Interventions for preventing weight gain after smoking cessation

Hartmann-Boyce, Jamie; Theodoulou, Annika; Farley, Amanda; Hajek, Peter; Lycett, Deborah; Jones, Laura L; Kudlek, Laura; Heath, Laura; Hajizadeh, Anisa; Schenkels, Marika; Aveyard, Paul

DOI:
10.1002/14651858.CD006219.pub4

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Interventions for preventing weight gain after smoking cessation.
Cochrane Database of Systematic Reviews 2021, Issue 10. Art. No.: CD006219.
DOI: 10.1002/14651858.CD006219.pub4.

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[Intervention Review]

Interventions for preventing weight gain after smoking cessation

Jamie Hartmann-Boyce[1a], Annika Theodoulou[2b], Amanda Farley[3], Peter Hajek[4], Deborah Lycett[5], Laura L Jones[3], Laura Kudlek[2], Laura Heath[1], Anisa Hajizadeh[2], Marika Schenkels[6], Paul Aveyard[1]

[1]Nuffield Department of Primary Care Health Sciences, University of Oxford, Oxford, UK. [2]UK. [3]Public Health, Epidemiology and Biostatistics, University of Birmingham, Birmingham, UK. [4]Wolfson Institute of Preventive Medicine, Barts & The London School of Medicine and Dentistry, Queen Mary University of London, London, UK. [5]Coventry, UK. [6]Canada

[a]Joint first author. [b]Joint first author

Contact address: Jamie Hartmann-Boyce, jamie.hartmann-boyce@phc.ox.ac.uk.

Editorial group: Cochrane Tobacco Addiction Group.
Publication status and date: Edited (no change to conclusions), published in Issue 10, 2021.

Citation: Hartmann-Boyce J, Theodoulou A, Farley A, Hajek P, Lycett D, Jones LL, Kudlek L, Heath L, Hajizadeh A, Schenkels M, Aveyard P. Interventions for preventing weight gain after smoking cessation. *Cochrane Database of Systematic Reviews* 2021, Issue 10. Art. No.: CD006219. DOI: 10.1002/14651858.CD006219.pub4.

ABSTRACT

Background

Most people who stop smoking gain weight. This can discourage some people from making a quit attempt and risks offsetting some, but not all, of the health advantages of quitting. Interventions to prevent weight gain could improve health outcomes, but there is a concern that they may undermine quitting.

Objectives

To systematically review the effects of: (1) interventions targeting post-cessation weight gain on weight change and smoking cessation (referred to as 'Part 1') and (2) interventions designed to aid smoking cessation that plausibly affect post-cessation weight gain (referred to as 'Part 2').

Search methods

Part 1 - We searched the Cochrane Tobacco Addiction Group's Specialized Register and CENTRAL; latest search 16 October 2020.

Part 2 - We searched included studies in the following 'parent' Cochrane reviews: nicotine replacement therapy (NRT), antidepressants, nicotine receptor partial agonists, e-cigarettes, and exercise interventions for smoking cessation published in Issue 10, 2020 of the Cochrane Library. We updated register searches for the review of nicotine receptor partial agonists.

Selection criteria

Part 1 - trials of interventions that targeted post-cessation weight gain and had measured weight at any follow-up point or smoking cessation, or both, six or more months after quit day.

Part 2 - trials included in the selected parent Cochrane reviews reporting weight change at any time point.

Data collection and analysis

Screening and data extraction followed standard Cochrane methods. Change in weight was expressed as difference in weight change from baseline to follow-up between trial arms and was reported only in people abstinent from smoking. Abstinence from smoking was expressed as a risk ratio (RR). Where appropriate, we performed meta-analysis using the inverse variance method for weight, and Mantel-Haenszel method for smoking.

Main results

Part 1: We include 37 completed studies; 21 are new to this update. We judged five studies to be at low risk of bias, 17 to be at unclear risk and the remainder at high risk.

An intermittent very low calorie diet (VLCD) comprising full meal replacement provided free of charge and accompanied by intensive dietitian support significantly reduced weight gain at end of treatment compared with education on how to avoid weight gain (mean difference (MD) −3.70 kg, 95% confidence interval (CI) −4.82 to −2.58; 1 study, 121 participants), but there was no evidence of benefit at 12 months (MD −1.30 kg, 95% CI −3.49 to 0.89; 1 study, 62 participants). The VLCD increased the chances of abstinence at 12 months (RR 1.73, 95% CI 1.10 to 2.73; 1 study, 287 participants). However, a second study found that no-one completed the VLCD intervention or achieved abstinence.

Interventions aimed at increasing acceptance of weight gain reported mixed effects at end of treatment, 6 months and 12 months with confidence intervals including both increases and decreases in weight gain compared with no advice or health education. Due to high heterogeneity, we did not combine the data. These interventions increased quit rates at 6 months (RR 1.42, 95% CI 1.03 to 1.96; 4 studies, 619 participants; I^2 = 21%), but there was no evidence at 12 months (RR 1.25, 95% CI 0.76 to 2.06; 2 studies, 496 participants; I^2 = 26%).

Some pharmacological interventions tested for limiting post-cessation weight gain (PCWG) reduced weight gain at the end of treatment (dexfenfluramine, phenylpropanolamine, naltrexone). The effects of ephedrine and caffeine combined, lorcaserin, and chromium were too imprecise to give useful estimates of treatment effects. There was very low-certainty evidence that personalized weight management support reduced weight gain at end of treatment (MD −1.11 kg, 95% CI −1.93 to −0.29; 3 studies, 121 participants; I^2 = 0%), but no evidence in the longer-term 12 months (MD −0.44 kg, 95% CI −2.34 to 1.46; 4 studies, 530 participants; I^2 = 41%). There was low to very low-certainty evidence that detailed weight management education without personalized assessment, planning and feedback did not reduce weight gain and may have reduced smoking cessation rates (12 months: MD −0.21 kg, 95% CI −2.28 to 1.86; 2 studies, 61 participants; I^2 = 0%; RR for smoking cessation 0.66, 95% CI 0.48 to 0.90; 2 studies, 522 participants; I^2 = 0%).

Part 2: We include 83 completed studies, 27 of which are new to this update.

There was low certainty that exercise interventions led to minimal or no weight reduction compared with standard care at end of treatment (MD −0.25 kg, 95% CI −0.78 to 0.29; 4 studies, 404 participants; I^2 = 0%). However, weight was reduced at 12 months (MD −2.07 kg, 95% CI −3.78 to −0.36; 3 studies, 182 participants; I^2 = 0%).

Both bupropion and fluoxetine limited weight gain at end of treatment (bupropion MD −1.01 kg, 95% CI −1.35 to −0.67; 10 studies, 1098 participants; I^2 = 3%); (fluoxetine MD −1.01 kg, 95% CI −1.49 to −0.53; 2 studies, 144 participants; I^2 = 38%; low- and very low-certainty evidence, respectively). There was no evidence of benefit at 12 months for bupropion, but estimates were imprecise (bupropion MD −0.26 kg, 95% CI −1.31 to 0.78; 7 studies, 471 participants; I^2 = 0%). No studies of fluoxetine provided data at 12 months.

There was moderate-certainty that NRT reduced weight at end of treatment (MD −0.52 kg, 95% CI −0.99 to −0.05; 21 studies, 2784 participants; I^2 = 81%) and moderate-certainty that the effect may be similar at 12 months (MD −0.37 kg, 95% CI −0.86 to 0.11; 17 studies, 1463 participants; I^2 = 0%), although the estimates are too imprecise to assess long-term benefit.

There was mixed evidence of the effect of varenicline on weight, with high-certainty evidence that weight change was very modestly lower at the end of treatment (MD −0.23 kg, 95% CI −0.53 to 0.06; 14 studies, 2566 participants; I^2 = 32%); a low-certainty estimate gave an imprecise estimate of higher weight at 12 months (MD 1.05 kg, 95% CI −0.58 to 2.69; 3 studies, 237 participants; I^2 = 0%).

Authors' conclusions

Overall, there is no intervention for which there is moderate certainty of a clinically useful effect on long-term weight gain. There is also no moderate- or high-certainty evidence that interventions designed to limit weight gain reduce the chances of people achieving abstinence from smoking.

PLAIN LANGUAGE SUMMARY

Interventions for preventing weight gain after smoking cessation

What is the best way to avoid putting on weight after stopping smoking?

Key messages

We are not certain which programmes or treatments work best to help people avoid gaining weight in the long term (up to 12 months) when stopping smoking, or how they affect success in stopping smoking. This is because the evidence shows varied and unclear effects on weight gain. Further studies should continue to look at how to limit weight gain in people who are stopping smoking. Future studies of new medicines to help people stop smoking should also measure changes in their weight.

Stopping smoking and weight gain

If you smoke, the best thing you can do for your health is to stop. But people often put on weight when they stop smoking, usually in the first few months of stopping. Gaining weight might undermine some of the benefits of stopping smoking, and might also affect the motivation of some people trying to stop smoking.

What did we want to find out?

Some programmes to help people stop smoking specifically target weight control. Other ways to help people stop smoking might also affect their weight; these include: exercise programmes, taking medicines, and using nicotine replacement therapy (NRT).

We wanted to find out the best ways to stop weight gain when stopping smoking.

What did we do?

In this update of a previously-published review, we searched for studies that tested:

- specific programmes for weight control while stopping smoking;

- other ways to help people stop smoking, if those studies also measured weight change.

We were interested in:

- how many people stopped smoking for six months or 12 months;

- people's weight at the end of treatment, then after six months and after 12 months.

What did we find?

We found 116 studies in total:

37 studies of specific programmes for weight control for people stopping smoking (21 new studies for this update); and 83 studies of other ways to help people stop smoking (27 new studies for this update). Four of these studies contributed to both.

The 37 studies of specific programmes tested behavioural programmes, including dieting, to manage weight in 11,514 people trying to stop smoking. Some of the behavioural programmes were acceptance-based, in which people also learn self-regulation skills (for example, how to deal with cravings) to help them keep to the behaviours needed to lose weight. Most studies (27) were done in the USA and others took place in Australia, Canada, China and Europe.

The 83 studies of other ways of stopping smoking included 46,248 people and looked at:

exercise programmes; taking NRT; taking a medicine called varenicline (used to help people stop smoking); or taking a medicine called fluoxetine (used to treat depression).

Of these studies, 39 were done in the USA and the rest took place in other countries around the world. Very few studies reported on side effects.

What are the main results of our review?

Programmes aimed at limiting weight gain

Compared with no programme or brief advice only, a personalized weight-management programme may reduce weight gain at the end of treatment, after six months and after 12 months. However, a weight-management programme without personalized assessment, planning and feedback may not reduce weight gain, and may reduce the number of people who stop smoking.

Compared with no programme, acceptance-based programmes for weight:

may help more people to stop smoking after six months and 12 months; but may make little to no difference to their weight gain**.**

Other programmes and treatments that might affect weight

Taking part in an exercise programme to help stop smoking may reduce weight gain after 12 months, compared with not taking part in one.

Using NRT probably reduces weight gain slightly after 12 months, compared with not using NRT.

Taking varenicline makes little difference to weight gain at the end of treatment, and may make little difference after six months or after 12 months.

Taking fluoxetine may reduce weight gain at the end of treatment, but we do not know how it affects weight gain after six months or 12 months.

What are the limitations of the evidence?

We are certain that there is no difference in weight gain at the end of treatment with varenicline, and further studies are unlikely to change this result. However, our confidence in all of the other evidence is limited, mainly because of small numbers of studies that could be compared, and small numbers of people taking part in them. The results varied widely, and there were not enough studies for us to be sure of the results. Our confidence is likely to change if further evidence becomes available.

How up to date is this evidence?

The evidence is current up to October 2020.

SUMMARY OF FINDINGS

Summary of findings 1. Behavioural weight management interventions compared to brief advice or no intervention for post-cessation weight control

Behavioural weight management interventions compared to brief advice or no intervention for post-cessation weight control for preventing weight gain after smoking cessation

Patient or population: People wanting to quit smoking
Setting: Community
Intervention: Behavioural weight management interventions
Comparison: advice or no intervention for post-cessation weight control

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with advice or no intervention for post-cessation weight control#	Risk with behavioural weight management interventions				
Mean weight change (kg) at end of treatment - Weight management education versus no weight intervention	1.45 kg	1.41 kg (0.88 to 1.95)	MD 0.04 kg lower (0.57 lower to 0.5 higher)	140 (2 RCTs)	⊕⊕⊖⊖ LOW[a,b]	-
Mean weight change (kg) at 6 months - Weight management education verses no weight intervention	0.97 kg	1.86 kg (0.19 to 3.52)	MD 0.89 kg higher (0.78 lower to 2.55 higher)	81 (2 RCTs)	⊕⊕⊖⊖ LOW[b,c]	-
Mean weight change (kg) at 12 months - Weight management education versus no weight intervention	0.46 kg	0.25 kg (-1.82 to 2.32)	MD 0.21 kg lower (2.28 lower to 1.86 higher)	61 (2 RCTs)	⊕⊖⊖⊖ VERY LOW[c,d]	-
Smoking cessation at 6 months - Weight management education versus no intervention	275 per 1000	280 per 1000 (214 to 365)	RR 1.02 (0.78 to 1.33)	660 (3 RCTs)	⊕⊕⊖⊖ LOW[d]	-
Smoking cessation at 12 months - Weight management education versus no intervention	294 per 1000	194 per 1000 (141 to 265)	RR 0.66 (0.48 to 0.90)	522 (2 RCTs)	⊕⊕⊖⊖ LOW[a,b]	-

Mean weight change (kg) at end of treatment - Personalised weight management support versus no weight intervention	1.45 kg	0.34 kg (-0.48 to 1.16)	MD 1.11 kg lower (1.93 lower to 0.29 lower)	121 (3 RCTs)	⊕⊕⊖⊖ LOW[a,b]	-
Mean weight change (kg) at 6 months - Personalised weight management support versus no weight intervention	0.97 kg	0.01 kg (-1.21 to 1.22)	MD 0.96 kg lower (2.18 lower to 0.25 higher)	816 (5 RCTs)	⊕⊖⊖⊖ VERY LOW[e,f]	-
Mean weight change (kg) at 12 months - Personalised weight management support versus no weight intervention	0.46 kg	0.02 kg (-1.88 to 1.92)	MD 0.44 kg lower (2.34 lower to 1.46 higher)	530 (4 RCTs)	⊕⊖⊖⊖ VERY LOW[a,d]	-
Smoking cessation at 6 months - Personalised weight management support versus no intervention	188 per 1000	178 per 1000 (154 to 206)	RR 0.95 (0.82 to 1.10)	5517 (7 RCTs)	⊕⊕⊖⊖ LOW[g,h]	-
Smoking cessation at 12 months - Personalised weight management support versus no intervention	475 per 1000	308 per 1000 (214 to 437)	RR 0.65 (0.45 to 0.92)	3441 (5 RCTs)	⊕⊕⊖⊖ LOW[a,i]	-

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

CI: Confidence interval; **RCT:** randomized controlled trial; **RR:** Risk ratio; **MD:** Mean difference

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[a]Downgraded one level due to risk of bias. All studies judged to be at unclear or high risk of bias. Results not sensitive to removal of studies at high risk of bias.
[b]Downgraded one level due to imprecision. Few studies and participants contributed data.
[c]Downgraded one level due to risk of bias. Of the two studies contributing data, one was at high risk of bias, and other at low risk. Results not sensitive to removal of study at high risk.[d]Downgraded two levels due to imprecision. Wide CIs incorporate clinically meaningful weight reduction and clinically meaningful weight increase.
[e]Downgraded two levels due to risk of bias. All studies judged to be at high risk.
[f]Downgraded one level due to imprecision. Wide CIs encompass benefit and no clinically meaningful difference.
[g]Downgraded one level due to risk of bias. All studies at high or unclear risk of bias, bar one small study at low risk of bias. Results not sensitive to removing studies at high risk of bias.
[h]Downgraded one level due to imprecision. Wide CIs incorporate clinically meaningful difference in favour of control group, as well as no clinically significant difference.
[i]Downgraded one level due to inconsistency due to substantial unexplained statistical heterogeneity (I^2 = 89%).
#Calculated as weighted means from control group data.

Summary of findings 2. Acceptance interventions for weight concern compared to no weight management intervention for post-cessation weight control

Acceptance interventions for weight concern compared to no weight management intervention for preventing weight gain after smoking cessation

Patient or population: People wanting to quit smoking
Setting: Community
Intervention: Acceptance interventions for weight concern
Comparison: No weight management intervention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no weight management intervention#	Risk with acceptance interventions for weight concern				
Mean weight change (kg) at end of treatment	see comment	see comment	see comment	169 (3 RCTs)	⊕⊖⊖⊖ VERY LOW[a,b]	Substantial unexplained statistical heterogeneity precluded meta-analysis. Of the 3 studies, 1 had wide CIs encompassing both benefit and harm, 1 suggested benefit with CIs excluding no difference, and 1 suggested harm with CIs excluding no difference.
Mean weight change (kg) at 6 months	3.5 kg	3.5 kg (1.97 to 5.03)	MD 0 kg (1.53 lower to 1.53 higher)	106 (3 RCTs)	⊕⊕⊖⊖ LOW[a,c,d]	-
Mean weight change (kg) at 12 months	4.39 kg	3.69 kg (1.44 to 5.95)	MD 0.7 kg lower (2.95 lower to 1.56 higher)	76 (2 RCTs)	⊕⊖⊖⊖ VERY LOW[a,c,d]	-
Smoking cessation at 6 months	218 per 1000	309 per 1000 (224 to 427)	RR 1.42 (1.03 to 1.96)	619 (4 RCTs)	⊕⊕⊖⊖ LOW[a,e]	-
Smoking cessation at 12 months	143 per 1000	179 per 1000 (109 to 294)	RR 1.25 (0.76 to 2.06)	496 (2 RCTs)	⊕⊖⊖⊖ LOW[a,d]	-

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the __relative effect__ of the intervention (and its 95% CI).

CI: Confidence interval; **RCT:** randomized controlled trial; **RR:** Risk ratio; **MD:** Mean difference

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[a]Downgraded one level due to risk of bias. All studies judged to be at unclear or high risk of bias. Results not sensitive to removal of studies at high risk of bias.
[b]Downgraded two levels due to inconsistency. Unexplained statistical heterogeneity prevented pooling data.
[c]Downgraded one level due to inconsistency. Moderate unexplained statistical heterogeneity.
[d]Downgraded two levels due to imprecision. CIs encompass clinically significant benefit and clinically significant harm.
[e]Downgraded one level due to imprecision. < 300 events overall and CIs encompass clinically significant benefit and no clinically significant difference.
[#]Calculated as weighted means from control group data.

Summary of findings 3. Exercise interventions for smoking cessation compared to no exercise intervention for preventing weight gain after smoking cessation

Exercise interventions for smoking cessation compared to no exercise intervention for preventing weight gain after smoking cessation

Patient or population: People who have quit smoking
Setting: Community
Intervention: Exercise interventions for smoking cessation
Comparison: no exercise intervention

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with no exercise intervention[#]	Risk with Exercise interventions for smoking cessation				
Mean weight change (kg) at end of treatment	2.85 kg	2.6 kg (2.07 to 3.14)	MD 0.25 kg lower (0.78 lower to 0.29 higher)	404 (4 RCTs)	⊕⊕⊝⊝ LOW[a,b]	-
Mean weight change (kg) at 12 months	4.67 kg	2.6 kg (0.89 to 4.31)	MD 2.07 kg lower (3.78 lower to 0.36 lower)	182 (3 RCTs)	⊕⊕⊝⊝ LOW[a,b]	-

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RCT:** randomized controlled trial; **RR:** Risk ratio; **MD:** Mean difference

GRADE Working Group grades of evidence

High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[a]Downgraded one level due to imprecision. CIs encompass clinically significant benefit as well as no clinically significant difference.
[b]Downgraded one level due to inconsistency - end of treatment and 12 month outcomes are clinically significantly different, with no clear or plausible reason for difference.
[#]Risk with no intervention from Aubin, 2012.

Summary of findings 4. Nicotine replacement therapy for smoking cessation compared to placebo for preventing weight gain after smoking cessation

Nicotine replacement therapy for smoking cessation compared to placebo for preventing weight gain after smoking cessation

Patient or population: People who have quit smoking
Setting: Community
Intervention: Nicotine replacement therapy for smoking cessation
Comparison: placebo

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo[#]	Risk with nicotine replacement therapy for smoking cessation				
Mean weight change (kg) at end of treatment	2.85 kg	2.33 kg (1.86 to 2.8)	MD 0.52 kg lower (0.99 lower to 0.05 lower)	2784 (21 RCTs)	⊕⊕⊕⊖ MODERATE[a,b,c]	-
Mean weight change (kg) at 6 months	4.23 kg	4.15 kg (3.72 to 4.58)	MD 0.08 kg lower (0.51 lower to 0.35 higher)	1021 (11 RCTs)	⊕⊕⊕⊖ MODERATE[a,d]	-
Mean weight change (kg) at 12 months	4.67 kg	4.3 (3.81 to 4.67)	MD 0.37 kg lower (0.86 lower to 0.11 higher)	1463 (17 RCTs)	⊕⊕⊕⊖ MODERATE[e]	-

*__The risk in the intervention group__ (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RCT:** randomized controlled trial; **RR:** Risk ratio; **MD:** Mean difference

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect

Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[a]Downgraded one level due to risk of bias. All studies at high or unclear risk. Results not sensitive to removal of studies at high risk of bias.
[b]Statistical heterogeneity was substantial due to one study (2 Abelin 1989), which showed a 4.3 kg difference between weight gain in the treatment and control arms. When this study was removed, statistical heterogeneity reduced to 0% and the overall estimate decreased. Not downgraded on this basis.
[c]Funnel plot showed some asymmetry, suggesting that smaller studies with less weight gain in intervention groups relative to control groups may be missing, but not downgraded on this basis, as asymmetry thought plausibly due to chance, given asymmetry in opposite direction at six months.
[d]Funnel plot showed some asymmetry, suggesting that smaller studies with greater weight gain in intervention groups relative to control groups may be missing, but not downgraded on this basis as asymmetry thought plausibly due to chance, given asymmetry in opposite direction at end of treatment.
[e]Downgraded one level due to imprecision. CIs encompass clinically significant benefit and no clinically significant difference.
[#]Risk with no intervention from Aubin, 2012.

Summary of findings 5. Varenicline for smoking cessation compared to placebo for preventing weight gain after smoking cessation

Varenicline for smoking cessation compared to placebo for preventing weight gain after smoking cessation

Patient or population: People who have quit smoking
Setting: Community
Intervention: Varenicline
Comparison: placebo for smoking cessation

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo for smoking cessation[#]	Risk with varenicline				
Mean weight change (kg) at end of treatment	2.85 kg	2.62 kg (2.32 to 2.91)	MD 0.23 kg lower (0.53 lower to 0.06 higher)	2566 (14 RCTs)	⊕⊕⊕⊕ HIGH	-
Mean weight change (kg) at 6 months	4.23 kg	4.14 kg (3.14 to 5.13)	MD 0.09 kg lower (1.09 lower to 0.9 higher)	384 (3 RCTs)	⊕⊕⊖⊖ LOW[a]	-
Mean weight change (kg) at 12 months	4.67 kg	5.72 kg (4.09 to 7.36)	MD 1.05 kg higher (0.58 lower to 2.69 higher)	237 (3 RCTs)	⊕⊕⊖⊖ LOW[b,c]	-

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; **RCT:** randomized controlled trial; **RR:** Risk ratio; **MD:** Mean difference

GRADE Working Group grades of evidence
High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
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Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[a]Downgraded two levels due to imprecision. CIs incorporate clinically significant benefit as well as clinically significant harm.
[b]Downgraded one level due to risk of bias. All studies at unclear risk.
[c]Downgraded one level due to imprecision. CIs incorporate clinically significant benefit and no difference.
[#]Risk with no intervention from Aubin, 2012.

Summary of findings 6. Fluoexetine compared to placebo for smoking cessation for preventing weight gain after smoking cessation

Fluoxetine compared to placebo for smoking cessation for preventing weight gain after smoking cessation

Patient or population: People who have quit smoking
Intervention: Fluoxetine for smoking cessation
Comparison: placebo for smoking cessation

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with placebo for smoking cessation[#]	Risk with all types of antidepressant				
Mean weight change (kg) at end of treatment	2.85 kg	1.84 kg (1.36 to 2.32)	MD 1.01 kg lower (1.49 lower to 0.53 lower)	144 (2 RCTs)	⊕⊕⊝⊝ LOW[a,b]	-
Mean weight change (kg) at 6 months	4.67 kg	3.66 kg (0.29 to 7.04)	MD 1.01 kg lower (4.38 lower to 2.37 higher)	124 (2 RCTs)	⊕⊕⊝⊝ VERY LOW[a,c]	no studies followed up participants at 12 months

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

CI: Confidence interval; RCT: randomized controlled trial; **RR:** Risk ratio;

GRADE Working Group grades of evidence

High certainty: We are very confident that the true effect lies close to that of the estimate of the effect
Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect
Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[a]Downgraded one level due to risk of bias. One study at unclear risk, one at high risk.
[b]Downgraded one level due to imprecision. Only two studies contributed data, overall; n < 150.
[c]Downgraded two levels due to imprecision; CIs incorporate clinically significant weight loss and clinically significant weight gain.
[#]Risk with no intervention from Aubin, 2012

BACKGROUND

Description of the condition

Although smoking cessation is associated with substantial health benefits, it is often accompanied by weight gain (Aubin, 2012; Audrain-McGovern 2011). Increases in weight are most marked in the first months after quitting (Aubin, 2012), and longer-term studies show further moderate increases in weight in quitters for a number of years compared with continuing smokers (2 Lycett 2011). Reports vary about the amount gained, but on average sustained quitters are likely to gain an additional two to five kilograms (kgs) in the first five years (Chiolero 2008; Klesges 1997; Tian 2015; Veldheer 2015; Williamson 1991), and up to seven kgs after eight years (2 Lycett 2011). It is important to note, however, that average weight gain masks a substantial variability at the individual level, with evidence suggesting some quitters may lose weight (Aubin, 2012; Bossé 1980), whereas around 10% to 15% gain 10 kgs or more (Aubin, 2012; Tian 2015; Williamson 1991). Factors that have been consistently associated with greater weight gain after smoking cessation include female sex, higher cigarettes smoked per day/nicotine dependency and higher body mass index (BMI) at quitting (Komiyama 2013; Scherr 2015; Veldheer 2015; Williamson 1991).

Description of the intervention

Interventions included in this review are discussed in two parts, described below.

Some smoking cessation interventions have been developed to promote smoking cessation and simultaneously control weight gain. They include behavioural interventions, such as exercise and energy restriction or healthy-eating advice. Some pharmacological treatments with known or potential efficacy for reducing weight have also been tested. Interventions may combine both behavioural components and pharmacological treatments, or these may be tested individually. They are often delivered concurrently with smoking cessation support during the first few months of quitting, when the rate of weight gain is at its highest. The effects of these interventions on both smoking abstinence and weight are included in**Part 1** of this review.

Several treatments for smoking cessation have been developed independently of concerns about weight gain, with the sole aim of assisting smoking cessation. Some of these, such as nicotine replacement therapy, e-cigarettes, antidepressants, varenicline and exercise might plausibly influence weight gain as well as smoking cessation. The effects of these interventions on smoking cessation are evaluated in the relevant Cochrane Reviews, but the effects on weight gain are summarised only in the exercise intervention review (Ussher 2019). The effects of these medications on weight gain are included in **Part 2** of this review.

How the intervention might work

Smoking (and quitting smoking) is likely to exert its effect on weight through the biological actions of nicotine and also through the influence of smoking on eating behaviours. Nicotine increases metabolic rate (Collins 1994; Dallosso 1984), and withdrawal of nicotine when people quit smoking results in a decrease in rate (Hofstetter 1986)

Nicotine may also be an appetite suppressant, and people may replace eating with smoking (Chiolero 2008). Particularly during the initial period of withdrawal from nicotine when quitting smoking, some people may eat more in order to deal with nicotine cravings/withdrawal, to satiate increases in appetite and replace the hand-to-mouth action of smoking (Audrain-McGovern 2011; Ward 2001). Through these mechanisms, it is likely that an energy imbalance is created favouring weight gain.

Behavioural interventions that limit energy intake (i.e. dieting or calorie restriction) or increase energy expenditure (i.e. exercise) may serve to reduce any energy imbalance that occurs during quitting, and thus reduce the amount of weight gained (Cheskin 2005; Gritz 1988; Hall 1986; 1 Hall 1992; Hughes 1991).

Pharmacological treatments may limit weight gain through several mechanisms. Appetite suppressants may offset the increased appetite that accompanies cessation, limiting any increase in calorie consumption after quitting to satiate increased hunger. Pharmacotherapies that replace nicotine included in Part 2 (nicotine replacement therapies or e-cigarettes) may reduce nicotine withdrawal effects on metabolism and appetite. Varenicline is a partial agonist of nicotinic receptors in the brain and so may also work through these mechanisms. Depressed mood is a recognised withdrawal symptom of nicotine, and antidepressants are known to affect bodyweight (Serretti 2010), although some increase and some decrease it.

The availability of interventions that limit weight gain might encourage smokers who are concerned about weight gain to try to stop smoking (Filozof 2004), and limiting weight gain may prevent people from returning to smoking to avoid an increase in weight. However, it is possible that some interventions that aim to limit energy intake might undermine the success of a quit attempt (1 Hall 1992). There is evidence that hunger and cigarette cravings are related, that hunger can undermine quit efforts (1 Hall 1992) and that hunger increases urges to smoke in current smokers (Cheskin 2005). There is evidence that early weight gain is associated with successful cessation (Gritz 1988; Hall 1986; Hughes 1991). It is important to investigate further the impact of these interventions on weight gain, and also to evaluate the effect on abstinence rates.

Why it is important to do this review

Among smokers there is a high prevalence of concerns about post-cessation weight gain, and it has been cited as a primary reason for putting off quit attempts, especially in women (Clark 2004; Klesges 1989; Klesges 1992). Weight consciousness has been found to predict current smoking (Weekley 1992), and weight gain experienced during or after smoking cessation has been associated with relapse (Klesges 1988; Klesges 1989; Klesges 1992). However there is inconsistent evidence that fear of weight gain or actual weight gain after quitting does lead to relapse, with some studies finding associations (1 Copeland 2006; Clark 2006; Meyers 1997; Pomerleau 2001) and others no associations (Fidler 2009; Hutter 2006; Killen 1996; Mizes 1998); methodological differences make it hard to draw a conclusion.

Post-cessation weight gain can have health consequences, although these do not outweigh the benefit of quitting smoking. In the shorter term, the incidence of diabetes is higher in people who quit smoking than in those who continue with it, an effect that appears to be explained by weight gain (Davey Smith 2005; Yeh 2010), although some evidence suggests in the longer term (more than 10 years) the risk is no higher in those who quit than

in those who continued smoking (Luo 2013). Hypertension can also be mediated by post-cessation weight gain (Gratziou 2009). Additionally, at least one study has suggested that cessation-related weight gain (more than 5 kgs) may attenuate reductions in cancer risk (Kim 2019). The extent to which these associations are clinically meaningful is unclear. The temporarily increased risk of type 2 diabetes amongst smokers who quit smoking with associated weight gain, is not associated with increased cardiovascular and all-cause mortality compared to non-quitters (Hu 2018). Weight gain after smoking cessation has been found not to modify its protective effect on heart attack and stroke (Clair 2013; Kim 2018).

Given the uncertainty of the risks surrounding cessation-related weight gain, and that concerns about weight gain are cited as a common reason for not attempting quitting, people who smoke, their healthcare providers, and policy-makers are keen to understand the effects of interventions that could potentially minimize post-cessation weight gain whilst not adversely affecting cessation. The 2012 version of this review found insufficient evidence to recommend any one type of intervention targeting post-cessation weight gain. Since then, considerable further literature has been published and new smoking cessation treatments have come onto the market. This updated review considers the entirety of the evidence to date on possible ways to limit post-cessation weight gain in people abstinent from smoking, and the impact of these interventions on smoking cessation as well as weight.

OBJECTIVES

To systematically review the effects of: (1) interventions targeting post-cessation weight gain on weight change and smoking cessation (referred to as 'Part 1') and (2) interventions designed to aid smoking cessation that may also plausibly affect weight on post-cessation weight change (referred to as 'Part 2').

METHODS

Criteria for considering studies for this review

Types of studies

Randomized controlled trials.

Types of participants

Adults who smoke and are attempting to quit smoking, excluding pregnant women.

In Part 1, we examine smoking cessation in everyone enrolled. In Part 1 and Part 2, we examine the effect of interventions on weight gain in people who have successfully quit smoking only. This is for several reasons. Firstly, if we included those who were not abstinent, mean weight gain would be reduced. This is because people who attempt quitting but fail after a few days do not gain weight, as those who relapse to smoking often lose the weight they gained previously (2 Lycett 2011; O'Hara 1998). Thus the average weight gain of a mixed population of abstinent and non-abstinent smokers would not reflect the weight gain of either. Secondly, this effect could bias results. If an intervention increased abstinence rates, it is very likely that it would appear to increase weight gain, regardless of whether it actually suppressed weight gain or had no effect. Thirdly, those who return to smoking tend not to attend clinics for follow-up. Authors typically only report weight data in abstinent smokers, and imputing missing data on weight in those who have relapsed to smoking is problematic. We have little data on the weight trajectory of people who try and fail to achieve abstinence. It is likely that the weight will depend on time since relapse and that imputing data using last observation carried forward or baseline observation carried forward is likely to be misleading. For these reasons, we eschew the intention-to-treat approach which is typically used in the Tobacco Addiction Review Group's reviews. This issue has been discussed elsewhere (Parsons 2009b; Parsons 2011; Spring 2011a; Spring 2011b).

Types of interventions

Part 1 - Interventions that are designed specifically to limit post-cessation weight gain.

Part 2 - Smoking cessation interventions that are not designed primarily to limit post-cessation weight gain but which might plausibly influence it, i.e. antidepressants, exercise, nicotine replacement therapy (NRT), electronic cigarettes and varenicline, but excluding trials in which all arms receive the same medication, regardless of differences in dose and schedule.

Types of outcome measures

There are two primary outcome measures:

- Smoking status at six and 12 months
- Mean (SD) change in body weight (kgs) at end of treatment, six, and 12 months.

Both outcomes are fully examined for studies that fit the criteria for Part 1. For Part 2 studies, effects of these interventions on smoking are reported in the parent Cochrane Reviews and we only report the effects of interventions on weight change.

For Part 1 studies of pharmacotherapies, we also evaluate adverse events and serious adverse events. We do not evaluate adverse and serious adverse events for behavioural interventions, following standard Cochrane Tobacco Addiction Group guidance. Information on adverse and serious adverse events for Part 2 studies can be found in the Cochrane Reviews on the relevant interventions (see Search methods for identification of studies).

Search methods for identification of studies

Electronic searches

Part 1 - For the most recent update, we searched the Cochrane Tobacco Addiction Group's Specialized Register (latest search 16 October 2020), using the following search terms in title, abstract or keywords: food, calorie restrict*, intake, diet*, body mass index (BMI), Quetelet, waist-hip ratio (WHR), weight, body-weight, weight-changes. At the search date the specialized register included the results of searches of the Cochrane Central Register of Controlled trials (CENTRAL), issue 9, 2020; MEDLINE (including in-process and Epub ahead of print, via OVID) to update 202000928; Embase (via OVID) to week 2020040; and PsycINFO (via OVID) to update 20200921, as well as online registers of controlled trials.

Searching other resources

Part 2 - We searched the following Cochrane Reviews: *Antidepressants for smoking cessation* (last updated 2020; Howes

2020); *Exercise interventions for smoking cessation* (last updated 2019; Ussher 2019); *Nicotine replacement therapy for smoking cessation* (last updated 2018; Hartmann-Boyce 2018); *Different doses, durations and modes of delivery of nicotine replacement therapy for smoking cessation* (last updated 2019; Lindson 2019); *Electronic cigarettes for smoking cessation* (last updated 2020; Hartmann-Boyce 2020), and *Nicotine receptor partial agonists for smoking cessation* (last updated 2016; Cahill 2016). We searched the text of references listed as included studies. For reviews last updated prior to 2019, we also searched the Cochrane Tobacco Addiction Group's Specialized Register on 16 October 2020, using the search terms outlined in the individual reviews.

Data collection and analysis

Selection of studies

For the 2020 searches, two review authors (for this update from: JHB, AT, LK, LH, AH and MS) independently screened all titles and abstracts obtained from the search using a piloted screening checklist. Full-text versions were then independently screened for inclusion. We also ran a 2016 search in which titles and abstracts of records identified were screened in singular by the group's Information Specialist (Lindsay Stead [LS]). Full-text records were then screened by AF and LS. Any discrepancies about eligibility throughout this update were resolved by discussion or with a third review author. Reasons for exclusion of key studies that required in-depth discussion are listed in Characteristics of excluded studies.

Data extraction and management

For this update, two review authors (from: JHB, AT, LK, LH, AH, MS, AF, PA, PH, LLJ, DL) independently undertook data extraction using a piloted form. Extractions were then compared and a final version agreed upon following discussion, or with referral to a third review author, when necessary. We extracted the following data for each study:

- Study design
- Study start and end date
- Recruitment
- Setting*
- Country
- Inclusion and exclusion criteria
- Summary of study participant characteristics
  - Total number randomized
  - Number per arm
  - Total percentage female
  - Mean age, baseline BMI, baseline weight, cigarettes per day (cpd), Fagerström Test for Nicotine Dependence (FTND) score
- Summary of intervention and comparative conditions
- Definition of smoking abstinence and type of biochemical validation (if any)
- How weight was measured
- Number of participants who were abstinent at end of treatment (EOT), 6 months, 12 months and/or at longest follow-up
- Mean weight change (kg) from baseline in abstinent smokers
- Abstinence rates (Part 1 studies only)
- Adverse events (AEs) and serious adverse events (SAEs) (Part 1 studies only)
- Risk of bias in domains specified below
- Study funding statement
- Author declarations of interest
- Any other notes

*studies identified during the 2020 search only.

One review author then entered the data into Review Manager 5 software for analyses (JHB), and another checked them (AT).

Assessment of risk of bias in included studies

Two review authors (for this update from: JHB, AT, LK, LH, MS, AF, PA, PH, LLJ, DL) independently assessed the risks of bias for each included study, using the Cochrane risk of bias tool v1 (Higgins 2011). This approach uses a domain-based evaluation that addresses different areas: random sequence generation; allocation concealment; blinding of participants and personnel; blinding of outcome assessment (smoking and weight); incomplete outcome data; and other potential sources of bias.

Specific considerations about judgements for individual domains for this review are outlined below:

- Blinding of participants and personnel: This domain was not evaluated for studies investigating behavioural interventions for smoking cessation where blinding was not possible; this is in accordance with standard guidance from the Cochrane Tobacco Addiction Group.
- Blinding of outcome assessments (detection bias) were evaluated separately for smoking and weight outcomes, given different considerations for each outcome. Risk of detection bias ratings were based on assessments of both weight and smoking outcomes.
- Following standard methods of the Cochrane Tobacco Addiction Review Group, we rated studies at high risk of attrition bias if loss to follow-up was greater than 50% overall or if there was a difference in follow-up rates of more than 20% between study arms.

We assigned a grade (low, high, or unclear) for risk of bias for each domain and resolved any disagreements by discussion or by consulting with a third review author. We judged studies to be at high risk of bias overall if they were rated at high risk in at least one domain, and at low risk of bias overall if they were judged to be at low risk across all domains evaluated. We judged the remaining studies to be at unclear risk of bias overall.

Measures of treatment effect

For Part 1, where possible we extracted smoking outcomes as continuous biochemically-confirmed abstinence, but we accepted less strict definitions if confirmed continuous abstinence was not available. Abstinence rates and their corresponding risk ratio (95% CI) were reported at six and 12 months of follow-up. We extracted adverse and serious adverse events for pharmacotherapy studies in Part 1 as the number of people experiencing an event, where these data were available. For studies in Part 2, we extracted data on weight change only.

We used the absolute mean (SD) difference in body weight (kgs) from baseline to follow-up by trial arm as a summary statistic for the treatment effect on weight. We estimated mean weight change only in those abstinent from smoking.

In some studies in Part 1 and 2, more than one trial arm had been compared with a control arm. Where this was the case, we took one of two approaches: where it was inappropriate to combine arms, we analyzed results separately and report them as such. Where appropriate, to create one comparison intervention arm we combined outcome data. For smoking we added together the numerator and denominator from each arm. We calculated weight outcomes from more than one trial arm using the following formulas:

$Mean_c$ = ((Mean1*n1)+(Mean2*n2))/(n1+n2)
Standard deviation = $\sqrt{var_c}$

$\sqrt{var_c}$= ($sumsq_c$ - (n_c * ($Mean_c$ ^{2})))/(n_c-1)

$sumsq_c$= (((n1-1)*(var1 + ((n1/n1-1))*(mean1^2) + ((n2-1)*(var2 + ((n2/n2-1))*(mean2^2))

Key: $Mean_c$= Combined mean; sumsq = sum of squares; var = variance

Unit of analysis issues

The cluster-randomized trial included reported results adjusted for intra-class correlation; we use these adjusted estimates in our analysis. All other trials were individually randomized and hence we did not encounter issues with unit of analysis.

Dealing with missing data

We checked that, for smoking abstinence estimates, participants lost to follow-up were coded as continuing to smoke and therefore all randomized participants were included in the denominator; if not, we corrected abstinence rates for this. Where weight gain had been measured but not reported at all or in full, we contacted authors or sponsors for clarification. If insufficient data were available for meta-analysis, we reported results narratively. As outlined below, where possible, we converted data for use in our meta-analysis.

In some studies mean (SD) weight change by trial arm was not reported in full. When the standard deviations for the changes in body weight were not present, we used several methods to calculate them using standard formulas, depending on the information available. This was mainly derived from confidence intervals and standard errors. To calculate standard deviations of the changes in weight from their associated confidence intervals for studies with a large sample size, we used the following formula:

SD = (√(n) x (upper limit - lower limit)) /standard error

For studies with 95% confidence intervals for difference in means we divided by 3.92 standard errors wide. If sample size was less than 60, the 3.92 standard error wide was replaced with numbers specific to both the t-distribution and the group sample size minus 1.

To calculate standard deviation from standard error we used the following formula:

SD = SE x √(n)

When the absolute mean differences in body weight were not reported explicitly, we calculated them by subtracting the baseline mean weights from the post-intervention mean weights for the intervention and control groups. We calculated SDs by using an estimated correlation coefficient of 0.99, which describes how similar the baseline and finishing weight were across participants. This was estimated in abstinent smokers from raw data that we have collected from a trial to prevent weight gain on smoking cessation (Parsons 2009a) and from any other included studies that report standard deviations for mean weight at baseline, final measurement, and changes in means. To estimate the correlation coefficient for the intervention and control groups from other studies reporting starting and finishing means with SDs, we used the following formula:

r = (SD (B)2 + SD (F)2 - SD (C)2) / (2 X SD(B) X SD (F))

(where r = correlation coefficient, SD = standard deviation for the changes in means, B = baseline, F = final measurement, and C = change in mean weight measurement).

The imputed correlation coefficient was used to calculate the missing standard deviations for changes in means for the intervention and control groups by using the following formula:

SD (C) = √((SD (B)2 + SD (F)2) - (2 X r X SD (B) X SD (F))

Assessment of heterogeneity

We used the I^2 statistic to investigate statistical heterogeneity, given by the formula [(Q-df)/Q] x 100%], where Q is the Chi^2 statistic and df is its degrees of freedom.

Assessment of reporting biases

We created funnel plots to visually investigate possible publication bias for meta-analyses with 10 or more studies.

Data synthesis

Smoking cessation outcome data are given based on the number of quitters in the treatment and control groups divided by the total number of participants receiving treatment. Adverse and serious adverse event data are given as the number of people experiencing an event divided by the total number of participants followed up at the relevant time point. Results for both are reported as risk ratios (RRs) with 95% confidence intervals (CIs). A risk ratio greater than 1.0 indicates that more people quit in the treatment group than in the control group, or that more people experienced an adverse event. We used the Mantel-Haenszel random-effects method for smoking cessation and adverse event outcomes where appropriate. Weight change outcome data are given as the difference in mean weight change between the intervention and control arms, and we combined estimates using the inverse variance method where appropriate.

Subgroup analysis and investigation of heterogeneity

Studies were subgrouped based on intervention type.

Sensitivity analysis

Following the standard approach of the Cochrane Tobacco Addiction Group, we conducted sensitivity analyses removing studies at high risk of bias.

Summary of findings and assessment of the certainty of the evidence

Following standard Cochrane methodology, we created summary of findings tables for the following comparisons, agreed prior to beginning this update, using GRADEpro GDT:

- Weight management education versus no weight intervention
- Personalized weight management support versus no weight intervention
- Interventions to allay concerns about weight gain versus no weight intervention
- Exercise interventions versus no exercise intervention for smoking cessation
- Nicotine replacement therapy versus placebo for smoking cessation
- Varenicline versus placebo for smoking cessation
- Fluoxetine versus placebo for smoking cessation

We selected these comparisons a priori as being the most clinically relevant. In the summary of findings tables, we present data on our primary outcomes (cessation and weight change) for these main comparisons. Also following standard Cochrane methodology, we used the five GRADE considerations (study limitations, consistency of effect, imprecision, indirectness and publication bias) to assess the certainty of the body of evidence for each outcome, and to draw conclusions about the certainty of evidence within the text of the review.

RESULTS

Description of studies

Studies are described by part below. Part 1 represents studies of interventions specifically designed to address post-cessation weight gain. Part 2 represents studies of smoking cessation interventions not specifically designed to address post-cessation weight gain.

Results of the search

Part 1

For Part 1 of this update, our 2020 searches identified 379 non-duplicate references (Figure 1). All references were then screened and 70 full-text articles were retrieved. For this update, we identified 21 new included studies and 10 new ongoing studies (Characteristics of ongoing studies). In total, we now include 37 studies in Part 1, i.e. 21 new included studies and 16 included studies identified in the 2012 review.

Figure 1. Study flow diagram for Part 1 2020 search plus studies from 2016 search and the 2012 review

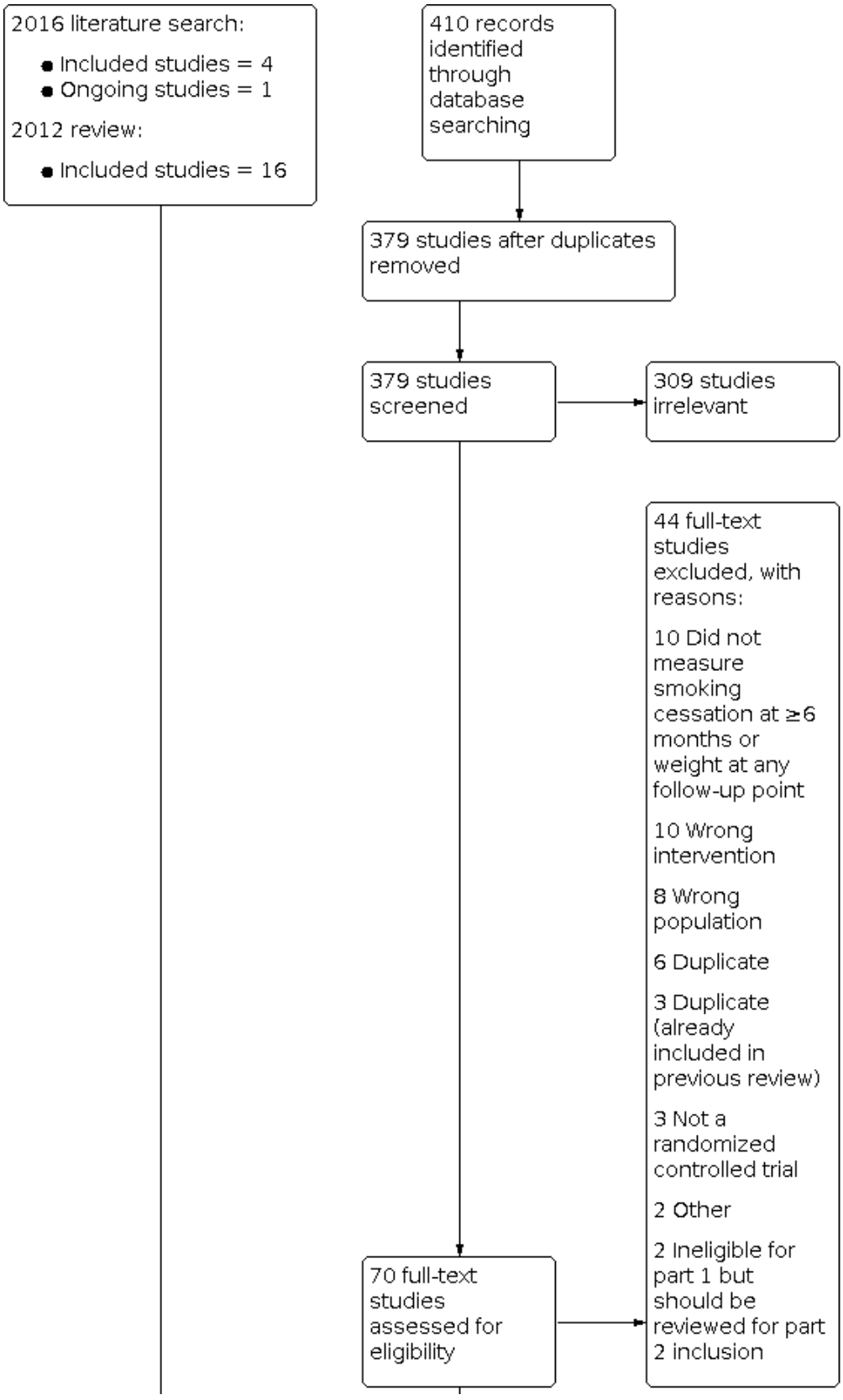
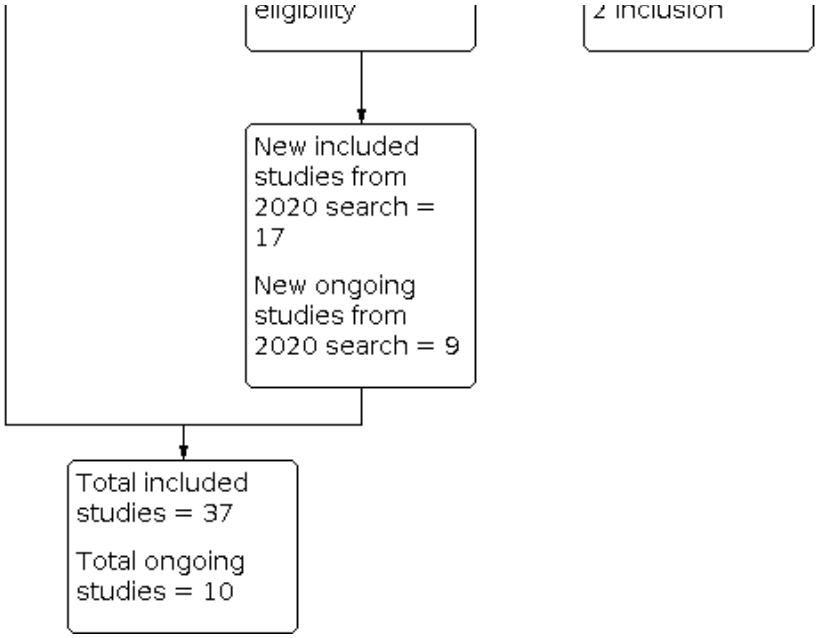


Figure 1. (Continued)



Part 2

For Part 2 of this update, our 2020 searches identified 1099 non-duplicate references (Figure 2). All references were then screened and 433 full-text articles were retrieved. We identified 27 new included studies and 10 new ongoing studies for this update (Characteristics of ongoing studies). In total, we now include 83 studies in Part 2. Four trials are also included in Part 1 that contributed data to Part 2 (1 Cooper 2005 (also Part 2); 1 Levine 2010 (also Part 2); 1 Pirie 1992 (also Part 2); 1 Spring 1995 (also Part 2))

Figure 2. Study flow diagram for Part 2 2020 search plus studies from 2016 search and the 2012 review

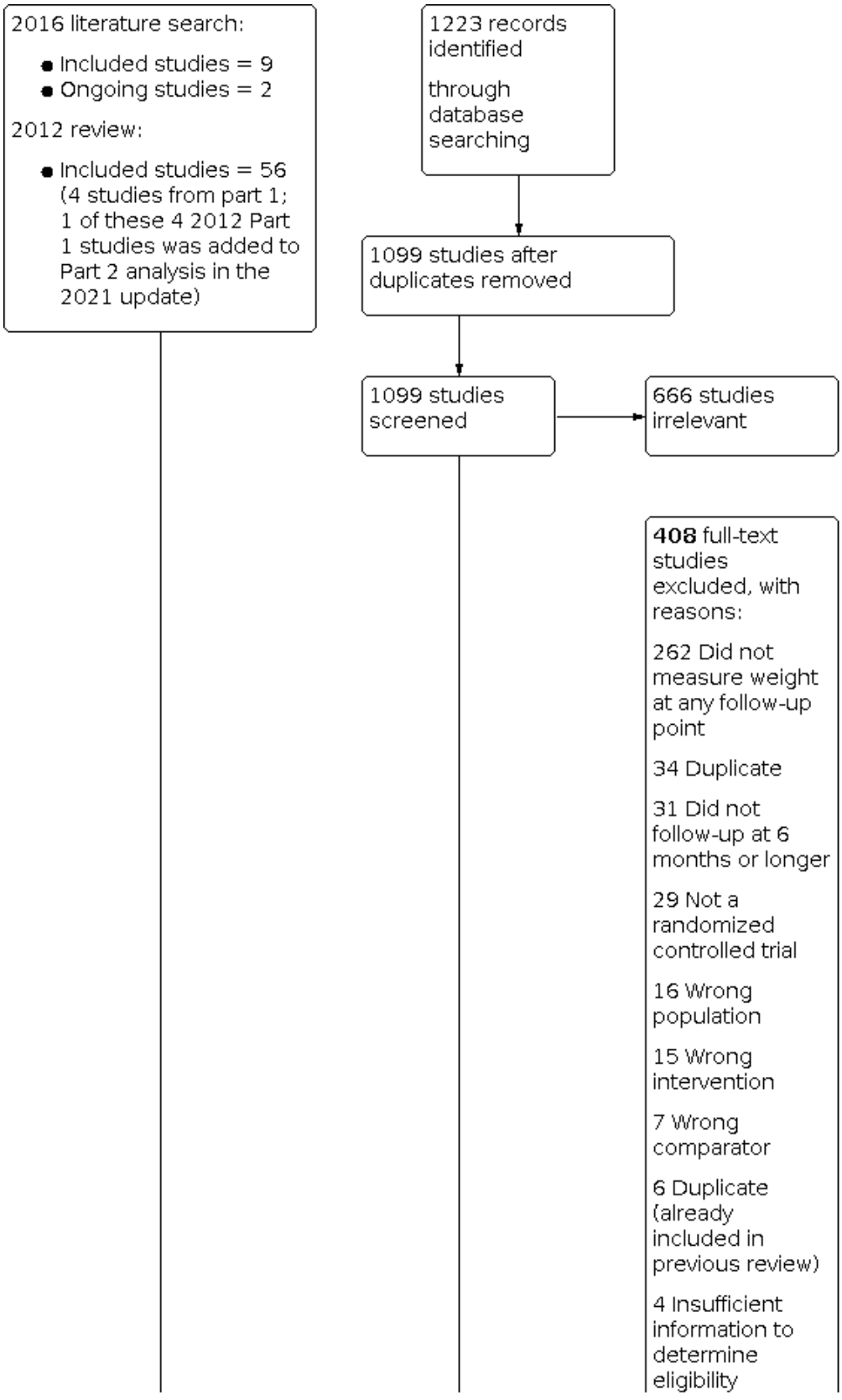
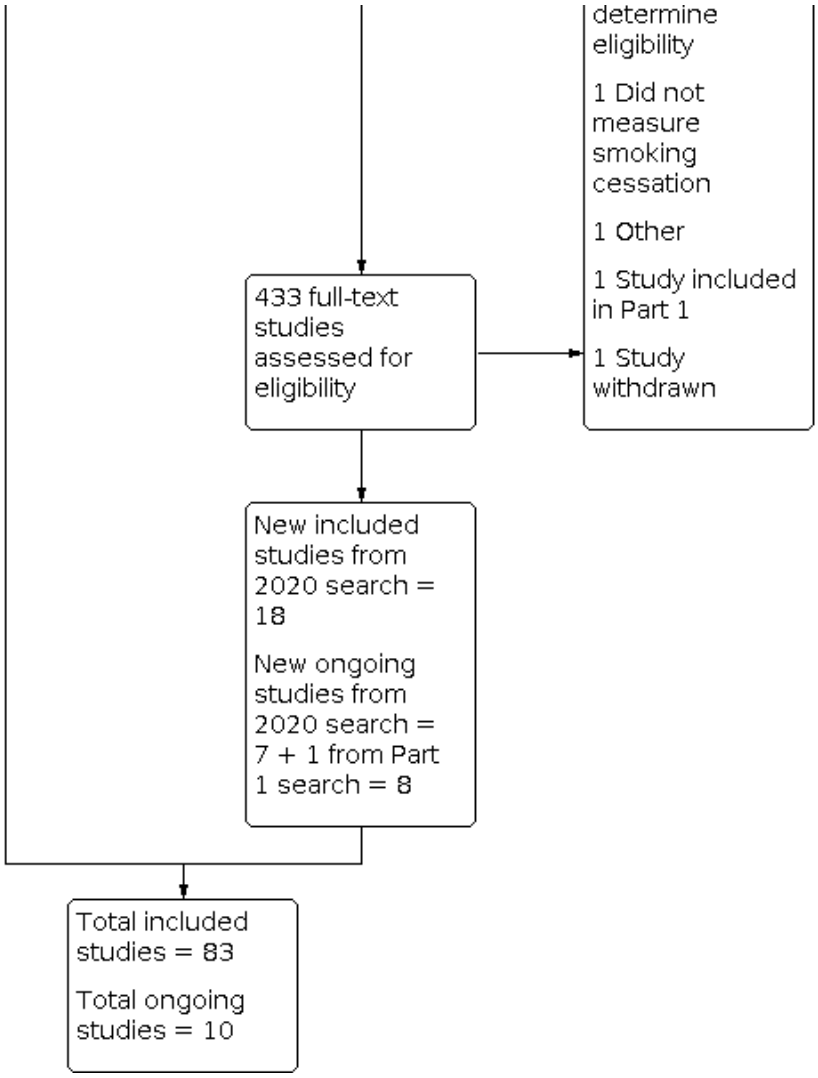


Figure 2. (Continued)



Included studies

Main features of studies included in Part 1 and Part 2 are summarized below, and further details on each included study can be found in the Characteristics of included studies table.

Participants

Part 1

A total of 11,514 participants were enrolled in the 37 included studies. Three-quarters of the studies (27 studies) were undertaken in the USA, three were conducted in England, and one each in Australia, Canada, China, Denmark, Norway, Scotland, and Sweden. A median age of 45.5 years was reported across 27 of the 37 included studies, and a median body mass index (BMI) of 28.5 kg/m^2 was reported across the 20 studies which provided these data at baseline. The median percentage of women across 35 studies reporting it was 75.4%, with 14 studies recruiting only women (1 Bloom 2020; 1 Cooper 2005 (also Part 2); 1 Copeland 2006; 1 Copeland 2015; 1 Danielsson 1999; 1 Klesges 1990; 1 Levine 2010 (also Part 2); 1 NCT03528304 2016; 1 Oncken 2019; 1 Perkins 2001; 1 Pirie 1992 (also Part 2); 1 Prapavessis 2018; 1 Spring 1995 (also Part 2); 1 Spring 2004). Participants smoked a median of 20 cigarettes per day at baseline, as reported across 26 studies. A median of 5.2 was scored on the Fagerström Test for Nicotine Dependence across the 12 studies that reported it.

Part 2

A total of 46,248 participants were enrolled in the 83 studies included in Part 2 of this review. Nearly half of the studies (39 studies) were conducted in the USA, and a further 15 studies were conducted across multiple countries. Four studies each were conducted in Sweden and England, three each in Switzerland and France and two each in Australia and Denmark. A single study was conducted each in Canada, China, Finland, Greece, India, Iceland, New Zealand, Japan, South Africa, Spain and Turkey.

Of the 83 included studies, 64 reported age, median 43 years, and 14 studies reported baseline BMI, median 27.2 kg/m^2.The median percentage of women was 55% as reported across 71 studies, with eight of these studies recruiting only women. Participants smoked a median of 22 cigarettes per day at baseline (across 57 studies) and a median of 5.6 was scored on the Fagerström Test for Nicotine Dependence (22 studies).

Interventions and comparators

Part 1

Behavioural interventions

Twenty-three studies assessed the effects of a behavioural intervention to prevent weight gain after a smoking cessation attempt.

Three trials examined an intervention consisting of education on weight management (1 Hall 1992; 1 Hankey 2009; 1 Pirie 1992 (also Part 2)) against standard smoking cessation support.

Seven trials examined the effects of personalized weight management against usual smoking cessation care (1 Bush 2012; 1 Bush 2018; 1 Johnson 2017; 1 Lycett 2020; 1 Sobell 2017; 1 Spring 2004; 1 Hall 1992). One study tested the efficacy of a very low calorie diet (VLCD), meaning food replacements providing less than 800 kcal/day, where participants in the intervention and control groups both received the weight management education as well as usual smoking cessation support. Both groups were advised to follow a 1600 kcal diet, while the intervention group received two two-week blocks of a VLCD provided free of charge. Treatment took place in a specialist obesity treatment centre (1 Danielsson 1999). One study compared 16 face-to-face one-hour motivational interviewing and cognitive behaviour therapy (CBT) counselling sessions, given mostly by telephone (1 Baker 2018).

Four studies compared the use of CBT to promote acceptance of moderate weight gain to no behavioural weight advice. (1 Bloom 2020; 1 Levine 2010 (also Part 2); 1 Perkins 2001; 1 White 2019). One of these studies was a three-arm RCT (1 Perkins 2001) and was also included in the aforementioned comparison on personalized weight management support versus no weight intervention.

Three studies new to this update directly compared behavioural weight management interventions. 1 Prapavessis 2018 tested an exercise maintenance condition with contact control to contact control alone, which included a behavioural weight management component, while 1 Heggen 2016 compared a low-carbohydrate diet to a moderately reduced-fat diet. 1 Copeland 2015 compared a minimally-tailored group intervention which provided information on smoking and weight with a highly tailored, multidisciplinary individual approach, but could not be included in the statistical analysis as no measures of variance were reported alongside weight-change data.

Five more studies could not be included in the statistical analyses. 1 Oncken 2019 tested the effect of 30 supervised exercise group sessions compared to relaxation group sessions. 1 Vander Weg 2016 compared a Quitline referral to a tailored tobacco intervention in which eligible participants who were worried about weight gain were offered support for weight management. Trial arms of interest in 1 NCT03528304 2016 compared a 16-week culturally-tailored contingency management intervention for smoking abstinence and weight loss to no intervention. 1 Lycett 2010 compared a VLCD to an individual dietary and activity-planning intervention either begun at baseline or at eight weeks post-quit. Finally, one study compared the effect of group to individual relapse-prevention follow-up sessions on smoking cessation and weight change after a two-week smoking cessation programme (1 Copeland 2006). Results from this study are also reported narratively.

Pharmacological interventions

Fourteen studies compared the effects of pharmacological interventions to placebo on smoking cessation and post-cessation weight change.

Pharmacological interventions included 8.33 mg phenylpropanolamine gum 16 pieces/day for 8 weeks (1 Cooper 2005 (also Part 2)), 9 pieces/day for 2 weeks (1 Klesges 1990) and up to 10 pieces/day for 4 weeks (1 Klesges 1995); 20 mg ephedrine plus 200 mg caffeine 3/day for 12 weeks (1 Norregaard 1996), 100, 50 and 25 mg/day naltrexone for 6 weeks (1 O'Malley 2006), 50 mg/day naltrexone for 12 weeks (1 King 2012), 25 mg/day naltrexone for 26 weeks (1 Toll 2010), 100 mg/day topiramate (up-titrated over 5 weeks) for 10 weeks (1 Oncken 2014), 400 mg/day chromium polynicotinate for 14 weeks (1 Parsons 2009) and 30 mg/day dexfenfluramine for 12 weeks (1 Spring 1995 (also Part 2)). This study also examined the efficacy of 40 mg/day of fluoxetine for preventing weight gain (1 Spring 1995 (also Part 2)). As the other fluoxetine studies were included in Part 2 of the reviews, this comparison is described in Part 2.

1 Rose 2019 provided two weeks of lorcaserin or placebo during the two-week pre-quit period, followed by an identical treatment regimen of lorcaserin plus a nicotine patch for 12 weeks post-quit date. Lorcaserin was also tested at 10 mg once or twice daily for 12 weeks in both 1 Shanahan 2017 and 1 Wilcox 2016, but data on the latter study were limited due to extraction from a conference abstract. Finally, 1 Lyu 2018 investigated a combination of adjunctive naltrexone (25 mg/day) and bupropion (300 mg/day) treatment for 24 weeks.

Part 2

Of the 83 included studies, 71 provided sufficient data to include in the meta-analysis. The outstanding studies were new to this update and measured weight at eligible time points, but data were not provided in a form that we could meta-analyze.

Of the 71 studies, 34 tested interventions with NRT, 19 with antidepressants, 17 with varenicline, four with exercise and two with electronic cigarettes. Five of these studies included multiple intervention arms or a combination of these interventions.

Nicotine replacement therapy was delivered in various forms, with most studies using a nicotine patch, while other studies delivered nicotine in the form of gum, lozenges, sublingual tablets, inhalers and intranasal spray. Some studies tested patches with varying nicotine dosing regimens, which were assessed separately.

Nineteen studies on antidepressants were included in this review, three of which compared bupropion to varenicline as well as placebo (2 Gonzales 2006; 2 Jorenby 2006; 2 Nides 2006). Overall, 14 studies compared weight change in participants treated with bupropion to placebo (2 Gonzales 2006; 2 Hurt 1997; 2 Jorenby 2006; 2 Nides 2006;2 Piper 2007; 2 Rigotti 2006; 2 Simon 2004; 2 Simon 2009; 2 Uyar 2007; 2 Zellweger 2005; 2 Cox 2012; 2 Eisenberg 2013; 2 Piper 2009; 1 Levine 2010 (also Part 2)). One of these studies (2 Simon 2004) provided a nicotine patch to both the bupropion and placebo study arms, and two additional studies compared varenicline and bupropion to varenicline and placebo (2 Rose 2014; 2 Ebbert 2014). A further two studies compared fluoxetine to placebo (2 Niaura 2002; 2 Saules 2004). 2 Saules 2004 tested fluoxetine versus placebo; both intervention and control arms used

NRT, but we included it in the analyses with other fluoxetine-versus-placebo studies. One other study examined the efficacy of fluoxetine versus placebo (1 Spring 1995 (also Part 2)). It was not included in the parent Cochrane Review because smoking cessation at six months was not reported, but was identified and included here. All bupropion studies administered 300 mg/day and 2 Hurt 1997 also included a 100 mg/day and 150 mg/day arm. For the main comparison, we use the 300 mg/day arm for 2 Hurt 1997 and we use the lower-dose arms to compare to the standard 300 mg/day treatment to the lower-dose arms. Two fluoxetine studies compared two dosing levels (30 mg and 60 mg/day (2 Niaura 2002) and 20 mg and 40 mg/day (2 Saules 2004)) which we combined for the main comparison, while the lower doses and higher doses were compared in a separate comparison to examine for a dose-dependent effect. One other study examined 40 mg fluoxetine versus placebo (1 Spring 1995 (also Part 2)).

Fourteen studies included in this review compared varenicline to placebo, with some studies including additional intervention components (e.g. patch) which were balanced between study arms. Once again, some studies compared different dosing regimens which were assessed in additional analyses. One study compared 2 mg/daily varenicline to a 21 mg patch tapering to 7 mg (2 Aubin 2008). As mentioned above, 2 Gonzales 2006; 2 Jorenby 2006; 2 Nides 2006 also compared varenicline with bupropion, while 2 Ioakeimidis 2018 compared varenicline with electronic cigarette (12 mg/ml nicotine) use for 12 weeks.

We found no new studies on exercise interventions for smoking cessation for inclusion in this update. In the four original studies, all participants in the treatment arm received an exercise component in parallel with cognitive behavioural treatment for smoking cessation, which was supplemented with nicotine replacement therapy in 2 Ussher 2003 and 2 Bize 2010. The exercise component included supervised exercise in three studies. 2 Marcus 1999 tested three supervised exercise sessions/week for 12 weeks, 30 to 40 minutes resting heart rate plus 60% to 85% heart reserve; 2 Marcus 2005 tested one supervised, four unsupervised exercise sessions/week for eight weeks, at least 30 minutes at resting heart rate plus 45% to 59% heart reserve; and 2 Bize 2010 tested moderate-intensity (40% to 60% of maximal aerobic power) group-based cardiovascular (CV) activity under the supervision of a trained monitor for 45 minutes weekly for nine weeks. In contrast, 2 Ussher 2003 compared the effect of seven weeks of exercise counselling to participants receiving a smoking cessation intervention with brief health education.

Finally, two new studies investigated the use of electronic cigarettes. 2 Walker 2020 was a three-arm RCT comparing a nicotine patch versus nicotine-containing electronic cigarette plus patch versus nicotine-free electronic cigarette plus patch. 2 Ioakeimidis 2018, mentioned above,compared varenicline with electronic cigarette (12 mg/ml nicotine) use for 12 weeks.

Further information on dose or length or both of all interventions outlined above are available in the Characteristics of included studies table. Weight change from baseline in all of the studies included in the second part of the review was measured in abstainers only. Definition of abstinence varied between studies as in Part 1, and is also noted in the Characteristics of included studies table. Data for some time points were received following requests made to study authors, which is also noted in the Characteristics of included studies table.

Outcomes

Part 1

Of the 37 included studies:

- 28 reported data on weight change at end of treatment (EOT), six months, 12 months and/or at the longest follow-up time point (data for three studies described narratively)
- 25 reported data on abstinence at EOT, six months, 12 months and/or at the longest follow-up time point (data for one study are described narratively)
- 10 pharmacotherapy trials reported adverse or serious adverse outcomes, or both, six of which are described narratively.

Part 2

Of the 83 included studies:

- 71 reported data on weight change at EOT, six months or 12 months in sufficient detail to be included in the meta-analysis.

Excluded studies

We list 200 studies excluded at full-text stage along with reasons in Characteristics of excluded studies. The most common reasons for exclusion in the 2020 search were not measuring any of our outcomes (10 studies) or testing ineligible interventions (10 studies).

Risk of bias in included studies

Part 1: Overall, of the 37 included studies, we judged five studies to be at low risk of bias, 17 to be at unclear risk and the remaining 15 studies at high risk.

Part 2: Of the 83 studies not designed to address post-cessation weight gain included in Part 2, we judged overall risk of bias to be low for 13 studies, unclear for 46 studies, and high for 24 studies.

Details of risk of bias judgements for each domain of each included study can be found in the Characteristics of included studies table and are illustrated in Figure 3.

Figure 3. Methodological quality summary: review authors' judgements about each methodological quality item for each included study.

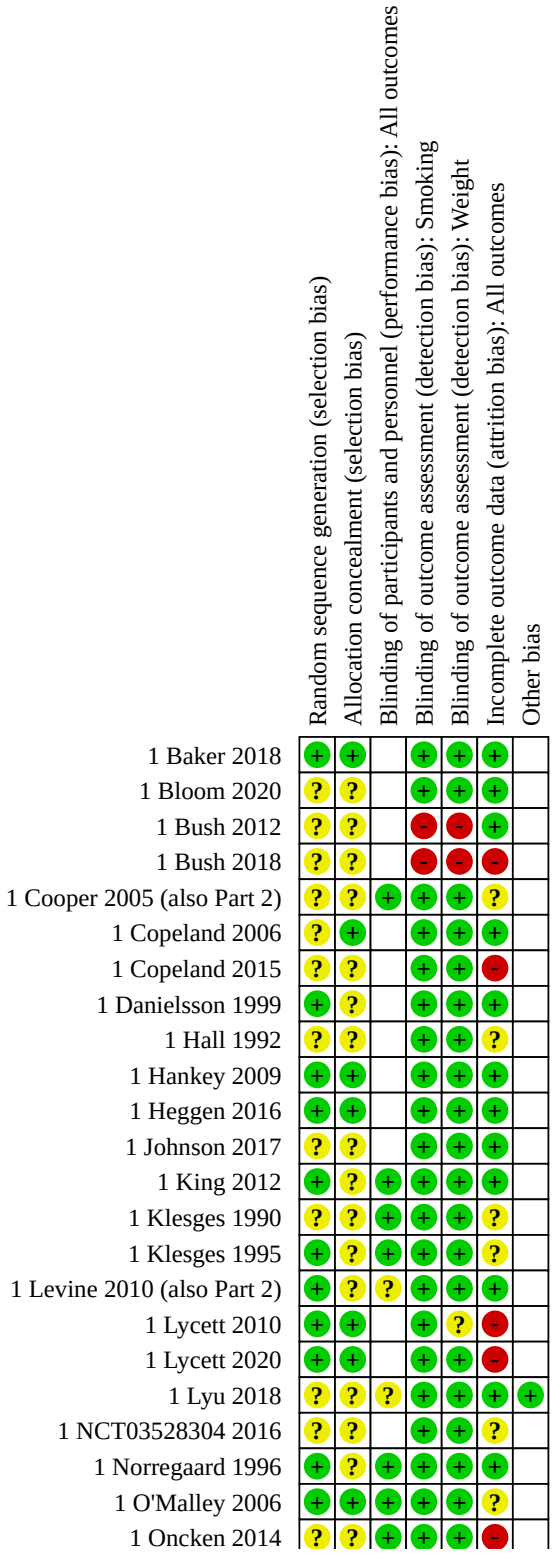
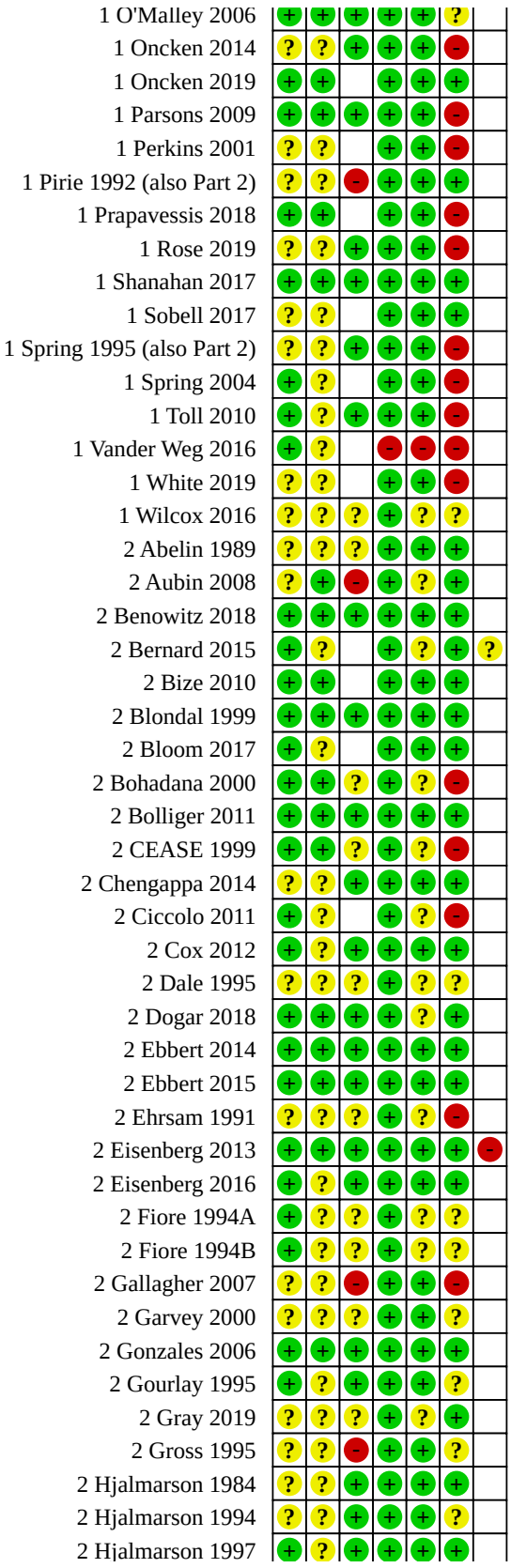


Figure 3. (Continued)



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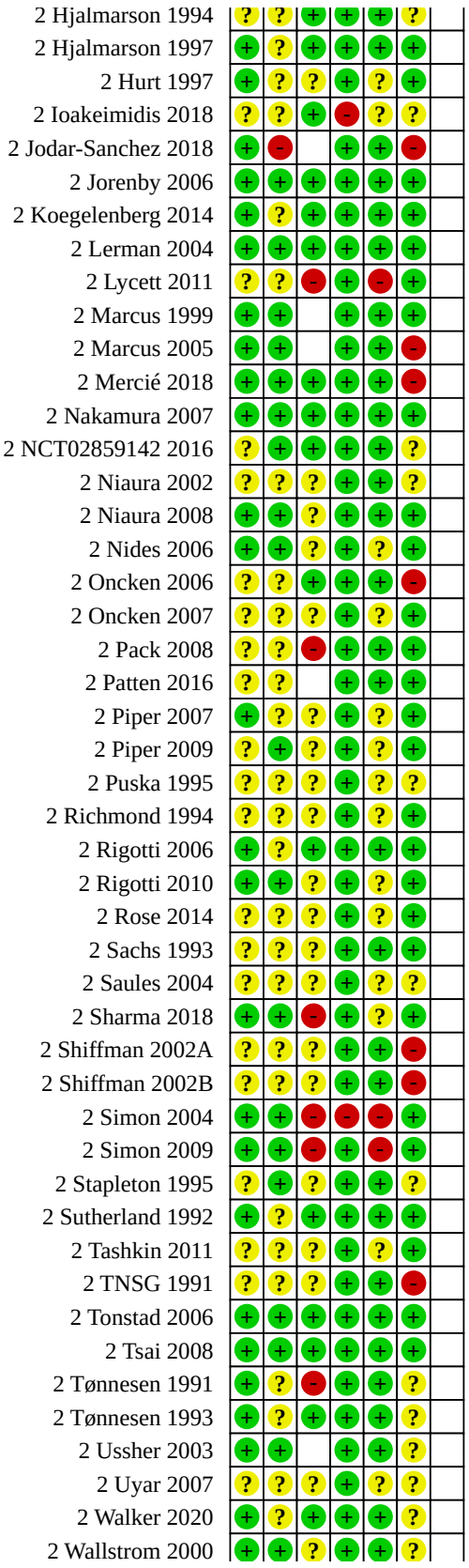

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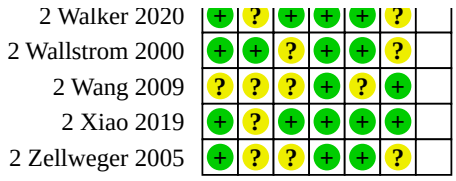


Allocation

For **Part 1.** we judged 10 studies to be at low risk of selection bias, and 27 studies to be at unclear risk of bias mainly due to limited information on allocation concealment.

