Interventions for preventing weight gain after smoking cessation (Review)

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[Intervention Review]

Interventions for preventing weight gain after smoking cessation

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ABSTRACT

Background

Most people who stop smoking gain weight, on average about 7kg in the long term. There are some interventions that have been specifically designed to tackle smoking cessation whilst also limiting weight gain. Many smoking cessation pharmacotherapies and other interventions may also limit weight gain.

Objectives

This review is divided into two parts.

(1) Interventions designed specifically to aid smoking cessation and limit post-cessation weight gain

(2) Interventions designed to aid smoking cessation that may also plausibly have an effect on weight

Search methods

Part 1: We searched the Cochrane Tobacco Addiction Group's Specialized Register which includes trials indexed in MEDLINE, EMBASE, SciSearch and PsycINFO, and other reviews and conference abstracts.

Part 2: We searched the included studies of Cochrane smoking cessation reviews of nicotine replacement therapy, antidepressants, nicotine receptor partial agonists, cannabinoid type 1 receptor antagonists (rimonabant), and exercise interventions, published in Issue 4, 2008 of The Cochrane Library.

Selection criteria

Part 1: We included trials of interventions designed specifically to address both smoking cessation and post-cessation weight gain that had measured weight at any follow-up point and/or smoking six months or more after quitting.

Part 2: We included trials from the selected Cochrane reviews that could plausibly modify post-cessation weight gain if they had reported weight gain by trial arm at end of treatment or later.

Data collection and analysis

We extracted data in duplicate on smoking and weight for part 1 trials, and on weight only for part 2. Abstinence from smoking is expressed as a risk ratio (RR), using the most rigorous definition of abstinence available in each trial, and biochemically validated rates if available. The outcome is expressed as the difference in weight change between trial arms from baseline. Where appropriate, we performed meta-analysis using the Mantel-Haenszel method for smoking and inverse variance for weight using a fixed-effect model.

Main results

We found evidence that pharmacological interventions aimed at reducing post-cessation weight gain resulted in a significant reduction in weight gain at the end of treatment (dexfenfluramine (-2.50kg [-2.98kg to -2.02kg], fluoxetine (-0.80kg [-1.27kg to -0.33kg], phenylpropanolamine (PPA) (-0.50kg [-0.80kg to -0.20kg], naltrexone (-0.76kg [-1.51kg to -0.01kg])). No evidence of maintenance of the treatment effect was found at six or 12 months.

Among the behavioural interventions, only weight control advice was associated with no reduction in weight gain and with a possible reduction in abstinence. Individualized programmes were associated with reduced weight gain at end of treatment and at 12 months (-2.58kg [-5.11kg to -0.05kg]), and with no effect on abstinence (RR 0.74 [0.39 to 1.43]). Very low calorie diets (-1.30kg (-3.49kg to 0.89kg] at 12 months) and cognitive behavioural therapy (CBT) (-5.20kg (-9.28kg to -1.12kg] at 12 months) were both associated with improved abstinence and reduced weight gain at end of treatment and at long-term follow up.

Both bupropion (300mg/day) and fluoxetine (30mg and 60mg/day combined) were found to limit post-cessation weight gain at the end of treatment (-0.76kg [-1.17kg to -0.35kg] I^2=48%) and -1.30kg [-1.91kg to -0.69kg]) respectively. There was no evidence that the weight reducing effect of bupropion was dose-dependent. The effect of bupropion at one year was smaller and confidence intervals included no effect (-0.38kg [-2.001kg to 1.24kg]).

We found no evidence that exercise interventions significantly reduced post-cessation weight gain at end of treatment but evidence for an effect at 12 months (-2.07kg [-3.78kg, -0.36kg]).

Treatment with NRT resulted in attenuation of post-cessation weight gain (-0.45kg [-0.70kg, -0.20kg]) at the end of treatment, with no evidence that the effect differed for different forms of NRT. The estimated weight gain reduction was similar at 12 months (-0.42kg [-0.92kg, 0.08kg]) but the confidence intervals included no effect.

There were no relevant data on the effect of rimonabant on weight gain.

We found no evidence that varenicline significantly reduced post-cessation weight gain at end of treatment and no follow-up data are currently available. One study randomizing successful quitters to 12 more weeks of active treatment showed weight to be reduced by 0.71kg (-1.04kg to -0.38kg). In three studies, participants taking bupropion gained significantly less weight at the end of treatment than those on varenicline (-0.51kg [-0.93kg to -0.09kg]).

Authors' conclusions

Behavioual interventions of general advice only are not effective and may reduce abstinence.

Individualized interventions, very low calorie diets, and CBT may be effective and not reduce abstinence.

Exercise interventions are not associated with reduced weight gain at end of treatment, but may be associated with worthwhile reductions in weight gain in the long term,

Bupropion, fluoxetine, nicotine replacement therapy, and probably varenicline all reduced weight gain while being used. Although this effect was not maintained one year after quitting for bupropion, fluoxetine, and nicotine replacement, the evidence is insufficient to exclude a modest long-term effect.

The data are not sufficient to make strong clinical recommendations for effective programmes.

PLAIN LANGUAGE SUMMARY

Interventions for preventing weight gain after smoking cessation

Most people who give up smoking put on weight. This is of concern to many smokers and often puts people off trying to quit or leads to people going back to smoking after managing to quit. A variety of drug and behavioural treatments have been tested to see if they

increase the chances of quitting whilst also limiting weight gain. Among the drug treatments, naltrexone showed the most promise, but there was no evidence of its effects on weight once drug treatment stopped or in the long term. Behavioural treatments were more successful when tailored to the individual, with very low calorie diets and cognitive behavioural therapy showing the most promise in limiting weight gain. Both treatments increased success in long-term quitting, but the long-term effect on weight was only found with cognitive behavioural therapy. There was not enough evidence to judge whether very low calorie diets helped people maintain their weight reduction long-term. Interventions to help smokers to quit may also have an effect on weight gain after quitting. Bupropion, fluoxetine and nicotine replacement therapy were all found to limit weight gain during treatment. However the effects on limiting weight gain were smaller once treatment had stopped, and there was not enough evidence to be sure that these effects persisted in the long term. Varenicline may also reduce weight gain during treatment, but there was not enough evidence to confirm this or to measure its long-term effect on weight. There was some evidence to suggest that exercise reduced long-term weight gain after quitting, but more studies are needed to confirm this effect.

BACKGROUND

Although smoking cessation is associated with substantial health benefits, it is usually accompanied by weight gain (Klesges 1997). In the USA it is estimated that 80% of people who quit smoking gain weight (USDHHS 1990). Studies have found that on average women gain more weight than men. Among people who sustained quitting for five years, O'Hara 1998 found that women gained 5.2 kg in year one and a mean of 3.4 kg in years one to five, while men gained a mean of 4.9 kg in year one and a mean of 2.6 kg in years one to five. A large cohort study showed that 13.4% of women compared with 9.8% of men had a weight gain greater than 13kg (Williamson 1991). This weight gain can have health consequences, with one study showing the incidence of diabetes to be higher in smokers who quit smoking than in those who continue to smoke. This effect appeared to be attributable to weight gain (Davey Smith 2005). Weight gain also reduces some of the benefits of quitting smoking on lung function (Chinn 2005).

There is widespread concern among smokers 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).

Some interventions have been developed to promote smoking cessation and simultaneously control weight gain in challenging populations, such as weight-concerned smokers. They include behavioural interventions, such as exercise and calorie restriction or eating advice. Dietary interventions might serve to encourage reluctant quitters to try to stop smoking if they can be reassured that weight gain might be limited. However, it is possible that such interventions might also risk undermining the success of the quit attempt (1 Hall 1992). There is evidence that hunger and cigarette cravings are related, and that hunger can undermine quit efforts and increase urges to smoke (West 2001). This suggests that interventions that limit dietary intake may potentially reduce smoking cessation success. The adage that smokers should stop smoking first and then tackle weight gain has become common in smoking cessation clinics.

There are a range of other treatments for smoking cessation that have been developed without reference to the risk of weight gain. Some of these, such as nicotine replacement therapy, 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 2008). The effects of these medications on weight gain will therefore be included in this review.

OBJECTIVES

To review the evidence from two kinds of trials:

Primary objectives:

(i) Part 1 - The effects of interventions specifically designed to limit weight gain on two outcomes: weight gain at end of treatment, at six and 12 months, and smoking cessation at six and 12 months.

(ii) Part 2 - The effects of antidepressants, exercise, nicotine replacement therapy, varenicline and rimonabant on weight gain at end of treatment, and at six and 12 months.

For (i) and (ii), weight gain is examined only in those biochemically validated as being abstinent from smoking.

Secondary objective:

(iii) To examine evidence of interactions between body characteristics, gender, and psychological variables such as fear of weight gain on (a) smoking cessation and (b) weight gain.

METHODS

Criteria for considering studies for this review

Types of studies

Randomized controlled trials

Types of participants

Adult smokers attempting to quit smoking.

Types of interventions

Part 1 - Interventions that are designed specifically to limit weight gain during and after smoking cessation.
Part 2 - Pharmacological and behavioural 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, varenicline and rimonabant.

Types of outcome measures

There are two primary outcome measures:
(i) Smoking status at least six months from the quit date for trials specifically designed to limit post-cessation weight gain only.
(ii) Mean (SD) change in body weight (kg) from baseline at the end of treatment and at least six months from the quit date in validated abstainers.
For studies designed to limit weight gain that are not included in other Cochrane reviews, we will fully examine both outcomes. For studies of interventions that might plausibly influence weight gain and where the effects of these interventions on quitting are already described in other Cochrane reviews, we will briefly report the smoking cessation outcomes and then assess the weight change outcomes in full.

Search methods for identification of studies

Part 1 - We searched the Cochrane Tobacco Addiction Group's Specialized Register, 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, bodyweight, weight-changes. The specialized register includes trials indexed in MEDLINE, EMBASE, PsycINFO and Web of Science, together with hand searching of specialist journals, conference proceedings, online registers of controlled trials and reference lists of previous trials and overviews. In addition, we performed citation searches of studies included in part 1 to exhaust possibilities of finding published weight data. The latest search was conducted in September 2008.
Part 2 - We searched the following Cochrane reviews: Antidepressants for smoking cessation, Exercise interventions for smoking cessation, Nicotine replacement therapy for smoking cessation, Cannabinoid type 1 receptor antagonists (rimonabant) for smoking cessation and Nicotine receptor partial agonists for smoking cessation, all published in Issue 4 2008 of The Cochrane Library. All references listed as included studies were searched except for the nicotine receptor partial agonists for smoking cessation review, where we were only interested in trials of varenicline.

Data collection and analysis

Two people independently identified and extracted data from studies that fulfilled the inclusion criteria. Any discrepancies were discussed and resolved. Papers published in a foreign language were translated into English. Where weight gain had been measured but not reported at all or in full, we contacted authors for clarification. If we were unable to successfully contact an author, studies were excluded from the review.
Part 1 - We extracted data on baseline characteristics, the intervention, smoking and weight. Where possible we extracted smoking outcomes as continuous abstinence, but we accepted less strict definitions if continuous abstinence was not available. For smoking abstinence estimates, participants lost to follow up were counted as smokers and therefore all randomized participants were included in the denominator. Abstinence rates and their corresponding risk ratio (95% Confidence Interval) were reported at six and 12 months follow up.
We used the absolute mean (standard deviation (SD)) difference in body weight (kg) from baseline to follow up by trial arm as the summary statistic for the treatment effect on weight. Mean weight change was estimated only in those abstinent from smoking. Smoking abstinence was variously defined across the studies, and we have recorded this in the Characteristics of included studies table. We used the difference between mean weight change in the treatment and control groups at the end of treatment, and at six and 12 months to analyse the effects of the weight gain prevention interventions. When studies reported mean differences in pounds we converted them to kilograms.
In some studies mean (SD) weight change by trial arm was not reported in full. When standard deviations for the changes in body weight were not reported, we used various methods to calculate them, mainly from confidence intervals (CI) and standard errors (SE) using standard formulae. For studies with large sample size, we used the following formula:

SD = $\sqrt{}$N x (upper limit - lower limit) /SE wide
For studies with 95% confidence intervals for difference in means we divided by 3.92 SEs wide. If sample size was less than 60, the 3.92 SEs 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*$\sqrt{}$(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. SDs were calculated by using an estimated correlation coefficient of 0.99, which describes how similar the baseline and finishing weights were across participants. This was estimated in abstinent smokers from raw data that we have collected from an unrelated trial of St John's Wort for smoking cessation 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) = $\sqrt{}$((SD (B)^2 + SD (F)^2) - (2 X r X SD (B) X SD (F)))
Part 2 - As data on the participants and interventions for included studies of the Cochrane reviews considered in the second part of this review have already been extracted and published by the Tobacco Addiction Cochrane Review Group, we only extracted data on our primary outcome, namely weight. Weight data were extracted using the approach described for part 1.
In some studies in parts 1 and 2, more than one trial arm had been compared with a control arm. We combined outcome data where appropriate, to create one comparison intervention arm. For the smoking outcome we added together the numerator and denominator from each arm. Weight outcomes from more than one trial arm were calculated using the following formulas:
Mean weight change = ((Mean1*n1)+(Mean2*n2))/(n1+n2)
Standard deviation= $\sqrt{}$Var$_{12}$
Var$_{12}$ = [Sumsq$_{12}$ - (n1+n2)*Mean weight change^2] / (n1+n2-1)
Sumsq$_{12}$=[(n1-1)*SD1^2]+[n1*Mean1] + [(n2-1)*SD2^2]+[n2*Mean2]
We rated the potential for bias in the included trials on methods of randomization and allocation concealment, using methods described in the Cochrane Handbook for Systematic Reviews of Interventions (Handbook 2008).
Smoking cessation outcome data are given on the number of quitters in the treatment and control groups divided by the total number of participants receiving treatment and reported as a risk ratio with 95% confidence intervals. A risk ratio greater than 1.0 indicates that more people quit in the treatment group than in the control group. Therefore, effective interventions appear to the right of the axis on the meta-analysis graph. We used the Mantel-Haenszel fixed-effect method for smoking cessation outcomes where appropriate. Weight change outcome data are given as the difference in mean weight change between the intervention and control arms and estimates were combined using the inverse variance method where appropriate. Effective weight change interventions appear to the left of the axis on the relevant meta-analysis graph, since less change is the desired outcome. We used the I² statistic to investigate statistical heterogeneity, given by the formula [(Q-df)/Q] x 100%, where Q is the chi-squared statistic and df is its degrees of freedom (Higgins 2003).