A similar risk of selection bias for all studies included in **Part 2**. We judged 27 studies to be at low risk, 55 studies to be at unclear risk of bias, and one study at high risk of bias (2 Jodar-Sanchez 2018). Most studies were again rated at unclear risk of bias due to insufficient information about allocation concealment.

Blinding

Of the 37 studies included in **Part 1**, we judged 11 out of 14 pharmacological studies to be at low risk of both performance and detection bias and the remaining three studies at unclear risk of bias. We judged 19 of the 23 behavioural studies to be at low risk of detection bias, one at unclear risk and three at high risk of detection bias; performance bias was not assessed in included studies on behavioural interventions.

Of the 83 studies included in **Part 2**, 74 tested a pharmacological intervention. Of these 74 studies, 29 were judged to be at low risk of both performance and detection bias, 34 at unclear risk and 11 at high risk. Many of these studies were rated at unclear or high risk of bias due to a lack of blinding when blinding was possible or due to insufficient information about blinding, mainly by not specifying who within the study were blinded. As with Part 1, performance bias was not assessed in the remaining nine behavioural studies included in Part 2. Of these nine studies, eight were judged to be at low risk of detection bias, while one study was rated at unclear risk because it did not specify how weight was measured.

Incomplete outcome data

We rated 16 out of the 37 studies included in **Part 1** at low risk of attrition bias. We rated 14 studies with greater than 50% loss to follow-up overall or a follow-up difference of more than 20% between study arms, or both, at high risk of attrition bias. The remaining seven studies were judged to at unclear risk.

Similarly, of the 83 studies included in **Part 2**, most (49 studies) were judged to be at low risk of attrition bias. Twenty-one studies were rated at unclear risk and 13 studies at high risk.

Other potential sources of bias

No studies in **Part 1** were judged to be at unclear or high risk of other bias.

2 Bernard 2015 from **Part 2** was rated at unclear risk of other bias as participants in the control group may have participated in exercise (contamination effect).

Effects of interventions

See: **Summary of findings 1** Behavioural weight management interventions compared to brief advice or no intervention for post-cessation weight control; **Summary of findings 2** Acceptance interventions for weight concern compared to no weight management intervention for post-cessation weight control; **Summary of findings 3** Exercise interventions for smoking cessation compared to no exercise intervention for preventing weight gain after smoking cessation; **Summary of findings 4** Nicotine replacement therapy for smoking cessation compared to placebo for preventing weight gain after smoking cessation; **Summary of findings 5** Varenicline for smoking cessation compared to placebo for preventing weight gain after smoking cessation; **Summary of findings 6** Fluoexetine compared to placebo for smoking cessation for preventing weight gain after smoking cessation

Part 1

Effects of pharmacological interventions to prevent post-cessation weight gain versus placebo

Weight change

For three pharmacotherapies, there was evidence of reduced weight gain at end of treatment (EOT), and confidence intervals (CIs) excluded no difference (Analysis 1.1):

- Dexfenfluramine: mean difference (MD) −2.50 kg, 95% confidence interval (CI) −2.98 to −2.02; 1 study at high risk of bias, 33 participants
- Phenylpropanolamine (PPA): MD −0.50 kg, 95% CI −0.80 to −0.20; I^2 = 0%; 3 studies, 112 participants; results not sensitive to removal of one study at high risk of bias
- Naltrexone: MD −0.91 kg, 95% CI -1.49 to -0.34; I^2 = 0%; 3 studies, 254 participants; results not sensitive to removal of one study at high risk of bias

For a further three pharmacotherapies, point estimates suggested reduced weight gain at end of treatment, but CIs included the possibility of no difference (Analysis 1.1):

- Ephedrine + caffeine: MD −1.30 kg, 95% CI −2.87 to 0.27; 1 study at high risk of bias, 40 participants
- Lorcaserin: MD −1.14 kg, 95% CI −3.65 to 1.37; 1 study at low risk of bias, 41 participants
- Chromium: MD −0.81 kg, 95% CI −3.05 to 1.43; 1 study at high risk of bias, 15 participants

The one study of topiramate did not have any quitters in the placebo arm and hence an effect estimate could not be calculated

(1 Oncken 2014). A further study comparing different treatment regimens of lorcaserin did not provide data by treatment arm (1 Rose 2019).

Four pharmacotherapies were tested in trials that reported at six (Analysis 1.2) and 12 months (Analysis 1.3). All had point estimates suggesting benefit, but only one study contributed data at each time point and in all cases CIs were wide and included no difference:

- PPA 6 months: MD −2.06, 95% CI −5.56 to 1.44; 12 months MD −1.04, 95% CI −5.03 to 2.95; 38 participants; at unclear risk of bias
- Ephedrine + caffeine 6 months: MD −0.70 kg, 95% CI −2.72 to 1.32; 32 participants; 12 months MD 1.20 kg, 95% CI −1.84 to 4.24; 24 participants; at unclear risk of bias
- Chromium 6 months only: MD −3.87 kg, 95% CI −12.01 to 4.27; 9 participants; at unclear risk of bias
- Naltrexone 6 months: MD −0.29 kg, 95% CI −2.23 to 1.65; 68 participants; 12 months MD −2.30 kg, 95% CI −4.92 to 0.32; 61 participants; at unclear risk of bias

Smoking cessation

For studies which measured smoking cessation at six (Analysis 1.4) or 12 months (Analysis 1.5), or both, CIs for all comparisons were wide and included no difference:

- PPA 6 months: RR 1.38, 95% CI 0.76 to 2.53; 12 months RR 1.48, 95% CI 0.80 to 2.73; 1 study at unclear risk of bias, 295 participants
- Ephedrine + caffeine 6 months: RR 1.06, 95% CI 0.53 to 2.11; 12 months RR 1.44, 95% CI 0.60 to 3.48; 1 study at unclear risk of bias, 225 participants
- Naltrexone 6 months: RR 1.02, 95% CI 0.79 to 1.32; I^2 = 0%; 3 studies, 890 participants; removing one at high risk did not impact results; 12 months: RR 1.25, 95% CI 0.67 to 2.31; 1 study at unclear risk of bias, 385 participants
- Chromium 6 months only: RR 0.48, 95% CI 0.12 to 1.84; 1 study at unclear risk of bias,143 participants
- Naltrexone and bupropion 6 months only: not estimable due to no quitters in either arm; 1 study at unclear risk of bias, 22 participants

Adverse and serious adverse events (SAEs)

For the most part, data were sparsely and heterogeneously reported, often precluding pooled analyses.

In both studies of lorcaserin, adverse events (AEs) were higher in the intervention arms, but CIs were wide and incorporated no difference: Analysis 1.6; compared to placebo: RR 1.12, 95% CI 0.95 to 1.32; 1 study at low risk of bias, 401 participants; longer duration compared to shorter duration: RR 1.41, 95% CI 0.88 to 2.25; 1 study at high risk of bias, 83 participants. The latter study was the only one of lorcaserin to also report measuring SAEs, with one event occurring in the control arm (Analysis 1.7).

One study of topiramate, judged to be at high risk of bias, measured SAEs, with none reported in either arm (38 participants, Analysis 1.7). In the same study (1 Oncken 2014), authors report that when examining the frequency of all adverse events, only paraesthesia was reported by more participants in the topiramate group than in the placebo group. No participants using placebo reported paraesthesia, compared to 47% (9 of 19) participants in the topiramate group (P = 0.011).

One study of naltrexone measured SAEs and found no difference: RR 0.98, 95% CI 0.14 to 6.89; 1 study at unclear risk of bias, 333 participants; Analysis 1.7. 1 King 2012 reported a higher incidence of dizziness and nausea in those randomized to naltrexone compared to placebo; these data could not be used in our statistical analysis. 1 O'Malley 2006 found no statistically significant between-group differences in adverse events by type. 1 Toll 2010 found that "the percentage of unique participants reporting non-serious adverse events rated moderate or severe with a prevalence of ≥5% differed by treatment group for depression and decreased appetite [in each case there were 4 (5%) naltrexone participants vs 0 (0%) placebo participants, Chi^2 = 4.21, P = 0.04]."

One study of PPA reported "only one side effect"; heartburn in the placebo group (1 Klesges 1990).

In their study of dexfenfluramine and fluoxetine, 1 Spring 1995 (also Part 2) detected no differences in number of participants stopping treatment due to adverse events.

1 Norregaard 1996, (ephedrine + caffeine) reported a higher incidence of palpitations, sweating, dizziness and nausea in the intervention than in the control group.

No other studies reported data on adverse or serious adverse events.

Effects of behavioural interventions to prevent post-cessation weight gain

Compared to no support

There was no evidence at any follow-up that weight management education alone reduced weight gain: At EOT MD −0.04 kg, 95% CI −0.57 to 0.50; I^2 = 0%; 2 studies, 140 participants; at 6 months MD 0.89, 95% CI −0.78 to 2.55; I^2 = 0%; 2 studies, 81 participants; and 12 months MD −0.21 kg, 95% CI −2.28 to 1.86; I^2 = 0%; 2 studies, 61 participants (Analysis 2.1; Analysis 2.2; Analysis 2.3). Results were not sensitive to removing the one study at high risk of bias. At six months, there was no evidence of a difference in quit rates, but CIs incorporated clinically significant benefit and clinically significant harm: RR 1.02, 95% CI 0.78 to 1.33; I^2 = 9%; 3 studies, 660 participants; results not sensitive to exclusion of one study at high risk of bias; Analysis 2.4. However, at 12 months there were fewer quitters in the weight-management education group, with CIs excluding no difference: RR 0.66, 95% CI 0.48 to 0.90; I^2 = 0%; 2 studies, 522 participants; results not sensitive to removal of one study at high risk of bias; Analysis 2.5.

Personalized weight-management support programmes reduced weight gain at end of treatment: MD −1.11 kg, 95% CI −1.93 to −0.29; I^2 = 0%; 3 studies, 121 participants; results not sensitive to the removal of the two studies at high risk of bias; Analysis 2.1, with CIs excluding no difference. Weight gain was also reduced relative to control at six months: MD −0.96 kg, 95% CI −2.18 to 0.25; I^2 = 46%; 5 studies, 816 participants; results not sensitive to removal of two studies at high risk of bias; Analysis 2.2; and at 12 months: MD −0.44 kg, 95% CI −2.34 to 1.46; I^2 = 41%; 4 studies, 530 participants; results not sensitive to exclusion of two studies at high risk of bias; Analysis 2.3, but CIs incorporated no difference.

As with weight-management education, at six months there was no evidence of difference in quit rates: RR 0.95, 95% CI 0.82 to 1.10; I^2 = 33%; 7 studies, 5517 participants; results not sensitive to removal of five studies at high risk of bias; Analysis 2.4, but significantly fewer people had quit in the intervention arm at 12 months: RR 0.65, 95% CI 0.45 to 0.92; I^2 = 89%; 5 studies, 3441 participants; removal of three studies at high risk of bias widened CIs to include no difference but did not substantially alter the point estimate; Analysis 2.5. 1 Sobell 2017 did not report data in a way that could be used in our analyses, but reported no differences in weight between groups. In 1 Vander Weg 2016, participants in the intervention arm could choose to engage in a weight-management intervention; results were not reported by randomized group.

Comparisons between weight-management interventions

The within-study comparison from 1 Hall 1992 suggested that personalized weight management support is more effective than educating participants about weight management at the end of smoking cessation treatment: MD −1.12 kg, 95% CI −2.17 to −0.07; Analysis 3.1, and at 12 months: MD −2.49 kg, 95% CI −5.51 to 0.53; Analysis 3.3. There was no difference in smoking cessation at six or 12 months, although again CIs were wide (Analysis 3.4; Analysis 3.5).

Data from 1 Danielsson 1999 (unclear risk of bias) showed the benefit of VLCD at end of treatment: MD −3.70, 95% CI −4.82 to −2.58; 121 participants 121; Analysis 3.1; and at 12 months: MD −1.30 kg, 95% CI −3.49 to 0.89; 62 participants; Analysis 3.3; although in the latter case CIs included no difference. This intervention improved abstinence at 12 months with CIs excluding no difference: RR 1.73, 95% CI 1.10 to 2.73, Analysis 3.5.

One study compared providing weight-management support at the start of a quit attempt versus some weeks after attaining abstinence. Confidence intervals were wide and included no difference in weight at end of treatment: 1 Spring 2004; unclear risk of bias; Analysis 3.1; and at six months Analysis 3.2. Cessation not measured. One study compared 16 x one-hour counselling sessions comprising motivational interviewing and CBT with 16 x 10-minute telephone calls aiming to reduce weight gain after cessation (1 Baker 2018; low risk of bias). There was no evidence of benefit for weight but outcomes were imprecisely estimated; Analysis 3.3; Analysis 3.5. One study compared advice to follow a low-carbohydrate diet with advice to follow a low-fat one and found no evidence of a difference in weight: 1 Heggen 2016, low risk of bias, Analysis 3.1; Analysis 3.2; Analysis 3.4.

1 Prapavessis 2018 (high risk of bias, 41 participants) randomized participants to an intensive exercise programme or no exercise support. There was no evidence of differences in cessation (Analysis 3.4; Analysis 3.5); weight was not measured. We include this trial in Part 1 as the intervention was delivered specifically in the context of reducing weight gain. 1 Copeland 2006 and 1 Copeland 2015 randomized menopausal women to either group-based education on CBT principles for weight management or to CBT based on individualized counselling based on questionnaire scores. They found no evidence that weight differed by end of treatment. :A further study compared a very low calorie diet to an individualized diet and exercise plan which began either at baseline or eight weeks post quit-date (step-by-step group), but all participants in two of the three study arms had relapsed or dropped out of the study by end of treatment (1 Lycett 2010). Average weight change in abstinent smokers in the step-by-step study arm was 1.15 (SD 2.22) kg (4 participants) at end of treatment and no one in the other groups was abstinent and provided weight data .

Effects of acceptance interventions for weight concern

There was mixed evidence that CBT to support acceptance of weight gain affected weight after stopping smoking. Statistical heterogeneity for weight at all time points precluded statistical synthesis (I^2 > 70% in all cases; Analysis 4.1; Analysis 4.2; Analysis 4.3). This heterogeneity was driven by the two studies in which no pharmacotherapy was provided; 1 Levine 2010 (also Part 2) (42 participants) found a point estimate favouring control at all time points, and 1 Perkins 2001 (63 participants) found a point estimate favouring the intervention at all time points; both excluded no difference at end of treatment (Analysis 4.1). Removing the one study at high risk of bias (1 Perkins 2001) did not meaningfully reduce statistical heterogeneity at end of treatment. However, at six months and 12 months, removing this study reduced statistical heterogeneity to 0%. At both time points, results from sensitivity analyses favoured control arms but CIs were wide and for 12 months incorporated no difference: six months: MD 0.89, 95% CI 0.39 to 1.40; 2 studies, 77 participants, at unclear risk of bias; Analysis 4.2; MD 0.37, 95% CI −0.50 to 1.24; 1 study, 54 participants at unclear risk of bias; Analysis 4.3. One further study (1 White 2019) did not provide data in a way that could be incorporated into the meta-analysis, but weight gain was reduced in the intervention compared to control group.

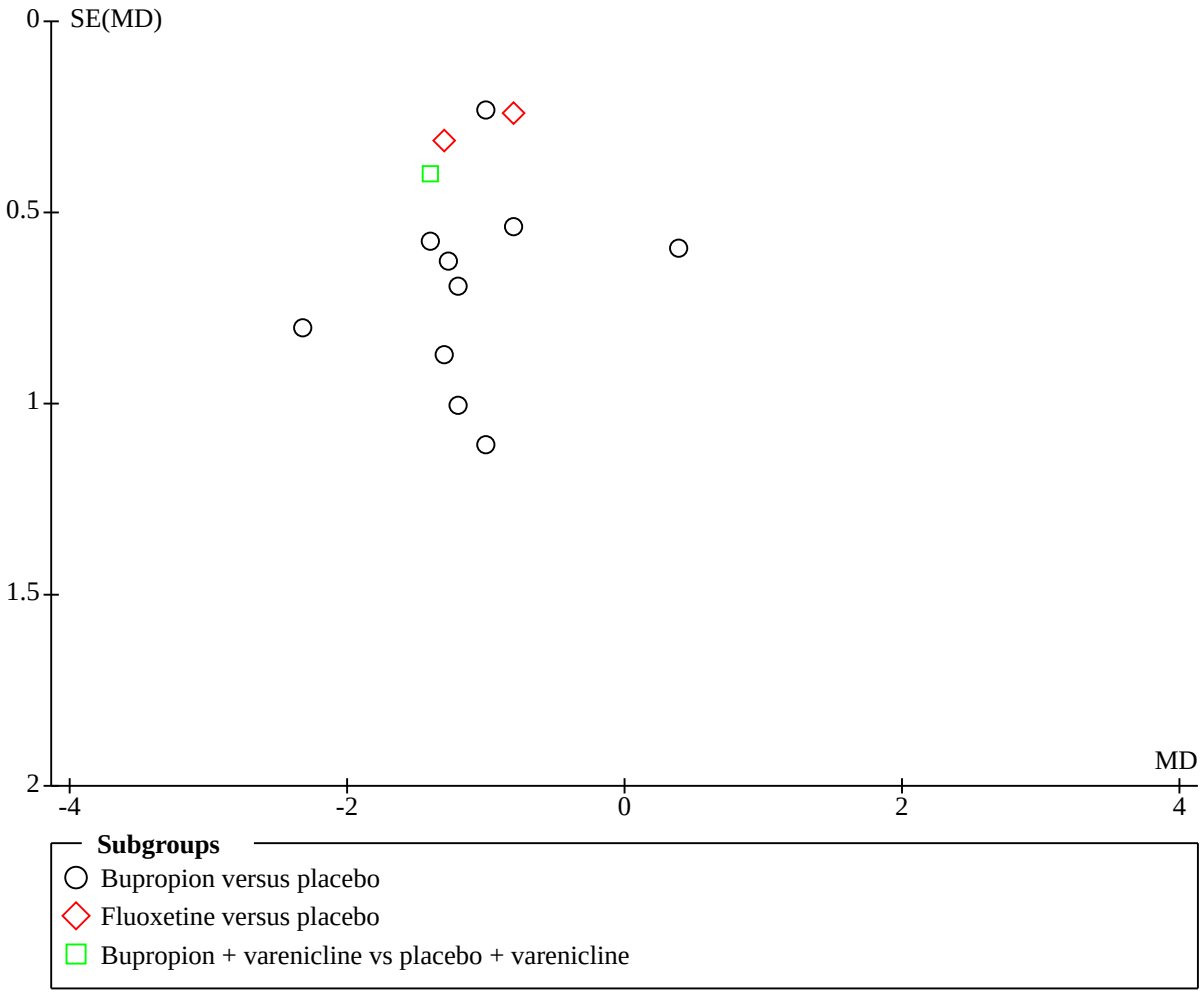
There was some evidence that interventions that promoted acceptance of weight gain increased smoking abstinence at six and 12 months. At six months the RR was 1.42, 95% CI 1.03 to 1.96; I^2 = 21%; 4 studies, 619 participants; removing two at unclear risk of bias decreased the point estimate and led to CIs incorporating no difference; Analysis 4.4. At 12 months, the RR was 1.25, 95% CI 0.76 to 2.06; ; I^2 = 26%; 2 studies, 496 participants; removing one at unclear risk of bias decreased the point estimate; Analysis 4.5.

Part 2

Effect of antidepressants on post-cessation weight gain

Bupropion (300 mg/day) limited post-cessation weight gain compared with placebo at the end of treatment, with CIs excluding no difference: MD −1.01 kg, 95% CI −1.35 to −0.67; I^2 = 3%; 10 studies, 1098 participants; results not sensitive to removal of one study at high risk of bias; Analysis 5.1. A funnel plot showed no evidence of asymmetry (Figure 4). At six and 12 months the reduction in weight was lower than at end of treatment and CIs incorporated no difference: six months: MD −0.38 kg, 95% CI −1.19 to 0.44; I^2 = 0%; 7 studies, 420 participants; results not sensitive to removal of two studies at high risk of bias; Analysis 5.3; 12 months: MD −0.26 kg, 95% CI −1.31 to 0.78; I^2 = 0%, 7 studies, 471 participants; results not sensitive to removal of two studies at high risk of bias; Analysis 5.5. There was no evidence of a dose-dependent response for bupropion at end of treatment, six or 12 months (Analysis 5.2, Analysis 5.4, Analysis 5.6), with wide CIs consistent with both benefit and harm. In a further study of bupropion, 2 Ebbert 2014 (low risk of bias), all participants received varenicline. At end of treatment (243 participants), the point estimate favoured bupropion and CIs excluded no difference; at six and 12 months the point estimate still favoured bupropion but CIs included no difference (Analysis 5.1; Analysis 5.3; Analysis 5.5).

Figure 4. Funnel plot of comparison: 5 All types of antidepressant versus placebo for smoking cessation, outcome: 5.1 Mean weight change (kg) at end of treatment.



The one study comparing post-cessation weight gain in bupropion versus NRT measured weight change at 12 months and detected no evidence of difference (2 Piper 2009, unclear risk of bias, 115 participants; Analysis 7.1).

Fluoxetine reduced weight gain at end of treatment: MD −1.01 kg, 95% CI −1.49 to −0.53; I^2 = 38%; 2 studies, 144 participants; results not sensitive to removal of one study at high risk of bias, Analysis 5.1. At six months, statistical heterogeneity was substantial (I^2 = 76%) and hence we do not present pooled results, but results from the two studies contributing data (both at unclear risk of bias) had CIs incorporating no difference (Analysis 5.3), Two studies of fluoxetine randomized participants to higher and lower doses as well as to placebo (2 Niaura 2002 to 60 mg and 30 mg and 2 Saules 2004 to 40 mg or 20 mg). There was no evidence that higher doses were more effective at six months and in fact people randomized to 60 mg had significantly greater weight gain at six months than people randomized to 30 mg, an effect not seen in the 40 mg versus 20 mg comparison (Analysis 5.4).

Effect of exercise interventions on post-cessation weight gain

Neither individual nor pooled data for the four trials of exercise programmes showed any reduction in weight gain at the end of the programme (Analysis 6.1), with a summary estimated mean difference of MD −0.25, 95% CI −0.78 to 0.29; I^2 = 0%; 4 studies, 404 participants; results not sensitive to removal of one study at high risk of bias. However, three studies (none at high risk of bias) provided data at 12 months follow-up which when pooled showed a significant reduction in weight gain favouring treatment (Analysis 6.2), with a summary estimate of MD −2.07 kg, 95% CI −3.78 to −0.36; I^2 = 0%; 3 studies, 182 participants.

Effect of nicotine replacement therapy (NRT) on post-cessation weight gain

Participants taking any type of NRT gained less weight than placebo referents at the end of treatment, with CIs excluding no difference: MD −0.52 kg, 95% CI −0.99 to −0.05; I^2 = 81%; 21 studies, 2784 participants; results not sensitive to removal of eight studies at high risk of bias; Analysis 8.1. Statistical heterogeneity was substantial

due to one study (2 Abelin 1989), which showed a 4.3 kg difference between weight gain in the treatment and control arms. When this study was removed, statistical heterogeneity reduced to 0% and the overall estimate decreased but CIs continued to exclude no difference: MD −0.41 kg, 95% CI −0.60 to −0.22; I^2 = 0%; 20 studies, 2667 participants; Analysis 8.1. A funnel plot showed some asymmetry, suggesting that smaller studies with less weight gain in intervention groups may be missing (Figure 5). Overall, weight gain was less for those taking NRT at six and 12 months although the point estimate was reduced compared to end of treatment, and CIs included no difference: six months: MD −0.08 kg, 95% CI −0.51 to 0.35; I^2 = 0%; 11 studies, 1021 participants; Analysis 8.2; and 12 months: MD −0.37 kg, 95% CI −0.86 to 0.11; I^2 = 0%; 17 studies, 1463 participants; Analysis 8.3. Whereas six-month results were not sensitive to removing the four studies at high risk of bias, removing the six studies at high risk of bias from the pooled 12-month estimate increased the magnitude of benefit, with CIs no longer excluding no difference: MD −0.77, 95% CI −1.45 to −0.08; I^2 = 0%; 11 studies, 630 participants. A funnel plot with data at six months showed some asymmetry but this time in the opposite direction to the end-of-treatment plot (Figure 6); at 12 months there was no asymmetry present (Figure 7). In 2 Lycett 2011 data were only available at eight-year follow-up, and weight change was similar between arms.

Figure 5. Funnel plot of comparison: 8 All types of NRT versus placebo for smoking cessation, outcome: 8.1 Mean weight change (kg) at end of treatment.

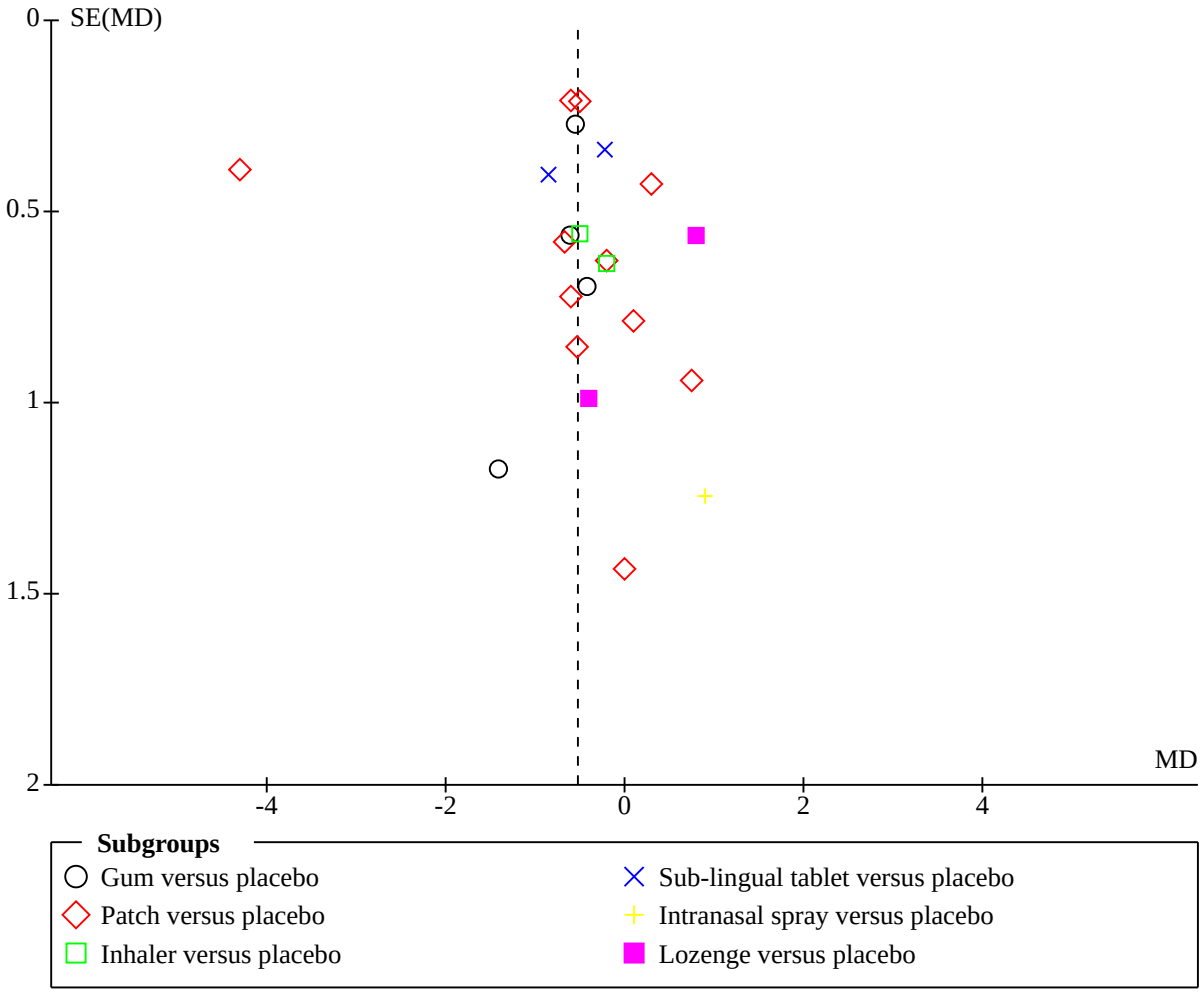


Figure 6. Funnel plot of comparison: 8 All types of NRT versus placebo for smoking cessation, outcome: 8.2 Mean weight change (kg) at 6 months.

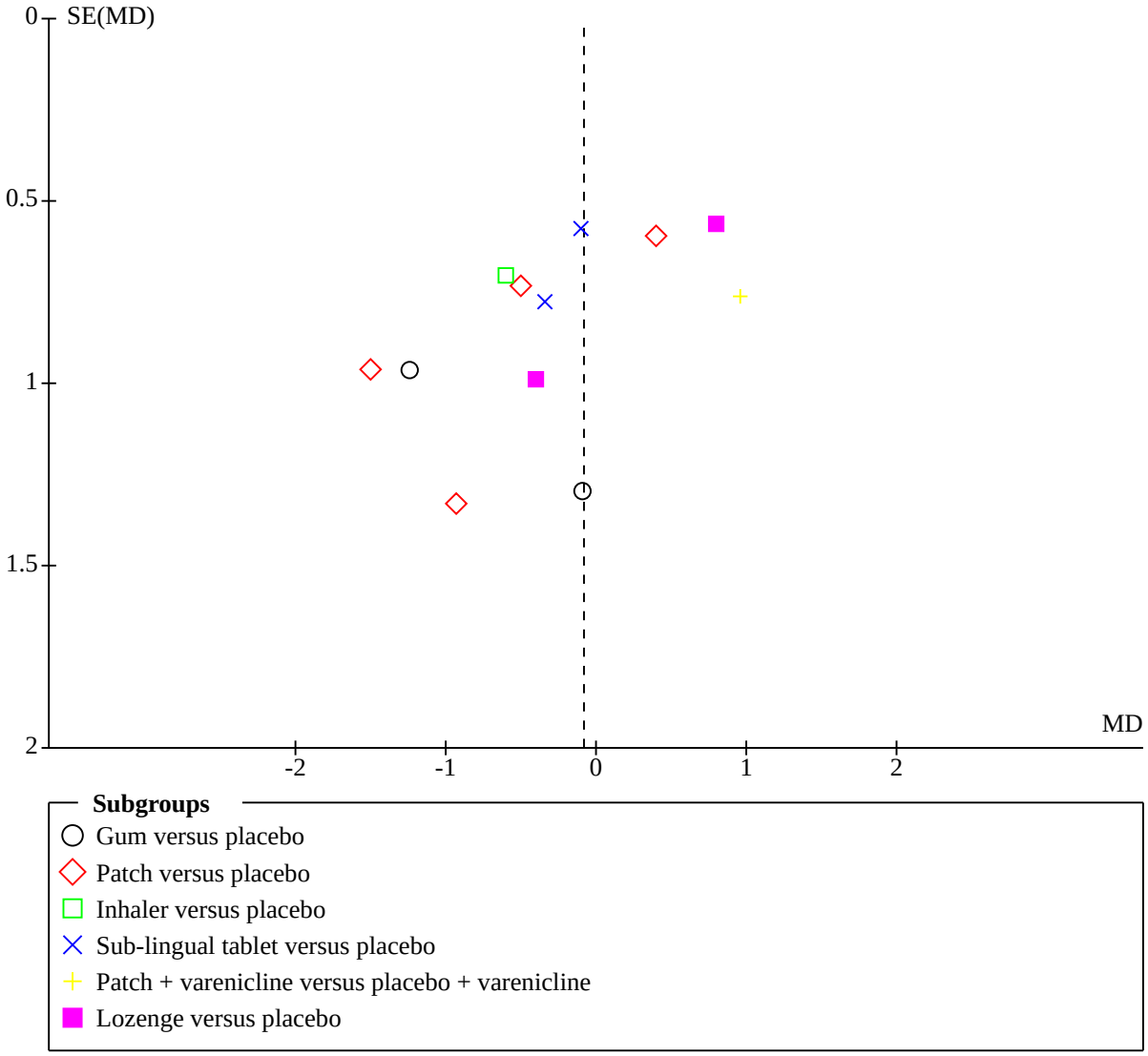
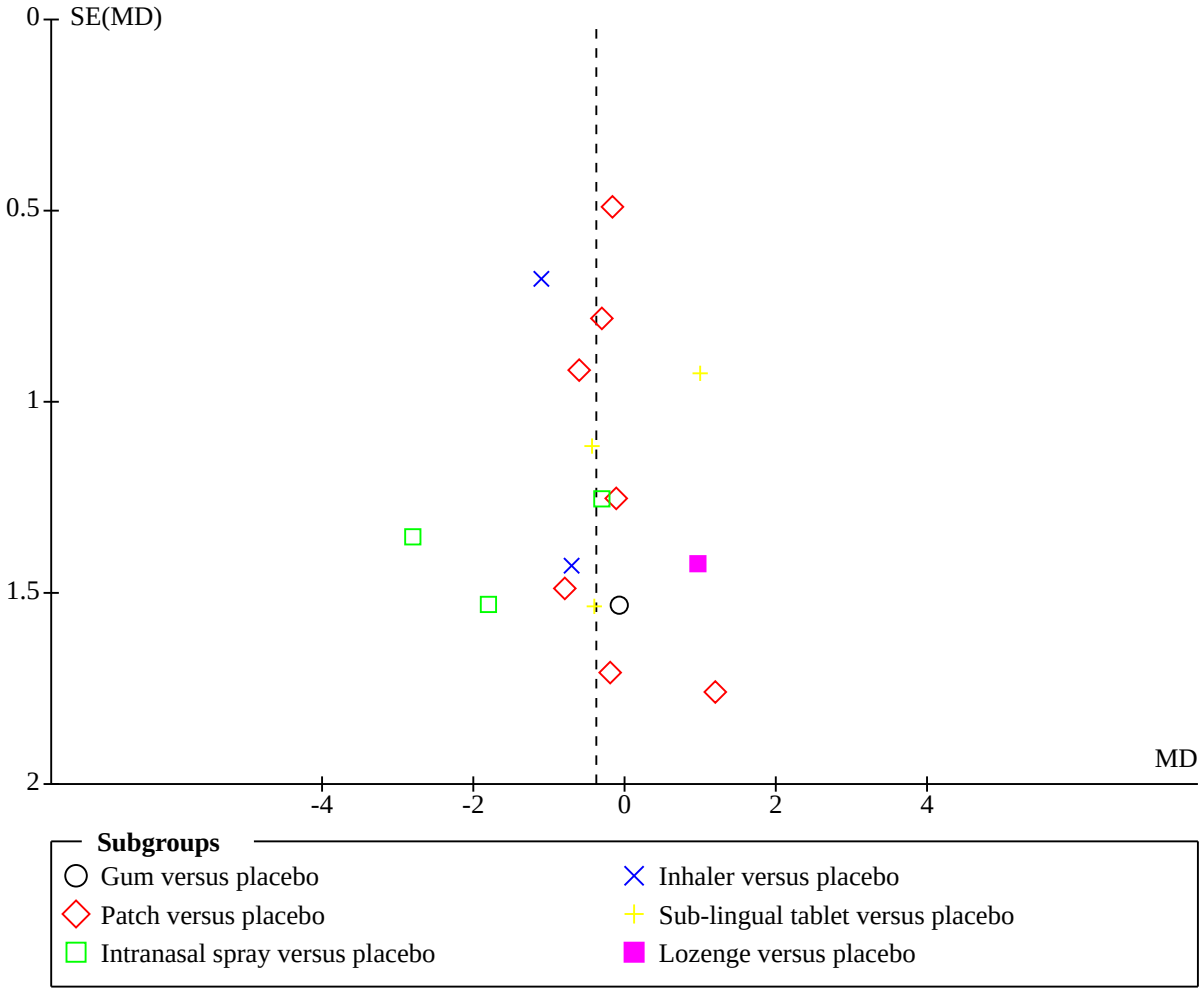


Figure 7. Funnel plot of comparison: 8 All types of NRT versus placebo for smoking cessation, outcome: 8.3 Mean weight change (kg) at 12 months.



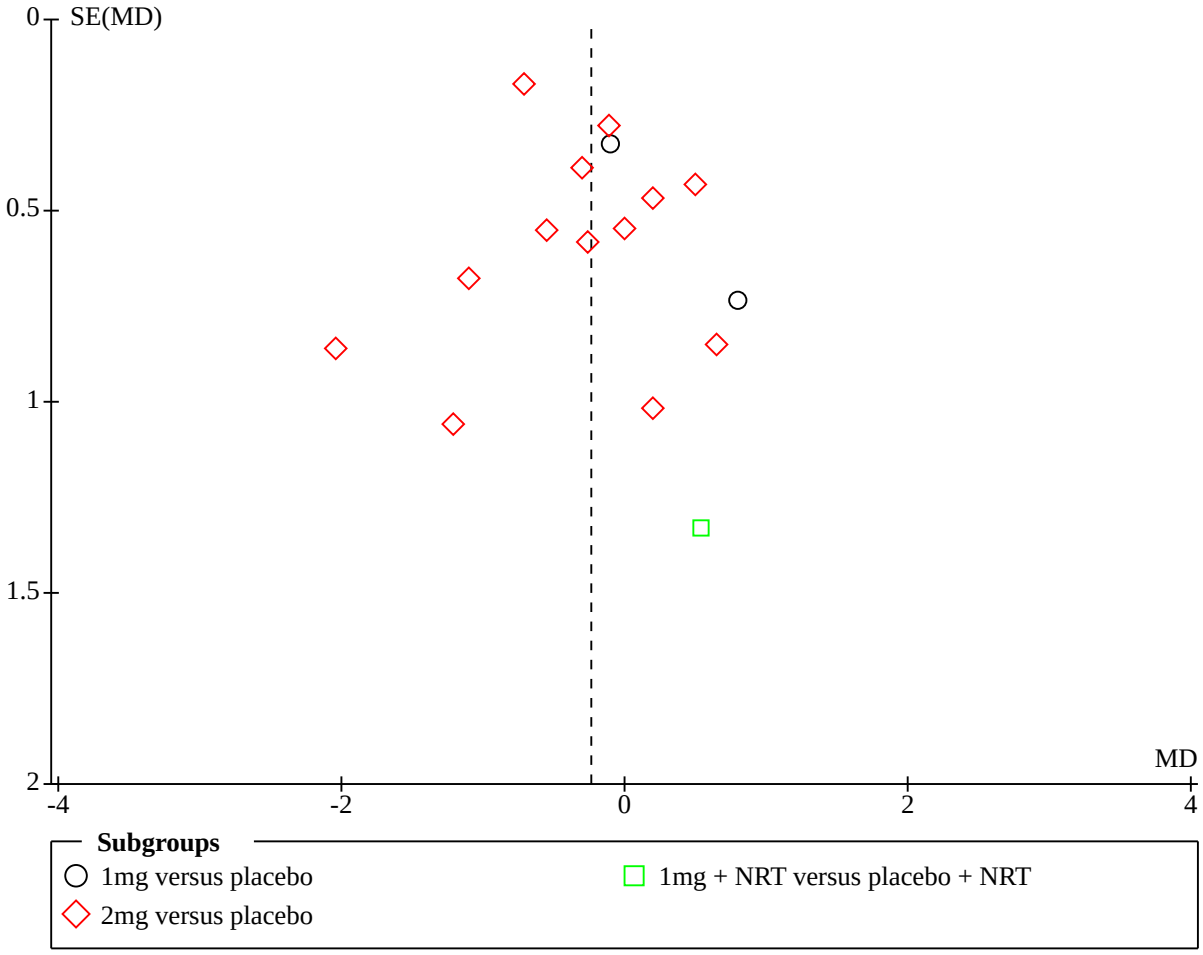
There was no evidence from direct comparisons (Analysis 9.1; Analysis 9.2; Analysis 9.3) or from subgroup analyses that results differed by type of NRT (I^2 < 10% for all tests of subgroup differences), with the exception of one study. In 2 Pack 2008 (high risk of bias, 54 participants), weight gain was less in lozenge compared to gum groups, with CIs excluding no difference at end of treatment: MD −2.45 kg, 95% CI −4.43 to −0.47; Analysis 9.1.

Pooled data from two studies (both at high risk of bias) comparing longer courses of NRT with 15 mg or 25 mg patches to shorter courses resulted in a point estimate favouring longer courses at 12 months, but CIs incorporated no difference: MD −0.24 kg, 95% CI −0.97 to 0.48; I^2 = 0%; 1 study, 404 participants; Analysis 9.4. Point estimates for pooled data of studies comparing higher versus lower doses of NRT were close to no difference, with CIs including no difference at both time points with data available: end of treatment: MD 0.22 kg, 95% CI −0.04 to 0.48; I^2 = 0%; 4 studies, 1038 participants; not sensitive to removal of four studies at high risk of bias; Analysis 9.5; 12 months: MD 0.27 kg, 95% CI −0.41 to 0.96; I^2 = 0%; 3 studies, 554 participants; not sensitive to removal of two studies at high risk of bias; Analysis 9.6.

Effect of varenicline on post-cessation weight gain

At end of treatment and six months, pooled data on the effect of varenicline on post-cessation weight gain had point estimates close to no difference and CIs incorporating no difference. At end of treatment, the MD was −0.23 kg, 95% CI −0.53 to 0.06; I^2 = 32%; 14 studies, 2566 participants; a funnel plot did not show asymmetry (Figure 8), and results were not sensitive to removal of two studies at high risk of bias (Analysis 10.1). At six months, the MD was −0.09 kg, 95% CI −1.09 to 0.90; I^2 = 19%; 3 studies, 384 participants; unclear risk, 1 low risk; Analysis 10.2. At 12 months, the point estimate favoured the intervention but CIs were wide and incorporated no difference: MD 1.05 kg, 95% CI −0.58 to 2.69; I^2 = 0%; 3 studies, 237 participants; at unclear risk of bias; Analysis 10.3.

Figure 8. Funnel plot of comparison: 10 Varenicline versus placebo for smoking cessation, outcome: 10.1 Mean weight change (kg) at end of treatment.



Three studies (two at low risk of bias, one at unclear risk) compared treatment with bupropion to varenicline and provided usable data. Participants taking varenicline gained more weight at the end of treatment. although CIs narrowly included no difference: MD 0.53 kg, 95% CI 0.00 to 1.05; I^2 = 29%; 3 studies, 598 participants; Analysis 11.1. One further study (2 Rose 2014) did not provide data in a form we could analyse.

There was no evidence that weight gain differed in the one trial of varenicline versus NRT (2 Aubin 2008, high risk of bias, Analysis 12.1).

Effect of e-cigarettes on post-cessation weight gain

Two studies of e-cigarettes (one as an adjunct to NRT, the other compared to varenicline) both had very wide CIs at all time points, encompassing clinically significant weight loss and weight gain (Analysis 13.1; Analysis 14.1; Analysis 14.2; Analysis 15.1; Analysis 15.2; Analysis 16.1).

DISCUSSION

Summary of main results

Since the previous version of this review, published in 2012, we have found 21 additional, completed trials fitting criteria for Part 1 (interventions targeting post-cessation weight gain on weight change and smoking cessation), so there are now 37 trials of interventions specifically designed to limit post-cessation weight gain. Although a range of pharmacological interventions were tested, none showed evidence that weight gain was prevented in the longer term (beyond six months), but most trials followed up participants only in the short term, primarily at end of treatment, and newer medications have since come on the market. Although some behavioural interventions suggested benefit, certainty in the evidence was limited across all comparisons. There was low- to very low-certainty evidence that personalized weight-management support, which included weight-management education with both feedback on personal goals and a personal energy prescription, reduced weight gain at end of treatment, at six, and 12 months (Summary of findings 1). There was low- to very low-certainty evidence that detailed weight-management education without personalized assessment, planning and feedback did not reduce

weight gain and may have reduced smoking cessation rates (Summary of findings 1). There was very low-certainty evidence that acceptance-based interventions for weight concern had no impact on weight, and low-certainty evidence that these interventions increased cessation rates (Summary of findings 2).

We identified 27 new, completed trials during the update that fitted the criteria for Part 2 (interventions designed to aid smoking cessation that plausibly affect post-cessation weight gain) of this review, bringing the total to 83 trials included in this part. In total, we examined evidence for six different interventions used to support smoking cessation that might incidentally reduce weight gain on cessation. There was low-certainty evidence that exercise interventions did not impact weight at end of treatment but that they reduced weight gain at 12 months by approximately 2 kg (Summary of findings 3). There was also moderate-certainty evidence that nicotine replacement therapy reduced weight at 12 months relative to control, although here the reduction was very modest (approximately 0.4 kg) (Summary of findings 4). There was low-certainty evidence that varenicline made little difference to weight at any time point (Summary of findings 5). Studies of fluoxetine showed low-certainty evidence of benefit at end of treatment and very low-certainty evidence of benefit at six months; no studies provided data at 12 months (Summary of findings 6). Bupropion appeared to limit weight gain at end of treatment, but there was no evidence of this at six or 12 months. There was insufficient evidence to draw any conclusions about the potential role of electronic cigarettes in limiting post-cessation weight gain.

Overall completeness and applicability of evidence

As described below, the major limitation to the evidence base was imprecision, meaning there are many places in which the evidence is too uncertain to assess whether interventions have worthwhile benefits on weight gain or pose a risk to attaining abstinence from smoking. Studies in Part 2 are probably broadly applicable to the general population of people motivated to quit smoking; these studies were of cessation that measured weight as a secondary outcome. Studies in Part 1, however, may not be as generalizable, with many selecting study populations based on weight concern. In addition, some of the pharmacotherapies tested in Part 1 are no longer widely available due to safety and tolerability concerns, and newer weight-loss medications have yet to be tested in the context of smoking cessation.

Certainty of the evidence

Part 1

We rated all outcomes in Part 1 to be of low to very low certainty, primarily due to imprecision (small numbers of studies and participants, resulting in wide CIs) and risk of bias (Summary of findings 1; Summary of findings 2). Although sensitivity analyses removing studies at high risk of bias did not affect results, in many cases all of the studies contributing to a given outcome were judged to be at high or unclear risk of bias. A further limitation to Part 1 studies is that most enrolled people who were weight-concerned in some way; such participants may have been more likely to default from the control programme than when allocated the active intervention that they presumably wanted, especially in studies such as 1 Danielsson 1999 and 1 Spring 2004, where this included free meals. The open-label design is unavoidable in this field, but it is important to note that it could bias the smoking abstinence results in favour of the intervention and decrease the difference in weight at follow-up.

Part 2

At end of treatment and six months, there was low- and very low-certainty evidence of benefit from fluoxetine, due to issues with serious imprecision (end of treatment) and very serious imprecision (six months) (Summary of findings 6). There were no data on fluoxetine at 12 months. Certainty of the evidence in the longer-term impact of nicotine replacement therapy on weight change was downgraded to moderate, due to issues with imprecision (Summary of findings 3). Further studies may increase certainty in these estimates. Evidence on exercise showed low-certainty evidence of no benefit at end of treatment, but benefit at 12 months (Summary of findings 4). In most trials of interventions in weight management, the difference between intervention and control is most marked at end of treatment and declines over follow-up. In this context, it is puzzling that there was no evidence of effectiveness of exercise on weight at end of programme, but there was at 12-month follow-up. This might either represent a chance finding or reflect the fact that the programme encouraged people to go on exercising after it had finished. Further evidence is required before we can be confident that physical activity programmes provide an effective intervention.

Evidence of no difference in weight at end of treatment with varenicline was high certainty, meaning we think further studies are unlikely to meaningfully change the estimate of no clinically significant difference. Longer-term outcomes (six and 12 months) were low certainty for varenicline, due to imprecision and to the fact that all studies contributing data at these time points were judged to be at unclear risk of bias (Summary of findings 5).

Potential biases in the review process

Several aspects of our methodological approach warrant consideration.

Firstly, in Part 2, we used existing Cochrane Reviews of interventions for smoking cessation to identify relevant studies. In effect, this means that to be included in Part 2, studies must have measured cessation at six months or longer, as this was an inclusion criterion of the parent review. This means that some studies reporting weight data at earlier than six months may have been missed. For example, we encountered studies of fluoxetine in Part 1 and Part 2 of the review. The study of fluoxetine in Part 1 was excluded from the parent Cochrane Review because it did not incorporate at least a six-month follow-up. It was included in the Part 1 search because the aim was to reduce weight gain. This means that it is possible that we did not include some other studies of fluoxetine that were not specifically aimed at reducing weight gain and did not incorporate a six- or 12-month follow-up. There is, however, no reason to imagine that excluding them would create a bias. Moreover, it is long-term weight gain that is relevant to health and all such studies would have been included. Second, in this and the 2012 update, but not in the original version of our review, we include 2 Tonstad 2006 in our main analysis of the effect of varenicline on weight gain. In this trial, participants had taken 12 weeks of varenicline before the abstinent participants were randomized to a further 12 weeks or placebo. Thus this study examines weight gain in months three to six of a quit attempt, not from months zero to three as in the other studies. Weight gain is less

rapid in months three to six (O'Hara 1998), meaning any effect of varenicline in preventing weight gain is likely to be lower, slightly biasing the effect downwards.

Thirdly, we split the behavioural interventions for weight control in Part 1 of the review into two categories: those that provided weight-management education only, and those that provided personalized weight-management support. This split was chosen based on meta-analysis evidence that healthy eating and physical activity interventions combining self-monitoring with at least one other technique derived from control theory, (such as specific goal setting, feedback on progress or review of goals set) are significantly more effective than those that do not (Michie 2009).

Finally, as noted in the Methods, the data here relate to weight gain in abstinent smokers only. It is practically difficult to follow up non-abstinent smokers as they have no motive to attend smoking cessation clinics and thus authors do not usually provide data on continuing smokers. However, most people gain weight on cessation and most people make repeated attempts to quit. It is possible that this leads to incremental weight gain and it would be useful if data could be collected on this.

Agreements and disagreements with other studies or reviews

English smoking cessation guidelines from the National Institute for Health and Care Excellence (NICE) make no specific recommendations about preventing post-cessation weight gain. However, the public-facing NHS website suggests exercise, varenicline, nicotine replacement, bupropion and dieting as options (NHS 2021). Similarly, US guidance recommends either bupropion, NRT, or exercise as interventions. A common perception is that concurrent behavioural treatment for smoking and weight undermines smoking cessation, and the advice is to establish smoking cessation before tackling weight (McEwen 2006). Some of the reason for this is the evidence from laboratory studies which show increased urges to smoke during periods of food restriction (Cheskin 2005; Leeman 2010).

Our review produced mixed evidence of this, with some data at 12 months suggesting that perhaps it undermines abstinence. However, data earlier in the quit attempt show no evidence of this and are rather more precise. Given that the putative mechanism relates to the similarity of hunger pangs and smoking urges, it is perhaps most likely that the somewhat lower abstinence in those who had weight-management interventions could be chance findings. However, other interpretations are possible, and only more data will clarify the issue.

AUTHORS' CONCLUSIONS

Implications for practice

- There is no moderate- or high-quality data that any intervention tested reduces weight gain in the long term.
- There is low-certainty evidence that weight-management education may reduce abstinence and is not effective at controlling weight .
- There is low- to very low-certainty evidence that personalized weight-management support programmes, incorporating both feedback on personal goals and a personal energy prescription, may reduce weight gain. There is mixed and low-certainty evidence of their effects on abstinence.
- Very low calorie diets may increase abstinence and prevent weight gain in the short term at least, but these conclusions are based on a single trial only, and another small trial found no one adhered to the intervention.
- There was low- to very low-certainty evidence that interventions designed to allay concerns about weight gain did not meaningfully affect weight gain but low certainty that they increase abstinence.
- There was low-certainty evidence that exercise interventions for smoking cessation did not affect weight by the end of treatment, so the 12-month reduction in weight is unexplained.
- Nicotine replacement therapy, bupropion, fluoxetine and varenicline all slightly reduced weight gain in the short term, but the size of benefit, if any, at 12 months was very uncertain, and evidence suggests was modest at best.

Implications for research

- As none of the existing pharmacotherapies tested to limit weight gain appear promising, testing newer agents now licensed for weight control to prevent weight gain may be helpful. Studies could also explore combining behavioural support and pharmacotherapy.
- Fluoxetine for smoking cessation was associated with reduced weight gain at end of treatment and six months, but evidence was very uncertain. Further studies are needed, particularly following up participants at six months and beyond.
- Behavioural weight management programmes are the mainstay of treatment for weight management and further trials to assess the impact of programmes tailored to people's concerns about weight gain would clarify the evidence on whether they limit long-term weight gain and their impact on abstinence from smoking.
- Further studies of interventions to allay people's concerns about weight gain are required to clarify its effect on smoking cessation.
- Further studies of exercise interventions are needed. The finding that an intervention aimed at increasing exercise levels had no effect initially but somehow affected weight one year later seems counterintuitive, as adherence to exercise regimens usually declines rather than increases with time.
- Future trials of interventions for limiting post-cessation weight gain should report mean weight change, standard deviation for the weight change and the number contributing to the mean in biochemically-confirmed continuous or prolonged abstinent participants only rather than in those abstinent for only one week. Weight change in those who continue to smoke should be reported separately.
- Trials of current and future pharmacotherapies for smoking cessation should measure weight change, reporting mean weight change, standard deviation of the change and numbers contributing to the mean, separating abstinent from smoking participants as described above.
- Future studies could also report results separately in those with overweight or obesity at baseline, or focus on recruiting from this population.
- Data are needed on whether using e-cigarettes to quit smoking affects post-cessation weight change.

ACKNOWLEDGEMENTS

We thank the Cochrane Tobacco Addiction Review Group for their support and advice. Specifically the content of the table of included studies in part two of this review is mainly populated by data extracted by the authors of the parent reviews (Lindsay Stead, Kate Cahill, Michael Ussher) with statistical advice given by Rafael Perera. We also thank Cynthia Pomerleau and colleagues, and Michael Ussher, for reading and commenting on earlier drafts of this protocol. We would also like to thank the many authors of the primary studies that responded to our requests for data.

For previous versions of the review, we thank the following authors for their contributions: Mujahed Shraim (MS) wrote and submitted the review protocol, and extracted data for Part 1 studies. Jennie Inglis (JS) extracted data for Part 2 studies. Both contributed to the first version of the review only, published in 2009. MS and Amanda Parsons (AP) carried out searches for the first part of the review and AP, Deborah Lycett (DL), MS and JI independently identified relevant studies and extracted data. AP drafted the review. DL, Paul Aveyard and Peter Hajek gave conceptual and editorial support.

For this update, we acknowledge the help of Min Gao in screening a paper published in Chinese and James Schulte for statistical support. We would also like to gratefully acknowledge and thank the following study authors who responded to our requests and provided additional data: Professor Amanda Baker and Associate Professor Terry J. Lewin, Assistant Professor Erika Litvin Bloom, Professor Bonnie Spring and Dr Harold Javitz, Professors Fridtjof Thomas and Karen Chandler Johnson, Dr Eli Heggen, Professor Andrea King, Professor Mark J. Eisenberg, Professor Kevin M. Gray, Dr Ashley Vena, Dr Nikos Ioakeimidis, and Associate Professor Natalie Walker. We thank Henri-Jean Aubin, Université Paris-Saclay, Inserm, CESP, AP-HP. Villejuif, France and Serena Tonstad, Oslo University Hospital, Norway, for providing peer review. We thank Charles Vicary for providing consumer review.

The National Institute for Health Research (NIHR) Oxford Biomedical Research Centre (BRC) Diet and Obesity provided funding to support this update. The views expressed are those of the review author(s) and not necessarily those of the NIHR or the Department of Health and Social Care.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

1 Baker 2018

Study characteristics	
Methods	Country: Australia Recruitment: "…referral sources included health services (148, 63%), media campaigns (59, 25%) and research programmes or registers (28, 12%).") Setting: Research will be conducted in three sites: Centre for Brain and Mental Health Research, University of Newcastle, New South Wales (NSW); School of Public Health, University of NSW, Sydney, NSW; and the Monash Alfred Psychiatry Research Centre (MAPrc), Monash University and The Alfred, Melbourne, Victoria, Australia Study start date: 4 August 2009. Study end date: 30 April 2014
Participants	Total N: 235 English-speaking smokers with psychotic disorders, smoking at least 15 cpd, aged at least 18 years N per arm: Healthy lifestyles condition = 122; Telephone condition = 113 41.5% female, av age 41.7, av baseline BMI: 30.6, av cpd: 28.6
Interventions	• Telephone condition: 16 telephone couselling sessions (approx. 10 min) weekly for 8 weeks, fortnightly for 3 sessions, followed by monthly calls for 6 months 2 out of the 16 sessions were delivered face-to-face. Session content designed to control for administration of NRT, number of and interval between counselling sessions and monitoring of nicotine withdrawal, medication side effects, distress, smoking, diet and physical activity • Healthy lifestyles: 16 face-to-face 1-hour motivational interviewing MI and CBT counselling sessions delivered by psychologists over 9 months. A further 7 weekly sessions were then offered (8 weekly sessions including session 1), after which participants received 3 fortnightly sessions and 6 monthly sessions. Session content: incorporated motivational techniques to increase readiness to change tobacco use, physical inactivity and poor dietary behaviours; cognitive behaviour strategies to build skills to make these changes; contingency reinforcement to support and encourage initiation and maintenance of change; NRT use and tapering; and relapse prevention All participants received a 90-minute face-to-face intervention session on feedback about smoking and other CVD risk factors; a case formulation was developed with the participant about CVD status and unhealthy behaviours, using a combination of MI and CBT, after which they received up to 24 weeks' supply of NRT, delivered at weeks 1, 4 and 8, and thereafter by arrangement
Outcomes	• Self-reported PPA (at 7 days) confirmed by an expired CO reading of # 10 ppm (unless the participant indicated they had smoked cannabis in the past week), measured at 12 months and longest follow-up (36 months) • Mean (SD) weight change (kg) in abstainers at 12 months and longest follow-up (36 months)

1 Baker 2018 *(Continued)*

Study funding	This work was supported by the Australian National Health and Medical Research Council (NHMRC project grant numbers 569210 and 1009351) and the Commonwealth Department of Health and Ageing
Author declarations	The author(s) declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article
Notes	Nicotine replacement therapy (NRT) was provided free of charge by GlaxoSmith Kline Participants were reimbursed AUD 20 for their travel, time and participation on each assessment occasion Additional information provided by authors upon request This study is new to the 2021 update

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "A permuted block randomisation approach was used so that the distribution of these characteristics across conditions was maintained." Quote: “Following the baseline assessment, study therapists were issued with a sealed randomisation envelope (by an independent person) displaying a participant identification code.” (Baker 2015)
Allocation concealment (selection bias)	Low risk	Quote: "Following completion of the baseline assessment for each participant, the clinicians will be issued with a sealed randomisation envelope (by an independent person) which displays the participant identification code. The envelope will be opened by the participant at the conclusion of the initial session."
Blinding of outcome assessment (detection bias) Smoking	Low risk	Confirmed PPA (at 7 days) was analyzed as self-reported abstinence from smoking, confirmed by an expired CO reading of # 10 ppm (unless the participant indicated they had smoked cannabis in the past week)
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: “…Using Seca 770 digital scales.”
Incomplete outcome data (attrition bias) All outcomes	Low risk	12 month = Intervention = 70/122 = 57%; Control: 69/113 = 61% 18 month = Intervention = 70/122 = 57%; Control: 62/113 = 55% 30 month = Intervention = 65/122 = 53%; Control: 64/113 = 56%

1 Bloom 2020

Study characteristics

Methods	Country: USA Recruitment: “Female participants (N = 69) were recruited from the local community via paper and electronic advertisements.” Setting: Not specified

1 Bloom 2020 *(Continued)*

	Study start date: May 2015; Study end date: December 2018
Participants	Total N: 69 female smokers, aged at least 18 years, smoked ≥ 5 cpd for at least the past year, motivated to quit, and concerned about post-cessation weight gain; N per arm: Health Education (HE) = 36; DT-W = 33 100% female, av age 49.7, av baseline BMI: 31.4, av cpd: 16.2, av FTND: 4.8
Interventions	• Health Education: 9 weeks of didactic education sessions about general health topics as they relate to the effects of smoking. 1 x 60-minute individual session was followed by 8 weekly 90-minute group sessions (TQD at session 4) and a 20-minute individual telephone session between sessions 4 and 5 (I.e. quit week) • DT-W: Acceptance and commitment therapy/Distress tolerance treatment for weight concern over 9 weeks. Session 1: Psychoeducation; Session 1 - 3: Distress tolerance skills; Session 3 - 5: Values Oriented Living Skills (including willingness, appetite awareness, mindful eating skills, committed action). 1 x 60-minute individual session followed by 8 weekly 90-minute group sessions (TQD at session 4) and a 20-minute individual telephone session between sessions 4 and 5 (I.e. quit week) All participants received standard CBT for smoking cessation in sessions 3 - 8, and 8 weeks of nicotine patches beginning on the target quit date (session 4)
Outcomes	• 7-day PPA at 6 months (Validation: CO ≤ 6 ppm) • 2. Mean (SD) weight change (kg) in abstainers at EOT and at 6 mont
Study funding	"This work was supported by the National Institute on Drug Abuse (grant number K23DA035288 to ELB)."
Author declarations	"RAB has equity ownership in Health Behavior Solutions, Inc., which is developing products for tobacco cessation that are not related to this study. The terms of this arrangement have been reviewed and approved by the University of Texas at Austin in accordance with its policy on objectivity in research. The other authors have no interests to declare."
Notes	"Participants were compensated up to $225 for completing all assessments." Baseline weight data was taken at the initial baseline appointment, which was usually 1 - 2 months before the quit date Additional information provided by authors upon request This study is new to the 2021 update

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Randomization occurred by cohort due to the group delivery of treatments. Cohort treatment assignments were randomly chosen without replacement from a fixed pool of 10 options (5 DT-W, 5 HE)."
Allocation concealment (selection bias)	Unclear risk	Not specified
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "Our primary smoking cessation outcome was 7-day point prevalence abstinence from combustible cigarette smoking, verified by expired breath carbon monoxide (CO) testing (≤6 ppm)43 with a Bedfont Micro Smokerlyzer. Self-reported smoking behavior was assessed at all individual assessments and group treatment sessions using a Timeline Followback procedure.44 Participants whose point prevalence abstinence data were missing were assumed to be smoking."

1 Bloom 2020 *(Continued)*

Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: "Participants were weighed on a calibrated medical scale at baseline, post-treatment, and 1-, 3-, and 6-month follow-ups."
Incomplete outcome data (attrition bias) All outcomes	Low risk	1 Month follow-up: DT-W = 26/33*100 = 78.8%; HE = 28/36*100 = 77.8% 3 Month follow-up: DT-W = 26/33*100 = 78.8%; HE = 25/36*100 = 69.4% 6 Month follow-up: DT-W = 26/33*100 = 78.8%; HE = 28/36*100 = 77.8%

1 Bush 2012

Study characteristics	
Methods	Country: USA Recruitment: Callers to the Oklahoma Tobacco Helpline (OKHL) Study start date: March 2008; Study end date: November 2008
Participants	Total n: 2000 (1000 per trial arm) 77% female, av age 41.3, av baseline BMI 30.4
Interventions	• Intervention (WCP): Standard quitline service (The Oklahoma Tobacco Helpline) with integrated brief telephone-based weight concerns programme. Weight-concern counselling embedded in each call, plus 3 additional calls with a weight coach (counselling to help people quit smoking and accept weight concerns). Encouraged use of self-monitoring (not specified of what) and goal setting on snacks and activity • Control (STD): Standard quitline service (The Oklahoma Tobacco Helpline) – mailed quit guide, 5 counselling calls, and 2 (insured) or 8 (uninsured) free weeks of NRT. Counselling intensity not described
Outcomes	• 90-day self-reported PPA at 6 months • Mean (SD) weight change (kg) at 6 months in abstainers (30-day PPA)
Study funding	"This study was funded by TSET, the Oklahoma State Department of Health, the Oklahoma Tobacco Research Center and Alere Wellbeing. NCT01162577"
Author declarations	Not specified
Notes	This study is new to the 2021 update.

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "Automated randomisation procedure" . Comment: Not described other than it was preprogrammed
Allocation concealment (selection bias)	Unclear risk	Not specified
Blinding of outcome assessment (detection bias) Smoking	High risk	Quote: "Blinded outcome assessments were collected 6 months following randomization" However, smoking abstinence was self-reported and participants were likely aware of their allocation: "The primary outcome was 30-day point prevalent abstinence. (…). Tobacco use was assessed with the question: "When was the last time you smoked a cigarette, even a puff?". Abstinence

1 Bush 2012 *(Continued)*

		rates were calculated in two ways: (1) including only participants who completed the survey in the denominator ("respondent analysis") and (2) using the intent-to-treat methodology (ITT) in which those not completing the survey were assumed to be tobacco users."
Blinding of outcome assessment (detection bias) Weight	High risk	Quote:"Blinded outcome assessments were collected 6 months following randomization" However, weight was self-reported and participants were likely aware of their allocation: Weight: "Secondary outcomes were … and change in weight amongst those who were abstinent at 6 months. (…). Change in weight was calculated in two ways: (1) by reporting participants perceived change in weight (…) and (2) calculated change in weight based on the difference between self reported weight in pounds at baseline and 6 months"
Incomplete outcome data (attrition bias) All outcomes	Low risk	6-month completion intervention group: 470/1000 (47%); 6-month completion control group: 532/1000 (53.2%); Overall number of participants lost to follow-up is 1002/2000*100 = 50.1%; Less than 20% difference in dropout between groups.

1 Bush 2018

Study characteristics	
Methods	Country: USA Recruitment: "Study participants were recruited from three state quitlines (Indiana, Maryland and North Carolina) and 10 commercial (employer-provided) quitlines…" Setting: Alere Wellbeing provided tobacco Quitline services and a phone/web-based weight management programme (Weight Talk) Study start date: August 2013; Study end date: March 2016 (trial record) or "…ended in 2017"
Participants	Total N: 2540 English-speaking smokers, aged ≥ 18, BMI ≥ 18.5, smoking a minimum of 10 cpd and motivated to quit smoking within the next 30 days N per arm: Control = 844; Simultaneous = 845; Sequential = 851 66% female, av age: 43.2, av baseline BMI: "76% overweight/obese", av baseline weight: 86.2 kg, cpd: 19.8
Interventions	• Control: standard Quitline + 5 healthy living control telephone calls • Simultaneously integrated: standard Quitline smoking and weight management programme (Weight Talk) adapted to focus on the prevention of weight gain. Programme includes individualized telephone counselling, written materials and an interactive online programme • Sequential: standard Quitline followed by weight management programme (Weight Talk) All participants received 5 standard Quitline smoking-cessation counselling calls and were offered free NRT in the form of patch, gum and/or lozenge (0 - 8 weeks), depending on the contract and appropriateness based on the participant's medical condition. All participants also received access to 1 or more web-based programmes and were mailed a Quit Kit containing a printed guide
Outcomes	• Self-reported 30-day multiply imputed point prevalence abstinence at 6 and 12 months • Self-reported mean (SD) weight change (kg) in abstainers at 6 and 12 months
Study funding	"This work was supported solely by funding from the National Institutes of Drug Addiction NIDA (RO1DA31147). The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health."

1 Bush 2018 *(Continued)*

Author declarations	"The authors at Alere Wellbeing declare that they are employed by Alere Wellbeing (a subsidiary of Optum) which provides tobacco cessation and weight management services to states and commercial clients. They have no other competing interests. JL declares that she has no competing interests. HJ declares that he has no competing interests. BS declares that she has no competing interests. MT declares that she has no competing interests."
Notes	Additional information provided by authors upon request This study is new to the 2021 update

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Eligible and consenting participants are immediately randomized by a computer generated program into one of three study arms…"
Allocation concealment (selection bias)	Unclear risk	Quote: "Candidates who met eligibility requirements and expressed interest in a research study about smoking and weight were transferred to a quit coach who described the study and obtained verbal informed consent to participate, while remaining blind to treatment assignment. Requiring written consent would have placed additional burden on participants, delayed treatment initiation and reduced the generalizability of study findings. We received approval from the Western Institutional Review Board to collect verbal consent." Comment: Unclear if the same coach also allocated participants to groups
Blinding of outcome assessment (detection bias) Smoking	High risk	Self-reported
Blinding of outcome assessment (detection bias) Weight	High risk	Self-reported weight
Incomplete outcome data (attrition bias) All outcomes	High risk	6 months follow-up: Control: 410/844 = 48.6%; Simultaneous: 359/845 = 42.5%; Sequential: 395/851 = 46.4%

1 Cooper 2005 (also Part 2)

Study characteristics

Methods	Country: USA Recruitment: community volunteers Study start date: not specified; Study end date: not specified
Participants	439 weight-concerned female smokers (≥ 10 cpd) av.age 38, av.cpd 23, av baseline weight 64 - 66 kg
Interventions	• Phenylpropanolamine (PPA) gum 8.33 mg 16 pieces/d 8 wks, weaning last 3 wks • Nicotine gum (2 mg), 10 - 12 pieces/day recommended, for 8 wks, weaning last 3 wks.