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies; Characteristics of studies awaiting classification.

Part 1: Interventions specifically designed to address post-cessation weight gain

We found 11 trials which matched our inclusion criteria for the first part of the review. All studies recruited community volunteers who wanted to stop smoking and avoid weight gain. Seven studies recruited women only (1 Cooper 2005; 1 Copeland 2006; 1 Danielsson 1999; 1 Klesges 1990; 1 Perkins 2001; 1 Pirie 1992; 1 Spring 1995) and the remainder included smokers of both sexes (1 Hall 1992; 1 Klesges 1995; 1 O'Malley 2006; 1 Norregaard 1996). Participants averaged 20 to 25 cigarettes per day, with the exception of four studies with a slightly higher average of 26 to 32 (Hall 1992; 1 O'Malley 2006; 1 Pirie 1992; 1 Spring 1995). Mean baseline weight and/or body mass index (BMI) were reported in all but two studies (1 Klesges 1990; 1 Klesges 1995) and ranged from 64 to 73kg/BMI 20 to 29.
Six studies compared the effects of pharmacological interventions to placebo for smoking cessation and post-cessation weight change. Pharmacological interventions included: Phenylpropanolamine gum 8.33 mg, 16 pieces a day for eight weeks (1 Cooper 2005), nine pieces a day for two weeks (1 Klesges 1990) and up to 10 pieces a day for four weeks (1 Klesges 1995); Ephedrine 20 mg plus 200 mg caffeine three times a day for 12 weeks (1 Norregaard 1996); Naltrexone 100, 50 and 25 mg a day for six weeks (1 O'Malley 2006); Dexfenfluramine 30 mg a day for 12 weeks (1 Spring 1995). Fluoxetine 40 mg a day (1 Spring

1995) was also included in this part of the review although the effects of fluoxetine are addressed in the second part of the review. This study tested specifically for its effect on weight in smokers who are weight-concerned, and has not been included in the antidepressant review (Hughes 2007).

Four studies assessed the effects of multicomponent behavioural smoking and weight-targeted programmes. In two studies the intervention consisted of advice on weight management without forming individual plans (Hall 1992; 1 Pirie 1992). Two studies assessed individualized weight management plans and incorporated individual feedback on progress (Hall 1992; 1 Perkins 2001). One study provided general dietary advice to all participants but the intervention group also received four weeks of an intermittent very low calorie diet provided free of charge at a specialist obesity research unit (1 Danielsson 1999). The duration, number and format of multicomponent weight-targeted programme sessions varied. In two of the four studies, participants were also given an exercise programme (1 Hall 1992; 1 Pirie 1992). As well as a weight programme arm, 1 Perkins 2001 tested the effect of cognitive behavioural therapy (CBT) to promote acceptance of modest weight gain. Finally, 1 Copeland 2006 compared the effect of group and individual relapse prevention follow-up sessions on smoking cessation and weight change after a two-week smoking cessation programme. As there was no control group without the weight advice, the study is not included in our meta-analyses.

Smoking cessation therapy was provided for all participants in all studies of pharmacological and behavioural interventions. The number, format and duration of sessions of the behavioural therapy varied from brief individual advice for two weeks to hour-long group sessions conducted over 16 weeks, but the content was similar and included the following components: cognitive behavioural skills such as anticipating and planning for high-risk situations, coping skills, relapse prevention and the benefits of quitting smoking. In three studies all participants were also supplied with nicotine replacement therapy (NRT) (1 Copeland 2006; 1 Danielsson 1999;1 O'Malley 2006) and in 1 Pirie 1992 two of the four comparison arms received NRT.

Seven studies (1 Cooper 2005; 1 Copeland 2006; 1 Danielsson 1999; Hall 1992; 1 Norregaard 1996; 1 Perkins 2001; 1 Pirie 1992) reported smoking as an outcome at either six or 12 months, or both. Smoking was recorded either as point prevalence (1 Cooper 2005; Hall 1992) or as prolonged or continuous abstinence (the remaining ten studies). Continuous abstinence was defined as biochemically validated, with not one single puff since the quit date. Definitions of prolonged abstinence varied, but mainly allowed for a grace period during the first week(s) after quit day or for small lapses that did not lead to full relapse. All twelve studies reported weight gain as an outcome in abstainers at end of treatment, and some reported weight at either six or 12 months, or both.

Part 2: Interventions not specifically designed to address post-cessation weight gain

For the second part of our review, we found 49 studies from the 'parent' Cochrane reviews of smoking cessation which had extractable data and matched our inclusion criteria. These were antidepressants (Hughes 2007: 9/54 studies, three of which also appear in varenicline list), exercise (Ussher 2008: 4/11 studies), nicotine replacement therapy (NRT) (Stead 2008: 28/133 studies), and varenicline (Cahill 2008: 8/9 studies). We were unable to obtain published or unpublished data from the authors of any studies in the cannabinoid receptor antagonists parent review (Cahill 2007). Included studies in the 'parent' reviews which did not report any data on weight are not referenced in this review. Participants were adult smokers who had typically volunteered from the community (although a small number of studies recruited participants from a primary care setting and one study recruited hospitalised patients). All were motivated to quit smoking and smoked an average of 20 to 30 cigarettes a day. Twenty-three studies reported baseline weight which was within normal weight to slightly overweight (with mean body mass index (BMI) of 24 to 25 or mean weight no greater than 85kg). The remaining 26 studies were not carried out in populations with specific weight characteristics and are also likely to represent the normal to slightly overweight range. One study recruited participants based on cigarette consumption, with an average of 17 to 18 (2 NRT Shiffman 2002A) and 25 to 26 (2 NRT Shiffman 2002B) cigarettes a day.

Nine studies from the antidepressant 'parent' review were included in this review. Three of them compared bupropion to varenicline as well as to placebo and therefore also appear in the list of included studies for varenicline (2 VA Gonzales 2006; 2 VA Jorenby 2006; 2 VA Nides 2006). Overall, seven studies compared weight change in participants treated with bupropion to placebo (2 AD Gonzales 2006; 2 AD Hurt 1997; 2 AD Jorenby 2006; 2 AD Nides 2006; 2 AD Rigotti 2006; 2 AD Simon 2004; 2 AD Zellweger 2005). Two studies compared fluoxetine to placebo (2 AD Niaura 2002; 2 AD Saules 2004). All bupropion studies administered 300 mg a day, and 2 AD Hurt 1997 also included arms with 100 mg a day and 150 mg a day. We used the 300 mg a day arm for the main comparison, and a separate comparison for the two lower dose arms against the standard 300 mg a day treatment group. Both fluoxetine studies compared two dosing regimens (30 and 60 mg a day, and 20 and 40 mg a day) which were combined for the main comparison. The lower doses were tested against the higher doses in a separate comparison to test for a dose-dependent effect. Length of treatment period for all antidepressant studies ranged from seven to 14 weeks, with a run-in to quit day of between one and four weeks.

Four studies provided data from the exercise 'parent' review. In all four, participants in the treatment arm received an exercise component in parallel with cognitive behavioural treatment (CBT) for smoking cessation, supplemented with nicotine replacement therapy in 2 EX Ussher 2003 and 2 EX Cornuz 2007. The exercise component included supervised exercise in three studies. 2

EX Marcus 1999 tested three supervised exercise sessions a week for 12 weeks, 30-40 minutes at resting heart rate plus 60-85% heart reserve. 2 EX Marcus 2005 tested one supervised and four unsupervised exercise sessions a week for eight weeks, at least 30 minutes at resting heart rate plus 45-59% heart reserve. 2 EX Cornuz 2007 tested moderate-intensity (40-60% of maximal aerobic power) group-based cardiovascular activity under the supervision of a trained monitor for 45 minutes a week for nine weeks. In contrast, 2 EX Ussher 2003 compared the effect of seven weeks of exercise counselling to participants receiving a smoking cessation intervention with brief health education.

Eleven studies provided data on weight change whilst using a patch compared with placebo (2 NRT Abelin 1989; 2 NRT CEASE 1999; 2 NRT Ehrsam 1991; 2 NRT Fiore 1994A; 2 NRT Fiore 1994B; 2 NRT Gourlay 1995, 2 NRT Richmond 1994, 2 NRT Sachs 1993; 2 NRT Stapleton 1995; 2 NRT Tonnesen 1991; 2 NRT TNSG 1991) and one study provided data comparing three different dosing regimens (11, 22 and 44 mg) (2 NRT Dale 1995), which has been included in a separate comparison. Dosing regimens in the 11 placebo-controlled studies varied although usually contained a mixture of participants treated with either a lower dose patch (e.g. 14 or 15 mg) and/or a higher dose patch (e.g. 21/22 or 25 mg) for those who were more addicted or opted for the extra support.

Five studies provided data on weight change whilst using nicotine gum, in two cases compared to placebo (2 NRT Garvey 2000; 2 NRT Hjalmarson 1984), and in three cases compared to no gum (1 Cooper 2005; 2 NRT Gross 1995; 1 Pirie 1992). In two of the studies, participants used 2 mg with ad libitum dosing instructions (2 NRT Hjalmarson 1984; 1 Pirie 1992). One study asked participants to chew 10 to 12 pieces daily (1 Cooper 2005). In 2 NRT Gross 1995, participants were given 2 mg gum but then randomized to instruction to chew seven, 15, or 30 pieces daily. 2 NRT Garvey 2000 randomized smokers to placebo, 9 to 15 pieces of 2 mg gum, or 9 to 15 pieces of 4 mg gum. Treatment length varied from eight weeks to one year, with a median of 12 weeks.

Other trials of nicotine replacement treatments included: two placebo-controlled studies of nicotine spray up to 40 mg a day (2 NRT Hjalmarson 1994; 2 NRT Sutherland 1992), two placebo-controlled study of up to six months use of nicotine inhaler (2 NRT Hjalmarson 1997; 2 NRT Tonnesen 1993), two placebo-controlled studies of nicotine lozenge 2 mg for smokers of a lower daily consumption (2 NRT Shiffman 2002A) and 4 mg for smokers of higher daily consumption (2 NRT Shiffman 2002B), one placebo-controlled study of 2 mg nicotine sublingual tablet (2 NRT Wallstrom 2000), one placebo-controlled study of nicotine inhaler added to 15 mg nicotine patch (2 NRT Blondal 1999), one placebo-controlled study of 16hr/15 mg nicotine patch added to nicotine inhaler (2 NRT Bohadana 2000), one placebo-controlled study of nicotine patch added to nicotine gum (2 NRT Puska 1995), and one study directly comparing nicotine patch to gum (2 NRT Lerman 2004).

The median length of treatment period for all NRT studies was 12 weeks (range 4 to 52). Fifteen studies included a period after treatment for reducing the dose (2 NRT Abelin 1989; 2 NRT Blondal 1999; 2 NRT Ehrsam 1991; 2 NRT Fiore 1994B; 2 NRT Garvey 2000; 2 NRT Gross 1995; 2 NRT Lerman 2004; 2 NRT Hjalmarson 1997; 2 NRT Puska 1995; 2 NRT Sachs 1993; 2 NRT Shiffman 2002A; 2 NRT Shiffman 2002B; 2 NRT Stapleton 1995; 2 NRT Tonnesen 1991; 2 NRT Wallstrom 2000).