1 Cooper 2005 (also Part 2) *(Continued)*

	• Placebo gum All participants received 13 x 1hr weekly CBT group sessions focused on smoking and weight. Participants cut down weeks 1 - 4 by 25% and quit week 5
Outcomes	• PPA at 6 and 12 months (validation: CO < 10 ppm) • Mean (SD) weight change (kg) in abstainers at EOT, 6 and 12 months
Study funding	Not specified
Author declarations	Not specified
Notes	PPA defined as validated self-report of no smoking at the time of the assessment Although these treatments are specifically tested for their effect on smoking and on weight gain the NRT arm is included in the second part of the review as it is included in the parent Cochrane Review

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Methods not described
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: “All group facilitators and participants were blind to treatment conditions” + placebo controlled"
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "Point prevalence abstinence at each assessment was defined by self-report of no smoking at the time of the assessment and a carbon monoxide (CO) level of < 10 ppm at the current assessment. (...) In instances in which smoking status could not be verified because of absence from that intervention session, the participants were categorized as smoking, indicating intention to treat analyses.“
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: "Participants’ weights were taken, in clothing but without shoes or heavy garments, at all sessions. Weight was recorded as absolute weight in pounds with a Detecto Electronics Scale accurate to + 2 oz.“
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: “Of the 89 participants who quit smoking, 27 cases were rejected because of missing data, resulting in a sample of 62 women“

1 Copeland 2006

Study characteristics

Methods	Country: USA Recruitment: Community volunteers Study start date: not specified; Study end date: not specified

1 Copeland 2006 *(Continued)*

Participants	79 women smokers motivated to quit and weight-concerned (at least 10 cpd for 1 yr); av cpd 20.1, av FTND: 4, av BMI: 24
Interventions	All participants completed a smoking cessation programme (6 sessions over 2 wks) involving smoking cessation and relapse prevention advice, and given an 8-wk supply of NRT Randomized to follow-up in either individual or group format: 6 follow-up relapse prevention sessions including psychological, dietary, and exercise components over 38 wks
Outcomes	1. Continuous abstinence at 6 months (validation: CO ≤ 10 ppm) 2. Mean (SD) weight change (kg) in continuous abstainers at 6 months
Study funding	"This study was funded by grants from the National Institutes on Health and Bristol-Myers Squibb Better Health for Women Program."
Author declarations	Not specified
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Low risk	Quote: "Statisticians generated the random assignment sequence for follow up condition"
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "Biological verification: carbon monoxide (CO) measurement. We used a BreathCo monitor (Vitalograph, Inc.) and used a cutoff level of b10 ppm to confirm nonsmoking status.“
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: "Anthropometric data. Baseline body weight and height were converted into body mass index (BMI; kg/m2). Participants were also weighed at each of the six follow-up sessions.“
Incomplete outcome data (attrition bias) All outcomes	Low risk	24-week completion tailored follow-up group: 33/40 (82.5%); 24-week completion follow-up group: 25/36 (69.44%)

1 Copeland 2015

Study characteristics

Methods	Country: USA Recruitment: from the Baton Rouge, LA community by way of newspaper and billboard advertisements Setting: Pennington Biomedical Research Center Study start date: 2003; Study end date: 2005 (end of recruitment)
Participants	Total N: 92 weight-concerned post-menopausal female smokers, smoking at least 10 cpd for ≥ 1 year, BMI ≥ 18, CO ≥10 ppm N per arm: Group = 54; Individual = 38

1 Copeland 2015 *(Continued)*

	100% female, av age 52.3, av baseline BMI 27.4, av cpd 20.3, av FTND 6.4
Interventions	• Minimally-tailored group format: In-person group sessions covering information on smoking and weight with a multidisciplinary team (clinical psychologists, registered dietitians, exercise physiologists) • Highly-tailored, multidisciplinary individual format: Tailored participants were counselled about specific eating patterns and food preferences from their Block Food Questionnaire and diet records. Weight management information was based on each woman's food intake data, and dietary counselling focused on vulnerability to overeating and changes in participants' food choices and caloric intake from pre- to post-cessation. The exercise physiologists also counselled participants on energy expenditure requirements based on their specific anthropometric information from baseline All participants received 6 sessions of in-person group CBT for smoking cessation and 8 wks of the nicotine transdermal patch
Outcomes	Mean weight change (kg) in abstainers at EOT (reported narratively)
Study funding	"This research was supported by the National Institute on Aging (NIA), grant AG18239. NIA had no other role other than financial support."
Author declarations	"None of the authors have any conflict(s) of interest that may inappropriately impact or influence the research and interpretation of the findings."
Notes	"Participants were provided a $40 monetary incentive for completion of the pretreatment assessment phase, and $40 for completion of the research requirements throughout the follow-up period." No control group. 2 formats of a post-cessation weight gain prevention follow-up intervention (comparing minimally-tailored vs highly-tailored only). Only successfully abstinent smokers randomized to follow-up weight prevention Longest follow-up at 16 weeks; no 6-month follow-up This study is new to the 2021 update.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Statisticians generated the random assignment sequence for follow-up condition" Comment: No further information given.
Allocation concealment (selection bias)	Unclear risk	Not specified
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "BreathCo monitors were used (Vitalograph Inc.) to determine expired CO level (ppm). A cut-off of b10 ppm was used to confirm non-smoking status"
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: "Participants were also weighed at each of the 6 follow-up sessions."
Incomplete outcome data (attrition bias) All outcomes	High risk	16 week post-treatment follow-up: Group: 28/54*100 = 51.9% Individual: 15/38*100 = 39.5%

1 Danielsson 1999

Study characteristics	
Methods	Country: Sweden Recruitment: community volunteers Study start date: not specified; Study end date: not specified
Participants	287 weight-concerned female smokers, age range 30 - 60, ≥ 10 cpd, av cpd 20, av BMI 26
Interventions	• Nicotine gum (2 or 4 mg) with moderate behavioural advice: 11 sessions (45 mins) in 16 weeks in combination with behavioural weight control programme and intermittent very low energy diet as total food replacement ((Nutrilett 1.76 MJ/day), 2-week periods (weeks 1 and 2, 7 and 8, 13 and 14). All participants were recommended a standardized balanced diet of about 6.7 MJ/day • Control group received the same as intervention but without the very low energy diet
Outcomes	• Prolonged abstinence 12 months (validated: CO < 10 ppm) • Mean (SD) weight change (kg) in prolonged abstainers at EOT and 12 months
Study funding	Not specified
Author declarations	Not specified
Notes	Prolonged abstinence defined as "completely and continuously stopped from week 2 onwards"

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Open consecutive randomization (in the order their questionnaires were received at the clinic)
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: “Successful smoking cessation was defined as self reported complete abstinence from week 2 to week 16, verified by a carbon monoxide concentration less than 10 ppm (New Smokerlyzer, Bedfont). Two missed visits between weeks 2 and 16 were allowed. If the week 2 visit was missing, the woman had to be abstinent from week 1 until endpoint. Women had to attend the week 16 visit to be eligible for the success criteria”
Blinding of outcome assessment (detection bias) Weight	Low risk	Not specified how weight was assessed, so that self-report cannot be ruled out. Participants were not blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: “After 12 months, 35 and 51 women had dropped out from the diet and control groups respectively”

1 Hall 1992

Study characteristics	
Methods	Country: USA

1 Hall 1992 *(Continued)*

	Recruitment: community volunteers Study start date: not specified; Study end date: not specified
Participants	180 smokers, 27% female, av age 39 - 42, av cpd 26 - 32, av baseline weight 67 - 73 kg
Interventions	Participants received treatment in groups. All groups completed 2-wk behavioural smoking cessation programme. Participants were randomly assigned to follow-up group for weight management: • Innovative intervention - individualized multifactorial intervention including exercise, daily weight monitoring, individual energy prescription to result in 2lb/wk weight loss if weight was gained (based on weight, age, gender, activity level), healthy eating advice and behavioural advice to manage triggers for uncontrolled eating (4 wks) • Standard treatment condition - given an information pack on good nutrition and exercise, not targeted for SC-induced weight gain at end of 2-wk SC programme • Non-specific control - non-individualized weight gain prevention intervention without the specific elements of the innovative intervention arm. Non-specific elements (1) a rationale based on gaining insight into eating styles, (2) a structured programme based on insight-oriented discussion, (3) nutritional and exercise information, (4) group support, and (5) therapeutic attention. The sessions centered around both self-tests adapted from the Smokers' Self-test Kit8 and informational presentations by the nutritionists and the exercise consultant
Outcomes	• PPA at 6 and 12 months (validation: CO < 10.5 at 6,12 and 26 wks, cotinine blood levels below 50 ng/ml at 12 months) • Mean (SD) weight change (kg) in abstainers at EOT and 12 months
Study funding	"This study was funded in part by grants DA02356 and DA00065, both from the National Institute on Drug Abuse, and by a Research Career Scientist Award from the Department of Veterans Affairs to Dr.Hall"
Author declarations	Not specified
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method not described
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: “At each assessment, subjects were coded as abstinent if they reported no cigarettes smoked during the prior week and had a carbon monoxide lvel below 10.5 ppm at the assessment. At week 52, subjects were coded as abstinent only if their blood cotinine levels were also less than 50ng/mL.”
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: “Body weights were taken at all assessments on the same balance beam scale”
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: “165 of the 180 subjects who began treatment completed the smoking cessation portion. Dropouts did not differ from the rest of the sample in age, gender, ethnicity, level of education, socioeconomic status, number of previous quit attempts, cessation induced weight gain, pretreatment carbon monoxide, cigarette intake, or body weight”

1 Hankey 2009

Study characteristics	
Methods	Country: Scotland Recruitment: Smokers at a smoking cessation clinic Study start date: January 2008; Study end date: August 2008
Participants	138 smokers, 75.4% female, av baseline weight 76.2 (18.1) kg, av age 50 yrs, av BMI 28.2 (5.5), av cpd, 25.2 (12.6)
Interventions	• 24-wk dietary stage of change-based interventions focusing advice and self-monitoring of physical activity (participants given pedometers), portion control, fruit and vegetable intake and fat intake for 4 wks post-quit. Also included bolster session at wks 8, 12, 16 and 20 post-quit. No individual targets set • No dietary intervention Both conditions were embedded within a smoking cessation clinic that followed the Maudsley model
Outcomes	• Abstinence at 6 months (validation: CO monitoring). Definition of abstinence or CO level not given • Mean (SD) weight change (kg) in abstainers at 6 months
Study funding	"The research was commissioned by the Food Standards Agency UK (FSA). The FSA had no role in the study design, collection, analysis or interpretation of data, or the decision to submit the paper for publication."
Author declarations	"The authors declare there are no conflicts of interest."
Notes	

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	computer-generated
Allocation concealment (selection bias)	Low risk	Randomization carried out via an interactive voice response system
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "Measurements of exhaled carbon monoxide (CO) were made at weeks 6 and 24 to assess smoking status (piCO + breath CO monitors, Bedfont Scientific Ltd)“
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: “Intervention and control participants had measurements of body weight, waist circumference and food choice/ intake made at baseline, weeks 6 and 24.“
Incomplete outcome data (attrition bias) All outcomes	Low risk	24-wk completion intervention group: 40/68 (59%); 24-wk completion placebo group: 43/70 (61%)

1 Heggen 2016

Study characteristics	
Methods	Country: Norway Recruitment: referrals to the Section for Preventive Cardiology at Oslo University Hospital and by newspaper advertisement Study start date: 4 January 2010; Study end date: 24 September 2013
Participants	Total N: 122 smokers with overweight or obesity (BMI 25 - 40) N per arm: Low-carb diet = 64; Moderately fat-reduced diet = 58 72.8% females, av age 50.1, av baseline BMI 30.5, av baseline weight 89.9 kg, av cpd 17.7, av FTND score 4.6
Interventions	• Low-carb diet with individual meal plans for 500 kcal/day reduction in energy based on individual calorie requirement (20 E% from carbohydrates, 25 E% from proteins, remaining 55 E% from fats) • Moderately fat-reducing diet with individual meal plans for 500 kcal/day reduction in energy based on individual calorie requirement (at most 30 E% from fats, at most 20 E% from proteins, remaining E% from carbohydrates) Energy requirements were based on measured RMR and level of physical activity In both conditions, participants received a 12-wk course of varenicline, motivational smoking cessation counselling (10 mins), and dietary advice and support by trained dieticians. Participants were given written dietary information, substitution lists, tips for planning meals and recipes to achieve targets for macronutrients, and for the first 7 days after the TQD were provided a daily lunch and snack specific to assigned diet
Outcomes	• Continuous abstinence at 6 months (validation: CO < 10 ppm) • Mean (SD) weight change (kg) at 12 weeks post-TQD (study wk 15; EOT) in abstainers (7-day point prevalence CO < 10 ppm) and at 6 months
Study funding	"This work was supported by Local Departmental Resources, including provision of varenicline. Tine AB, Kavli Holding AS, Lantmännen Cerealia AS, and the Norwegian Meat and Poultry Council sponsored study meals. These companies had no role in the conduct, writing or interpretation of the trial"
Author declarations	"EH and ST have received honorarium for lectures and consultancy for Pfizer, the manufacturer of varenicline, as well as from other pharmaceutical companies producing smoking cessation aids"
Notes	Additional information provided by authors upon request This study is new to the 2021 update

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	A block randomization procedure was used. The randomization list was computer-generated by a statistician using blocks of 8 with a 1:1 allocation ratio
Allocation concealment (selection bias)	Low risk	The study co-ordinator identified predetermined randomization assignment by consecutively opening sealed envelopes. Allocation of grouping through predetermined randomization contained in sealed envelopes
Blinding of outcome assessment (detection bias)	Low risk	Quote: “To be counted as a quitter a report of “not a single puff of a cigarette” and carbon monoxide < 10 ppm was required“

1 Heggen 2016 *(Continued)*
Smoking

Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: "Height was measured by a standard wall-scale. Body weight in kg was measured at every visit on a digital and calibrated scale (Seca 770) in light indoor clothing without shoes"
Incomplete outcome data (attrition bias) All outcomes	Low risk	24-wk post-TQD visit attendance low carbohydrate group: 48/64 (75%); 24-week post-TQD visit attendance moderately fat-reduced group: 47/58 (81%)

1 Johnson 2017

Study characteristics	
Methods	Country: USA Recruitment: "Traditional recruitment approaches included media (i.e., television, radio), print (i.e., mass mailings of postcards to age appropriate persons identified by driver's license registries, newspaper ads, rack cards, flyers), and community (i.e., events at college campuses, health fairs, word of mouth). Technology recruitment approaches included website (TARGIT study), internet (i.e., Google ads, Craig's List), social media (TARGIT Facebook page) and email list serves (i.e., academic, healthcare, corporate, professional)." Setting: Department of Preventive Medicine, clinical trials research cente in Memphis, TN Study start date: August 2009; Study end date: October 2014
Participants	Total N: 330 smokers, aged 18 - 35 years, at risk for weight gain (e.g. plan to quit smoking), BMI ≥ 22 decreased ≥ 20, self-report smoking ≥ 10 cpd N per arm: Comparison = 164; Intervention = 166 48.8% females, av age 29.7, av baseline BMI 29.2, av baseline weight 85.7, av cpd 17.9
Interventions	• Smoking cessation alone programme: a smoking cessation handbook, 6 weeks of nicotine patches, access to the interactive smoking cessation study website and 1 in-person session and 5 intervention calls via a proactive quit line over a 6-month period. Text, email messages App also used for the delivery of the smoking cessation programme for 24 months • Smoking cessation programme + behavioural weight loss or weight gain prevention intervention (depending on baseline weight category) programme, delivered via interactive technology (live online webinars). Intervention adapted from the Look AHEAD behavioural weight loss programme and tailored to young adult smokers. Frequency of scheduled contacts varied from weekly to monthly, and then to quarterly throughout the 24-month study period
Outcomes	• 7-day PPA at 6, 12 and 24 months (longest follow-up) (validation: CO ≤ 10 ppm) • Mean (SD) weight change (kg) in abstainers at 6, 12 and 24 months (longest follow-up)
Study funding	"This work was supported by grant funding from the National Heart, Lung, and Blood Institute, National Institutes of Health."
Author declarations	"The authors declared no conflict of interest."
Notes	Additional information provided by authors upon request This study is new to the 2021 update.
Risk of bias	

1 Johnson 2017 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Participants were individually randomized in blocks of four (allocation ratio 1:1)" No further information given
Allocation concealment (selection bias)	Unclear risk	Quote: "Neither the participants nor the study staff who provided the intervention were blinded to group assignment. However, study personnel who were collecting and assessing outcome data, such as weight, and the investigators, including the principal investigator, were blinded to treatment assignment (did not know a participant's group assignment status). All participants were asked not to reveal their study group assignment to blinded clinic personnel."
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "…smoking cessation, was assessed as biochemically verified 7-day point prevalence abstinence. Abstinence was only concluded if a participant self-reported not smoking and exhaled carbon monoxide was</=10 ppm. Salivary cotinine was collected only at the 24-month visit, and values >/=100 ng/mL were considered to be consistent with smoking."
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: "Weight was measured in the study clinic by using a standardized protocol created by the EARLY consortium on a calibrated scale."
Incomplete outcome data (attrition bias) All outcomes	Low risk	At 24 months: Comparison arm: 118/164 = 72%; Internvention arm: 107/166 = 64%

1 King 2012

Study characteristics	
Methods	Country: USA Recruitment: Internet, print, and radio advertisements Study start date: June 2006; Study end date: April 2010
Participants	Total N: 333 N per arm: Naltrexone = 168; Placebo = 165 53.3% females, av age 41.9, av baseline BMI 27.0, av cpd 19.7, av FTND 5.1
Interventions	• 12 wks post-TQD Oral Naltrexone (50 mg) with 1 wk pre-TQD dose titration • Placebo oral naltrexone All participants received nicotine patch during the first 4 wks post-TQD and attended 6 x 45-minute weekly individual CBT smoking cessation counselling (pre- and post-TQD)
Outcomes	• 7-day PPA at 6 and 12 months • Mean (SD) weight change (kg) in abstainers at EOT (12 weeks post-TQD), 6 and 12 months (CO confirmed prolonged abstinence, allowing a 1-week grace period) • Adverse events reported per study arm at 1 week and 4 weeks post-TQD
Study funding	"This study was supported by grants from the National Institute of Drug Abuse/the National Institutes of Health (R01-DA016834), CTSA Grant Number ULI-RR024999 from the National Center for Advancing Translational Sciences (its contents are solely the responsibility of the authors and do not necessarily

1 King 2012 *(Continued)*

	represent official views of the National Center for Advancing Translational Sciences or the National Institutes of Health), and the National Cancer Institute (P30-CA14599)."
Author declarations	"Andrea King is part of the advisory board and is a consultant for Lundbeck and the US Food and Drug Administration. Dingcai Cao is part of the advisory board and is a consultant for the US Food and Drug Administration. Stephanie S. O'Malley received research support from NABI Biopharmaceuticals, Pfizer Inc; is part of the advisory board and is a consultant for the American College of Neuropsychopharmacogy workgroup, the Alcohol Clinical Trial Initiative Group; is sponsored by Alkermes, Abbott Laboratories, Eli Lilly & Company, GlaxoSmithKline, Johnson & Johnson Pharmaceuticals, Lundbeck, Schering Plough, Pfizer, and Gilead Pharmaceuticals. Dr O'Malley was an inventor on a patent on naltrexone for smoking cessation held by Yale University, which has been abandoned. Henry R. Kranzler is part of the advisory board and is a consultant for the American College of Neuropsychopharmacogy Alcohol Clinical Trial Initiative Group, Lundbeck, GlaxoSmithKline, Alkermes, Gilead, Roche, Pfizer, and Lilly. Dr Kranzler received grants from Merck. Harriet deWit received grants from Unilever. Dr deWit is part of the advisory board and is a consultant for the US Food and Drug Administration. Alicia K. Matthews is part of the advisory board and is a consultant for US Food and Drug Administration. Xiaochen Cai and Ryan J. Stachoviak report no financial conflicts of interest."
Notes	Additional information provided by authors upon request This study is new to the 2021 update.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Randomly assigned by computer"
Allocation concealment (selection bias)	Unclear risk	Not specified
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: “Participants and study staff were blinded to treatment assignment.”
Blinding of outcome assessment (detection bias) Smoking	Low risk	Biochemical validation in clinic. Participants who reported smoking abstinence during the past 7 days at telephone follow-up were asked to attend an in-person visit to provide biochemical validation
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: "At each study visit, participants underwent weight measurement … Weight was measured by the research assistant with a digital medical scale (Tanita, Tokyo, Japan), and weight values were not shared with the participant to reduce undue stress”
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: “The 12-week completion rates did not differ by group (placebo, 115/154 participants [75%]; naltrexone, 123/161 participants [76%]).“ Quote: “Follow-up rates were high and did not differ by group or sex (telephone follow-up at 26 weeks, 99% completion in both groups; at 52 weeks, 98% placebo vs 96% naltrexone; in-person follow-up of abstainers at 26 weeks, 95% vs 89%, respectively; at 52 weeks, 92% vs 88%).“

1 Klesges 1990

Study characteristics

1 Klesges 1990 *(Continued)*

Methods	Country: USA Recruitment: Community volunteers Study start date: not specified; Study end date: not specified
Participants	57 adult female smokers who had previously experienced post-cessation weight gain, av age 27, av 22.4 cpd, mean CO 49.8 ppm
Interventions	• PPA gum 8.33 mg 9/day 2w • Placebo gum All participants received a "brief but intensive stop-smoking intervention" and were offered a cash reward and opportunity to win prizes if they were successful at quitting for 2 weeks
Outcomes	• Mean (SD) weight change (kg) in continuous abstinent smokers at EOT (validation: CO ≤ 7 ppm) • Adverse events at EOT (reported narratively)
Study funding	"Supported by a grant awarded to Dr. Klesges and Dr. Meyers (HL-3932) by the National Heart, Lung, and Blood Institute (Be- thesda, Md.). Support was also received from a Centers of Excellence grant awarded to the Department of Psychology, Memphis State University, by the state of Tennessee. Schering-Plough Corporation provided both the phenylpropanolamine and the placebo gum for this investigation."
Author declarations	Not specified
Notes	Intervention only 2 wks long. No 6-month follow-up

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method not described
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: “double-blind” “Neither the investigators, not the subjects knew which gum contained the active gradient” + placebo gum in same shape, colour and size"
Blinding of outcome assessment (detection bias) Smoking	Low risk	Biochemical verification of smoking status (by mean of carbon monoxide testing) + a random carbon monoxide abstinence verification check
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: “height and weight measurements were taken privately” Comment: Unclear if self-report or objective assessment of weight, but participants were blinded to treatment condition
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not specified

1 Klesges 1995

Study characteristics	
Methods	Country: USA Recruitment: community volunteers Study start date: not specified; Study end date: not specified
Participants	107 male and female smokers, age between 18 and 60, cpd 20+, CO > 15 ppm
Interventions	• PPA gum 8.33 mg up to 10 pieces/day 4 wks • 2. Placebo gum, same regimen All participants received 1 x 30-min session on smoking cessation and relapse prevention
Outcomes	• Mean (SD) weight change (kg) in continuous abstainers at EOT (validation: CO < 8 ppm)
Study funding	"This study was supported by two grants (HL45057, HL46352) awarded by the National Heart, Lung, and Blood Institute. We also appreciate the financial support from Schering-Plough Corporation and for providing the placebo and PPA gum. Support was also received from a Centers of Excellence grant awarded to the Department of Psychology, Memphis State University, by the state of Tennessee."
Author declarations	Not specified
Notes	No 6 months follow-up data

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Independent randomization
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: “Assignment of product was independently randomized and group membership (e.g., gum A versus Gum B) was not revealed to the researchers until all data were coded. Identification of those using active gum was not revealed until statistical analyses were complete.”
Blinding of outcome assessment (detection bias) Smoking	Low risk	CO < 8 ppm
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: “Height and weight in subjects were assessed using a sensitive scale (Detecto Electronic) (..). The unit was zero calibrated by project staff prior to each use.”
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: “five male subjects were dropped from the study due to elevated blood pressure … four of these subjects had been assigned to the PPA group and the remaining subject to the placebo group”

1 Levine 2010 (also Part 2)

Study characteristics

1 Levine 2010 (also Part 2) *(Continued)*

Methods	Country: USA Recruitment: community volunteers Study start date: September 2000; Study end date: December 2009
Participants	349 weight-concerned women smokers, aged between 18 and 65 yrs, motivated to quit smoking, av 20.7 cpd, av age 42
Interventions	• Weight concerns CBT + bupropion 300 mg/day • Weight concerns CBT + placebo • Standard cessation counselling + bupropion 300 mg/day • Standard cessation counselling + placebo CBT was delivered weekly for buproprion/placebo was taken for 26 wks
Outcomes	• Prolonged abstinence at 6 and 12 months (validation: CO ≤ 8 ppm, or urinary cotinine < 15µg/L) • Mean (SD) weight change (kg) at EOT, 6 and 12 months
Study funding	"This research was supported by grant R01 DA 04174 from the National Institute on Drug Abuse (Dr Marcus). Dr Levine's effort was partially supported by grant K01DA15396 from the National Institute on Drug Abuse (Dr Levine). GlaxoSmithKline provided bupropion hydrochloride SR, 150 mg, and matching placebo oral administration free of charge." Role of the Sponsor: "The funding agencies had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; and preparation, review, or approval of the manuscript."
Author declarations	"Dr Marcus has served as a consultant to GlaxoSmithKline and Sanofi-Aventis. Dr Perkins has served as a consultant for GlaxoSmithKline."
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Block randomization sequence
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double-blind, placebo-controlled. No further information given (Judgement only relevant for part 2 analyses)
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "… expired-air carbon monoxide (CO) was collected using a Vitalograph BreathCO monitor (Vitalograph Inc, Lenexa, Kansas). Salivary samples were collected immediately after each assessment visit (1, 3, 6, and 12 months). A CO reading of 8 ppm or less and cotinine level of less than 15 µg/L (to convert to nanomoles per liter, multiply by 5.675) were used to confirm non- smoking"
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: "Women were weighed in street clothing without shoes prior to each session. Height was measured at baseline using a mounted stadiometer, and body mass index was calculated as weight in kilograms divided by height in meters squared"

1 Levine 2010 (also Part 2) *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	24 week completion CONCERNS + B group: 64/106 (60%); 24 week completion CONCERNS + P group: 40/87 (45%); 24 week completion STANDARD + B group: 47/89 (52%); 24 week completion STANDARD + P group: 32/67 (47%); 48 week completion CONCERNS + B group: 57/106 (53%); 48 week completion CONCERNS + P group: 37/87 (42%); 48 week completion STANDARD + B group: 46/89 (51%); 48 week completion STANDARD + P group: 28/67 (41%); RoB assessment based on 6m attrition rate 6M overall retention rate = 52.4%; 12-month rate = 48.1%; diff between groups is < 20%

1 Lycett 2010

Study characteristics	
Methods	Country: England Recruitment: Listed on GP database; Invited by letter from their GP; Interested participants telephoned trial office Setting: GP practices Study start date: 22 December 2008; Study end date: Not specified
Participants	Total N: 16 smokers with an exhaled CO ≥ 10 ppm for at least 15 mins after last smoking, aged > 18 years, with a BMI ≥ 25*, N per arm: Step by step control (SBS) = 6; Individual dietary and activity planning (IDAP) = 6; Very low calorie diet (VLCD) = 4 81% female, av age 46, av baseline BMI 29.5, av baseline weight 79.9, av cpd 23, av FTND: 5
Interventions	• SBS Control: Participants receive IDAP 8 weeks after quitting (wk 8 to wk 12; stage 2) • IDAP: Energy prescription based on individual basal metabolic rate (BMR) aiming for daily reduction of 600 kcal. (week -1 to week +4 stage 1; week 8 - week 12; stage 2) • VLCD: 429 - 559 kcal/day liquid formula beginning 1 week before quitting and continuing for 4 weeks (stage 1). After this, they received IDAP (week 5 to week 12; stage 2) All participants received identical behavioural support and NRT patches (25 mg (8 wks),15 mg (2 wks),10 mg (2 wks))
Outcomes	1. Mean (SD) weight change (kg) in abstainers at EOT (narrative discussion)
Study funding	"This trial is funded by UK Centre for Tobacco Control Studies (UKCTCS), a UKCRC Public Health Research: Centre of Excellence. Funding from British Heart Foundation, Cancer Research UK, Economic and Social Research Council, Medical Research Council, and the Department of Health, under the auspices of the UK Clinical Research Collaboration, is gratefully acknowledged."

1 Lycett 2010 *(Continued)*

Author declarations	"Deborah Lycett declares no competing interests. Paul Aveyard has done consultancy work on smoking cessation for Pfizer, McNeil, and Xenova Biotechnology. Peter Hajek received research funding and provided consultancies to manufacturers of stop-smoking medications."
Notes	* Inclusion criteria were widened once study began. “We no longer excluded those who were unsuitable for a VLCD and we opened the trial to all smokers, regardless of BMI, this meant we were effectively running two trials, side by side. DeMiST 1, which used the original exclusion criteria, and randomised participants into three arms and DeMiST 2 which independently randomised participants into either the SBS or the IDAP arm.” This study is new to the 2021 update

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Randomisation was computer generated by an independent statistician within the Primary Care Clinical Research and Trials Unit (PCCRTU) using random permuted blocks of length 6, stratified by practice. The numbers were entered into the trial database by an independent computer programmer within the trials unit. The database concealed randomisation until after participants were screened and entered into the trial."
Allocation concealment (selection bias)	Low risk	Quote: "At week -3 the nurses clicked on the randomisation tab in the database and this revealed the arm to which the participant was allocated. The database was set up so that the randomisation „tab“ would not work until all data from week -2 was complete. Therefore, it was impossible for anyone to see treatment allocation beforehand. This greatly minimised any risk of the trial randomisation being undermined"
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "Twenty-four hour point prevalence abstinence is measured by participants achieving 24 consecutive hours of abstinence as verified by exhaled CO < 10 ppm. Seven day point prevalence abstinence is defined as those not smoking over the last 7 days as verified by exhaled CO < 10 ppm. Participants achieving 1, 6 and 12 month abstinence as defined using the Russell Standard which states that no more than 5 cigarettes since have been smoked since week +2, this is verified by CO < 10 ppm at each consultation [34]. Participants who have not achieved abstinence but are still attempting to quit are termed ‘lapsed"
Blinding of outcome assessment (detection bias) Weight	Unclear risk	Quote: “These are measured as described below. The schedule of measurements is contained in table 2. 1. Weekly weight, waist to hip ratio, % body fat composition, blood pressure, and heart rate.”
Incomplete outcome data (attrition bias) All outcomes	High risk	High loss to follow-up, including 100% of participants in 1 arm. > 50% loss to follow-up End of treatment: SBS = 3/6 = 50% IDAP = 0/6 = 0% VLCD = 1/4 = 25%

1 Lycett 2020

Study characteristics	
Methods	Country: England Recruitment: NHS commissioned Stop Smoking Services were first recruited from Bristol and North Somerset Primary Care Trusts, then across the West Midlands and South-West England due to poor recruitment of clinics. “All individuals attending the Stop Smoking Services were invited to take part in the trial at their first visit when they set their quit date.” ”Participating services located within pharmacies, general practices and community centers will display an A3 poster advertising the trial.” Setting: National Health Service commissioned Stop Smoking Services; Commercial weight management programme (Slimming world) Study start date: October 2012; Study end date: 6 May 2013
Participants	Total N: 76 daiily smokers with expired CO > 10 ppm, aged ≥ 18 years and BMI ≥ 23 N per arm: Usual care = 39; Intervention = 37 65% female, av age 46.7, av baseline BMI 30.5, av FTND 5.8
Interventions	• Usual care: NHS stop smoking advisers provided standard smoking cessation support: withdrawal oriented behavioural support focusing on key behavioural change techniques with 6 weekly sessions begining 2 weeks before target quit date and a prescription of nicotine replacement or varenicline to relieve withdrawal symptoms • Usual care plus Slimming World for 12 weeks receiving support to lose weight or prevent weight gain
Outcomes	• Prolonged abstinence at EOT and 6 months (self-report of no more than 5 cigarettes since 2 weeks following quit day; validation: CO < 10 ppm) • Mean (SD) weight change (kg) in abstainers at EOT and 6 months. As EOT time point varied for each study arm, outcome data for EOT is reported narratively
Study funding	This work was supported by funding of the salary for DL, provided by a fellowship from the NIHR-SPCR during the active trial period. Additional funds to set up the trial and buy equipment were provided by the NIHR-SPCR and UKCTCS. The UKCTCS is one of five UK Public Health Research Centres of Excellence. We also gratefully acknowledge funding from the British Heart Foundation, Cancer Research UK, the Economic and Social Research Council, Medical Research Council and the Department of Health, under the auspices of the UK Clinical Research Collaboration. AL’s salary was paid by NIHR-SPCR during the trial period, and the salaries of AF, MM and PA were paid by their respective institutions. PA is an NIHR senior investigator and funded by NIHR Oxford Biomedical Research Centre and CLAHRC. All funding is gratefully acknowledged.
Author declarations	DL has received hospitability from manufacturers of smoking cessation products, Pfizer, Tadworth, UK. DL’s institution during the active phase of the trial has received smoking cessation products for use in a clinical trial from Johnson & Johnson, New Brunswick, New Jersey, USA. DL has received Slimming World membership vouchers for use in this trial. DL has received expenses and consultancy fees from the NHS and Universities for teaching about cessation-related weight gain. DL has received grant funding from UKCTCS and the NIHR-SPCR for research relating to cessation-related weight gain. PA is an NIHR senior investigator and is funded by NIHR Biomedical Research Centre and the CLAHRC, Oxford. AF is an NIHR Senior Investigator and receives funding from NIHR Oxford Biomedical Research Centre. AL has received hospitality from Weight Watchers. In the last 5 years, MM has received grant funding from Pfizer and varenicline, for research purposes.
Notes	This study is new to the 2021 update.
Risk of bias	

1 Lycett 2020 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Randomisation sequence was computer generated and concealed until allocation."
Allocation concealment (selection bias)	Low risk	Quote: "Stop smoking advisors were unaware of the randomisation sequence; they opened sealed, numbered, opaque envelopes in turn."
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "Abstinence is prolonged abstinence, defined according to the Russell Standard as self-report of no more than five cigarettes since 2 weeks following quit day and expired CO less than 10 ppm..."
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: "The primary outcome was objectively measured weight…"
Incomplete outcome data (attrition bias) All outcomes	High risk	At week 4: Usual care: 20/39*100 = 51.3%; Intervention: 20/37*100 = 54.1% At week 12: Usual care: 15/39*100 = 38.5%; Intervention: 15/37*100 = 40.5% At week 26: Usual care: 10/39*100 = 25.6%; Intervention: 12/37*100 = 32.4%

1 Lyu 2018

Study characteristics	
Methods	Country: China Recruitment: Inpatient unit at Xuhui Mental Health Center located in Shanghai Setting: Inpatient unit at Xuhui Mental Health Center Study start date: May 2016; Study end date: July 2018
Participants	Total N: 22 men with schizophrenia, on stable antipsychotic medication treatment for at least 1 month, aged 18 - 65, smoking ≥ 10 cpd for 1 year or longer, BMI > 28 or 27 in the presence of dslipidaemia or waist circumference over 90 cm, with a desire to lose weight and quit smoking. N per arm: Control: 11 (10 reported at baseline (1 was lost to follow-up and excluded from analysis)); Intervention: 11; 0% female, av age 55.3, av baseline BMI 26.9, av baseline weight 76.6, av cp week 74.8
Interventions	1. Placebo naltrexone and placebo bupropion for 24 weeks 2. Adjunctive naltrexone (25 mg/day) and bupropion (300 mg/day) combination treatment for 24 weeks
Outcomes	• Abstinence at 6 months (EOT) (CO level measured) • Mean (SD) weight change (kg) at EOT in abstainers (not possible as "none of participants had sucesfully stopped smoking") Adverse events reported per study arm at 6 months (EOT) in narrative discussion
Study funding	"Program of Shanghai Academic Research Leader (17XD1403300), Shanghai Key Laboratory of Psychotic Disorders (13DZ2260500), Shanghai Municipal Health and Family Planning Commission (2017ZZ02021)."
Author declarations	"The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest."

1 Lyu 2018 *(Continued)*

Notes	This study is new to the 2021 update.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Following screening and confirmation that inclusion and exclusion criteria were met, participants were randomized to receive the combination treatment or placebo." Comment: No further information
Allocation concealment (selection bias)	Unclear risk	Quote: "Following screening and confirmation that inclusion and exclusion criteria were met, participants were randomized to receive the combination treatment or placebo." Comment: No further information
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "The purpose of the present 24-week, randomized, double blind, placebo controlled pilot trial was to examine the feasibility, safety, and initial benefit of using naltrexone and bupropion combination in treating obesity and smoking cessation in patients with schizophrenia" Comment: No further information given
Blinding of outcome assessment (detection bias) Smoking	Low risk	Expired CO level measured at baseline and 24-weeks
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: "Medical and psychiatric histories were obtained, and physical exam was performed for each participant." "The following measures were completed at baseline and week 24: (1) height, weight and waist circumference…"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Among 28 patients who fit the inclusion and exclusion criteria, 22 of them were enrolled in the study. One patient in the placebo group dropped out of the study after week-12 because of loss of follow up after being discharged from the inpatient unit. Therefore 21 patients (11 in the treatment group, 10 in the control group) completed the 24-week trial and were included in the final analysis."
Other bias	Low risk	Quote: "In the treatment group, 5 patients were on clozapine, 7 on olanzapine, 8 on other antipsychotic agents (risperidone, amisulpride, quetiapine, and chlorpromazine); in the placebo group, 5 patients were on clozapine, 4 on olanzapine, 11 on other antipsychotic agents (risperidone, amisulpride, paliperidone, and chlorpromazine. There were no significant differences between the two groups in the numbers of patients on clozapine or olanzapine (p's > 0.05)."

1 NCT03528304 2016

Study characteristics

Methods	Country: USA Recruitment: Not specified Setting: Clinic Study start date: September 2010; Study end date: January 2015

1 NCT03528304 2016 *(Continued)*

Participants	Total N: 125 female daily smokers of reproductive age (18 - 44 years) with overweight or obesity, of American Indians and Alaska Native hertigate
Interventions	• Control arm • 16-week culturally-tailored contingency management intervention for smoking abstinence • 16-week culturally-tailored contingency management intervention for weight loss (ineligible study arm) • 16-week culturally-tailored contingency management (CM) intervention for smoking abstinence and weight loss All participants attended face-to-face clinic visits, the control arm attended these visits for assessment only
Outcomes	Data measured during the trial but not available for extraction at the time of this update. • Abstinence at EOT (validation: urine test) • Mean (SD) weight change (kg) in abstainers at EOT
Study funding	5U48DP001911-02 (U.S. NIH Grant/Contract); Sponsor: Washington State University (reported on clinical trial register).
Author declarations	NS (information extracted from a clinical trial registry only)
Notes	Information extracted from clinical trial record only This study is new to the 2021 update.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not specified
Allocation concealment (selection bias)	Unclear risk	Not specified
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: “In each intervention session the women participants will complete a urine test to determine if they have smoked a cigarette within the past 3-4 days…”
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: “In each intervention session the women participants will complete a urine test to determine if they have smoked a cigarette within the past 3-4 days, and will be weighed on a dedicated, standardized scale”
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not specified

1 Norregaard 1996

Study characteristics

Methods	Country: Denmark Recruitment: Community volunteers

1 Norregaard 1996 *(Continued)*

	Study start date: not specified; Study end date: not specified
Participants	225 smokers who wanted to quit without gaining weight, 65% female, av BMI 23 - 24, av age 38 - 39, av 20 cpd
Interventions	• 20 mg Ephedrine plus 200 mg caffeine combination 3/day 12 wks then decreased until 39 wks. TQD - first session. 8 visits were scheduled for the 52-week study period (at the beginning of the study and after weeks 1, 3, 6, 12, 26, 39, and 52) • Placebo All participants given advice on how to quit smoking and prevent weight gain (inc booklet about low-fat food)
Outcomes	• Prolonged abstinence at 6 and 12 months (validation: CO < 10 ppm) • Mean (SD) weight change (kg) in prolonged abstainers at EOT, 6 and 12 months • Frequency of side effects at wks 1, 3, 6, and 12 (narratively discussed)
Study funding	Not specified
Author declarations	Not specified
Notes	Prolonged abstinence defined as no smoking after wk 1 post-quit

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Minimization
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: “double blind, placebo controlled” but “Blinding was incomplete because 68% in the ephedrine plus caffeine-treated group and 63% in the placebo group correctly guessed their treatment at trial termination (p<0.001)”
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: “self-reported abstinence with validation by carbon monoxide in expired air and serum cotinine“
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: “subjects were weighed by means of the same scales at each visit without shoes and overcoats”
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Three subjects (two in the ephedrine plus caffeine-treated group) moved from the area or were lost to follow-up. Seven subjects (one in the ephedrine plus caffeine-treated group) were excluded because they started treatment with ephedrine plus caffeine or nicotine replacement (prescribed by their own doctor). Six subjects (all in the the ephedrine plus caffeine-treated group) were withdrawn because of side effects, and an additional six subjects (all in the the ephedrine plus caffeine-treated group) left the trial for other reasons“

1 O'Malley 2006

Study characteristics	
Methods	Country: USA Recruitment: Community volunteers Study start date: not specified; Study end date: not specified
Participants	400 smokers, 46% female, av BMI 27 - 28, av 26 - 29 cpd, av age 45 - 47
Interventions	• 1. Naltrexone 25 mg 6 wks • 2. Naltrexone 50 mg 6 wks • 3. Naltrexone 100 mg 6 wks • 4. Placebo All participants also given 6 wks supply of 21 mg patches and 6 sessions of behavioural support (1 x 45 mins, 5 x 15 mins)
Outcomes	• 7-day PPA at 6 and 12 months • Mean (SD) weight change (kg) in continuous abstainers at EOT • Number of adverse events by treatment group (narrative discussion)
Study funding	"This study was supported by grants P50-DA-13334 from the National Institute on Drug Abuse and grants P50AA15632, K02-AA00171, and R01- AA11197 from the National Institute on Alcohol Abuse and Alcohol Dependence, National Institutes of Health, Bethesda, Md; grant 039787 from the Robert Wood Johnson Foundation, Princeton, NJ; and by the Department of Veterans Affairs, Newington, Conn."
Author declarations	"Nicotine patches were donated by GlaxoSmithKline Inc. Naltrexone hydrochloride and matching placebo were purchased from Mallinckrodt Pharmaceuticals. Drs O'Malley, Krishnan-Sarin, and Meandzija are coinventors on a patent held by Yale University for smoking cessation treatments using naltrexone and related compounds. Dr O'Malley has received research support from Alkermes Inc (a manufacturer of an investigational injectable naltrexone), DuPont (a manufacturer of naltrexone), GlaxoSmithKline Inc, Forest Laboratories, Lipha Pharmaceuticals, Ortho-McNeil, Inc, Bristol-Myers Squibb, Pfizer Inc, Sanofi-Aventis, and Mallinckrodt Pharmaceuticals; served as a consultant to Alkermes Inc, Forest Laboratories, GlaxoSmithKline Inc, Ortho-McNeil, Inc, Pfizer Inc, and Johnson & Johnson; and received travel reimbursement from Alkermes Inc. Dr Krishnan-Sarin has received grant support from and served as a consultant to Pfizer Inc. In separate company- sponsored studies held at Yale University, Dr Meandzija and Ms Romano-Dahlgard received a portion of their salary from Alkermes Inc, Bristol-Myers Squibb, and Ortho-McNeil, Inc, and Dr McKee received a portion of her salary from Pfizer Inc."
Notes	Arms 1 - 3 combined for the main comparisons No 6-month follow-up data

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Block randomization, stratified by sex after the first 150 participants
Allocation concealment (selection bias)	Low risk	Random sequence was provided to the pharmacist, who assigned participants
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Random sequence was provided to the pharmacist, who assigned participants; others were blinded to treatment assignment." + Placebo controlled

1 O'Malley 2006 *(Continued)*

Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "self-reported abstinence... was verified by an exhaled CO of 10ppm or less"
Blinding of outcome assessment (detection bias) Weight	Low risk	Unclear if weight was assessed objectively or by means of self-report but participants were blinded to treatment allocation
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Treatment completion placebo group: 75/98 (76%); Treatment completion 25 mg naltrexone group: 75/94 (79%); Treatment completion 50 mg naltrexone group: 71/99 (71%); Treatment completion 100mg naltrexone group: 74/109 (67%) --> Attrition rates at follow-up not reported

1 Oncken 2014

Study characteristics	
Methods	Country: USA Recruitment: Advertising Study start date: 1 April 2006; Study end date: 1 December 2008
Participants	Total N: 57 N per arm: Placebo = 19; Topirimate = 19; Topirimate plus NRT = 19 60% female, av age 47.2, av baseline BMI 28.1, av cpd 21.4, av FTND 5.9
Interventions	• Topiramate (100 mg titrated up over 5 wks) 10 wks • Topiramate + nicotine patch 10 wks (21 mg/24h for 7 weeks then 14 mg for 3 days, then 7 mg for 4 days) • Placebo 10 wks TQD 2 wks after baseline visit. All groups received weekly behavioural counselling (10 mins) from a nurse from baseline, and *Clearing the Air: Quit smoking today* booklet
Outcomes	• Mean (SD) weight change (kg) at EOT (8 wks post-TQD; study week 10) in abstainers (CO ≤ 10 ppm confirmed prolonged abstinence during last 4 weeks of treatment) • Adverse events (narrative discussion) • Number of serious adverse events
Study funding	"This project was supported by funds from the Department of Medicine at the University of Connecticut Health Center and the General Clinical Research Center (M01RR006192). HRK's participation was funded by National Institute on Alcohol Abuse and Alcoholism (K24 AA13736)"
Author declarations	"CO currently is receiving study medication (nicotine inhaler and placebo) from Pfizer Pharmaceuticals for a National Institutes of Health–funded study of nicotine inhaler for smoking cessation during pregnancy. MS has served as an expert witness on behalf of Pfizer in lawsuits related to varenicline. HRK has served as a consultant or advisory board member for Alkermes, Lilly, Lundbeck, Pfizer, and Roche and as a member of the American Society of Clinical Psychopharmacology's Alcohol Clinical Trials Initiative, supported by AbbVie, Lilly, Lundbeck, and Pfizer"
Notes	This study is new to the 2021 update
Risk of bias	

1 Oncken 2014 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Urn randomization procedure to balanced on sex and FTND score. No description
Allocation concealment (selection bias)	Unclear risk	No description
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Participants and research personnel blinded to trial arms 1 and 3, but not 2. The group on NRT knew this, as did those who were not on NRT but the topiramate (hypothesized to impact on weight) was blinded
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "biochemically confirmed cigarette abstinence was assessed at Weeks 8–11 (…) no posttreatment abstinence rates were reported"
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: "We assessed vital signs, weight, adverse effects and tolerability of the medication, and exhaled CO levels at each weekly visit". Comment: Participants and assessors were blinded.
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "Thirty-eight subjects (66.7%) completed the 10-week study with the highest completion rate in the TOP/NIC group (16 of 19 or 84%). The rate of treatment completion in both the PLC and the TOP groups was 58% (i.e., 11 of 19 subjects in each group). The rate of completion did not differ significantly by group ($\chi 2(2) = 3.95$; $p = .14$). Reasons for dropout included: adverse events (one PLC, four TOP, and one TOP/NIC), lack of efficacy (two PLC), lost to follow-up (five PLC, three TOP, and one TOP/NIC), and other (one TOP and one TOP/NIC)." Comment: Difference in follow-up between groups is greater than 20%

1 Oncken 2019

Study characteristics	
Methods	Country: USA Recruitment: "We recruited participants through local mass media advertisements (eg, radio), mass media (eg, Facebook), and through flyers placed in medical clinics." Setting: Universities of Connecticut and Minnesota Study start date: March 2009; Study end date: 29 April 2017
Participants	Total N: 301 women who smoked ≥ 10 cpd, were postmenopausal (i.e., with no menstruation for at least 1 year), and were motivated to quit smoking N per arm: Relaxation = 151; Exercise = 150 100% female, av age 55.9, av baseline BMI 28.5, av cpd 18.9
Interventions	• Relaxation arm: 30 supervised relaxation group sessions in 3 phases over 24 wks • Exercise arm: 30 supervised exercise group sessions in 3 phases over 24 wks All participants were provided with 12 weeks of varenicline to support smoking cessation, a *Clearing the Air* smoking cessation manual and diary for daily entries. All participants were also encouraged to

1 Oncken 2019 *(Continued)*

	practise techniques (relaxation or exercise) at home, and an interactive Voice Response tool was to improve adherence outside of supervised sessions. Weekly feedback provided on IVR recordings and diaries
Outcomes	Data measured during the trial but not available for extraction at the time of this update. • Continuous abstinence (Validation: CO ≤ 5 ppm) at 24 weeks (EOT), 12 months and longest follow-up (15 months) • Mean weight change (kg) at 24 weeks (EOT), 12 months and longest follow-up (15 months)
Study funding	"The study was supported by R01DA024872 and the Lowell P. Weicker Clinical Research Center at the UConn Health."
Author declarations	"Dr. Oncken has received free nicotine and placebo inhalers from Pfizer Pharmaceuticals for an NIH-funded smoking cessation study in pregnant women. The remaining authors report no conflict of interest."
Notes	This study is new to the 2021 update

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "After baseline measurements, we randomized participants in block assignments of 4–8 participants to either the Exercise or the Relaxation condition using a computerized urn randomization procedure that assigned groups to treatment conditions by balancing on FTCD score (with a cutoff of 6) and history of depression (yes–no)."
Allocation concealment (selection bias)	Low risk	Quote: "Allocation of patients to condition was concealed to study personnel prior to random assignment but not during the treatment period."
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "We defined continuous abstinence weeks 9–12 as no recorded smoking, not even a puff, biochemically verified by CO ≤ 5 ppm."
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: "Follow-up visits to assess smoking status occurred at 3, 6, 9, and 12 months after treatment. At each of these visits we measured cigarettes per day, exhaled carbon monoxide, weight and height, and self-reported minutes per day of exercise and relaxation, and we administered questionnaires."
Incomplete outcome data (attrition bias) All outcomes	Low risk	Flow-chart: 24-week completion relaxation: 95/151; exercise: 100/150 9 months completion relaxation: 91/151; exercise: 89/150 12 months completion relaxation: 82/151; exercise: 82/150 15 months completion relaxation: 93/151; exercise: 92/150

1 Parsons 2009

Study characteristics

Methods	Country: England Recruitment: community volunteers

1 Parsons 2009 *(Continued)*

	Study start date: May 2006; Study end date: June 2007
Participants	143 smokers 63% female, av age 45.5, av baseline weight 75.1 kg, av cpd 20
Interventions	• St John's Wort (SJW (Jarsin preparation (LI 160, Lichtwer Pharma, Berlin, Germany), standard hypericin content 0.12% - 0.28%)) 900 mg daily and chromium polynicotinate 400 micrograms daily for 14 wks • SJW active, Chromium placebo • SJW placebo, Chromium active • SJW placebo, Chromium placebo All participants received 7 wks of behavioural counselling with TQD coinciding with the 3rd visit
Outcomes	• Prolonged abstinence at 6 months (self-report) • Mean (SD) weight change (kg) in prolonged abstainers at EOT and 6 months • Number of serious adverse events (narrative discussion)
Study funding	Not specified
Author declarations	Not specified
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	independent statistician prepared an excel spreadsheet using Stata to generate 2 lists of randomly-sequenced blocks of 2, 4, or 6, which were passed to the medication packing company
Allocation concealment (selection bias)	Low risk	Lists were used to package together medication of SJW or placebo and CR or placebo, which were allocated in sequence to participants in clinic
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Participants, therapists, and outcome assessors were blind to the treatment allocation“ + Placebo controlled
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: “abstinence was confirmed by exhaled carbon monoxide (CO) concentration of less than 10 parts per million (ppm)“
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: “Weight and percentage body fat were measured using a Tanita TBF300MA body composition analyser. Baseline weight was defined as the mean of the two pre-quit weights measured at the baseline visit and 1 week later. The mean was used to give a better measure of pre-quit weight less sensitive to fluctuations”
Incomplete outcome data (attrition bias) All outcomes	High risk	24-week completion SJWa-CRa group: 34/36 (94.4%) provided smoking data; 24-week completion SJWa-CRa group: 9/36 (25%) provided weight data; 24-week completion SJWa-CRp group: 33/35 (94.3%) provided smoking data; 24-week completion SJWa-CRp group: 3/35 (8.6%) provided weight data;

1 Parsons 2009 *(Continued)*

	24-week completion SJWp-CRa group: 32/37 (86.5%) provided smoking data; 24-week completion SJWp-CRa group: 3/37 (8.1%) provided weight data; 24-week completion SJWp-CRp group: 31/35 (88.6%) provided smoking data; 24-week completion SJWp-CRp group: 8/35 (22.9%) provided smoking data

1 Perkins 2001

Study characteristics	
Methods	Country: USA Recruitment: community volunteers Study start date: not specified; Study end date: not specified
Participants	219 weight-concerned women, av age 44, av body weight 69 kg, mean cpd 21
Interventions	• Weight control - Programme to attenuate weight gain, with a 500 kcal deficit of the energy required to maintain baseline weight, behavioural support (stimulus control techniques), self-monitoring and constructive feedback. 10 x 90-min sessions over 7 wks • Standard - No additional support given for weight, session time used to talk about smoking cessation • CBT - therapy to promote the acceptance of modest weight gain, reduce concerns and encourage healthy eating All participants received standard CB SC counselling at each session
Outcomes	• Continuous abstinence 6 and 12 m (validation: CO ≤ 8 ppm) • Mean (SD) weight change (kg) for continuous abstainers at 6 and 12 m
Study funding	"This research was supported by National Institute on Drug Abuse Grant DA04174."
Author declarations	Not specified
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	After a sufficient number of participants to form a group recruited, group assigned to a treatment condition
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: “point-prevalence was defined as self-report of no smoking at all during the 7 days prior to the follow-up point, confirmed by CO<= 8 ppm. (…) Those who dropped out or were otherwise lost to follow up at any point were presumed to have relapsed to smoking and coded as such in all outcome analyses”
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: “Body weight was measured at each session fully clothed on an electronic scale”

1 Perkins 2001 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: “Attrition by the end of the 7 weeks of treatment (4 weeks postquit) was 19%, 10%, and 21% for CBT, weight control, and standard, respectively, and the difference between weight control and standard was significant, x2 (l, N = 145) = 3.75, p = .05.”

1 Pirie 1992 (also Part 2)

Study characteristics	
Methods	Country: USA Recruitment: community volunteers Study start date: not specified; Study end date: not specified
Participants	417 women smokers, av cpd 25 - 27, av age 42 - 44, av BMI 23 - 24, 30 - 40% expressed great weight concern
Interventions	• Group SC therapy 8 wks • Group SC therapy plus weight control programme (general calorie restriction 100 - 300 kcal based on cigarette consumption, increased exercise to 1 hour daily walking, encouraged to self-monitor, acceptance of weight gain) • Group therapy plus nicotine gum 8 wks • Group therapy plus weight control programme and nicotine gum 8 wks Gum type: 2mg ad lib 8-wk treatment period + 3 months supply
Outcomes	• Continuous abstinence at 6 and 12 months (alidation: expired CO ≤ 10 ppm) • Mean (SD) weight change (kg) in continuous abstainers at EOT, 6 and 12 months
Study funding	"This research was supported by grant no. CA41647 from the National Cancer Institute"
Author declarations	Not specified
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method not stated
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	no blinding for (Part 2 only; not applicable for Part 1)
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: “expired air carbon monoxide” + “saliva was collected for biochemical validation .. only for those individuals reporting themselves to be abstinent”
Blinding of outcome assessment (detection bias)	Low risk	Quote: “weight was measured with a balance beam scale at each group session”

1 Pirie 1992 (also Part 2) *(Continued)*
Weight

Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Data were collected in the follow-up clinics on 98% of participants at 6 months and on 98.1% of participants at 12 months. Those few participants who had moved out of the area were allowed to complete self-report assessments by telephone and mail, resulting in 100% participation in the follow-up assessments"

1 Prapavessis 2018

Study characteristics	
Methods	Country: Canada Recruitment: "...from local businesses, hospitals, academic institutions and organizations and through advertisements placed in newspapers, radio stations and city buses in London, Ontario." Setting: Exercise and Health Psychology Laboratory (EHPL) Study start date: October 2009; Study end date: April 2014
Participants	Total N: 413 (411 in secondary analysis) female smokers between 18 - 65 years, smoked > 10 cpd for the previous 2 years, want to quit smoking, engaged in ≤ 2 30-minute bouts of moderate- or vigorous-intensity exercise/week over the past 6 months and were able to read and write in English N per arm: Contact Control = 95; Exercise Maintenance + Contact Control = 106; Smoking cessation Maintenance + Contact Control = 100; Exercise Maintenance + Smoking Cessation Maintenance = 108 100% female, av age 42.4, av cpd 16.9
Interventions	All participants received a 14-week facility-based group exercise programme (Week 0 - 8: 3 x 45-min sessions/week; week: 9 - 11: 2 x sessions/week; Week 12 - 14: 1 x session/week) with individualised exercise prescriptions. At week 4, all participants also received the NicoDerm 3-step, 10-week transdermal patch programme • Contact Control: Messaging on reinforcing women's health issues (e.g. vitamin D intake, oral hygiene, sleep disorders) were communicated during contact control sessions (Weeks 8-14). Contact control sessions from Week 14 included 10 phone messages reinforcing health issues covered over the next 12 months. • Exercise Maintenance + Contact Control: 5 x 25-min weekly exercise adherence group-based CBT sessions at weeks 8 - 14 followed by 7 x 15-min bi-weekly (Month 1), monthly (Month 2 - 3) and then bi-monthly (for last 8 months) telephone counselling sessions. Contact control messaging also provided • 3. Smoking Cessation Maintenance + Contact Control Smoking cessation relapse prevention booklets (Brandon's *Forever Free* booklets) containing evidence-based information on urges, weight gain, stress and lifestyle balance. Contact control included 7 x group-based sessions discussing women's health issues during weeks 8 - 14 plus 10 phone messages reinforcing health issues covered over the next 12 months • 4. Exercise Maintenance + Smoking Cessation Maintenance: As above
Outcomes	• Continuous abstinence (lapse free) at week 26 and 56 (validation: CO < 6 ppm) • Mean (SD) weight change (kg) in abstainers at week 56 (data not available)
Study funding	"This was an investigator initiated study funded by a grant from the Canadian Cancer Society (#019876-PI-HP). The Exercise and Health Psychology Lab (www.ehpl.uwo.ca) where this work was conducted, is supported by a Canadian Foundation Innovation infrastructure grant (#312466) award to the PI-HP. Clinical Trials Registration Number: NCT01305447."

1 Prapavessis 2018 *(Continued)*

Author declarations	"All authors declare that they have no conflict of interest."
Notes	All participants received exercise treatment This study is new to the 2021 update

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Participants will be randomized to one of four conditions: (a) exercise adherencebased group-mediated cognitive behavioural therapy, or GMCB (Exercise Maintenance), (b) GMCB plus smoking cessation relapse prevention booklets (Exercise Maintenanceþ Relapse Prevention Booklets), (c) smoking cessation relapse prevention booklets plus group-mediated discussions of women's health issues (Relapse Prevention Bookletsþ Contact), or (d) group-mediated discussions of women's health issues (Contact Control) using a central computerized system"
Allocation concealment (selection bias)	Low risk	Quote: "The project manager for trial used numbered containers to implement the random allocation sequence, and the sequence was concealed until interventions were assigned"
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "To be considered smoke-free for analyses participants had to show CO levels<6 ppm for the full 10 weeks of the treatment program (i.e., weeks 4–14). Those who provided CO levels ≥6 ppm or failed to provide CO level at any time over the treatment program were considered a smoker."
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: "Height and weight were collected (Health-o-meter professional, Pelstar 500KL) after asking participants to remove their shoes and heavy clothing (e.g., sweater)."
Incomplete outcome data (attrition bias) All outcomes	High risk	Week 14 follow-up: EM +SCM = 75/108 *100 = 69.4%; EM + CC = 79/106*100 = 74.5%; SCM + CC = 67/100 *100 = 67%; CC = 64/95 *100 = 67% Week 26 Follow-up: EM +SCM = 66/108 *100 = 61%; EM + CC = 68/106*100 = 64.2%; SCM + CC = 55/100 *100 = 55%; CC = 55/95 *100 = 57.9% Week 56 Follow-up: EM +SCM = 51/108 *100 = 47.2%; EM + CC = 55/106*100 = 51.8%; SCM + CC = 48/100 *100 = 48%; CC = 35/95 *100 = 36.8%

1 Rose 2019

Study characteristics

Methods	Country: USA Recruitment: "Subjects were recruited from a metropolitan area via advertisements targeting smokers who were concerned about gaining weight after quitting smoking." Setting: Duke Center for Smoking Cessation clinic

1 Rose 2019 *(Continued)*

	Study start date: 8 November 2016; Study end date: 18 October 2018
Participants	Total N: 61 smokers, 18 - 65 years, smoking ≥ 10 cpd for at least 1 cumulative year with CO ≥ 10 ppm, body weight of > 50 kg (110 lbs.) and want to quit smoking in the next 30 days N per arm: Patch = 30; Lorcaserin + Patch = 31 75.4% female, av age 45.5, av baseline BMI 30.9, av baseline weight 88.2 kg, av cpd 16.3, av FTND 5.3
Interventions	• Patch: Placebo plus nicotine patch for 2 weeks pre-quit period, then identical treatment (lorcaserin plus nicotine patch) for 12 weeks. • Lorcaserin + Patch: Lorcaserin plus nicotine patch for 2 weeks pre-quit period, then identical treatment (lorcaserin plus nicotine patch) for 12 weeks All participants received behavioural treatment: 30 mins of smoking cessation counselling, time-based monetary incentives to delay smoking and diaries to record medication use and the number of cigarettes smoked per day
Outcomes	• 1. Mean (SD) weight change (kg) in abstainers at EOT (Data not available for analysis) • 2. Number of serious adverse events per study arm at EOT • 3. Types of adverse events reported per study arm (narrative discussion) Also measured continuous 4-wk abstinence at EOT (CO validation)
Study funding	"This study was funded by a grant from the National Institute on Drug Abuse (P50-DA027840)."
Author declarations	"J.R. received funding from Philip Morris International, Altria, JUUL Labs. He discloses consulting with Philip Morris International and Revive Therapeutics LLC. He obtained patent purchase agreement in 2011 with Philip Morris International for nicotine inhalation system. J.R.'s privately funded projects are limited to the development and evaluation of reduced-risk tobacco products. J.M.D. received funding from Pfizer Inc. and Axsome Therapeutics Inc. J.M.D. privately funded projects are limited to evaluation of programs or development of drugs designed to treat tobacco use."
Notes	"Subjects will be reimbursed up to $417.42 for attending seven study visits and one follow up visit. There will be a payment of $40 per study visit attended. In addition, subjects will receive a payment of $10 for each of the 7 sessions attended in which they return their completed take-home forms (brief questionnaires which describe withdrawal symptoms and record smoking behavior and medication use). Subjects will also receive additional compensation up to $7.42 (per Sherry McKee protocol) for completing the laboratory session (P2). Subjects who do not complete each visit will still receive payment for the sessions attended. Thus, subjects who attend seven visits and hand in their take-home forms each time will receive a total payment of $350 plus the amount earned in the P2 laboratory session. Subjects who come back for a follow up session six months after their Quit Day will receive an additional $60. Subjects will not be compensated for the screening session." Both arms received the same pharmacotherapy in different schedules. This study is new to the 2021 update

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Participants will be randomized to receive nicotine patch + lorcaserin or nicotine patch + placebo for the first 2 weeks" Comment: No further detail provided in the protocol or primary publication.
Allocation concealment (selection bias)	Unclear risk	Quote: "Participants will be randomized to receive nicotine patch + lorcaserin or nicotine patch + placebo for the first 2 weeks" Comment: No further detail provided in the protocol or primary publication

1 Rose 2019 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "In order to maintain a double-blind assignment to treatment conditions, subjects receiving nicotine patch alone (Group B) will receive placebo lorcaserin tablets during the first two weeks." Clinical trial record: "Masking: Double (Participant, Care Provider)"
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "Ad libitum smoking was assessed weekly via daily diary recordings of cigarettes smoked per day as well as the objective index of expired air carbon monoxide (CO) levels measured at the study visits."
Blinding of outcome assessment (detection bias) Weight	Low risk	Weight objectively measured
Incomplete outcome data (attrition bias) All outcomes	High risk	Week 2 (from baseline; 2 weeks pre-quit date) Patch: 27/30*100 = 90%; Lorcaserin + Patch: 30/31*100 = 96.8% Week 14 (from baseline; 10 weeks from Quit date): Patch: 20/30*100 = 66.7%; Lorcaserin + Patch: 17/31*100 = 54.8% 6 months post-quit date Patch: 16/30*100 = 53.3%; Lorcaserin + Patch: 14/31*100 = 45.2%

1 Shanahan 2017

Study characteristics	
Methods	Country: USA Recruitment: Not specified Setting:30 clinical research sites in the USA experienced in smoking cessation trials Study start date: 28 February 2014; Study end date: 15 May 2014
Participants	Total N: 603 smokers, 18 - 65 years, smoking ≥ 10 cpd for the past year with no period of abstinence > 3 months, motivated to quit smoking, BMI 18.5 – 38.0 and at least 50 kg N per arm: Placebo = 200; Lorcaserin 10 mg daily = 202; Lorcaserin 10 mg twice a day = 201 54.4% female, av age 45.6, av baseline BMI 27.8, av baseline weight 80.4 kg, av cpd 18, av FTND 5.6.
Interventions	• Placebo for 12 weeks • Lorcaserin 10 mg once daily (daily) for 12 weeks • Lorcaserin 10 mg twice daily (twice a day) for 12 weeks. All participants received standard smoking cessation counselling by a trained counsellor. Counselling sessions were individual, face-to-face and 10 mins long
Outcomes	• Mean (SD) weight change (kg) in abstainers at EOT • Adverse events by intervention arm at EOT
Study funding	"This study was funded by Arena Pharmaceuticals, Inc. and Eisai, Inc."

1 Shanahan 2017 *(Continued)*

Author declarations	"JER is a consultant to Arena Pharmaceuticals. All other authors (WRS, AG, SS, and MS-K) were full-time employees of Arena Pharmaceuticals, Inc. at the time of trial design and execution, data analysis, and manuscript preparation and are shareholders."
Notes	This study is new to the 2021 update

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The contract research organization created the randomization codes using a random number generator."
Allocation concealment (selection bias)	Low risk	Quote: "Qualifying participants were centrally randomized in a 1:1:1 ratio to the three treatment options."
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "The contract research organization maintained the database and the treatment blind until after database lock. All site, contract, and sponsor personnel involved with conduct or analysis of the trial remained blinded until after database lock."
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "…weekly exhaled carbon monoxide measurements (MicroCO™/Carefusion)…" "The prespecified primary endpoint was the continuous abstinence rate for the last 4 weeks of the trial, weeks 9–12 (month 3) in the modified Intent-to-Treat (mITT) population. Secondary endpoints included continuous abstinence for weeks 5–8 (month 2) and for weeks 3–12, the weekly point prevalence of abstinence for weeks 3–12. To meet abstinence endpoints, participants had to specify no nicotine use, not even one puff, during the evaluated period, confirmed by weekly exhaled carbon monoxide values of ≤10 ppm."
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: "Weight was measured in the fasting state post voiding in the morning, in patient gown and undergarments using certified scales sensitive to within 100 grams supplied by the sponsor."
Incomplete outcome data (attrition bias) All outcomes	Low risk	"Week 12 completion rates were 70.0% for placebo, 72.8% for lorcaserin QD, and 85.1% for lorcaserin BID participants"

1 Sobell 2017

Study characteristics

Methods	Country: USA Recruitment: "Participants were recruited during 2006 to 2008 from military primary care centers in the San Antonio, Texas, area. Potential participants learned about the study through referrals from staff or from fliers posted at the centers." Setting: Not specified Study start date: 2006; Study end date: 2008 (recruitment end date)

1 Sobell 2017 *(Continued)*

Participants	Total N: 317 millitary personnel regularly consuming alcohol (≥ 4 drinks per week (1 standard drink = 0.6 oz. or 14 g ethanol)) and regularly smoking (≥ 5/day during past year), have CO ≥ 8 ppm when screened, 21 – 75 years of age, interested in quitting and willing to set quit date within 6 weeks and concerned about weight gain N per arm: Standard Smoking Cessation = 159; Smoking cessation plus group = 158 29% female, av age 37.4, av baseline weight 84.9, av FTND 3.9
Interventions	• Standard Smoking Cessation: Provided pamplet that discussed behavioural change strategies for tobacco cessation, provided encouragement to not let weight gain be an obstacle to quitting, suggested reducing alcohol use, and provided encouragement to quit again should they relapse. Initial 15-min face-to-face session, 3-month follow-up session with discussion if cessation attempt failed. All participants who requested medication were medically screened and provided with NRT (nicotine patch) and/or bupropion and instructions if there were no medical contraindications • Smoking cessation plus group: received standard smoking cessation as arm 1, plus 4 counselling sessions, 2 face-to-face, and 2 by telephone over 8 wks. Provided educational materials, cessation plans and workbook. Sesssions included discussion of strategies for weight control and reducing alcohol consumption to decrease caloric intake
Outcomes	• Abstinence at 6 and 12 months (validation: CO < 8 ppm) • Mean (SD) weight change (kg) in abstainers at EOT (not broken down by treatment arm - narrative discussion only)
Study funding	"This study was supported by a grant from the Department of Defense Peer Review Medical Research Program of the Office of the Congressionally Directed Medical Research Programs, Grant Number W81XWH-05-2-0015. The opinions expressed herein and the interpretation and reporting of these data are the responsibility of the authors and in no way should be seen as an official recommendation, interpretation, or policy of the National Institutes of Health, the Department of Health and Human Services, the Department of Defense, or the U.S. Government."
Author declarations	"The authors declare that they have no conflict of interest."
Notes	This study is new to the 2021 update

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Participants randomly assigned to the SCP intervention were scheduled to take part in four sessions, two face-to-face, and two by telephone." Comment: No further information provided
Allocation concealment (selection bias)	Unclear risk	Quote: "Participants randomly assigned to the SCP intervention were scheduled to take part in four sessions, two face-to-face, and two by telephone." Comment: No further information provided
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "For available participants, an absence of smoking was confirmed by having a CO level of < 8 ppm"
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: "Weight in pounds was measured at the 12-month follow-up, with the exception of a small number of cases (e.g., deployed and overseas, stationed at a facility in another part of the country)."
Incomplete outcome data (attrition bias)	Low risk	3-month follow-up:

1 Sobell 2017 *(Continued)*

All outcomes	SSC: 151/159*100 = 95%; SCP: 141/158*100 = 89.2% 6-month follow-up: SSC: 144/159*100 = 90.6%; SCP: 144/158*100 = 91.1% 12-month follow-up: SSC: 127/159*100 = 79.9%; SCP: 141/158*100 = 89.2%

1 Spring 1995 (also Part 2)

Study characteristics

Methods	Country: USA Recruitment: community volunteers Study start date: not specified; Study end date: not specified
Participants	144 female weight-concerned smokers, av age 41, av cpd 27, av BMI 23 - 25
Interventions	• Dexfenfluramine 30 mg/day 12 wks • Fluoxetine 40 mg/day 12 wks • Placebo All participants received weekly group behavioural support for first 4 wks and fortnightly support for remaining 8 wks
Outcomes	• Mean (SD) weight change (kg) in prolonged abstainers at EOT (validation: CO < 10 ppm) • Number of adverse events by treatment arm (narrative discussion)
Study funding	"Supported by awards from the Center for Brain Sciences and Metabolism Charitable Trust and National Institutes of Health grant #MOI-RR00088 to the MIT Clinical Research Center, as well as by VA Merit Review and American Cancer Society awards to BS"
Author declarations	"MIT holds patents governing the use of both dexfenfluramine and fluoxetine for various weight control applications with JW and RW as co-patent assignees. BS is co-patent assignee for the application to prevent post-cessation weight gain"
Notes	No 6 months follow-up data Prolonged abstinence defined as validated continuous abstinence after a 2-week grace period Fluoxetine arm used in first part of review as taken specifically to prevent post-cessation weight gain and this study is not included in the parent antidepressant review.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method not stated
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias)	Low risk	Double blind + placebo controlled. Quote: "All subjects received identical packets of three pills"

1 Spring 1995 (also Part 2) *(Continued)*
All outcomes

Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: “to be considered abstinent from smoking, all of the following were required: self-report of no smoking, expired carbon monoxide < 8 ppm and plasma cotinine < 10 ug/L.”
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: “Body weight of subjects without shoes was always measured by using the same balance-beam scale.”
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: “The three treatment groups differed significantly in their rates of attrition. More dexfenfluramine (30/47, 63.8%) than fluoxetine (21/49, 42.9%) subjects completed the trial, and the number of placebo subjects who completed the study (27/48, 56.3%) was intermediate.”

1 Spring 2004

Study characteristics	
Methods	Country: USA Recruitment: community volunteers Study start date: not specified; Study end date: not specified
Participants	315 mildly weight-concerned women, av age 42.7 (10.3) yrs, av 20.3 (9.5) cpd, av BMI 27.4 (7.6)
Interventions	• Early diet group. Diet during 1 - 8 wks of treatment programme (Pre-packaged Nutri/system foods: high-carbohydrate, low-fat, balanced diet based on baseline precessation energy intake from food diaries minus 150 kcal per day). Participants led on a 30-minute walk after the treatment programme session • Late diet group. Diet during 9 - 16 wks of treatment programme • Control. Final smoking cessation group session focused on weight loss strategies. All participants received 16 weekly CBT smoking cessation group support sessions
Outcomes	1. Mean (SD) weight change (kg) at EOT and at 6 months in continuous abstainers (validation: CO ≤ 10 ppm)
Study funding	"The work described in this article was supported in part by National Institutes of Health Grants HL52577 and HL63307 and a Veterans Affairs Merit Review Award to Bonnie Spring."
Author declarations	Not specified
Notes	

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Block randomization
Allocation concealment (selection bias)	Unclear risk	Not described

1 Spring 2004 *(Continued)*

Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "Seven-day point prevalence smoking status was evaluated via self-report and ecolyzer measurement of expired carbon monoxide (CO)“
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: “Participants were weighed weekly with a balance beam scale throughout the treatment portion of the study and monthly throughout the follow-up period. Weight change at each visit was calculated by subtracting out participants’ baseline weight“
Incomplete outcome data (attrition bias) All outcomes	High risk	Treatment completion early diet group: 75/104 (72%); Treatment completion late diet group: 86/104 (82%); Treatment completion control group: 75/107 (70%); 36-week completion early diet group: 45/104 (43%); 36-week completion late diet group: 45/104 (43%); 36-week completion control group: 40/107 (37%)

1 Toll 2010

Study characteristics	
Methods	Country: USA Recruitment: community volunteers Study start date: 3 February 2005; Study end date: 27 April 2009
Participants	127 weight-concerned smokers, 28.5% men, mean BMI 28.4 ± 6.16, mean 25.5 ± 10.76 expired CO
Interventions	• 25-mg naltrexone daily beginning the week before quitting, continuing until 26 wks • Placebo All participants received 21 mg patches for 6 wks and then 14 mg for 2 wks, starting on quit day. All received CBT for weight concerns weekly for 4 wks, bimonthly twice and then monthly
Outcomes	• PPA at end of treatment (26 wks) • Mean (SD) weight change (kg) at end of treatment (26 wks) in continuous abstainers (validation: CO < 10 ppm) • Number of adverse events by treatment arm (narrative discussion)
Study funding	"This research was supported by National Institutes of Health grants [P50-AA15632 (to SOM), K12-DA000167 (to BAT), K05- AA014715 (to SOM), K23 DK071646 (to MAW)] from the National Institute on Alcohol Abuse and Alcoholism (NIAAA), National Institute on Drug Abuse (NIDA), National Institute on Diabetes and Digestive and Kidney Diseases (NIDDK), and by the State of Connecticut, Department of Mental Health and Addictions Services (DMHAS). Portions of the naltrexone and nicotine patches used in this study were donated by Mallinckrodt Pharmaceuticals and GlaxoSmithKline, respectively. The content is solely the responsibility of the authors and does not necessarily represent the official views of the NIAAA, NIDA, NIDDK, the National Institutes of Health (NIH), or DMHAS. The NIAAA, NIDA, NIDDK, DMHAS, Mallinckrodt Pharmaceuticals, and GlaxoSmithKline had no further role in study design; in the collection, analysis and interpretation of data; in the writing of the report; or in the decision to submit the paper for publication"
Author declarations	"At the time the study was conducted, Drs. O’Malley and Meandzija were inventors on an unlicensed patent held by Yale University regarding the use of naltrexone for smoking cessation treatment that has since been abandoned. Dr. O’Malley received honoraria as a member of the American College of Neuropsychopharmacology workgroup, the Alcohol Clinical Trial Initiative, sponsored by Eli Lilly, Janssen, Schering Plough, Lundbeck, Glaxo-Smith Kline and Alkermes. She received travel reimbursement for talks at the Controlled Release Society, the Drug Information Association and the Association for Medical Education and Research in Substance Abuse, and an honorarium from the Medical Education

1 Toll 2010 *(Continued)*

	Speaker Network. She has consulted to the University of Chicago, Brown University, and the Medical University of South Carolina on studies of naltrexone. She is a partner in Applied Behavioral Research, and a Scientific Panel Member, Butler Center for Research at Hazelden. All other authors declare that they have no conflicts of interest"
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Block stratified for gender, sequence provided by author and given to pharmacist
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: “Random sequence was provided by one of the authors (RW) to the pharmacist who assigned participants; all others were blind to treatment assignment.“ + placebo controlled
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: “If they reported abstinence, they were only coded as abstinent when an in-person breath CO measurement was obtain bio- logically verifying their self-report. Serum cotinine was measured at intake and post-treatment follow-ups.“
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: "Participant weight (in street clothes, without shoes) was measured using a cali- brated balance beam scale“
Incomplete outcome data (attrition bias) All outcomes	High risk	Treatment completion placebo group: 30/85 (35%); Treatment completion intervention group: 28/87 (32%)

1 Vander Weg 2016

Study characteristics

Methods	Country: USA Recruitment: “Recruitment letters were mailed to 847 rural Veterans, of whom 706 were excluded.” Setting: Quitline Study start date: June 2012; Study end date: June 2013
Participants	Total N: 63 rural Veterans, 18+ years, smoking at least daily, receiving primary care from the Iowa City VAMC or Coralville Clinic and willing to make a quit attempt in the next 30 days N per arm: Quitline referral = 32; Tailored tobacco intervention = 31 12.7% female, av age 56.8, av cpd 24.7, av FTND 5.7
Interventions	• Quitline referral: Telephone sessions delivered by regional Quitline

1 Vander Weg 2016 *(Continued)*

	• Tailored tobacco intervention: 6 telephone couselling sessions, 20 – 30 mins each and consisting of 4 phases:
	  * 1) preparing to quit;
	  * 2) going through the quitting process;
	  * 3) maintaining short-term abstinence; and
	  * 4) relapse prevention.
	• Baseline survey screened for depressive symptoms, risky alcohol use, and concerns about weight gain. Eligible participants were offered 0 to 3 additional voluntary supplemental modules for
	  * (1) Mood Management;
	  * (2) Alcohol risk reduction;
	  * (3) Weight management.
	• Small, manageable changes in diet and physical activity were encouraged. Counseling related to each of the supplemental modules was delivered concurrently with the smoking cessation intervention
	
	"The approach to pharmacotherapy was the same for both groups. Medication options were based on the Clinical Practice Guideline [35] and the VA formulary and included several forms of NRT (patch, gum, lozenge), bupropion, and varenicline. Combination therapy was also available as appropriate."

Outcomes	• Penalised imputation of 7-day self-reported PPA at 6 months (discussed narratively) • Mean (SD) weight change (kg) in all participants who recieved the weight management component at 6 months (data in abstainers measured but not available)
Study funding	"The work reported in this manuscript was funded by the Department of Veterans Affairs Office of Rural Health (Project number 12-CR6). The Office of Rural Health played no role in the design or conduct of the study, the interpretation of the results, or the preparation of the manuscript."
Author declarations	"The authors declare that they have no competing interests."
Notes	This study is new to the 2021 update

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "The computerized random allocation sequence was generated by the study data manager."
Allocation concealment (selection bias)	Unclear risk	Quote: "The computerized random allocation sequence was generated by the study data manager. Participants were enrolled and informed of their treatment assignment by the Project Coordinator (AJC)."
Blinding of outcome assessment (detection bias) Smoking	High risk	Quote: "Cessation was determined based on self-reported 7-day point prevalent abstinence (PPA). To meet criteria for abstinence, participants had to report no tobacco or ecigarette use during the prior 7 days."
Blinding of outcome assessment (detection bias) Weight	High risk	Quote: "Health-related items included self-reported height, weight, and self-rated health."
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "Twelve-week data were available for 74 % of those in the Tailored intervention group and 94 % of those assigned to Quitline Referral." Quote: "Six month data were obtained for 74 and 88 % of those in the Tailored and Quitline Referral groups, respectively."

1 White 2019

Study characteristics	
Methods	Country: USA Recruitment: "Participants were recruited through advertising and physician referral, with primary emphasis in online advertising outlets." Setting: Not specified Study start date/Study end date: Not specified
Participants	Total N: 54 regular current smokers, ≥ 10 cpd, with < 3 consecutive months of abstinence in the past year N per arm: Internet-administered smoking cessation treatment with health education = 27 Internet-administered smoking cessation plus CBT for weight concerns = 27 72% female, av age 45.9, av baseline BMI 33.1, av cpd 19.7
Interventions	• Internet-administered smoking cessation treatment with health education: * Online education sessions on general health topics including stress management, sleep hygiene, general nutrition, physical activity, economic stress, alcohol use, and use of medications and drugs. Weekly clinician email contact also provided to match for contact time provided for trial arm 2. • Internet-administered smoking cessation plus CBT for weight concerns: "Lessons on cognitive restructuring; CBT treatment was administered through the study website, with weekly clinician contact via email. Submission of CBT assignments—for example, thought restructuring exercises— occurred via forms provided on the study website. Clinicians prompted participants to complete the assignments via weekly emails." All participants recieved smoking cessation treatment: 21-mg nicotine patch daily for 10 weeks, beginning in the second week of treatment and 12-weekly online behavioural smoking cessation treatment lessons + clinician reminders
Outcomes	• 14-day continuous abstinence CO < 10 ppm verified at 6 months • Mean (SD) weight change (kg) in abstainers at 12 weeks (EOT; SD not provided - weight change discussed narratively)
Study funding	"The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: The study was funded by the American Heart Association, Grant-in-Aid awarded to Dr White."
Author declarations	"The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article."
Notes	This study is new to the 2021 update.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Quote: "Randomization. Eligible participants were randomized in equal allocation to one of two conditions: Internet-administered smoking cessation treatment with health education (QUIT + HE) or Internet-administered smoking cessation plus CBT for weight concerns (QUIT + CBT). No blocking or stratification was used." Comment: No further detail provided.

1 White 2019 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Quote: "Randomization. Eligible participants were randomized in equal allocation to one of two conditions: Internet-administered smoking cessation treatment with health education (QUIT + HE) or Internet-administered smoking cessation plus CBT for weight concerns (QUIT + CBT). No blocking or stratification was used." Comment: No further detail provided.
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "CO levels were measured using a Vitalograph Breath CO Monitor, which is a precision instrument for detecting carbon monoxide in exhaled breath. A cutoff of 10 ppm for CO was used."
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: "Height and weight were self reported online and subsequently measured during in-person evaluations and at all clinic meetings using a high capacity digital scale."
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "Of the 54 randomized participants, 27 received QUIT + CBT and 27 received QUIT + HE. Overall, 44 (81.5%) participants completed the trial. Attrition varied by treatment condition ($\chi 2 = 7.86$, $p = .005$), with 67 percent (n = 18) of the QUIT + HE participants and 96 percent (n = 26) of the QUIT + CBT participants attending the post-treatment (12 weeks) assessment."