Eight studies in the nicotine receptor partial agonist 'parent' review reported weight change when using varenicline. Seven studies were placebo-controlled and included a 2 mg a day arm. 2 VA Nakamura 2007, 2 VA Nides 2006 and 2 VA Oncken 2006 also provided comparative data for 0.3 mg and/or 1mg a day with or without titration. The study without a placebo arm (2 VA Aubin 2008) compared 2 mg daily varenicline to 21 mg to 7 mg tapering nicotine patch. As mentioned above, three studies (2 VA Gonzales 2006; 2 VA Jorenby 2006; 2 VA Nides 2006) also compared varenicline with bupropion. Three of the eight studies were phase II trials (2 VA Nakamura 2007; 2 VA Nides 2006; 2 VA Oncken 2006). The treatment phase lasted for 12 weeks in seven studies (2 VA Aubin 2008; 2 VA Gonzales 2006; 2 VA Jorenby 2006; 2 VA Nakamura 2007; 2 VA Oncken 2006; 2 VA Tonstad 2006; 2 VA Tsai 2008) and for six weeks in one study (2 VA Nides 2006). In Tonstad 2006, all participants received a 12-week course of open-label treatment with varenicline, and successful quitters were randomized to an additional 12 weeks of varenicline or placebo; the effect of an extra 12 weeks of treatment is explored in a separate comparison. All studies used a one-week medication run-in period before the target quit day.

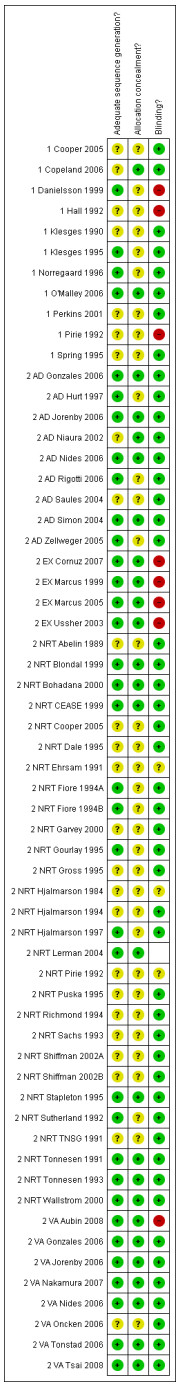
Weight change from baseline in all of the studies included in the second part of the review was measured in abstainers only. Definitions of abstinence varied between studies as in the first part of the review, and are noted in the table of Characteristics of included studies. In most studies, all participants received some form of behavioural support in addition to the pharmacotherapy/exercise therapy. Some of the end-of-treatment data and longer term follow-up data were received through personal communication with authors (noted in the table). Altogether, we collected six-month follow-up data from eight NRT trials and two bupropion trials, and 12-month follow-up data from 13 NRT trials, four bupropion trials and one fluoxetine + NRT trial. One exercise trial reported weight gain at 60 weeks. No varenicline studies reported weight change beyond the end of treatment.

Risk of bias in included studies

We extracted information about randomization, allocation concealment and blinding, and assessed the potential for bias in each domain as either being unlikely (Yes), likely (No) or insufficient information to be able to tell (Unclear) (Figure 1). None of the included studies were found to have used methods of randomization or allocation concealment likely to introduce bias. However, a

large proportion of studies did not report the method of generating the random allocation sequence (27/59 studies) or allocation concealment (35/59 studies) in enough detail for us to assess the likelihood of bias. As the majority of these studies were published before the CONSORT statement guidelines were issued (CONSORT 2001), it is likely that this is due to lack of reporting rather than to bias. Given the nature of the behavioural interventions and exercise interventions, blinding was not possible and therefore there was some potential risk of bias. However in 1 Perkins 2001 participants were blinded to their allocation until after they had completed baseline information. The degree to which unblinding occurred was reported in two studies. 1 Norregaard 1996 found that 68% of the treatment group and 63% of the placebo group had correctly guessed their allocation and in 2 NRT Tonnesen 1993 46% on active treatment and 58% on placebo treatment guessed correctly. A more serious potential for bias concerns the weight management interventions in the group of 'behavioural treatment' studies. Four of the five studies recruited women concerned about post-cessation weight gain. It is feasible that in these 'open label' studies women allocated to 'no weight help' interventions were more likely to drop out.

Figure 1. Methodological quality summary: review authors' judgements about each methodological quality item for each included study.



Effects of interventions

Effect of pharmacological interventions for smoking cessation and post-cessation weight gain on smoking cessation and weight

Due to heterogeneity of treatments, the treatment effect of the different pharmacological interventions were not pooled and were estimated separately. No pharmacological interventions significantly increased the quit rate at six or 12 months (Analysis 1.1; Analysis 1.2). However, some treatments resulted in a significant reduction in mean weight gain at the end of treatment: Dexfenfluramine -2.50 kg (-2.98 to -2.02), Fluoxetine -0.80 kg (-1.27 to -0.33), Phenylpropanolamine (PPA) -0.50 kg (-0.80 to -0.20), Naltrexone -0.76 kg (-1.51 to -0.01) (Analysis 2.1). The naltrexone estimate was pooled from three treatment groups receiving 25, 50 and 100 mg a day. Weight gain was greatest in those on higher doses of naltrexone (mean (standard deviation (SD)) 0.7(1.91), 1.1 (1.90) and 1.5 (1.95) respectively) with only the 25 mg dosage limiting weight gain significantly compared with placebo (-1.20 kg (-2.10 to -0.30: Analysis 2.1.6). This effect was maintained at three months (mean (SD) 25 mg 1.42 (0.54), placebo 3.17 (0.55) P = 0.02). Difference in mean weight gain for pharmacological treatments remained lower than for placebo at six and 12 months, but not significantly so (Analysis 2.2; Analysis 2.3). For all treatments, the effect on weight was estimated in each case from a single study, except for PPA at the end of treatment which is a meta-analysis of three studies. These studies showed no statistical heterogeneity although one study reported smoking outcome as point prevalence.

Effect of behavioural interventions for smoking cessation and post-cessation weight gain on smoking cessation and weight

Interventions providing weight control advice only compared with no intervention showed reduced quit rates at end of treatment (Analysis 3.1) and at six months (Analysis 3.2) which were small and not significant 0.90 (0.76 to 1.06) and 0.95 (0.72 to 1.26). At 12 months, however, the reduction was significant 0.66 (0.48 to 0.90) (Analysis 3.3). There was no evidence at any follow up that advice only reduced weight gain (-0.04 kg (-0.57 to 0.50) and -0.21kg (-2.28 to 1.86)) (Analysis 4.1; Analysis 4.2).

Interventions with an individualized weight control programme compared with no intervention showed no evidence that they influence quit rates, although the confidence intervals were wide 1.11 (0.84 to 1.46), 0.88 (0.54 to 1.43) and 0.79 (0.47 to 1.33) (Analysis 3.1; Analysis 3.2; Analysis 3.3). These programmes significantly reduced weight gain at the end of treatment and this effect was strengthened at 12 months (-1.05 kg (-2.01 to -0.09: Analysis 4.1) and -2.58 kg (-5.11 to -0.05: Analysis 4.2)). The within-study comparison from 1 Hall 1992 also suggested that individualized programmes are more effective than advice only (-1.12 kg (-2.17 to -0.07: Analysis 4.1) and -2.49 kg (-5.51 to 0.53: Analysis 4.2)).

The single study (1 Danielsson 1999) addressing incorporation of intermittent very low calorie diets into a weight control advice intervention showed a significant improvement in abstinence at end of treatment and 12 months 1.40 (1.07 to 1.85: analysis 3.1.4) and 1.73 (1.10 to 2.73: analysis 3.3.4) (Analysis 3.1; Analysis 3.3). This intervention significantly reduced weight gain at end of treatment and at 12 months although significance was not maintained (-3.70 kg (-4.82 to -2.58: Analysis 4.1) and -1.30 kg (-3.49 to 0.89: Analysis 4.2)).

Cognitive behavioural therapy to accept moderate weight gain (1 Perkins 2001) was found to increase the quit rate at six and 12 months (1.81 (1.22 to 2.70: Analysis 5.1) and 2.43 (1.19 to 4.95: Analysis 5.2)) and to decrease post-cessation weight gain at end of treatment (-1.10 kg (-1.82 to -0.38: Analysis 6.1)), at six months (-3.50 (-6.05 to -0.95: Analysis 6.2)) and at 12 months (-5.20 kg (-9.28 to -1.12: Analysis 6.3)).

Effect of antidepressants on post-cessation weight gain

Both bupropion (300 mg a day) and fluoxetine (30 mg a day arm + 60 mg a day arm) were found to limit post-cessation weight gain compared with placebo at the end of treatment (bupropion -1.11 kg (-1.47 to -0.76), six studies, 774 participants, I^2=0%; and fluoxetine -1.30 kg (-1.91 to -0.69) one study, 119 participants: Analysis 7.1). At six months, participants using fluoxetine were reported to gain more weight than the controls. This is due to a large increase in weight gain for participants taking 60mg compared with those taking 30mg (Analysis 7.3; Analysis 7.4). 2 AD Saules 2004 tested fluoxetine versus placebo, but both intervention and control arms used NRT. Weight was reported at six months and treatment showed no significant advantage over placebo (Analysis 7.3). At six and 12 months a reduction in weight was maintained in participants on bupropion 300 mg a day compared with placebo, although it was not statistically significant (-0.58 kg (-2.16 to -1.00); Analysis 7.3 and -0.38 kg (-2.00 to 1.24); Analysis 7.5). There was no evidence of a dose-dependent response for bupropion at end of treatment, six or 12 months or for fluoxetine at the end of treatment (Analysis 7.2; Analysis 7.4; Analysis 7.6).

Effect of exercise interventions on post-cessation weight gain

Neither individual nor pooled data for the four trials of exercise treatment showed evidence of a significant effect for change in weight from baseline to the end of treatment, with a summary estimate of -0.25 kg (-0.78 to 0.29); Analysis 8.1. However, three studies provided data at 12 months follow up which when pooled showed a significant reduction in weight gain favouring treatment, with a summary estimate of -2.07 kg (-3.78 to -0.36); Analysis

8.2.

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

Participants taking any type of NRT gained less weight than those taking placebo at the end of treatment (-0.69 kg (-0.88 to -0.51); 19 studies, 2600 participants, I^2=82%; Analysis 9.1). Statistical heterogeneity was due to one study 2 NRT Abelin 1989, which showed a 4.3 kg difference in weight gained between the treatment and control arms. When this study was removed, statistical heterogeneity reduced to 0% and the overall estimate decreased but remained statistically significant (-0.46 kg (-0.66 to -0.27)). Estimates of difference in weight gain for different types of NRT were:

- Gum -0.58 kg (-1.02 to -0.13) four studies, 345 participants, I^2=0%
- Patch (without 2 NRT Abelin 1989) -0.45 kg (-0.70 to -0.20) nine studies, 1502 participants, I^2=0%
- Inhaler -0.37 kg (-1.19 to 0.45) two studies, 111 participants I^2=0%
- Sublingual tablet -0.48 kg (-0.99 to 0.03) two studies, 478 participants, I^2=30%
- Intranasal spray (+ patch) 0.90 kg (-1.54 to 3.34) one study, 47 participants

Overall, weight gain was less for those taking NRT at six and 12 months, although not significantly so (six months: -0.37 kg (-0.88 to 0.14) 9 studies, 771 participants, I^2=0%; Analysis 9.4, and 12 months: -0.42 kg (-0.92 to 0.08) 15 studies, 1334 participants, I^2=0%; Analysis 9.6).

Longer courses of NRT with 15 or 25 mg patches were not associated with reduced weight gain at 12 months Analysis 9.8. 2 NRT Lerman 2004 compared patch to spray and found no significant difference in weight gain at end of treatment or at six months. Four trials compared the effects of different doses of NRT. 2 NRT Garvey 2000 compared 4 mg and 2 mg NRT gum to placebo, 2 NRT Dale 1995 compared 44, 22 and 11mg patches to placebo, 2 NRT CEASE 1999 compared 25 and 15 mg patches to placebo, and 2 NRT Gross 1995 compared different amounts of 2 mg NRT gum per day. There was no significant dose-dependent difference in weight gain at the end of treatment (Analysis 9.3) or at 12 months (Analysis 9.7).

Effect of rimonabant on post-cessation weight gain

We were unable to obtain data on the effect of rimonabant on post-cessation weight gain. The Food and Drug Administration have never authorised the use of rimonabant in the USA, and the European Medicines Agency have recommended the suspension of marketing authorisation for rimonabant as a weight loss treatment in Europe, because of concerns about serious adverse events (Cahill 2007).

Effect of varenicline on post-cessation weight gain

Varenicline (all treatment arms combined within studies) had no significant effect on post-cessation weight gain compared with placebo at end of treatment (Analysis 10.1). No significant effect was found when comparing different doses or titration against non-titration (Analysis 10.2, Analysis 10.3, Analysis 10.4, Analysis 10.5, Analysis 10.6, Analysis 10.7). No studies reported differences in weight gain at longer term follow up. One relapse prevention study (2 VA Tonstad 2006) randomized abstinent smokers who had completed 12 weeks of open-label varenicline to either 12 more weeks of either active or placebo treatment. This extended course significantly reduced weight gain by -0.71 kg (-1.04 to -0.38) (Analysis 10.8). The two estimates of the effects of 12 weeks of varenicline on weight gain are therefore discrepant. In an exploratory analysis, we excluded the two studies from the Far East, where weight gain was about half that seen in the studies on western populations. The pooled estimate of effect of varenicline was then -0.52 kg (-1.16 to 0.11), which is more similar to the estimate from 2 VA Tonstad 2006.