1 Wilcox 2016

Study characteristics	
Methods	Country: USA Recruitment and setting: Not specified Study start date/Study end date: Not specified
Participants	Total N: 59 smokers, ages 18 - 65 inclusive, smoking ≥ 10 cpd for at least the past year, who were motivated to stop smoking
Interventions	• Placebo plus in-person smoking cessation counselling at day -1 and weekly through to week 12, 10 mins per session • Lorcaserin 10 mg once daily (low dose) plus smoking cessation counselling as per placebo arm • Locaserin 10 mg twice daily (high dose) plus smoking cessation counselling as per placebo arm
Outcomes	• Mean (SD) weight change (kg) in abstainers at 12 wks (EOT; data measured but not available)
Study funding	Not specified
Author declarations	"Nothing to disclose."
Notes	Information extracted from a conference abstract. This study is new to the 2021 update

Risk of bias

Bias	Authors' judgement	Support for judgement

1 Wilcox 2016 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Quote: "Fifty-nine (59) eligible smokers were randomly assigned to one of three treatment groups: lorcaserin 10 mg once daily; lorcaserin 10 mg twice daily, or placebo in a 3:3:2 ratio."
Allocation concealment (selection bias)	Unclear risk	Not specified
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "This was a randomized, double-blind, twelve-week [dosing], placebo-controlled, parallel-group dose selection study."
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "…end-expiratory carbon monoxide- (CO-) confirmed Continuous Abstinence Rate (CAR) from study weeks 9-12, defined as zero reported smoking via Nicotine Use Inventory (NUI) with exhaled CO measurement ≤ 10 ppm."
Blinding of outcome assessment (detection bias) Weight	Unclear risk	How weight was measured is not reported and blinding is unclear
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not specified

2 Abelin 1989

Study characteristics	
Methods	Country: Switzerland Recruitment: 21 primary care clinics Study start date: not specified; Study end date: not specified
Participants	199 primary care patients, 40% female, av.age 41, av.cpd 27
Interventions	• Nicotine patch, 24-hr, 12 wks with weaning; 21mg smokers of > 20 cpd, 14 mg for < 20 cpd • Placebo patch Participants did not receive any psychological support
Outcomes	Mean (SD) weight change (kg) in prolonged abstainers at end of treatment (validation: CO content 0 - 11 ppm)
Study funding	Not specified
Author declarations	Not specified
Notes	Abstinence defined as participants who smoked 0 - 3 cigarettes per wk with validation

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method not stated

2 Abelin 1989 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double-blind + placebo-controlled. No further information given
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "Abstinence was verified by measurement of the CO content of exhaled air. Participants who smoked 0-3 cigarettes per week and had a CO content of 0-11 ppm in expired air were deemed abstinent"
Blinding of outcome assessment (detection bias) Weight	Low risk	Unclear how weight was measured; self-report cannot be ruled out and it is also unclear if participants were blinded to treatment allocation.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Altogether there were 20 drop-outs in the nicotine group after 3 months and 21 in the placebo group – i.e. a total rate of about 20%."

2 Aubin 2008

Study characteristics	
Methods	Country: Belgium, France, Netherlands, UK, USA Recruitment: smoking cessation clinics or community volunteers Study start date: 17 January 2005; Study end date: 28 June 2006
Participants	Healthy adults, Mean age 42.9 yrs, 50.8% female, Mean cpd 22.7.
Interventions	• Varenicline 1 mg x 2/day for 12 wks, titrated 1st wk; 376 participants • Nicotine patch (21 mg wks 2 - 6, 14 mg wks 7 - 9, 7 mg wks 10 - 11); 370 participants No placebo control group. All participants received *Clearing the Air,* S-H booklet at baseline, and brief counselling (≤ 10 mins) at each clinic visit or by phone
Outcomes	Mean (SD) weight change (kg) in prolonged abstainers at EOT (email communication) (validation: CO ≤ 10 ppm)
Study funding	"This study was funded by Pfizer Inc. Editorial support was provided by Brenda Smith PhD and Abegale Templar PhD of Envision Pharma and was funded by Pfizer Inc."
Author declarations	"H-JA has received sponsorship to attend scientific meetings, speaker honorariums and consultancy fees from GlaxoSmithKline, Pierre-Fabre Sante, Sanofi-Aventis, Merck-Lipha and Pfizer Inc. AB has received sponsorship to attend scientific meetings, speaker honorariums and consultancy fees from Boehringer Ingelheim, GlaxoSmithKline, Novartis and Pfizer Inc. In the past 5 years JRB has received consultancy fees from Xenova and Novartis and his employing institution has received consultancy fees and honoraria on his behalf from Pfizer Inc. CO has received honoraria and consulting fees from Pfizer, nicotine and placebo products for research studies at no cost from GlaxoSmithKline and honoraria from Pri-Med and CME outfitters. CBB, JG, KEW and KRR are employees of Pfizer Inc."
Notes	Prolonged abstainers defined as completely quit from wk 9
Risk of bias	

2 Aubin 2008 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Central computer-generated sequence
Allocation concealment (selection bias)	Low risk	Central allocation
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open-label. 2 active pharmacological interventions.
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "The primary end point was the self-reported continuous abstinence rate (CAR), confirmed by exhaled carbon monoxide (CO) levels of 10 ppm or below, during the last 4 weeks of treatment (varenicline, weeks 9–12; NRT, weeks 8–11)“
Blinding of outcome assessment (detection bias) Weight	Unclear risk	Comment: Self-report cannot be ruled out. Follow-up weight was likely self-reported. Participants not blinded, but both arms were active interventions. Quote: “Blood chemistry, haematology, urinalysis tests, vital signs, physical examinations, body weight measures and electrocardiograms were assessed during the treatment period."
Incomplete outcome data (attrition bias) All outcomes	Low risk	Follow-up completion: Varenicline group: 312/376 (83%); NRT group: 305/370 (82.3%)

2 Benowitz 2018

Study characteristics	
Methods	Country: USA, Argentina, Australia, Brazil, Bulgaria, Canada, Chile, Denmark, Finland, Germany, Mexico, New Zealand, Russian Federation, Slovakia, South Africa, Spain Recruitment: From the investigators’ own clinics; through newspaper, radio, and television advertising; and fliers and posters Setting: 140 multinational centres in 16 countries across 5 continents. Study sites included clinical trial centres, academic centres, and outpatient clinics treating patients with and without psychiatric disorders Study start date: EAGLES: November 2011; Extrension trial: May 2012; Study end date: EAGLES: January 2015; Extension trial: July 2015
Participants	**EAGLES trial** Total N: 8144 smokers aged between 18 - 75 years, motivated to stop smoking, smoking 10+ cpd over the previous year and a CO > 10 ppm at screening N per arm (received treatment): Varenicline = 2016; Bupropion = 2006; NRT = 2022; Placebo = 2014 55.9% female, av age 46.5; av baseline BMI: 28.1, av cpd 20.7, av FTND 5.8. **EAGLES non-treatment extension trial**

2 Benowitz 2018 *(Continued)*

	Total N: 4595; N per arm: varenicline = 1192; bupropion = 1166; NRT = 1116; Placebo = 1121 55.5% female, av age 47.9, av baseline BMI: 28.6
Interventions	• Placebo varenicline + placebo bupropion + placebo nicotine patches for 12 wks • Active varenicline (2 x 1 mg per day) + placebo bupropion + placebo nicotine patches for 12 wks. • Placebo varenicline + active bupropion (2 x 150 mg per day) + placebo nicotine patches for 12 wks • Placebo varenicline + placebo bupropion + active nicotine patches (1 x 21 mg per day, reduced to 14 mg per day at week 8 and 7 mg per day at week 10) for a total of 12 wks All participants were asked to complete up to 15 face-to-face visits and 11 telephone visits during the 24-week EAGLES trial Smoking cessation counselling of at most 10 mins based on Agency for Healthcare Research and Quality guidelines was given at each clinic visit
Outcomes	The following outcomes were measured during the trial but were not available for extraction at the time of this update • Mean (SD) weight change (kg) in abstainers at EOT, 6 and 12 months
Study funding	This work was supported by Pfizer and GlaxoSmithKline Role of the Funder/Sponsor: Evaluating Adverse Events in a Global Smoking Cessation Study (EAGLES) and the EAGLES extension trial are postmarketing requirements in the United States and Europe for Pfizer and GlaxoSmithKline. As such, sponsor employees, with input from academic authors, designed both studies. The sponsors supported the conduct of the trials, monitored the study sites, and collected and analyzed the data. All authors had full access to the data in the studies. Dr Benowitz prepared the initial draft of the manuscript and had final responsibility for the decision to submit for publication.
Author declarations	Dr Benowitz has served as a consultant to pharmaceutical companies, including Pfizer, which markets smoking cessation medications, and has been a paid expert witness in litigation against tobacco companies. Dr Pipe has served as a consultant to pharmaceutical companies that market smoking cessation medications, including Pfizer, and has received research funding from Pfizer for conduct of this study and from Johnson & Johnson. Dr West is a consultant to Pfizer, Johnson & Johnson, and GlaxoSmithKline and has received research funding from Pfizer and Johnson & Johnson; Dr West's salary is funded by Cancer Research UK. Dr Hays has received research support from Pfizer for the conduct of this study. Dr Tonstad has received honoraria for lectures and consulting for Pfizer. Drs McRae, Lawrence, and St Aubin are employees and stockholders of Pfizer. Dr Anthenelli reports his university receiving grants from Pfizer and Alkermes, and providing consulting and/or advisory board services to Pfizer, Arena Pharmaceuticals, and Cerecor; Dr Anthenelli's contributions to this article were supported, in part, by National Institute on Alcohol Abuse and Alcoholism grants U01 AA013641 and R01 AA019720, and National Institute on Drug Abuse/Veterans Affairs Cooperative Studies 1031 and 1032.
Notes	Weight gain is reported for the EAGLES extension trial, which was a non-treatment follow-up to the EAGLES trial monitoring cardiovascular adverse events, including the collection of weight data In the EAGLES trial, participants were divided into a non-psychiatric cohort and 4 sub-cohorts in the psychiatric cohort This study is new to the 2021 update

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "A randomisation administrator, independent from the clinical study team, prepared the computer-generated randomisation schedule used to as-

2 Benowitz 2018 *(Continued)*

		sign participants to treatment using a block size of 8 (1:1:1:1 ratio) for each of the 20 diagnosis by region combinations."
Allocation concealment (selection bias)	Low risk	Quote: "Investigators obtained participant identification numbers via a web-based or telephone call-in drug management system. Study product kit codes did not allow deciphering of randomised treatment or block size."
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "As such, participants, investigators, and research personnel were masked to treatment assignments."
Blinding of outcome assessment (detection bias) Smoking	Low risk	Objectively measured
Blinding of outcome assessment (detection bias) Weight	Low risk	Objectively measured. Quote: "Body weight will be measured at the initiation visit of study A3051148 and Week 52 or ET52 Weight will be measured in indoor clothing without shoes"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Study completion rates for the 24-week EAGLES trial were similar across all treatment arms, with a high of 79.3% (varenicline) vs a low of 77.0% (NRT). Of those who completed EAGLES, 964 NPC participants and 734 PC participants declined enrollment in the 28- week extension trial. Thus, 4595 participants (73.0% of EAGLES completers or 56.4% of those randomized to EAGLES) enrolled in the extension trial; similar numbers of participants enrolled in each of the 4 treatment arms (Figure 3 and Figure 1). Extension trial completion rates were high (4139 of 4595 [90.1%]) and similar across the 4 treatment groups."

2 Bernard 2015

Study characteristics	
Methods	Country: France Recruitment: news releases and advertisements in local print and electronic media over a 17-month recruitment period Setting: Montepellier University Hospital Study start date: October 2010; Study end date: March 2013
Participants	Total N: 70 smokers aged between 18 - 65 years, sedentary for the previous 6 months with elevated depressive symptoms and a Fagerström score ≥ 4 N per arm: Standard smoking cessation treatment plus exercise and counselling = 35; Health education = 35 58.6% female, av age 48.5; av baseline BMI: 24.6, av cpd 21.5; av FTND 6.4
Interventions	• Health education control: • Standard smoking cessation treatment plus face-to-face group sessions of supervised exercise and counselling + home-based exercise and paper reminders describing the home exercise sessions All participants recieved an initial individual session with medical doctor encouraging to stop smoking and selecting a quit date within 2 weeks + optional NRT (adjusted to expired CO level) or optional

2 Bernard 2015 *(Continued)*

	varenicline (2 x 1 mg per day for 12 weeks) + couselling (10-session, 8-week group programme, with bi-weekly meetings for weeks 1 and 2 and weekly meetings for weeks 3 through 8. 75 minutes of clinician contact time per session)
Outcomes	The following outcomes were measured during the trial but were not available for extraction at the time of this update. • Mean (SD) weight change (kg) in abstainers at EOT, 6 and 12 months
Study funding	"This work was supported by the University Hospital of Montpellier (AOI 2009) and French Committee against Respiratory Diseases"
Author declarations	"Pr Quantin received research funds and served on the scientific board of Lilly, Bohringer, Roche, and Pfizer. Pr Courtet has received grants and served as consultant or speaker for the following entities: AstraZeneca, Roche, Servier, Bristol-Myers Squibb, Janssen-Cilag, Lundbeck, Otsuka, Pfizer, SanofiAventis, and Servier. Dr. Guillaume has received compensa- tion as a consultant for AstraZeneca, Bristol-Myers Squibb, Lundbeck, Otsuka, Servier, and Janssen Cilag. These companies manufacture and/or distribute some antidepressant, mood stabilizer, and/or antipsychotic medications. Drs. Bernard, Cyprien, and Georgescu have no conflict of interest. Pr Ninot and Taylor have no conflict of interest."
Notes	This study is new to the 2021 update

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Following their baseline assessment, the participants were randomized using TENALEA, an online randomization service (TENALEA, 2010). The randomization was not stratified on depression level, antidepressant treatment, or any other variable."
Allocation concealment (selection bias)	Unclear risk	Not specified
Blinding of outcome assessment (detection bias) Smoking	Low risk	CO < 10 verified
Blinding of outcome assessment (detection bias) Weight	Unclear risk	Not specified
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "The dropout rate did not vary significantly between the intervention (7 out of 35, 20%) and control (13 out of 35, 37.1%) groups; $\chi 2(1) = 1.75$, $p = .18$."
Other bias	Unclear risk	Patients in control group may have participated in exercise (contamination effect)

2 Bize 2010

Study characteristics

Methods	Country: Switzerland Recruitment: Community volunteers

2 Bize 2010 *(Continued)*

	Study start date: June 2002; Study end date: January 2006
Participants	481, av age 42, av cpd 27, sedentary: < 150 mins moderate-intensity physical activity per wk and < 60 mins vigorous-intensity activity, av BMI 24 - 25
Interventions	• Intervention: moderate-intensity group-based CV activity, 45 mins, weekly for 9 weeks + 15 mins cessation counselling for 9 weeks (including NRT prescription) • Control: 9 weeks of 15 mins per week cessation counselling (including NRT prescription) + Health Education for equal time as exercise intervention (not exercise) Exercise started 5 weeks before quit date
Outcomes	Mean (SD) weight change (kg) in continuous abstainers at end of treatment and 12 m (validation: CO < 10 ppm)
Study funding	"This trial was supported by a grant from the Swiss National Science Foundation (SNSF 3200-067085). Other funders: Swiss National Science Foundation"
Author declarations	"None"
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Remotely and randomly generated by a computer
Allocation concealment (selection bias)	Low risk	Secured by means of sealed envelopes
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "Smoking cessation was defined as self-reported abstinence from smoking, confirmed by a carbon monoxide (CO) concentration in expired air of less than 10 ppm“
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: "Body weight was recorded to the nearest 0.1 kg with the participant wearing only underwear and socks. Height was measured to the nearest 0.5 cm.“
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: “The 52-week follow-up visit was completed by 127/229 participants in the physical activity group (follow-up rate: 55%) and 155/252 in the control group (follow-up rate: 62%).”

2 Blondal 1999

Study characteristics

Methods	Country: Iceland Recruitment: community volunteers Study start date: November 1991; Study end date: not specified
Participants	237 smokers 67% F, av.age 41 - 43, av tobacco use 25 g/day

2 Blondal 1999 *(Continued)*

Interventions	• Nicotine nasal spray (NNS) (0.5 mg/dose) + 15 mg nicotine patches for 3m, weaning over further 2m. NNS could be continued for 1 yr • Placebo nasal spray + 15 mg nicotine patches on same schedule
Outcomes	Mean (SD) weight change (kg) in continuous abstainers at EOT (email communication) and 12m (email communication) (validation: CO < 11 ppm)
Study funding	"Pharmacia and Upjohn provided the drugs and placebo"
Author declarations	"TB was a consultant for Pharmacia and Upjohn, and GG and AW are employed by Pharmacia and Upjohn"
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated code at pharmacy
Allocation concealment (selection bias)	Low risk	Quote: "participants allocated their treatment by generated randomisation code at a local pharmacy"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: “The pharmacy staff were blinded to the content of the bottles“; “The staff of the smoking clinic had no knowledge of the treatment assigned to each participant.“; “Blinding among participants was successful. At the 1 year follow up we found no significant relation between type of treatment and the participants’ responses, which proved they had been unable to guess their treatment“
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "Participants were considered to be smokers if they had, after stopping smoking, taken a single puff of a cigarette, used other forms of tobacco, used a nicotine drug other than that prescribed, had a carbon monoxide concentration of >10 ppm, or were lost to follow up“
Blinding of outcome assessment (detection bias) Weight	Low risk	Unclear how weight was measured but participants were blinded to treatment allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	48-week completion patch and nicotine spray group: 117/120 (97.5%) (1 was excluded due to non-compliance and 1 for Illness); 48-week completion patch and placebo spray group: 119/119 (100%)

2 Bloom 2017

Study characteristics

Methods	Country: USA Recruitment: “Participants were recruited from newspaper and radio advertisements.” Setting: Not specified Study start date: Not specified; Study end date: Not specified

2 Bloom 2017 *(Continued)*

Participants	Total N: 61 participants 18 – 65 years old, smoked ≥ 10 cpd and had not engaged in regular aerobic exercise (≥ 20 min/day on ≥ 3 days/wk) for ≥ 6 months N per arm: Health Education programme Control = 31; Aerobic Exercise programme = 30 65.6% female, av age 47.3, av baseline BMI: 28.7, av cpd 19.9, av FTND 5.8
Interventions	• Health education (weekly hour-long health information sessions conveyed through lectures, handouts, in-group exercises, and Internet resources) + financial incentives • Aerobic exercise programme (12 weekly group, supervised exercise sessions at a fitness facility) + cognitive–behavioral counselling (20-min weekly group sessions) + financial incentives All participants recieved telephone counselling smoking cessation treatment delivered in 8 x 20-min weekly telephone counselling sessions beginning in week 1 of the intervention + 8 weeks of transdermal nicotine patch (Nicoderm CQ, 24-hr TNPs (21-mg strength for weeks 5 – 8, 14-mg strength for weeks 9 – 10, and 7-mg strength for weeks 11 – 12))
Outcomes	The following outcomes were measured during the trial but were not available for extraction at the time of this update • Mean (SD) weight change (kg) in abstainers at EOT, 6 and 12 months
Study funding	"This work was supported by the National Institute on Drug Abuse [grant number K23 DA019950] awarded to Ana M. Abrantes, PhD."
Author declarations	"No potential conflict of interest was reported by the authors."
Notes	This study is new to the 2021 update.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Upon receiving medical clearance to exercise, participants were assigned to one of two conditions using urn randomization (Stout, 1988), with body mass index (BMI), level of nicotine dependence, gender, and age included as blocking variables…"
Allocation concealment (selection bias)	Unclear risk	Not specified
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "Self-reported 7-day point prevalence abstinence at follow-ups was verified by expired carbon monoxide (CO; < 10 ppm cutoff) or, in one instance, by the report of a family member of the participant because the participant was unable to provide CO."
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: "Height and weight was obtained by utilizing a Detecto medical scale."
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "Assessments occurred at baseline, 3(EOT)-, 6-, and 12-month follow-ups, with 85%, 80%, and 74% completion rates, respectively."

2 Bohadana 2000

Study characteristics	
Methods	Country: France Recruitment: community volunteers Study start date: March 1996; Study end date: Feburary 1998
Participants	400 smokers, 18 - 70 yrs, 51% F, Av cpd: Group 1 26.1, Group 2 23.5; FTND > 6
Interventions	• Nicotine inhaler, 26 wks, combined with nicotine patch (15 mg/16hr) for first 6 wks, placebo patch for next 6 wks • Nicotine inhaler, 26 wks, placebo patch for first 12 wks All received brief counselling and support from investigator at each visit
Outcomes	Mean (SD) weight change (kg) in prolonged abstainers at end of treatment (email communication) and 12 m (email communication) (validation: CO < 10 ppm)
Study funding	"This study was supported by a grant from Pharmacia & Upjohn Consumer Healthcare, Helsingborg, Sweden"
Author declarations	Not specified
Notes	Prolonged abstinence defined as validated self-report from 2 wks

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated code
Allocation concealment (selection bias)	Low risk	Quote: "sealed randomisation envelopes were provided for each subject and were held by the hospital pharmacy, which was responsible for dispensing medication"
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double-blind, placebo-controlled. No further information given
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "self-reported nonsmoking between week 2 and month 12 and an expired carbon monoxide level less than 10 ppm." Comment: Smokers not attending follow-up were classified as relapsing smokers
Blinding of outcome assessment (detection bias) Weight	Unclear risk	Unclear how weight was measured and also unclear if participants were blinded to treatment allocation
Incomplete outcome data (attrition bias) All outcomes	High risk	24-wk completion active patch group: 67/200 (33.5%); 24-wk completion placebo patch group: 66/200 (33%); 48-wk completion active patch group: 52/200 (26%); 48-wk completion placebo patch group: 45/200 (22.5%)

2 Bolliger 2011

Study characteristics	
Methods	Country: Multiple sites in Latin America Recruitment: Not specified Study start date: 10 April 2008; Study end date: 17 August 2009
Participants	Total N: 588 N per arm: Varenicline = 390; Placebo = 198 40% female, av age 43.4, av baseline weight 75.5 kg, av baseline BMI 26.4, av cpd 23.7, av FTND 6
Interventions	• 12 weeks of varenicline treatment: 1 week of dose titration (0.5 mg once daily for 3 days followed by 0.5 mg twice a day for 4 days) followed by 11 weeks of varenicline 1 mg twice a day • Placebo (matching tablets and regimen) All participants provided with *You can Quit Smoking* education booklet, brief 1-2-1 smoking cessation advice counselling (up to 10 minutes) at each visit during treatment and follow-up phases. Assigned TQD – first scheduled treatment visit. 3 days after TQD phone call with brief counselling. Clinic assessment visits at weeks 2, 3, 4, 6, 8, 10, 12 (treatment phase) and 13, 16, 20, 24 (non-treatment follow-up phase), Telephone assessments at week 14, 18, 22
Outcomes	• Mean (SD) weight change (kg) at EOT (week 12) and 24 weeks in abstainers (CO ≤ 10 ppm validated 4-week continuous abstinence rate (CAR) at weeks 9 to 12 and weeks 9 to 24)
Study funding	"This work was supported by Pfizer Inc, which was the sponsor and funding source for the clinical trial reported here"
Author declarations	All of the authors completed the Unified Competing Interest form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare that: (1) the institutions of Drs. Bolliger, Issa, Posadas-Valay, and Safwat received financial support from Pfizer for the clinical trial; (2) Drs. Bolliger, Issa, Posadas-Valay, and Safwat received no financial support from Pfizer for the submitted work; (3) Drs. Bolliger, Issa, Posadas-Valay, and Safwat have specified relationships with Pfizer that might have an interest in the submitted work in the previous 3 years, including investigator payments, consulting honoraria, and grants; (4) their spouses, partners, and children have no financial relationships that may be rele- vant to the submitted work; and (5) Drs. Bolliger, Issa, Posadas-Valay, and Safwat have no nonfinancial interests that may be relevant to the submitted work. Drs. Bolliger, Issa, Posadas-Valay, and Safwat did not receive financial support with respect to the writing or development of the manuscript. Dr. Abreu, Mr. Correia, Dr. Park, and Mr. Chopra are employees of, and stockholders in, Pfizer. Dr. Abreu and Mr. Chopra participated in the design of the study. Drs. Bolliger, Issa, Posadas-Valay, and Safwat participated in the collection of data. Dr. Abreu, Mr. Correia, and Mr. Chopra were involved in data analysis. All of the authors were involved in interpretation of data, drafting the article, reviewing the article for important intellectual content, and the decision to submit the article for publication. Drs. Bolliger, Issa, Posadas-Valay, and Safwat acted as investigators for this study and were remunerated for this role. They did not receive honoraria for this publication. All of the authors had full access to all of the data (including statistical reports and tables) in the study and are responsible for the integrity of the data and the accuracy of the data analysis. Dr. Bolliger was the guarantor of the study. Pfizer was involved in study design; in the collection, analysis, and interpretation of data; in the writing of the report; and in the decision to submit the article for publication. Editorial assistance (proofreading, collation of review comments, formatting the manuscript for submission, preparation of figures, and formatting of references) was provided by Penny Gorringe, MSc, and Fiona Nitsche, PhD, of UBC Scientific Solutions and was funded by Pfizer.
Notes	This study is new to the 2021 update
Risk of bias	

2 Bolliger 2011 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Using a block randomization within each site, eligible participants were randomly assigned in a 2:1 ratio to receive varenicline or placebo"
Allocation concealment (selection bias)	Low risk	Quote: "a web-based or telephone call-in drug management system directed by the sponsor"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "All of the study personnel and participants were blinded to treatment assignment until the end of the nontreatment follow-up phase" + placebo-controlled
Blinding of outcome assessment (detection bias) Smoking	Low risk	CO-validated 4 week CAR ('not a puff' rule enforced)
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: "Vital signs and weight were measured at each clinic visit throughout the study period" Comment: self-reported weight assessment cannot be ruled out, but participants were blinded to treatment allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "A total of 336 of 394 (85.3%) participants assigned to receive varenicline and 156 of 199 (78.4%) assigned to receive placebo completed the study. Overall, the study-completion rates at week 24 were 336 of 390 (86.2%) in the varenicline group and 156 of 198 (78.8%) in the placebo group. Overall, 54 (13.8%) participants in the verenicline and 42 (21.2%) participants in the placebo arm discontinued the study"

2 CEASE 1999

Study characteristics	
Methods	Country: Multicentre - 36 clinic centres in 17 European countries Recruitment: community volunteers Study start date: January 1994; Study end date: December 1995
Participants	3575 smokers 48% female, av age 41, av cpd 27, av weight 71 - 73 kg
Interventions	Factorial design compared 2 patch doses and 2 treatment durations. Dose 15 mg or 25 mg (16 hr), duration of active treatment 28 wks (incl 4 wk fading) or 12 wks (incl 4 wk fading) • 25 mg patch for 28 wks (L-25) • 25 mg patch for 12 wks (S-25) • 15 mg patch for 28 wks (L-15) • 15 mg patch for 12 wks (S-15) • Placebo All participants received brief advice and self-help brochure
Outcomes	Mean (SD) weight change (kg) in prolonged abstainers at end of treatment (email communication) and 12m (email communication) (validation: CO < 10 ppm)

2 CEASE 1999 *(Continued)*

Study funding	"This trial was conducted on behalf of the ERS by the Occupational and Epidemiology Assembly and with the sponsorship of Pharmacia & Upjohn, Helsingborg, Sweden"
Author declarations	Not specified
Notes	Prolonged abstinence defined as validated self-report from 2 wks Doses and durations collapsed in main analyses

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Stratified only by centre
Allocation concealment (selection bias)	Low risk	Quote: "A computer-generated allocation list was prepared centrally and allocated subjects to treatment numbers"
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double-blind, placebo-controlled. No further information given
Blinding of outcome assessment (detection bias) Smoking	Low risk	CO level < 10 ppm
Blinding of outcome assessment (detection bias) Weight	Unclear risk	Unclear how weight was measured and also unclear if participants were blinded to treatment allocation.
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: “Of the participants, 867 (24%) completed the study at 12 months and 2,708 (76%) withdrew during the 12 months. Reasons for withdrawal were: never stopped smoking (122; 3%), started smoking (1,089; 30%), elevated CO (43; 1%), not willing to continue in study (250; 7%), adverse events (73; 2%), exclusion criteria (20; 1%), and other or several reasons (320; 9%). The remaining group consisted of 769 (22%) subjects lost to follow-up i.e. either no contact despite at least two telephone calls, or who withdrew by telephone.”

2 Chengappa 2014

Study characteristics

Methods	Country: USA Recruitment: recruited from Western Psychiatric Institute and Clinic and Dubois Regional Medical Center Setting: Not specified Study start date: January 2010; Study end date: March 2013
Participants	Total N: 60 smokers diagnosed with DSM-IV bipolar disorder aged between 18 - 65 years, smoking > 10 cpd with expired breath CO level > 10 ppm at screening and randomization. Women of child-bearing potential must have a negative serum and must agree to a birth control method N per arm: placebo = 29; varenicline = 31

2 Chengappa 2014 *(Continued)*

	68.3% female; av age 46.0, av baseline weight 91.1 kg, av cpd 18.2, av FTND 6.2
Interventions	1. Placebo for 12 weeks 2. Varenicline (Chantix) 2 x 1.0 mg per day for 12 wks All participants recieved cognitive-behavioural counselling for smoking cessation (15-min sessions face-to-face counselling)
Outcomes	Data measured during the trial but not available for extraction at the time of this update • Mean (SD) weight change (kg) in abstainers at EOT, 6 and 12 months
Study funding	"The National Institute of Mental Health (NIMH) of the NIH, under award R21MH087928 (Dr Chengappa), provided the main funding for this study. Pfizer provided drug/placebo and an investigator- initiated grant, WS-515343 (Dr Chengappa). These monies channeled through the University of Pittsburgh were used to offset costs of study procedures, participant payments, and a percentage of the time and effort of research staff and faculty salaries. Role of the sponsor: Neither the NIMH of the NIH nor Pfizer had a role in the conduct or the publication of the study. As part of the letter of agreement with Pfizer, they reviewed the original manuscript that was submitted but did not request changes to the content."
Author declarations	"Dr Turkin has served on the speaker'bureau of Forest, Sunovion, and Otsuka; and owns shares of Pfizer stock. Dr George has received investigator-initiated and contract research support from Pfizer, served as a consultant to Novartis, and received honoraria from National Institutes of Health (NIH) and American College of Neuropsychopharmacology. Drs Chengappa, Perkins, Brar, and Levine, and Mss Schlicht and Hetrick and have no financial disclosures with regards to this study."
Notes	This study is new to the 2021 update.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Using a 1:1 Randomization, which also takes into account gender, subjects who sign an informed consent document will be randomized to receive Chantix or placebo." "We will be using placebo in a randomized, controlled, and blinded trial to compare to varenicline in subjects with bipolar disorder"
Allocation concealment (selection bias)	Unclear risk	Not specified
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "The treatment assignment was blinded to participating subjects, raters, investigators, and statisticians."
Blinding of outcome assessment (detection bias) Smoking	Low risk	Biochemically-verified abstinence (CO < 10 ppm)
Blinding of outcome assessment (detection bias) Weight	Low risk	Unclear how weight was measured, but participants were blinded to treatment allocation

2 Chengappa 2014 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "The dropout rate in the current 24-week study was 23% in the varenicline arm and 31% among the placebo- assigned subjects. (…) 80% completed the 12-week treatment phase and 73% completed the follow-up“

2 Ciccolo 2011

Study characteristics	
Methods	Country: USA Recruitment: newspaper, Internet, and television advertisements Study start date: Not specified; Study end date: Not specified
Participants	Total N: 25 N per arm: Exercise = 13; Control = 12 52% female, av age 36.5, av baseline weight 81.8 kg, av cpd 18, av FTND 4.0
Interventions	• Exercise group: Resistance training with equipment for 12 weeks: alone, facility, 60 min, 2 times/week for 12 weeks, 10 exercises, 65 - 75% est max, 10 reps, weeks 1 - 3: 1 set, weeks 4 - 2: 2 sets • Control group: 25 min health education video watched 2 times/week for 12 weeks Prior to randomization, all ppts received a 15 - 20 mins cessation support and nicotine patches (total 8 weeks)
Outcomes	Data measured during the trial but not available for extraction at the time of this update • Mean (SD) weight change (kg) in abstainers at EOT (3 months) and 6 months
Study funding	"National Cancer Institute (R03 CA132475 to J.T.C.)"
Author declarations	"None declared"
Notes	This study is new to the 2021 update.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomly-generated by a computer
Allocation concealment (selection bias)	Unclear risk	No detail given
Blinding of outcome assessment (detection bias) Smoking	Low risk	Validated 7-day PPA
Blinding of outcome assessment (detection bias) Weight	Unclear risk	Not described how body weight was measured. Likely to be objectively assessed, but self-report cannot be ruled out

2 Ciccolo 2011 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	High risk	16 week completion resistance training group: 12/13 (92.31%); 16 week completion control group: 11/13 (84.81%); 24 week completion resistance training group: 7/13 (53.84%); 24 week completion control group: 6/13 (46.15%)

2 Cox 2012

Study characteristics	
Methods	Country: USA Recruitment: Clinic- and community-based efforts Study start date: 27 December 2007; Study end date: 13 May 2010
Participants	Total N: 540 African-American light smokers (< 10 cpd) N per arm: Arm 1: 270; Arm 2: 270 66.1% female, av age 46.5, av baseline weight 88.7 kg, av baseline BMI 31.1,av cpd 8, av FTND 3.2
Interventions	• 300 mg bupropion 7 wks • Placebo 7 wks All participants received a total of 6 x 15 - 20 mins health education counselling by trained counsellors at weeks 0, 1, 3, 7 in person and weeks 5 and 16 by telephone and a culturally-targeted smoking cessation guide developed for African-American light smokers (Kick It at Swope: Stop smoking Guide)
Outcomes	1. Mean (SD) weight change (kg) at EOT (7 weeks) and 6 months in abstainers (cotinine-verified 7-day point prevalence)
Study funding	"This work was supported by the National Cancer Institute at the National Institutes of Health (CA 091912 to L.S.C.). This work was also supported in part by the National Institute for Minority Health and Disparities (1P60MD003422 to J.S.A.). Support was also provided by the Centre for Addiction and Mental Health and by a Canada Research Chair in Pharmacogenetics (to R.F.T.)"
Author declarations	"Dr J. S. Ahluwalia serves as a consultant to Pfizer Pharmaceuticals, Inc; Dr N. L. Benowitz serves as a consultant to Pfizer Pharmaceuticals, Inc, and has been a paid expert witness in litigation against tobacco companies; Dr R. F. Tyndale holds shares in Nicogen Research, Inc, a company that is focused on novel smoking cessation treatment approaches; no Pfizer or Nicogen funds were used in this work"
Notes	This study is new to the 2021 update.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	A computer-generated table of random numbers was used to randomly assign ppts to intervention or control
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Specified who was blinded: Quote: “Study staff and participants were blinded to treatment condition” + Placebo controlled: Quote: “Participants received 7 weeks of pharmacotherapy (bupropion SR or placebo)“

2 Cox 2012 *(Continued)*

Blinding of outcome assessment (detection bias) Smoking	Low risk	Cotinine-verified 7-day PPA
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: "Study staff verbally administered all self-report measures. Demographic information included age, sex, marital status, income, employment status, and education. Height and weight were measured to calculate body mass index (kg/m^2)" Comment: How weight was measured is unclear but both participants and study staff were blinded to treatment condition.
Incomplete outcome data (attrition bias) All outcomes	Low risk	26-week completion bupropion group: 192/270 (71%); 26-week completion placebo group: 187/270 (69%)

2 Dale 1995

Study characteristics	
Methods	Country: USA Recruitment: community volunteers and smoking clinic attenders Study start date: not specified; Study end date: not specified
Participants	71 smokers stratified according to light, moderate and heavy smoking rates. 56% female, av.age 48, av.cpd 26, av weight 79.4 kg
Interventions	• 11 mg/24-hr nicotine patch • 22 mg/24-hr nicotine patch • 44 mg/24-hr nicotine patch • Placebo patch for 1 wk followed by 11 or 22 mg patch for 7 wks Duration of patch use 8 wks. High level of support including 6-day inpatient stay
Outcomes	Mean (SD) weight change (kg) in continuous abstainers at EOT (email communication) and 12 m (email communication) (validation: blood cotinine)
Study funding	"This study was supported by a grant from Lederle Laboratories, Pear River, NY"
Author declarations	"Drs Hurt and Croghan and Mr Offord have worked on clinical research studies funded in part by Lederle Laboratories, Elan Pharmaceutical Research Corporation, Burroughs-Wellcome, and Kabi. Dr Hurt has received honoraria for educational activities from Ciba Geigy Corporation, Marion Merrell Dow, Inc, and McNeil Pharmaceuticals. Mr Offord has received honoraria for educational activities from Elan Pharmaceutical Research corporation"
Notes	

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method not stated

2 Dale 1995 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double-blind, placebo-controlled. No further information given
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "At each visit, self-reported smoking status was obtained, and expired air was tested for carbon monoxide concentration. Self-reported abstinence in the previous 7 days was considered biochemically confirmed if the expired air carbon monoxide level was 8 ppm or lower."
Blinding of outcome assessment (detection bias) Weight	Unclear risk	Unclear how weight was measured and also unclear if participants were blinded to treatment allocation
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not specified

2 Dogar 2018

Study characteristics	
Methods	Country: Bangladesh and Pakistan Recruitment: Sites were designated tuberculosis treatment centres run by the national tuberculosis control programmes of Bangladesh and Pakistan and were chosen on the basis of having the required resources and ability to recruit participants and take part in the research. Setting: "TB treatment centres integrated into public health care systems in Bangladesh and Pakistan." 30 sites in Bangladesh (17) and Pakistan (13) Study start date: 1 November 2015; Study end date: 31 October 2019
Participants	Total N: 2471 newly-diagnosed (in the last 4 weeks) pulmonary tuberculosis patients aged 15 years (18 years for Bangladesh) and above, who have been smoking tobacco on a daily basis and wish to quit N per arm: Placebo = 1233; Cytisine = 1239 1% female, av age 42.5, av baseline BMI 18.6, av cpd 11.1
Interventions	• Placebo • Cytisine: standard 25-day course with start drug dose of 9 mg cytisine (Desmoxan; Aflofarm, Pabianice, Poland) administered orally as 6 x 1.5 mg capsules per day, which was gradually reduced to 1.5 mg (1 capsule) by day 25, with a quit date set for day 5 All participants recieved 2 x face-to-face behavioural support sessions on days 0 and 5 (for 10 mins and 5 mins, respectively) by the clinical team (Health Worker/TB paramedic). Further encouragement and support offered, if needed, at the week 5 visit.
Outcomes	The following outcomes were measured during the trial but were not available for extraction at the time of this update • Mean (SD) weight change (kg) in abstainers at EOT, 6 and 12 m

2 Dogar 2018 *(Continued)*

Study funding	"This project has received funding from the European Union's Horizon 2020 research and innovation programme, under Grant Agreement No. 680995. Aflofarm Pharma Poland provided cytisine (Desmoxan) and placebo free of cost for the trial; however, they have no role in the trial conduct, its analysis or dissemination of results."
Author declarations	"K.S. received a research grant from Pfizer (2015–2017) to study the effect of varenicline (a smoking cessation medicine) on waterpipe smoking cessation. E.K. received payment from pharmaceutical companies providing smoking cessation medications for clinical studies, educational and consultation activities.
Notes	"Participants will not receive financial incentives except nominal travel costs for any follow-up visits that fall outside routine TB care." This study is new to the 2021 update.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Allocation to the trial arms is by pre-prepared block randomization lists for each country, generated by the trial statistician."
Allocation concealment (selection bias)	Low risk	Quote: "Allocation to the trial arms is by pre-prepared block randomization lists for each country, generated by the trial statistician. IMP packs are labelled sequentially in their randomized order and distributed to trial sites in batches. Once a patient has consented to participate, the researcher at the site calls the country coordinating office to obtain the patient's allocated trial number and confirm the next IMP pack number in the sequence to dispense to the patient."
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Investigators, clinicians, and patients were masked to treatment allocation. To maintain masking, medication packs were identical and cytisine and placebo capsules were identical in appearance, smell, and taste. Codebreak envelopes were prepared separately for each medication pack, which contained the true allocation, for emergency unmasking as per the protocol."
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "Self-report of not using more than five cigarettes/bidis/water pipe sessions/chewing tobacco products from the quit date (5 +/ 2 days) to the reporting date, supported by a negative biochemical test at 6 months."
Blinding of outcome assessment (detection bias) Weight	Unclear risk	Not specified
Incomplete outcome data (attrition bias) All outcomes	Low risk	6-months follow-up: Placebo: 1130/1233*100 = 91.6% Cytisine: 1142/1239*100 = 92.3% 12 months follow-up: Placebo: 1056/1233*100 = 85.6% Cytisine: 1048/1239*100 = 84.6% Quote: "Of the 2472 patients enrolled, 1142 (92%) of 1239 patients in the cytisine group and 1130 (92%) of 1233 patients in the placebo group completed the 6-month follow-up assessment."

2 Ebbert 2014

Study characteristics	
Methods	Country: USA Recruitment: Not specified Study start date: October 2009; Study end date: April 2013
Participants	Total N: 506 N per arm: varenicline plus bupropion = 249; varenicline plus placebo group = 257 47% females, av age 42.0, av cpd 20, av FTND 5.2
Interventions	• 12 wks varenicline (2 mg/d) and bupropion SR (300 mg/d) • 12 wks varenicline (2 mg/d) and placebo All participants received 11 clinic visits with brief (≤ 10 mins) behavioural counselling and 3 follow-up telephone calls. Medication started day after baseline visit and titrated up to full dose, and TQD was day 8
Outcomes	• 1. Mean (SD) weight change (kg) at EOT (12 wks), 26-wk and 52-wk follow-up in abstainers (CO ≤ 8 ppm prolonged abstinence from 2 weeks after TQD)
Study funding	"The clinical trial was supported by National Institutes of Health (NIH) grant CA 138417 (primary investigator, Dr Ebbert). Medication (varenicline) was provided by Pfizer. Role of the Sponsors: NIH and Pfizer had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication"
Author declarations	"All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr Ebbert reports serving as an investigator for clinical trials funded by Pfizer, receipt of consultancy fees from GlaxoSmithKline, research support from Pfizer, and research support from Orexigen and JHP Pharmaceuticals outside of the current study. Dr Hatsukami reports receipt of research support from Nabi Biopharmaceuticals outside of the current study. Dr Hays reports serving as an investigator for clinical trials funded by Pfizer. Dr Hurt reports receipt of consulting fees from Pfizer, an unrestricted grant from Pfizer Medical Education Group, and provision of expert testimony in Florida tobacco litigation cases. The other authors report no disclosures"
Notes	This study is new to the 2021 update.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	A central pharmacy randomly assigned study medication in a 1:1 ratio using a computer-generated randomization sequence with variable-sized blocks ranging from 2 to 8 stratified by study site
Allocation concealment (selection bias)	Low risk	A central pharmacy randomly assigned study medication in a 1:1 ratio using a computer-generated randomization sequence with variable-sized blocks ranging from 2 to 8 stratified by study site
Blinding of participants and personnel (performance bias)	Low risk	Study medication was labelled and dispensed according to participant identification, ensuring that treatment assignment remained concealed from the participant, investigators, and all study personnel having participant contact

2 Ebbert 2014 *(Continued)*
All outcomes

Blinding of outcome assessment (detection bias) Smoking	Low risk	Biochemically-confirmed (CO 8 ppm or less) prolonged abstinence (no smoking from 2 weeks after TQD)
Blinding of outcome assessment (detection bias) Weight	Low risk	Unclear how weight was assessed. Likely to be objective, but self-report cannot be ruled out. Quote: "During clinic visits, participants received brief (≤10 minutes) behavioral counseling,12 and tobacco use status, vitals signs, exhaled-air carbon monoxide (CO) measurements (measured in parts per million [ppm]), and weight were obtained." Participants and personnel were blinded to treatment condition
Incomplete outcome data (attrition bias) All outcomes	Low risk	12-wk completion varenicline + bupropion SR group: 182/249 (73%); 12-wk completion varenicline group: 184/257 (71%); 52-wk completion varenicline + bupropion SR group: 158/249 (63%); 52 wk completion varenicline group: 157/257 (61%)

2 Ebbert 2015

Study characteristics	
Methods	Country: Australia, Canada, Czech Republic, Egypt, Germany, Japan, Mexico, Taiwan, UK, and USA Recruitment: Advertisments Setting: clinical trial centres, academic centres, and outpatient clinics (61 centres in 10 countries) Study start date: July 2011; Study end date: July 2013
Participants	Total N: 1510 smokers aged ≥ 18, smoking an average of ≥ 10 cpd with no continuous abstinence period > 3 months in the previous year, had an exhaled CO > 10 ppm and wished to quit smoking gradually rather than abruptly N per arm: Placebo = 750; Varenicline = 760 43.6% females, av age 44.6, av cpd 20.7, av FTND 5.6
Interventions	• Placebo for 24 weeks (12 weeks reduction, 12 weeks post-quit attempt) • Varenicline for 24 weeks (12 weeks reduction, 12 weeks post-quit attempt); Day 0 - 3: 0.5 mg once daily; Day 4 - 7: 0.5 mg twice daily; Day 8 - end of treatment at 24 weeks: 1 mg twice daily; Tolerability issues resulted in temporary or permanent lowering of dosage to 0.5 mg All participants recieved tailored counselling for treating tobacco use and dependence: ≤ 10 minutes per visit, 18 in-person clinic visits, 10 telephone visits + *Clearing the Air – Quit Smoking Today* booklet
Outcomes	The following outcomes were measured during the trial but were not available for extraction at the time of this update. • Mean (SD) weight change (kg) in abstainers at EOT (week 24)
Study funding	This study was funded by Pfizer Inc.; Pfizer Inc was involved in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, and approval of the manuscript; and decision to submit the manuscript for publication.

2 Ebbert 2015 *(Continued)*

Author declarations	The authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr. Ebbert reports grants from Pfizer, Orexigen and JHP Pharmaceuticals and personal fees from GlaxoSmithKline during the conduct of the study. Dr. Hughes reports personal fees from Alere/ Free and Clear, Equinox, GlaxoSmithKline, Healthwise, Pfizer, Embera, Selecta, DLA Piper, Dorrffermeyer, Nicoventures, Pro Ed, Publicis, Cicatelli, and non-financial support from Swedish Match, outside the submitted work. Dr. West reports grants, personal fees and non-financial support from Pfizer, GlaxoSmithKline, and Johnson & Johnson outside the submitted work. Dr. Rennard reports personal fees from Almirall, Novartis, Nycomed, Pfizer, A2B Bio, Dalichi Sankyo, APT Pharma/Britnall, AstraZeneca, Boehringer Ingelheim, Chiesi, Decision Resource, Dunn Group, Easton Associates, Gerson, GlaxoSmithKline, Roche, Theravance, Almirall, CSL Behring, MedImmune, Novartis, Pearl, Takeda, Forest, CME Incite, Novis, PriMed, Takeda, grants from AstraZeneca, Novartis, Otsuka, Boehringer Ingelheim, GlaxoSmithKline, and Johnson & Johnson, outside the submitted work. Dr. Russ, Dr. McRae, Ms. Treadow, Dr. Yu, Dr. Dutro, and Dr. Park are employees and stock holders of Pfizer Inc.
Notes	This study is new to the 2021 update.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Participants were randomized (…) in a 1:1 ratio using a computer-generated block randomization schedule within site.“
Allocation concealment (selection bias)	Low risk	Quote: "Investigators obtained participant identification numbers and treatment group assignments through a web- based or telephone call-in drug management system.“
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Participants, investigators, and research personnel were blinded to randomization until after the database was locked.“
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "CO-confirmed continuous smoking abstinence rate (CAR)”
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: "Body weight will be measured at the screening and baseline visits and at the Weeks 12 and 24 visits (or ET24). Height will be measured at the screening visit. Both will be measured in indoor clothing without shoes.“
Incomplete outcome data (attrition bias) All outcomes	Low risk	Flowchart: Study completion placebo group: 516/750; Study completion varenicline group: 559/760

2 Ehrsam 1991

Study characteristics

Methods	Country: Switzerland Recruitment: University (primary care) Study start date: not specified; Study end date: not specified
Participants	112 smokers Av.age 26, av cpd 23
Interventions	• Nicotine patch (21 or 14 mg/24-hr, 9 wks, tapered)

2 Ehrsam 1991 *(Continued)*

	• Placebo patch
Outcomes	Mean (SD) weight change (kg) in abstainers at the end of treatment
Study funding	Not specified
Author declarations	Not specified
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double-blind, placebo-controlled. No further information given
Blinding of outcome assessment (detection bias) Smoking	Low risk	CO < 12 ppm, cotinine < 100 ng/ml
Blinding of outcome assessment (detection bias) Weight	Unclear risk	Unclear how weight was measured, self-report cannot be ruled out (although unlikely, as face-to-face visits with doctors were conducted to assess CO, take pictures of the skin where the patch was and weight was "assessed")
Incomplete outcome data (attrition bias) All outcomes	High risk	36% dropouts in the experimental group vs 55% dropouts in the placebo group. This difference was significant

2 Eisenberg 2013

Study characteristics

Methods	Country: Canada Recruitment: Based on admission to hospital Study start date: Not specified; Study end date: Not specified
Participants	Total N: 392 participants hospitaliezd with acute myocardial infarction N per arm: bupropion = 192; placebo = 200 16.5% female, av age 53.9, av baseline weight 78.2 kg, av baseline BMI 27.3, av cpd 23.2, median FTND 4 - 6
Interventions	• Bupropion 300 mg/day for 9 wks (150 mg for 3 d, then 150 mg 2 x d for remainder) • Placebo on same schedule

2 Eisenberg 2013 *(Continued)*

	Both arms: 7 x one-to-one counselling sessions by research nurses at baseline and all follow-ups of < 20 mins (avg. 5) - mix of phone and in-person
Outcomes	• Mean (SD) weight change (kg) at EOT (9 weeks), 6 and 12 m in abstainers (CO ≤ 10 ppm validated continuous abstinence at 12 months)
Study funding	"This study was funded by the Canadian Institutes of Health Research (Grant NCT64989) and the Heart and Stroke Foundation of Quebec. The funding organizations were not involved in the design and conduct of the study; in the collection, management, analysis, and interpretation of the results; or in the preparation, review, or approval of the manuscript."
Author declarations	"Dr. Pilote is a Chercheur National of the Fonds de la Recherche du Québec-Santé (FRQS). Dr. Pilote also holds a James McGill Chair at McGill University. Dr. O'Loughlin holds the Canada Research Chair in the Early Determinants of Adult Chronic Disease. Dr. Paradis holds a Canadian Institutes of Health Research Chair in Applied Public Health Research. Dr. Rinfret is a Junior 2 Physician-Scientist of the FRQS. Drs. Eisenberg and Gervais reported that they served as paid consultants for Pfizer Canada Inc.'s Varenicline Advisory Board. Dr. Gervais reported that he received funds from Pfizer Canada Inc., for lectures including service on speaker bureaus, development of educational presentations, and travel/accommodations/meeting expenses. Dr. Eisenberg received funding from Pfizer Canada Inc., to perform the Evaluation of Varenicline (Champix) in Smoking Cessation for Patients Post-Acute Coronary Syndrome [EVITA] Trial; NCT00794573). All other authors have reported that they have no relationships relevant to the contents of this paper to disclose. "
Notes	Participants were not allowed to smoke whilst hospitalized This study is new to the 2021 update.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Randomization was done via an internet website using random blocks of 2 and 4 and was stratified by center to ensure that similar numbers of patients were randomized to the 2 arms of the study at each study center"
Allocation concealment (selection bias)	Low risk	Allocation performed centrally, see above
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Double-blind." Quote: "All clinical end points were adjudicated by members of the Endpoints Evaluation Committee who were blinded to treatment assignment." Comment: No further information provided
Blinding of outcome assessment (detection bias) Smoking	Low risk	Biochemically-confirmed continuous abstinence
Blinding of outcome assessment (detection bias) Weight	Low risk	Not specified, but participants were blinded to treatment allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	52-week completion bupropion group: 146/192 (76.04%); 9-52-week completion placebo group: 159/200 (79.5%)
Other bias	High risk	Data on weight at all time points is only for those abstinent at 12 months

2 Eisenberg 2016

Study characteristics	
Methods	Country: Canada and the United States Recruitment: "Enrolment took place during hospital admission for acute coronary syndrome, including myocardial infarction and unstable angina with clinically significant coronary artery disease." Setting: 40 clinical centres Study start date: September 2009; Study end date: December 2015
Participants	Total N: 302 active smokers (≥ 10 cpd on average for the past year), ≥ 18 years, suffered an acute coronary syndrome (ACS) and hospitalized and motivated to quit smoking N per arm: Placebo = 151; Varenicline = 151 24.8% female, av age 55, av baseline weight 86.5, av cpd 21.5
Interventions	• Low-intensity counselling plus placebo for 12 weeks • Low-intensity counselling plus varenicline (Champix; Day 0 - 3: 0.5 mg once daily; Day 4 - 7: 0.5 mg twice daily; Day 8 - 12 weeks: 1 mg twice daily) All participants recieved ≥ 5 mins smoking cessation or relapse-prevention counselling (face-to-face and telephone) plus educational materials. Following completion of the 12-wk treatment period, participants who relapsed could use open-label smoking cessation therapies
Outcomes	• Mean (SD) weight change (kg) in abstainers at EOT, 6 and 12 months
Study funding	EVITA was an investigator-initiated trial, which received funding and study drug/placebo from Pfizer Inc. Pfizer Inc had no role in the design, conduct, analysis, interpretation of data, or reporting of the EVITA trial
Author declarations	Drs Eisenberg, Dehghani, and Madan received honoraria from Pfizer Inc for providing continuing medical education on smoking cessation. The other authors report no conflicts. From Windle 2018 #707: Shamir Mehta reports funding from AstraZeneca, Boston Scientific, Bayer and Abbott. Beth Abramson has received grants or research support from AstraZeneca and Sanofi; honoraria from Amgen, AstraZeneca, Boehringer Ingelheim, Bristol–Myers Squibb, Novartis, Fournier, Merck, Pfizer, Servier and Sanofi; and consulting fees from Amgen, Bayer, Boehringer Ingelheim, Sanofi and Servier. She authored *Heart Health for Canadians*.
Notes	Participants were also permitted to seek counselling outside of the study; however, only 2.7% of participants did so at any point (equal in each treatment arm) Following the 12-week treatment period, participants who had relapsed were also permitted to use nonstudy pharmacotherapy treatments for smoking cessation. Use of a nonstudy treatment at any point in the trial was 18.3% overall (14.9% in the varenicline group v. 21.8% in the placebo group) Additional information provided by authors upon request This study is new to the 2021 update.

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**

2 Eisenberg 2016 *(Continued)*

Random sequence generation (selection bias)	Low risk	Quote: “Randomization was performed by enrolling center personnel and stratified by center using a computer-generated list of permuted blocks of 2 and 4."
Allocation concealment (selection bias)	Unclear risk	Quote: "Computer-generated permutated block randomization was used to produce comparable groups and conceal treatment allocation.“ Comment: No further information given
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: “Participants and study personnel are blinded to participant treatment allocation“
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: “Point prevalence smoking abstinence was defined by self-report of complete abstinence in the 7 days before the 24 week clinic visit confirmed by a measured exhaled carbon monoxide ≤10 ppm.”
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: "Participants’ heights and weights were measured at baseline. At each clinic visit, a research nurse also measured weight and assessed participants’ smoking status. We calculated body mass index (BMI) using the standard formula (weight in kilograms divided by height in square meters)“
Incomplete outcome data (attrition bias) All outcomes	Low risk	24-week completion rate placebo group: 114/151 24-week completion rate varenicline group: 118/151 (3 died)

2 Fiore 1994A

Study characteristics	
Methods	Country: USA Recruitment: community volunteers Study start date: Not specified; Study end date: Not specified
Participants	88 smokers, av cpd 28 - 31, av age 42 - 44 yrs, av weight 79 - 81 kg
Interventions	• Nicotine patch (22 mg/24-hr, 8 wks, no weaning) • Placebo patch All participants received intensive group counselling
Outcomes	Mean (SD) weight change (Kg) in point prevalence abstainers at EOT (email communication) (validation: CO < 10 ppm)
Study funding	"This study was supported by a research grant provnided by Elan Pharmaceutical Research Corporation, Gainesville, Ga, and Athlone, Ireland"
Author declarations	Not specified
Notes	PPA was defined as validated self-reported abstinence for 7 days prior to measurement Different participants to 2 Fiore 1994B added in separately in the main comparison
Risk of bias	

2 Fiore 1994A *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Pregenerated computer sequence
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double-blind, placebo-controlled. No further information given
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: “abstinence was defined as a self-report of zero cigarettes smoked in the preceding 7 days, confirmed by a CO value of <10 ppm”
Blinding of outcome assessment (detection bias) Weight	Unclear risk	Unclear how weight was measured, and also unclear if participants were blinded to treatment allocation
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: “Of the 88 subjects who were enrolled and randomized, 77 completed the cessation treatment phase (first 8 weeks on study). Of the the 11 who failed to complete treatment, 10 had placebo patches and 1 had active treatment. Of the 87 subjects (one disqualified due to nicotine gum use), 62 were interviewed at the 6-month follow-up mark.”

2 Fiore 1994B

Study characteristics	
Methods	Country: USA Recruitment: community volunteers Study start date: Not specified; Study end date: Not specified
Participants	112 smokers, av age 43 - 45 yrs, av weight 72 - 73 kg
Interventions	• Nicotine patch (22 mg/24-hr, 6 wks incl weaning) • Placebo patch All participants received x 8 weekly 10 - 20 min individual counselling
Outcomes	Mean (SD) weight change (kg) in point prevalence abstainers at end of treatment (email communication) (validation: CO < 10 ppm)
Study funding	"This study was supported by a research grant provided by Elan Pharmaceutical Research Corporation, Gainesville, Ga, and Athlone, Ireland"
Author declarations	Not specified
Notes	PPA was defined as validated self-report abstinence for 7 days prior to measurement Different participants to 2 Fiore 1994A added in separately in the main comparison
Risk of bias	

2 Fiore 1994B *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Pregenerated computer sequence
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double-blind, placebo-controlled. No further information given
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote “a CO level >= 10 ppm indicated smoking”
Blinding of outcome assessment (detection bias) Weight	Unclear risk	Unclear how weight was measured and also unclear if participants were blinded to treatment allocation
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: “Of the 112 subjects who were enrolled and randomized, 79 completed the active treatment phase of the study. Of the 33 who failed to complete the treatment phase (first 6 weeks on study), 18 had placebo patches and 15 active treatment. 72 were interviewed at the 6-month follow-up mark.”

2 Gallagher 2007

Study characteristics	
Methods	Country: USA Recruitment: Potential participants were identified by LFC case management staff or self-referred Setting: 3 La Frontera Center case management sites in Tucson, Arizona Study start date: March 2003; Study end date: July 2004 (end of randomisation period)
Participants	Total N: 120 smokers, ≥ 18 years, diagnosed with DSM-IV Axis I psychotic-spectrum or affective disorders that have resulted in long-term mental illness, experienced significant symptoms and functional impairment(s) due to their disorder, smoked ≥ 10 cpd, and regularly for ≥ 3 years and registered a breath CO level ≥ 10 ppm after at least 15 smoke-free minutes at the baseline visit N per arm: Control = 60; CR = 60; CR + NRT = 60 47.7% female, av age 42.9, av cpd 24.5, av FTND 6.1
Interventions	• Self-quit control: 3 face-to-face visits; encouraged to use available community resources (e.g. Smoker's Helpline) and received smoking cessation literature • Contingent reinforcement: 12 face-to-face visits across 3 phases: Phase 1: weekly; Phase 2: bimonthly; Phase 3 monthly over 24 weeks. Participants were compensated USD 25 for completing the baseline and follow-up assessments and earned USD 5 per regular visit for attending and completing study measures. In addition, they received compensation for maintaining abstinence. Participants earned progressively more money for each visit where they demonstrated abstinence • Contingent reinforcement (as per arm 2) for 24 weeks plus nicotine patch (21 mg) for the first 16 weeks

2 Gallagher 2007 *(Continued)*

	All received a brief smoking-related educational information packet and referral to community-based cessation programmes
Outcomes	The following outcomes were measured during the trial but were not available for extraction at the time of this update • Mean (SD) weight change (kg) in abstainers at EOT, 6 and 36 months (longest follow-up)
Study funding	Was funded by the Arizona Biomedical Research Commission (formerly theArizona Disease Control Research Commission), Grant # 7014.
Author declarations	Not specified
Notes	People who attended the baseline assessment session but did not meet inclusion criteria or chose to withdraw at that time received USD 5.00 as compensation for their time and travel. In addition, they received a brief smoking-related educational information packet and referral to community-based cessation programmes. If necessary, participants were provided with bus passes This study is new to the 2021 update.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Participants were randomly assigned to one of the three groups (CR, CR+NRf, self-quit)“ Comment: No further information provided.
Allocation concealment (selection bias)	Unclear risk	Not specified
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "Due to the nature of the intervention groups, research staff were not blind to treatment condition. Ideally, those assessing outcomes should be blind to study condition but because staff delivered immediate reinforcement based on CO outcomes, this was not possible.“ Comment: Participants not blinded and contact control not provided
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "Carbon monoxide in expired air, after at least 15 smoke-free minutes, was assessed at each visit via a Bedfont portable carbon monoxide analyzer. (…) 10 ppm or below is appropriate for a sample with high prevalence (50% or above) of smoking.“ Note: "Quit rates significantly differed between exhaled carbon monoxide level (CO in ppm) and salivary cotinine levels. These data suggest that participants were able to abstain from smoking long enough to register below 10 ppm CO in order to earn the CR. When cotinine was the criterion, quit rates were much lower and lower even than our expectations based on other studies with this population“
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: “Weight, pulse rate and blood pressure were taken at every visit.“
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: “Attrition rates for the groups did not significantly differ at week 20 Cx2=1.39, p= 0.50) nor at week 36 Cx2 = 2.75, p = 0.25). At week 20 and 36 respectively, the CR group lost 37% and 43% of participants, the CR+NRT group lost 35% and 36%, while the self-quit comparison group lost 52% by both follow-up points.”

2 Garvey 2000

Study characteristics	
Methods	Country: USA Recruitment: community volunteers Study start date: Not specified; Study end date: Not specified
Participants	608 smokers, aged > 20, 51% female, avcpd 23, av weight (men) 80 - 81 kg, av weight (women) 64 - 69
Interventions	• 4 mg nicotine gum (recommended 9 - 15 pieces), weaning from 2 m + weaning • 2 mg nicotine gum, use as 1 • Placebo gum All received brief counselling (5 - 10 mins) at each study visit (1, 7, 14, 30 days, 2, 3, 6, 9, 12m)
Outcomes	Mean (SD) weight change (kg) in prolonged abstainers at end of treatment (email communication) (validation: CO ≤ 8 ppm)
Study funding	"Support for this research was provided by Grants DA06183 and DA10073 from the National Institute on Drug Abuse, and by the Department of Veterans Affairs. The Normative Aging Study is supported by the Cooperative Studies Program/ERIC, U. S. Department of Veterans Affairs, and is a research component of the Massachusetts Veterans Epidemiology Research and Information Center (MAVERIC). The authors wish to thank Marion Merrell Dow, Inc. (now Hoechst Marion Roussel, Inc.) for supplying the nicotine gum used in this study"
Author declarations	Not specified
Notes	Prolonged abstinence defined as participants who had not returned to smoking for 7 or more consecutive days or episodes 4 + 2 mg doses combined in main comparison

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method not stated, stratified by high- and low-dependence
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double-blind, placebo-controlled. No further information given
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "Subjects for whom follow-up information was lacking were classified as relapsers; i.e., an intent-to-treat analysis was used. Self-reports of abstinence were considered valid if they were confirmed by CO values of 8 ppm or less.“
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: "Body weight and height were assessed using a standard upright scale, which was calibrated frequently. Height and weight were obtained with shoes off, and heavy outer clothing removed“

2 Garvey 2000 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not specified

2 Gonzales 2006

Study characteristics	
Methods	Country: USA Recruitment: community volunteers Study start date: May 2003; Study end date: April 2005
Participants	1025 smokers, 55% female (placebo), 48% female (bupropion); av age 45, av cpd not specified
Interventions	• Varenicline 1 mg x 2/day for 12 wks • Bupropion 300 mg/day for 12 wks • Placebo All participants received brief individual counselling at visits wks 1 - 7, 9, 12, + telephone counselling at 4 and 5m
Outcomes	Mean (SD) weight change (kg) in prolonged abstainers at EOT (validation: CO < 10 ppm)
Study funding	"This study was supported by Pfizer Inc, which provided funding, study drug and placebo, and monitoring"
Author declarations	"**Financial Disclosures:** Dr Gonzales reports having received research contracts from Pfizer, Sanofi Aventis, GlaxoSmithKline, and Nabi Biopharmaceuticals; consulting fees and honoraria from Pfizer, Sanofi Aventis, and GlaxoSmithKline; and owning 5 shares of Pfizer stock. Dr Rennard reports having had or currently having a number of relationships with companies who provide product and/or services relevant to outpatient management of chronic obstructive pulmonary disease. These relationships include serving as a consultant for Adams, Almirall, Altana, Array Bio- pharma, AstraZeneca, Aventis, Biolipox, Centocor, Dey, Critical Therapeutics, GlaxoSmithKline, Johnson & Johnson, Merck, Novartis, Ono Pharma, Otsuka, RJ Reynolds, Roche, Sankyo, Schering-Plough, Scios, and Wyeth; advising regarding clinical trials for Altana, AstraZeneca, Aventis, Centocor, GlaxoSmithKline, Novartis, Pfizer, and Philip Morris; and speaking at continuing medical education programs and performing funded research both at basic and clinical levels for Altana, AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, and Novartis. Dr Nides reports having received research grants, consulting fees, and honoraria from Pfizer, SanofiAventis, and GlaxoSmithKline. Dr Oncken reports having received research grants, consulting fees, and honoraria from Pfizer; receiving, at no cost, nicotine replacement and placebo products from GlaxoSmithKline for smoking cessation studies; and receiving honoraria from Pri-Med. Drs Azoulay, Watsky, Gong, Williams, and Reeves and Mr Billing report owning Pfizer stock or having stock options in Pfizer. **Role of Sponsor:** The database containing the findings of the 19 individual investigator sites was maintained by Pfizer Inc, and statistical analyses were performed at Pfizer Inc by Mr Billing and by Ann Pennington, MS. **Independent Statistical Analysis:** Barbara Pizacani, PhD, Adjunct Faculty at the School of Nursing at Oregon Health & Science University (OHSU) and Epidemiologist in Program Design and Evaluation Services for Multnomah Health Department and Orgeon Department of Human Services, and Clyde Dent, PhD, of the Program Design and Evaluation Services of Multnomah County Health Department and Oregon Department of Human Services, had access to all of the data used in the study and performed an independent analysis in consultation with Dr Gonzales. The independent analysis replicated the analyses of the primary and secondary end points reported in the manuscript using cross tabulations, logistic regression, and mixed-model procedures. Repeat tabulations for other end points were performed.

2 Gonzales 2006 *(Continued)*

	Results for the adverse events were also replicated. Results were comparable with those obtained by the sponsor. While there were several small discrepancies, all were resolved prior to submission of the manuscript and none affected the inferences made in the manuscript. Compensation for Drs Pizacani and Dent was provided by OHSU. Pfizer Inc provided no funds to support the independent analysis."
Notes	Prolonged abstinence defined as complete abstinence from weeks 9 - 12 Arm 2 compared with 3 (same study as 4 VA Gonzales)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomization: computer-generated sequence 1:1:1
Allocation concealment (selection bias)	Low risk	Participants were randomized according to a predefined central computer sequence
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: “Participants and investigators were blinded to drug treatment assignments.” + placebo-controlled
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: “self-report of no smoking and an exhaled carbon monoxide measurement of less than 10 part per million … was measured at baseline and each clinic visit to confirm smoking status”
Blinding of outcome assessment (detection bias) Weight	Low risk	Unclear how weight was measured, self-report cannot be ruled out but participants were blinded to treatment allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: “The 52-week study completion rates were 60.5% (213/ 352) for varenicline, 56% (184/329) for bupropion SR, and 54% (187/344) for placebo. Most study discontinuations occurred during the drug treatment phase. The most common reason for discontinuation for both treatment and nondrug follow-up was loss to follow- up. Compliance with medication dosing was similar across all treatment groups, with a median duration of treatment of 84 days in each of the 3 groups”

2 Gourlay 1995

Study characteristics

Methods	Country: Australia Recruitment: community volunteers Study start date: Not specified; Study end date: Not specified
Participants	629 smokers (> 15 cpd) who had relapsed after transdermal nicotine and behavioural counselling in an earlier phase of the study Minimal additional support
Interventions	• Nicotine patch 30 cm^2 (21 mg/24-hr) for 4 wks, 20 cm^2 (14 mg/24-hr) for 4 wks, 10 cm^2 (7 mg/24-hrs) for 4 wks • Placebo patch

2 Gourlay 1995 *(Continued)*

Outcomes	Mean (SD) weight change (kg) in continuous abstainers at EOT (validation: expired CO < 9 ppm)
Study funding	"Ciba-Geigy Australia, the Anti Cancer Council of Victoria, and the Victorian Health Promotion Foundation. Ciba-Geigy Australia provided the transdermal nicotine patches"
Author declarations	"GG has received research funding from and has been a paid consultant to Ciba-Geigy Australia, manufacturers of transdermal nicotine. DP is medical director of Ciba-Geigy New Zealand"
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Treatments were randomly allocated to study numbers by using a 1:1 ratio within blocks of 10
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind + placebo controlled. Quote: “Treatment assignment was guessed correctly by 63/281 (22.4%) of those allocated to achieve treatment and by 109/272 (38.8%) of those allocated to placebo”
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "Continuous abstinence was defined as self reported non-smoking from the quit day, verified by attendance at each scheduled visit and by carbon monoxide levels =< 8 ppm at each visit“
Blinding of outcome assessment (detection bias) Weight	Low risk	Unclear how weight was measured but participants were successfully blinded
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: “After the first four weeks of treatment with patches of 30 cm2, 152/315 (48%) subjects allocated to active treatment and 124/314 (39%) allocated to placebo continued treatment. After the 20 cm2 patches, 113/315 (36%) and 58/314 (19%) subjects, respectively, continued. The rates of permanent discontinuation of treatment because of adverse experiences were 7/179 (3.9%) and 5/143 (3.5%) subjects, respectively (p=0.919).” ; Comment: Number of participants followed-up not reported.

2 Gray 2019

Study characteristics

Methods	Country: USA Recruitment: "...primarily through media advertisements. Recruited from the community, schools, and clinical settings. (…) utilizing high school-based clinics, internet/media advertisements, pediatric/primary care clinic referrals, and College of Charleston postings.” + respondent-driven sampling (RDS), where participants can win coupons for referring eligible friends and acquaintances Setting: Medical University of South Carolina outpatient clinic Study start date: August 2012; Study end date: 26 January 2018

2 Gray 2019 *(Continued)*

Participants	Total N: 157 adolescent smokers, aged 14 - 21 years, smoking daily for ≥ 6 months who want to quit smoking, with at least 1 prior failed quit attempt; if female, must agree to use birth control N per arm: placebo = 80; varenicline = 77 40.1% female, av age 19.1, av baseline weight 75.2, av cpd 11.5
Interventions	• Placebo for 12 weeks • Varenicline for 12 weeks; Dose regimen: Participants who weighed > 55 kg: Days 1 - 3: 0.5 mg 1 x daily; Days 4 - 7: 0.5 mg 2 x daily; Day 7 - Week 12: 1.0 mg 2 x daily; Participants who weighed <55 kg:Days 1-7: 0.5mg 1x daily; Day 7-Week 12: 0.5mg 2x daily All participants were provided with brief individual, face-to-face skills-based cessation counselling and quit-smoking brochures
Outcomes	• Mean (SD) weight change (kg) in abstainers at EOT and 6 months
Study funding	This study was supported by grants U01 DA031779 (Dr Gray), K01 DA036739 (Dr McClure), K12 HD055885 (Dr Tomko), and K23 AA025399 (Dr Squeglia) from the NIH. Varenicline and placebo tablets were supplied at no cost by Pfizer, Inc. Role of the Funder/Sponsor: The sponsor had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; or preparation, review, and approval of the manuscript.
Author declarations	Dr Gray reported consulting for Pfizer, Inc, and receiving grant support from the National Institutes of Health (NIH). Mr Baker reported receiving grant support from the NIH. Dr McClure reported receiving grant support from the NIH. Dr Tomko reported receiving grant support from the NIH during the conduct of the study and outside the submitted work. Dr Squeglia reported receiving grant support from the NIH. Dr Saladin reported receiving grant support from the NIH. Dr Carpenter reported consulting for Pfizer, Inc, during the conduct of the study. No other disclosures were reported.
Notes	The study recruited adolescent smokers. However, authors provided weight data restricted to participants greater than or equal to age 18 at study entry. This study is new to the 2021 update.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "In order to avoid accidental bias, we will utilize a stratified urn randomization procedure“; "Treatment-seeking adolescent smokers were randomized in 1:1 parallel group allocation to receive a double-blind 12-week course of varenicline or placebo added to weekly cessation counseling.“
Allocation concealment (selection bias)	Unclear risk	Quote: "If assessment procedures reveal that a participant meets inclusion criteria, the MUSC Investigational Drug Service (IDS) will randomize the participant to varenicline or placebo in double-blind fashion."
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: "… randomize the participant to varenicline or placebo in double-blind fashion.“

2 Gray 2019 *(Continued)*

Blinding of outcome assessment (detection bias) Smoking	Low risk	CO–confirmed (≤ 8 ppm) abstinence
Blinding of outcome assessment (detection bias) Weight	Unclear risk	Quote: "Vital Signs: Blood pressure, pulse, height, and weight will be monitored to assess medical stability and monitor for any changes during study participation.“
Incomplete outcome data (attrition bias) All outcomes	Low risk	26-week follow-up completion: Placebo group: 41/80 (51.25%) Varenicline group: 42/77 (54.54%)

2 Gross 1995

Study characteristics	
Methods	Country: USA Recruitment: community volunteers Study start date: Not specified; Study end date: Not specified
Participants	177 smokers, 51% female, av age 42, avcpd 33, av FTND score 7.8
Interventions	• Nicotine gum (2 mg), tapered from wk 12. Active gum groups further randomized to chew 7, 15 or 30 pieces of gum per day • No gum All participants received 1 pre-quit group counselling session, 14 clinic visits in 10 wks
Outcomes	Mean (SD) weight change (kg) in prolonged abstainers at end of treatment (validation: CO ≤ 10 ppm)
Study funding	"This study was supported by grant #DA 03893and training grant T 32 DA 07209from the National Institute on Drug Abuse to Dr. Stitzer. We gratefully acknowledge the support of Marion Merrell Dow, Inc. in providing the nicotine gum for this study"
Author declarations	Not specified
Notes	Prolonged abstinence defined as validated self-reported abstinence (allowed up to 3 cigs) Long-term abstinence rates not affected by amount of gum chewed, so these groups collapsed for comparison with no-gum condition

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method not stated
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias)	High risk	Quote: "Neither staff nor subjects were blind to the gum-group assignment“

2 Gross 1995 *(Continued)*
All outcomes

Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: “subjects were classified as having relapsed when they (a) submitted a breath sample with CO > 10 ppm, or (b) had a cumulative self-reported number of cigarettes =3, or (c) had a salivary thiocyanate level that exceeded 2000 ng/ml at the 2.5 post-cessation visit.”
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: "Biological measures at each laboratory visit included body weight and expired-breath carbon monoxide (CO).”
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not specified

2 Hjalmarson 1984

Study characteristics	
Methods	Country: Sweden Recruitment: smoking cessation clinic Study start date: 1981; Study end date: 1982
Participants	206 smokers, 56% female, avage 42, av cpd 24
Interventions	• Nicotine gum (2 mg) (no restrictions on amount or duration of use) • Placebo gum All participants received 6 group sessions of SC behavioural support in 6 wks
Outcomes	Mean (SD) weight gain (kg) in continuous abstainers at 6 months (email communication)(validation: CO < 10 ppm)
Study funding	Not specified
Author declarations	Not specified
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomized by therapy group
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind + placebo-controlled. Nurse distributing gum and therapists did not know about treatment allocation

2 Hjalmarson 1984 *(Continued)*

Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: “Those who claimed to be ex-smokers were validated by measurement of expired-air and was then excluded from the analysis.”
Blinding of outcome assessment (detection bias) Weight	Low risk	Unclear how weight was measured but participants were blinded to treatment allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: “three subjects in the nicotine group and three in the placebo group were unavailable for follow-up and counted as smokers”

2 Hjalmarson 1994

Study characteristics	
Methods	Country: Sweden Recruitment: smoking cessation clinic Study start date: November 1989; Study end date: November 1990
Participants	248 smokers, 57% female, av age 45, av cpd 22, av weight (male) 77 - 83 kg, av weight (female) 64 - 66 kg
Interventions	• Nicotine nasal spray (0.5 mg/spray) used as required up to 40 mg/day for up to 1 yr • Placebo spray All participants received x 8 45 - 60 min group sessions over 6 wks with clinical psychologist
Outcomes	Mean (SD) weight change (kg) in continuous abstainers at 12m (validation: CO < 10 ppm)
Study funding	"This study was supported by a grant from Kabi Pharmacia AB, Helsingborg, Sweden"
Author declarations	Not specified
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method not described
Allocation concealment (selection bias)	Unclear risk	Treatment allocater not blinded if more than 1 participant from the same household so that they could be given same medication
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: “Procedure was blind to both subject and therapist”
Blinding of outcome assessment (detection bias) Smoking	Low risk	CO < 10 ppm to validate abstinence

2 Hjalmarson 1994 *(Continued)*

Blinding of outcome assessment (detection bias) Weight	Low risk	Weight likely objectively assessed: Quote: “weight was measured at intervals throughout the study in subjects who were abstinent”; Participants blinded
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not specified

2 Hjalmarson 1997

Study characteristics	
Methods	Country: Sweden Recruitment: smoking cessation clinic Study start date: October 1992; Study end date: June 1994
Participants	247 smokers, 64% female, av age 48, av cpd 21
Interventions	• Nicotine Inhaler (recommended minimum 4/day, tapering after 3 m, use permitted to 6 m) • Placebo inhaler All participants attended 8 group meetings over 6 wks
Outcomes	Mean (SD) weight change (kg) in prolonged abstainers end of treatment and 12 months (validation: CO < 10 ppm)
Study funding	"This study was supported by a grant from Pharmacia & Upjohn, Helsingborg, Sweden (Dr Wiklund)"
Author declarations	Not specified
Notes	Prolonged abstainers defined as validated self-reported abstinence from week 2

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Participants assigned a number on attending first group session. Numbers on a list randomising to medication. Participants from the same household randomised to same treatment
Allocation concealment (selection bias)	Unclear risk	Treatment allocater not blinded if more than 1 participant from the same household so that they could be given same medication
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: “The randomization was blinded to both the participant and the therapist.” + placebo controlled
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: “exhaled-air carbon monoxide concentration of less than 10 ppm”

2 Hjalmarson 1997 *(Continued)*

Blinding of outcome assessment (detection bias) Weight	Low risk	Likely objectively measured: Quote: “Participants' body weight, blood pressure, and pulse rate were recorded at all visits.“ Participants blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "At 12 months, responses were received from 231 (94%) of 247 participants. The 16 individuals (10 used active and 6 used placebo inhalers) who could not be reached at 1 year were counted as smokers."