In three studies compared bupropion to varenicline, participants taking varenicline gained significantly more weight at the end of treatment (0.51 kg (0.09 to 0.93; Analysis 11.1). In the one trial of varenicline versus NRT (2 VA Aubin 2008) there was no evidence that weight gain differed (Analysis 12.1).

DISCUSSION

This review has collated the evidence for the effect of two types of intervention on smoking and/or weight. We found 11 trials of interventions specifically designed to aid smoking cessation and to limit post-cessation weight gain. Trials were pharmacological or behavioural in nature. Pharmacological trials were too different clinically to combine and their effects have been assessed separately. Although the design of behavioural interventions differed, they all had similar components and gave estimates that when combined showed no statistical heterogeneity. We have considered the combined treatment effect on smoking and weight for some of these interventions. We also found that a small proportion of studies testing smoking cessation interventions and not specifically targeting post-cessation weight gain nonetheless reported weight change at end of treatment and at follow up. These included trials of antidepressants, exercise, nicotine replacement therapy and varenicline.

Interventions to aid smoking cessation and limit post-cessation weight gain

To date, five pharmacological interventions (phenylpropanolamine (PPA), ephedrine plus caffeine, naltrexone, dexfenfluramine and fluoxetine) have been combined with standard smoking cessation treatments to test their effect on post-cessation weight gain compared with smoking cessation treatments alone. Trials of PPA, ephedrine plus caffeine, and naltrexone

also reported effects on quit rates. Dexfenfluramine, a serotonergic anorectic drug, showed superiority in effect on post-cessation weight gain at the end of treatment, yielding a weight reduction of about 2½ kilograms. However, this drug was removed from the US market by the Food and Drug Administration (FDA) in 1997 and from other markets around the world. PPA, an appetite suppressant, which has also been withdrawn from the US market and restricted in the UK, also attenuated weight gain compared with placebo at the end of treatment, with an effect size of a similar magnitude to that of nicotine replacement therapy (NRT). However, studies testing PPA used dosages above the UK recommended limit of 100 mg a day. The most promising pharmacological intervention of those tested to date is naltrexone, an opioid receptor antagonist licensed in the UK for use in alcohol and opioid dependence. However, the confidence interval for the effect estimate is wide, suggesting some imprecision in the findings. One study of fluoxetine (1 Spring 1995), a selective serotonergic reuptake inhibitor, compared with placebo found significant attenuation of weight gain at end of treatment. It is likely that fluoxetine used specifically to reduce weight gain is comparable with its limited success as an aid to smoking cessation, since the estimates and confidence intervals were similar. This study was not included in the meta-analysis for fluoxetine in the second part of the review because it was not included in the parent Cochrane review, and was used specifically to test its effect on post-cessation weight gain. For those pharmacotherapies that did attenuate weight gain at end of treatment, follow-up data were only reported for PPA, which by six months showed rebound in weight to match that gained in the placebo arm. The association between long-term quitting and limiting weight gain during treatment phase could not be assessed, as quit rates were not reported beyond end of treatment for those interventions that limited weight gain. However, at end of treatment higher quit rates were reported for dexfenfluramine, for naltrexone (100 mg dose) and in one small trial of PPA. The remaining trials of PPA and fluoxetine reported lower quit rates in the intervention arms at the end of treatment.

Although not stated in the National Institute for Health and Clinical Excellence (NICE) guidance for smoking cessation, there is a widely-held clinical view that concurrent behavioural treatment for smoking and weight control may lead to worse smoking cessation outcomes. Our review suggests that the effects may depend upon the type of programme that is used to control weight, although with few studies in this area and the small sample sizes of existing studies conclusions must be tentative. We noted that advice-only for weight control appeared ineffective in reducing weight gain and also that it may be detrimental to success in quitting, since there was a trend towards reduced quitting by end of treatment and at six and 12 months. Hunger is associated with increased urges to smoke (Cheskin 2005), and it might be expected that dieting would significantly increase relapse. But the trend was only significant at 12 months, which leaves the interpretation unclear. Individualized planning was more successful as a weight control strategy and it did not seem to reduce smoking cessation, although the confidence interval for this was wide and therefore no firm conclusion can be reached. Very low calorie diets and cognitive behavioural therapy to accept weight gain were associated with improved abstinence and weight outcomes.

There is a caveat regarding the open-label design of the behavioural intervention studies. With the exception of 1 Hall 1992, they all enrolled women who had had problems with weight gain in earlier cessation attempts and were therefore seeking weight control programmes. Such participants when assigned to the control group may have been more likely to default from the programme and resume smoking to avoid weight loss compared with those assigned to the treatment they wanted, especially in studies such as 1 Danielsson 1999, where the intervention included free meals and intensive specialist care versus advice only. 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. Another possible explanation of the positive result of the very low calorie diet is that it induced ketosis, which may have suppressed hunger and nicotine withdrawal. Finally, both the weight control intervention and the cognitive behavioural therapy in 1 Perkins 2001 were associated with reduced withdrawal discomfort while quitting. Hence improvements in abstinence may be due to this effect. Further studies are needed, but advice-only weight control interventions may be harmful and should not be recommended.

1 Copeland 2006 compared group and individual relapse prevention programmes after a two-week smoking cessation intervention. The relapse prevention programme included cognitive restructuring regarding body image and weight concern. Although no differences in abstinence rates or weight gain were found between those randomized to group or individual therapy, regression analysis showed that weight gain was more strongly associated with relapse in the group setting, indicating that individual cognitive restructuring treatment may help patients to tolerate weight gain. More studies are needed to test these findings and clarify the mechanism of action.

Interventions to aid smoking cessation only

Attenuation of weight gain was greatest for antidepressants, with fluoxetine showing the greatest reduction in weight gain, closely followed by bupropion (300 mg a day). The bupropion estimate is based on six studies with a combined participant number of 774, compared with one fluoxetine study with 119 participants. It was not possible to conclude whether or not the effect of bupropion was dose-dependent, as different doses were assessed in only one study, and the number of abstinent participants was low. However, there is a suggestion of dose-response because the high dose regimen (300 mg) led to almost twice the magnitude of weight attenuation as the lower doses (100 or 150 mg). We found no studies that measured the effect of nortriptyline, an antidepressant licensed as a second line treatment for smoking cessation, on post-cessation

weight gain. The point estimate for the reduction in weight gain for bupropion at 6 and 12 months was about half that seen at the end of treatment. However, with fewer studies and fewer abstinent participants, the effects were not significant and it is not possible to say whether bupropion reduces weight gain in long-term.

There was mixed evidence for the effect of exercise on post-cessation weight gain. Two trials compared an exercise plus cognitive behavioural smoking cessation intervention to a cognitive behavioural smoking cessation intervention alone. Two others compared NRT plus cognitive behavioural smoking cessation treatment to the same programme plus exercise, and found no difference in weight gain at the end of treatment. Weight gain at the end of treatment in the two studies using NRT was markedly less than in those without NRT. Although the pooled estimate for end-of-treatment effect was non-significant, the exercise condition achieved significantly lower weight gain at 12 months follow up. It is not clear whether this represents a delayed effect of exercise on weight gain. It is possible that participants receiving the exercise intervention remained more motivated to exercise after the intervention had ended, but post-treatment exercise behaviour is not reported in either study. Smoking cessation is associated with a decrease in metabolic rate and increased energy intake (Filozof 2004). In this context, maintaining or reducing weight is likely to require intensive levels of exercise, which may explain why exercise interventions have not shown much success in reducing weight gain at the end of treatment. However, although no intervention effect was seen at the end of treatment, NRT might have reduced the effect of exercise on suppressing weight gain in the two NRT/exercise trials, while participant numbers were small in the other two. More studies are needed to clarify the effect of exercise on post-cessation weight gain.

Nicotine replacement therapy was found to reduce post-cessation weight gain during treatment, but to a lesser extent than antidepressants. The greatest weight of evidence was found for patch and gum preparations, which both independently attenuated weight gain. It is likely that the inhaler and sublingual tablet would have a similar effect, although sample size of the trials limited the findings. As with antidepressants, attenuation of weight gain was reversed after pharmacotherapy, with no significant attenuation by six or 12 months. One trial (2 NRT Sutherland 1992) tested intranasal nicotine spray against placebo and reported a large significant reduction in weight gain at 12 months, but this may be attributable to just under half of the participants abstinent at 12 months continuing to use the nasal spray. However, overall the point estimate for NRT favours a continuing reduction in weight, but there may be differences between types of NRT which could be explained by differences in the propensity to use types of NRT in the long term. Evidence of an additional benefit for combination treatment was not demonstrated, although this is based on one trial with small numbers (2 NRT Blondal 1999).

No trials of varenicline tartrate reported weight outcomes beyond the end of treatment, so it was not possible to estimate any long-term effects. The overall picture at the end of treatment is of a non-significant small effect on weight. This is surprising, as the mode of action of varenicline is similar to nicotine and could therefore be expected to suppress weight gain in a similar way. The effect estimate is derived from four studies conducted in western populations (America, Norway) and two studies conducted in the east (Japan, Korea and Taiwan). Absolute weight gain in eastern populations was lower than in the west, and it is possible that these studies mask the true effect, since greater weight gain may allow for greater weight suppression. Removing 2 VA Tsai 2008 and 2 VA Nakamura 2007 from the meta-analysis gives a similar estimate to that seen for nicotine replacement therapy, although it still does not achieve statistical significance. An effect is also suggested by the findings of 2 VA Tonstad 2006. Participants abstinent after 12 weeks of open-label varenicline were randomized to a further 12 weeks of either active or placebo treatment. At 24 weeks, participants receiving active treatment had gained significantly less weight than those taking placebo.

AUTHORS' CONCLUSIONS

Implications for practice

- Smoking cessation is usually accompanied by weight gain and quitters can expect to gain an average of 4 to 6 kilograms over one year of continuous abstinence.

- There are no pharmacological interventions specifically to reduce weight gain that can be recommended with promise of long-term benefit to smokers trying to quit. Fluoxetine could be tried, but evidence for long-term benefit is unclear.

- Advice to prevent weight gain by reducing calories may reduce abstinence, and is not effective for controlling weight. It should not be used.

- Individualized behavioural weight control plans, very low calorie diets, and cognitive behavioural therapy may all reduce weight gain, and there is no strong evidence they reduce abstinence. They should be used cautiously, ideally in research settings.

- Nicotine replacement therapy, antidepressants and probably varenicline for smoking cessation all reduce weight gain in the short term, but patients need to be advised that it is unclear whether they reduce weight gain in the long term.

- There is mixed evidence that exercise limits post-cessation weight gain.

- The long-term effect of all combined smoking cessation and weight control interventions on weight gain is small at best, at less than one kilogram, compared with a typical weight gain of about five kilograms for continuous abstinence over one year,

and is of borderline clinical relevance. The only possible exceptions are individualized weight control interventions, cognitive behavioural therapy and very low calorie diets.

Implications for research

- Drugs that suppress appetite and that have been tested have other serious health consequences that limit their use, although they have been successful in the short term. However, other drugs that suppress appetite, such as sibutramine, are worth investigating.

- It is important to know whether the effects of individualized behavioural programmes, very low calorie diets, and cognitive behavioural therapy on possible increases in cessation rate can be generalised to all smokers trying to stop, or whether the effect is specific to smokers concerned about weight gain.

- Single studies of cognitive behavioural therapy and very low calorie diet were both successful interventions for increasing abstinence reducing weight gain in the long term. Replication of these findings are needed.

- More and larger studies of exercise interventions are needed.

- Trials of current and future pharmacotherapies for smoking cessation should measure and report weight gain, standard deviation of the change, and numbers of prolonged abstinent participants.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

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

1 Cooper 2005

Methods	Country: USA Recruitment: Community volunteers
Participants	439 weight-concerned female smokers (≥10 cpd) Av.age 38, av.cpd 23, av baseline weight 64-66 kg
Interventions	1. Phenylpropanolamine (PPA) gum 8.33 mg 16 pieces/d 8 wks, weaning last 3 wks 2. Nicotine gum (2 mg), 10-12 pieces/day recommended, for 8 wks, weaning last 3 wks. 3. Placebo gum All participants received x13 1hr weekly cognitive behavioural group sessions focused on smoking and weight. Ppts cut down weeks 1-4 by 25% and quit week 5
Outcomes	1. PP abstinence at 12m (Validation: CO<10ppm) 2. Mean (SD) weight change (kg) in abstainers at 6m and 12m
Notes	PP abstinence defined as validated self report of no smoking at the time of the assessment

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	Methods not described
Allocation concealment?	Unclear	Not described
Blinding? All outcomes	Yes	All group facilitators and participants were blind to treatment conditions

1 Copeland 2006

Methods	Country: USA Recruitment: Community volunteers
Participants	79 women smokers motivated to quit and weight concerned (at least 10 cpd for 1yr) av cpd 20.1, av FTND score 4, av BMI 24
Interventions	All participants completed a smoking cessation programme (6 sessions over 2w) involving smoking cessation and relapse prevention advise and given an 8w supply of NRT. randomized to follow up in either individual or group format: Six follow up relapse prevention sessions including psychological, dietary, and exercise components over 38 weeks

1 Copeland 2006 (*Continued*)

Outcomes	1. Continuous abstinence at 6 months (Validation: CO<=10ppm) 2. Mean (SD) weight change (kg) in continuous abstainers at 6m
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	Not described
Allocation concealment?	Yes	"Statisticians generated the random assignment sequence for follow up condition"
Blinding? All outcomes	Yes	"Therapists were blind to participant follow-up treatment condition assignment until the last meeting of the cessation program."

1 Danielsson 1999

Methods	Country: Sweden Recruitment: community volunteers
Participants	287 weight concerned female smokers age range 30-60 >=10cpd, av cpd 20, av BMI 26
Interventions	1. Nicotine gum (2 or 4 mg) with moderate behavioural advice: 11 sessions (45 min) 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), two week periods (weeks 1 and 2, 7 and 8, 13 and 14). All participants were recommended a standardised balanced diet of about 6.7 MJ/day. 2. Control group received the same as intervention but without the very low energy diet
Outcomes	1. Prolonged abstinence 12m (Validated: CO<10ppm) 2. Mean (SD) weight change (kg) in prolonged abstainers at 6m
Notes	Prolonged abstinence defined as "completely and continuously stopped from week 2 onwards"

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Yes	Open consecutive randomization (in the order their questionnaires were received at the clinic)
Allocation concealment?	Unclear	Not described
Blinding? All outcomes	No	Open study

1 Hall 1992

Methods	Country: USA Recruitment: community volunteers
Participants	180 smokers, 27% F, av age 39-42, av cpd 26-32, av baseline weight 67-73kg
Interventions	Participants received treatments in groups. All groups completed 2 week behavioural smoking cessation programme. Participants were randomly assigned to follow up group for weight management: (1) Innovative intervention - individualised multifactorial intervention including exercise, self-monitoring, dieting and behavioural advice (4w) (2) Standard treatment condition - given an information pack on good nutrition and exercise not targeted for SC induced weight gain at end of 2w SC programme
Outcomes	1. Point prevalence abstinence at 6 and 12m (Validation: CO < 10.5 at 6,12 and 26w, Cotinine blood levels below 50 ng/ml at 12 m) 2. Mean (SD) weight change (kg) in abstainers at end of treatment and 12 months
Notes	Non individualised weight programme arm also in this study that has not been used

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Method not described
Allocation concealment?	Unclear	Not described
Blinding? All outcomes	No	Open study

1 Klesges 1990

Methods	Country: USA Recruitment: Community volunteers
Participants	57 adult female smokers who had previously experienced post-cessation weight gain, av age 27, av 22.4 cpd, mean CO 49.8ppm
Interventions	(1) PPA gum 8.33mg 9/day 2w (2) 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 end of treatment (Validation: CO <=7ppm)
Notes	Intervention only 2 weeks long. No 6 month follow up.

Risk of bias

1 Klesges 1990 (*Continued*)

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	Method not described
Allocation concealment?	Unclear	Not described
Blinding? All outcomes	Yes	Double blind

1 Klesges 1995

Methods	Country: USA Recruitment: community volunteers
Participants	107 male and female smokers, age between 18-60, cpd 20+, CO>15ppm
Interventions	(1) PPA gum 8.33mg up to 10 pieces/day 4w (2) Placebo gum same regime All participants received one 30 min session on smoking cessation and relapse prevention
Outcomes	Mean (SD) weight change (kg) in continuous abstainers at end of treatment (validation: CO<8ppm)
Notes	No 6 months follow up data

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Yes	Independent randomisation
Allocation concealment?	Unclear	Not described
Blinding? All outcomes	Yes	"Neither the investigators nor the subjects knew which gum contained the active ingredients"

1 Norregaard 1996

Methods	Country: Denmark Recruitment: Community volunteers
Participants	225 smokers who wanted to quit without gaining weight, 65% F, av BMI 23-24, av age 38-39, av 20 cpd
Interventions	(1) 20mg Ephedrine plus 200mg caffeine combination 3/day 12w then decreased until 39w. TQD -first session. Eight 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).

1 Norregaard 1996 (*Continued*)

	(2) Placebo All participants given advice on how to quit smoking and prevent weight gain (inc booklet about low fat food)
Outcomes	(1) Prolonged abstinence at 6 and 12m (validation: CO<10ppm) (2) Mean (SD) weight change (kg) in prolonged abstainers at end of treatment, 6 and 12m
Notes	Prolonged abstinence defined as no smoking after week 1 post quit

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Minimisation
Allocation concealment?	Unclear	Not described
Blinding? All outcomes	Yes	"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 ($p < 0.001$)"

1 O'Malley 2006

Methods	Country: USA Recruitment: Community volunteers
Participants	400 smokers, 46% F, av BMI 27-28, av 26-29 cpd, av age 45-47
Interventions	(1) Naltrexone 25mg 6w (2) Naltrexone 50mg 6w (3) Naltrexone 100mg 6w (4) Placebo All participants also given 6w supply of 21mg patches and 6 sessions of behavioural support (1x45mins, 5x15mins)
Outcomes	Mean (SD) weight change (kg) in continuous abstainers at end of treatment
Notes	Arms 1-3 combined for the main comparison No 6 month follow up data

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Block randomization, stratified by sex after the first 150 participants

1 O'Malley 2006 (*Continued*)

Allocation concealment?	Yes	Random sequence was provided to the pharmacist, who assigned participants
Blinding? All outcomes	Yes	All were blinded to the treatment assignment

1 Perkins 2001

Methods	Country: USA Recruitment: community volunteers
Participants	219 weight concerned women av age 44, av body weight 69kg, mean 21 cpd
Interventions	1. Weight control - Programme to attenuate weight, with daily calorie goals, behavioural support, self monitoring and constructive feedback. 10x 90min sessions over 7 weeks 2. Standard - No additional support given for weight, session time used to talk about smoking cessation 3. CBT - therapy to promote the acceptance of modest weight gain, reduce concerns and encourage healthy eating. All participants received standard cognitive behavioral SC counselling at each session
Outcomes	(1) Continuous abstinence 6 and 12m (validation: CO </=8ppm) (2) Mean (SD) weight change (kg) for continuous abstainers 6 and 12m
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	After a sufficient number of participants to form a group recruited, group assigned to a treatment condition
Allocation concealment?	Unclear	Not described
Blinding? All outcomes	Yes	"Participants did not learn of their treatment condition assignment until the first treatment session, after all baseline information had been received"

1 Pirie 1992

Methods	Country: USA Recruitment: community volunteers
Participants	417 women smokers, av cpd 25-27, av age 42-44, av BMI 23-24, 30-40% expressed great weight concern
Interventions	1. Group SC therapy plus weight control programme (calorie restriction, increased exercise, self monitoring, acceptance of weight gain) 2. Group SC therapy
Outcomes	(1) Continuous abstinence at 6 and 12m (Validation: expired CO </=10ppm) (2) Mean (SD) weight change (kg) in continuous abstainers at 6 and 12m
Notes	2 additional arms in the study that haven't been used in this review- SC therapy + 2mg nicotine gum ad lib and SC therapy + weight control programme + 2mg NRT ad lib

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Method not stated
Allocation concealment?	Unclear	Not described
Blinding? All outcomes	No	Not possible due to nature of the interventions

1 Spring 1995

Methods	Country: USA Recruitment: community volunteers
Participants	144 female weight concerned smokers, av age 41, av cpd 27, av BMI 23-25
Interventions	(1) Dexfenfluramine 30mg/day 12w (2) Fluoxetine 40mg/day 12w (3) Placebo All participants received weekly group behavioural SC support for first 4w and fortnightly support for remaining 8w
Outcomes	Mean (SD) weight change (kg) in prolonged abstainers at end of treatment (validation: CO <10ppm)
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

1 Spring 1995 (*Continued*)

Risk of bias		
Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Method not stated
Allocation concealment?	Unclear	Not described
Blinding? All outcomes	Yes	"All subjects received identical packets of three pills"

2 AD Gonzales 2006

Methods	Country: USA Recruitment: community volunteers
Participants	1025 smokers 55% female (Placebo), 48% female (Bup); av age 45, av CPD not specified
Interventions	1. Varenicline 1mg x2/day for 12w 2. Bupropion 300 mg/day for 12w 3. Placebo All participants received brief individual counselling at visits w1-7, 9, 12, + telephone counselling at 4 and 5m
Outcomes	Mean (SD) weight change (kg) in prolonged abstainers at end of treatment (validation: CO <10ppm)
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		
Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Randomization: computer-generated sequence 1:1:1
Allocation concealment?	Yes	Participants were randomised according to a pre-defined central computer sequence
Blinding? All outcomes	Yes	Double blind

2 AD Hurt 1997

Methods	Country: USA, multi-centre Recruitment: community volunteers
Participants	615 smokers, 55% F, av age 44, av CPD 27
Interventions	1. Bupropion 100 mg/day for 7w, begun 1w before TQD 2. Bupropion 150 mg/day 3. Bupropion 300 mg/day 4. Placebo All participants received physician advice, S-H materials, and brief individual SC 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 < 11ppm)
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Yes	Stratified by site, method not specified
Allocation concealment?	Unclear	Not described
Blinding? All outcomes	Yes	Double blind

2 AD Jorenby 2006

Methods	Country: USA, multi centre Recruitment: community volunteers
Participants	1027 smokers, 41% F, av age 42, av CPD 22
Interventions	1. Bupropion 300mg for 12 w + placebo varenicline 2. Varenicline 2mg for 12 w + placebo bupropion 3. Placebo bupropion + placebo varenicline All participants received brief (< 10 min) individual counselling at each weekly assessment for 12w & 5 follow-up visits. One telephone call 3 days after quit day
Outcomes	Mean (SD) weight gain (kg) in prolonged abstainers at end of treatment (validation: CO < 10ppm)
Notes	Prolonged abstinence defined as validated self reported abstinence w 8-12 Arm 1 and 3 in main comparison (same study as VA Jorenby 2006)

Risk of bias

2 AD Jorenby 2006 (*Continued*)

Item	Authors' judgement	Description
Adequate sequence generation?	Yes	Centralised, computer-generated
Allocation concealment?	Yes	"SItes used an electronic system to assign participants to treatment"
Blinding? All outcomes	Yes	Double blind

2 AD Niaura 2002

Methods	Country: USA, multi-centre, 16 sites Recruitment: Community volunteers
Participants	989 smokers, 61% F, av age 42 av CPD 28
Interventions	1. Fluoxetine 30 mg for 10w, starting 2w before TQD 2. Fluoxetine 60 mg for 10w, starting 2w before TQD 3. Placebo All participants received 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 end of treatment (Validation: CO less than 8ppm and salivary cotinine less than 20ng/ml)
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	Method not stated
Allocation concealment?	Yes	Not described
Blinding? All outcomes	Yes	Double blind

2 AD Nides 2006

Methods	Country: USA, multi-centre, 7 sites Recruitment: Volunteers (phase II study)
Participants	638 smokers, 51% F, av age 41, av CPD 20, av BMI 25-27

2 AD Nides 2006 (*Continued*)

Interventions	1. Varenicline 0.3mg 1/d for 6w, + 1wk placebo 2. Varenicline 1.0mg 1/d for 6w, + 1wk placebo 3. varenicline 1.0mg 2/d for 6w, + 1wk placebo 4. Bupropion 150mg 2/d (titrated in wk 1) for 7 wks 5. Placebo tablets 2/d for 7 wks All participants received up to 10 mins counselling at 7 weekly clinic visits, 12 & 24w
Outcomes	Mean (SD) weight gain (kg) in prolonged abstainers at end of treatment (email communication)
Notes	Prolonged abstinence defined as self reported quit for 4 weeks during treatment period (not validated) Arms 4 and 5 in main comparison (same study as 3 AD Nides)

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Computer-generated list
Allocation concealment?	Yes	"Investigators assigned medication to subjects in numerical order of acceptance into the study" from computer generated list
Blinding? All outcomes	Yes	Double blind

2 AD Rigotti 2006

Methods	Country: USA Recruitment: hospital patients with cardiovascular disease
Participants	248 smokers, 31% F, av age 56, av CPD 21-23.
Interventions	1. Bupropion 300 mg for 12w 2. Placebo All participants received multi component CBT cessation & relapse prevention programme 30-45 mins and 5 X10 min post-discharge contacts (2 days,1,3,8, 12w)
Outcomes	Mean (SD) weight gain (kg) in point prevalence abstainers at end of treatment (email communication) and 12m (email communication) (Validation: <=20ng/ml cotinine)
Notes	Point prevalence abstinence defined as validated self report of no smoking in previous 7 days

Risk of bias

Item	**Authors' judgement**	**Description**

2 AD Rigotti 2006 (*Continued*)

Adequate sequence generation?	Yes	Computer-generated stratified
Allocation concealment?	Unclear	"The study pharmacist used the computer generated sequence, concealed from enrolment staff, to assign participants to study arm."
Blinding? All outcomes	Yes	Double blind