2 Hurt 1997

Study characteristics	
Methods	Country: USA, multicentre Recruitment: community volunteers Study start date: not specified; Study end date: not specified
Participants	615 smokers, 55% F, av age 44, av cpd 27
Interventions	• Bupropion 100 mg/day for 7 wks, begun 1 wk before TQD • Bupropion 150 mg/day • Bupropion 300 mg/day • Placebo All participants received physician advice, S-H materials, and brief individual counselling by study assistant at each visit
Outcomes	Mean (SD) weight change (kg) in continuous abstainers at end of treatment (email communication), 6 (email communication) and 12 m (email communication) (validation: CO < 11 ppm)
Study funding	Not specified
Author declarations	Not specified
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Stratified by site, method not specified
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double-blind + placebo-controlled. No further information given
Blinding of outcome assessment (detection bias)	Low risk	Quote: "For the point-prevalence rates, subjects were classified as abstinent if they reported not smoking during the previous seven days and this report

2 Hurt 1997 *(Continued)*

Smoking		was confirmed by an expired carbon monoxide value of 10 ppm or less. To be classified as continuously abstinent, the subjects had to be confirmed as not smoking on the basis of carbon monoxide measurement at each visit.“
Blinding of outcome assessment (detection bias) Weight	Unclear risk	Blinding unclear and how weight was measured was not described
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: “A total of 219/615 subjects (148 during the treatment phase and 71 subsequently) did not complete the 12-month study. Of these subjects, 196 (89 percent) withdrew their consent for various reasons (e.g., scheduling difficulties or perceived lack of benefit); 15 stopped participating because of an adverse event, 6 because of protocol deviations, and 1 for administrative reasons; 1 subject died. The rate of completion of the study increased with the dose and was 57 percent, 65 percent, 64 percent, and 71 percent for the placebo, 100-mg, 150-mg, and 300-mg groups, respectively (P=0.01 by logistic-regression analysis in which dose was treated as a continuous variable).“

2 Ioakeimidis 2018

Study characteristics	
Methods	Country: Greece Recruitment: Unclear, had previously been hospitalized with acute coronary syndrome Setting: Follow-up conducted over the telephone and in clinics Study start date/Study end date: Not specified
Participants	Total N: 54 smokers ≥ 18 years old, smoking ≥ 10 cpd ib average in the past year and were hospitalized with acute coronary syndrome N per arm: varenicline = 27; electronic Cigarettes = 27 64.8% female, av age 52, av baseline weight 71.8, av cpd 21, av FTND 5.6
Interventions	• 12-wk use of varenicline • 12-wk use of electronic cigarettes (EC; 12 mg/ml nicotine) All participants received low-intensity counselling
Outcomes	1. Mean (SD) weight change (kg) in abstainers at EOT
Study funding	Not specified
Author declarations	Not specified
Notes	Information extracted from a conference poster and abstract Authors provided weight change data upon request for EOT; weight not measured at 26 week follow-up This study is new to the 2021 update

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**

2 Ioakeimidis 2018 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	No information provided
Allocation concealment (selection bias)	Unclear risk	No information provided
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Similar amount of low-intensity counselling between arms. Unable to blind participants due to nature of trial (varenicline vs EC)
Blinding of outcome assessment (detection bias) Smoking	High risk	Point prevalence smoking abstinence was defined by self-report of complete abstinence in the 7 days before the 24-week clinic visit
Blinding of outcome assessment (detection bias) Weight	Unclear risk	No information provided
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No information provided

2 Jodar-Sanchez 2018

Study characteristics	
Methods	Country: Spain Recruitment: "Smokers were recruited during routine visits to our outpatient clinic." Setting: Smoking Cessation Unit at Virgen del Rocío University Hospital, Seville Study start date: 24 October 2016; Study end date: October 24, 2018 (Final data collection date for primary outcome measure)
Participants	Total N: 240 N per arm: Usual care = 120; Intervention = 120 48.8% female, av age 49.7, av baseline BMI 27.0, av cpd 21.1, av FTND 5.8
Interventions	• Usual care: Pharmacological therapy with bupropion (Zyntabac usually prescribed at a daily dose of 300 mg after the first week of 150 mg per day for 7 to 9 weeks or up to 12 weeks in severe cases) or varenicline (Champix 0.5 mg/1.0 mg (dose progressively increased in the first days to facilitate tolerance) for 12 weeks or longer for severe cases); Behavioural therapy: face-to-face follow-up consultations which used techniques e.g. motivational interviewing and CBT • Usual care plus digital therapeutic solution (Social-Local-Mobile Intervention): App sent personalized motivational messages generated using AI. Algorithm dynamically determined the type and content on individual messages according to the phase of the transtheoretical model of behavior change that the individual was at, user health conditions, user feedback, and user filtering strategies. Message categories included: reduce tobacco consumption, increase risk perception, and increase benefit perception during the preparation phase; and general motivation, diet tips, exercise and active life recommendations, personal physical activity level, and positive facts of being a former smoker during the action and maintenance phases.

2 Jodar-Sanchez 2018 *(Continued)*

	The App also provided a User profile linked to the performed physical activity level collected by Google Fit, four smoking cessation benefit indicators (savings, smoke-free days, regained life hours by not smoking, and number of nonsmoked cigarettes since quitting), text-based information about smoking cessation, and a section containing relaxing and distracting elements (breathing exercises and minigames).
Outcomes	The following outcome was measured during the trial but was not available for extraction at the time of this update • Mean (SD) weight change (kg) in abstainers at EOT
Study funding	"This research was funded by the H2020 European Commission research and innovation program (grant agreement 681120) as part of the SmokeFreeBrain project (www.smokefreebrain.eu)."
Author declarations	"SHF is a product manager at Salumedia Tecnologías SLU, the company with exploitation rights to the digital therapeutic solution used in the So-Lo-Mo study (DigiQuit). He contributed to technical data extraction for the precision, time-to-open the messages, and perceived quality metrics and their analysis. He was not involved in the clinical trial design, execution, or analysis of the resulting clinical data. Some institutions of all the other authors (University of Seville, the Aristotle University of Thessaloniki, and the Servicio Andaluz de Salud as a legal representative institution for the Virgen del Rocío University Hospital) signed an exploitation agreement with Salumedia Tecnologías SLU to benefit from DigiQuit commercialization. This agreement was elaborated and signed before publishing the present results but after the trial was finished and its results were generated."
Notes	"To facilitate recruitment and avoid bias associated with treatment cost, the SmokeFreeBrain project financed the drugs for usual care. Thus, all participants received their assigned treatments free of charge." This study is new to the 2021 update.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "We generated a list of 240 consecutive items by randomly assigning 1 of the study groups to each item. Participants were assigned to each of the study groups according to this list and following their order of enrollment." (protocol publication) Quote: "A technician generated a random-group table (n=240) using computer methods and following a 1:1 ratio between groups." (primary paper)
Allocation concealment (selection bias)	High risk	Quote: "Clinicians enrolled the participants and assigned them to the group mentioned in the table according to their enrolment sequence. Participants were blinded to this allocation, as those in the IG were told that the provided mobile app was part ofusual care. Participants in the CG were not informed about the existence of the app and did not have access to it."
Blinding of outcome assessment (detection bias) Smoking	Low risk	Participants with an exhaled CO level greater than 6 ppm were considered smokers Participants with a cotinine concentration greater than 200 ng/ml were considered smokers Participants were considered smokers when at least one of the aforementioned conditions was met.

2 Jodar-Sanchez 2018 *(Continued)*

Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: "Healthy lifestyle will be measured in terms of the subject's BMI (weight in kg / height in m^2) at baseline (first evaluation in the study) and at the end of the intervention (after 1 year of follow-up)" Comment: Unclear if weight objectively measured, but participants were blinded
Incomplete outcome data (attrition bias) All outcomes	High risk	12 month follow-up: Usual care: 47/120*100 = 39.2% Intervention group: 51/120*100 = 42.5%

2 Jorenby 2006

Study characteristics	
Methods	Country: USA, multicentre Recruitment: community volunteers Study start date: June 2003; Study end date: March 2005
Participants	1027 smokers, 41% F, av age 42, av cpd 22
Interventions	• Bupropion 300 mg for 12 wks + placebo varenicline • Varenicline 2 mg for 12 wks + placebo bupropion • Placebo bupropion + placebo varenicline All participants received brief (< 10 mins) individual counselling at each weekly assessment for 12 wks & 5 follow-up visits. One telephone call 3 days after quit day
Outcomes	Mean (SD) weight change (kg) in prolonged abstainers at end of treatment (validation: CO < 10 ppm)
Study funding	"The data reported in this article were derived from a clinical trial sponsored by Pfizer Inc, which provided funding, study drug and placebo, and monitoring"
Author declarations	"**Financial Disclosures:** Dr Jorenby reported receiving research support from Pfizer, Nabi Biopharmaceutical, Sanofi-Aventis and consulting fees from Nabi Biopharmaceutical. Dr Hays reported receiving a research grant from Pfizer. Dr Rigotti reported receiving research grant funding and consulting fees from GlaxoSmithKline, which markets smoking cessation medications, and Pfizer and Sanofi-Aventis, which are developing smoking cessation medications. Dr Rigotti also reported receiving consulting fees from Merck, which is developing smoking cessation medications. **Role of Sponsor:** Drs Azoulay, Watsky, Williams, Gong, and Reeves, and Mr Billing, employees of Pfizer Inc, were involved in all elements of this study, including but not limited to the study design and monitoring. In addition, the database containing the findings of the 14 investigator sites was maintained by Pfizer Inc, and statistical analyses were performed at Pfizer Inc by Mr Billing and Ann Pennington, MS. All of the authors including those employed by Pfizer Inc, reviewed and edited the manuscript prior to publication of this article. **Independent Statistical Analyses:** Daniel Bolt, PhD, associate professor of Educational Psychology at the University of Wisconsin, had access to all of the data used in the study and performed an independent analysis in consultation with Dr Jorenby. The independent statistical analyses involved the primary and key secondary outcomes, including participant demographics, self-reported data, and safety as described in this article. The re-

2 Jorenby 2006 *(Continued)*

	sults confirm what is presented in this article. Dr Bolt received compensation from the University of Wisconsin for this reanalysis."
Notes	Prolonged abstinence defined as validated self reported abstinence w 8-12 Arm 1 and 3 in main comparison

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Centralized, computer-generated
Allocation concealment (selection bias)	Low risk	Quote: "SItes used an electronic system to assign participants to treatment"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind + placebo-controlled. Participants specified as blinded. No further information given
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "Abstinence at each visit was defined as a self-report of no smoking or use of other nicotine-containing products (or other tobacco during followup) since the previous visit or contact (or previous 7 days in the case of the point prevalence measure), confirmed by an expired carbon monoxide level of 10 ppm or less.“
Blinding of outcome assessment (detection bias) Weight	Low risk	Unclear how weight was measured, self-report cannot be ruled out but participants were blinded to treatment allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: “Overall study completion rates at week 52 were 70% (240/344 participants) in the varenicline group, 65% (221/342 participants) in the bupropion SR group, and 60% (204/341 participants) in the placebo group. More participants in the placebo group failed to complete the study. There were no differences in demographic variables or baseline characteristics across the 3 groups.“

2 Koegelenberg 2014

Study characteristics

Methods	Country: South Africa Recruitment: not specified Study start date: April 2011; Study end date: October 2012
Participants	Total N: 446 N per arm: varenicline + active nicotine patch = 222; varenicline + placebo patch = 224 61.7% female, av age 46.3, av baseline BMI 27.3, av cpd 15.8, av FTND 4.5
Interventions	• Varenicline + active nicotine patch: Active 15-mg nicotine patches (Nicorette, McNeil) administered for 16 h/d beginning at the randomization visit, 2 weeks before the TQD, and continued until week 12 (total duration, 14 weeks).

2 Koegelenberg 2014 *(Continued)*

	• Varenicline + placebo patch: placebo patches (supplied by the same manufacturer and were similar in appearance and packaging) administered for 16 hrs/day beginning at the randomization visit, 2 weeks before the TQD, and continued until week 12 (total duration, 14 weeks) 1 wk before the TQD, all participants began taking varenicline (Pfizer), 0.5 mg once daily for 3 days, titrated to 0.5 mg twice daily for days 4 to 7 and then to the maintenance dose of 1 mg twice daily through week 12. Varenicline was tapered off and stopped at the end of week 13 (0.5 mg twice daily for 4 days, followed by 0.5 mg in the evenings for 3 days; total duration, 14 weeks). All participants received 10 minutes of smoking cessation counselling based on the 2008 update of the US Public Health Service guidelines. Participants were followed up weekly from randomization until the TQD (2 weeks later) and subsequently at 1, 2, 4, 8, and 12 weeks during the treatment period. Follow-up visits were conducted at weeks 13 (telephone), 16, and 24 during the non-treatment period
Outcomes	1. Mean (SD) weight change (kg) at 24 weeks in abstainers (CO < 10 ppm validated continuous abstinence at 6 months)
Study funding	"This study was supported by unrestricted grants from Pfizer, New York, New York, and McNeil, Helsingborg, Sweden. Varenicline was supplied by Pfizer, and both active and placebo NRT patches were supplied by McNeil. The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication."
Author declarations	"All authors have completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Dr Koegelenberg reported receiving grants for studies (for his institution) from Pfizer, McNeil, Bayer, and GlaxoSmithKline and personal fees from AstraZeneca. Dr Noor reported receiving grants for studies (for her institution) from Pfizer, McNeil, and GlaxoSmithKline. Dr Bateman reported receiving grants for studies (for his institution) from Actelion, Almirall, AstraZeneca, Boehringer Ingelheim, Chiesi, GlaxoSmithKline, Hoffman la Roche, Merck, Novartis, Takeda Aeras, Cephalon, and sanofi- aventis and personal fees from Elevation Pharma, Napp Pharma, Forest, Pfizer, Navigant Consulting, IMS Consulting Group, ALK-Abello, and ICON. Dr van Zyl-Smit reported receiving grants for studies (for his institution) from Pfizer and personal fees from Pfizer and GlaxoSmithKline. Dr Bruning reported receiving grants for studies (for his institution) from Pfizer and McNeil. Dr O'Brien reported receiving grants for studies (for his institution) from Pfizer and McNeil and personal fees from Pfizer, Boehringer Ingelheim, Astra Zeneca, and GlaxoSmithKline. Dr Smith reported receiving personal fees from Pfizer. Dr Irusen reported receiving grants for studies (for his institution) from Pfizer, Astra Zeneca, GlaxoSmithKline, Merck Sharp and Dohme, and Boehringer Ingelheim and personal fees from Merck Sharp and Dohme, Novartis, GlaxoSmithKline, Boehringer Ingelheim, Astra Zeneca, and Nycomed. No other disclosures were reported."
Notes	This study is new to the 2021 update.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Participants randomized in a 1:1 ratio using centrally-generated block randomization within each site (blocks of 4 with 2 active and 2 placebo patches)
Allocation concealment (selection bias)	Unclear risk	No information provided
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Both the investigators and the participants were blinded" + placebo controlled

2 Koegelenberg 2014 *(Continued)*

Blinding of outcome assessment (detection bias) Smoking	Low risk	Continuous (validated CO < 10 ppm) and point prevalence rates presented.
Blinding of outcome assessment (detection bias) Weight	Low risk	Not specified how weight was measured, but participants and assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	24-wk completion NRT + varenicline group: 144/222 (64.86%) Placebo patch + varenicline group: 134/224 (59.82%)

2 Lerman 2004

Study characteristics	
Methods	Country: USA Recruitment: community volunteers and referrals Study start date: February 2000; Study end date: March 2002
Participants	350 smokers (includes 51 who withdrew before treatment) 54% F, av age 46, av cpd 21
Interventions	• Nicotine patch (21 mg/24-hr) for 8 wks incl tapering • Nicotine nasal spray (8 - 40 doses/day, max 5/hr) for 8 wks, tapering over final 4 wks All participants received 7 x 90-min behavioural group counselling sessions. TQD in wk 3.
Outcomes	Mean (SD) weight change (kg) in unvalidated continuous abstainers at EOT and 6 months
Study funding	"By Transdisciplinary Tobacco Use Research Center grant P5084718 from the National Cancer Institute and the National Institute on Drug Abuse and Public Health Services Research grant M01-RR0040 from the National Institutes of Health. Dr. Lerman was supported by the Abramson Cancer Center and Annenberg Public Policy Center. Dr. Benowitz was supported by Public Health Services grants DA02277, DA12393, and CA078703, as well as the University of Cal- ifornia, San Francisco, Comprehensive Cancer Center. Nicotine nasal spray (Nicotrol) was provided by Pharmacia and Upjohn, Helsingborg, Sweden"
Author declarations	"Consultancies: N. Benowitz (GlaxoSmithKline); Grants received: C. Lerman (National Cancer Institute), N. Benowitz (GlaxoSmithKline)"
Notes	For prolonged abstinence, relapse was defined as 7 consecutive days of smoking at any point during follow-up period

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated, operated by data manager.
Allocation concealment (selection bias)	Low risk	After allocation only outcome assessors blind

2 Lerman 2004 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: “Interviewers were blinded to study group assignment”
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "The point prevalence measure required 7 days of continuous abstinence immediately before the follow-up point, which was confirmed by a carbon monoxide reading of less than 10 parts per million (ppm)“
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: “Height and weight were measured at the medical screening visit“
Incomplete outcome data (attrition bias) All outcomes	Low risk	Follow-up completion transdermal nicotine treatment group: 153/175 (87%); Follow-up completion nicotine nasal spray treatment group: 147/175 (84%)

2 Lycett 2011

Study characteristics	
Methods	Country: England Recruitment: Invitation letter from GP Setting: 19 general practices in Oxfordshire Study start date: 1 June 1991; Study end date: 1 March 1992; “An unplanned follow-up took place 8 years later“
Participants	Total N: 1686 smokers aged 25 - 64 years, smoking ≥15 cpd. N per arm: Nicotine patch and 16-page pamphlet = 422; Nicotine patch and 46-page booklet = 420; Placebo patch and 16-page pamphlet = 422; Placebo patch and 46-page booklet = 422 55.1% female, av age 42.6, av cpd 24.3
Interventions	• 1. Nicotine patch and 16-page pamphlet: Pamphlet was a standard 16-page Health Education Authority pamphlet on smoking cessation entitled *So you want to quit smoking?* • Nicotine patch and 46-page booklet: Booklet gave specific and more detailed information on smoking cessation with the help of patches entitled *Smoker’s quit plan* • Placebo patch and 16-page pamphlet • Placebo patch and 46-page booklet Nicotine patch used was Nicotinell TTS. Participants used an initial 30 cm^2 patch for the first 4 weeks, reducing to 20 cm^2 for 4 weeks and then 10 cm^2 for 4 weeks. The patches delivered 21 mg, 14mg, and 7mg nicotine per 24 hours respectively The total treatment period was 12 weeks. Participants were advised to stop smoking completely from the first day. By the end of the final 3m assessment, participants were scheduled to have been seen (for 10-15 minutes) on 4 occasions by a nurse and on 1 occasion by a GP

2 Lycett 2011 *(Continued)*

Outcomes	1. Mean (SD) weight change (kg) in abstainers at longest follow-up (8 years) (discussed narratively)
Study funding	**Burke 1993:** "This study was supported by Ciba-Geigy Pharmaceuticals, who also supplied the nicotine and placebo patches. We thank Ciba-Geigy for help in conducting the study and for ensuring that it met the sandards set by the Declaration of Helsinki and the "Good clinical practice" guidelines. We thank Ciba-geigy for undertaking the time consuming tasks of packaging and data entry. The central oxford ethics committee gave advice and formal consent to the trial, and Professor Nicholas Wals and colleagues at St Bartholomew's Medical College, London, carried out the cotinine measurements." **Lycett 2011:** "The original trial and 8-year follow-up was funded by Cancer Research UK. Deborah Lycett has a PhD studentship funded by UK Centre for Tobacco Control Studies (UKCTCS), a UKCRC Public Health Research: Centre of Excellence. Funding from British Heart Foundation, Cancer Research UK, Economic and Social Research Council, Medical Research Council, and the Department of Health, under the auspices of the UK Clinical Research Collaboration, is gratefully acknowledged. Paul Aveyard is funded by National Institute of Health Research (NIHR)."
Author declarations	Paul Aveyard has conducted consultancy work on smoking cessation for Pfizer, McNeil and Xenova Biotechnology. Marcus Munafo` has received fees for invited lectures from the National Health Service, GlaxoSmithKline, Novartis, the Moffitt Cancer Research Center and the Karolinska Institutet, and received benefits in kind (hospitality, etc.) from various pharmaceutical companies. He has received research and travel support from the European Research Advisory Board, GlaxoSmithKline, Pfizer Consumer Healthcare and Novartis. Consultancy has been provided to the European Commission, The American Institutes for Research, the National Audit Office and G-Nostics Ltd. Elaine Johnstone has received consultancy income from European Network for Smoking Prevention. Michael Murphy has received consultancy income from the European Network for Smoking Prevention and has provided scientific consultancy services through the University of Oxford ISIS Innovation to the National Audit Office and G-Nostics Ltd.
Notes	This study is new to the 2021 update.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Randomisation was carried out by prior random allocation of study numbers to each intervention group and by sequential allocation of a study number to patients on entry."
Allocation concealment (selection bias)	Unclear risk	Quote: "Randomisation was carried out by prior random allocation of study numbers to each intervention group and by sequential allocation of a study number to patients on entry." Quote: "prepared precoded packages containing the patches were handed to the patients"
Blinding of participants and personnel (performance bias) All outcomes	High risk	Quote: "it was not possible to blind the nurse or patient to the support material provided" Quote: "more of those using the nicotine patch (70.7%) than the placebo patch (48.6%) guessed correctly"
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "Abstainers were defined as having stopped smoking on or around quit day and declared continuous total abstinence from 3 months to 1 year and were still abstinent 8 years later. Abstinence was verified biochemically at 3, 6 and 12 months and 8 years."
Blinding of outcome assessment (detection bias) Weight	High risk	Quote: "Height and weight were measured at trial entry, although this was self-reported in 19% of participants. At 8-year follow-up, weight was self-reported as the questionnaire was completed by post."

2 Lycett 2011 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	> 50% follow-up at 8 years

2 Marcus 1999

Study characteristics	
Methods	Country: USA Recruitment: not described Study start date: not specified; Study end date: not specified
Participants	20 women, av age 39, av cpd 28, av BMI 24 - 27
Interventions	• CV equipment: group, facility 30 - 45 mins, 60 - 85% HR max, 3 times/wk for 12 wks + cessation programme (twice a week for 4 weeks) • Cessation programme only (twice a week for 4 weeks)
Outcomes	Mean weight change (kg) in continuous abstainers at end of treatment (8 wks) and at 60 wks (validation: CO < 8 ppm and cotinine level less than 57 nmol/L (10ng/ml])
Study funding	"This project was supported in part through grants K07CA01757 and R29CA59660 from the National Cancer Institute, Bethesda, Md, and an R29CA59660 supplementary grant from the Office of Research on Women's Health, National Institutes of Health, Bethesda, Md (Dr Marcus)"
Author declarations	Not specified
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated
Allocation concealment (selection bias)	Low risk	Quote: "randomisation code for group assignment was generated by a computer code"
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "To be considered abstinent, subjects needed to have a carbon monoxide level less than 8ppm and a cotinine level less than 57 nmol/L."
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: "Body weight and height were measured … using a calibrated scale; subjects were clothed in examination gowns"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "There was no differential loss to follow-up. Of those randomized, 64.6% of control subjects and 68.7% of exercise subjects returned at end of treatment (P = .47). At the 3-month follow-up, 46.9% of control subjects and 58.2% of exercise subjects returned (P = .06); at the 12- month follow-up, 50.3% of control subjects and 56.0% of exercise subjects returned (P = .35)"

2 Marcus 2005

Study characteristics	
Methods	Country: USA Recruitment: community volunteers Study start date: not specified; Study end date: not specified
Participants	217 women, mean age 43, mean cpd 21 exercise ≤ 90 mins /wk
Interventions	• 1 x 1hr facility (group) session + 4 x 30-min session home (individual) or facility (group), 45 - 59% HR reserve or 50% - 69% maximum HR, goal: 165 mins/wk for 8 wks plus 8 wks of SC CBT • Smoking cessation therapy as 1. once/week for 8 weeks + health education once/week for 8 wks Exercise began before quit date, time in therapy matched for 2 groups
Outcomes	Mean (SD) weight change (kg) in continuous abstainers at EOT; (validation: saliva cotinine < 10 ng/ml, CO < 8 ppm)
Study funding	"This project was supported in part through grants from the National Cancer Institute (CA77249) and the National Heart, Lung, and Blood Institute (HL64342, HL68422)"
Author declarations	Not specified
Notes	Published paper of Marcus 2003a conference abstract (included study in exercise interventions parent review)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated
Allocation concealment (selection bias)	Low risk	Quote: "Group assignment was based on a randomisation code generated by a computer software program"
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: “Criteria for 7-day point- prevalence abstinence was a cotinine level less than 57 nmol/l (10 ng/ml) and a carbon monoxide level less than 8ppm”
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: “We used a calibrated scale to assess height and weight”
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "We found no differential loss to follow-up between the two groups. For the CBT+EX group, 54.1% attended the end-of-treatment assessment session, 39.4% attended the 3-month follow-up session, and 24.8% attended the 12-month follow-up session. For the CBT group, 58.9% attended the end-of-treatment assessment session, 42.1% attended the 3-month follow-up session, and 31.8% attended the 12-month follow-up session.“

2 Mercié 2018

Study characteristics

2 Mercié 2018 *(Continued)*

Methods	Country: France Recruitment: Not specified Setting: 30 HIV clinics located in French university hospitals or other referral hospitals that are usually involved in the management of people living with HIV Study start date: October 2009; Study end date: July 2014
Participants	Total N: 248 regular smokers (≥ 10 cpd during past year) with documented HIV infection and motivated to quit smoking N per arm: placebo = 125; varenicline = 123 17% female, av age 45, av baseline weight 69 kg, av cpd 20, av FTND 5.4
Interventions	• Placebo for 12 weeks + behavioural change counselling • Varenicline for 12 weeks (Days 1 - 3: 0.5 mg/day; Days 4 - 7: 0.5 mg twice daily; Day 8 to Week 12: 2 x 0.5 mg daily + behavioural change counselling Behavioural change counselling: The duration of the programme and the precise number of sessions were tailored to participants' needs. The programme aimed to include 10 to 15 face-to-face sessions over 1 year
Outcomes	The following outcome was measured during the trial but was not available for extraction at the time of this update • Mean (SD) weight change (kg) in abstainers at EOT and longest follow-up (week 48)
Study funding	The French National Institute for Health and Medical Research (INSERM)–French National Agency for Research on AIDS and Viral Hepatitis (ANRS) and Pfizer. The funder had no role in study design, collection, analysis, and interpretation of data, writing the report, or in the decision to submit the paper for publication. PM had full access to all data and had final responsibility for the decision to submit for publication
Author declarations	The institution of JR has received funds from Institut national de la santé et de la recherche médicale (Inserm)-France Recherche Nord et sud Sida-hiv hépatites (ANRS). XD has received grant support from Pfizer. J-MM is a member of scientific advisory boards of Merck laboratories, Gilead, Bristol-Myers Squibb, ViiV Healthcare, and Janssen and has received grant support from Merk laboratories and Gilead. BS has received honoraria for seminars from Merck laboratories, Gilead, and Janssen and support for the IAS 2014 conference from Merck laboratories. The institution of CF and GC has received grant support from Inserm-ANRS and Pfizer. GC has received grant support for International Workshop on HIV and Hepatitis Observational Databases from Gilead, Tibotec-Janssen, Roche, Merck laboratories, Janssen Pharmaceuticals, Boehringer Ingelheim, Bristol-Myers Squibb, GlaxoSmithKline, ViiV Healthcare, Mylan, Abbvie, and Abbott and grant support for ongoing clinical trials of Inserm-ANRS from Gilead, Tibotec-Janssen, Merck laboratories, Boehringer Ingelheim, and Abbott. All other authors declare no competing interests.
Notes	This study is new to the 2021 update.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Randomisation (1:1) was done centrally via electronic case report software (CS software, Ennov-Clinsight), on the basis of a list generated with SAS software, version 9.2 (PROC PLAN procedure, block size 8). Randomisation was stratified according to whether the quit-smoking counsellor was an infectious

2 Mercié 2018 *(Continued)*

		diseases specialist or tobaccologist and whether or not the centre had participated in an ancillary study on lung ageing."
Allocation concealment (selection bias)	Low risk	Quote: "Only the trial statistician (JA) had access to the randomisation list during the trial. JA was involved in the data analysis."
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Participants and investigators remained masked to treatment groups until the database lock (after week 48), and therefore did not know which group the participant was originally assigned to"
Blinding of outcome assessment (detection bias) Smoking	Low risk	< 10 ppm CO verified continuous abstinence
Blinding of outcome assessment (detection bias) Weight	Low risk	Not specified but participants were blinded
Incomplete outcome data (attrition bias) All outcomes	High risk	Placebo = 46/124 completed follow-up Varenicline = 35/123 completed follow-up

2 Nakamura 2007

Study characteristics	
Methods	Country: Japan Recruitment:community volunteers Study start date: Not specified; Study end date: Not specified
Participants	619 healthy smokers, aged 20 - 75, smoking 10+ cpd. 1 ppt excluded from ITT denominator as withdrew prior to treatment. Demographic data only supplied for nicotine-dependent group (515/618): 75% male, mean age 39.8, mean cpd 24, mean FTND score 5.6
Interventions	• Varenicline 0.25 mg x 2/day 12 wks • Varenicline 0.50 mg x 2/day 12 wks • Varenicline 1.00 mg x 2/day 12 wks • Placebo tablet x 2/day 12 wks All participants received S-H booklet *Clearing the Air* at baseline, + brief counselling (≤ 10 mins) at each clinic visit
Outcomes	Mean (SD) weight change (kg) in prolonged abstainers at end of treatment (validation: CO ≤ 10 ppm)
Study funding	"The study was funded by Pfizer Inc. (ClinicalTrials. gov Identifier: NCT00139750)"
Author declarations	"Drs. Nakamura and Oshima were the primary study investigators, had full access to all study data, and had the final responsibility for the decision to submit the results for publication. Dr. Nakamura has received research contracts from Pfizer Japan Inc. (Tokyo, Japan), Novartis Pharma K.K. (Tokyo, Japan), and Sanofi-Aventis K.K. (Tokyo, Japan), and a research grant from Pfizer Research Foundation (Tokyo, Japan). Dr. Oshima has received research contracts from Pfizer Japan Inc."
Notes	Prolonged abstinence defined as continuous abstinence during weeks 9 - 12

2 Nakamura 2007 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated random number lists
Allocation concealment (selection bias)	Low risk	Quote: "randomised to 1 of the 4 treatment groups in a 1:1:1:1 ratio using a central procedure"
Blinding of participants and personnel (performance bias) All outcomes	Low risk	“double-blinding of subjects and investigators was maintained throughout the study using matching placebo tablets”
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "If CO levels were found to be >10 ppm, the subject was considered nonabstinent for the period as- sociated with that measurement“
Blinding of outcome assessment (detection bias) Weight	Low risk	Weight likely objectively measured: Quote: “Blood pressure, heart rate, and body weight were measured at each clinic visit from baseline to week 52 or early termination of treatment/follow-up.“ Comment: Participants blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Flowchart: Study completion varenicline 0.25 mg group: 126/153 (82%); Study completion varenicline 0.50 mg group: 128/156 (82%); Study completion varenicline 1 mg group: 124/156 (79%); Study completion placebo group: 132/154 (85%)

2 NCT02859142 2016

Study characteristics

Methods	Country: USA Recruitment: Advertisements Setting: Real-world clinic-based setting; Chicago, Illinois. 4 x in-person visits and 1 telephone call Study start date: 29 March 2018; Study end date: 15 October 2020
Participants	Total N: 122 heavy drinkers (consume > 14 (men) or > 7 (women) standard alcohol drinks per week), aged 18 - 85 years, who smoke 3 - 30 cpd and want to quit smoking N per arm: Not specified
Interventions	• Placebo + nicotine patches (NicodermCQ) + behavioural counseling • Varenicline tartrate (Chantix; up-titration week prior to the TQD (0.5 mg per day for 3 days, 0.5 mg twice daily for 4 days,12 weeks of target dosing, and a down-titration week as per Pfizer recommendations) + nicotine patches (NicodermCQ) + behavioural counseling

2 NCT02859142 2016 *(Continued)*

	Behavioural counselling: 1-on-1 sessions with a trained therapist at each of 4 study visits (pre-quit, quit date, week 2, and week 12)
Outcomes	1. Mean (SD) weight change (kg) in abstainers at EOT
Study funding	Not specified: Sponsors and Collaborators; University of Chicago; Pfizer
Author declarations	Not specified
Notes	Information extracted from the clinicaltrial.gov record. Authors provided weight change data upon request This study is new to the 2021 update.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Eligible participants will be randomized into one of two treatment groups…" Comment: No further information provided
Allocation concealment (selection bias)	Low risk	No information Quote: "Placebo tablets, triple blinding (participant, caer provider and investigator)" Comment: Do not explicitly discuss allocation concealment but given blinding practices assumed to be low
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Placebo tablets, triple blinding (participant, care provider and investigator)
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "Biochemical verification from breath tests for CO, as well as vital signs and weight, will be measured at each visit along with survey responses measuring smoking urge and withdrawal, negative affect, neurocognition, and alcohol and smoking behaviors. These will also be used at a 26-week follow-up by telephone with biochemical verification for CO in those reporting being smoke-free."
Blinding of outcome assessment (detection bias) Weight	Low risk	Weight was measured at clinic visits. Do not explicitly discuss what was used to measure weight but given blinding practices assumed to be low.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number of participants randomized per group not available

2 Niaura 2002

Study characteristics

Methods	Country: USA, multicentre, 16 sites Recruitment: Community volunteers

2 Niaura 2002 *(Continued)*

	Study start date: not specified; Study end date: not specified
Participants	989 smokers, 61% F, av age 42 av cpd 28
Interventions	• Fluoxetine 30 mg for 10 wks, starting 2 wks before TQD • Fluoxetine 60 mg for 10 wks, starting 2 wks before TQD • 3. Placebo All arms: 9 sessions (60 - 90 mins) individual CBT. Included coping skills, stimulus control techniques and relapse prevention
Outcomes	Mean (SD) weight change (kg) in continuous abstainers at EOT (validation: CO < 8 ppm and salivary cotinine < 20 ng/ml) and 6 months
Study funding	"Financial support of Elo Lilly & Company, as well as Veterans Affairs Merit Review and National Institutes of Health Grants HL52577 and HL59348"
Author declarations	Not specified
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method not stated
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double-blind + placebo controlled. No further information given
Blinding of outcome assessment (detection bias) Smoking	Low risk	CO level < 8 ppm + salivary cotinine < 20 ng/ml
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: "we measured participants' weight in kilograms with shoes off at each visit using a balance beam scale"
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not specified

2 Niaura 2008

Study characteristics

Methods	Country: USA Setting: 5 research centres Study start date: December 2001; Study end date: June 2003

2 Niaura 2008 *(Continued)*

Participants	320 healthy adult volunteers, aged 18 - 65, smoking ≥ 10 cpd. 52% M, 91% white, mean age 42, mean cpd 22, mean Fagerström score 5.4
Interventions	• Varenicline tartrate 12 wks (wk 1: titrated from 0.5 to 1.0 mg/day) followed by a self-regulated flexible schedule (wks 2 – 12: 0.5 – 2.0 mg/day). • Placebo
Outcomes	Mean (SD) weight change (kg) in continuous abstainers at EOT (12 wks). (validation: CO ≤ 10 ppm)
Study funding	"This study was funded by Pfizer, Inc"
Author declarations	"KEW, KRR, and CBB are employees of Pfizer and have stock or stock options in Pfizer. RN has received consulting fees from Pfizer, GlaxoSmithKline, Sanofi-Aventis, Merck, Constella, and LLC. DEJ has received consulting fees from Nabi Biopharmaceutical and receives research support from Pfizer, Nabi Biopharmaceutical, and Sanofi-Aventis. FTL serves on speakers' bureaus for Pfizer and Merck and is a consultant on an advisory panel with Pfizer. JTH received grant support from Pfizer. JEP received grant support from Merck, DepoMed, Pfizer, Novartis, Takeda, Sanofi-Aventis, Symbollon, TAP, and GlaxoSmithKline. Editorial support was provided by Ray Beck, Jr, PhD of Envision Pharma and was funded by Pfizer, Inc. The ClinicalTrials.gov registra- tion number is NCT00150228"
Notes	Continuous abstinence defined as self-report abstinence weeks 4 - 12 with biochemical validation

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	randomly permuted blocks and a pseudo-random number generator
Allocation concealment (selection bias)	Low risk	participants were assigned in a 1:1 ratio to varenicline treatment or placebo in the numerical order that they were accepted to the study
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double-blind + placebo-controlled. No further information given
Blinding of outcome assessment (detection bias) Smoking	Low risk	Self-reported abstinence validated by a CO concentration of < 10 ppm
Blinding of outcome assessment (detection bias) Weight	Low risk	Weight likely objectively measured: Quote: "Vital signs and weight were documented at all clinic visits"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Flowchart: 52-week completion varenicline group: 100/160 (64%); 52-week completion placebo group: 89 (57%)

2 Nides 2006

Study characteristics

Methods	Country: USA, multicentre, 7 sites Recruitment: Volunteers (phase II study)

2 Nides 2006 *(Continued)*

	Study start date: 21 February 2000; Study end date: 3 January 2003
Participants	638 smokers, 51% F, av age 41, av cpd 20, av BMI 25 - 27
Interventions	• Varenicline 0.3 mg 1/d for 6 wks, + 1 wk placebo • Varenicline 1.0 mg 1/d for 6 wks, + 1 wk placebo • Varenicline 1.0 mg 2/d for 6 wks, + 1 wk placebo • Bupropion 150 mg 2/d (titrated in wk 1) for 7 wks • Placebo tablets 2/d for 7 wks All participants received up to 10 mins counselling at 7 weekly clinic visits, 12 & 24 wks
Outcomes	Mean (SD) weight change (kg) in continuous abstainers at end of treatment (validation: CO ≤ 10 ppm) (email communication)
Study funding	"As the sponsor, Pfizer provided funding and was involved in all elements of the study, including, but not limited to, the study design and monitoring"
Author declarations	"Dr Nides has received research grants, consulting fees, and honoraria from Pfizer, Sanofi-Aventis, and GlaxoSmithKline. Dr Oncken has received research grants, consulting fees, and honoraria from Pfizer; received, at no cost, nicotine replacement and placebo products from GlaxoSmithKline for smoking cessation studies; and received honoraria from Pri-Med. Dr Gonzales reports having received research contracts from Pfizer, Sanofi-Aventis, GlaxoSmithKline and Nabi Biopharmaceuticals; consulting fees and honoraria from Pfizer, Sanofi-Aventis, and GlaxoSmithKline; and owning 5 shares of Pfizer stock. Dr Rennard has had or currently has a number of relationships with companies that provide product and/or services relevant to outpatient management of chronic obstructive pulmonary disease. These relationships include serving as a consultant (Adams, Almirall, Altana, Array Biopharma, AstraZeneca, Aventis, Biolipox, Centocor, Dey, Critical Therapeutics, GlaxoSmithKline, Johnson & Johnson, Merck, Novartis, Ono Pharma, Otsuka, RJ Reynolds, Roche, Sankyo, Schering-Plough, Scios, and Wyeth); advising regarding clinical trials (Altana, AstraZeneca, Aventis, Cen- tocor, GlaxoSmithKline, Novartis, Pfizer, and Philip Mor- ris); speaking at continuing medical education programs; and performing funded research at both basic and clinical levels (Altana, AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, and Novartis). He owns no stock in any pharmaceutical companies. Drs Watsky and Reeves and Mr Anziano are employees of Pfizer and own Pfizer stock or have stock options"
Notes	Continuous abstinence defined as self-reported quit from TQD with biochemical validation. Arms 1 - 3 and 5 in main comparison

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated list
Allocation concealment (selection bias)	Low risk	Quote: "Investigators assigned medication to subjects in numerical order of acceptance into the study" from computer generated list
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double-blind + placebo-controlled. No further information given
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "The primary efficacy measure was the continuous quit rate (CQR) for any 4 weeks, defined as abstinence for any consecutive 28-day period during the treatment phase (determined by diary data). This measure was chosen to give the best possibility of detecting an efficacy signal in this early phase 2 study. Secondary efficacy measures included the CO-confirmed (≤ 10 ppm) 4-week CQR for weeks 4 to 7, as well as CQRs from week 4 to weeks 12, 24, and

2 Nides 2006 *(Continued)*

		52. Subjects who dropped out for any reason were considered to be smokers at all subsequent time points.“
Blinding of outcome assessment (detection bias) Weight	Unclear risk	Unclear how weight was measured, self-report cannot be ruled out and unclear if participants were blinded to treatment allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	52-week completion varenicline tartrate 0.3 mg once-daily group: 65/128 (51.6%); 52-week completion varenicline tartare 1.0 mg once daily group: 77/128 (61.1%); 52-week completion varenicline tartrate 1.0 mg twice daily group: 77/127 (61.1%); 52-week completion bupropion hydrochloride, 150 mg twice daily group: 68/128 (54.0%); 52-week completion placebo group: 66/127 (53.7%)

2 Oncken 2006

Study characteristics	
Methods	Country: USA Recruitment: community volunteers Study start date: Not specified; Study end date: Not specified
Participants	647 smokers, 50.5% female, av cpd 21, av age 42 - 44 yrs, av BMI 26 - 28
Interventions	• Varenicline 0.5 mg nontitrated (2/d for 12 wks) • Varenicline 0.5 mg titrated (wk1 1/d, wks 2 - 12 2/d) • Varenicline 1.0 mg nontitrated (2/d for 12 wks) • Varenicline 1.0 mg titrated (0.5 mg 1/d for 3 days, 0.5 mg 2/d for 4 days, 1.0 mg 2/d wks 2 - 12) • Placebo tablets 2/d 12 wks All participants received S-H booklet at baseline, + brief (≤ 10 mins) counselling at weekly clinic visits throughout treatment phase
Outcomes	Mean (SD) weight change (kg) in continuous abstainers at end of treatment (validation: CO ≤ 10 ppm)
Study funding	"Pfizer Inc provided funding for this study. Pfizer Inc was involved in all elements of this study, including, but not limited to, the study design and monitoring"
Author declarations	"Dr Oncken has received research grants, consulting fees, and honoraria from Pfizer; nicotine replacement and placebo products from GlaxoSmithKline at no cost for smoking cessation studies; and honoraria from PriMed. Dr Gonzales has received research contracts, consulting fees, and honoraria from Pfizer, SanofiAventis, and GlaxoSmithKline and owns 5 shares of Pfizer stock that he received as a gift from his parents. Dr Rennard has had or currently has a number of relationships with companies who provide products and/or services relevant to outpatient management of chronic obstructive pulmonary disease. These relationships include serving as a consultant (for Adams, Almirall, Altana, Array Biopharma, AstraZeneca, Aventis, Biolipox, Centocor, Dey, Critical Therapeu tics, GlaxoSmithKline, Johnson & Johnson, Merck, Novartis, Ono Pharma, Otsuka, RJ Reynolds, Roche, Sankyo, Schering-Plough, Scios, and Wyeth), advising regarding clinical trials (Altana, AstraZeneca, Aventis, Centocor, GlaxoSmithKline, Novartis, Pfizer, and Philip Morris), speaking at continuing medical education programs and performing funded research at both basic and clinical levels (Altana, AstraZeneca, Boehringer Ingelheim, GlaxoSmithKline, and Novartis). He does not own any stock in any pharmaceutical companies. Dr Nides has received research grants, consulting fees, and honoraria from Pfizer, Sanofi-Avenits, and GlaxoSmithKline. Drs Watsky and Reeves and Messrs Billing and Anziano are employees of Pfizer and own Pfizer stock or hold Pfizer stock options."

2 Oncken 2006 *(Continued)*

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Subjects and investigators were blinded to the study drug treatment assignment.“
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "Continuous abstinence was defined as self-report of no cigarette use during the specified time period confirmed by an exhaled carbon monoxide measurement of 10 ppm or lower.“
Blinding of outcome assessment (detection bias) Weight	Low risk	Weight likely objectively assessed: Quote: "Vital signs, weight, and adverse event information were collected at each visit.“ Comment: Participants blinded.
Incomplete outcome data (attrition bias) All outcomes	High risk	Flowchart: 0.5 mg twice a day: Nontitrated 129 Randomized 124 Treated, 63 Completed Week 52 Visit (48.3%); 0.5 mg twice a day: Titrated 130 Randomized 129 Treated, 60 Completed Week 52 Visit (46.1%); 1.0 mg twice a day: Nontitrated 129 Randomized 124 Treated, 69 Completed Week 52 Visit (53.4%); 1.0 mg twice a day: Titrated 130 Randomized 129 Treated, 77 Completed Week 52 Visit (59.2%); Placebo 129 Randomized 121 Treated, 40 Completed Week 52 Visit (31%)

2 Oncken 2007

Study characteristics

Methods	Country: USA Recruitment: local newspaper advertisements and through flyers placed in general medicine clinics Study start date: Not specified; Study end date: Not specified
Participants	The original study had n = 152 but weight analysis paper focuses on 119 participants who provided data on body weight at 12 weeks and 12 months. Only this sample is extracted below: N per arm: Nicotine patch = 47; Placebo = 72 100% female, av age 55.8, av baseline weight 71.5, av baseline BMI 27.1, av cpd 21.1, av FTQ score 5.5
Interventions	• 12 wk 21 mg active nicotine patch • 12 wk placebo patch

2 Oncken 2007 *(Continued)*

	In both treatment conditions, participants came for 7 clinic visits where a research nurse monitors the progress and adverse effects of the medication. In session 2 - 5 ppt also participated in group counselling session which lasted about 2 hours
Outcomes	1. Mean (SD) weight change (kg) at EOT (12 weeks) and 12 months in abstainers (7-day point prevalence CO < 8 ppm)
Study funding	"This study was supported in part by The Patrick and Catherine Weldon Donaghue Foundation, The University of Connecticut Center on Aging, and NIH grants R01 DA13334, and M01 RR06192 (University of Connecticut General Clinical Research Center) and P50AA15632. Glaxo-SmithKline Pharmaceuticals donated nicotine and placebo patches"
Author declarations	Not specified
Notes	This study is new to the 2021 update. Weight data from Allen 2013

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of generating random-number sequence not described
Allocation concealment (selection bias)	Unclear risk	Method of concealing allocation not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double-blind + placebo, who was blinded is not described
Blinding of outcome assessment (detection bias) Smoking	Low risk	Biochemically validated (CO levels ≤ 8 ppm) 7-day point prevalence smoking abstinence
Blinding of outcome assessment (detection bias) Weight	Unclear risk	Not specified how weight was measured, and blinding was unclear
Incomplete outcome data (attrition bias) All outcomes	Low risk	12-wk completion nicotine group: 49/57 (85.96%); 12-wk completion placebo group: 47/57 (82.46%); 64-wk completion nicotine group: 80/95 (84.21%); 64-wk completion placebo group: 72/95 (75.79%)

2 Pack 2008

Study characteristics

Methods	Country: USA Recruitment: community volunteers 2 x 2 factorial design Study start date: June 2004; Study end date: July 2005

2 Pack 2008 *(Continued)*

Participants	408 smokers, 56% F, av age 40 - 44 yrs, av cpd 22 - 24
Interventions	• Nicotine lozenge + 4 calls from Wisconsin Tobacco Quit Line • Nicotine gum + 4 calls from Wisconsin Tobacco Quit Line • Nicotine lozenge + Self-help brochure • Nicotine gum + Self-help brochure Participants were treated with 8 wks of NRT. Follow-up at 8 wks, 6m and 12m
Outcomes	Mean (SD) weight change (kg) in 7-day point prevalence abstainers at EOT, 6m, 12m
Study funding	"This research was supported by the National Cancer Institute Grant P50CA084724 and the National Institute on Drug Abuse Grant # P50DA19706"
Author declarations	Not specified
Notes	Weight data from arms 1&2 and 3&4 were combined for the analysis

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	No information on blinding given. No placebo
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "Seven-day point prevalence of smoking abstinence was biochemically confirmed by exhaled carbon monoxide levels of less than 10 ppm measured at 8 weeks with follow-up at 6 and 12 months“
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: “…measurements were taken and included height, weight ...” taken at baseline, 8 week post-TQD clinic visit and at further follow-up clinic visits if reporting abstinence
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: “Overall follow-up rates at 8 weeks, 6 months, and 12 months were 64.0%, 72.8% and 69.9% respectively, with little variation between groups. Of those reporting abstinence via phone follow-up who were subsequently invited for a clinic visit for CO confirmation at 6 and 12 months, 81.3% and 64.3 % completed the clinic visit respectively, with little variation across the groups.”

2 Patten 2016

Study characteristics

Methods	Country: USA Recruitment: by provider referrals and flyers posted in the clinic and radio and newspaper advertisements

2 Patten 2016 *(Continued)*

	Setting: The treatment was mainly held in a community (YMCA) setting and 4 sessions were conducted at a worksite fitness centre Study start date: September 2013; Study end date: December 2015
Participants	Total N: 30 female, sedentary smokers, 18 - 55 years of age, smoking ≥ 10 cpd, with moderate to severe depression and willing to make a quit attempt N per arm: Health Education = 15; Exercise = 15 100% female, av age 37.5, av baseline BMI 30.5, av FTND 4.5
Interventions	• Health education: Lectures, handouts, films, and discussions covered various women's health and lifestyle issues • Supervised, vigorous-intensity exercise + exercise counselling: provided Kinetic Activity Monitor For both conditions, the 12-week programme comprised 3 x 30 – 40-minute individual-based sessions per week delivered by wellness coaches. All participants received a nicotine patch and behavioural smoking cessation counselling (weekly 15 – 20 minutes of smoking cessation counselling)
Outcomes	Data measured during the trial but not available for extraction at the time of this update • 1. Mean (SD) weight change (kg) in abstainers at EOT
Study funding	This study was supported by CTSA grant number UL1 TR000135 from the National Center for Advancing Translational Sciences (NCATS), a component of the National Institutes of Health (NIH). Its contents are solely the responsibility of the authors and do not necessarily represent the official view of NIH. Funding for this study was also provided by a Mayo Clinic NIH-relief award, and a small grant award from the Department of Psychiatry and Psychology.
Author declarations	None declared.
Notes	Participants received USD 25 for completing the baseline assessment and USD 50 after completing each follow-up. All participants received a free 6-month YMCA membership (HE participants received this after the final assessment). No incentives were offered for treatment adherence. This study is new to the 2021 update

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Participants were stratified according to current depression severity (baseline Patient Health Questionnaire [PHQ-9]score: mild/moderate vs. severe) and antidepressant medication use (yes/no) and randomly assigned to the exercise intervention group (EX, n = 15) or to the health education contact control group (HE, n = 15). The conditions were matched for wellness coach contact time and duration of treatment." Comment: No further information given
Allocation concealment (selection bias)	Unclear risk	Quote: "Allocation to treatment conditions was unknown to the study staff or investigators prior to assignment, and participants completed baseline assessments prior to being informed of their allocation to treatment condition."
Blinding of outcome assessment (detection bias) Smoking	Low risk	7-day point-prevalence, self-reported, saliva cotinine confirmed cigarette smoking status was obtained at Week 12 and at 6-month follow-up. Participants are classified as abstinent if the reading is a 0 (<10 ng/mL cotinine). At each time point, participants who self-reported no cigarette smoking (not

2 Patten 2016 *(Continued)*

		even a puff) in the last 7 days confirmed with a cotinine test strip were classified as nonsmokers
Blinding of outcome assessment (detection bias) Weight	Low risk	Height and weight were recorded at baseline and at Week 12 using a calibrated scale
Incomplete outcome data (attrition bias) All outcomes	Low risk	In both groups 13/15 completed end of treatment assessments

2 Piper 2007

Study characteristics	
Methods	Setting: USA Recruitment: volunteers Study start date: 2001; Study end date: January 2004
Participants	608 smokers of 10 cpd; 58% F, av age 42, av cpd 22, no details of depression history
Interventions	• Nicotine gum (4 mg) and bupropion (300 mg) • Placebo gum and bupropion • Double placebo All arms: 3 x 10 min counselling over 3 weeks
Outcomes	1. Mean (SD) weight change (kg) in point prevalent abstainers at EOT (data from email communication) (validation: CO < 10 ppm)
Study funding	"This research was supported by National Institutes of Health grants CA84724-05 and DA0197-06"
Author declarations	"Dr. Fiore neither consults for nor accepts honoraria from the pharmaceutical industry effective January 1, 2006. In 1998 the University of Wisconsin appointed Dr. Fiore to a named chair, made possible by an unrestricted gift to the university from GlaxoWellcome. Dr. Baker has received monies to conduct clinical trials from pharmaceutical companies (Nabi, Glaxo, Pfizer, Sanofi); he has received no personal remuneration from these companies"
Notes	

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Block randomization
Allocation concealment (selection bias)	Unclear risk	Methods not stated
Blinding of participants and personnel (performance bias)	Unclear risk	Double-blind + placebo-controlled. No further information given

2 Piper 2007 *(Continued)*
All outcomes

Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "Participants who reported 7-day point-prevalence abstinence (no smoking, not even a puff, during the 7 days prior to the follow-up call) at their 6- or 12-month follow-up calls were scheduled to return to the clinic and provide either a breath sample for CO analysis (6 and 12 months) or a blood sample for cotinine analysis (12 months). Participants who could not be reached at follow-up were considered to be smoking for the purposes of follow-up analyses. Both 7-day point-prevalence abstinence and continuous abstinence were used as outcome measures.“
Blinding of outcome assessment (detection bias) Weight	Unclear risk	Unclear how weight was measured and insufficient information to confirm if participants were blinded to treatment allocation.
Incomplete outcome data (attrition bias) All outcomes	Low risk	24-week completion active bupropion & active gum group: 180/228 (78.94%); 24-week completion active bupropion & placebo gum group: 162/224 (72.32%); 24-week completion placebo bupropion & placebo gum group: 102/156 (65.38%); 48-week completion active bupropion & active gum group: 164/228 (71.93%); 48-week completion active bupropion & placebo gum group: 153/224 (68.30%); 48-week completion placebo bupropion & placebo gum group: 100/156 (64.10%)

2 Piper 2009

Study characteristics	
Methods	Country: USA Recruitment: television, radio, and newspaper advertisements; flyers; earned media, including press conferences; and television and radio news interviews Study start date: January 2005; Study end date: June 2007
Participants	Total N: 1504 • 264 bupropion • 262 bupropion + lozenge • 260 nicotine lozenge • 262 nicotine patch • 267 nicotine patch + lozenge • 189 placebo 58.3% female, av age 44.7, av cpd 21.4, av FTND 5.4
Interventions	• Bupropion SR (150 mg twice a day, 1 week pre-quit, 8 weeks post-quit) • Bupropion + NRT (lozenge) (duration and dosage as below) • Nicotine lozenge 2 or 4 mg for 12 weeks (based on dose-for-dependence level as per instructions) • Nicotine patch (24-hr, 21, 14, and 7 mg titrated down over 8-week period post-quit) • Lozenge + patch (duration and dosage as above) • Placebo (bupropion, bupropion + placebo lozenge, lozenge, patch, lozenge + placebo patch) All arms: In addition received 6 x 10 - 20-minute counselling sessions
Outcomes	1. Mean (SD) weight change (kg) at 12-month in abstainers (CO < 10 ppm validated continuous abstinence at 12 months)

2 Piper 2009 *(Continued)*

Study funding	"This research was conducted at the University of Wisconsin–Madison and was supported by grant P50 DA019706 from the National Institute on Drug Abuse and by grant M01 RR03186 from the General Clinical Research Centers Program of the National Center for Research Resources. Dr Piper was supported by an Institutional Clinical and Translational Science Award, University of Wisconsin–Madison (KL2 grant 1KL2RR025012-01). Medication was provided to patients at no cost under a research agreement with GlaxoSmithKline"
Author declarations	"The authors report the following potential conflicts of interest for the last 5 years: Dr Smith has received research support from Elan Corporation. Dr Baker has served as an investigator on research projects sponsored by pharmaceutical companies, including Sanofi-Synthelabo, Pfizer Inc, and Nabi Biopharmaceuticals. Dr Jorenby has received research support from the National Institute on Drug Abuse, the National Cancer Institute, Pfizer Inc, Sanofi-Synthelabo, and Nabi Biopharmaceuticals. He has received support for educational activities from the National Institute on Drug Abuse and the Veterans Administration and consulting fees from Nabi Biopharmaceuticals. Dr Fiore has received honoraria from Pfizer. He has served as an investigator on research studies at the University of Wisconsin that were funded by Pfizer, Sanofi- Synthelabo, GlaxoSmithKlein, and Nabi Biopharmaceuticals. In 1998, the University of Wisconsin appointed Dr Fiore to a named chair funded by an unrestricted gift to University of Wisconsin from Glaxo Wellcome. All authors had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis."
Notes	This study is new to the 2021 update.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method of sequence generation not specified. Quote: “participants were randomised to1 of 6 treatment conditions…. used a blocked randomization scheme with sex and self-reported race (white/non-white) as the blocking variables”
Allocation concealment (selection bias)	Low risk	Staff did not know to which type(s) of medication
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double-blind but no further detail provided. Quote: “Study staff were blinded to whether the medication was active or placebo” but (type of medication (i.e. patch, gum, pill) would have been apparent to both groups)
Blinding of outcome assessment (detection bias) Smoking	Low risk	7d PPA at 6m; initial cessation. Validation: CO < 10 ppm
Blinding of outcome assessment (detection bias) Weight	Unclear risk	Weight data provided from email. No information on how weight was measured.
Incomplete outcome data (attrition bias) All outcomes	Low risk	8-week treatment completion NP group: 253/262 (96.56%); 8-week treatment completion NL group: 243/260 (93.46%); 8-week treatment completion NP + NL group: 261/267 (97.75%); 8-week treatment completion bupropion SR group: 249/264 (94.31%); 8-week treatment completion bupropion SR + NL group: 253/262 (96.56%); 8-week treatment completion placebo group: 176/189 (93.12%); 12/26-week completion NP group: 250/262 (95%); 12/26-week completion NL group: 238/260 (91.54%); 12/26-week completion NP + NL group: 258/267 (96.63%); 12/26-week completion bupropion SR group: 244/264 (92.42%); 12/26-week completion bupropion SR + NL group: 250/262 (95%); 12/26-week completion placebo group: 174/189 (92.06%)

2 Puska 1995

Study characteristics	
Methods	Country: Finland Recruitment: community volunteers Study start date: Spring 1992; Study end date: Autumn 1993
Participants	300 volunteers aged 20 - 65, smoking > 10 cpd for > 3 yrs, no serious illness
Interventions	• Nicotine patch (15 mg/16 hrs, 12 wks+ 6 wks taper) plus nicotine gum (2 mg at least 4 daily) • Placebo patch plus nicotine gum (same regimen)
Outcomes	Mean (SD) weight change (kg) in prolonged abstainers at end of treatment (email communication) and 12m (email communication) (validation: CO < 10 ppm)
Study funding	Not specified
Author declarations	Not specified
Notes	Prolonged abstinence defined as verified continuously lapse-free abstinence after week 1

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Quote: “The study was carried out in a strictly double blind fashion” + placebo
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: “Success was defined as continuously lapse-free abstinence after week 1 verified with a CO level in expired air of less than 10 ppm at all visits after week 1”
Blinding of outcome assessment (detection bias) Weight	Unclear risk	Weight was “recorded at each visit”. Self-report cannot be ruled out and it is unclear if participants were blinded
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not specified

2 Richmond 1994

Study characteristics	
Methods	Country: Australia

2 Richmond 1994 *(Continued)*

	Recruitment: community volunteers Study start date: Not specified; Study end date: Not specified
Participants	315 smokers, av cpd 29
Interventions	• Nicotine patch (24 hr, 22mg/24 hr, 10 wks incl tapering) • Placebo patch All participants received group smoking cessation behavioural support
Outcomes	Mean (SD) weight change (kg) in prolonged abstainers at end of treatment (email communication), 6 months (email communication) and 12 months (email communication) (validation: CO ≤ 10 ppm)
Study funding	This study was supported by a grant from Marion Merrell Dow in USA and was monitored under Food and Drug Administration (FDA) regulations
Author declarations	Not specified
Notes	Prolonged abstainers were defined as continuous abstinence for a sustained period preceding the assessment point at 12 months

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double-blind + placebo-controlled. No further information given.
Blinding of outcome assessment (detection bias) Smoking	Low risk	CO level < 10 ppm
Blinding of outcome assessment (detection bias) Weight	Unclear risk	Unclear how weight was measured and unclear if participants were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "The dropout rate at 12 months was 20% for the active patch group and %1% for placebo. This difference in dropout rate was statistically significant."

2 Rigotti 2006

Study characteristics

Methods	Country: USA Recruitment: hospital patients with cardiovascular disease

2 Rigotti 2006 *(Continued)*

	Study start date: October 1999; Study end date: December 2003
Participants	248 smokers, 31% F, av age 56, av cpd 21 - 23
Interventions	• Bupropion 300 mg for 12 wks • Placebo All participants received multicomponent CBT cessation & relapse prevention programme 30 - 45 mins and 5 X 10-min post-discharge contacts (2 days,1, 3, 8, 12 wks)
Outcomes	Mean (SD) weight change (kg) in point prevalence abstainers at EOT (email communication) and 12m (email communication) (validation: ≤ 20 ng/ml cotinine)
Study funding	"This study was funded by grants from NHLBI (#R01 HL 61779 and #K24-HL04440), the NIH General Clinical Re- search Centers Program (#M01-RR-01066) and an unrestricted research grant from GlaxoSmithKline, Inc (GSK). GSK provided free drug and placebo and an unrestricted research grant to permit data collection to be completed when NHLBI funds were exhausted"
Author declarations	Not specified
Notes	PPA defined as validated self-report of no smoking in previous 7 days

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated stratified
Allocation concealment (selection bias)	Unclear risk	Quote: "The study pharmacist used the computer generated sequence, concealed from enrolment staff, to assign participants to study arm."
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Subjects and study personnel, except the statistician and pharmacist, were blind to treatment assignment“ + placebo controlled
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: “Subjects were considered smokers if they were lost to follow-up, failed to provide a saliva sample, or had a cotinine concentration >20 ng/ml.“
Blinding of outcome assessment (detection bias) Weight	Low risk	Weight measurement not specified but participants were blinded to treatment allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: “completed study” bupropion SR + counselling group: 85/127 (69%) (à 28 (23%) lost to follow-up); Quote: “completed study” placebo + counselling group: 80/127 (65%) (à 28 (23%) lost to follow-up)

2 Rigotti 2010

Study characteristics

Methods	Country: 15 countries in Europe, Asia, Americas

2 Rigotti 2010 *(Continued)*

	Setting: 39 research centres Study start date: February 2006; Study end date: August 2008
Participants	714 adult smokers, aged 35 - 75, smoking at least 10 cpd, with stable CVD and motivated to quit. 79% male, 80% white, mean cd 22, mean Fagerström 5.6
Interventions	• Varenicline 1.0 mg 2/d for 12 wks, preceded by 1 wk titrated dose • Placebo tablets as above Both groups received brief (10 mins) counselling at weekly clinic visits throughout treatment phase, and phone call 3d post-TQD
Outcomes	Mean (SD) weight change (kg) in wks 9 - 12 continuous abstainers at end of treatment (12 wks) and 12 months (Validation: expired CO ≤ 10 ppm)
Study funding	"This study was funded by Pfizer Inc. Editorial support for the development of this manuscript was provided by Alexandra Bruce, PhD, of UBC Scientific Solutions and was funded by Pfizer Inc."
Author declarations	"Drs Rigotti, Pipe, Benowitz, and Tonstad have consulted for Pfizer. Dr Rigotti has been the site principal investigator for clinical trials of smoking cessation medications funded by Pfizer, sanofi-aventis, and Nabi Biopharmaceuticals. Dr Pipe has received educational and research support in the past from Bristol Myers Squibb, Johnson & Johnson, GlaxoSmithKline, and Merrell Dow. Drs Benowitz and Tonstad served on the scientific planning committee for this study and have been paid consultants to Pfizer and other pharmaceutical companies that are developing and/or marketing smoking cessation medications. Dr Benowitz has been a paid expert witness in litigation against tobacco companies. At the time of the study, his family owned a small amount of Pfizer stock, but no longer does. Dr Tonstad has been the site principal investigator for clinical trials of smoking cessation medication and other medications funded by Pfizer and other pharmaceutical companies. Dr Arteaga is a statistical director at Pfizer Inc, supporting the varenicline studies. Dr Garza is a senior medical director of clinical research and development at Pfizer Inc, and the medical monitor for this study. The other authors report no conflicts."
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	The study sponsor conducted the randomization centrally using a computer-generated list that prespecified the order of treatment allocation
Allocation concealment (selection bias)	Low risk	see above
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double-blind + placebo-controlled. Quote: "Reported or observed cardiovascular events or deaths resulting from any cause were reviewed separately and adjudicated under blinded conditions by an independent event committee made up of 3 board-certified cardiologists who used a standard events manual". No further information given
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "Continuous abstinence was defined as self-reported abstinence from any tobacco- or nicotine-containing product since the last visit, but a subject with CO > 10 ppm was classified as a smoker regardless of self-reported abstinence.“

2 Rigotti 2010 *(Continued)*

Blinding of outcome assessment (detection bias) Weight	Unclear risk	Unclear how weight was measured and unclear of participants were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Flowchart: Of 355 assigned to varenicline group, 353 Received study drug, 293 (82.5%) completed treatment and 302 (85.1%) completed study (53 (14.9%) discontinued study); Of 359 assigned to placebo group, 350 received study drug, 186 (79.7%) completed treatment and 189 (80.5%) completed study (70 (19.7%) discontinued study).

2 Rose 2014

Study characteristics	
Methods	Country: USA Recruitment: newspaper, radio, and television advertisements Setting: Duke Center for Nicotine and Smoking Cessation Research In Charlotte, Durham, Raleigh and Winston-Salem, North Carolina. Study start date: March 2011; Study end date: July 2013
Participants	Total N: 222 18 - 65 years old, smoked an average ≥ 10 cpd for 3 cumulative years, have an expired air CO reading at screening of ≥ 10 ppm, express a desire to quit smoking within the next 30 days and were not responsive to early nicotine patch treatment (failing to show a decrease of 50% in ad lib smoking, assessed using expired-air CO) N per arm: varenicline + placebo = 109; varenicline + bupropion = 113 54.3% female, av age 44.1, av cpd 20.7, av FTND 6.1
Interventions	• Brief support + varenicline + placebo • Brief support + varenicline + sustained release bupropion (days 1 - 3: 150 mg once daily; Day 4 – 12 weeks: 150 mg twice daily) All participants recieved brief support (< 15-minute sessions held weekly for 2 weeks before the quit date and at 1, 3, 7 and 11 weeks after the quit date) and varenicline (up-titration, then 1 mg 2 x daily from day 8 to Week 12)
Outcomes	1. Mean weight change (kg) in abstainers at EOT (narrative discussion)
Study funding	Supported by National Institute on Drug Abuse grant 1P50 DA027840 and a grant from Philip Morris USA. The sponsors had no role in the planning or execution of the study, data analysis, or publication of results. Active bupropion sustained-release and placebo tablets were supplied by Murty Pharmaceuticals, under contract from the National Institute on Drug Abuse
Author declarations	The authors have consulting and patent purchase agreements with Philip Morris International for nicotine inhalation technology and consulting agreements with Targacept and Novartis
Notes	Participants provided written informed consent after receiving a complete description of the study, and they were compensated up to USD 330 for study participation The nicotine patch prequit responders were entered into a separate study to explore combination nicotine replacement therapy treatment, the results of which will be reported elsewhere
Risk of bias	

2 Rose 2014 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not specified
Allocation concealment (selection bias)	Unclear risk	Not specified
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double-blind, placebo-controlled design. No further information given
Blinding of outcome assessment (detection bias) Smoking	Low risk	Abstinence was identified by self-report of no smoking confirmed by expired-air CO levels #10 ppm Point (7-day) abstinence at 6 months (self-reported abstinence confirmed by expired-air CO level at the follow-up)
Blinding of outcome assessment (detection bias) Weight	Unclear risk	Not specified
Incomplete outcome data (attrition bias) All outcomes	Low risk	Withdrew/lost to follow-up placebo = 38/109 Withdrew/lost to follow-up bupropion = 41/113

2 Sachs 1993

Study characteristics	
Methods	Country: USA Recruitment: community volunteers Study start date: Jaunary 1990; Study end date: April 1990
Participants	220 adult smokers. av cpd 28 - 9, av weight 72 - 76 kg
Interventions	• Nicotine patch (15 mg/16-hr, 12 wks + 6 wks tapering) • Placebo patch All participants received physician advice at 8 visits during treatment period
Outcomes	Mean (SD) weight change (kg) in continuous abstainers at 6m (validation: CO < 10 ppm)
Study funding	"This research was supported in part by US Public Health Service grant DA-04986 from the National Institute on Drug Abuse and by research grants from Kabi Pharmacia AB and Parke-Davis"
Author declarations	Not specified
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement

2 Sachs 1993 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Method not stated
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double-blind + placebo-controlled. No further information given
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "Smoking abstinence was defined as (1) patient self-report of no smoking from the previous visit, with no slips of any kind allowed (if the subject reported even one puff from a cigarette, then the subject was classified as a failure); and (2) an exhaled air carbon monoxide level of 9 ppm or less at each visit. After all patch use was discontinued, at week 18, an additional objective confirmation was used: serum cotinine level of 15 ng/mL or less."
Blinding of outcome assessment (detection bias) Weight	Low risk	Weight objectively measured Quote: "At each visit, project personnel … measured vital signs, including weight …"
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "One subject in the active patch group dropped out due to a potential medication side effect. The total drop-out rate secondary to actual or potential adverse drug events was 0.9% (1/114) in the active treatment group vs 0.0% (0/107) in the placebo treatment group (P=0.3294)"

2 Saules 2004

Study characteristics	
Methods	Country: USA Recruitment: community volunteers Study start date: not specified; Study end date: not specified
Participants	150 smokers, 20% history of MDD, 55% F, av age 40
Interventions	• Fluoxetine 40 mg for 14 wks, nicotine patch for 10 wks • Fluoxetine 20 mg for 14 wks, nicotine patch for 10 wks • Placebo & nicotine patch All participants received CBT 6 sessions
Outcomes	Mean (SD) weight change (kg) in continuous abstainers at 6 months (email communication) (validation: CO < 10 ppm)
Study funding	"This work was supported by grant R01 DA I0492-01A1 (Dr. Schuster) from the National Institute on Drug Abuse, Bethesda, Md., and a Joe Young, Sr. research grant from the State of Michigan (Dr. Schuster). Nicotine transdermal patches were donated by McNeil Consumer Healthcare."
Author declarations	Not specified
Notes	

2 Saules 2004 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double-blind + placebo-controlled. No further information given
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "self- reported abstinence combined with CO less than 10 ppm.“
Blinding of outcome assessment (detection bias) Weight	Unclear risk	Weight likely self-reported. Quote: “Participants received additional compensation of $25 per visit for … provision of weight data … at three, six and twelve months post-quit date.“ Comment: Participants likely blinded to treatment but this is unclear.
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: “Overall, 60% of the participants completed the active phase of the study. The completion rate did not differ by group, nor did the rate of drop-out during the study differ by group (as assessed by log rank statistic)”

2 Sharma 2018

Study characteristics	
Methods	Country: India Recruitment: by invitation Setting: Trial centres were at the All India Institute of Medical Sciences (AIIMS), New Delhi and neighbouring tuberculosis and chest clinics in the National Capital Region of Delhi and the Sri Venkateswara Institute of Medical sciences (SVIMS), Tirupati, Andhra Pradesh Study start date: November 2010; Study end date: September 2016
Participants	Total N: 800 adult smokers, > 18 years with recently-diagnosed (primary TB/Relapse TB) smear-positive tuberculosis who self-report to smoke ≥ 10 whole cigarettes or bidis (rolled tobacco leaf) per day, every day N per arm: Control = 400; Intervention = 400 0.25% female, av age 34.6, av baseline BMI 18.6, av baseline weight 49.8, av FTND 6.8
Interventions	• Counselling • Counselling + nicotine replacement therapy (gum for 6 weeks) All participants received anti-tuberculosis treatment and behaviour-change counselling for smoking cessation (10 minutes at baseline, second and fourth week by healthcare workers trained by an expert in smoking cessation; Pamphlets and educational material provided at each follow-up visit)

2 Sharma 2018 *(Continued)*

Outcomes	Data measured during the trial but not available for extraction at the time of this update. • Mean (SD) weight change (kg) in abstainers at 6 months (24 weeks)
Study funding	Funding for the study was provided by EU-FP7 and ICMR. Professor S K Sharma was supported by the JC Bose Fellowship (No. SB/SB2/JCB-04/2013) of the Ministry of Science & Technology, Govt. of India.
Author declarations	The authors declare no competing interests
Notes	This study is new to the 2021 update.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "Patients were randomised in a 1:1 ratio to the arm receiving behaviour change counselling with NRT in the form of nicotine chewing gums (intervention arm) or only behaviour change counselling (control arm). Randomisation was performed by generation of random numbers through sequentially numbered, opaque sealed envelopes using a block randomisation scheme with variable block size."
Allocation concealment (selection bias)	Low risk	Quote: "…opaque sealed envelopes…"
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not placebo controlled although blinding would have been possible given this is a pharmacological trial.
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "biochemical quit rates defined as serum cotinine levels less than 10 ng/mL or BAT less than six parts per million."
Blinding of outcome assessment (detection bias) Weight	Unclear risk	Not specified
Incomplete outcome data (attrition bias) All outcomes	Low risk	Loss to follow-up: Control group = 18/400 Intervention group = 19/400

2 Shiffman 2002A

Study characteristics

Methods	Country: USA and UK (15 sites) Recruitment: community volunteers, low dependence (time to first cigarette > 30 mins) Study start date: Not specified; Study end date: Not specified
Participants	917 smokers, 58% female, av age 41, av cpd 17 - 18, av weight 74 - 76 kg
Interventions	• Nicotine lozenge, 2 mg. Recommended dose 1 every 1 - 2 hrs, min 9, max 20/day for 6 wks, decreasing 7 - 12 wks, available as needed 13 - 24 wks

2 Shiffman 2002A *(Continued)*

	• Placebo lozenge, same schedule All participants received brief advice at 4 visits.
Outcomes	Mean (SD) weight change (kg) in prolonged abstainers at end of treatment (email communication), 6 (email communication) and 12 months (email communication) (validation: CO ≤ 10 ppm)
Study funding	"This study was supported by GlaxoSmithKline Consumer Healthcare, Parsippany, NJ"
Author declarations	"Dr Shiffman provides consulting to GlaxoSmithKline Healthcare on matters relating to smoking control, and was compensated for his work on this project. Dr Shiffman also has an interest in a novel nicotine replacement product that is not addressed by this article. Dr Hajek has provided consulting to and received research funding from pharmaceutical companies, including GlaxoSmithKline Consumer Healthcare and Pharmacia Consumer Healthcare, Peapack, NJ. Drs Dresler, Gilburt, and Strahs and Mr Targett are employed by GlaxoSmithKline Consumer Healthcare"
Notes	Prolonged abstinence defined as sustained from 2 wks, no slips allowed

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method not stated
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double-blind + placebo-controlled. No further information given
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: “Participants’ reports of abstinence were subject to verification by an exhaled carbon monoxide level of no greater than 10 ppm.”
Blinding of outcome assessment (detection bias) Weight	Low risk	Weight likely objectively assessed: Quote: “Weight was measured at each study visit.“
Incomplete outcome data (attrition bias) All outcomes	High risk	Flowchart: 24-week completion low dependency, 2 mg lozenge group: 124/459 (27%) 24-week completion low dependency, placebo group: 78/458 (17%)

2 Shiffman 2002B

Study characteristics

Methods	Country: USA and UK (15 sites) Recruitment: community volunteers, high dependence (time to first cigarette < 30 mins) Study start date: Not specified; Study end date: Not specified
Participants	901 smokers, 55% female, av age 43 - 44, av cpd 25 - 26

2 Shiffman 2002B *(Continued)*

Interventions	• Nicotine lozenge, 4mg. Recommended dose 1 every 1-2 hrs, min 9, max 20/day for 6 wks, decreasing 7-12 wks, available as needed 13-24 wks • Placebo lozenge, same schedule
Outcomes	Mean (SD) weight change (kg) in prolonged abstainers at EOT (email communication), 6 (email communication) and 12 months (email communication) (validation: CO ≤ 10 ppm)
Study funding	"This study was supported by GlaxoSmithKline Consumer Healthcare, Parsippany, NJ"
Author declarations	"Dr Shiffman provides consulting to GlaxoSmithKline Healthcare on matters relating to smoking control, and was compensated for his work on this project. Dr Shiffman also has an interest in a novel nicotine replacement product that is not addressed by this article. Dr Hajek has provided consulting to and received research funding from pharmaceutical companies, including GlaxoSmithKline Consumer Healthcare and Pharmacia Consumer Healthcare, Peapack, NJ. Drs Dresler, Gilburt, and Strahs and Mr Targett are employed by GlaxoSmithKline Consumer Healthcare"
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method not stated
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double-blind + placebo-controlled. No further information given
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: “Participants’ reports of abstinence were subject to verification by an exhaled carbon monoxide level of no greater than 10 ppm.”
Blinding of outcome assessment (detection bias) Weight	Low risk	Weight likely objectively assessed: Quote: “Weight was measured at each study visit.“
Incomplete outcome data (attrition bias) All outcomes	High risk	Flowchart: 24-week completion high dependency, 4 mg lozenge group: 117/450 (26%); 24-week completion high dependency, placebo group: 51/451 (11%)

2 Simon 2004

Study characteristics

Methods	Country: USA Recruitment: outpatients Study start date: 1 September 1998; Study end date: 31 March 2001

2 Simon 2004 *(Continued)*

Participants	244 smokers, 79% veterans, 15% F, av age 50, av cpd 24, av BMI 26 - 28
Interventions	• Bupropion 300 mg for 7 wks, nicotine patch for 2m • Placebo bupropion, nicotine patch for 2m All participants received 3m of CBT counselling, S-H materials and telephone follow-up counselling
Outcomes	Mean (SD) weight change (kg) in continuous abstainers at 12m (email communication) (validation: salivary cotinine of < 15 ng/ml)
Study funding	"This study was entirely funded by grant 7RT-0033 from the California Tobacco-Related Disease Research Program, Oakland, Calif"
Author declarations	Not specified
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated
Allocation concealment (selection bias)	Low risk	Participants allocated according to computer-generated list
Blinding of participants and personnel (performance bias) All outcomes	High risk	Double-blind + placebo-controlled. Quote: “All study personnel engaged in providing interventions to participants were blinded to treatment assignment.“ “A significant percentage of participants were able to guess whether they were taking either active bupropion or placebo“
Blinding of outcome assessment (detection bias) Smoking	High risk	Quote: “We collected only self-reported data on smoking cessation at all time points except for the final 12 month follow-up hence, we were unable to verify biochemically the smoking cessation point prevalences at the other times.”
Blinding of outcome assessment (detection bias) Weight	High risk	Quote: "Body mass index (calculated as weight in kilograms divided by the square of height in meters) and change in weight over time were determined using self- reported or medical record data“ Comment: Participants were blinded to treatment condition, but a significant percentage correctly guessed allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: “Of the 244 participants enrolled, 3 (1%) were lost to follow-up (all randomized to the placebo arm) and an additional 5 participants (2%) died during the study (2 bupropion- and 3 placebo-treated subjects).”