2 AD Saules 2004

Methods	Country: USA Recruitment: community volunteers
Participants	150 smokers, 20% history of MDD 55% F, av age 40
Interventions	1. Fluoxetine 40 mg for 14w, nicotine patch for 10w 2. Fluoxetine 20 mg for 14w, nicotine patch for 10w 3. Placebo & nicotine patch All participants received CBT for SC, 6 sessions.
Outcomes	Mean (SD) weight gain (kg) in continuous abstainers at 6 months (email communication) (Validation: CO<10ppm)
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Not described
Allocation concealment?	Unclear	Not described
Blinding? All outcomes	Yes	Double blind

2 AD Simon 2004

Methods	Country: USA Recruitment: outpatients
Participants	244 smokers, 79% veterans, 15% F, Av age 50, Av CPD 24, av BMI 26-28
Interventions	1. Bupropion 300 mg for 7w, nicotine patch for 2m 2. Placebo bupropion, nicotine patch for 2m All participants received 3m of CBT counselling, S-H materials and telephone follow-up counselling

2 AD Simon 2004 (*Continued*)

Outcomes	Mean (SD) weight gain (kg) in continuous abstainers at 12m (email communication) (Validation: salivary cotinine of less than 15ng/ml)
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Yes	Computer-generated
Allocation concealment?	Yes	Participants allocated according to computer-generated list
Blinding? All outcomes	Yes	"All study personnel engaged in providing interventions to participants were blinded to treatment assignment"

2 AD Zellweger 2005

Methods	Country: 12 European countries, 26 centres Recruitment: volunteers, healthcare professionals (qualified practising physician or nurse)
Participants	667 smokers (>= 10 CPD) (excludes 1 centre enrolling 20 people, and 3 people who took no medication) 64% female, av CPD 23
Interventions	1. Bupropion SR 300 mg/day for 7w 2. Placebo All participants received brief (10-15 min) motivational support at weekly clinic visits and telephone support one day before TQD, 3 days after TQD, monthly during follow up
Outcomes	Mean (SD) weight gain (kg) in prolonged abstainers at end of treatment (email communication), 6m (email communication) and 12m (email communication) (Validation: CO <= 10 ppm)
Notes	Prolonged abstinence defined as continuous abstinence from week 4

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Yes	3:1 ratio
Allocation concealment?	Unclear	Not described
Blinding? All outcomes	Yes	Double blind

2 EX Cornuz 2007

Methods	Country: Switzerland Recruitment: Community volunteers
Participants	481, av age 42, av cpd 27, sedentary: < 150 mins moderate intensity physical activity per week and <60 mins vigorous intensity activity, av BMI 24-25
Interventions	(a) Intervention: moderate-intensity group-based CV activity, 45 mins, weekly for 9 weeks + 15 mins cessation counselling for 9 weeks (including NRT prescription) (b) 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 gain (kg) in continuous abstainers at end of treatment and 12m (Validation: CO <10ppm)
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Yes	Remotely and randomly generated by a computer.
Allocation concealment?	Yes	Secured by means of sealed envelopes
Blinding? All outcomes	No	Not possible

2 EX Marcus 1999

Methods	Country: USA Recruitment: not described
Participants	20 women, av age 39, av cpd 28, av BMI 24-27.
Interventions	1. CV equipment: group, facility 30-45 min, 60-85% HR max, 3 times/week for 12 weeks + cessation programme (twice a week for 4 weeks) 2. Cessation programme only (twice a week for 4 weeks)
Outcomes	Mean weight gain (kg) in continuous abstainers at end of treatment (8w) and at 60w (validation: CO <8ppm and cotinine level less than 57 nmol/L [10ng/ml])
Notes	

Risk of bias

Item	Authors' judgement	Description

2 EX Marcus 1999 (*Continued*)

Adequate sequence generation?	Yes	Computer generated
Allocation concealment?	Yes	"randomisation code for group assignment was generated by a computer code"
Blinding? All outcomes	No	Not possible

2 EX Marcus 2005

Methods	Country: USA Recruitment: community volunteers
Participants	217 women, mean age 43, mean cpd 21 exercise <= 90 mins /wk.
Interventions	1. 1x 1hr facility (group) session + 4x 30min session home (individual) or facility (group), 45-59% HR reserve or 50%-69% maximum HR, goal: 165 min/week for 8w plus 8w of cognitive behavioural smoking cessation therapy 2. Smoking cessation therapy as 1. once/week for 8 weeks + health education once/week for 8 weeks Exercise began before quit date, time in therapy matched for two groups
Outcomes	Mean (SD) weight gain (kg) in continuous abstainers at end of treatment (Validation: saliva cotinine < 10ng/ml, CO < 8ppm)
Notes	Published paper of Marcus 2003a conference abstract (included study in exercise interventions parent review)

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Computer-generated
Allocation concealment?	Yes	"Group assignment was based on a randomisation code generated by a computer software program"
Blinding? All outcomes	No	Not possible

2 EX Ussher 2003

Methods	Country: UK Recruitment: community volunteers
Participants	309 sedentary smokers, 60% female, av age 43, av cpd 22, av BMI 25-26
Interventions	1. Exercise counselling (once a week for 7 weeks) + cessation programme (once a week for 7 weeks) + NRT. 2. Cessation programme as 1. once/week for 7 weeks + brief health education once/week for 7 weeks + NRT
Outcomes	Mean weight gain (kg) in continuous abstainers at end of treatment & 12 months
Notes	12 month data reported in Ussher et al 2007

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	computer-generated
Allocation concealment?	Yes	Allocated in order of attendance
Blinding? All outcomes	No	Not possible

2 NRT Abelin 1989

Methods	Country: Switzerland Recruitment: 21 Primary care clinics
Participants	199 primary care patients 40% female, av.age 41, av.cpd 27
Interventions	1. Nicotine patch, 24hr, 12 wk with weaning; 21mg smokers of >20 cpd, 14 mg for <20 cpd 2. Placebo patch Participants did not receive any psychological support
Outcomes	Mean (SD) weight change (kg) in abstainers at end of treatment (Validation: CO content 0-11ppm)
Notes	Abstainence defined as participants who smoked 0-3 cigarettes per wk with validation

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Method not stated
Allocation concealment?	Unclear	Not described

2 NRT Abelin 1989 (*Continued*)

Blinding? All outcomes	Yes	"Double blind"

2 NRT Blondal 1999

Methods	Country: Iceland Recruitment: community volunteers
Participants	237 smokers 67% female, av.age 41-43, av. tobacco use 25g/day
Interventions	1. Nicotine nasal spray (NNS) (0.5mg/dose) + 15mg nicotine patches for 3m, weaning over further 2m. NNS could be continued for 1 yr 2. Placebo nasal spray + 15 mg nicotine patches on same schedule
Outcomes	Mean (SD) weight gain (kg) in continuous abstainers at end of treatment (email communication) and 12m (email communication) (Validation: CO<11ppm)
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Computer-generated code at pharmacy
Allocation concealment?	Yes	"participants allocated their treatment by generated randomisation code at a local pharmacy"
Blinding? All outcomes	Yes	Double blind

2 NRT Bohadana 2000

Methods	Country: France Recruitment: community volunteers
Participants	400 smokers, 18-70 yrs, 51% female, Av cpd: Group 1 26.1, Group 2 23.5; FTND>6
Interventions	1: Nicotine inhaler, 26wks, combined with nicotine patch (15 mg/16hr) for first 6wks, placebo patch for next 6wks 2: Nicotine inhaler, 26wks, placebo patch for first 12wks All received brief counselling and support from investigator at each visit
Outcomes	Mean (SD) weight gain (kg) in prolonged abstainers at end of treatment (email communication) and 12 m (email communication) (Validation: CO<10ppm)
Notes	Prolonged abstinence defined as validated self report from 2 wks

2 NRT Bohadana 2000 (*Continued*)

Risk of bias		
Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Computer-generated code
Allocation concealment?	Yes	"sealed randomisation envelopes were provided for each subject and were held by the hospital pharmacy, which was responsible for dispensing medication"
Blinding? All outcomes	Yes	Double blind

2 NRT CEASE 1999

Methods	Country: Multicentre - 36 clinic centres in 17 European countries Recruitment: community volunteers
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 15mg or 25mg (16hr), duration of active treatment 28 wks (incl 4 wk fading) or 12 wks (incl 4 wk fading) 1. 25mg patch for 28 wks (L-25) 2. 25mg patch for 12 wks (S-25) 3. 15mg patch for 28 wks (L-15) 4. 15mg patch for 12 wks (S-15) 5. Placebo All participants received brief advice & self-help brochure
Outcomes	Mean (SD) weight gain (kg) in prolonged abstainers at end of treatment (email communication) and 12m (email communication) (validation: CO <10ppm)
Notes	Prolonged abstinence defined as validated self report from 2wks. Doses and durations collapsed in main analyses.

Risk of bias		
Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Stratified only by centre
Allocation concealment?	Yes	"A computer-generated allocation list was prepared centrally and allocated subjects to treatment numbers"

2 NRT CEASE 1999 (*Continued*)

Blinding? All outcomes	Yes	Double blind

2 NRT Cooper 2005

Methods	Country: USA Recruitment: community volunteers
Participants	439 weight concerned female smokers (≤10 cpd) Av.age 38, av.cpd 23, av. baseline weight 64-66kg
Interventions	1. Phenylpropanolamine (PPA) gum 8.33mg 16 pieces/d 8wks, weaning last 3 wks 2. Nicotine gum (2mg), 10-12 pieces/day recommended, for 8 wks, weaning last 3 wks 3. Placebo gum All participants received 13x1hr weekly cognitive behavioural group sessions focused on smoking and weight. Participants cut down wks 1-4 by 25% and quit wk 5
Outcomes	1. PP abstinence at 12m (Validation: CO<10ppm) 2. Mean (SD) weight change (kg) in abstainers at 6m and 12m
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

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Method not stated
Allocation concealment?	Unclear	Not described
Blinding? All outcomes	Yes	All group facilitators and participants were blind to treatment conditions

2 NRT Dale 1995

Methods	Country: USA Recruitment: community volunteers and smoking clinic attenders
Participants	71 smokers stratified according to light, moderate and heavy smoking rates. 56% female, av.age 48, av.cpd 26, av weight 79.4kg
Interventions	1. 11mg/24hr nicotine patch 2. 22mg/24hr nicotine patch 3. 44mg/24hr nicotine patch 4. Placebo patch for 1 wk followed by 11 or 22mg patch for 7 wks

2 NRT Dale 1995 (*Continued*)

	Duration of patch use 8 wks. High level of support including 6 day inpatient stay
Outcomes	Mean (SD) weight gain (kg) in continuous abstainers at end of treatment (email communication) and 12m (email communication) (Validation: Blood cotinine)
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	Method not stated
Allocation concealment?	Unclear	Not described
Blinding? All outcomes	Yes	Double blind

2 NRT Ehrsam 1991

Methods	Country: Switzerland Recruitment: university (primary care)
Participants	112 smokers, av.age 26, av.cpd 23
Interventions	1. Nicotine patch (21 or 14mg/24hr, 9 wks, tapered) 2. Placebo patch
Outcomes	Mean (SD) weight change (kg) in abstainers at the end of treatment
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	Not described
Allocation concealment?	Unclear	Not described
Blinding? All outcomes	Unclear	Not described

2 NRT Fiore 1994A

Methods	Country: USA Recruitment: community volunteers
Participants	88 smokers, av cpd 28-31, av age 42-44yrs, av weight 79-81kg
Interventions	1. Nicotine patch (22mg/24hr, 8 wks, no weaning) 2. Placebo patch All participants received intensive group counselling.
Outcomes	Mean (SD) weight change in point prevalence abstainers at end of treatment (email communication) (Validation: CO <10ppm)
Notes	PPA was defined as validated abstinence for 7 days prior to measurement. Different participants to Fiore 1994B added in separately in the main comparison

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Pregenerated computer sequence
Allocation concealment?	Unclear	Not described
Blinding? All outcomes	Yes	Double blind

2 NRT Fiore 1994B

Methods	Country: USA Recruitment: community volunteers
Participants	112 smokers, av age 43-45yrs, av weight 72-73kg
Interventions	1. Nicotine patch (22mg/24hr, 6 wks incl weaning) 2. Placebo patch All participants received 8x weekly 10-20 min individual counselling
Outcomes	Mean (SD) weight change in point prevalence abstainers at end of treatment (email communication) (Validation: CO <10ppm)
Notes	PPA was defined as validated abstinence for 7 days prior to measurement. Different participants to Fiore 1994A added in separately in the main comparison

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Pregenerated computer sequence

2 NRT Fiore 1994B (*Continued*)

Allocation concealment?	Unclear	Not described
Blinding? All outcomes	Yes	Double blind

2 NRT Garvey 2000

Methods	Country: USA Recruitment: community volunteers
Participants	608 smokers, aged>20 51% female, av.cpd 23, av weight (males) 80-81kg, av weight (female) 64-69
Interventions	1. 4mg nicotine gum (recommended 9-15 pieces), weaning from 2m + weaning 2. 2mg nicotine gum, use as 1. 3. 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≤ 8ppm)
Notes	Prolonged abstinence defined as participants who had not returned to smoking for 7 or more consecutive days or episodes 4 + 2mg doses combined in main comparison.

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Method not stated, stratified by high- and low-dependence
Allocation concealment?	Unclear	Not described
Blinding? All outcomes	Yes	Double blind

2 NRT Gourlay 1995

Methods	Country: Australia Recruitment: community volunteers
Participants	629 smokers (>15 cpd) who had relapsed after transdermal nicotine and behavioural counselling in an earlier phase of the study. Minimal additional support

2 NRT Gourlay 1995 (*Continued*)

Interventions	1. Nicotine patch 30cm^2 (21mg/24 hr) for 4 wks, 20cm^2 (14mg/24 hr) for 4 wks, 10cm^2 (7mg/24 hrs) for 4 wks. 2. Placebo patch
Outcomes	Mean (SD) weight change (kg) in continuous abstainers at end of treatment (Validation: expired CO<9ppm)
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Yes	Treatments were randomly allocated to study numbers by using a 1:1 ratio within blocks of 10
Allocation concealment?	Unclear	Not described
Blinding? All outcomes	Yes	Double blind

2 NRT Gross 1995

Methods	Country: USA Recruitment: community volunteers
Participants	177 smokers, 51% female, av. age 42, av.cpd 33, av. FTND score 7.8
Interventions	1. Nicotine gum (2mg), tapered from wk 12. Active gum groups further randomized to chew 7, 15 or 30 pieces of gum per day. 2. 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≤10ppm)
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

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	Method not stated
Allocation concealment?	Unclear	Not described

2 NRT Gross 1995 (*Continued*)

Blinding? All outcomes	Yes	Not possible

2 NRT Hjalmarson 1984

Methods	Country: Sweden Recruitment: smoking cessation clinic
Participants	206 smokers, 56% female, av.age 42, av. cpd 24
Interventions	1. Nicotine gum (2mg) (no restrictions on amount or duration of use) 2. Placebo gum All participants received 6 group sessions of SC behavioural support in 6wks
Outcomes	Mean (SD) weight gain (kg) in continuous abstainers at 6m (email communication)(Validation: CO)
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Randomized by therapy group.
Allocation concealment?	Unclear	Not described
Blinding? All outcomes	Unclear	Unclear if enroller blind, but therapists blind

2 NRT Hjalmarson 1994

Methods	Country: Sweden Recruitment: smoking cessation clinic
Participants	248 smokers, 57% female, av.age 45, av. cpd 22, av weight (male) 77-83kg, av weight (female) 64-66kg
Interventions	1. Nicotine nasal spray (0.5 mg/spray) used as required up to 40 mg/day for up to 1 yr 2. Placebo spray All participants received 8x45-60 min group sessions over 6 wks with clinical psychologist
Outcomes	Mean (SD) weight gain (kg) in continuous abstainers at 12m (Validation: CO<10ppm)
Notes	

Risk of bias		
Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Method not described
Allocation concealment?	Unclear	Treatment allocater not blinded if more than 1 participant from the same household so that they could be given same medication
Blinding? All outcomes	Yes	Therapists and participants

2 NRT Hjalmarson 1997

Methods	Country: Sweden Recruitment: smoking cessation clinic
Participants	247 smokers, 64% female, av.age 48, av.cpd 21
Interventions	1. Nicotine Inhaler (recommended minimum 4/day, tapering after 3m, use permitted to 6m) 2. Placebo inhaler All participants attended 8 group meetings over 6 wks
Outcomes	Mean (SD) weight change (kg) in prolonged abstainers end of treatment and 12m (Validation: CO<10ppm)
Notes	Prolonged abstainers defined as validated self reported abstinence from wk 2

Risk of bias		
Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Participants assigned a number on attending first group session. Numbers on a list randomizing to medication. Participants from the same household randomized to same treatment
Allocation concealment?	Unclear	Treatment allocater not blinded if more than 1 participant from the same household so that they could be given same medication
Blinding? All outcomes	Yes	Participant and therapist blinded

2 NRT Lerman 2004

Methods	Country: USA Recruitment: community volunteers and referrals
Participants	350 smokers (includes 51 who withdrew before treatment) 54% female, av.age 46, av. cpd 21
Interventions	1. Nicotine patch (21 mg/24hr) for 8 wks incl tapering 2. Nicotine nasal spray (8-40 doses/day, max 5/hr) for 8 wks, tapering over final 4 wks All participants received 7x90 min behavioural group counselling sessions. TQD in wk 3
Outcomes	Mean (SD) weight change (kg) in unvalidated continuous abstainers
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Yes	Computer-generated, operated by data manager.
Allocation concealment?	Yes	After allocation only outcome assessors blind

2 NRT Pirie 1992

Methods	Country: USA Recruitment: community volunteers
Participants	417 women smokers. Av cpd 25-27. av BMI 23-25
Interventions	1. Group therapy 8 wks 2. Group therapy plus weight control programme 8 wks 3. Group therapy plus nicotine gum 8 wks 4. Group therapy plus weight control programme and nicotine gum 8 wks Gum type: 2mg ad lib 8 wk treatment period + 3m supply
Outcomes	Mean (SD) weight change (kg) in continuous abstainers end of treatment, 6 and 12m (Validation: expired CO $\leq$10ppm)
Notes	Group 3 compared with group 1. Group 1, 3 and 4 compared in first part of review

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	Not described
Allocation concealment?	Unclear	Not described

2 NRT Pirie 1992 (*Continued*)

Blinding? All outcomes	Unclear	Not described

2 NRT Puska 1995

Methods	Country: Finland Recruitment: community volunteers
Participants	300 volunteers aged 20-65, smoking >10 cpd for >3 yrs, no serious illness
Interventions	1. Nicotine patch (15mg/16hrs, 12 wks+ 6 wks taper) plus nicotine gum (2mg at least 4 daily) 2. Placebo patch plus nicotine gum (same regimen)
Outcomes	Mean (SD) weight gain (kg) in prolonged abstainers at end of treatment (email communication) and 12m (email communication) (Validation: CO<10ppm)
Notes	Prolonged abstinence defined as verified continuously lapse-free abstinence after wk 1

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Not described
Allocation concealment?	Unclear	Not described
Blinding? All outcomes	Yes	Double blind

2 NRT Richmond 1994

Methods	Country: Australia Recruitment: community volunteers
Participants	315 smokers, av. cpd 29.
Interventions	1. Nicotine patch (24 hr, 22mg/24 hr, 10 wks incl tapering) 2. Placebo patch All participants received group smoking cessation behavioural support
Outcomes	Mean (SD) weight gain (kg) in continuous and prolonged abstainers at end of treatment (email communication), 6m (email communication) and 12m (email communication) (Validation: expired CO)
Notes	Prolonged abstainers were defined as continuous abstinence for a sustained period preceding the assessment point at 12m

2 NRT Richmond 1994 (*Continued*)

Risk of bias		
Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Not described
Allocation concealment?	Unclear	Not described
Blinding? All outcomes	Yes	Double blind

2 NRT Sachs 1993

Methods	Country: USA Recruitment: community volunteers
Participants	220 adult smokers. Av. cpd 28-9, av weight 72-76kg
Interventions	1. Nicotine patch (15mg/16hr, 12 wks + 6 wks tapering) 2. 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 <10ppm)
Notes	

Risk of bias		
Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Method not stated
Allocation concealment?	Unclear	Not described
Blinding? All outcomes	Yes	Double blind

2 NRT Shiffman 2002A

Methods	Country: USA & UK (15 sites) Recruitment: community volunteers, low dependence (time to first cigarette >30mins)
Participants	917 smokers, 58% female, av age 41, av cpd 17-18, av weight 74-76kg
Interventions	1. Nicotine lozenge, 2mg. 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. Placebo lozenge, same schedule

2 NRT Shiffman 2002A (*Continued*)

	All participants received brief advice at 4 visits.	
Outcomes	Mean (SD) weight gain (kg) in prolonged abstainers at end of treatment (email communication), 6m (email communication) and 12m (email communication) (Validation: CO≤10ppm)	
Notes	Prolonged abstinence defined as sustained from 2 wks, no slips allowed	
Risk of bias		
Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Method not stated
Allocation concealment?	Unclear	Not described
Blinding? All outcomes	Yes	Double blind

2 NRT Shiffman 2002B

Methods	Country: USA & UK (15 sites) Recruitment: community volunteers, high dependence (time to 1st cigarette <30mins)	
Participants	901 smokers, 55% female, av age 43-44, av cpd 25-26	
Interventions	1. 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 2. Placebo lozenge, same schedule	
Outcomes	Mean (SD) weight gain (kg) in prolonged abstainers at end of treatment (email communication), 6m (email communication) and 12m (email communication) (Validation: CO≤10ppm)	
Notes		
Risk of bias		
Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Method not stated
Allocation concealment?	Unclear	Not described
Blinding? All outcomes	Yes	Double blind

2 NRT Stapleton 1995

Methods	Country: UK Recruitment: General practice patients
Participants	1200 smokers, av. cpd 23-4, av weight 71-72kg
Interventions	1. Nicotine patch standard dose (15mg/16 hr for 18 wks) 2. Nicotine patch with dose increase to 25mg at 1 wk if required 3. Placebo patch group The nicotine patch groups were further randomized to gradual tapering or abrupt withdrawal from wk 12 All participants received physician advice & 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<10ppm)
Notes	Prolonged abstinence defined as validated self-reported abstinence from wk 2. The dose increase after 1 wk did not affect cessation, 1+2 vs 3 in main comparison

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Computer-generated list
Allocation concealment?	Yes	"Study subjects were assigned a treatment according to a computer generated list compiled in blocks of six"
Blinding? All outcomes	Yes	Double blind

2 NRT Sutherland 1992

Methods	Country: UK Recruitment: Smoking cessation clinic patients
Participants	227 male and female smokers. Av. cpd 25-27, av age 38-41yrs, av weight women 62-64kg, av weight men 75-77kg
Interventions	1. Nicotine nasal spray, maximum 40 mg/day 2. Placebo spray All participants received 4 wks of group support
Outcomes	Mean (SD) weight change (kg) in prolonged abstainers at 12 months (Validation: CO<10ppm)
Notes	Prolonged abstinence defined as validated self-reported no smoking from the start of the last wk of group treatment to the 12m follow up

2 NRT Sutherland 1992 (*Continued*)

Risk of bias		
Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Drew card with A or P for active or placebo allocation
Allocation concealment?	Unclear	Not described
Blinding? All outcomes	Yes	"Subjects and therapist were blind to spray assignment"

2 NRT TNSG 1991

Methods	Country: USA (9 sites) Recruitment: community volunteers (treated at smoking cessation clinics)
Participants	808 smokers 60% female, av.age 43, av. cpd 31, av weight 72.4 kg
Interventions	1. Nicotine patch (21mg /24 hr, 6 wks+) 2. Nicotine patch 14mg 3. Placebo patch All participants received group smoking cessation behavioural support
Outcomes	Mean (SD) weight change (kg) in continuous abstainers at end of treatment (6 wks) (Validation: CO<9ppm)
Notes	2 trials pooled and data relating to a 7mg patch group used in only 1 trial omitted

Risk of bias		
Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Unclear	Method not stated
Allocation concealment?	Unclear	Not described
Blinding? All outcomes	Yes	Double blind

2 NRT Tonnesen 1991

Methods	Country: Denmark Recruitment: community volunteers
Participants	289 smokers 70% female, av.age 45, av. cpd 22
Interventions	1. Nicotine patch (15mg/16 hr for 12 wks with tapering) 2. Placebo patch All participants receive brief behaviour support at clinic visits
Outcomes	Mean (SD) weight gain (kg) in prolonged abstainers at end of treatment (email communication) and 12m (email communication) (validation: CO≤10ppm)
Notes	Prolonged abstinence was defined as validated self report abstinence after 1 wk of quitting

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	According to a computer-generated randomization code
Allocation concealment?	Yes	"packages labelled with consecutive numbers from computer-generated random code"
Blinding? All outcomes	Yes	Double blind

2 NRT Tonnesen 1993

Methods	Country: Denmark Recruitment: community volunteers
Participants	286 smokers, av cpd 20 60% female, av.age 39
Interventions	1. Nicotine inhaler (2-10/day) up to 6m 2. Placebo inhaler All participants received brief advice at 8 clinic visits, 0, 1, 2, 3, 6,12, 24, 52 wks)
Outcomes	Mean (SD) weight gain (kg) in continuous abstainers at end of treatment (email communication) and 12m (email communication) (Validation: expired CO<10ppm)
Notes	

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Computer-generated randomization code

2 NRT Tonnesen 1993 (*Continued*)

Allocation concealment?	Yes	"participants were randomly assigned according to code generated by a computer"
Blinding? All outcomes	Yes	Double blind

2 NRT Wallstrom 2000

Methods	Country: Sweden Recruitment: community volunteers
Participants	247 smokers (≥10 cpd) 59% female, av.age 45, av. cpd 18-20, av weight (male) 80-81kg, av weight (female) 66-67kg
Interventions	1. Nicotine sublingual tablet 2mg. 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 2. Placebo tablet All participants received brief 5 mins counselling at study visits
Outcomes	Mean (SD) weight change (kg) in prolonged abstainers at 12m (Validation: CO<10ppm)
Notes	Prolonged abstinence defined as complete abstinence from wk 2

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Computer assignment
Allocation concealment?	Yes	"Subjects were randomised to receive either active or placebo treatment using a computer program"
Blinding? All outcomes	Yes	Double blind

2 VA Aubin 2008

Methods	Country: Belgium, France, Netherlands, UK, USA Recruitment: smoking cessation clinics or community volunteers
Participants	Healthy adults, Mean age 42.9 yr, 50.8% female, mean cpd 22.7
Interventions	1. Varenicline 1mg x2/day for 12 wks, titrated 1st wk. 2. Nicotine patch (21mg wks 2-6, 14mg wks 7-9, 7mg wks 10-11). No placebo control group. All participants received *Clearing the Air* S-H booklet at baseline, and brief counselling (≤10 mins)

2 VA Aubin 2008 (*Continued*)

	at each clinic visit or by phone
Outcomes	Mean (SD) weight change (kg) in prolonged abstainers at end of treatment (email communication) (Validation: CO≤10ppm)
Notes	Prolonged abstainers defined as completely quit from wk 9.