2 Simon 2009

Study characteristics

Methods	Setting: San Francisco Veterans Affairs Medical Center, USA Recruitment: hospitalized volunteers

2 Simon 2009 *(Continued)*

	Study start date: January 2004; Study end date: August 2006
Participants	85 inpatient smokers, 3.5% female, av age 56 yrs, av BMI 27.5, av cpd 16
Interventions	• Bupropion 300 mg for 7 wks • Placebo All ppts received Individual cognitive behavioural 30 - 60 mins during hospital stay + 5 phone calls at wk 1, wk 3, wk 5, wk 8, wk 12; recycling encouraged
Outcomes	Mean (SD) weight change (kg) in continuous abstainers at 6m (data from email communication) validation: saliva cotinine < 15 ng/ml
Study funding	"California Tobacco-Related Disease Research Program (12RT-0148)"
Author declarations	"None declared"
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	used a computer algorithm to generate a random list of treatment assignments
Allocation concealment (selection bias)	Low risk	All study personnel engaged in providing interventions to participants were blinded to treatment assignment
Blinding of participants and personnel (performance bias) All outcomes	High risk	Double-blind + placebo controlled. Quote: “All study personnel engaged in providing interventions to participants were blinded to treatment assignment.“ “A significant percentage of participants were able to guess whether they were taking either active bupropion or placebo“
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "Because many of the participants live great distances from the SF-VAMC, we used salivary cotinine levels (≥ 15 ng/ml) as an indicator of current tobacco use, rather than measuring carbon monoxide in person (Jarvis, Tunstall-Pedoe, Feyerabend, Vesey, & Saloojee, 1987). We permitted the mailing of saliva samples in special envelopes when necessary. For self-reported quitters who had salivary cotinine levels of 15 ng/ml or higher, we ascertained by telephone interview whether they were using NRT at the time the sample was provided. We considered three participants (two in the bupropion arm and one in the placebo arm) to be nicotine dependent and, thus, smokers"
Blinding of outcome assessment (detection bias) Weight	High risk	Quote: "Body mass index and change in weight over time were determined using self-reported or medical record data“. Comment: Participants were blinded to treatment condition, but a significant percentage correctly guessed allocation
Incomplete outcome data (attrition bias) All outcomes	Low risk	24-week completion bupropion + counselling group: 38/42 (90.47%) (2 withdrew, 1 died, 1 lost to follow-up); 24-week completion placebo + counselling group: 36/43 (83.72%) (5 withdrew, 1 died, 1 lost to follow-up)

2 Stapleton 1995

Study characteristics	
Methods	Country: UK Recruitment: General practice patients Study start date: Not specified; Study end date: Not specified
Participants	1200 smokers, av cpd 23 - 4, av weight 71 - 72 kg
Interventions	• Nicotine patch standard dose (15 mg/16-hr for 18 wks) • Nicotine patch with dose increase to 25 mg at 1 wk if required • Placebo patch group The nicotine patch groups were further randomized to gradual tapering or abrupt withdrawal from wk 12 All participants received physician advice and brief support at 1, 3, 6, 12 wks
Outcomes	Mean (SD) weight change (kg) in prolonged abstainers at end of treatment (email communication) and 12m (email communication) (validation: CO < 10 ppm)
Study funding	"This study was funded by Pharmacia AB, who also supervised and monitored procedures and data collection in the practices. We thank the MRC and Imperial Cancer Research Fund for financial support of the Health Behaviour Unit. The Unit`s staff designed the study, analysed and wrote up the results, and assayed saliva cotinine concentrations"
Author declarations	Not specified
Notes	Prolonged abstinence defined as validated self-reported abstinence from week 2. The dose increase after 1 wk did not affect cessation, 1+2 vs 3 in main comparison.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Computer-generated list
Allocation concealment (selection bias)	Low risk	Quote: "Study subjects were assigned a treatment according to a computer generated list compiled in blocks of six"
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double-blind + placebo-controlled. No further information given
Blinding of outcome assessment (detection bias) Smoking	Low risk	Self-reported abstinence was validated by ECO < 10 ppm and saliva cotinine < 20 ng/ml
Blinding of outcome assessment (detection bias) Weight	Low risk	Weight likely objectively measured: Quote: “at week 0 and all subsequent visits data collection included body weight, …”
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not specified

2 Sutherland 1992

Study characteristics	
Methods	Country: UK Recruitment: Smoking cessation clinic patients Study start date: January 1989; Study end date: March 1990
Participants	227 male and female smokers, av cpd 25 - 27, av age 38 - 41 yrs, av weight women 62 - 64 kg, av weight men 75 - 77 kg
Interventions	• Nicotine nasal spray, maximum 40 mg/day • Placebo spray All participants received 4 wks of group support
Outcomes	Mean (SD) weight change (kg) in prolonged abstainers at 12 months (validation: CO < 10 ppm)
Study funding	"We thank the Medical Research Council and the Imperial Cancer Research fund for financial support; (…) Kabi Pharmacia Therapeutics AB for supplying the nasal sprays, and their representative, Dr Mikael Franzon"
Author declarations	Not specified
Notes	Prolonged abstinence defined as validated self-reported no smoking from the start of the last week of group treatment to the 12-month follow-up

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Drew card with A or P for active or placebo allocation
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: “subjects and therapists were blind to spray assignment”
Blinding of outcome assessment (detection bias) Smoking	Low risk	Self-reported abstinence validated by a CO concentration of < 10 ppm
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: “Subjects were weighed (indoor clothes, minus shoes) at assessment, after 4 weeks, and at all follow-ups”
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: “On average, 96% in the active group and 95% in the placebo group were followed up at each of the five occasions”

2 Tashkin 2011

Study characteristics	
Methods	Country: USA (17 centres), Spain (3 centres), France (4 centres), Italy (3 centres) Setting: 27 research centres. Study start date: 2 May 2006; Study end date: 30 April 2009
Participants	504 adult smokers with mild-to-moderate COPD, aged 35+, smoking 10+ cpd, motivated to quit; allocated to varenicline (250), or placebo (254). 62% male, mean age 57, cpd 24 - 25, Fagerström score 5.9 - 6.2., av BMI 26.6 (SD 5.5)
Interventions	• Varenicline 1.0 mg 2/d for 12 wks, preceded by 1 wk titrated dose. • Placebo tablets as above. Both groups received SC educational booklet, + brief (10 mins) counselling at weekly clinic visits throughout treatment phase, and phone call 3d post-TQD.
Outcomes	Mean (SD) weight change at in continuous abstainers EOT (12 wks) and 12m (Validation: CO ≤ 10 ppm)
Study funding	"This study was funded by Pfizer Inc. Role of sponsors: Editorial support for the development of this manuscript was provided by Brenda Smith, PhD, and administrative support was provided by Sue Francis, both of UBC Scientific Solutions with funding from Pfizer Inc."
Author declarations	"Dr Tashkin received grant support from Pfizer Inc and Nabi Pharmaceuticals and fees for attending advisory board meetings from Pfizer Inc. Dr Hays received a research grant from Pfizer Inc for the conduct of the clinical trial described in this manuscript. In the past 3 years, Dr Rennard has been a consultant or a member of an advisory board for Able Associates, Adelphi Research, Almirall/Prescott, APT Pharma/Britnall, Aradigm, AstraZeneca, Boehringer Ingelheim, Chiesi, CommonHealth, Consult Complete, COPDForum, Data Monitor, Decision Resources, Defined Health, Dey, Dunn Group, Eaton Associates, Equinox, Gerson, GlaxoSmithKline, Infomed, KOL Connection, M Pankove, MedaCorp, MDRx Financial, Mpex, Novartis, Nycomed, Oriel Therapeutics, Otsuka, Pennside Partners, Pfizer Inc (varenicline), Pharma Ventures, Pharmaxis, Price Waterhouse, Propagate, Pulmatrix, Reckner Associates, Recruiting Resources, Roche, Schlesinger Medical, SciMed, Sudler and Hennessey, TargeGen, Theravance, UBC, Uptake Medical, and VantagePoint Management. Dr Rennard has lectured for the American Thoracic Society, AstraZeneca, Boehringer Ingelheim, California Allergy Society, Creative Educational Concept, France Foundation, Information TV, Network for Continuing Ed, Novartis, Pfizer, and SOMA and has received industry-sponsored grants from AstraZeneca, Biomarck, Centocor, Mpex, Nabi Pharmaceuticals, Novartis, and Otsuka. Ms Ma and Drs Lawrence and Lee are all employees of Pfizer Inc, own Pfizer Stock, and have Pfizer stock options"
Notes	

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Methods not described
Allocation concealment (selection bias)	Unclear risk	Methods not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double-blind + placebo-controlled. No further information given

2 Tashkin 2011 *(Continued)*

Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "A CO value of ≤ 10 parts per million (ppm) was the criterion to confirm smoking abstinence."
Blinding of outcome assessment (detection bias) Weight	Unclear risk	Unclear how weight was measured and unclear if participants were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: "A larger proportion of participants receiving varenicline than placebo completed the treatment phase (83.5% vs 76.9%, respectively), and the entire 52-week study (71.0% vs 62.5%, respectively)"

2 TNSG 1991

Study characteristics	
Methods	Country: USA (9 sites) Recruitment: community volunteers (treated at smoking cessation clinics) Study start date: Not specified; Study end date: Not specified
Participants	808 smokers, 60% female, av age 43, av cpd 31, av weight 72.4 kg
Interventions	• Nicotine patch (21 mg /24-hr, 6 wks+) • Nicotine patch 14 mg • Placebo patch All participants received group smoking cessation behavioural support
Outcomes	Mean (SD) weight change (kg) in continuous abstainers at EOT (6 wks) (validation: CO < 9 ppm)
Study funding	This research was supported in part by the Merell Dow Pharmaceutical Comany and by Research Grant DA 03893 and Training Grant T32DA07209 from the National Institute on Drug Abuse
Author declarations	Not specified
Notes	2 trials pooled and data relating to a 7 mg patch group used in only 1 trial omitted

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method not stated
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Randomized placebo-controlled. No further information given
Blinding of outcome assessment (detection bias)	Low risk	CO level < 8 ppm

2 TNSG 1991 *(Continued)*
Smoking

Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: "At each lab visit, subjects were weighed on a standard balance beam scale"
Incomplete outcome data (attrition bias) All outcomes	High risk	Quote: "Over the course of the 10-week trial, there were 44 (50.6%) dropouts"

2 Tonstad 2006

Study characteristics	
Methods	Country: USA (6 centres) and "international" (18 centres, across Canada, Czech Republic, Denmark, Norway, Sweden, UK) Recruitment: smoking cessation clinics Study start date: 13 April 2003; Study end date: 17 February 2004
Participants	1210 successful quitters (62.8% of initial cohort) following a 12-wk open-label course of varenicline for smoking cessation. 51% female, av age 45, av cpd 21
Interventions	• Varenicline 1 mg x 2/day for 11 wks after 1wk titrated dosage • Placebo tablets, same regimen Participants had already received 12 wks of varenicline. All participants received brief counselling (≤ 10 mins) at each clinic visit throughout treatment phase (wks 13 - 24). Treatment phase clinic visits were at wks 13, 14, 16, 20 and 24
Outcomes	Mean (SD) weight change (kg) in continuous abstainers at 6m (validation: CO ≤ 10 ppm)
Study funding	"This study was sponsored by Pfizer Inc, which provided funding, study drug and placebo, and monitoring. **Role of the Sponsor:** Pfizer Inc was involved in all elements of this study, including but not limited to the study design and monitoring. In addition, the database containing the findings of the 25 individual investigator sites was maintained by Pfizer Inc, and statistical analyses were performed at Pfizer Inc by Mr Billing and Ann Pennington, MS. **Independent Statistical Analysis:** Ingar Holme, PhD, professor of biostatistics, University of Oslo, and Ullevål University Hospital, had access to all of the data used in the study and performed an independent analysis. Dr Holme performed analyses of the primary and key secondary end points using logistic regression and cross-tabulations. Results were identical to those obtained by the sponsor. Dr Holme received compensation for this reanalysis from Pfizer Inc."
Author declarations	"Dr Tonstad reports receiving honoraria for lecturing and consultancies for Pfizer and other manufacturers of smoking cessation medications; Dr Tønnesen reports receiving honoraria for participation in advisory boards for Pfizer and Sanofi-Aventis and for presentations relating to smoking cessation from Pfizer and GlaxoSmithKline; Dr Hajek reports consulting for manufacturers of smoking cessation medications, including Pfizer; Dr Williams reports stock ownership in Pfizer; and Dr Reeves reports stock ownership in Pfizer. No other disclosures were reported"
Notes	Continuous abstinence was defined as validated complete abstinence during week 13 - 24
Risk of bias	

2 Tonstad 2006 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated lists stratified by centre, x 4 random block design
Allocation concealment (selection bias)	Low risk	computer-generated sequence used for allocation of participants
Blinding of participants and personnel (performance bias) All outcomes	Low risk	double-blind + placebo-controlled. Participants blinded
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "participants whose CO value was more than 10 ppm were classified as smokers“
Blinding of outcome assessment (detection bias) Weight	Low risk	Unclear how weight was measured but participants were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	Flowchart: Of 603 assigned to varenicline, 602 received treatment as assigned, 555 completed the treatment period (47 discontinued) and 494 completed the study (61 discontinued follow-up); Of 607 assigned to receive placebo, 604 received placebo as assigned, 510 completed the treatment period (94 discontinued) and 463 completed the study (47 discontinued follow-up)

2 Tsai 2008

Study characteristics	
Methods	Country: Taiwan and Republic of Korea Recruitment: community volunteers Study start date: February 2005; Study end date: March 2006
Participants	250 healthy adult volunteers, motivated to quit, aged 18 to 75; allocated to varenicline (126), or placebo (124). 11% female, av age 40.3, BMI > 15 or < 38 or weight > 45.5 kg, av cpd 24
Interventions	• Varenicline 1.0 mg x 2/day 12 wks, 1st wk titrated • Placebo tablet x 2/day 12 wks All participants received a smoking cessation booklet *Clearing the Air* at baseline + brief counselling (≤ 10 mins) at each clinic visit
Outcomes	Mean (SD) weight change (kg) in prolonged abstainers at end of treatment (validated: CO ≤ 10 ppm)
Study funding	"Varenicline and placebo were supplied by Pfizer and the study was funded by Pfizer Inc. (ClinicalTrials.gov Identification Number NCT00141167)"
Author declarations	"Drs. Tsai and Cho have been members of Pfizer-sponsored advisory panels and, together with Drs. Cheng, Kim, and Hsueh, were investigators for a Pfizer- sponsored clinical trial. Editorial assistance was provided by Christopher Grantham, PhD, of Envision Pharma, Horsham, United Kingdom, and funded by Pfizer Inc., New York, New York."
Notes	Prolonged abstinence is defined as validated complete abstinence during weeks 9 - 12

2 Tsai 2008 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Permutated blocks (block = 4)
Allocation concealment (selection bias)	Low risk	web- and telephone-based assignment
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind + placebo-controlled. Quote: "Knowledge of treatment assignments was withheld from those directly involved with the operation of the study, including study subjects, study investigators and their staffs, and sponsor personnel involved in clinical operations."
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: “no reported smoking (not even a puff) or other nicotine use during the final 4 weeks of treatment, verified by end-expiratory CO levels of ≤10 ppm“
Blinding of outcome assessment (detection bias) Weight	Low risk	Weight likely objectively assessed: Quote: "Vital signs and physical measurements were determined either at screening or baseline (height and body temperature) or at all clinic visits in both the treatment and nontreatment follow-up phases (body weight ..)”
Incomplete outcome data (attrition bias) All outcomes	Low risk	Quote: “Study completion rates were 95.2% in the varenicline group and 94.4% in the placebo group. The numbers of subjects discontinuing during the 12-week treatment phase of the study were 4 (3.2%) and 3 (2.4%) in the varenicline and placebo groups, respectively. The numbers of subjects discontinuing during the 12-week, nontreatment, follow-up phase were 2 (1.6%) in the varenicline group and 4 (3.2%) in the placebo group.”

2 Tønnesen 1991

Study characteristics

Methods	Country: Denmark Recruitment: community volunteers Study start date: Not specified; Study end date: Not specified
Participants	289 smokers, 70% female, av age 45, av cpd 22
Interventions	• Nicotine patch (15 mg/16-hr for 12 wks with tapering) • Placebo patch All participants receive brief behavioural support at clinic visits
Outcomes	Mean (SD) weight change (kg) in prolonged abstainers at EOT (email communication) and 12m (email communication) (validation: CO ≤ 10 ppm)
Study funding	"Supported in part by a grant from Kabi Pharmacia Therapeutics"

2 Tønnesen 1991 *(Continued)*

Author declarations	"Dr Tonnesen has been consultant for Kabi Pharmacia Therapeutics, developer of the nicotine patch and has received grants from the company. Dr. Säwe is medical director of Kabi Pharmacia Therapeutics"
Notes	Prolonged abstinence was defined as validated self-report abstinence after 1 wk of quitting

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	According to a computer-generated randomisation code
Allocation concealment (selection bias)	Unclear risk	Quote: "packages labelled with consecutive numbers from computer-generated random code"
Blinding of participants and personnel (performance bias) All outcomes	High risk	Double-blind + placebo-controlled Quote: “the blinding of this study was imperfect, in that 67 percent of the subjects guessed correctly which treatment they had received”
Blinding of outcome assessment (detection bias) Smoking	Low risk	Self-reported abstinence validated by a CO concentration of < 10 ppm
Blinding of outcome assessment (detection bias) Weight	Low risk	Likely objectively measured: Quote: “The same two nurses conducted the assessments (recording weight …)”
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: "3 subjects completely lost to follow up from 26 weeks" Comment: No further information given

2 Tønnesen 1993

Study characteristics

Methods	Country: Denmark Recruitment: community volunteers Study start date: Not specified; Study end date: Not specified
Participants	286 smokers, av cpd 20, 60% F, av age 39
Interventions	• Nicotine inhaler (2 - 10/day) up to 6m • Placebo inhaler All participants received brief advice at 8 clinic visits, 0, 1, 2, 3, 6,12, 24, 52 wks)
Outcomes	Mean (SD) weight change (kg) in continuous abstainers at EOT (email communication) and 12m (email communication) (validation: expired CO < 10 ppm)
Study funding	"This investigation was supported by a grant from Kabi Pharmacia Therapeutics, Helsingborg, Sweden"

2 Tønnesen 1993 *(Continued)*

Author declarations	"Drs Tonnesen, Norregaard, Mikkelsen, and Jorgensen have received fees from Kabi Pharmacia for consultancies and honoraria for educational activities. Mr Nilsson is employed by Kabi Phamacia"
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated randomization code
Allocation concealment (selection bias)	Unclear risk	Quote: "participants were randomly assigned according to code generated by a computer".
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind + placebo-controlled. Quote: “Forty-six percent on active treatment and 58% on placebo identified the treatment correctly, 13% on active treatment and 15% on placebo guessed wrong, and 42% on active treatment and 27% on placebo did not know which treatment they had received”
Blinding of outcome assessment (detection bias) Smoking	Low risk	Self-reported abstinence validated by a CO concentration of < 10 ppm
Blinding of outcome assessment (detection bias) Weight	Low risk	Likely objectively measured: Quote: “Two nurses conducted the assessments (weight, …)”
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: “Six subjects were unavailable for follow-up, and seven subjects were excluded because of protocol violation”

2 Ussher 2003

Study characteristics

Methods	Country: England Recruitment: community volunteers Study start date: not specified; Study end date: not specified
Participants	309 sedentary smokers, 60% female, av age 43, av cpd 22, av BMI 25 - 26
Interventions	• Exercise counselling (once a week for 7 weeks) + cessation programme (once a week for 7 weeks) • Cessation programme as 1. once/week for 7 weeks + brief health education once/week for 7 weeks
Outcomes	Mean (SD) weight change (kg) in continuous abstainers at end of treatment
Study funding	"This study was supported through grant CE1198/0101 from the Cancer Research Campaign (now Cancer Research UK) to the authors"
Author declarations	Not specified

2 Ussher 2003 *(Continued)*

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated
Allocation concealment (selection bias)	Low risk	Allocated in order of attendance
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "Smoking abstinence was verified with expired air CO concentration (cut-off, 10 p.p.m.)“
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: “clothed weight and height, without shoes, were measured on calibrated scales to the nearest 0.25 kg and 0.5 cm, respectively.“
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: “Attendance at the quit day visit was slightly, although not significantly, higher for the control group than for the exercise group [89% (129/145) versus 83.1% (128/ 154), respectively]; this reduced the chance of finding a significant effect for the exercise intervention.” Comment: No further information.

2 Uyar 2007

Study characteristics

Methods	Country: Turkey Setting: cessation clinic Recruitment: cessation clinic patients Study start date: September 2002; Study end date: Not specified
Participants	131 smokers; 81% M, av age 36, av baseline weight 70 - 75kg, av FTND score 3.9 - 4.8
Interventions	• Bupropion 300mg for 7 weeks (150 mg daily for the first 3 days, then 150 mg twice daily for 6 weeks) • Nicotine patch 21 mg for 6 wks incl tapering • Advice and follow-up only All arms: Brief counselling and booklet on consequences of smoking with follow-up for 24 wks
Outcomes	Mean (SD) weight change (kg) in continuous abstainers at 24 weeks (data from email communication) Validation: CO levels < 10 ppm
Study funding	None specified
Author declarations	None specified
Notes	

2 Uyar 2007 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	no mention of blinding and no placebo used
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "Declaration of quitting and exhaled carbon monoxide level less than 10 ppm was accepted as success criteria."
Blinding of outcome assessment (detection bias) Weight	Unclear risk	Quote: "…weight gain were recoded at follow-up visits at 2, 4, 8, 12, 24 weeks." No further information on how weight was measured was provided
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No mention of any losses to follow-up

2 Walker 2020

Study characteristics

Methods	Country: New Zealand Recruitment: via media advertising/social media and directed to contact the study centre at the University of Auckland's National Institute for Health Innovation by freephone, email, Facebook or through the study website Setting: Telephone Study start date: March 2016; Study end date: August 2018
Participants	Total N: 1124 smokers who want to quit in the next 3 months, reside in New Zealand, ≥18 years N per arm: NP = 125; NP + NEC = 500; NP + Non-EC = 499 68.3% female, av age 41.6, av cpd 17.3
Interventions	• Moderate-intensity smoking cessation behavioural support (10 - 15 mins weekly telephone calls for 6 weeks) + nicotine patch (21 mg, 24-h nicotine patch (Habitrol) for 14 weeks) • Arm 1 + E-cigarette containing nicotine (second-generation eVOD (Kangertech, Shenzhen GuangDong, China); choice of 1 of 2 tobacco e-liquid flavours, nicotine content: 18 mg/mL, written and online video device instructions provided) • Arm 1 + E-cigarette not containing nicotine (as per Arm 2 but with 0 mg/mL nicotine content)
Outcomes	• Mean (SD) weight change (kg) in abstainers at EOT (self-reported abstinence) and 6 months (abstinence CO-verified)

2 Walker 2020 *(Continued)*

Study funding	Health Research Council of New Zealand; Role of the funding source: The sponsor of the study had no role in the study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.
Author declarations	NW, CB, MV, GL, ML, and VP report grants from the Health Research Council of New Zealand, during the conduct of the study. NW, CB, MV, and VP report grants from Pfizer, outside of the submitted work. GL chairs the organisation End Smoking New Zealand, which advocates for harm reduction approaches to tobacco control. E-cigarettes were purchased from a New Zealand e-cigarette online retailer (NZVAPOR, https://www.nzvapor.com/), e-liquid was purchased from Nicopharm, Australia (www.nicopharm.com.au/), and nicotine patches were supplied by the New Zealand Government via their contract with Novartis (Sydney, Australia). NZVAPOR also provided, at no cost to participants, on-line and phone support regarding use of the e-cigarettes. Neither NZVAPOR nor Nicopharm have links with the tobacco industry. None of the above parties had any role in the design, conduct, analysis, or interpretation of the trial findings, or writing of this publication.
Notes	Authors provided additional data upon request This study is new to the 2021 update.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "participants will be allocated to one of the three study groups in a 1:4:4 ratio (21mg nicotine patch alone: 21mg nicotine patch plus 18 mg/mL nicotine e-cigarette: 21 mg nicotine patch plus nicotine-free e-cigarette) using stratified block randomisation (block size of nine). Randomisation will be stratified by ethnicity (Māori, non-Māori) to ensure an equal balance in this key prognostic factor. The computer-generated randomisation sequence will be prepared by the study statistician.“
Allocation concealment (selection bias)	Unclear risk	Not specified
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "Participants and all research staff (except the project manager) are blinded to the nicotine content of the e-juice (the e-juice is stored in a brown bottle), until after data lock. The project manager is not involved in any data collection or interaction with trial participants. If required, the medical practitioner who reviews all adverse event reports may request that the participant’s data be un-blinded. This un-blinding will be undertaken by the study statistician.“
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: “The primary outcome was continuous smoking abstinence 6 months after the agreed quit date (self-reported abstinence since quit date, allowing five or fewer cigarettes in total). Abstinence was verified by a researcher or community-based cessation provider using standardised exhaled carbon monoxide (CO) measurement with a Bedfont Smokerlyzer (Bedfont Scientific Ltd, Kent, UK), with a reading of 9 ppm or lower signifying abstinence.” Comment: Continuous abstinence (CO-verified at 12 months) was secondary outcome
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: "We asked a subsample of participants for their self-reported weight and height at baseline, then their weight (self-reported) at three and six months post-quit“ Comment: Participants were blinded to treatment allocation

2 Walker 2020 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	24-week assessment: NP group: 63/125 (50.4%) NP + NEC group: 339/500 (67.8%) NP + Non-NEC: 337/499 (67.5%)

2 Wallstrom 2000

Study characteristics	
Methods	Country: Sweden Recruitment: community volunteers Study start date: Not specified; Study end date: Not specified
Participants	247 smokers (10+ cpd), 59% female, av age 45, av cpd 18 - 20, av weight (male) 80 - 81kg, av weight (female) 66 - 67 kg
Interventions	• Nicotine sublingual tablet 2 mg. Recommended dosage 1 tab/hr for smokers with FTND < 7, 2 tabs/hr for scores ≥ 7. After 3m treatment, tapering period of 3m if necessary • Placebo tablet All participants received brief 5 mins counselling at study visits
Outcomes	Mean (SD) weight change (kg) in prolonged abstainers at 12 months (validation: CO < 10 ppm)
Study funding	Not specified
Author declarations	Not specified
Notes	Prolonged abstinence defined as complete abstinence from wk 2

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer assignment
Allocation concealment (selection bias)	Low risk	Quote: "Subjects were randomised to receive either active or placebo treatment using a computer program".
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double-blind + placebo-controlled. No further information given
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "Success without slips: continuous, self-reported complete abstinence from week 2 until end-point, verifjed by exhaled CO level, 10 p.p.m. from week 3 onwards“
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: "Subjects were also weighed, using the same scales, at each visit.“

2 Wallstrom 2000 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Quote: “In the highly dependent group .. there was a high dropout rate between the 6- and 12-month follow-up visits”

2 Wang 2009

Study characteristics	
Methods	Setting: Not described Country: China (10 sites), Singapore (3 sites), Thailand (2 sites)udy start date: Not specified; Study end date: Not specified
Participants	333 healthy adult volunteers, aged 18 to 75; 97% male, mean age 39, BMI > 15 and < 38 or weight > 45.5 kg, mean cpd 20, mean Fagerström score 5.4
Interventions	• Varenicline 1.0 mg x 2/day • Placebo tablet x 2/day Treatment period 12 wks, 1st wk titrated dosage. All participants received a smoking cessation booklet at baseline, + brief counselling (10 mins) at each clinic visit, except for wks 5 and 7, when counselling was conducted by phone
Outcomes	Mean (SD) weight change (kg) in continuous abstainers at EOT (12 wks) and 6 months (Validation: CO ≤ 10 ppm)
Study funding	"Pfizer Inc. funded the study"
Author declarations	"Pfizer Inc. funded the study and was involved with its design, analysis and writing the manuscript. All authors had complete access to all relevant data. Dahlia Garza and Simon Davies are employees of Pfizer Inc., and therefore hold shares in the company. Editorial support was provided by Aideen Young, PhD, of UBC Scientific Solutions and funded by Pfizer Inc. None of the other authors hold shares in any companies. Chen Wang and Dan Xiao are affiliated with the WHO Collaborating Centre for Tobacco or Health. WHO had no role in the study’s funding, design, analysis or write-up."
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	eligible participants were randomised in a 1:1 ratio
Allocation concealment (selection bias)	Unclear risk	not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double-blind + placebo-controlled. No further information given
Blinding of outcome assessment (detection bias) Smoking	Low risk	Self-reported abstinence validated by a CO concentration of < 10 ppm

2 Wang 2009 *(Continued)*

Blinding of outcome assessment (detection bias) Weight	Unclear risk	Unclear how weight was measured
Incomplete outcome data (attrition bias) All outcomes	Low risk	Flowchart: Of those randomized to the varenicline group, 165 received at least one dose, 160 (97%) completed treatment (5 (3.0%) discontinued) and 158 (95.8%) completed the study (7 (4.2%) discontinued); Of those randomized to the placebo group, 168 received at least one dose, 162 (96.4%) completed treatment (6 (3.6%) discontinued) and 161 (95.8% completed the study (7 (4.2%) discontinued).

2 Xiao 2019

Study characteristics	
Methods	Country: China Recruitment: from smoking cessation clinics and via advertisements published in the hospitals Setting: 10 academic or hospital-associated smoking cessation clinics in 6 cities (Beijing, Shenyang, Tianjin, and Shanghai [2 sites each]; Hangzhou and Guangzhou [1 site each]) Study start date: May 2009; Study end date: March 2011
Participants	**Total sample** Total N: 722 smokers, ≥ 18 years, smoking regularly everyday for ≥ 1 year and strongly motivated to quit (using nicotine mint lozenge) 3.2% female, av age 39.1, av FTND 4.3 **Low-dependence stratum** Total N: 438 participants who smoked their first cigarette > 30 mins after awakening N per arm: Nicotine = 241; Placebo = 242 3.7% female, av age 39.2, av baseline weight 72.1, av FTND 2.6 **High-dependence stratum** Total N: 240 participants who smoked their first cigarette within 30 mins after awakening N per arm: Nicotine = 120; Placebo = 120 (1 participant withdrew and not included in analysis) 2.1% female, av age 42.2, av baseline weight 75.1, av FTND 5.9
Interventions	**Low-dependence stratum** 1. 0 mg nicotine placebo lozenge 2. 2 mg nicotine placebo lozenge **High-dependence stratum** 1. 0 mg nicotine placebo lozenge 2. 4 mg nicotine lozenge Dosing schedule for all groups:

2 Xiao 2019 *(Continued)*

	Week 1 - 6: 1 lozenge every 1 - 2 hours, 9 - 15/day Week 7 - 9: 1 lozenge every 2 - 4 hours, 3 - 6/day Week 10 - 12: 1 lozenge every 4 - 8 hours, 3 - 6/day After week 12: Use 1 - 2 lozenges/day; Discontinue use after 24 week. All participants received low-intensity behavioural support sessions for 10 minutes at visit 2 through to visit 5 (i.e. weeks 0, 1, 2, and 4 of treatment). Diary cards were provided to record cravings, withdrawal symptoms, and daily lozenge usage
Outcomes	**Low-dependence stratum** • Mean (SD) weight change (kg) in abstainers at EOT and 6 months **High-dependence stratum** • Mean (SD) weight change (kg) in abstainers at EOT and 6 months.
Study funding	"This study was sponsored by Tianjin Sino-American SmithKline & French Laboratory Ltd. Medical writing assistance was provided by Peloton Advantage, LLC, an OPEN Health company, and was funded by GlaxoSmithKline Consumer Healthcare. GlaxoSmithKline Consumer Health- care provided a full review of the article.“ All study treatments were provided by Sino-American Tianjin Smith Kline & French Laboratories Ltd, Tianjin, China
Author declarations	The authors report no conflicts of interest
Notes	This study is new to the 2021 update.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	The randomization schedule was computer-generated and was provided to the site by the GSK Biostatistics Department
Allocation concealment (selection bias)	Unclear risk	Not specified
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Quote: "This was a double-blind study. Sponsors, sponsor’s representatives, the investigator, staff, and subjects were blinded to treatment regimen“
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: "Abstinence was confirmed by expiratory CO levels threshold of <= 10 ppm at each in-person visit to the study site. Subjects who failed to meet the success criteria and those with unknown smoking status were counted as failures.“
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: “Body weight, concomitant medications, and vital signs were recorded.” Not entirely clear if weight was objectively recorded. Self-report cannot be ruled out, but participants were blinded.
Incomplete outcome data (attrition bias) All outcomes	Low risk	2 mg Placebo: 48/242 dropped out 2 mg NRT: 48/241 dropped out 4 mg placebo: 26/120 dropped out

2 Xiao 2019 *(Continued)*

	4 mg NRT: 22/120 dropped out

2 Zellweger 2005

Study characteristics	
Methods	Country: 12 European countries, 26 centres Recruitment: volunteers, healthcare professionals (qualified practising physician or nurse) Study start date: not specified; Study end date: not specified
Participants	667 smokers (≥ 10 cpd) (excludes 1 centre enrolling 20 people, and 3 people who took no medication) 64% female, av cpd 23
Interventions	• Bupropion SR 300 mg/day for 7 wks • Placebo All participants received brief (10 - 15 mins) motivational support at weekly clinic visits and telephone support 1 day before TQD, 3 days after TQD, monthly during follow-up
Outcomes	Mean (SD) weight change (kg) in prolonged abstainers at EOT (email communication), 6m (email communication) and 12m (email communication) (validation: CO ≤ 10 ppm)
Study funding	Not specified
Author declarations	Not specified
Notes	Prolonged abstinence defined as continuous abstinence from week 4

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	3:1 ratio
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Double-blind + placebo-controlled. No further information given
Blinding of outcome assessment (detection bias) Smoking	Low risk	Quote: “Expiratory CP level <ppm”
Blinding of outcome assessment (detection bias) Weight	Low risk	Quote: “subjects were weighed”
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Not specified

BMI: body mass index; CBT: (E)CO: (expired) carbon monoxide; CBT: cognitive behavioural therapy; COPD: chronic obstructive pulmonary disease; cpd: cigarettes per day: EOT: end of treatment; FTND: Fagerström test for nicotine dependence; MI: motivational interviewing; CVD: cardiovascular disease; MDD: major depressive disorder; NRT: nicotine replacement therapy; PPA: point prevalence abstinence; ppm: parts per million; RMR: resting metabolic rate; SC: smoking cessation; SD: standard deviation; SH: self-help; TQD: target quit date.

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
1 Ames 2007	Not an intervention designed specifically to tackle post-cessation weight gain
1 Chaney 2008	Exercise intervention excluded by parent Cochrane Review
1 Hughes 1997	Effect of NRT on post-cessation weight gain, not identified in NRT parent review
1 ISRCTN47776579	Study on ineligible population as participants were not immediately ready to quit smoking
1 Jeffery 1990	Study testing effect on intervention on weight control in general rather than on post-cessation control
1 Killen 1990	Effect of minimal contact smoking relapse prevention trial with NRT, not included in parent review
1 Kim 2017	Did not measure smoking cessation at 6+ months OR weight at any follow-up point
1 King 2006	Weight only measured at end of 1 month (2-month intervention)
1 Lagrue 1994	Intervention on overweight participants only
1 Leischow 1992	Unable to obtain full data
1 Love 2011	Participants not randomized
1 NCT02412631	Study terminated; (lorcaserin removed from market)
1 NCT03362372	Not a smoking cessation trial
1 Patterson 2006	Not an intervention designed to address weight gain
1 Pomerleau 1991	Excluded from antidepressant parent review
1 Rohsenow 2007	No weight data
1 Russo 2016	Ineligible population as participants were not intending to quit smoking.
1 Spring 1991	Unable to obtain data
1 Thompson 2015	Weight not measured at baseline for the usual-care study arm
1 Toll 2008	Participants not randomized to experimental or control conditions
1 Wilcox 2010	Uncontrolled trial

Study	Reason for exclusion
2 AD Ahluwalia 2002	Unable to obtain full data
2 AD Aubin 2004	Unable to obtain full data
2 AD Berlin 1995	No weight data
2 AD Blondal 1999	No weight data
2 AD Brown 2006	No weight data
2 AD Cinciripini 05	No weight data
2 AD Collins 2004	No weight data
2 AD Covey 2002	No weight data
2 AD Covey 2007	All participants received 8 weeks of open-label bupropion and NRT
2 AD Da Costa 2002	No weight data
2 AD Dalsgareth 2004	Unable to obtain full data
2 AD Evins 2001	Unable to obtain full data
2 AD Evins 2005	No weight data
2 AD Evins 2006	No weight data
2 AD Evins 2008	Less than 6 months follow-up
2 AD Ferry 1992	No weight data
2 AD Ferry 1994	No weight data
2 AD George 2002	No weight data
2 AD GlaxoSmithK SMK20001	No weight data
2 AD Gonzales 2001	No weight data
2 AD Haggsträm 2006	No weight data
2 AD Hall 1998	No weight data
2 AD Hall 2002	No weight data
2 AD Hall 2004	No weight data
2 AD Hatsukami 2004	No weight data
2 AD Hays 2001	Unable to obtain full data
2 AD Hertzberg 2001	No weight data
2 AD Holt 2005	No weight data

Study	Reason for exclusion
2 AD Hurt 2003	No weight data
2 AD Killen 2000	No weight data
2 AD Killen 2004	No weight data
2 AD Killen 2006	No weight data
2 AD Myles 2004	No weight data
2 AD Piper 2004	No weight data
2 AD Piper 2009	No weight data
2 AD Prochazka 1998	No weight data
2 AD Prochazka 2004	No weight data
2 AD Rovina 2009	No weight data
2 AD Selby 2003	No weight data
2 AD Swan 2003	No weight data
2 AD Tashkin 2001	No weight data
2 AD Tonstad 2003	Unable to obtain full data
2 AD Tønnesen 2003	Unable to obtain full data
2 AD Uyar 2005	Unable to obtain full data
2 AD Wagena 2005	No weight data
2 Aveyard 2018	ineligible intervention
2 Drovandi 2018	This trial was deemed eligible for inclusion but the author confirmed that "the funding fell through and I was unable to conduct this RCT as intended"
2 EX Hill 1985	No weight data
2 EX Hill 1993	No weight data
2 EX Kinnunen 2008	Unable to get data [Check Korhonen T, Goodwin A, Miesmaa P, Dupuis EA, Kinnunen T. Smoking cessation program with exercise improves cardiovascular disease biomarkers in sedentary women *Journal of Women's Health (2002)* 2011 20(7) 1051-64]
2 EX Marcus 1991	No weight data
2 EX Marcus 1995	No weight data
2 EX Martin 1997	No weight data
2 EX Prapavessis 2007	Unable to get data

Study	Reason for exclusion
2 EX Russell 1988	No weight data
2 EX Taylor 1988	No weight data
2 LeMao 2020	Insufficient information to determine eligibility
2 NRT Ahluwalia 1998	No weight data
2 NRT Ahluwalia 2006	No weight data
2 NRT Areechon 1988	No weight data
2 NRT Blondal 1989	No weight data
2 NRT Blondal 1997	Unable to obtain full data
2 NRT Bolin 1999	No weight data
2 NRT Br Thor Soc 83	No weight data
2 NRT Buchkremer 88	No weight data
2 NRT Bullen 2010	Participants took medication before quit day
2 NRT Campbell 1987	No weight data
2 NRT Campbell 1991	No weight data
2 NRT Campbell 1996	No weight data
2 NRT Cinciripini 96	No weight data
2 NRT Clavel 1985	No weight data
2 NRT Clavel-Cha '92	No weight data
2 NRT Croghan 2003	No weight data
2 NRT Croghan 2007	No weight data
2 NRT Daughton 1991	No weight data
2 NRT Daughton 1998	No weight data
2 NRT Dautzenberg 01	No weight data
2 NRT Davidson 1998	No weight data
2 NRT Etter 2009	Participants took medication before the quit date
2 NRT Fagerström 1982	No weight data
2 NRT Fagerström 1984	No weight data
2 NRT Fee 1982	No weight data

Study	Reason for exclusion
2 NRT Fortmann 1995	No weight data
2 NRT Garcia 1989	No weight data
2 NRT Gilbert 1989	No weight data
2 NRT Glavas 2003a	No weight data
2 NRT Glavas 2003b	No weight data
2 NRT Glover 2002	Unable to obtain full data
2 NRT Goldstein 1989	No weight data
2 NRT Hall 1985	No weight data
2 NRT Hall 1987	No weight data
2 NRT Hall 1996	No weight data
2 NRT Hand 2002	No weight data
2 NRT Harackiewicz 1988	No weight data
2 NRT Hatsukami 2007	Less than 6 months follow-up
2 NRT Hays 1999	No weight data
2 NRT Herrera 1995	No weight data
2 NRT Hilleman 1994	No weight data
2 NRT Huber 1988	No weight data
2 NRT Hughes 1989	No weight data
2 NRT Hughes 1990	No weight data
2 NRT Hughes 1991	No weight data
2 NRT Hughes 1999	No weight data
2 NRT Hughes 2003	No weight data
2 NRT Hurt 1990	No weight data
2 NRT Hurt 1994	No weight data
2 NRT ICRF 2007	No weight data
2 NRT Jamrozik 1984	No weight data
2 NRT Jarvis 1982	No weight data
2 NRT Jensen 1991	No weight data

Study	Reason for exclusion
2 NRT Jorenby 1995	No weight data
2 NRT Jorenby 1999	Unable to obtain full data
2 NRT Joseph 1996	No weight data
2 NRT Kalman 2006	No weight data
2 NRT Killen 1984	No weight data
2 NRT Killen 1990	No weight data
2 NRT Killen 1997	No weight data
2 NRT Killen 1999	Unable to obtain full data
2 NRT Kornitzer 1987	Unable to obtain full data
2 NRT Kornitzer 1995	No weight data
2 NRT Kralikova 2002	No weight data
2 NRT Kralikova 2009	Participants could reduce smoking or quit smoking
2 NRT Leischow 1996	No weight data
2 NRT Leischow 1999	No weight data
2 NRT Leischow 2004	No weight data
2 NRT Lewis 1998	No weight data
2 NRT Llivina 1988	No weight data
2 NRT Malcolm 1980	No weight data
2 NRT Marshall 1985	No weight data
2 NRT McGovern 1992	No weight data
2 NRT Molyneux 2003	No weight data
2 NRT Moolchan 2005	No weight data
2 NRT Mori 1992	No weight data
2 NRT Müller 1990	No weight data
2 NRT Nakamura 1990	No weight data
2 NRT Nebot 1992	No weight data
2 NRT Niaura 1994	No weight data
2 NRT Niaura 1999	No weight data

Study	Reason for exclusion
2 NRT Ockene 1991	No weight data
2 NRT Oncken 2007	No weight data
2 NRT Otero 2006	No weight data
2 NRT Page 1986	No weight data
2 NRT Paoletti 1996	No weight data
2 NRT Peng 2007	Less than 6 months follow up
2 NRT Perng 1998	No weight data
2 NRT Piper 2007	No weight data
2 NRT Puska 1979	No weight data
2 NRT Richmond 1993	No weight data
2 NRT Rose 1994	No weight data
2 NRT Rose 1998	No weight data
2 NRT Rose 2006	No weight data
2 NRT Rose 2009	Participants took medication before quit day
2 NRT Roto 1987	Unable to obtain full data
2 NRT Russell 1983	No weight data
2 NRT Schneider 1985A	No weight data
2 NRT Schneider 1985B	No weight data
2 NRT Schneider 1995	No weight data
2 NRT Schneider 1996	No weight data
2 NRT Schnoll 2010	No weight data
2 NRT Schuurmans 04	No weight data
2 NRT Segnan 1991	No weight data
2 NRT Shiffman 2009	Not abrupt quitting
2 NRT Sonderskov 97	No weight data
2 NRT Stapleton 2011	Less than 6 months follow up
2 NRT Tønnesen 1988	No weight data
2 NRT Tønnesen 2000	No weight data

Study	Reason for exclusion
2 NRT Tønnesen 2006	No weight data
2 NRT Veaugh-Geiss 2010	No weight data
2 NRT Villa 1999	No weight data
2 NRT Westman 1993	No weight data
2 NRT Wisborg 2000	No weight data
2 NRT Wong 1999	No weight data
2 NRT Zelman 1992	No weight data
2 Prapavessis 2016	Identified and included in Part 1 of this review.
2 Urdapilleta-Herrera 2013	Insufficient information to determine eligibility.
2 VA Carson 2010	Less than 6 months follow-up
2 VA Hajek 2011	Participants took medication before quit day
2 VA Tsukahara 2010	No weight data for abstainers
2 VA Williams 2007	No weight data

Characteristics of ongoing studies *[ordered by study ID]*

1 Komiyama 2018

Study name	A randomized, multicenter trial for the effects of dietary instruction on cardiovascular risk markers after smoking cessation
Methods	Randomized multicenter controlled trial Country: Japan Recruitment: smoking cessation clinics (SC), enrolling by invitation
Participants	Target sample: 250 Key inclusion criteria: • Aged 20+ and < 80 years • Patients who succeed in smoking cessation at the time of the 5th visit (definition of success in smoking cessation: expired carbon monoxide concentration of less than 7 ppm and the patient affirmation of no smoking for 1 week) • Patients within 1 month from the 5th visit • Patients with weight gain more than 1kg from the first visit to the 5th visit to smoking cessation clinic • Patients who gave informed written consent Key exclusion criteria: • Patients who receive nourishment instruction regularly

1 Komiyama 2018 *(Continued)*

	• Patients in an unfavourable state for nourishment instruction enforcement (e.g. shock state, serious infectious disease, acute phase of cerebral infarction or myocardial infarction, terminal stage of cancer, remarkable gastrointestinal weakness) • Pregnancy or breastfeeding patients • Patients who take steroid regularly • Patients with uncontrolled diabetes mellitus (with HbA1c level more than 10.0%) • Patients who are judged to be unsuitable to participate in this clinical trial by a doctor (e.g. patients with advanced dementia)
Interventions	(1) 3 sessions of nutritional guidance provided by a registered dietician every 3 months (1, 4 and 7 months after enrolment). An instructional plan to meet an individual's estimated energy requirements and nutrient intake will be formulated based on the Dietary Reference Intake for Japanese (2015) as stipulated by the Ministry of Health, Labor, and Welfare (2) No nutritional guidance
Outcomes	Mean (SD) weight change (kg) at 9-month follow-up in abstainers (CO < 7 ppm and self-report of 30-day abstinence)
Starting date	Study start date: April 2016; Expected study end date: March 2022
Contact information	Maki Komiyama: nikonikomakirin@yahoo.co.jp; Clinical Research Institute, National Hospital Organization Kyoto Medical Center, 1-1 Mukaihata-cho, Fukakusa, Fushimi-ku, Kyoto 612-8555, Japan
Notes	

1 NCT01892813 2013

Study name	Dissemination of a tailored tobacco quitline for rural veteran smokers
Methods	Randomized, double-blind, clinical trial Country: United States Recruitment: Not specified
Participants	Target sample: 411 Inclusion criteria: • Veteran status • 18+ years of age • Smoke cigarettes on at least a daily basis • Receive primary care from the Iowa City VA Health Care System or an affiliated Community-based Outpatient Clinic (CBOC) • Live in a non-metropolitan area (based on Rural-Urban Commuting Area Codes (RUCA) codes) • Be willing to make an attempt to quit smoking in the next 30 days • Be capable of providing informed consent • Have access to a telephone (land line or cell phone) • Have a stable residence Exclusion criteria: • Planning to move within the next 12 months • Presence of a terminal illness • Pregnancy

1 NCT01892813 2013 *(Continued)*

	• Unstable psychiatric disorder (e.g. acute psychosis) • Currently pregnant • Incarcerated • Institutionalized
Interventions	• Tailored intervention: Participants will receive a combined behavioral and pharmacological intervention. The behavioral component will consist of a 6-session cognitive behavioural telephone intervention combined with supplemental treatment modules to address common issues (symptoms of depression, weight gain, risky alcohol use) associated with cigarette smoking based on eligibility and preference. * Participants with concerns about gaining weight after quitting smoking may receive this 6-session telephone-based behavioural self-management intervention designed to help attenuate post-cessation weight gain • Enhanced standard care: Participants assigned to the enhanced standard of care condition will receive referral to their state tobacco quitline along with pharmacotherapy to assist with smoking cessation
Outcomes	Mean (SD) weight change (kg) at 6-month follow-up in abstainers (self-reported abstinence in the past 30 days)
Starting date	July 2013; Expected study end date: January 2018
Contact information	Mark W. Vander Weg, Ph.D., mark-vanderweg@uiowa.edu
Notes	

1 NCT02424188 2015

Study name	Trial of integrated smoking cessation, exercise and weight management in serious mental illness: TRIUMPH
Methods	Randomized controlled trial Country: United States Recruitment: Based on attending 1 of 2 community mental health organizations in Maryland
Participants	Total final enrolment: 192 Inclusion criteria: • Diagnosis of schizophrenia, schizoaffective disorder, bipolar disorder, or recurrent major depression meeting criteria for serious mental illness • Fagerström Test for Nicotine Dependence of ≥ 3 and daily cigarette smoking for at least the past 6 months (on days that cigarettes were available) • On stable psychotropic medication for mental illness for at least 30 days (i.e. antipsychotic medication for those with schizophrenia spectrum illness, mood stabilizer for those with bipolar disorder) • Competent and willing to give informed consent • Completion of baseline data collection • Willing to participate in smoking cessation intervention that includes combination of evidence-based behavioural (group and individual sessions) and pharmacotherapeutic smoking cessation aids Exclusion criteria: • Serious cardiovascular event (e.g. myocardial infarction, stroke) within the past 6 months

1 NCT02424188 2015 *(Continued)*

	• Serious unstable medical condition that limits life expectancy • Pregnant, breastfeeding, or planning a pregnancy during study period • Alcohol or illicit substance use disorder if not sober/abstinent for ≥ 30 days • Planning to leave mental health programme or move out of geographic area within 18 months Review by treating psychiatrist required for those with inpatient psychiatric hospitalization within 6 months of enrolment
Interventions	• TRIUMPH: 18-month-long group and individual smoking cessation and weight management counselling, pharmacotherapy with varenicline or bupropion and nicotine replacement therapy, group exercise, and text messaging support • Treatment as usual: Referral to quit line
Outcomes	Mean (SD) weight change (kg) at 6 and 18-months follow-up in abstainers (CO-verified 7-day point prevalence)
Starting date	7 July 2016; Expected study end date: March 2020
Contact information	Gail L Daumit: gdaumit@jhmi.edu Johns Hopkins University 2024 East Monument Street Suite 2-620 Baltimore, Maryland 21287
Notes	

1 NCT02906787 2016

Study name	Behavioral activation for smoking cessation and the prevention of post-cessation weight gain
Methods	Randomized clinical trial Country: United States Recruitment: Not specified
Participants	Targeted sample: 340 Key eligibility criteria: • Male and female treatment-seeking smokers who are between 18 and 65 years of age and self-report smoking at least 5 cigarettes (menthol or non-menthol, or both) per day for at least the last 6 months • Provide a carbon monoxide (CO) breath test reading ≥ 5 parts per million (ppm) at the intake visit • Smokers who wish to make a permanent quit attempt in the next 1 - 2 months (treatment-seeking)
Interventions	• Transdermal nicotine (TN) and BAS+: Participants will attend 8 counselling sessions and receive a behavioural activation intervention to smoking cessation and to post-cessation weight gain (BAS +). The goal of the BAS+ is to maintain a level of overall reward after cessation by structuring and enhancing opportunities for reinforcement to: * ensure that not smoking is as reinforcing as smoking; and * prevent an over-reliance on food as a substitute reinforcer for smoking so that PCWG does not precipitate smoking relapse. Standard, 8-week; open-label TN will begin on the TQD • Transdermal nicotine (TN) and SC: Participants will attend 8 counselling sessions and receive standard smoking cessation counselling (SC). Per convention, SC will address overeating and weight gain concerns through standard recommendations to consume low-calorie snack foods,

1 NCT02906787 2016 *(Continued)*

	drink water, eat nutritious meals, and exercise, but will not include skills to shape the use of these suggestions. Standard, 8-week; open-label TN will begin on the TQD.
Outcomes	Mean (SD) weight change (kg) at EOT (10 weeks), 12-week follow-up and 26-week follow-up in abstainers (CO < 5 ppm 7-day PPA; Saliva cotinine < 15 ng/ml)
Starting date	Study start date: 31 August 2016; Expected study end date: February 2021
Contact information	Benjamin F Albelda: albeldab@mail.med.upenn.edu Janet Audrain-McGovern: audrain@pennmedicine.upenn.edu
Notes	

1 NCT03204396 2017

Study name	Smoking cessation facilitated by glucagon-like peptide-1 (GLP-1) analogues
Methods	Randomized, double-blind, placebo-controlled trial Country: Switzerland Recruitment: Not specified
Participants	Target sample: 256 Inclusion criteria: • Age 18 to 75 years • Daily smokers who are willing to quit and exhibit 1 of the following criteria: ≥ cpd or • At least moderate nicotine dependence, defined by a Fagerström score of ≥ 5 points or • Tobacco-associated disease treatment with varenicline (Champix) Exclusion criteria: • Pregnancy (incl. wish to become pregnant within next 3 months) or breast feeding • Pre-existing treatment with GLP-1 agonists • History of pancreatitis • Severe renal insufficiency (estimated glomerular filtration rate smaller than 30 ml/min/1.73 m^2) • Unstable psychiatric conditions • Anorexia nervosa
Interventions	• Intervention: Dulaglutide (Trulicity) 1.5 mg in 0.5 ml, via pen s.c. once weekly for 12 weeks • Placebo: 0.5 ml normal saline (0.9% sodium chloride (NaCl)), injection s.c. via syringe once weekly for 12 weeks
Outcomes	Mean (SD) weight change (kg) at 4, 8, 12, 24 and 52 weeks in abstinent smokers (CO < 10 ppm PPA)
Starting date	Study start date: 26 June 2017; Expected study end date: 31 March 2021
Contact information	Dr Bettina Winzeler, Tel: +41615565075, Bettina.winzeler@usb.ch Dr Nica Jeanloz, Tel:+41613285523, nicaanna.jeanloz@usb.ch
Notes	

1 NCT03712098 2018

Study name	Daily liraglutide for nicotine dependence (DAL)
Methods	Randomized, double-blind, placebo-controlled, parallel arm pilot study with 1 between-subjects factor of medication group (liraglutide vs. placebo) Country: United States Recruitment: Not specified
Participants	Target sample: 80 Key eligibility criteria: • 18 years of age or older who self-report smoking cigarettes (menthol and non-menthol) at least 10 times per day, on average, for the past 6 months • Interested in quitting smoking (defined as "intend to quit within one month") • BMI ≥ 27 kg/m^2 with 1 weight-related comorbidity (e.g. high blood pressure, high cholesterol, dyslipidaemia) or ≥ 30 kg/m^2 per the manufacturer label for weight management
Interventions	• Smoking cessation counselling and liraglutide: Participants receive 8 sessions of smoking cessation behavioural counselling and 32 weeks of the medication liraglutide. Liraglutide comes in a pre-filled pen and is self-injected once a day into the abdomen, thigh, or upper arm area. The dosing regimen, which follows FDA guidelines and is documented to be safe and well-tolerated in prior clinical studies, will begin at 0.6 mg and increase weekly by 0.6 mg until the recommended dose of 3 mg is reached (Weeks 1 through 5) and will continue at the 3 mg dose through the end of the study (Week 32) • Smoking cessation counselling and placebo: Participants receive 8 sessions of smoking cessation behavioural counselling and 32 weeks of placebo. The placebo comes in a pre-filled pen and is self-injected once a day into the abdomen, thigh, or upper arm area. The dosing regimen, which is the same as the liraglutide regimen, will begin at 0.6 mg and increase weekly by 0.6 mg until 3 mg is reached (Weeks 1 through 5) and will continue at the 3 mg dose through the end of the study (Week 32)
Outcomes	Mean (SD) weight change (kg) at 12 weeks post-TQD (study week 18) and 26-weeks post-TQD (study week 32) in abstainers (CO < 5 ppm 7-day PPA)
Starting date	Study start date: 29 November 2018; Expected study end date: May 2021
Contact information	Rebecca L. Ashare, Ph.D; 215-746-5789; rlashare@pennmedicine.upenn.edu Kristina D. Roose, MSW; 215-746-8430; kroose@pennmedicine.upenn.edu
Notes	

1 NCT04130698 2019

Study name	Comparing two treatments that both target smoking cessation and weight loss at the same time (BREATH)
Methods	Randomized clinical trial Country: United States Recruitment: Not specified

1 NCT04130698 2019 *(Continued)*

Participants	Target sample: 48 Inclusion criteria: • between 18 - 64 years old • have been a regular smoker for at least 3 years • meet DSM-IV criteria for nicotine dependence • smoke on average 10 cigarettes per day • are overweight or obese (25 < BMI < 40) • report motivation to quit smoking and lose weight • speak English Exclusion criteria: • engaged in a smoking cessation or weight loss intervention • use medications known to affect smoking cessation or weight loss • have a medical condition that is a contraindication for transdermal nicotine patch (TNP) • regularly use other tobacco products • endorse active suicidal or homicidal ideation • self-report or meet diagnostic criteria for an alcohol or drug dependence • self-report or meet diagnostic criteria for an eating or neurocognitive disorder
Interventions	• Distress tolerance + transdermal nicotine patch (TN): * group-level intervention comprising 1 x 2-hour weekly group session to learn skills and strategies to quit smoking and lose weight. Treatment rationale: RAs will explain that there are 3 (not 2 as in the control) key factors that maintain smoking behaviour and excess weight: ☐ learned habits, ☐ the addictive properties of smoking and food, and ☐ a way to manage distress. * Therefore, to be effective, an intervention designed to simultaneously treat smoking cessation and weight loss must address all 3 key factors. This condition includes both key factors in the control but introduces the third key factor: 'distress tolerance' (DT). Toward that end, modules will include: a values discussion; experiential avoidance; distress tolerance; and mindfulness-based ways to manage distress. ☐ Module 1: Orientation & ACT; ☐ Module 2: Avoidance; ☐ Module 3: Cognitive Fusion vs. Defusion; ☐ Module 4: Self-As-Context; ☐ Module 5: Present-Moment-Awareness; and ☐ Module 6: Values and Committed Action. * TN patch for 8 weeks as outlined by the recommended usage for steps 1 - 3 going from 21 mg for 4 weeks, 14 mg for 1 week, and 7 mg for 1 week. • Active health control + transdermal nicotine patch (TN): * group-level intervention comprised 1 x 2-hour weekly group sessions to learn skills and strategies to quit smoking and lose weight. Treatment rationale: RAs will explain that there are 2 key factors that maintain smoking behaviour and excess weight: ☐ learned habits and ☐ the addictive properties of smoking and food. * Therefore, to be effective, an intervention designed to simultaneously treat smoking cessation and weight loss must address both key factors. Toward that end, modules will include standard treatment on: the dangers of smoking, excess weight, unhealthy diets and sedentariness; the importance of healthy behaviours; and relaxation exercises to manage stress. These are all key aspects of standard treatment for smoking cessation and weight loss. ☐ Module 1: Orientation and Health; ☐ Module 2: Game Plan; ☐ Module 3: Stress and Coping Strategies;

1 NCT04130698 2019 *(Continued)*

	☐ Module 4: Physical Activity; ☐ Module 5: Changes in Activities, Habits and Lifestyle; and ☐ Module 6: Long-Term Rewards * TN patch for 8 weeks as outlined by the recommended usage for steps 1 - 3 going from 21 mg for 4 weeks, 14 mg for 1 week, and 7 mg for 1 week
Outcomes	Mean (SD) weight change (kg) at 6-month follow-up in abstainers (saliva cotinine verified 7-day PPA)
Starting date	Study start date: 1 June 2019; Expected study end date: 31 May 2022
Contact information	Nadia Petrovic; 1-401-456-8000; npetrovic@ric.edu
Notes	Based on a previously conducted pilot study of Distress Tolerance (DT)

1 NCT04332029 2020

Study name	Smoking cessation treatment for smokers with obesity
Methods	Randomized clinical trial Country: Spain Recruitment: Not specified
Participants	Target sample: 120 Inclusion criteria: • Being aged 18 or over • Having smoked 10 or more cigarettes/day within the last year • Meeting the diagnostic criteria for nicotine dependence according to the Diagnostic and Statistical Manual of Mental Disorders-5th ed. (American Psychiatric Association 2013) • Having overweight or obesity (BMI above 25) Exclusion criteria: • Not being able to attend the entire treatment • Currently receiving other psychological/pharmacological treatment for smoking cessation or weight control • Being diagnosed with a current severe psychiatric disorder, eating disorder other than Binge-Eating Disorder or Substance Use Disorder other than nicotine • Being pregnant, lactating or in the postpartum period • Have any health condition that requires a specialized diet or affected eating • Participants must not be taking a medication that impacts weight

1 NCT04332029 2020 *(Continued)*

Interventions	• Experimental (CBT + WGP + CM): The intervention will be implemented in 8-week group-based sessions and includes: * A cognitive behavioural treatment (CBT) for smoking cessation with quit date occurring at 6th session. Participants will be asked to reduce their nicotine intake gradually (i.e. 20% each week); * A Weight Gain Prevention module (WGP) which will consist of providing CBT and Dialectical-Behavioral Therapy (DBT) techniques targeting weight stability and associated disordered eating, and * Contingency Management procedure reinforcing smoking abstinence. This component will consist of providing vouchers to reinforce abstinence contingent on biochemical verification. The schedule will incorporate an increasing magnitude of reinforcement • Active comparator (CBT + WGP): The intervention will be implemented in 8-week group-based sessions and will include only the first 2 components of the experimental intervention
Outcomes	Mean (SD) weight change (kg) at end of treatment (8 weeks) and 1, 3, 6, and 12 months follow-up in abstainers (CO-verified continuous abstinence)
Starting date	Study start date: 7 October 2020; Expected study end date: December 2022
Contact information	Gloria Garcia-Fernandez, PhD; +34985103252; garciafgloria@uniovi.es
Notes	

1 RBR-682px9 2018

Study name	Evaluation of the effect of dietary control in the treatment of female smokers
Methods	Clinical trial of treatment, randomized controlled, parallel, open, 2 arms Country: Brazil Recruitment: Not specified
Participants	Target sample: 205 Inclusion criteria: “women smokers enrolled in the smoking control program at health units in the western zone of the municipality of Rio de Janeiro.” Exclusion criteria: “pregnant women unable to walk.”
Interventions	• “Control group: 128 women will receive only the standard treatment of smoking cessation…” • “77 women enrolled in the smoking control program in health units will receive guidelines for weight control associated with the standard smoking cessation treatment, through dietary guidance, performed in a group, consisting of menu suggestions with 6 meals a day and recipes with low glycaemic index foods, with an average caloric value of 1800 kcal; will also receive guidance on attitudinal techniques, through tips on behavior changes, food purchases in supermarkets and meal preparation; and exercise techniques to increase physical activity with everyday tasks.”
Outcomes	Mean (SD) weight change (kg) at 6 months follow-up in abstainers
Starting date	Study start date: 5 September 2018; Expected study end date: Not specified
Contact information	Cláudia Christina Sobrinho do Nascimento; +55-021-997332776; claudiachrisnutri@gmail.com
Notes	

1 Salgado Garcia 2018

Study name	Efficacy of two novel behavioral post-cessation weight gain interventions
Methods	Randomized clinical trial Country: United States Recruitment: Multifaceted. Both traditional (e.g. flyers, business cards, postcards, posters, recruitment through medical referrals, radio, and local media advertising) and electronic strategies (e.g. institution emails, electronic advertisements on Facebook). Sites will include local universities and colleges, local physician and dentist offices, barbershops, police stations, fire department stations, and community resource websites. In addition, recruitment will include a "refer a friend" incentive where participants can refer up to 10 friends to the study. Each randomized friend will earn the referrer USD 10 in incentives (i.e. Amazon gift certificates)
Participants	Target sample: 400 Inclusion criteria: • Wish to quit smoking in the next 30 days • Have smoked 5 or more cigarettes a day for at least 1 year • 18 years or older • Have a BMI of 22 kg/m^2 or greater • Have access to a telephone and daily access to email (if using a cell phone, participants must be willing to use their cell phone minutes for weekly phone interventions) • Able to understand consent process in English • If female and of childbearing age, participant must have a negative pregnancy test and must agree to use contraception during participation in the study • Willing to be randomized to the study conditions and wait 8 weeks prior to beginning smoking cessation • Participants must have BP < 150/95 and a heart rate of > 40 beats per minute and < 120 beats per minute Exclusion criteria: • Not have a known contraindication, allergy or hypersensitivity to varenicline therapy • Not currently (in the previous 30 days) be participating in other behavioural or pharmacologic weight or smoking cessation interventions • Not have had weight loss surgery (hx of gastric bypass, stomach stapling or banding) • Not have lost ≥ 10 lbs in the past 6 months • Not be taking a medication that impacts weight • Not have used an investigational drug within the last 30 days • Not have current suicidal thoughts or have a lifetime history of a suicide attempt as defined by the Columbia-Suicide Severity Rating Scale (C-SSRS) • No history of psychosis, bipolar disorder, or anorexia nervosa • Not have self-reported current alcohol abuse or illicit substance use • Not have kidney or liver disease, unstable cardiovascular conditions, HIV, or history of cancer in last 5 years • Not have another member of their household already participating in this study • Pregnant, lactating or planning to become pregnant in the next 12 months, or have been pregnant within the last 6 months • Weight limit of 385 pounds
Interventions	All participants will receive 6 sessions of a highly efficacious telephonic smoking cessation intervention delivered in groups plus varenicline (Chantix) prior to the start of the smoking cessation intervention

1 Salgado Garcia 2018 *(Continued)*

- Weight gain prevention: Participants will be asked to keep their weight stable during the initial 8 weeks of the study.
  * Intervention components:
    - Lesson materials adapted from the Small Changes intervention, which will provide guidance for meeting the goals of this intervention (i.e. increasing steps by 2000 steps per day, making 1 Small dietary Change each day).
    - Daily self-monitoring of steps and number of Small Changes
    - Daily weight self-monitoring on the BodyTraceTM e-scale
    - Fit Bit Alta activity trackers to self-monitor steps
- Weight loss intervention: Participants will be asked to achieve a weight loss goal of at least 5% of their baseline weight by week 8.
  * Intervention components:
    - Tailored calorie and fat goals based on their baseline weight
    - Daily dietary intake and physical activity self-monitoring using a website or app
    - Daily weight self-monitoring on the BodyTraceTM e-scale
    - Lesson materials for each session, drawn from the Look AHEAD intensive lifestyle intervention
    - Meal replacements for 2 meals and 1 snack for 8 weeks as a method to achieve the study's calorie and fat goals and as a strategy to control portions
    - Graded physical activity goals of 175 minutes of moderate intensity exercise (e.g. brisk walking) per week, or 10,000 steps per day
    - Fit Bit Alta activity trackers to self-monitor steps
- Self-guided intervention: Participants will wait for 8 weeks before initiating the same smoking cessation intervention as the other 2 conditions, while they review the provided weight management focused book
  * Intervention components:
    - EatingWell Diet book.
    - Daily weight self-monitoring on the BodyTraceTM e-scale

Outcomes	Mean (SD) weight change (kg) at 2, 4, 8 and 12 months follow-up in abstainers (CO < 10 ppm 7-day PPA)
Starting date	Study start date: 30 November 2017; Expected study end date: April 2022
Contact information	Salgado Garcia; fsalgado@uthsc.edu
Notes	

2 Berlin 2019

Study name	Randomized trial of electronic cigarettes with or without nicotine in smoking cessation (ECSMOKE)
Methods	Randomized, placebo and reference treatment controlled, multicenter, double-blind, double-dummy, parallel group, pivotal, phase III trial Country: France Recruitment: either local (a) directly by the centres or centralized (b) using a web page and a centralized study-specific phone number and email address • Smokers intending to quit smoking are recruited by advertisement in pharmacies, physicians' offices situated in the catchment area of each investigator's centre, by local newspapers and in public places of the centres' healthcare facilities • Candidates to participate can register by the study's website, unique email address and phone number. Registration is followed by a phone screening before dispatching to the study centres

2 Berlin 2019 *(Continued)*

Participants	Target sample: 650 Inclusion criteria: • smoking at least 10 cigarettes/day (factory-made or roll-your-own) in the past year • Aged 18 to 70 years • Motivated to quit, defined as a score > 5 on a visual rating scale ranging from 0 (not motivated at all) to 10 (extremely motivated) • Women of childbearing age can be included if they use an effective contraceptive method: either hormonal contraception or an intrauterine device started at least 1 month before the first research visit • Individual affiliated to a health insurance system as defined by the sponsor (except Aide Médicale d'État = AME) • Previous failure of nicotine replacement therapy for smoking cessation • Signed written informed consent • Understanding and speaking French Exclusion criteria: • any unstable disease condition within the last 3 months defined by the investigator as major change in symptoms or treatments such as 1.1.recent myocardial infarction, 1.2.unstable or worsening angina 1.3.severe cardiac arrhythmia 1.4.unstable or uncontrolled arterial hypertension 1.5.recent stroke 1.6.cerebrovascular disease 1.7.obliterative peripheral arterial disease 1.8.cardiac insufficiency 1.9.diabetes 1.10.hyperthyroidism 1.11.pheochromocytoma 1.12.severe hepatic insufficiency 1.13.history of seizures 1.14.severe depression 1.15.chronic obstructive pulmonary disease (COPD) • any life-threatening condition with life expectancy of less than 3 months • alcohol use disorder defined as a score ≥ 10 on the AUDIT-C questionnaire • abuse of or dependence on illegal drugs in the last 6 months revealed by the medical history • regular use of tobacco products other than cigarettes • current or previous (last 6 months) use of electronic cigarette • pregnant women • breast feeding women • protected adults • current or past 3 months participation in another interventional research • current or past (last 3 months) use of smoking cessation medication such as varenicline, bupropion, nicotine replacement therapies • known lactose intolerance (placebo tablets contain lactose) • hypersensitivity to the active substance or to any of the excipients • known severe renal failure

Interventions	• Experimental: electronic cigarette + placebo varenicline tablets
	  * Ad libitum use of EC liquids containing 12 mg/mL of nicotine for 1 month
	• Active comparator: electronic cigarette without nicotine + active varenicline tablets;
	  * Varenicline (Champix) of 0.5 mg
	• Placebo comparator: electronic cigarette without nicotine + placebo varenicline tablets
	
	Brief behavioural smoking cessation counselling based on the national guidelines for smoking cessation is administered for all participants at all visits by the investigators specialized in smoking cessation

Outcomes	Mean (SD) weight change (kg) at 24-week follow-up in abstainers (CO ≤ 8 ppm) Confirmed continuous abstinence rate from weeks 9 to 12
Starting date	Study start date: 17 October 2018; Expected study end date: March 2022

2 Berlin 2019 *(Continued)*

Contact information	Ivan Berlin: ivan.berlin@aphp.fr, +33 1 42 16 16 78; Groupe Hospitalier Pitié-Salpétrière, Paris, France, 75013
Notes	

2 Caponnetto 2019

Study name	Smoking cessation with varenicline plus counselling for e-cigarettes users (VAREVAPE)
Methods	Double-blind, placebo-controlled, randomized clinical trial Country: Italy Recruitment: Not specified
Participants	Target sample: 140 + 140 • White e-cigarette users, vaping nicotine-containing liquids daily for > 3 months and willing to quit (single users) • White e-cigs users, vaping nicotine-containing liquids daily for > 3 months; who also smoke at least 1 conventional cpd and willing to quit (i.e. dual users) Inclusion criteria: • Adults of any gender aged between 18 and 75 years • Motivated to stop smoking • Women of childbearing potential may be included provided that they are not pregnant, not nursing, and are practising effective contraception Exclusion criteria: • History of alcoholism • History of epilepsy • Comorbid/history of psychiatric disorders (schizophrenia, major depression, bipolar disorder) • History of suicide attempts within the past 3 months and/or current suicidal ideation/plan and people at risk of the development of depressive symptom • Pregnant and breast feeding • Severe renal impairment and symptomatic vascular disease (including a history of ischaemic heart disease, stroke)

Interventions	• 12 weeks of varenicline + counselling
	  * First 3 days: 1 x 0.5 mg per day
	  * Day 4 - 8: 2 x 0.5 mg per a day
	  * Day 9 - end of 12 weeks: 4 x 0.5 mg per day
	• 12 weeks matching placebo + counselling

Outcomes	Mean (SD) weight change (kg) at follow-up in abstainers
Starting date	Study start date: June 2019; Expected study end date: 2020
Contact information	Centro per la Prevenzione e Cura del Tabagismo (CPCT), Azienda Ospedaliero-Universitaria “Policlinico-V. Emanuele”, Universita` di Catania, Via S. Sofia 78, 95123, Catania, Italy; p.caponnetto@unict.it (P. Caponnetto), m.maglia@unict.it (M. Maglia), polosa@unict.it (R. Polosa)
Notes	

2 Cinciripini 2009

Study name	Combining varenicline and bupropion for smoking cessation
Methods	Randomized clinical trial Country: United States Recruitment: Not specified
Participants	Target sample: 385 Inclusion criteria: • Age: 25 - 70 years old • Smoking 5 or more cigarettes per day, on average, within the 2 months preceding the screening visit, and expired CO ≥ 6ppm • Able to follow verbal and written instructions in English and complete all aspects of the study • Provide informed consent and agree to all assessments and study procedures • Have an address and home telephone number where they may be reached • Be the only participant in their household Exclusion criteria: • Within the month immediately preceding the screening visit, use of any form of tobacco products other than cigarettes on 3 or more days within a week if the individual refuses to refrain from such tobacco use during the course of the study • Within the month immediately preceding the screening visit, use of marijuana in any form on 3 or more days within a week • Within the 2 weeks immediately preceding the screening visit, involvement on more than 3 days in any formal smoking cessation activities • Treatment on a continuous basis within 2 weeks before the screening visit: any contraindicated medication for varenicline or bupropion. Classes of contraindicated medications include, but are not limited to, antiasthmatics, antipsychotics, some antidepressants, antihypertensives, antiarrhythmics, antineoplastics, some antiseizures, and MAO inhibitors (See Appendix U for specific list of excluded and precautionary medications) • Uncontrolled hypertension (average reading of systolic blood pressure greater than 150 or diastolic blood pressure greater than 95) or other major contraindications for bupropion or varenicline (See section on Screening) • Severe renal impairment (creatinine clearance less than 30 ml/min/1.73 m^2) • Laboratory evaluations outside normal limits and of potential clinical significance in the opinion of the investigator • Meet current criteria for psychiatric disorders or substance abuse as assessed by the MINI plus (major depressive episode) and the MINI for items B, D, I, J (Alcohol Addendum-past 6 months only), K, L, M and N including a past manic or hypomanic episode as well as a lifetime psychotic disorder • Individuals rated as moderate (6 - 9) to high (10 or greater) on suicidality as assessed by Module C of the MINI • Psychiatric hospitalization within 1 year of screening date • A positive urine pregnancy test during the screening period. Women who are 2 years postmenopausal, or who have had a tubal ligation or a partial or full hysterectomy will not be subject to a urine pregnancy test • Pregnant, breast feeding or of childbearing potential and is not protected by a medically acceptable, effective method of birth control while enrolled in the study. Medically-acceptable contraceptives include: (1) approved hormonal contraceptives (such as birth control pills, patches, implants or injections), (2) barrier methods (such as a condom or diaphragm) used with a spermicide, or (3) an intrauterine device (IUD). Contraceptive measures sold for emergency use after unprotected sex, are not acceptable methods for routine use • Use of varenicline or bupropion within 2 weeks before the screening visit

2 Cinciripini 2009 *(Continued)*

	• History of hypersensitivity or allergic reaction to varenicline, tricyclic antidepressant, bupropion (Wellbutrin, Zyban) or similar chemical classes or any component of these formulations • Current or previous history of a seizure disorder • Current or previous history of anorexia. • Subject considered by the investigator as unsuitable candidate for receipt of an investigational drug or unstable to be followed up throughout the entire duration of the study

Interventions	• Active varenicline and active bupropion
	  * 12-weeks varenicline: On Days 1 - 3, 0.5 mg tablet by mouth in the morning. Beginning on Day 4, and then every day after that, 0.5 mg tablet by mouth in the morning and 0.5 mg tablet by mouth in the evening (for a total of 2 doses). Other Name: Chantix
	  * 12-weeks bupropion: On Days 1 - 3, 150 mg tablet by mouth in the morning. Beginning on Day 4, and then every day after that, 150 mg tablet by mouth in the morning and 150 mg tablet by mouth in the evening (for a total of 2 doses). Other Name: Zyban
	  * Brief behavioural counselling sessions (10 - 15 minutes) provided to all participants once a week for 12 weeks. One support phone call conducted 3 days after the target quit date
	• Active varenicline and placebo bupropion
	  * 12-weeks varenicline as above
	  * 12-weeks placebo bupropion in the same schedule as active bupropion above
	  * Brief behavioural counselling as above
	• Placebo varenicline and placebo bupropion
	  * 12-weeks placebo varenicline in the same schedule as active varenicline above
	  * 12-weeks placebo bupropion in the same schedule as active bupropion above
	  * Brief behavioural counselling as above

Outcomes	Mean (SD) weight change (kg) at 3, 6 and 12-month follow-up in abstainers (prolonged abstinence verified by CO < 10 ppm at each in-person measurement occasion)
Starting date	17 May 2010; Expected study end date: 31 May 2021
Contact information	Paul M Cinciripini, PhD, pcinciri@mdanderson.org, Anderson Cancer Center
Notes	

2 Hebert-Losier 2020

Study name	Evaluating the efficacy of e-cigarette use for smoking cessation (E3) trial
Methods	Interventional (clinical trial) Country: Canada Recruitment: Community-based advertisements (e.g. printed fliers, newspaper ads) and online platforms (e.g. Craigslist, Kijiji, Facebook), as well as in outpatient, smoking cessation, and walk-in clinics
Participants	Target sample: 376 Inclusion criteria: • Active smoker, 10 or more cigarettes per day, on average, for the past year • Age of 18 years or older • Motivated to quit according to the Motivation To Stop Scale (MTSS) (level 5 or higher) • Able to understand and to provide informed consent in English or French • Likely to be available for follow-up (1 year)

2 Hebert-Losier 2020 *(Continued)*

	Exclusion criteria: • Medical condition with a prognosis < 1 year • Current or recent cancer (less than 1 year in remission) • Pregnant or lactating women • Current or recent use (in the past 30 days) of any pharmacotherapy or behavioural therapy for smoking cessation (e.g. NRTs, bupropion, varenicline, or counselling); • Any e-cigarette use (nicotine or non-nicotine) in the past 60 days, or ever use of any e-cigarette for more than 7 days consecutively • History of psychosis, schizophrenia, or bipolar disorder • Less than one month following a myocardial infarction, life-threatening arrhythmia, severe or worsening angina pectoris, or cerebral vascular accident • Use of any illegal drugs in the past year (excluding marijuana) • Planned use of tobacco products other than conventional cigarettes (e.g. cigarillos, cigars, snuff, shisha, etc.) or marijuana during the study period
Interventions	• Nicotine e-cigarettes (15 mg nicotine) for 12 weeks plus counselling • Non- nicotine (0 mg nicotine) for 12 weeks plus counselling • Counselling alone
Outcomes	Mean (SD) weight change (kg) at 12-month follow-up in abstainers
Starting date	Study start date: November 2016; Study end date: 28 January 2021
Contact information	Dr Mark J. Eisenberg, Jewish General Hospital, McGill University, 3755 Côte Ste-Catherine Road, Suite H-421.1, Montreal, Quebec H3T 1E2, Canada 1-514-340-8222, ext.: 23564; mark.eisenberg@mcgill.ca
Notes	

2 ISRCTN34399445 2020

Study name	IMPACT Smoking cessation Support for people with Severe mental illness in South Asia (IMPACT 4S): a randomised controlled pilot and feasibility trial for a combined behavioural and pharmacological support intervention
Methods	Open-label parallel randomised controlled trial Country: India, Pakistan Recruitment: Not specified
Participants	Target sample: 172 Inclusion criteria: • Adults (≥ 18 years old) with SMI (i.e. schizophrenia, schizoaffective disorder, bipolar affective disorder, psychosis, severe depression with psychosis) • Considered to be stable by the mental health clinical team • Self-reported current smoker of any form of smoked tobacco product (including cigarettes, bidis, waterpipe, etc) for at least 6 months • Smoking on > 25 days in the past month • Able to provide informed consent • Attending included institutions during the study period • Willing to cut down or quit smoking

2 ISRCTN34399445 2020 *(Continued)*

	• Willing and able to attend up to 10 face-to-face counselling sessions • Living in the Rawalpindi district in Pakistan, or in Bangalore urban and rural districts in India Exclusion criteria: • Pregnant or breast feeding women • Comorbid drug or alcohol problems, or both
Interventions	• Brief advice for smoking cessation * One-off, face-to-face, one-to-one, counselling session of 5 minutes * Information leaflet on the harmful effects of tobacco • IMPACT 4S intervention * up to 10 face-to-face, one-to-one counselling sessions which are about 45 minutes long * pharmacotherapy (bupropion or nicotine replacement therapy, or both) provided for a minimum of 3 months. Participants who opt to take bupropion will be referred to their medical doctor for assessing the suitability of prescribing bupropion. Participants will be offered sustained-release bupropion, 75 mg/d for the first week and 150 mg/d thereafter * breath CO monitoring and feedback on breath CO levels at every counselling session * Information leaflet on the harmful effects of tobacco
Outcomes	• Mean (SD) weight change (kg) at follow-up in abstainers • Mean (SD) weight change (kg) at 6-months follow-up in abstainers (CO verified < 7 ppm, self-reported or family/carer reported continuous smoking abstinence for at least six months (only five instances of smoking allowed during the total 6 months)
Starting date	Study start date: 01/07/2018; Expected study end date: 01/05/2021
Contact information	Prof. Pratima Murthy, pratimamurthy@gmail.com Department of Psychiatry National Institute of Mental Health and Neurosciences Bangalore 560029 INDIA, Bangalore +91 (0)8026995250
Notes	

2 NCT02106637 2014

Study name	Early In-hospital Initiation of pharmacotherapy for smoking cessation, concomitant with nurse-led support, in patients after an Acute Coronary Syndrome (ACS)
Methods	Prospective, double-blind, randomized, placebo-controlled, multicenter study Country: Israel Recruitment: hospitalized ACS smokers
Participants	Target sample: 300 Inclusion criteria: • Stable clinical condition following a recent (< 10 days) ACS event • Active smoking status 30 days prior to ACS • Age > 21

2 NCT02106637 2014 *(Continued)*

	• Life expectancy > 1 year Exclusion criteria: • Severe pulmonary disease (FEV1 < 30% predicted) • End-stage renal failure (eGFR < 20 ml/min/m2) • Uncontrolled depression or history of psychosis or bipolar disorder or active substance abuse • Uncontrolled stage IV hypertension • Unresolved life-threatening arrhythmia • Planned surgical intervention (within < 3 months) • Known hypersensitivity to study drug components • Inability to comply with study protocol • Active malignancy other than basal cell carcinoma (BCC) • End-stage congestive heart failure - NYHA IV or decompensated heart failure • Pregnancy or lactation
Interventions	• 12-week course of varenicline • 12-week course of matching placebo
Outcomes	Mean (SD) weight change (kg) at 12-month follow-up in abstainers (CO-verified continuous abstinence rate (CAR) at 12 months)
Starting date	October 2016; Expected study end date:December 2018
Contact information	Prof. IIan Goldenberg, Sheba Medical Center, ilan.goldenberg@sheba.health.gov.il
Notes	

2 NCT02162849 2015

Study name	Reward sensitivity and pharmacotherapy for smoking cessation
Methods	Randomized, double-blind, placebo-controlled clinical trial Country: United States Recruitment: Not specified
Participants	Target sample: 204 Inclusion criteria: • Age: 18 - 75 years old • Smoking 5 or more cigarettes, little cigars or cigarillos per day, on average, within the 2 months preceding the screening visit and expired carbon monoxide (CO) ≥ 6 ppm. (if ≤ 5, then NicAlert Strip > 2) • Interested in treatment that might change smoking behaviour • Able to follow verbal and written instructions in English and complete all aspects of the study • Provide informed consent and agree to all assessments and study procedures • Have an address and telephone number where they may be reached • Be the only participant in their household Exclusion criteria:

2 NCT02162849 2015 *(Continued)*

- Within the month immediately preceding the screening visit, use of any form of tobacco products other than cigarettes, little cigars or cigarillos on 3 or more days within a week if the individual refuses to refrain from such tobacco use during the course of the study
- Current enrolment or plans to enrol in another smoking cessation programme in the next 12 months
- Plan to use other nicotine substitutes (i.e. OTC or prescription medication for smoking cessation) or smoking cessation treatments in the next 12 months
- Uncontrolled hypertension (systolic blood pressure; SBP greater than 180 or diastolic blood pressure greater than 110)
- History of severe kidney disease (e.g. chronic or acute kidney failure) with creatinine clearance below 30 and/or severe liver disease with liver tests over 4 times the upper normal level
- Laboratory evaluations (kidney and liver) outside normal limits and of potential clinical significance in the opinion of the investigator
- Serious or unstable disease within the past 3 months
- History (last 3 months) of abnormal heart rhythms, cardiovascular disease (stroke, angina, heart attack) may result in ineligibility. These conditions will be evaluated on a case-by-case basis by the study physician
- Current use of certain medications:
  * Smoking cessation meds (last 7 days), i.e. Wellbutrin, Zyban, NRT, Chantix
  * Certain medications to treat depression (last 14 days), i.e. MAOIs and Elavil (Amitriptyline)
  * A case-by-case determination will be made by study physician for medication on precautionary list, i.e. nitroglycerin, or
  * Daily use of opioids for 30 days or more on phone screen or at screening is exclusionary, but PRN use is allowed (i.e. 3:7 days per week or less or if more frequent, use less than a month's duration.)
- Meet criteria for the following psychiatric and/or substance use disorders as assessed by the MINI International Neuropsychiatric Interview (MINI): items C (current manic or hypomanic episode only), I (alcohol abuse - Alcohol Addendum-past 6 months only; current alcohol dependence), J (substance abuse -Substance Abuse Addendum - past 6 months only; current substance dependence), K (current/lifetime psychotic disorder or current/lifetime mood disorder with psychotic features). Individuals who meet criteria for non-exclusionary psychiatric disorders that are considered clinically unstable and/or unsuitable to participate as determined by the principal investigator or study physician, or both
- Individuals rated as moderate (9 - 16) to high (17 or greater) on suicidality as assessed by Module B of the MINI
- Psychiatric hospitalization within 1 year of screening date
- A positive urine pregnancy test during the screening period. Women who are 2 years postmenopausal, or who have had a tubal ligation or a partial or full hysterectomy will not be subject to a urine pregnancy test
- Pregnant, breast feeding or of childbearing potential and is not protected by a medically-acceptable, effective method of birth control while enrolled in the study. Medically-acceptable contraceptives include: (1) approved hormonal contraceptives (such as birth control pills, patches, implants or injections), (2) barrier methods (such as a condom or diaphragm) used with a spermicide, or (3) an intrauterine device (IUD). Contraceptive measures sold for emergency use after unprotected sex are not acceptable methods for routine use
- History of hypersensitivity or allergic reaction to Varenicline, NRT, or any component of these formulations.
- Any medical or psychiatric condition, illness, disorder, or concomitant medication that could compromise participant safety or treatment, as determined by the principal investigator or study physician, or both
- Subject considered by the investigator as unsuitable candidate for receipt of an investigational drug, or unstable to be followed up throughout the entire duration of the study.

2 NCT02162849 2015 *(Continued)*

	• Positive toxicology screen for any of the following drugs: cocaine, opiates, methadone, benzodiazepines, barbiturates, amphetamines, methamphetamines, PCP, or THC.
	  * A. Participants with valid prescriptions for opiates, benzodiazepines, barbiturates, amphetamines or methadone will not be excluded.
	  * B. Participants failing the toxicology screen will be allowed to re-screen once. If they test positive again, they will not be allowed to return.
	• Must not have visual problems that in the investigators opinion would interfere in the completion of the study assessments
	• Unwilling to change hairstyle or remove a wig as necessary for the appointment to accommodate the net that is required to be worn on the scalp during the study procedure
	• Reports diagnosis of seizure disorder or a history of neurological illness or closed head injury that in the opinion of the PI feels that it would affect the results of the EEG

Interventions	• Active varenicline + placebo patch
	  * Varenicline following recommended 12-week course (0.5 mg/day by mouth for days 1 - 3; 0.5 mg twice a day for says 4 - 7, and 1 mg twice a day thereafter)
	  * Patch applied for 11 weeks daily from day 8 onwards
	  * All participants receive 7 behavioural smoking cessation counselling sessions of 15 minutes duration, 4 of which delivered over the phone
	• Placebo varenicline + active nicotine patch:
	  * Placebo varenicline following the same recommended 12-week schedule as above
	  * 21 mg nicotine patch applied as above
	  * Behavioural smoking cessation counselling as above

Outcomes	Mean (SD) weight change (kg) at 6-month follow-up in abstainers (CO-verified prolonged abstinence at 6-months post-quit-date)
Starting date	Study start date: 14 December 2015; Expected study end date: December 2020
Contact information	Paul Cinciripini, PHD, MS, BS, pcinciri@mdanderson.org
Notes	

2 NCT03722966 2018

Study name	Effectiveness of combination varenicline and oral nicotine replacement therapy (COMBO)
Methods	Randomized clinical trial Country: United States Recruitment: Not specified
Participants	Target sample: 100 Inclusion criteria: • ≥ 18 years of age • ≥ 6th grade English literacy • agree to use personal or study-provided smartphone/applications • agree to complete phone-based or in-person surveys throughout 26-week study • expired CO > 7 at baseline visit (suggesting current smoker) • currently smoke ≥ 5 cigarettes per day • willing to make quit attempt 7 days after baseline visit Exclusion criteria:

2 NCT03722966 2018 *(Continued)*

	• < 18 years of age • history of seizures or allergic reaction to varenicline • report current suicidality • taking antidepressants or antipsychotic medications • pregnant or planning to become pregnant • currently breast feeding

Interventions	• Varenicline + behavioural counselling
	  * Participants will receive behavioural tobacco cessation counselling, a 13-week course of varenicline, and no automated medication reminders
	• Varenicline + behavioural counselling + medication reminders
	  * Participants will receive behavioural tobacco cessation counselling, a 13-week course of varenicline, and automated medication reminders via their smartphones
	• Varenicline + behavioural counselling + oral NRT
	  * Participants will receive behavioural tobacco cessation counselling, a 13-week course of varenicline, 12 weeks of oral nicotine replacement therapy (NRT; gum or lozenge), and no automated medication reminders
	• Varenicline + behavioural counselling + oral NRT + medication reminders
	  * Participants will receive behavioural tobacco cessation counselling, a 13-week course of varenicline, 12 weeks of oral nicotine replacement therapy (NRT; gum or lozenge), and automated medication reminders via their smartphones

Outcomes	Mean (SD) weight change (kg) at 26-week follow-up in abstainers (CO-verified < 8 ppm 7-day PPA at 26 weeks post-quit date)
Starting date	Study start date: 2 December 2019; Expected study end date: 30 December 2021
Contact information	Joseph Waring, 4052718001 ext 31153, joseph-waring@ouhsc.edu Jocelyn Barton, PhD, 4052718001 ext 31324, jocelyn-barton@ouhsc.edu
Notes	

2 NCT04088942 2019

Study name	TOBacco STOP in Chronic Obstructive Pulmonary Disease-Trial - Study Protocol
Methods	Randomized, open-label, superiority, 2-arm intervention study Country: Denmark Recruitment: in general practice is done by the project-trained nurse
Participants	Target sample: 600 Inclusion criteria: • Competent and mature • Have diagnosed COPD (spirometry verified and evaluated by pulmonary specialist) • Current daily smoker (minimum 1 cigarette daily) • Have smoked minimum 20 pack years (1 pack year = 20 cigarettes daily in 1 year) • Want to or try to stop smoking • Do not mind taking varenicline or NRT during the trial • Are willing to give blood and urine samples according to the protocol Exclusion criteria:

2 NCT04088942 2019 *(Continued)*

	• Previously included in the trial • Hospitalized with COPD exacerbation within the last 24 months • Are associated with hospital outpatient clinic for COPD disease treatment • Have FEV1 < 50%. • Pregnancy/breastfeeding • Life expectancy less than 1 year • Severe linguistic problems or inability to give informed consent • Severe mental illness that is not controlled with medication • Active alcohol or substance abuse • Active cancer disease* *The person can participate if he or she has had a cancer disease that is now referred to as curative/radically treated. Basal cell carcinoma of the skin does not count as an exclusion criterion

Interventions	• Low-intensity group:
	  * Varenicline prescribed for 12 weeks - Day 1-3: 0.5 mg daily. Day 4-7: 0.5 mg two times daily. Thereafter 1 mg 2 times daily plus encouraged to quit smoking via own doctor.
	• High-intensity group:
	  * Varenicline for 12 weeks - day 1 - 3: 0.5 mg daily. Day 4 - 7: 0.5 mg twice daily. Thereafter 1 mg twice daily
	  * Group sessions: 5 sessions Day 1 - 14: 5 sessions Day 15 - 30: 5 sessions Day 31 - 60: 5 sessions Day 61 - 90: 5 sessions Day 90 - 180: 5 sessions
	  * Hotline
	  * Scheduled phone consultations (weekly for 26 weeks; 5 - 10 min calls; “If the patient has not had relapse, there will be called week 34 and week 42. If the patient has had relapse, calls continue until relapse-free for 10 weeks, then week 34 and week 42.”
	  * Buddy arrangement: A meeting frequency of approx. every 7 - 14 days

Outcomes	Mean (SD) weight change (kg) at follow-up in abstainers at 12 months
Starting date	Study start date: 1 August 2021; Expected study end date: 1 January 2024
Contact information	Jens-Ulrik S Jensen, MD, PhD; +45 3867 3057; jens.ulrik.jensen@regionh.dk
Notes	

2 Roelsgaard 2017

Study name	REU-stop – effect of intensive smoking cessation intervention on smoking cessation and disease activity in patients with rheumatoid arthritis
Methods	International, multicentre, randomized trial Country: Denmark, Norway Recruitment: daily smokers with RA in remission or with low-moderate disease activity will be recruited from the Center for Rheumatology and Spine Diseases, Rigshospitalet, Denmark, and from the Preventive Cardio-Rheuma Clinic, Department of Rheumatology, Diakonhjemmet Hospital, Oslo, Norway
Participants	Target sample: 150 Inclusion criteria: • have RA in clinical remission or low-moderate disease activity for the 3 months prior to enrolment • are over 18 years of age

2 Roelsgaard 2017 *(Continued)*

	• smoking tobacco daily • able to understand and speak Danish or Norwegian, respectively Exclusion criteria: • scheduled or actual change of dose or preparation in anti-rheumatic medical treatment within the previous 3 months (including glucocorticoid injection during the previous month) • are cognitively or otherwise unable to give informed consent • are pregnant or breast feeding
Interventions	• **Intervention:** Intensive smoking cessation intervention * 6-weeks individual motivational counselling: * 5 sessions with a trained smoking cessation counsellor 20 - 40 minutes * The principles of motivational counselling are based on the transtheoretical model of change. The smoking cessation counsellor has also been trained in motivational counselling techniques specific to this intervention. * Nicotine replacement therapy: ☐ NRT free of charge tailored to an individual's Fagerstöm Test for Nicotine Dependence • Participants will note their tobacco and NRT consumption in a smoking diary • **Control:** no intervention * The control group will receive the standard treatment and care in the rheumatology outpatient clinic. The participants will be encouraged to write a diary describing their tobacco use during the trial period. If participants in the control group express an interest in receiving smoking cessation counselling, they will be informed about municipal programmes
Outcomes	Mean (SD) weight change (kg) at 3-, 6- and 12- month follow-up in abstainers (continuous cessation validated by CO reading < 10 ppm)
Starting date	Study start date: April 2020; Expected study end date: January 2021
Contact information	Ida Kristiane Roelsgaard, ida.kristiane.roelsgaard@regionh.dk; Copenhagen Center for Arthritis Research (COPECARE), Center for Rheumatology and Spine Diseases, Rigshospitalet, Glostrup, Denmark
Notes	

COPD: chronic obstructive pulmonary disease; cpd: cigarettes per day; NRT: nicotine replacement therapy; OTC: over the counter; PPA: point prevalence abstinence; ppm: part per million; TQD: target quit date

DATA AND ANALYSES

Comparison 1. Pharmacological interventions versus placebo for post cessation weight control

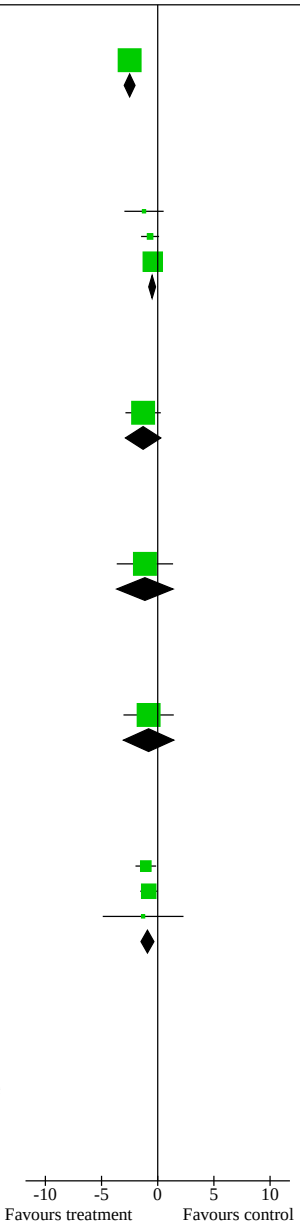
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Mean weight change (kg) at end of treatment	11		Mean Difference (IV, Random, 95% CI)	Subtotals only
1.1.1 Dexfenfluramine versus placebo	1	33	Mean Difference (IV, Random, 95% CI)	-2.50 [-2.98, -2.02]
1.1.2 Phenylpropanolamine versus Placebo	3	112	Mean Difference (IV, Random, 95% CI)	-0.50 [-0.80, -0.20]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1.3 Ephedrine + Caffeine versus Placebo	1	40	Mean Difference (IV, Random, 95% CI)	-1.30 [-2.87, 0.27]
1.1.4 Lorcaserin versus placebo	1	41	Mean Difference (IV, Random, 95% CI)	-1.14 [-3.65, 1.37]
1.1.5 Chromium versus placebo	1	15	Mean Difference (IV, Random, 95% CI)	-0.81 [-3.05, 1.43]
1.1.6 Naltrexone versus placebo	3	254	Mean Difference (IV, Random, 95% CI)	-0.91 [-1.49, -0.34]
1.1.7 Topiramate versus placebo	1	6	Mean Difference (IV, Random, 95% CI)	Not estimable
1.2 Mean weight change (kg) at 6 months	4		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.2.1 Phenylpropanolamine versus Placebo	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.2.2 Ephedrine + caffeine versus placebo	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.2.3 Chromium versus placebo	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.2.4 Naltrexone versus placebo	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.3 Mean weight change (kg) at 12 months	3		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.3.1 Phenylpropanolamine versus placebo	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.3.2 Ephedrine + Caffeine versus placebo	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.3.3 Naltrexone versus placebo	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
1.4 Smoking cessation at 6 months	7		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
1.4.1 Phenylpropanolamine gum versus placebo	1	295	Risk Ratio (M-H, Random, 95% CI)	1.38 [0.76, 2.53]
1.4.2 Ephedrine + Caffeine versus placebo	1	225	Risk Ratio (M-H, Random, 95% CI)	1.06 [0.53, 2.11]
1.4.3 Naltrexone versus placebo	3	890	Risk Ratio (M-H, Random, 95% CI)	1.02 [0.79, 1.32]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.4.4 Chromium versus placebo	1	143	Risk Ratio (M-H, Random, 95% CI)	0.48 [0.12, 1.84]
1.4.5 Naltrexone & bupropion versus placebo	1	22	Risk Ratio (M-H, Random, 95% CI)	Not estimable
1.5 Smoking cessation at 12 months	3		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
1.5.1 Phenylpropanolamine gum versus placebo	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
1.5.2 Ephedrine + Caffeine versus Placebo	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
1.5.3 Naltrexone versus placebo	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
1.6 Adverse events	2		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
1.6.1 Lorcaserin versus placebo	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
1.6.2 Lorcaserin (longer duration) versus placebo + lorcaserin (shorter duration)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
1.7 Serious adverse events	3		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
1.7.1 Topiramate versus placebo	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
1.7.2 Naltrexone versus placebo	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
1.7.3 Lorcaserin (longer duration) versus placebo + lorcaserin (shorter duration)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

Analysis 1.1. Comparison 1: Pharmacological interventions versus placebo for post cessation weight control, Outcome 1: Mean weight change (kg) at end of treatment

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
1.1.1 Dexfenfluramine versus placebo								
1 Spring 1995 (also Part 2)	1	0.7	18	3.5	0.7	15	100.0%	-2.50 [-2.98 , -2.02]
Subtotal (95% CI)			**18**			**15**	**100.0%**	**-2.50 [-2.98 , -2.02]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 10.22 (P < 0.00001)								
1.1.2 Phenylpropanolamine versus Placebo								
1 Cooper 2005 (also Part 2)	0.59	3.04	16	1.81	2.18	22	3.0%	-1.22 [-2.97 , 0.53]
1 Klesges 1990	0.04	1.07	15	0.72	1.04	12	14.2%	-0.68 [-1.48 , 0.12]
1 Klesges 1995	0.34	0.54	19	0.78	0.61	28	82.8%	-0.44 [-0.77 , -0.11]
Subtotal (95% CI)			**50**			**62**	**100.0%**	**-0.50 [-0.80 , -0.20]**
Heterogeneity: Tau² = 0.00; Chi² = 0.97, df = 2 (P = 0.61); I² = 0%								
Test for overall effect: Z = 3.23 (P = 0.001)								
1.1.3 Ephedrine + Caffeine versus Placebo								
1 Norregaard 1996	0.2	2.22	27	1.5	2.45	13	100.0%	-1.30 [-2.87 , 0.27]
Subtotal (95% CI)			**27**			**13**	**100.0%**	**-1.30 [-2.87 , 0.27]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.62 (P = 0.11)								
1.1.4 Lorcaserin versus placebo								
1 Shanahan 2017 (1)	-0.41	3.18	30	0.73	3.78	11	100.0%	-1.14 [-3.65 , 1.37]
Subtotal (95% CI)			**30**			**11**	**100.0%**	**-1.14 [-3.65 , 1.37]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.89 (P = 0.37)								
1.1.5 Chromium versus placebo								
1 Parsons 2009	0.98	1.88	4	1.79	2.15	11	100.0%	-0.81 [-3.05 , 1.43]
Subtotal (95% CI)			**4**			**11**	**100.0%**	**-0.81 [-3.05 , 1.43]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.71 (P = 0.48)								
1.1.6 Naltrexone versus placebo								
1 King 2012	2.26	2.15	40	3.32	1.91	35	39.1%	-1.06 [-1.98 , -0.14]
1 O'Malley 2006	1.1	1.9	123	1.9	2	34	58.4%	-0.80 [-1.55 , -0.05]
1 Toll 2010	3.1	4.1	8	4.4	4.2	14	2.6%	-1.30 [-4.89 , 2.29]
Subtotal (95% CI)			**171**			**83**	**100.0%**	**-0.91 [-1.49 , -0.34]**
Heterogeneity: Tau² = 0.00; Chi² = 0.23, df = 2 (P = 0.89); I² = 0%								
Test for overall effect: Z = 3.12 (P = 0.002)								
1.1.7 Topiramate versus placebo								
1 Oncken 2014	-1.36	1.06	5	-4.99	0	1		Not estimable
Subtotal (95% CI)			**5**			**1**		**Not estimable**
Heterogeneity: Not applicable								
Test for overall effect: Not applicable								
Test for subgroup differences: Chi² = 48.34, df = 5 (P < 0.00001), I² = 89.7%								

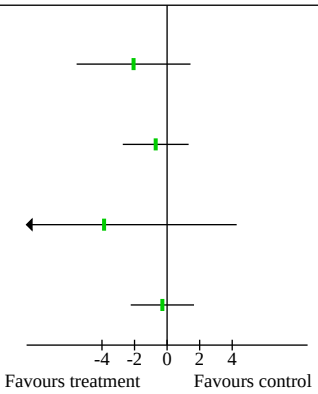


Footnotes

(1) Intervention is twice daily 10mg. Once daily arm has comparable outcomes.

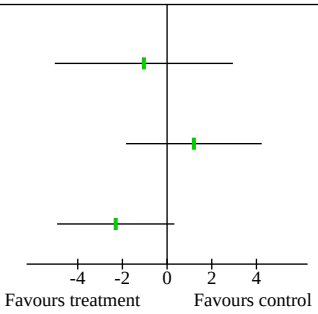
Analysis 1.2. Comparison 1: Pharmacological interventions versus placebo for post cessation weight control, Outcome 2: Mean weight change (kg) at 6 months

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
1.2.1 Phenylpropanolamine versus Placebo								
1 Cooper 2005 (also Part 2)	1.64	6.36	16	3.7	3.8	22	-2.06 [-5.56 , 1.44]	
1.2.2 Ephedrine + caffeine versus placebo								
1 Norregaard 1996	3.1	2	22	3.8	2.97	10	-0.70 [-2.72 , 1.32]	
1.2.3 Chromium versus placebo								
1 Parsons 2009	4.72	6.59	3	8.59	4.09	6	-3.87 [-12.01 , 4.27]	
1.2.4 Naltrexone versus placebo								
1 King 2012	3.92	3.73	36	4.21	4.37	32	-0.29 [-2.23 , 1.65]	



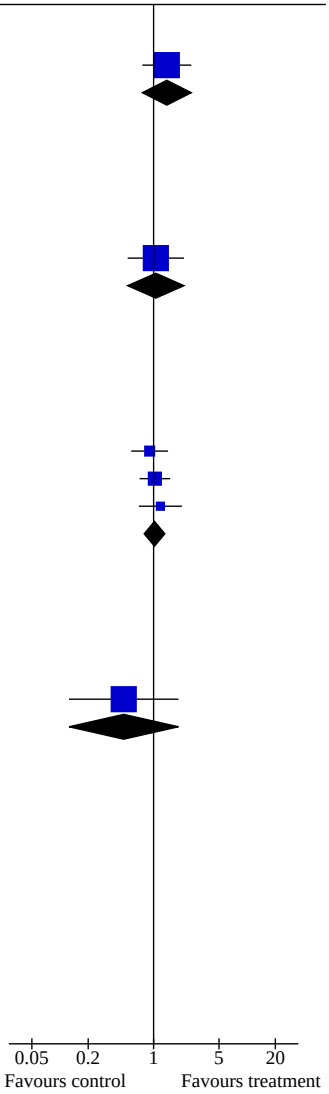
Analysis 1.3. Comparison 1: Pharmacological interventions versus placebo for post cessation weight control, Outcome 3: Mean weight change (kg) at 12 months

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
1.3.1 Phenylpropanolamine versus placebo								
1 Cooper 2005 (also Part 2)	0.82	7.14	16	1.86	4.58	22	-1.04 [-5.03 , 2.95]	
1.3.2 Ephedrine + Caffeine versus placebo								
1 Norregaard 1996	5.9	3.56	18	4.7	3.19	6	1.20 [-1.84 , 4.24]	
1.3.3 Naltrexone versus placebo								
1 King 2012	4.18	5.58	26	6.48	4.56	35	-2.30 [-4.92 , 0.32]	



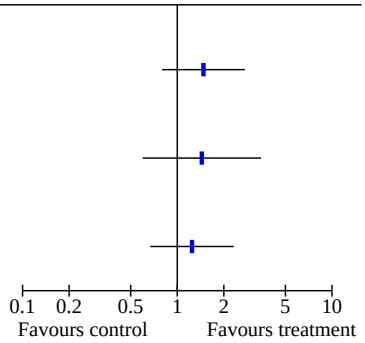
Analysis 1.4. Comparison 1: Pharmacological interventions versus placebo for post cessation weight control, Outcome 4: Smoking cessation at 6 months

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
1.4.1 Phenylpropanolamine gum versus placebo						
1 Cooper 2005 (also Part 2)	22	147	16	148	100.0%	1.38 [0.76 , 2.53]
Subtotal (95% CI)		**147**		**148**	**100.0%**	**1.38 [0.76 , 2.53]**
Total events:	22		16			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.06 (P = 0.29)						
1.4.2 Ephedrine + Caffeine versus placebo						
1 Norregaard 1996	22	152	10	73	100.0%	1.06 [0.53 , 2.11]
Subtotal (95% CI)		**152**		**73**	**100.0%**	**1.06 [0.53 , 2.11]**
Total events:	22		10			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.16 (P = 0.88)						
1.4.3 Naltrexone versus placebo						
1 O'Malley 2006	57	292	20	93	31.4%	0.91 [0.58 , 1.43]
1 King 2012	42	168	40	165	45.6%	1.03 [0.71 , 1.50]
1 Toll 2010	23	87	19	85	23.0%	1.18 [0.70 , 2.01]
Subtotal (95% CI)		**547**		**343**	**100.0%**	**1.02 [0.79 , 1.32]**
Total events:	122		79			
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.56$, df = 2 (P = 0.76); $I^2 = 0\%$						
Test for overall effect: Z = 0.17 (P = 0.86)						
1.4.4 Chromium versus placebo						
1 Parsons 2009	3	73	6	70	100.0%	0.48 [0.12 , 1.84]
Subtotal (95% CI)		**73**		**70**	**100.0%**	**0.48 [0.12 , 1.84]**
Total events:	3		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.07 (P = 0.28)						
1.4.5 Naltrexone & bupropion versus placebo						
1 Lyu 2018	0	11	0	11		Not estimable
Subtotal (95% CI)		**11**		**11**		**Not estimable**
Total events:	0		0			
Heterogeneity: Not applicable						
Test for overall effect: Not applicable						



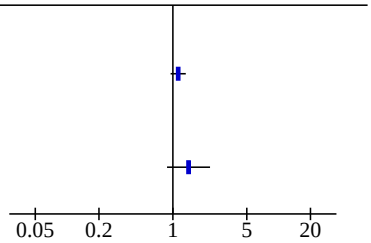
Analysis 1.5. Comparison 1: Pharmacological interventions versus placebo for post cessation weight control, Outcome 5: Smoking cessation at 12 months

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Risk Ratio M-H, Random, 95% CI
1.5.1 Phenylpropanolamine gum versus placebo					
1 Cooper 2005 (also Part 2)	22	147	15	148	1.48 [0.80 , 2.73]
1.5.2 Ephedrine + Caffeine versus Placebo					
1 Norregaard 1996	18	152	6	73	1.44 [0.60 , 3.48]
1.5.3 Naltrexone versus placebo					
1 O'Malley 2006	43	292	11	93	1.25 [0.67 , 2.31]



Analysis 1.6. Comparison 1: Pharmacological interventions versus placebo for post cessation weight control, Outcome 6: Adverse events

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Risk Ratio M-H, Random, 95% CI
1.6.1 Lorcaserin versus placebo					
1 Shanahan 2017 (1)	124	200	111	201	1.12 [0.95 , 1.32]
1.6.2 Lorcaserin (longer duration) versus placebo + lorcaserin (shorter duration)					
1 Rose 2019	35	56	12	27	1.41 [0.88 , 2.25]

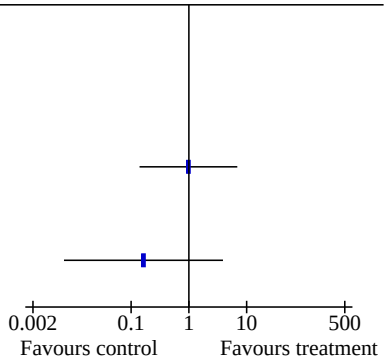


Footnotes

(1) Intervention is twice daily 10mg. Once daily arm has same rate as placebo. Events calculated from percentages provided.

Analysis 1.7. Comparison 1: Pharmacological interventions versus placebo for post cessation weight control, Outcome 7: Serious adverse events

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Risk Ratio M-H, Random, 95% CI
1.7.1 Topiramate versus placebo					
1 Oncken 2014	0	19	0	19	Not estimable
1.7.2 Naltrexone versus placebo					
1 King 2012	2	168	2	165	0.98 [0.14 , 6.89]
1.7.3 Lorcaserin (longer duration) versus placebo + lorcaserin (shorter duration)					
1 Rose 2019	0	56	1	27	0.16 [0.01 , 3.89]

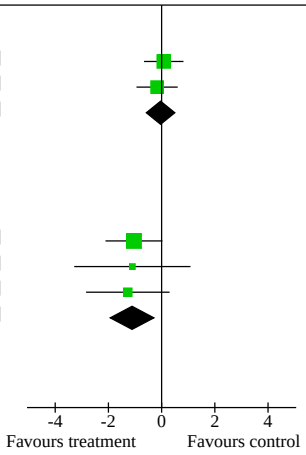


Comparison 2. Behavioural weight management interventions versus advice or no intervention for post-cessation weight control

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2.1 Mean weight change (kg) at end of treatment	4		Mean Difference (IV, Random, 95% CI)	Subtotals only
2.1.1 Weight management education versus no weight intervention	2	140	Mean Difference (IV, Random, 95% CI)	-0.04 [-0.57, 0.50]
2.1.2 Personalised weight management support versus no weight intervention	3	121	Mean Difference (IV, Random, 95% CI)	-1.11 [-1.93, -0.29]
2.2 Mean weight change (kg) at 6 months	7	897	Mean Difference (IV, Random, 95% CI)	-0.51 [-1.55, 0.53]
2.2.1 Weight management education verses no weight intervention	2	81	Mean Difference (IV, Random, 95% CI)	0.89 [-0.78, 2.55]
2.2.2 Personalised weight management support versus no weight intervention	5	816	Mean Difference (IV, Random, 95% CI)	-0.96 [-2.18, 0.25]
2.3 Mean weight change (kg) at 12 months	5		Mean Difference (IV, Random, 95% CI)	Subtotals only
2.3.1 Weight management education versus no weight intervention	2	61	Mean Difference (IV, Random, 95% CI)	-0.21 [-2.28, 1.86]
2.3.2 Personalised weight management support versus no weight intervention	4	530	Mean Difference (IV, Random, 95% CI)	-0.44 [-2.34, 1.46]
2.4 Smoking cessation at 6 months	9		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
2.4.1 Weight management education versus no intervention	3	660	Risk Ratio (M-H, Random, 95% CI)	1.02 [0.78, 1.33]
2.4.2 Personalised weight management support versus no intervention	7	5517	Risk Ratio (M-H, Random, 95% CI)	0.95 [0.82, 1.10]
2.5 Smoking cessation at 12 months	6		Risk Ratio (M-H, Random, 95% CI)	Subtotals only
2.5.1 Weight management education versus no intervention	2	522	Risk Ratio (M-H, Random, 95% CI)	0.66 [0.48, 0.90]
2.5.2 Personalised weight management support versus no intervention	5	3441	Risk Ratio (M-H, Random, 95% CI)	0.65 [0.45, 0.92]

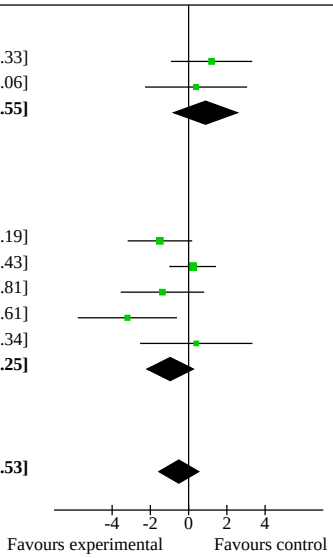
Analysis 2.1. Comparison 2: Behavioural weight management interventions versus advice or no intervention for post-cessation weight control, Outcome 1: Mean weight change (kg) at end of treatment

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
2.1.1 Weight management education versus no weight intervention								
1 Hall 1992	1.2	1.18	21	1.12	1.54	31	52.2%	0.08 [-0.66 , 0.82]
1 Pirie 1992 (also Part 2)	0.5	1.85	39	0.67	1.83	49	47.8%	-0.17 [-0.94 , 0.60]
Subtotal (95% CI)			**60**			**80**	**100.0%**	**-0.04 [-0.57 , 0.50]**
Heterogeneity: Tau² = 0.00; Chi² = 0.21, df = 1 (P = 0.65); I² = 0%								
Test for overall effect: Z = 0.14 (P = 0.89)								
2.1.2 Personalised weight management support versus no weight intervention								
1 Hall 1992	0.08	2.4	26	1.12	1.54	31	58.7%	-1.04 [-2.11 , 0.03]
1 Perkins 2001	2.6	3.4	17	3.7	3	16	14.1%	-1.10 [-3.28 , 1.08]
1 Spring 2004	2.44	2.77	21	3.71	1.66	10	27.3%	-1.27 [-2.84 , 0.30]
Subtotal (95% CI)			**64**			**57**	**100.0%**	**-1.11 [-1.93 , -0.29]**
Heterogeneity: Tau² = 0.00; Chi² = 0.06, df = 2 (P = 0.97); I² = 0%								
Test for overall effect: Z = 2.66 (P = 0.008)								
Test for subgroup differences: Chi² = 4.61, df = 1 (P = 0.03), I² = 78.3%								



Analysis 2.2. Comparison 2: Behavioural weight management interventions versus advice or no intervention for post-cessation weight control, Outcome 2: Mean weight change (kg) at 6 months

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
2.2.1 Weight management education verses no weight intervention								
1 Hankey 2009	3.9	3.1	23	2.7	3.7	18	14.1%	1.20 [-0.93 , 3.33]
1 Pirie 1992 (also Part 2)	4.09	4.17	25	3.7	4.17	15	10.5%	0.39 [-2.28 , 3.06]
Subtotal (95% CI)			**48**			**33**	**24.7%**	**0.89 [-0.78 , 2.55]**
Heterogeneity: Tau² = 0.00; Chi² = 0.22, df = 1 (P = 0.64); I² = 0%								
Test for overall effect: Z = 1.04 (P = 0.30)								
2.2.2 Personalised weight management support versus no weight intervention								
1 Bush 2012 (1)	-0.5	7.8	173	1	8.3	177	18.1%	-1.50 [-3.19 , 0.19]
1 Bush 2018 (2)	0.56	6.2	181	0.35	5.8	193	23.4%	0.21 [-1.01 , 1.43]
1 Johnson 2017	1.21	5.27	31	2.58	3.37	33	13.7%	-1.37 [-3.55 , 0.81]
1 Lycett 2020	-0.9	2.5	8	2.3	2.2	5	11.0%	-3.20 [-5.79 , -0.61]
1 Spring 2004	6	3.3	11	5.6	2.24	4	9.2%	0.40 [-2.54 , 3.34]
Subtotal (95% CI)			**404**			**412**	**75.3%**	**-0.96 [-2.18 , 0.25]**
Heterogeneity: Tau² = 0.85; Chi² = 7.47, df = 4 (P = 0.11); I² = 46%								
Test for overall effect: Z = 1.56 (P = 0.12)								
Total (95% CI)			**452**			**445**	**100.0%**	**-0.51 [-1.55 , 0.53]**
Heterogeneity: Tau² = 0.82; Chi² = 10.63, df = 6 (P = 0.10); I² = 44%								
Test for overall effect: Z = 0.97 (P = 0.33)								
Test for subgroup differences: Chi² = 3.11, df = 1 (P = 0.08), I² = 67.8%								



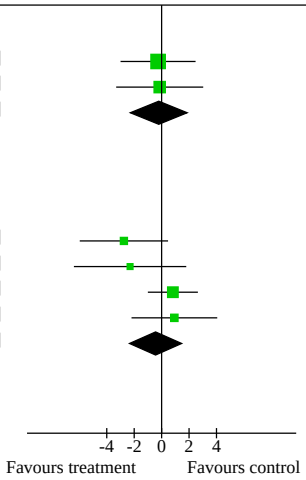
Footnotes

(1) Contained both weight acceptance and weight management components

(2) Intervention data is for sequential delivery. 3rd arm testing simultaneous delivery of weight and smoking intervention also found no difference. Results not sensitive to which

Analysis 2.3. Comparison 2: Behavioural weight management interventions versus advice or no intervention for post-cessation weight control, Outcome 3: Mean weight change (kg) at 12 months

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
2.3.1 Weight management education versus no weight intervention								
1 Hall 1992	3.35	2.38	7	3.61	3.99	14	57.4%	-0.26 [-2.99 , 2.47]
1 Pirie 1992 (also Part 2)	4.43	4.95	25	4.57	4.96	15	42.6%	-0.14 [-3.31 , 3.03]
Subtotal (95% CI)			**32**			**29**	**100.0%**	**-0.21 [-2.28 , 1.86]**
Heterogeneity: Tau² = 0.00; Chi² = 0.00, df = 1 (P = 0.96); I² = 0%								
Test for overall effect: Z = 0.20 (P = 0.84)								
2.3.2 Personalised weight management support versus no weight intervention								
1 Hall 1992	0.86	3.95	10	3.61	3.99	14	22.1%	-2.75 [-5.97 , 0.47]
1 Perkins 2001	5.4	3.3	9	7.7	4.7	7	15.9%	-2.30 [-6.40 , 1.80]
1 Bush 2018 (1)	0.44	9.7	214	-0.38	9.7	221	39.0%	0.82 [-1.00 , 2.64]
1 Johnson 2017	4.01	5.56	23	3.08	6.19	32	23.0%	0.93 [-2.19 , 4.05]
Subtotal (95% CI)			**256**			**274**	**100.0%**	**-0.44 [-2.34 , 1.46]**
Heterogeneity: Tau² = 1.54; Chi² = 5.11, df = 3 (P = 0.16); I² = 41%								
Test for overall effect: Z = 0.45 (P = 0.65)								
Test for subgroup differences: Chi² = 0.03, df = 1 (P = 0.87), I² = 0%								

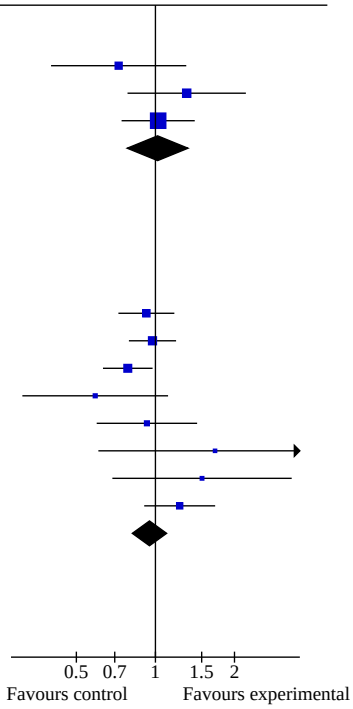


Footnotes

(1) Intervention data is for sequential delivery. 3rd arm testing simultaneous delivery of weight and smoking intervention also found no difference. Results not sensitive to which

Analysis 2.4. Comparison 2: Behavioural weight management interventions versus advice or no intervention for post-cessation weight control, Outcome 4: Smoking cessation at 6 months

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
2.4.1 Weight management education versus no intervention						
1 Hall 1992	13	51	19	54	19.0%	0.72 [0.40 , 1.31]
1 Hankey 2009	23	68	18	70	24.3%	1.32 [0.78 , 2.21]
1 Pirie 1992 (also Part 2)	55	206	55	211	56.7%	1.02 [0.74 , 1.41]
Subtotal (95% CI)		**325**		**335**	**100.0%**	**1.02 [0.78 , 1.33]**
Total events:	91		92			
Heterogeneity: Tau² = 0.01; Chi² = 2.20, df = 2 (P = 0.33); I² = 9%						
Test for overall effect: Z = 0.14 (P = 0.89)						
2.4.2 Personalised weight management support versus no intervention						
1 Bush 2012 (1)	109	1000	118	1000	19.8%	0.92 [0.72 , 1.18]
1 Bush 2018 (2)	201	845	103	422	23.4%	0.97 [0.79 , 1.20]
1 Bush 2018 (3)	163	851	103	422	22.4%	0.78 [0.63 , 0.98]
1 Hall 1992	11	53	19	54	4.9%	0.59 [0.31 , 1.12]
1 Johnson 2017	31	166	33	164	9.1%	0.93 [0.60 , 1.44]
1 Lycett 2020	8	37	5	39	2.1%	1.69 [0.61 , 4.69]
1 Perkins 2001	13	72	9	75	3.4%	1.50 [0.69 , 3.30]
1 Sobell 2017 (4)	59	158	48	159	15.0%	1.24 [0.91 , 1.69]
Subtotal (95% CI)		**3182**		**2335**	**100.0%**	**0.95 [0.82 , 1.10]**
Total events:	595		438			
Heterogeneity: Tau² = 0.01; Chi² = 10.46, df = 7 (P = 0.16); I² = 33%						
Test for overall effect: Z = 0.68 (P = 0.50)						



Footnotes

(1) Contained both weight acceptance and weight management components

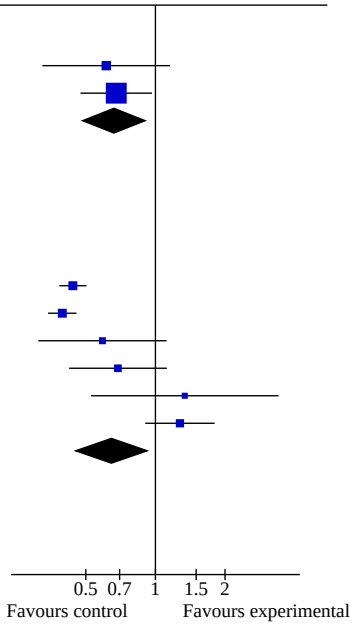
(2) Intervention data is simultaneous arm.

(3) Intervention arm sequential

(4) Note this intervention also focused on alcohol reduction, both as means of weight management and to aid cessation

Analysis 2.5. Comparison 2: Behavioural weight management interventions versus advice or no intervention for post-cessation weight control, Outcome 5: Smoking cessation at 12 months

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
2.5.1 Weight management education versus no intervention						
1 Hall 1992	11	51	19	54	23.8%	0.61 [0.32 , 1.16]
1 Pirie 1992 (also Part 2)	39	206	59	211	76.2%	0.68 [0.47 , 0.97]
Subtotal (95% CI)		**257**		**265**	**100.0%**	**0.66 [0.48 , 0.90]**
Total events:	50		78			
Heterogeneity: Tau² = 0.00; Chi² = 0.07, df = 1 (P = 0.79); I² = 0%						
Test for overall effect: Z = 2.61 (P = 0.009)						
2.5.2 Personalised weight management support versus no intervention						
1 Bush 2018 (1)	227	845	258	422	21.8%	0.44 [0.38 , 0.50]
1 Bush 2018 (2)	205	851	257	422	21.8%	0.40 [0.34 , 0.46]
1 Hall 1992	11	53	19	54	13.1%	0.59 [0.31 , 1.12]
1 Johnson 2017	23	166	33	164	15.9%	0.69 [0.42 , 1.12]
1 Perkins 2001	9	72	7	75	8.9%	1.34 [0.53 , 3.41]
1 Sobell 2017 (3)	52	158	41	159	18.6%	1.28 [0.90 , 1.80]
Subtotal (95% CI)		**2145**		**1296**	**100.0%**	**0.65 [0.45 , 0.92]**
Total events:	527		615			
Heterogeneity: Tau² = 0.15; Chi² = 47.16, df = 5 (P < 0.00001); I² = 89%						
Test for overall effect: Z = 2.41 (P = 0.02)						



Footnotes

(1) Intervention data is simultaneous arm.

(2) Intervention arm sequential

(3) Note this intervention also focussed on alcohol reduction, both as means of weight management and to aid cessation

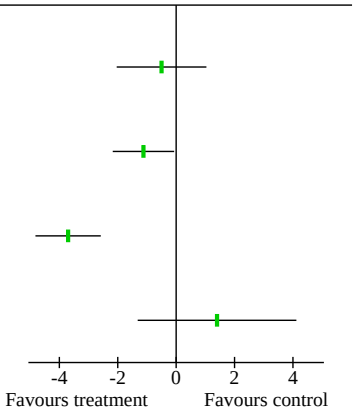
Comparison 3. Direct comparisons between behavioural weight management interventions

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.1 Mean weight change (kg) at end of treatment	4		Mean Difference (IV, Random, 95% CI)	Totals not selected
3.1.1 Low carb diet versus reduced fat diet	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
3.1.2 Personalised weight management support versus weight management education	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
3.1.3 VLCD + advice versus advice	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
3.1.4 Early versus late personalised weight management support	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
3.2 Mean weight change (kg) at 6 months	2		Mean Difference (IV, Random, 95% CI)	Totals not selected
3.2.1 Low carb diet versus reduced fat diet	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.2.2 Early versus late personalised weight management support	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
3.3 Mean weight change (kg) at 12 months	3		Mean Difference (IV, Random, 95% CI)	Totals not selected
3.3.1 Personalised weight management support versus weight management education	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
3.3.2 VLCD + advice versus advice	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
3.3.3 Motivational interviewing + CBT versus telephone support	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
3.4 Smoking cessation at 6 months	3		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
3.4.1 Exercise maintenance condition + standard care versus standard care (incl. behavioural weight management)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
3.4.2 Low carb diet versus reduced fat diet	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
3.4.3 Personalised weight management support versus weight management education	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
3.5 Smoking cessation at 12 months	4		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
3.5.1 Exercise maintenance condition + standard care versus standard care (incl. behavioural weight management)	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
3.5.2 Personalised weight management support versus weight management education	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
3.5.3 VLCD + advice versus advice	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected
3.5.4 Motivational interviewing + CBT versus telephone support	1		Risk Ratio (M-H, Random, 95% CI)	Totals not selected

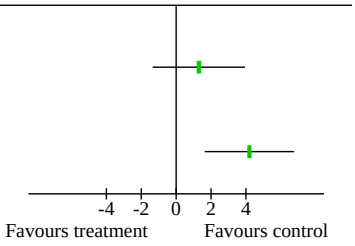
Analysis 3.1. Comparison 3: Direct comparisons between behavioural weight management interventions, Outcome 1: Mean weight change (kg) at end of treatment

Study or Subgroup	Intervention Mean	SD	Total	Comparator Mean	SD	Total	Mean Difference IV, Random, 95% CI
3.1.1 Low carb diet versus reduced fat diet							
1 Heggen 2016	-0.2	3.4	31	0.3	2.6	28	-0.50 [-2.04 , 1.04]
3.1.2 Personalised weight management support versus weight management education							
1 Hall 1992	0.08	2.4	26	1.2	1.18	21	-1.12 [-2.17 , -0.07]
3.1.3 VLCD + advice versus advice							
1 Danielsson 1999	-2.1	3.37	68	1.6	2.9	53	-3.70 [-4.82 , -2.58]
3.1.4 Early versus late personalised weight management support							
1 Spring 2004	2.44	2.77	21	1.04	5.58	20	1.40 [-1.32 , 4.12]



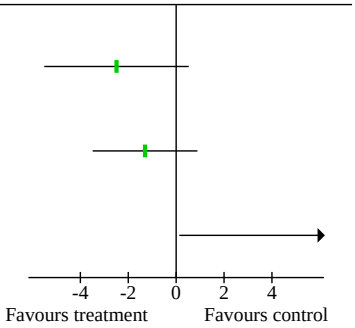
Analysis 3.2. Comparison 3: Direct comparisons between behavioural weight management interventions, Outcome 2: Mean weight change (kg) at 6 months

Study or Subgroup	Intervention Mean	SD	Total	Comparator Mean	SD	Total	Mean Difference IV, Random, 95% CI
3.2.1 Low carb diet versus reduced fat diet							
1 Heggen 2016	4.3	4.4	22	3	4	17	1.30 [-1.34 , 3.94]
3.2.2 Early versus late personalised weight management support							
1 Spring 2004	6	3.3	11	1.8	2.83	11	4.20 [1.63 , 6.77]



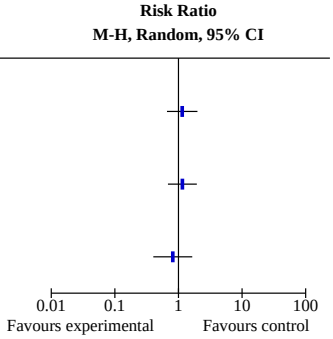
Analysis 3.3. Comparison 3: Direct comparisons between behavioural weight management interventions, Outcome 3: Mean weight change (kg) at 12 months

Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Mean Difference IV, Random, 95% CI
3.3.1 Personalised weight management support versus weight management education							
1 Hall 1992	0.86	3.95	10	3.35	2.38	7	-2.49 [-5.51 , 0.53]
3.3.2 VLCD + advice versus advice							
1 Danielsson 1999	2.5	5.55	38	3.8	3.23	24	-1.30 [-3.49 , 0.89]
3.3.3 Motivational interviewing + CBT versus telephone support							
1 Baker 2018	1.94	6.6	8	-5.13	6.52	6	7.07 [0.13 , 14.01]



Analysis 3.4. Comparison 3: Direct comparisons between behavioural weight management interventions, Outcome 4: Smoking cessation at 6 months

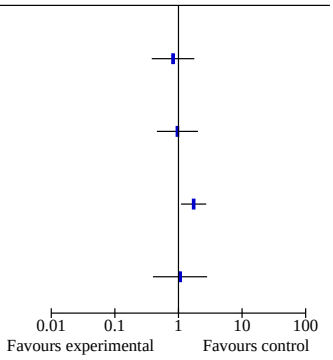
Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Risk Ratio M-H, Random, 95% CI
3.4.1 Exercise maintenance condition + standard care versus standard care (incl. behavioural weight management)					
1 Prapavessis 2018 (1)	23	106	18	95	1.15 [0.66 , 1.99]
3.4.2 Low carb diet versus reduced fat diet					
1 Heggen 2016	22	64	17	57	1.15 [0.68 , 1.94]
3.4.3 Personalised weight management support versus weight management education					
1 Hall 1992	11	53	13	51	0.81 [0.40 , 1.65]



Footnotes
(1) Standard care (incl. behavioural weight management)

Analysis 3.5. Comparison 3: Direct comparisons between behavioural weight management interventions, Outcome 5: Smoking cessation at 12 months

Study or Subgroup	Experimental Events	Experimental Total	Control Events	Control Total	Risk Ratio M-H, Random, 95% CI
3.5.1 Exercise maintenance condition + standard care versus standard care (incl. behavioural weight management)					
1 Prapavessis 2018 (1)	11	106	12	95	0.82 [0.38 , 1.77]
3.5.2 Personalised weight management support versus weight management education					
1 Hall 1992	11	53	11	51	0.96 [0.46 , 2.02]
3.5.3 VLCD + advice versus advice					
1 Danielsson 1999	38	137	24	150	1.73 [1.10 , 2.73]
3.5.4 Motivational interviewing + CBT versus telephone support					
1 Baker 2018	8	122	7	113	1.06 [0.40 , 2.82]



Footnotes
(1) Standard care (incl. behavioural weight management)

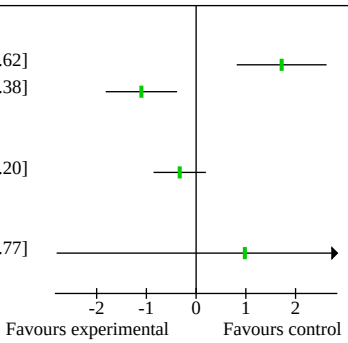
Comparison 4. Acceptance interventions for weight concern

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.1 Mean weight change (kg) at end of treatment	3		Mean Difference (IV, Random, 95% CI)	Totals not selected
4.1.1 Acceptance intervention, no additional pharmacotherapy	2		Mean Difference (IV, Random, 95% CI)	Totals not selected
4.1.2 Acceptance intervention, with bupropion in both arms	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
4.1.3 Acceptance intervention, with NRT in both arms	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
4.2 Mean weight change (kg) at 6 months	3	106	Mean Difference (IV, Random, 95% CI)	-0.00 [-1.53, 1.53]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.2.1 CBT to accept moderate weight gain versus no behavioural weight advice, no additional pharmacotherapy	2	55	Mean Difference (IV, Random, 95% CI)	-1.05 [-5.55, 3.45]
4.2.2 CBT to accept moderate weight gain versus no behavioural weight advice, with bupropion	1	46	Mean Difference (IV, Random, 95% CI)	0.86 [0.30, 1.42]
4.2.3 Acceptance intervention versus health education, with NRT	1	5	Mean Difference (IV, Random, 95% CI)	-0.53 [-5.72, 4.66]
4.3 Mean weight change (kg) at 12 months	2	76	Mean Difference (IV, Random, 95% CI)	-0.70 [-2.95, 1.56]
4.3.1 CBT to accept moderate weight gain versus no behavioural weight advice, no additional pharmacotherapy	2	44	Mean Difference (IV, Random, 95% CI)	-2.15 [-7.54, 3.24]
4.3.2 CBT to accept moderate weight gain versus no behavioural weight advice, with bupropion	1	32	Mean Difference (IV, Random, 95% CI)	0.38 [-0.57, 1.33]
4.4 Smoking cessation at 6 months	4	619	Risk Ratio (M-H, Random, 95% CI)	1.42 [1.03, 1.96]
4.4.1 CBT to accept moderate weight gain versus no behavioural weight advice (no additional pharmacotherapy)	3	355	Risk Ratio (M-H, Random, 95% CI)	1.53 [0.92, 2.55]
4.4.2 CBT to accept moderate weight gain versus no behavioural weight advice (with bupropion)	1	195	Risk Ratio (M-H, Random, 95% CI)	1.36 [0.85, 2.16]
4.4.3 ACT for weight concern versus health education	1	69	Risk Ratio (M-H, Random, 95% CI)	0.73 [0.22, 2.35]
4.5 Smoking cessation at 12 months	2	496	Risk Ratio (M-H, Random, 95% CI)	1.25 [0.76, 2.06]
4.5.1 CBT to accept moderate weight gain versus no behavioural weight advice (no additional pharmacotherapy)	2	301	Risk Ratio (M-H, Random, 95% CI)	1.45 [0.58, 3.59]
4.5.2 CBT to accept moderate weight gain versus no behavioural weight advice (with bupropion)	1	195	Risk Ratio (M-H, Random, 95% CI)	1.06 [0.62, 1.81]

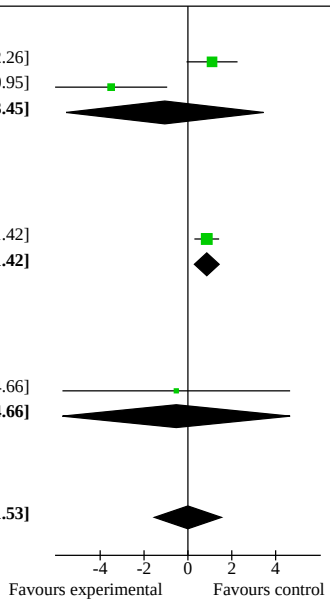
Analysis 4.1. Comparison 4: Acceptance interventions for weight concern, Outcome 1: Mean weight change (kg) at end of treatment

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Mean Difference IV, Random, 95% CI
4.1.1 Acceptance intervention, no additional pharmacotherapy							
1 Levine 2010 (also Part 2)	5.49	1.29	29	3.77	1.42	13	1.72 [0.82 , 2.62]
1 Perkins 2001	1.1	1.4	40	2.2	1.4	23	-1.10 [-1.82 , -0.38]
4.1.2 Acceptance intervention, with bupropion in both arms							
1 Levine 2010 (also Part 2)	4.98	0.79	43	5.31	0.96	16	-0.33 [-0.86 , 0.20]
4.1.3 Acceptance intervention, with NRT in both arms							
1 Bloom 2020	1.48	3.23	3	0.5	0.71	2	0.98 [-2.81 , 4.77]



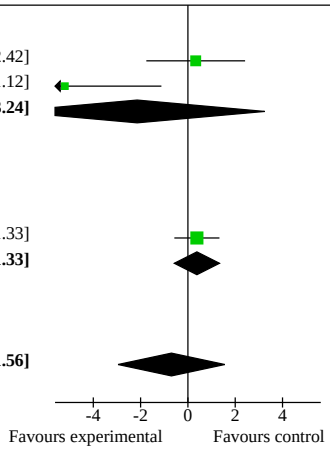
Analysis 4.2. Comparison 4: Acceptance interventions for weight concern, Outcome 2: Mean weight change (kg) at 6 months

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
4.2.1 CBT to accept moderate weight gain versus no behavioural weight advice, no additional pharmacotherapy								
1 Levine 2010 (also Part 2)	3.81	1.17	19	2.71	1.4	7	33.8%	1.10 [-0.06 , 2.26]
1 Perkins 2001	2.9	2.6	20	6.4	3.5	9	19.3%	-3.50 [-6.05 , -0.95]
Subtotal (95% CI)			**39**			**16**	**53.1%**	**-1.05 [-5.55 , 3.45]**
Heterogeneity: Tau² = 9.55; Chi² = 10.32, df = 1 (P = 0.001); I² = 90%								
Test for overall effect: Z = 0.46 (P = 0.65)								
4.2.2 CBT to accept moderate weight gain versus no behavioural weight advice, with bupropion								
1 Levine 2010 (also Part 2)	3.96	0.62	36	3.1	0.85	10	39.7%	0.86 [0.30 , 1.42]
Subtotal (95% CI)			**36**			**10**	**39.7%**	**0.86 [0.30 , 1.42]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 2.99 (P = 0.003)								
4.2.3 Acceptance intervention versus health education, with NRT								
1 Bloom 2020	2.51	3.1	3	3.04	2.76	2	7.2%	-0.53 [-5.72 , 4.66]
Subtotal (95% CI)			**3**			**2**	**7.2%**	**-0.53 [-5.72 , 4.66]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.20 (P = 0.84)								
Total (95% CI)			**78**			**28**	**100.0%**	**-0.00 [-1.53 , 1.53]**
Heterogeneity: Tau² = 1.44; Chi² = 11.35, df = 3 (P = 0.010); I² = 74%								
Test for overall effect: Z = 0.00 (P = 1.00)								
Test for subgroup differences: Chi² = 0.95, df = 2 (P = 0.62), I² = 0%								



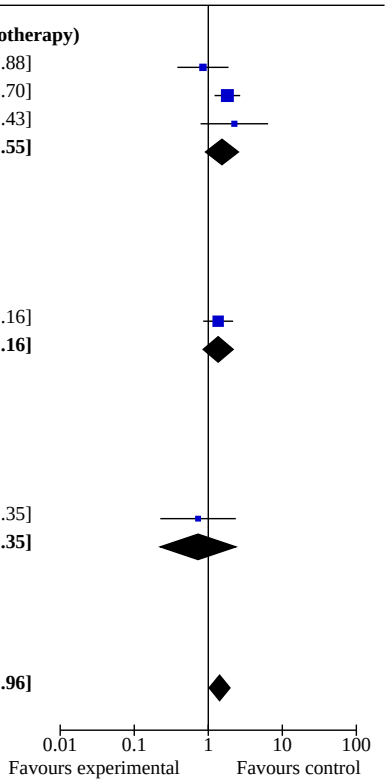
Analysis 4.3. Comparison 4: Acceptance interventions for weight concern, Outcome 3: Mean weight change (kg) at 12 months

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
4.3.1 CBT to accept moderate weight gain versus no behavioural weight advice, no additional pharmacotherapy								
1 Levine 2010 (also Part 2)	5.38	1.85	17	5.05	2.16	5	35.0%	0.33 [-1.76 , 2.42]
1 Perkins 2001	2.5	4.2	15	7.7	4.7	7	19.0%	-5.20 [-9.28 , -1.12]
Subtotal (95% CI)			**32**			**12**	**54.0%**	**-2.15 [-7.54 , 3.24]**
Heterogeneity: Tau² = 12.56; Chi² = 5.59, df = 1 (P = 0.02); I² = 82%								
Test for overall effect: Z = 0.78 (P = 0.44)								
4.3.2 CBT to accept moderate weight gain versus no behavioural weight advice, with bupropion								
1 Levine 2010 (also Part 2)	4.85	0.97	25	4.47	1.18	7	46.0%	0.38 [-0.57 , 1.33]
Subtotal (95% CI)			**25**			**7**	**46.0%**	**0.38 [-0.57 , 1.33]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.78 (P = 0.43)								
Total (95% CI)			**57**			**19**	**100.0%**	**-0.70 [-2.95 , 1.56]**
Heterogeneity: Tau² = 2.64; Chi² = 6.86, df = 2 (P = 0.03); I² = 71%								
Test for overall effect: Z = 0.61 (P = 0.54)								
Test for subgroup differences: Chi² = 0.82, df = 1 (P = 0.37), I² = 0%								

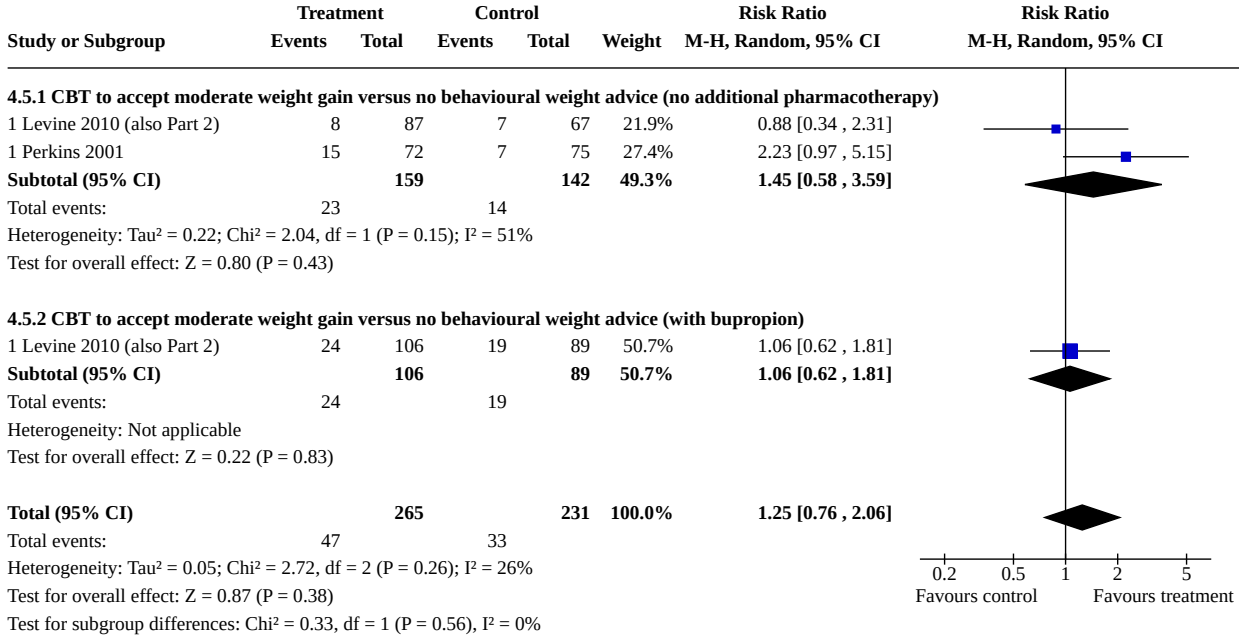


Analysis 4.4. Comparison 4: Acceptance interventions for weight concern, Outcome 4: Smoking cessation at 6 months

Study or Subgroup	Treatment Events	Treatment Total	Control Events	Control Total	Weight	Risk Ratio M-H, Random, 95% CI
4.4.1 CBT to accept moderate weight gain versus no behavioural weight advice (no additional pharmacotherapy)						
1 Levine 2010 (also Part 2)	11	87	10	67	14.0%	0.85 [0.38 , 1.88]
1 Perkins 2001	40	72	23	75	38.6%	1.81 [1.22 , 2.70]
1 White 2019	9	27	4	27	8.6%	2.25 [0.79 , 6.43]
Subtotal (95% CI)		**186**		**169**	**61.2%**	**1.53 [0.92 , 2.55]**
Total events:	60		37			
Heterogeneity: Tau² = 0.08; Chi² = 3.26, df = 2 (P = 0.20); I² = 39%						
Test for overall effect: Z = 1.63 (P = 0.10)						
4.4.2 CBT to accept moderate weight gain versus no behavioural weight advice (with bupropion)						
1 Levine 2010 (also Part 2)	34	106	21	89	31.8%	1.36 [0.85 , 2.16]
Subtotal (95% CI)		**106**		**89**	**31.8%**	**1.36 [0.85 , 2.16]**
Total events:	34		21			
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.29 (P = 0.20)						
4.4.3 ACT for weight concern versus health education						
1 Bloom 2020	4	33	6	36	7.0%	0.73 [0.22 , 2.35]
Subtotal (95% CI)		**33**		**36**	**7.0%**	**0.73 [0.22 , 2.35]**
Total events:	4		6			
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.53 (P = 0.59)						
Total (95% CI)		**325**		**294**	**100.0%**	**1.42 [1.03 , 1.96]**
Total events:	98		64			
Heterogeneity: Tau² = 0.03; Chi² = 5.07, df = 4 (P = 0.28); I² = 21%						
Test for overall effect: Z = 2.13 (P = 0.03)						
Test for subgroup differences: Chi² = 1.30, df = 2 (P = 0.52), I² = 0%						



Analysis 4.5. Comparison 4: Acceptance interventions for weight concern, Outcome 5: Smoking cessation at 12 months



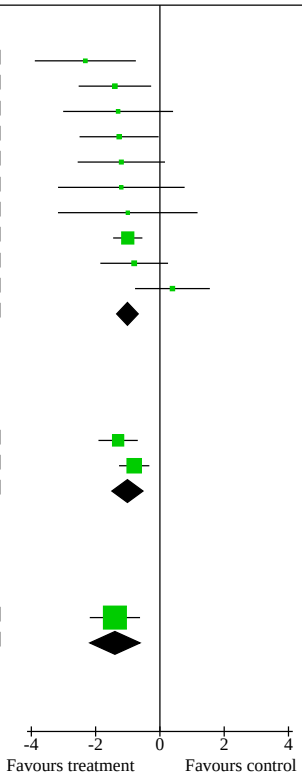
Comparison 5. All types of antidepressant versus placebo for smoking cessation

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5.1 Mean weight change (kg) at end of treatment	13		Mean Difference (IV, Random, 95% CI)	Subtotals only
5.1.1 Bupropion versus placebo	10	1098	Mean Difference (IV, Random, 95% CI)	-1.01 [-1.35, -0.67]
5.1.2 Fluoxetine versus placebo	2	144	Mean Difference (IV, Random, 95% CI)	-1.01 [-1.49, -0.53]
5.1.3 Bupropion + varenicline vs placebo + varenicline	1	243	Mean Difference (IV, Random, 95% CI)	-1.40 [-2.18, -0.62]
5.2 Mean weight change (kg) at end of treatment: dose response	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
5.2.1 Bupropion: 300mg/day v 150mg/day placebo	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
5.2.2 Bupropion: 300mg/day v 100mg/day placebo	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
5.3 Mean weight change (kg) at 6 months	10		Mean Difference (IV, Random, 95% CI)	Subtotals only
5.3.1 Bupropion versus placebo	7	420	Mean Difference (IV, Random, 95% CI)	-0.38 [-1.19, 0.44]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
5.3.2 Fluoxetine versus placebo	2	124	Mean Difference (IV, Random, 95% CI)	-1.01 [-4.38, 2.37]
5.3.3 Bupropion + varenicline vs placebo + varenicline	1	162	Mean Difference (IV, Random, 95% CI)	-0.40 [-1.71, 0.91]
5.4 Mean weight change (kg) at 6 months: dose response	3		Mean Difference (IV, Random, 95% CI)	Totals not selected
5.4.1 Bupropion: 300mg/day v 150mg/day	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
5.4.2 Bupropion: 300mg/day v 100mg/day	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
5.4.3 Fluoxetine: 40mg v 20mg	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
5.4.4 Fluoxetine: 60mg v 30mg	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
5.5 Mean weight change (kg) at 12 months	8		Mean Difference (IV, Random, 95% CI)	Subtotals only
5.5.1 Bupropion versus placebo	7	471	Mean Difference (IV, Random, 95% CI)	-0.26 [-1.31, 0.78]
5.5.2 Bupropion + varenicline vs placebo + varenicline	1	140	Mean Difference (IV, Random, 95% CI)	-1.20 [-3.18, 0.78]
5.6 Mean weight change (kg) at 12 months: dose response	1		Mean Difference (IV, Random, 95% CI)	Subtotals only
5.6.1 Bupropion: 300mg/day v 150mg/day	1	33	Mean Difference (IV, Random, 95% CI)	0.20 [-4.81, 5.21]
5.6.2 Bupropion: 300mg/day v 100mg/day	1	24	Mean Difference (IV, Random, 95% CI)	-2.00 [-8.04, 4.04]

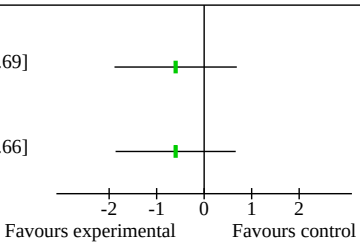
Analysis 5.1. Comparison 5: All types of antidepressant versus placebo for smoking cessation, Outcome 1: Mean weight change (kg) at end of treatment

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
5.1.1 Bupropion versus placebo								
2 Nides 2006	1.68	1.92	22	4	2.18	10	4.5%	-2.32 [-3.89 , -0.75]
2 Hurt 1997	1.5	2	38	2.9	1.9	16	8.6%	-1.40 [-2.53 , -0.27]
2 Piper 2007	1.3	6.2	69	2.6	2.3	26	3.8%	-1.30 [-3.01 , 0.41]
2 Jorenby 2006	1.88	3.4	102	3.15	4.1	60	7.3%	-1.27 [-2.50 , -0.04]
2 Cox 2012	0.3	3.36	64	1.5	2.81	26	6.0%	-1.20 [-2.56 , 0.16]
2 Rigotti 2006	1.2	3.9	31	2.4	3.6	25	2.9%	-1.20 [-3.17 , 0.77]
2 Eisenberg 2013	0.36	6.07	59	1.36	6.16	63	2.4%	-1.00 [-3.17 , 1.17]
2 Zellweger 2005	1.32	1.8	248	2.32	1.64	66	46.6%	-1.00 [-1.45 , -0.55]
2 Gonzales 2006	2.12	1.8	95	2.92	3.94	61	9.8%	-0.80 [-1.85 , 0.25]
1 Levine 2010 (also Part 2)	3.1	0.85	10	2.71	1.4	7	8.1%	0.39 [-0.77 , 1.55]
Subtotal (95% CI)			**738**			**360**	**100.0%**	**-1.01 [-1.35 , -0.67]**
Heterogeneity: Tau² = 0.01; Chi² = 9.24, df = 9 (P = 0.42); I² = 3%								
Test for overall effect: Z = 5.90 (P < 0.00001)								
5.1.2 Fluoxetine versus placebo								
2 Niaura 2002	1.3	1.4	73	2.6	1.8	46	42.1%	-1.30 [-1.91 , -0.69]
1 Spring 1995 (also Part 2)	2.7	0.5	10	3.5	0.7	15	57.9%	-0.80 [-1.27 , -0.33]
Subtotal (95% CI)			**83**			**61**	**100.0%**	**-1.01 [-1.49 , -0.53]**
Heterogeneity: Tau² = 0.05; Chi² = 1.61, df = 1 (P = 0.20); I² = 38%								
Test for overall effect: Z = 4.09 (P < 0.0001)								
5.1.3 Bupropion + varenicline vs placebo + varenicline								
2 Ebbert 2014	1.1	3.52	132	2.5	2.69	111	100.0%	-1.40 [-2.18 , -0.62]
Subtotal (95% CI)			**132**			**111**	**100.0%**	**-1.40 [-2.18 , -0.62]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 3.51 (P = 0.0004)								
Test for subgroup differences: Chi² = 0.85, df = 2 (P = 0.65), I² = 0%								



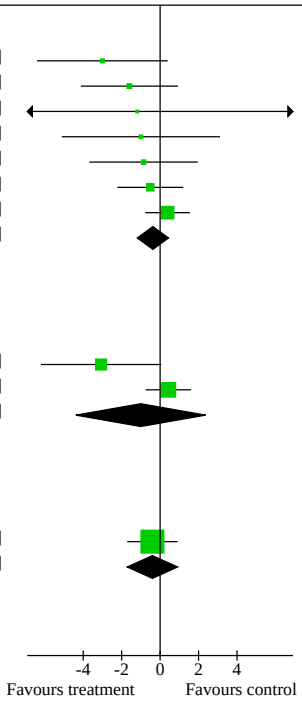
Analysis 5.2. Comparison 5: All types of antidepressant versus placebo for smoking cessation, Outcome 2: Mean weight change (kg) at end of treatment: dose response

Study or Subgroup	Higher dose Mean	Higher dose SD	Higher dose Total	Lower dose Mean	Lower dose SD	Lower dose Total	Mean Difference IV, Random, 95% CI
5.2.1 Bupropion: 300mg/day v 150mg/day placebo							
2 Hurt 1997	2.3	2.4	28	2.9	1.9	16	-0.60 [-1.89 , 0.69]
5.2.2 Bupropion: 300mg/day v 100mg/day placebo							
2 Hurt 1997	2.3	2	21	2.9	1.9	16	-0.60 [-1.86 , 0.66]



Analysis 5.3. Comparison 5: All types of antidepressant versus placebo for smoking cessation, Outcome 3: Mean weight change (kg) at 6 months

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
5.3.1 Bupropion versus placebo								
2 Eisenberg 2013	0.19	11.48	59	3.19	6.99	63	5.7%	-3.00 [-6.40 , 0.40]
2 Uyar 2007 (1)	0.9	3	13	2.5	2.2	5	10.4%	-1.60 [-4.13 , 0.93]
2 Simon 2009 (2)	0.5	19.71	6	1.69	15.23	13	0.2%	-1.19 [-19.00 , 16.62]
2 Hurt 1997	4.5	4.7	19	5.5	5.4	9	3.9%	-1.00 [-5.11 , 3.11]
2 Cox 2012	2.63	4.94	36	3.49	6.12	27	8.3%	-0.86 [-3.68 , 1.96]
2 Zellweger 2005	3.35	2.82	117	3.86	5	36	22.6%	-0.51 [-2.22 , 1.20]
1 Levine 2010 (also Part 2)	3.1	0.85	10	2.71	1.4	7	48.9%	0.39 [-0.77 , 1.55]
Subtotal (95% CI)			**260**			**160**	**100.0%**	**-0.38 [-1.19 , 0.44]**
Heterogeneity: Tau² = 0.00; Chi² = 5.09, df = 6 (P = 0.53); I² = 0%								
Test for overall effect: Z = 0.90 (P = 0.37)								
5.3.2 Fluoxetine versus placebo								
2 Saules 2004	3.09	3.43	34	6.16	4.45	9	41.1%	-3.07 [-6.20 , 0.06]
2 Niaura 2002	5.13	2.8	49	4.7	2.54	32	58.9%	0.43 [-0.75 , 1.61]
Subtotal (95% CI)			**83**			**41**	**100.0%**	**-1.01 [-4.38 , 2.37]**
Heterogeneity: Tau² = 4.67; Chi² = 4.21, df = 1 (P = 0.04); I² = 76%								
Test for overall effect: Z = 0.59 (P = 0.56)								
5.3.3 Bupropion + varenicline vs placebo + varenicline								
2 Ebbert 2014	3.4	4.38	91	3.8	4.08	71	100.0%	-0.40 [-1.71 , 0.91]
Subtotal (95% CI)			**91**			**71**	**100.0%**	**-0.40 [-1.71 , 0.91]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.60 (P = 0.55)								
Test for subgroup differences: Chi² = 0.13, df = 2 (P = 0.94), I² = 0%								



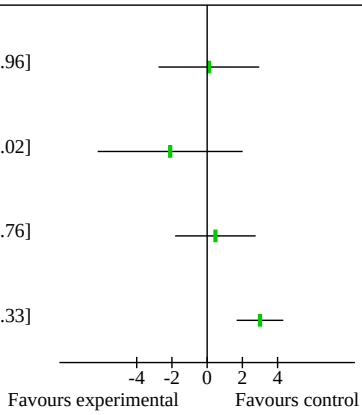
Footnotes

(1) Control group was no treatment (no placebo received)

(2) All participants received NRT

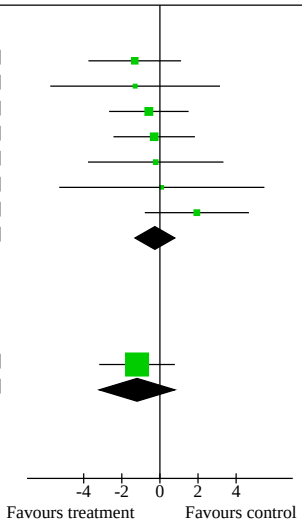
Analysis 5.4. Comparison 5: All types of antidepressant versus placebo for smoking cessation, Outcome 4: Mean weight change (kg) at 6 months: dose response

Study or Subgroup	Higher dose Mean	Higher dose SD	Higher dose Total	Lower dose Mean	Lower dose SD	Lower dose Total	Mean Difference IV, Random, 95% CI
5.4.1 Bupropion: 300mg/day v 150mg/day							
2 Hurt 1997	4.5	4.7	19	4.4	4.5	21	0.10 [-2.76 , 2.96]
5.4.2 Bupropion: 300mg/day v 100mg/day							
2 Hurt 1997	4.5	4.7	19	6.6	5.7	10	-2.10 [-6.22 , 2.02]
5.4.3 Fluoxetine: 40mg v 20mg							
2 Saules 2004	3.35	3	15	2.88	3.8	19	0.47 [-1.82 , 2.76]
5.4.4 Fluoxetine: 60mg v 30mg							
2 Niaura 2002	6.6	2.65	25	3.6	2.06	24	3.00 [1.67 , 4.33]



Analysis 5.5. Comparison 5: All types of antidepressant versus placebo for smoking cessation, Outcome 5: Mean weight change (kg) at 12 months

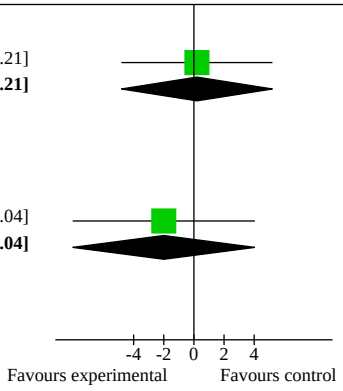
Study or Subgroup	Treatment Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
5.5.1 Bupropion versus placebo								
2 Eisenberg 2013	2.2	5.89	59	3.52	7.74	63	18.5%	-1.32 [-3.75 , 1.11]
2 Rigotti 2006	5.6	8.2	20	6.9	5.2	15	5.5%	-1.30 [-5.75 , 3.15]
1 Levine 2010 (also Part 2)	4.47	1.18	7	5.05	2.16	5	25.1%	-0.58 [-2.67 , 1.51]
2 Zellweger 2005	4.15	4.18	117	4.45	6.12	36	23.9%	-0.30 [-2.44 , 1.84]
2 Simon 2004 (1)	2.72	6.7	17	2.94	3.86	23	8.6%	-0.22 [-3.77 , 3.33]
2 Hurt 1997	6.1	7.9	16	6	5.4	8	3.8%	0.10 [-5.28 , 5.48]
2 Piper 2009	5.12	5.16	55	3.18	6.62	30	14.6%	1.94 [-0.79 , 4.67]
Subtotal (95% CI)			**291**			**180**	**100.0%**	**-0.26 [-1.31 , 0.78]**
Heterogeneity: Tau² = 0.00; Chi² = 3.54, df = 6 (P = 0.74); I² = 0%								
Test for overall effect: Z = 0.50 (P = 0.62)								
5.5.2 Bupropion + varenicline vs placebo + varenicline								
2 Ebbert 2014	4.9	5.82	77	6.1	6.07	63	100.0%	-1.20 [-3.18 , 0.78]
Subtotal (95% CI)			**77**			**63**	**100.0%**	**-1.20 [-3.18 , 0.78]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.19 (P = 0.24)								



Footnotes
(1) All participants received NRT

Analysis 5.6. Comparison 5: All types of antidepressant versus placebo for smoking cessation, Outcome 6: Mean weight change (kg) at 12 months: dose response

Study or Subgroup	Higher dose Mean	SD	Total	Lower dose Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
5.6.1 Bupropion: 300mg/day v 150mg/day								
2 Hurt 1997	6.1	7.9	16	5.9	6.7	17	100.0%	0.20 [-4.81 , 5.21]
Subtotal (95% CI)			**16**			**17**	**100.0%**	**0.20 [-4.81 , 5.21]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.08 (P = 0.94)								
5.6.2 Bupropion: 300mg/day v 100mg/day								
2 Hurt 1997	6.1	7.9	16	8.1	6.7	8	100.0%	-2.00 [-8.04 , 4.04]
Subtotal (95% CI)			**16**			**8**	**100.0%**	**-2.00 [-8.04 , 4.04]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.65 (P = 0.52)								
Test for subgroup differences: Chi² = 0.30, df = 1 (P = 0.58), I² = 0%								



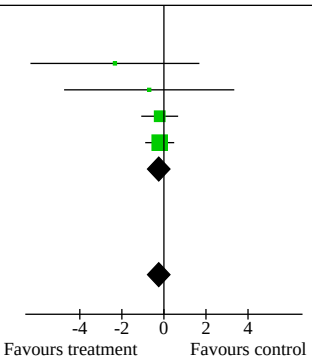
Comparison 6. Exercise interventions versus no exercise for smoking cessation

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
6.1 Mean weight change (kg) at end of treatment	4	404	Mean Difference (IV, Random, 95% CI)	-0.25 [-0.78, 0.29]
6.1.1 Exercise + SC versus SC only	4	404	Mean Difference (IV, Random, 95% CI)	-0.25 [-0.78, 0.29]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
6.2 Mean weight change (kg) at 12 months	3	182	Mean Difference (IV, Random, 95% CI)	-2.07 [-3.78, -0.36]
6.2.1 Exercise + SC versus SC only	3	182	Mean Difference (IV, Random, 95% CI)	-2.07 [-3.78, -0.36]

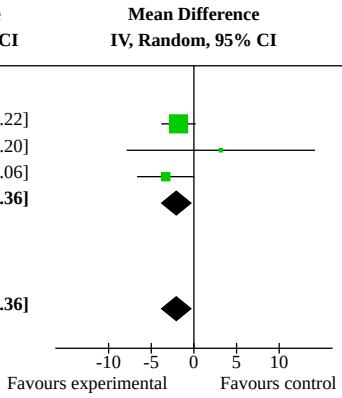
Analysis 6.1. Comparison 6: Exercise interventions versus no exercise for smoking cessation, Outcome 1: Mean weight change (kg) at end of treatment

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
6.1.1 Exercise + SC versus SC only								
2 Marcus 1999	3.03	3.45	24	5.36	6.94	13	1.8%	-2.33 [-6.35 , 1.69]
2 Marcus 2005	3.86	5.66	12	4.56	5.05	16	1.7%	-0.70 [-4.75 , 3.35]
2 Bize 2010	2.5	4.14	107	2.7	2.14	115	36.9%	-0.20 [-1.08 , 0.68]
2 Ussher 2003	1.8	1.9	61	2	1.9	56	59.6%	-0.20 [-0.89 , 0.49]
Subtotal (95% CI)			**204**			**200**	**100.0%**	**-0.25 [-0.78 , 0.29]**
Heterogeneity: Tau² = 0.00; Chi² = 1.11, df = 3 (P = 0.77); I² = 0%								
Test for overall effect: Z = 0.91 (P = 0.36)								
Total (95% CI)			**204**			**200**	**100.0%**	**-0.25 [-0.78 , 0.29]**
Heterogeneity: Tau² = 0.00; Chi² = 1.11, df = 3 (P = 0.77); I² = 0%								
Test for overall effect: Z = 0.91 (P = 0.36)								
Test for subgroup differences: Not applicable								



Analysis 6.2. Comparison 6: Exercise interventions versus no exercise for smoking cessation, Outcome 2: Mean weight change (kg) at 12 months

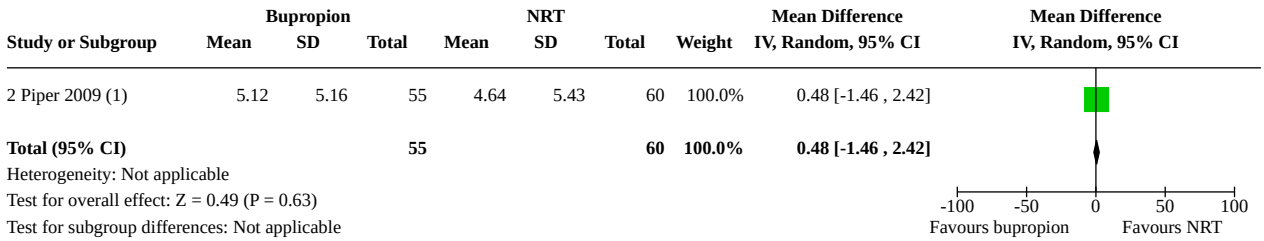
Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
6.2.1 Exercise + SC versus SC only								
2 Bize 2010	4.4	6.91	59	6.2	4.18	70	71.8%	-1.80 [-3.82 , 0.22]
2 Marcus 1999	8.92	8.9	15	5.76	12.6	6	2.4%	3.16 [-7.88 , 14.20]
2 Ussher 2003	3.9	5.3	14	7.2	4.1	18	25.8%	-3.30 [-6.66 , 0.06]
Subtotal (95% CI)			**88**			**94**	**100.0%**	**-2.07 [-3.78 , -0.36]**
Heterogeneity: Tau² = 0.00; Chi² = 1.45, df = 2 (P = 0.49); I² = 0%								
Test for overall effect: Z = 2.37 (P = 0.02)								
Total (95% CI)			**88**			**94**	**100.0%**	**-2.07 [-3.78 , -0.36]**
Heterogeneity: Tau² = 0.00; Chi² = 1.45, df = 2 (P = 0.49); I² = 0%								
Test for overall effect: Z = 2.37 (P = 0.02)								
Test for subgroup differences: Not applicable								



Comparison 7. Bupropion versus NRT

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
7.1 Weight change (kg) at 12 months	1	115	Mean Difference (IV, Random, 95% CI)	0.48 [-1.46, 2.42]

Analysis 7.1. Comparison 7: Bupropion versus NRT, Outcome 1: Weight change (kg) at 12 months



Footnotes

(1) NRT data is patch arm. Comparable to lozenge arm.

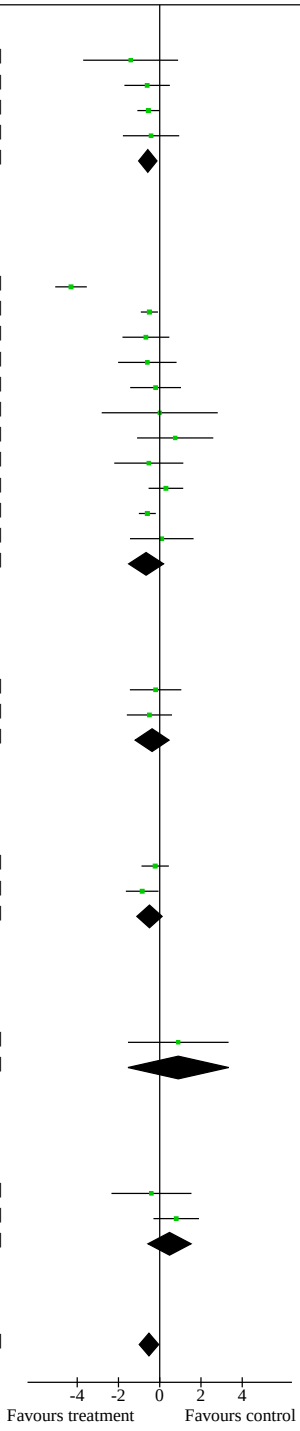
Comparison 8. All types of NRT versus placebo for smoking cessation

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
8.1 Mean weight change (kg) at end of treatment	21	2784	Mean Difference (IV, Random, 95% CI)	-0.52 [-0.99, -0.05]
8.1.1 Gum versus placebo	4	345	Mean Difference (IV, Random, 95% CI)	-0.58 [-1.02, -0.13]
8.1.2 Patch versus placebo	11	1666	Mean Difference (IV, Random, 95% CI)	-0.66 [-1.51, 0.19]
8.1.3 Inhaler versus placebo	2	111	Mean Difference (IV, Random, 95% CI)	-0.37 [-1.19, 0.45]
8.1.4 Sub-lingual tablet versus placebo	2	478	Mean Difference (IV, Random, 95% CI)	-0.50 [-1.11, 0.12]
8.1.5 Intranasal spray versus placebo	1	47	Mean Difference (IV, Random, 95% CI)	0.90 [-1.54, 3.34]
8.1.6 Lozenge versus placebo	1	137	Mean Difference (IV, Random, 95% CI)	0.48 [-0.57, 1.52]
8.2 Mean weight change (kg) at 6 months	11	1021	Mean Difference (IV, Random, 95% CI)	-0.08 [-0.51, 0.35]
8.2.1 Gum versus placebo	2	103	Mean Difference (IV, Random, 95% CI)	-0.83 [-2.35, 0.69]
8.2.2 Patch versus placebo	4	282	Mean Difference (IV, Random, 95% CI)	-0.33 [-1.16, 0.49]
8.2.3 Inhaler versus placebo	1	57	Mean Difference (IV, Random, 95% CI)	-0.60 [-1.98, 0.78]
8.2.4 Sub-lingual tablet versus placebo	2	329	Mean Difference (IV, Random, 95% CI)	-0.19 [-1.09, 0.72]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
8.2.5 Patch + varenicline versus placebo + varenicline	1	113	Mean Difference (IV, Random, 95% CI)	0.96 [-0.53, 2.45]
8.2.6 Lozenge versus placebo	1	137	Mean Difference (IV, Random, 95% CI)	0.48 [-0.57, 1.52]
8.3 Mean weight change (kg) at 12 months	17	1463	Mean Difference (IV, Random, 95% CI)	-0.37 [-0.86, 0.11]
8.3.1 Gum versus placebo	1	49	Mean Difference (IV, Random, 95% CI)	-0.07 [-3.07, 2.93]
8.3.2 Patch versus placebo	7	812	Mean Difference (IV, Random, 95% CI)	-0.23 [-0.89, 0.44]
8.3.3 Intranasal spray versus placebo	3	122	Mean Difference (IV, Random, 95% CI)	-1.55 [-3.09, -0.00]
8.3.4 Inhaler versus placebo	2	90	Mean Difference (IV, Random, 95% CI)	-1.03 [-2.23, 0.17]
8.3.5 Sub-lingual tablet versus placebo	3	303	Mean Difference (IV, Random, 95% CI)	0.27 [-0.99, 1.54]
8.3.6 Lozenge versus placebo	1	87	Mean Difference (IV, Random, 95% CI)	0.97 [-1.82, 3.76]

Analysis 8.1. Comparison 8: All types of NRT versus placebo for smoking cessation, Outcome 1: Mean weight change (kg) at end of treatment

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
8.1.1 Gum versus placebo								
1 Cooper 2005 (also Part 2)	2.19	4.14	24	3.6	3.82	22	2.6%	-1.41 [-3.71 , 0.89]
1 Pirie 1992 (also Part 2)	0.49	1.82	34	1.1	1.81	15	4.9%	-0.61 [-1.71 , 0.49]
2 Garvey 2000	0.95	1.6	161	1.5	1.65	47	6.2%	-0.55 [-1.08 , -0.02]
2 Gross 1995	2.07	2.26	35	2.49	1.54	7	4.3%	-0.42 [-1.78 , 0.94]
Subtotal (95% CI)			**254**			**91**	**18.0%**	**-0.58 [-1.02 , -0.13]**
Heterogeneity: Tau² = 0.00; Chi² = 0.57, df = 3 (P = 0.90); I² = 0%								
Test for overall effect: Z = 2.55 (P = 0.01)								
8.1.2 Patch versus placebo								
2 Abelin 1989	0.1	1.8	72	4.4	2.2	45	5.7%	-4.30 [-5.07 , -3.53]
2 CEASE 1999	1.7	2.1	497	2.2	2.3	147	6.4%	-0.50 [-0.92 , -0.08]
2 Ehrsam 1991	1.23	1.7	22	1.9	1.5	11	4.8%	-0.67 [-1.81 , 0.47]
2 Fiore 1994A	2.6	1.8	26	3.2	2.6	17	4.2%	-0.60 [-2.02 , 0.82]
2 Fiore 1994B	2.6	1.91	21	2.8	1.56	11	4.6%	-0.20 [-1.43 , 1.03]
2 Gourlay 1995	1.9	3.1	21	1.9	3.1	6	2.0%	0.00 [-2.81 , 2.81]
2 Oncken 2007	1.58	2.97	12	0.83	2.31	35	3.3%	0.75 [-1.10 , 2.60]
2 Richmond 1994	2.62	2.68	55	3.15	3.63	22	3.6%	-0.53 [-2.20 , 1.14]
2 Stapleton 1995	3.1	2.9	155	2.8	2.3	41	5.5%	0.30 [-0.54 , 1.14]
2 TNSG 1991	2	1.9	332	2.6	1.5	68	6.4%	-0.60 [-1.01 , -0.19]
2 Tønnesen 1991	2.6	2.1	43	2.5	1.9	7	3.9%	0.10 [-1.44 , 1.64]
Subtotal (95% CI)			**1256**			**410**	**50.5%**	**-0.66 [-1.51 , 0.19]**
Heterogeneity: Tau² = 1.61; Chi² = 95.28, df = 10 (P < 0.00001); I² = 90%								
Test for overall effect: Z = 1.53 (P = 0.13)								
8.1.3 Inhaler versus placebo								
2 Hjalmarson 1997	1.7	1.6	35	1.9	2.7	22	4.6%	-0.20 [-1.45 , 1.05]
2 Tønnesen 1993	3.3	2	36	3.8	1.9	18	4.9%	-0.50 [-1.59 , 0.59]
Subtotal (95% CI)			**71**			**40**	**9.5%**	**-0.37 [-1.19 , 0.45]**
Heterogeneity: Tau² = 0.00; Chi² = 0.13, df = 1 (P = 0.72); I² = 0%								
Test for overall effect: Z = 0.88 (P = 0.38)								
8.1.4 Sub-lingual tablet versus placebo								
2 Shiffman 2002A	2.32	2.57	158	2.54	2.68	99	5.9%	-0.22 [-0.88 , 0.44]
2 Shiffman 2002B	2.74	2.68	158	3.59	2.72	63	5.7%	-0.85 [-1.64 , -0.06]
Subtotal (95% CI)			**316**			**162**	**11.6%**	**-0.50 [-1.11 , 0.12]**
Heterogeneity: Tau² = 0.06; Chi² = 1.43, df = 1 (P = 0.23); I² = 30%								
Test for overall effect: Z = 1.59 (P = 0.11)								
8.1.5 Intranasal spray versus placebo								
2 Blondal 1999	6.5	5.6	29	5.6	2.9	18	2.4%	0.90 [-1.54 , 3.34]
Subtotal (95% CI)			**29**			**18**	**2.4%**	**0.90 [-1.54 , 3.34]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.72 (P = 0.47)								
8.1.6 Lozenge versus placebo								
2 Xiao 2019 (1)	2.4	4.05	29	2.8	2.8	19	3.1%	-0.40 [-2.34 , 1.54]
2 Xiao 2019 (2)	2	2.75	46	1.2	2.56	43	4.9%	0.80 [-0.30 , 1.90]
Subtotal (95% CI)			**75**			**62**	**8.1%**	**0.48 [-0.57 , 1.52]**
Heterogeneity: Tau² = 0.07; Chi² = 1.11, df = 1 (P = 0.29); I² = 10%								
Test for overall effect: Z = 0.89 (P = 0.37)								
Total (95% CI)			**2001**			**783**	**100.0%**	**-0.52 [-0.99 , -0.05]**
Heterogeneity: Tau² = 0.86; Chi² = 108.01, df = 21 (P < 0.00001); I² = 81%								
Test for overall effect: Z = 2.17 (P = 0.03)								
Test for subgroup differences: Chi² = 4.80, df = 5 (P = 0.44), I² = 0%								



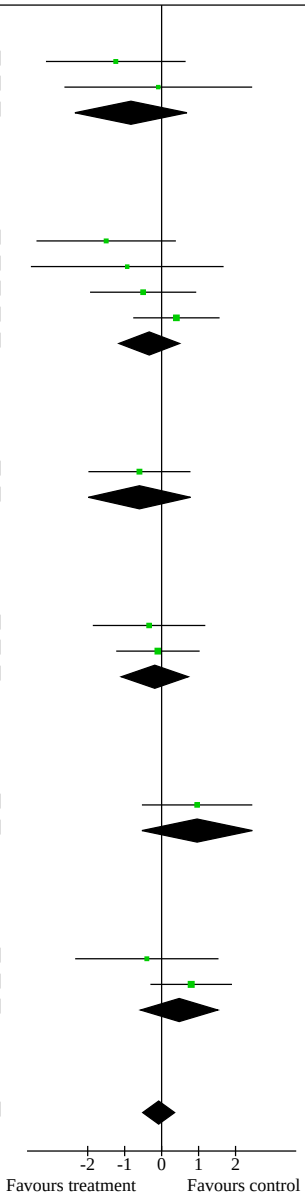
Footnotes

(1) High dependency stratum. N is those recorded as long-term abstinent, unclear whether weight was measured in all participants

(2) Low dependency stratum. N is those recorded as long-term abstinent, unclear whether weight was measured in all participants.

Analysis 8.2. Comparison 8: All types of NRT versus placebo for smoking cessation, Outcome 2: Mean weight change (kg) at 6 months

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
8.2.1 Gum versus placebo								
2 Hjalmarson 1984	1.34	3.6	36	2.58	3.2	18	5.2%	-1.24 [-3.13 , 0.65]
1 Pirie 1992 (also Part 2)	3.61	4.18	34	3.7	4.18	15	2.9%	-0.09 [-2.63 , 2.45]
Subtotal (95% CI)			**70**			**33**	**8.1%**	**-0.83 [-2.35 , 0.69]**
Heterogeneity: Tau² = 0.00; Chi² = 0.51, df = 1 (P = 0.48); I² = 0%								
Test for overall effect: Z = 1.07 (P = 0.28)								
8.2.2 Patch versus placebo								
2 Sachs 1993	4.3	3.5	38	5.8	2.8	13	5.2%	-1.50 [-3.39 , 0.39]
2 Richmond 1994	3.16	4.84	45	4.09	4.87	19	2.7%	-0.93 [-3.54 , 1.68]
2 Puska 1995	3.8	3.3	41	4.3	2.9	31	9.0%	-0.50 [-1.94 , 0.94]
2 Bohadana 2000	3.1	3.2	50	2.7	2.6	45	13.7%	0.40 [-0.77 , 1.57]
Subtotal (95% CI)			**174**			**108**	**30.7%**	**-0.33 [-1.16 , 0.49]**
Heterogeneity: Tau² = 0.05; Chi² = 3.23, df = 3 (P = 0.36); I² = 7%								
Test for overall effect: Z = 0.80 (P = 0.42)								
8.2.3 Inhaler versus placebo								
2 Hjalmarson 1997	3.8	2.4	35	4.4	2.7	22	9.8%	-0.60 [-1.98 , 0.78]
Subtotal (95% CI)			**35**			**22**	**9.8%**	**-0.60 [-1.98 , 0.78]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.85 (P = 0.39)								
8.2.4 Sub-lingual tablet versus placebo								
2 Shiffman 2002B	4.66	3.78	106	5	4.64	46	8.1%	-0.34 [-1.86 , 1.18]
2 Shiffman 2002A	3.24	3.76	111	3.34	3.67	66	14.7%	-0.10 [-1.23 , 1.03]
Subtotal (95% CI)			**217**			**112**	**22.7%**	**-0.19 [-1.09 , 0.72]**
Heterogeneity: Tau² = 0.00; Chi² = 0.06, df = 1 (P = 0.80); I² = 0%								
Test for overall effect: Z = 0.40 (P = 0.69)								
8.2.5 Patch + varenicline versus placebo + varenicline								
2 Koegelenberg 2014	4.28	4.64	71	3.32	3.41	42	8.4%	0.96 [-0.53 , 2.45]
Subtotal (95% CI)			**71**			**42**	**8.4%**	**0.96 [-0.53 , 2.45]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.26 (P = 0.21)								
8.2.6 Lozenge versus placebo								
2 Xiao 2019 (1)	2.4	4.05	29	2.8	2.8	19	5.0%	-0.40 [-2.34 , 1.54]
2 Xiao 2019 (2)	2	2.75	46	1.2	2.56	43	15.3%	0.80 [-0.30 , 1.90]
Subtotal (95% CI)			**75**			**62**	**20.3%**	**0.48 [-0.57 , 1.52]**
Heterogeneity: Tau² = 0.07; Chi² = 1.11, df = 1 (P = 0.29); I² = 10%								
Test for overall effect: Z = 0.89 (P = 0.37)								
Total (95% CI)			**642**			**379**	**100.0%**	**-0.08 [-0.51 , 0.35]**
Heterogeneity: Tau² = 0.00; Chi² = 10.09, df = 11 (P = 0.52); I² = 0%								
Test for overall effect: Z = 0.36 (P = 0.72)								
Test for subgroup differences: Chi² = 4.85, df = 5 (P = 0.43), I² = 0%								



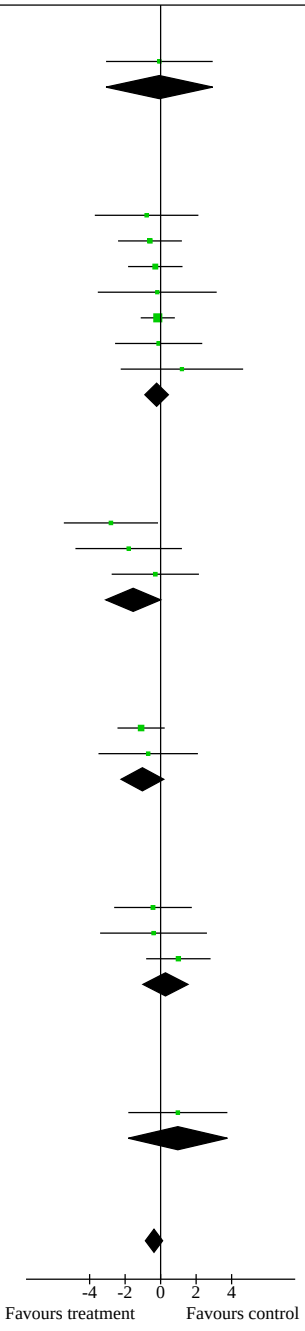
Footnotes

(1) High dependency stratum. N is those recorded as long-term abstinent, unclear whether weight was measured in all participants

(2) Low dependency stratum. N is those recorded as long-term abstinent, unclear whether weight was measured in all participants.

Analysis 8.3. Comparison 8: All types of NRT versus placebo for smoking cessation, Outcome 3: Mean weight change (kg) at 12 months

Study or Subgroup	Treatment Mean	Treatment SD	Treatment Total	Control Mean	Control SD	Control Total	Weight	Mean Difference IV, Random, 95% CI
8.3.1 Gum versus placebo								
1 Pirie 1992 (also Part 2)	4.5	4.95	34	4.57	4.94	15	2.6%	-0.07 [-3.07 , 2.93]
Subtotal (95% CI)			**34**			**15**	**2.6%**	**-0.07 [-3.07 , 2.93]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.05 (P = 0.96)								
8.3.2 Patch versus placebo								
2 Richmond 1994	5.25	5.09	34	6.04	4.97	17	2.8%	-0.79 [-3.71 , 2.13]
2 Puska 1995	5.9	3.9	36	6.5	3.3	26	7.3%	-0.60 [-2.40 , 1.20]
2 Bohadana 2000	4.8	3.7	39	5.1	2.7	28	10.0%	-0.30 [-1.83 , 1.23]
2 Oncken 2007	6.31	5.93	16	6.5	4.33	26	2.1%	-0.19 [-3.54 , 3.16]
2 CEASE 1999	4.9	3.7	404	5.06	3.8	70	25.5%	-0.16 [-1.12 , 0.80]
2 Stapleton 1995	5.4	4.69	76	5.51	4.8	18	3.9%	-0.11 [-2.57 , 2.35]
2 Tønnesen 1991	4.2	3.9	18	3	3	4	2.0%	1.20 [-2.25 , 4.65]
Subtotal (95% CI)			**623**			**189**	**53.5%**	**-0.23 [-0.89 , 0.44]**
Heterogeneity: Tau² = 0.00; Chi² = 1.00, df = 6 (P = 0.99); I² = 0%								
Test for overall effect: Z = 0.67 (P = 0.50)								
8.3.3 Intranasal spray versus placebo								
2 Sutherland 1992	3	4	13	5.8	2.9	14	3.3%	-2.80 [-5.45 , -0.15]
2 Blondal 1999	6.5	5.6	29	8.3	4.2	14	2.6%	-1.80 [-4.80 , 1.20]
2 Hjalmarson 1994	4.7	3.9	34	5	4.5	18	3.9%	-0.30 [-2.76 , 2.16]
Subtotal (95% CI)			**76**			**46**	**9.9%**	**-1.55 [-3.09 , -0.00]**
Heterogeneity: Tau² = 0.00; Chi² = 1.87, df = 2 (P = 0.39); I² = 0%								
Test for overall effect: Z = 1.96 (P = 0.05)								
8.3.4 Inhaler versus placebo								
2 Hjalmarson 1997	4.5	2.9	35	5.6	2.2	22	13.3%	-1.10 [-2.43 , 0.23]
2 Tønnesen 1993	4.4	5.3	24	5.1	2.8	9	3.0%	-0.70 [-3.50 , 2.10]
Subtotal (95% CI)			**59**			**31**	**16.3%**	**-1.03 [-2.23 , 0.17]**
Heterogeneity: Tau² = 0.00; Chi² = 0.06, df = 1 (P = 0.80); I² = 0%								
Test for overall effect: Z = 1.67 (P = 0.09)								
8.3.5 Sub-lingual tablet versus placebo								
2 Wallstrom 2000	5.37	3.5	45	5.8	6	37	4.9%	-0.43 [-2.62 , 1.76]
2 Shiffman 2002B	6.61	5.76	67	7.01	7.22	28	2.6%	-0.40 [-3.41 , 2.61]
2 Shiffman 2002A	4.8	5.52	82	3.8	4.62	44	7.1%	1.00 [-0.81 , 2.81]
Subtotal (95% CI)			**194**			**109**	**14.7%**	**0.27 [-0.99 , 1.54]**
Heterogeneity: Tau² = 0.00; Chi² = 1.21, df = 2 (P = 0.55); I² = 0%								
Test for overall effect: Z = 0.42 (P = 0.67)								
8.3.6 Lozenge versus placebo								
2 Piper 2009	4.15	5.68	57	3.18	6.62	30	3.0%	0.97 [-1.82 , 3.76]
Subtotal (95% CI)			**57**			**30**	**3.0%**	**0.97 [-1.82 , 3.76]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.68 (P = 0.50)								
Total (95% CI)			**1043**			**420**	**100.0%**	**-0.37 [-0.86 , 0.11]**
Heterogeneity: Tau² = 0.00; Chi² = 9.61, df = 16 (P = 0.89); I² = 0%								
Test for overall effect: Z = 1.51 (P = 0.13)								
Test for subgroup differences: Chi² = 5.47, df = 5 (P = 0.36), I² = 8.6%								

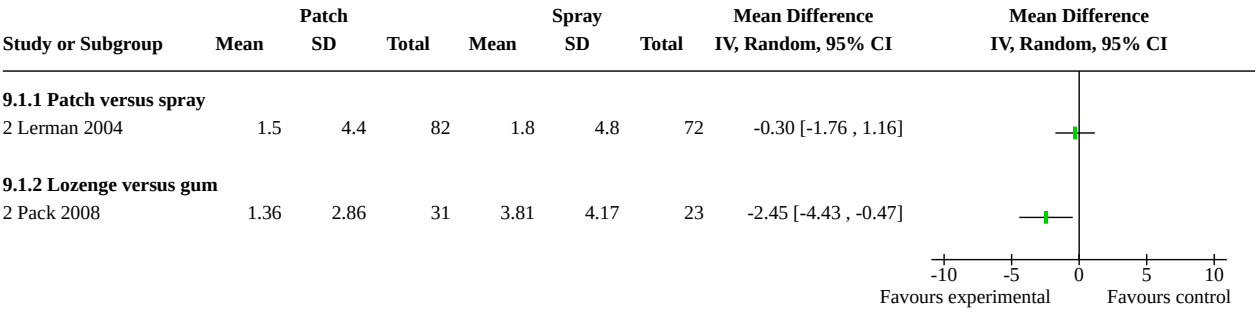


Comparison 9. Direct comparisons between NRT types for smoking cessation

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
9.1 Mean weight change (kg) at end of treatment: comparisons by type	2		Mean Difference (IV, Random, 95% CI)	Totals not selected
9.1.1 Patch versus spray	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
9.1.2 Lozenge versus gum	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
9.2 Mean weight change (kg) at 6 months: comparisons by type	2		Mean Difference (IV, Random, 95% CI)	Totals not selected
9.2.1 Lozenge versus gum	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
9.2.2 Patch versus spray	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
9.3 Mean weight change (kg) at 12 months: comparisons by type	2		Mean Difference (IV, Random, 95% CI)	Totals not selected
9.3.1 Loxenge versus gum	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
9.3.2 Lozenge versus patch	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
9.4 Mean weight change (kg) at 12 months: longer course vs. shorter	1	404	Mean Difference (IV, Random, 95% CI)	-0.24 [-0.97, 0.48]
9.4.1 22 weeks vs 8 weeks 25mg patch	1	222	Mean Difference (IV, Random, 95% CI)	-0.50 [-1.46, 0.46]
9.4.2 22 weeks vs 8 weeks 15mg patch	1	182	Mean Difference (IV, Random, 95% CI)	0.10 [-1.00, 1.20]
9.5 Mean weight change (kg) at end of treatment: dose response	4	1038	Mean Difference (IV, Random, 95% CI)	0.22 [-0.04, 0.48]
9.5.1 4mg vs 2mg gum	1	161	Mean Difference (IV, Random, 95% CI)	-0.10 [-0.61, 0.41]
9.5.2 22mg vs 11mg patch	1	15	Mean Difference (IV, Random, 95% CI)	-0.40 [-2.65, 1.85]
9.5.3 44mg vs 22mg patch	1	24	Mean Difference (IV, Random, 95% CI)	-0.20 [-1.99, 1.59]
9.5.4 25mg patch vs 15mg patch-8 week treatment course	1	497	Mean Difference (IV, Random, 95% CI)	0.40 [0.04, 0.76]
9.5.5 25mg patch vs 15mg patch-22 weeks treatment	1	299	Mean Difference (IV, Random, 95% CI)	0.20 [-0.57, 0.97]

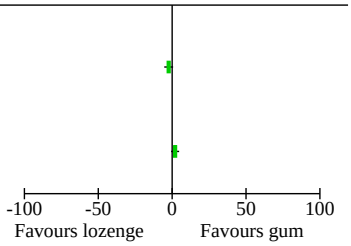
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
9.5.6 15x2mg gum vs 7x2mg gum	1	24	Mean Difference (IV, Random, 95% CI)	1.59 [-0.27, 3.45]
9.5.7 30x2mg gum vs 15x2mg gum	1	18	Mean Difference (IV, Random, 95% CI)	-0.27 [-1.83, 1.29]
9.6 Mean weight change (kg) at 12 months: dose response	3	554	Mean Difference (IV, Random, 95% CI)	0.27 [-0.41, 0.96]
9.6.1 22mg patch vs 11mg	1	7	Mean Difference (IV, Random, 95% CI)	-3.90 [-10.74, 2.94]
9.6.2 44mg patch vs 11mg	1	12	Mean Difference (IV, Random, 95% CI)	-2.20 [-10.12, 5.72]
9.6.3 25mg patch vs 15mg- 8 week treatment course	1	198	Mean Difference (IV, Random, 95% CI)	0.60 [-0.43, 1.63]
9.6.4 25mg patch vs 15mg- 22 weeks treatment course	1	206	Mean Difference (IV, Random, 95% CI)	0.00 [-1.04, 1.04]
9.6.5 Patch + lozenge vs lozenge	1	131	Mean Difference (IV, Random, 95% CI)	0.59 [-1.50, 2.68]

Analysis 9.1. Comparison 9: Direct comparisons between NRT types for smoking cessation, Outcome 1: Mean weight change (kg) at end of treatment: comparisons by type



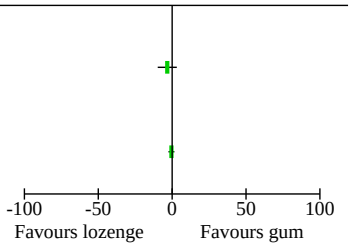
Analysis 9.2. Comparison 9: Direct comparisons between NRT types for smoking cessation, Outcome 2: Mean weight change (kg) at 6 months: comparisons by type

Study or Subgroup	lozenge Mean	lozenge SD	lozenge Total	gum Mean	gum SD	gum Total	Mean Difference IV, Random, 95% CI
9.2.1 Lozenge versus gum							
2 Pack 2008	3.95	5.26	22	6.3	4.4	18	-2.35 [-5.34 , 0.64]
9.2.2 Patch versus spray							
2 Lerman 2004	4.8	6	53	2.8	7.9	50	2.00 [-0.72 , 4.72]



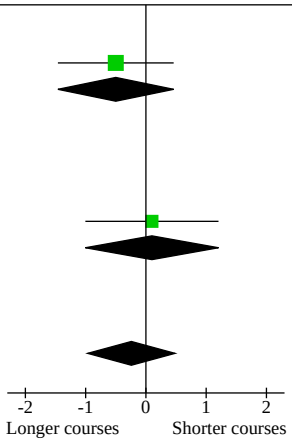
Analysis 9.3. Comparison 9: Direct comparisons between NRT types for smoking cessation, Outcome 3: Mean weight change (kg) at 12 months: comparisons by type

Study or Subgroup	Experimental Mean	Experimental SD	Experimental Total	Control Mean	Control SD	Control Total	Mean Difference IV, Random, 95% CI
9.3.1 Loxenge versus gum							
2 Pack 2008	2.86	12.43	19	6.17	6.17	14	-3.31 [-9.77 , 3.15]
9.3.2 Lozenge versus patch							
2 Piper 2009	4.15	5.68	57	4.64	5.43	60	-0.49 [-2.51 , 1.53]

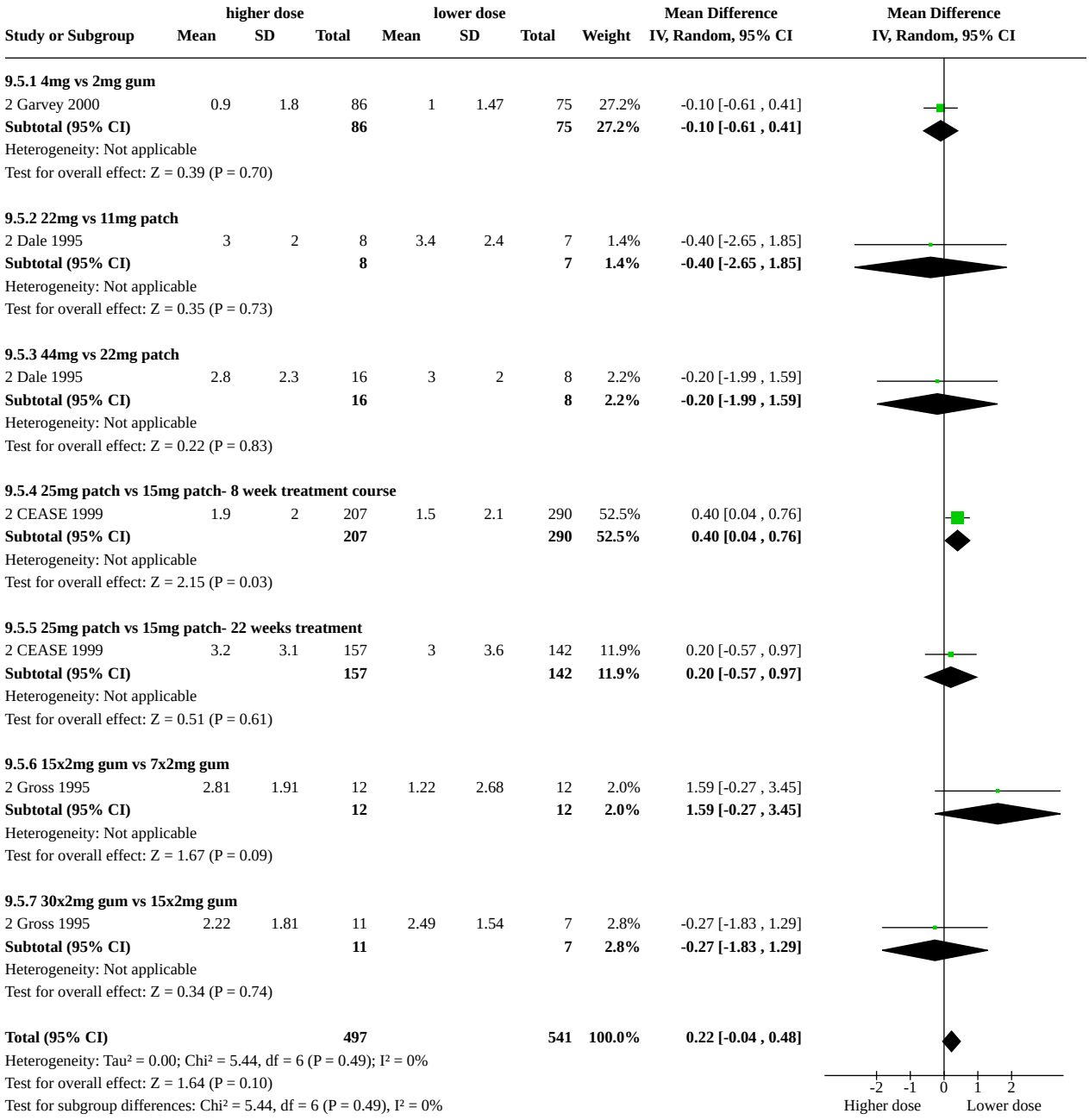


Analysis 9.4. Comparison 9: Direct comparisons between NRT types for smoking cessation, Outcome 4: Mean weight change (kg) at 12 months: longer course vs. shorter

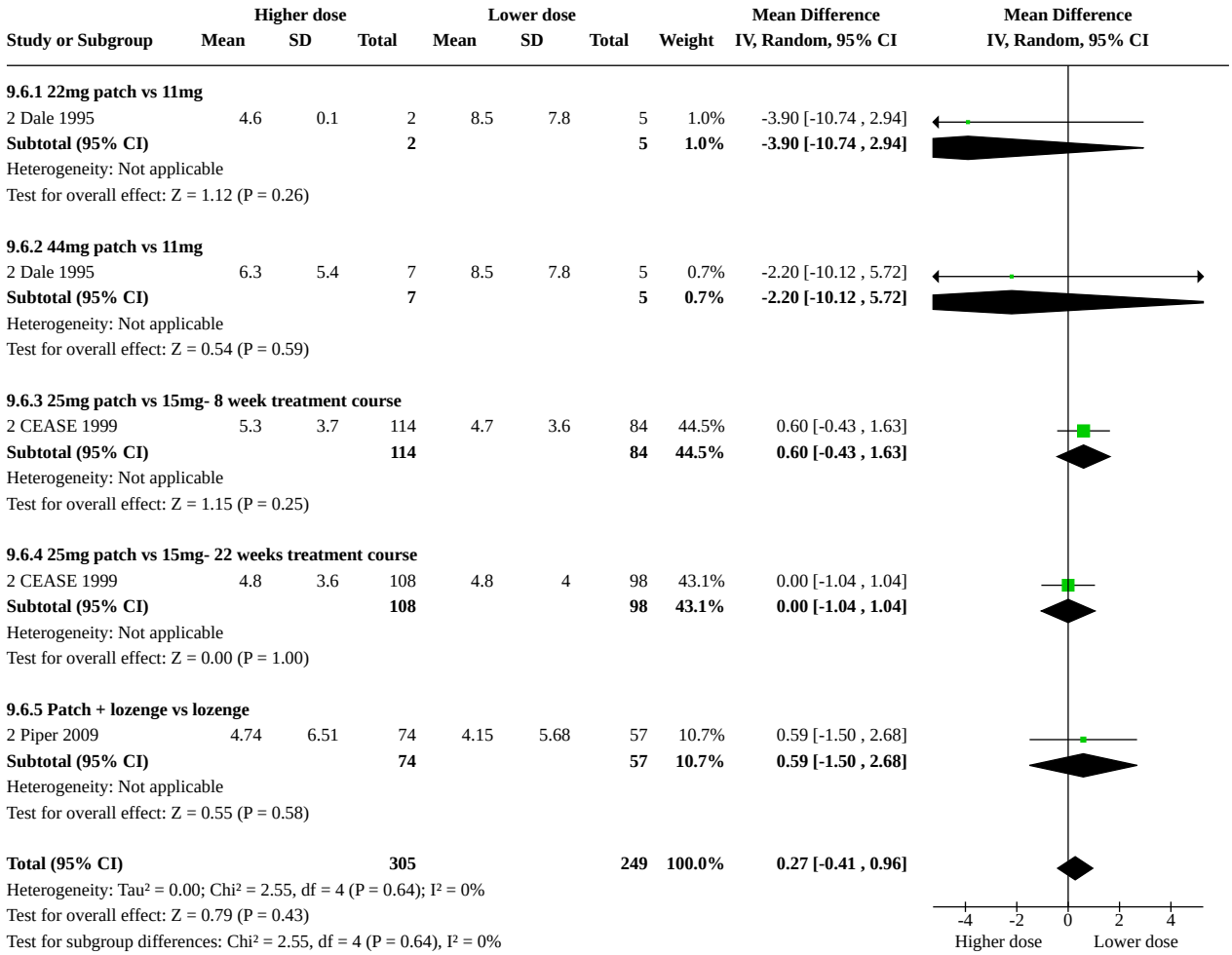
Study or Subgroup	Long course Mean	Long course SD	Long course Total	Short course Mean	Short course SD	Short course Total	Weight	Mean Difference IV, Random, 95% CI
9.4.1 22 weeks vs 8 weeks 25mg patch								
2 CEASE 1999	4.8	3.6	108	5.3	3.7	114	56.9%	-0.50 [-1.46 , 0.46]
Subtotal (95% CI)			**108**			**114**	**56.9%**	**-0.50 [-1.46 , 0.46]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.02 (P = 0.31)								
9.4.2 22 weeks vs 8 weeks 15mg patch								
2 CEASE 1999	4.8	4	98	4.7	3.6	84	43.1%	0.10 [-1.00 , 1.20]
Subtotal (95% CI)			**98**			**84**	**43.1%**	**0.10 [-1.00 , 1.20]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.18 (P = 0.86)								
Total (95% CI)			**206**			**198**	**100.0%**	**-0.24 [-0.97 , 0.48]**
Heterogeneity: Tau² = 0.00; Chi² = 0.65, df = 1 (P = 0.42); I² = 0%								
Test for overall effect: Z = 0.65 (P = 0.51)								
Test for subgroup differences: Chi² = 0.65, df = 1 (P = 0.42), I² = 0%								



Analysis 9.5. Comparison 9: Direct comparisons between NRT types for smoking cessation, Outcome 5: Mean weight change (kg) at end of treatment: dose response



Analysis 9.6. Comparison 9: Direct comparisons between NRT types for smoking cessation, Outcome 6: Mean weight change (kg) at 12 months: dose response



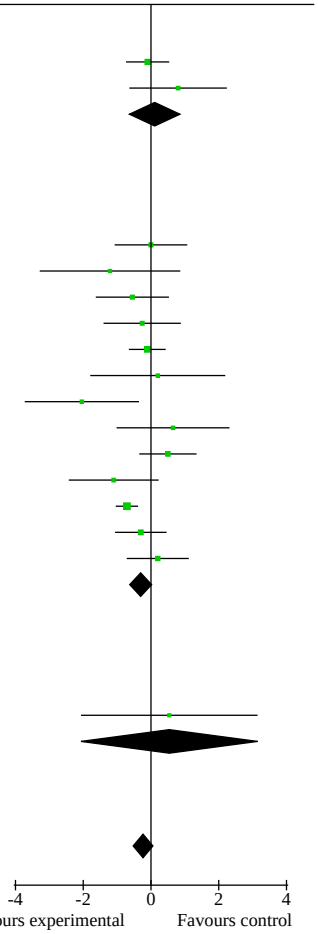
Comparison 10. Varenicline versus placebo for smoking cessation

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
10.1 Mean weight change (kg) at end of treatment	14	2566	Mean Difference (IV, Random, 95% CI)	-0.23 [-0.53, 0.06]
10.1.1 1mg versus placebo	2	230	Mean Difference (IV, Random, 95% CI)	0.11 [-0.64, 0.85]
10.1.2 2mg versus placebo	13	2308	Mean Difference (IV, Random, 95% CI)	-0.30 [-0.63, 0.02]
10.1.3 1mg + NRT versus placebo + NRT	1	28	Mean Difference (IV, Random, 95% CI)	0.54 [-2.07, 3.15]
10.2 Mean weight change (kg) at 6 months	3	384	Mean Difference (IV, Random, 95% CI)	-0.09 [-1.09, 0.90]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
10.3 Mean weight change (kg) at 12 months	3	237	Mean Difference (IV, Random, 95% CI)	1.05 [-0.58, 2.69]

Analysis 10.1. Comparison 10: Varenicline versus placebo for smoking cessation, Outcome 1: Mean weight change (kg) at end of treatment

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
10.1.1 1mg versus placebo								
2 Nakamura 2007	1.38	2.02	71	1.48	1.57	51	11.0%	-0.10 [-0.74 , 0.54]
2 Oncken 2006	2.94	3.65	94	2.14	2.36	14	3.5%	0.80 [-0.64 , 2.24]
Subtotal (95% CI)			**165**			**65**	**14.5%**	**0.11 [-0.64 , 0.85]**
Heterogeneity: Tau² = 0.08; Chi² = 1.26, df = 1 (P = 0.26); I² = 20%								
Test for overall effect: Z = 0.29 (P = 0.77)								
10.1.2 2mg versus placebo								
2 Bolliger 2011	2.2	2.4	150	2.2	2.5	24	5.6%	0.00 [-1.07 , 1.07]
2 Eisenberg 2016	1.42	5.79	75	2.63	5.86	51	1.8%	-1.21 [-3.28 , 0.86]
2 Gonzales 2006 (1)	2.37	2.76	155	2.92	3.94	61	5.5%	-0.55 [-1.63 , 0.53]
2 Jorenby 2006	2.89	2.94	151	3.15	4.11	60	5.1%	-0.26 [-1.40 , 0.88]
2 Nakamura 2007	1.37	1.55	84	1.48	1.57	51	12.9%	-0.11 [-0.65 , 0.43]
2 Niaura 2008	4	4.5	32	3.8	1.9	9	2.0%	0.20 [-1.79 , 2.19]
2 Nides 2006 (2)	1.96	2.3	24	4	2.28	10	2.6%	-2.04 [-3.73 , -0.35]
2 Oncken 2006	2.79	4.03	50	2.14	2.36	14	2.7%	0.65 [-1.02 , 2.32]
2 Rigotti 2010	2.2	2.7	161	1.7	2.6	48	7.9%	0.50 [-0.35 , 1.35]
2 Tashkin 2011	2.5	2.8	103	3.6	2.9	22	4.0%	-1.10 [-2.43 , 0.23]
2 Tonstad 2006	0.8	2.13	425	1.51	2.31	301	18.1%	-0.71 [-1.04 , -0.38]
2 Tsai 2008	1.29	2.42	75	1.59	1.7	40	9.0%	-0.30 [-1.06 , 0.46]
2 Wang 2009	1.58	2.75	82	1.38	2.51	50	7.1%	0.20 [-0.72 , 1.12]
Subtotal (95% CI)			**1567**			**741**	**84.3%**	**-0.30 [-0.63 , 0.02]**
Heterogeneity: Tau² = 0.10; Chi² = 18.37, df = 12 (P = 0.10); I² = 35%								
Test for overall effect: Z = 1.85 (P = 0.06)								
10.1.3 1mg + NRT versus placebo + NRT								
2 NCT02859142 2016	1.82	3.43	18	1.28	3.34	10	1.2%	0.54 [-2.07 , 3.15]
Subtotal (95% CI)			**18**			**10**	**1.2%**	**0.54 [-2.07 , 3.15]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.41 (P = 0.68)								
Total (95% CI)			**1750**			**816**	**100.0%**	**-0.23 [-0.53 , 0.06]**
Heterogeneity: Tau² = 0.09; Chi² = 22.07, df = 15 (P = 0.11); I² = 32%								
Test for overall effect: Z = 1.58 (P = 0.11)								
Test for subgroup differences: Chi² = 1.34, df = 2 (P = 0.51), I² = 0%								



Footnotes

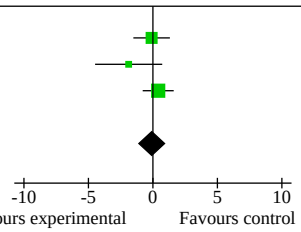
(1) 2 Gray 2019 could not be included, due to no abstainers in control arm. In intervention arm, n=16, mean 1.75 kg (SD 2.74)

(2) Third arm of 1 mg dose not included in this analysis to avoid double counting of control group. Weight change 2.14 kg, SD 2.28, n=14

Analysis 10.2. Comparison 10: Varenicline versus placebo for smoking cessation, Outcome 2: Mean weight change (kg) at 6 months

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
2 Bolliger 2011	2.9	3	152	3	3.4	25	38.1%	-0.10 [-1.52 , 1.32]
2 Eisenberg 2016 (1)	1.51	7.8	60	3.39	5.61	42	13.4%	-1.88 [-4.48 , 0.72]
2 Wang 2009	2.07	3.49	63	1.66	2.77	42	48.5%	0.41 [-0.79 , 1.61]
Total (95% CI)			**275**			**109**	**100.0%**	**-0.09 [-1.09 , 0.90]**

Heterogeneity: Tau² = 0.16; Chi² = 2.47, df = 2 (P = 0.29); I² = 19%
Test for overall effect: Z = 0.18 (P = 0.86)
Test for subgroup differences: Not applicable

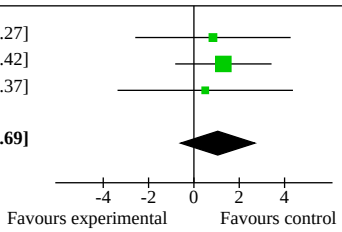


Footnotes
(1) 2 Gray 2019 could not be included, due to no abstainers in control arm. In intervention arm, n=4, mean 1.79 kg (SD 3.91)

Analysis 10.3. Comparison 10: Varenicline versus placebo for smoking cessation, Outcome 3: Mean weight change (kg) at 12 months

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
2 Eisenberg 2016	5.58	9.22	50	4.74	6.99	36	22.8%	0.84 [-2.59 , 4.27]
2 Rigotti 2010	5.2	4.4	67	3.9	4.8	26	59.3%	1.30 [-0.82 , 3.42]
2 Tashkin 2011	5.7	9.3	44	5.2	5.2	14	17.9%	0.50 [-3.37 , 4.37]
Total (95% CI)			**161**			**76**	**100.0%**	**1.05 [-0.58 , 2.69]**

Heterogeneity: Tau² = 0.00; Chi² = 0.15, df = 2 (P = 0.93); I² = 0%
Test for overall effect: Z = 1.26 (P = 0.21)
Test for subgroup differences: Not applicable



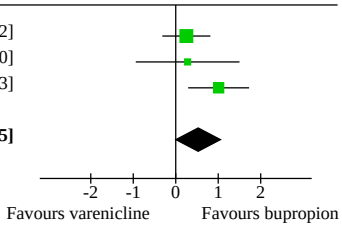
Comparison 11. Varenicline versus bupropion

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
11.1 Mean weight change (kg) at end of treatment	3	598	Mean Difference (IV, Random, 95% CI)	0.53 [0.00, 1.05]

Analysis 11.1. Comparison 11: Varenicline versus bupropion, Outcome 1: Mean weight change (kg) at end of treatment

Study or Subgroup	Varenicline Mean	SD	Total	Bupropion Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
2 Gonzales 2006	2.37	2.76	155	2.12	1.8	95	48.3%	0.25 [-0.32 , 0.82]
2 Nides 2006	1.96	2.3	24	1.68	1.92	22	15.8%	0.28 [-0.94 , 1.50]
2 Jorenby 2006	2.89	2.94	151	1.88	3.4	151	36.0%	1.01 [0.29 , 1.73]
Total (95% CI)			**330**			**268**	**100.0%**	**0.53 [0.00 , 1.05]**

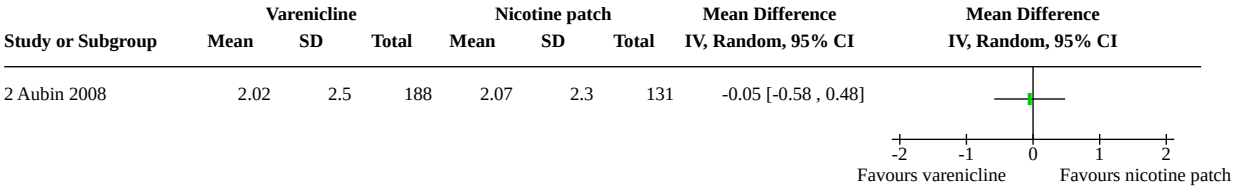
Heterogeneity: Tau² = 0.06; Chi² = 2.82, df = 2 (P = 0.24); I² = 29%
Test for overall effect: Z = 1.98 (P = 0.05)
Test for subgroup differences: Not applicable



Comparison 12. Varenicline versus NRT

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
12.1 Mean weight change (kg) at end of treatment	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

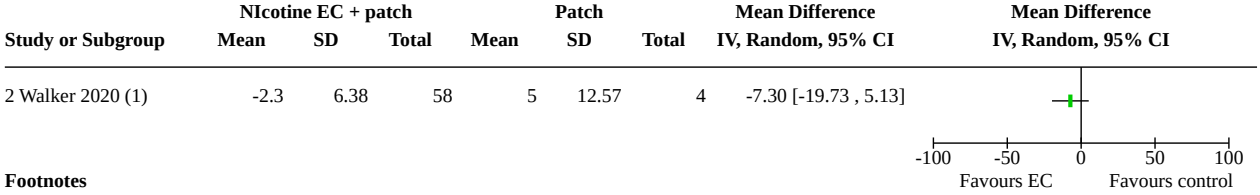
Analysis 12.1. Comparison 12: Varenicline versus NRT, Outcome 1: Mean weight change (kg) at end of treatment



Comparison 13. Nicotine EC + patch vs patch

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
13.1 Weight (kg) at EOT	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 13.1. Comparison 13: Nicotine EC + patch vs patch, Outcome 1: Weight (kg) at EOT



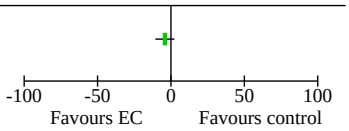
Footnotes
(1) EOT data is self-report only

Comparison 14. Nicotine EC + patch vs nicotine-free EC + patch

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
14.1 Weight (kg) at EOT	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
14.2 Weight (kg) at 6 months	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Analysis 14.1. Comparison 14: Nicotine EC + patch vs nicotine-free EC + patch, Outcome 1: Weight (kg) at EOT

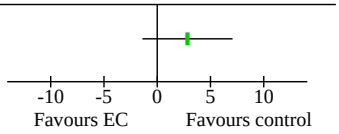
Study or Subgroup	NIcotine EC + patch Mean	SD	Total	Non-nicotine EC + patch Mean	SD	Total	Mean Difference IV, Random, 95% CI
2 Walker 2020 (1)	-2.3	6.38	58	1.83	16.96	28	-4.13 [-10.62 , 2.36]



Footnotes
(1) EOT data is self-report only

Analysis 14.2. Comparison 14: Nicotine EC + patch vs nicotine-free EC + patch, Outcome 2: Weight (kg) at 6 months

Study or Subgroup	NIcotine EC + patch Mean	SD	Total	Non-nicotine EC + patch Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
2 Walker 2020	1.01	5.47	21	-1.83	5.96	11	2.84 [-1.39 , 7.07]

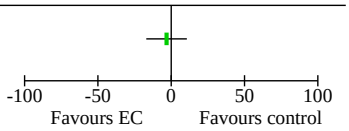


Comparison 15. Nicotine-free EC + patch vs patch

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
15.1 Weight (kg) at EOT	1		Mean Difference (IV, Random, 95% CI)	Totals not selected
15.2 Weight (kg) at 6 months	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Analysis 15.1. Comparison 15: Nicotine-free EC + patch vs patch, Outcome 1: Weight (kg) at EOT

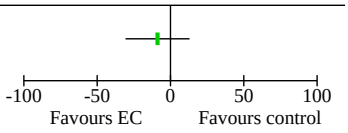
Study or Subgroup	NIcotine-free EC + patch Mean	SD	Total	Patch Mean	SD	Total	Mean Difference IV, Random, 95% CI
2 Walker 2020 (1)	1.83	16.96	28	5	12.57	4	-3.17 [-17.00 , 10.66]



Footnotes
(1) EOT data is self-report only

Analysis 15.2. Comparison 15: Nicotine-free EC + patch vs patch, Outcome 2: Weight (kg) at 6 months

Study or Subgroup	Non-nIcotine EC + patch Mean	SD	Total	Patch Mean	SD	Total	Mean Difference IV, Fixed, 95% CI
2 Walker 2020	-1.83	5.96	11	7	15.56	2	-8.83 [-30.68 , 13.02]

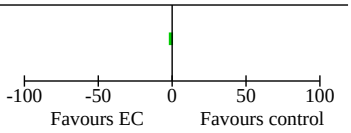


Comparison 16. Nicotine EC versus varenicline

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
16.1 Weight change (kg) at EOT	1		Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 16.1. Comparison 16: Nicotine EC versus varenicline, Outcome 1: Weight change (kg) at EOT

Study or Subgroup	Nicotine EC Mean	Nicotine EC SD	Nicotine EC Total	Varenicline Mean	Varenicline SD	Varenicline Total	Mean Difference IV, Random, 95% CI
2 Ioakeimidis 2018	1.1	1.79	10	1.93	1.34	16	-0.83 [-2.12 , 0.46]



WHAT'S NEW

Date	Event	Description
8 October 2021	Amended	Correction of PLS, to remove duplicated information

HISTORY

Protocol first published: Issue 4, 2006
Review first published: Issue 1, 2009

Date	Event	Description
20 April 2021	New citation required and conclusions have changed	Updated with 47 new included studies providing data on new comparisons and increasing certainty in effects of smoking cessation interventions on weight change.
20 April 2021	New search has been performed	Updated with 48 new included studies. Latest search 16 October 2020.
23 November 2011	New citation required but conclusions have not changed	Change of name for one author (Amanda Parsons is now Amanda Farley), one new author added (DL), and two authors of previous version removed (see Contributions of Authors).
23 November 2011	New search has been performed	Twelve additional studies added. Conclusions largely unchanged.
24 April 2008	Amended	Converted to new review format.
14 July 2006	New citation required and major changes	Substantive amendment

CONTRIBUTIONS OF AUTHORS

2021 update (includes 2016 searches and data extraction): All authors contributed to screening or data extraction or both. Analysis and write-up was led by JHB and AT. All authors reviewed and commented on the final manuscript.

DECLARATIONS OF INTEREST

JHB: co-applicant on an award from the Cochrane Review Support Programme. JHB also writes and publishes frequently on the evidence for smoking cessation interventions, and to a lesser extent about evidence on weight management. None of these represent a conflict with what is covered in this review.

AT: None

AF: co-applicant on a researcher-led grant from Ethicon (Johnson and Johnson).

PH: research grants, last held in 2015 from Pfizer (funds were received by the institution); Recieved payment for assessing grant applications (GRAND initiative) and attending global advisory board meeting (last attended in 2017); provides invited commentaries, usually concerning an article on e-cigarettes for journals (The Lancet, Tobacco Control, Lancet Respiratory and Addiction); was involved in the conduct of a study that was eligible for inclusion in this work which was funded by NIHR.

DL: published a press release following publication of a research report; was involved in the conduct studies that were eligible for inclusion in this work: The DeMist Trial: UKCTCS, VLCD provided by Lipotrim (2010) and The SWISSS Trial: NIHR-SPCR, Slimming Word vouchers for intervention provide by Slimming World (2013)

LLJ: None

LK: None

LH: None

AH: None

MS: None

PA: was involved in the conduct of a study that was eligible for inclusion in this work funded by the School for Primary Care Research.

PA and AF (nee Parsons) are also authors of a study included in this review testing the effect of St John's wort and chromium supplements on smoking cessation and post-cessation weight gain. The trial was funded by Cancer Research UK and the supplements were bought from the manufacturer. Paul Aveyard has done consultancy work for pharmaceutical and biotechnology companies that has led to payments to him and his institution. This includes work for companies providing smoking cessation medication, including McNeil, Xenova and Pfizer.

SOURCES OF SUPPORT

Internal sources

- University of Birmingham, UK

  Paid the salary of Amanda Parsons, Jennie Inglis and Paul Aveyard

  Mujahed Sharim studied for a masters in public health at the University and completed part of the work as part of his masters project
- UKCTCS, UK

  Paid the doctoral stipend of Deborah Lycett and contributed to the salaries of Amanda Parsons and Paul Aveyard. The UK Centre for Tobacco Control Studies is a UKCRC Public Health Research: Centre of Excellence. Funding from British Heart Foundation, Cancer Research UK, Economic and Social Research Council, Medical Research Council, and the National Institute of Health Research, under the auspices of the UK Clinical Research Collaboration, is gratefully acknowledged.
- Queen Mary's University of London, UK

  Paid the salary of Peter Hajek
- National Institute of Health Research, UK

  Contributed to the salary of Paul Aveyard
- NIHR Oxford Biomedical Research Centre, UK

  Paid the salary of Laura Kudlek

External sources

- No sources of support provided

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

In the 2021 version, we made the following changes:

- We changed from fixed- to random-effects models for our meta-analyses, in accordance with updated guidance from the Cochrane Tobacco Addiction Group;
- We added the review of electronic cigarettes for smoking cessation to Part 2 and removed the review of cannabinoid type 1 receptors, as these are not considered a frontline stop-smoking pharmacotherapy;
- We updated risk of bias assessments in accordance with updated guidance from the Cochrane Tobacco Addiction Group;
- We extracted and assessed data on adverse and serious adverse events for Part 1 studies of pharmacotherapies;
- We added summary of findings tables according to Cochrane guidance;
- We conducted sensitivity analyses removing studies at high risk of bias.

All of these changes were agreed with the Cochrane Tobacco Addiction Group prior to starting the review update.

INDEX TERMS

Medical Subject Headings (MeSH)

Antidepressive Agents [therapeutic use]; Benzazepines [administration & dosage]; Exercise; Nicotine [administration & dosage]; Nicotinic Agonists [administration & dosage]; Piperidines [administration & dosage]; Pyrazoles [administration & dosage]; Quinoxalines [administration & dosage]; Randomized Controlled Trials as Topic; Smoking Cessation [*methods]; *Weight Gain [drug effects]

MeSH check words

Female; Humans; Male