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Central computer-generated sequence.
Allocation concealment?	Yes	Central allocation
Blinding? All outcomes	No	open-label design

2 VA Gonzales 2006

Methods	Country: USA Recruitment: community volunteers
Participants	1025 smokers 55% female (placebo), 48% female (Bup); av age 45, av cpd not specified
Interventions	1. Varenicline 1mg x2/day for 12 wks 2. Bupropion 300 mg/day for 12 wks 3. Placebo All participants received brief individual counselling at visits wk1-7, 9, 12, + telephone counselling at 4 and 5m
Outcomes	Mean (SD) weight change (kg) in prolonged abstainers at end of treatment (validation: CO<10ppm)
Notes	Prolonged abstinence defined as complete abstinence from weeks 9-12 Arm 1 compared with 3 (same study as 3 AD Gonzales)

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Computer generated sequence 1:1:1
Allocation concealment?	Yes	Participants were randomized according to a pre-defined central computer sequence
Blinding? All outcomes	Yes	Double blind

2 VA Jorenby 2006

Methods	Country: USA, multicentre Recruitment: community volunteers
Participants	1027 smokers, 41% female, av age 42, av cpd 22
Interventions	1. Bupropion 300mg for 12 wks + placebo varenicline 2. Varenicline 2mg for 12 w + placebo bupropion 3. Placebo bupropion + placebo varenicline All participants recieved brief (<10 min) 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 gain (kg) in prolonged abstainers at end of treatment (validation: CO<10ppm)
Notes	Prolonged abstinence defined as validated self-reported abstinence wks 9-12. Arm 1 and 3 in main comparison

Risk of bias

Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Centralised, computer-generated
Allocation concealment?	Yes	"SItes used an electronic system to assign participants to treatment"
Blinding? All outcomes	Yes	Double blind

2 VA Nakamura 2007

Methods	Country: Japan Recruitment:community volunteers
Participants	619 healthy smokers, aged 20-75, smoking ≥10cpd. 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	1. Varenicline 0.25mg x 2/day 12 wks 2. Varenicline 0.50mg x 2/day 12 wks 3. Varenicline 1.00mg x 2/day 12 wks 4. 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 gain (kg) in prolonged abstainers at end of treatment (validation: CO≤10ppm)
Notes	Prolonged abstinence defined as continuous abstinence during wks 9-12

2 VA Nakamura 2007 (*Continued*)

Risk of bias		
Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Computer-generated random number lists
Allocation concealment?	Yes	'randomised to 1 of the 4 treatment groups in a 1:1:1:1 ratio using a central procedure'
Blinding? All outcomes	Yes	'double-blinding of subjects and investigators was maintained throughout the study'

2 VA Nides 2006

Methods	Country: USA, multi-centre, 7 sites Recruitment: Volunteers (phase II study)
Participants	638 smokers, 51% female, av age 41, av cpd 20, av BMI 25-27
Interventions	1. Varenicline 0.3mg 1/d for 6 wks, + 1wk placebo 2. Varenicline 1.0mg 1/d for 6 wks, + 1wk placebo 3. Varenicline 1.0mg 2/d for 6 wks, + 1wk placebo 4. Bupropion 150mg 2/d (titrated in wk 1) for 7 wks 5. 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 gain (kg) in prolonged abstainers at end of treatment (email communication)
Notes	Prolonged abstinence defined as self-reported quit for 4 wks during treatment period (not validated) . Arms 1-3 and 5 in main comparison (same study as 3 AD Nides 2006)

Risk of bias		
Item	**Authors' judgement**	**Description**
Adequate sequence generation?	Yes	Computer-generated list
Allocation concealment?	Yes	"Investigators assigned medication to subjects in numerical order of acceptance into the study" from computer generated list"
Blinding? All outcomes	Yes	Double blind

2 VA Oncken 2006

Methods	Country: USA Recruitment: community volunteers
Participants	647 smokers, 50.5% female, av cpd 21, av age 42-44yrs, av BMI 26-28
Interventions	1. Varenicline 0.5mg nontitrated (2/d for 12 wks) 2. Varenicline 0.5mg titrated (wk1 1/d, wks 2-12 2/d) 3. Varenicline 1.0mg nontitrated (2/d for 12 wks) 4. Varenicline 1.0mg titrated (0.5mg 1/d for 3 days, 0.5mg 2/d for 4 days, 1.0mg 2/d wks 2-12) 5. Placebo tablets 2/d 12 wks All participants received S-H booklet at baseline, + brief (≤10mins) counselling at weekly clinic visits throughout treatment phase
Outcomes	Mean (SD) weight gain (kg) in continuous abstainers at end of treatment (validation: CO≤10ppm)
Notes	

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Unclear	Not described
Allocation concealment?	Unclear	Not described
Blinding? All outcomes	Yes	"Subjects and investigators were blinded to the study drug treatment assignment"

2 VA Tonstad 2006

Methods	Country: USA (6 centres) and 'international' (18 centres, across Canada, Czech Republic, Denmark, Norway, Sweden, UK) Recruitment: smoking cessation clinics
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	1. Varenicline 1mg x2/day for 11 wks after 1wk titrated dosage 2. 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 gain (kg) in continuous abstainers at 6m (validation: CO≤10ppm)
Notes	Continuous abstinence was defined as validated complete abstinence during wks13-24

Risk of bias

2 VA Tonstad 2006 (*Continued*)

Item	Authors' judgement	Description
Adequate sequence generation?	Yes	Computer-generated lists stratified by centre, x4 random block design
Allocation concealment?	Yes	computer-generated sequence used for allocation of participants
Blinding? All outcomes	Yes	Double blind

2 VA Tsai 2008

Methods	Country: Taiwan and Korea Recruitment: community volunteers
Participants	250 healthy adult volunteers, motivated to quit, aged 18- 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	1. Varenicline 1.0mg x 2/day 12 wks 1st wk titrated 2. 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 gain (kg) in prolonged abstainers at end of treatment (validated: CO≤10ppm)
Notes	Prolonged abstinence is defined as validated complete abstinence during wks 9-12

Risk of bias

Item	Authors' judgement	Description
Adequate sequence generation?	Yes	Permutated blocks (block=4)
Allocation concealment?	Yes	web- and telephone-based assignment
Blinding? All outcomes	Yes	Subjects, investigators, study staff and sponsor personnel blind to treatment

BMI: body mass index
CO: carbon monoxide
cpd: cigarettes per day
d: day
FTND: Fagerström test for Nicotine Dependence
m: month
PPA: point prevalence abstinence

SC: smoking cessation
TQD: target quit date
wk: week

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

Study	Reason for exclusion
1 Hughes 1997	Effect of NRT on post-cessation weight gain, not identified in NRT parent review
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 Lagrue 1994	Intervention on overweight patients only
1 Leischow 1992	Unable to obtain full data
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 Toll 2008	Participants not randomized to experimental or control conditions
2 AD Dalsgareth 2004	Unable to obtain full data
2 AD Evins 2001	Unable to obtain full data
2 AD Hays 2001	Unable to obtain full data
2 AD Tonnesen 2003	Unable to obtain full data
2 AD Tonstad 2003	Unable to obtain full data
2 AD Uyar 2005	Unable to obtain full data
2 NRT Blondal 1997	Unable to obtain full data
2 NRT Glover 2002	Unable to obtain full data
2 NRT Jorenby 1999	Unable to obtain full data
2 NRT Killen 1999	Unable to obtain full data
2 NRT Kornitzer 1987	Unable to obtain full data

(*Continued*)

2 NRT Roto 1987	Unable to obtain full data

Characteristics of studies awaiting assessment *[ordered by study ID]*

1 Ames 2007

Methods	
Participants	
Interventions	
Outcomes	
Notes	

1 Chaney 2008

Methods	
Participants	
Interventions	
Outcomes	
Notes	

1 King 2006

Methods	
Participants	
Interventions	
Outcomes	
Notes	

1 Levine 2007

Methods	
Participants	
Interventions	
Outcomes	
Notes	

1 Spring 1991

Methods	
Participants	
Interventions	
Outcomes	
Notes	

2 AD Spring 2004

Methods	Country: USA Recruitment: community volunteers
Participants	247 smokers, >= 10 CPD 54% F, av age 44, av CPD 23, 44% history of MDD
Interventions	1. Fluoxetine 60 mg for 12w 2. Placebo Both arms: group behavioural counselling, 9 meetings over 12w
Outcomes	
Notes	

2 EX Kinnunen 2008

Methods	Country: USA Randomization: Method not stated
Participants	182 women, mean age 39, mean cpd 19, exercise < 3 times a week
Interventions	(a) Intervention 1: CV equipment, individual, facility, 40 min, 60-80% HR max (twice a week for 5 weeks, then once per week for 14 weeks) + CP (once a week for 19 weeks) + nicotine gum (b) Intervention 2: CP and nicotine gum as (a) + health education for same number of sessions as for exercise in (a) (c) Control: CP and nicotine gum as (a)

2 EX Kinnunen 2008 (*Continued*)

Outcomes	
Notes	

2 EX Prapavessis 2007

Methods	Country: NZ Randomization: Computer-generated
Participants	142 women, mean age 38, exercise < twice a week. (excludes 21 drop-outs)
Interventions	(a) Intervention 1: CV activity: various, group/facility, 45 min, 60-75% HR reserve, (3 times/week for 12 weeks) + CP (three times/week for 12 weeks). (b) Intervention 2: exercise as (a) plus nicotine patches (c) Intervention 3: Cognitive behavioural cessation programme three times/week for 12 weeks. (d) Intervention 4: as (c) plus nicotine patches. Exercise began before quit date
Outcomes	
Notes	

2 RM STRATUS-EU 2006

Methods	
Participants	
Interventions	
Outcomes	
Notes	

2 RM STRATUS-US 2006

Methods	
Participants	
Interventions	
Outcomes	
Notes	

2 RM STRATUS-WW 2005

Methods	
Participants	
Interventions	
Outcomes	
Notes	

2 VA Williams 2007

Methods	Country: USA and Australia
Participants	377 adult smokers, aged 18-75, smoking at least 10cpd. 49.9% male, 88.6% white, av cpd at baseline 23, mean Fagerstrom 5.5 in treatment group, 6.05 in control group
Interventions	1. Varenicline 1mg x2/day, titrated for first wk. 2. Placebo inactive tablets, same regimen All participants received S-H booklet *Clearing the Air*. Brief counselling (<=10 mins) at each visit. TQD was 1st day of wk 1 visit (7-10 days post-randomization)
Outcomes	
Notes	

DATA AND ANALYSES

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

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Abstinence at 6 months	3		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 Phenylpropanolamine gum versus placebo	1	295	Risk Ratio (M-H, Fixed, 95% CI)	1.38 [0.76, 2.53]
1.2 Ephedrine + Caffeine versus placebo	1	225	Risk Ratio (M-H, Fixed, 95% CI)	1.06 [0.53, 2.11]
1.3 Naltrexone versus placebo	1	385	Risk Ratio (M-H, Fixed, 95% CI)	0.91 [0.58, 1.43]
2 Abstinence at 12 months	3		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.1 Phenylpropanolamine gum versus placebo	1	295	Risk Ratio (M-H, Fixed, 95% CI)	1.48 [0.80, 2.73]
2.2 Ephedrine + Caffeine versus Placebo	1	225	Risk Ratio (M-H, Fixed, 95% CI)	1.44 [0.60, 3.48]
2.3 Naltrexone versus placebo	1	385	Risk Ratio (M-H, Fixed, 95% CI)	1.25 [0.67, 2.31]

Comparison 2. Pharmacological interventions versus placebo for post-cessation weight control: weight change

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean weight change (kg) at end of treatment	6		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
1.1 Dexfenfluramine versus placebo	1	33	Mean Difference (IV, Fixed, 95% CI)	-2.5 [-2.98, -2.02]
1.2 Fluoxetine versus placebo	1	25	Mean Difference (IV, Fixed, 95% CI)	-0.80 [-1.27, -0.33]
1.3 Phenylpropanolamine versus Placebo	3	112	Mean Difference (IV, Fixed, 95% CI)	-0.50 [-0.80, -0.20]
1.4 Ephedrine + Caffeine versus Placebo	1	40	Mean Difference (IV, Fixed, 95% CI)	-1.30 [-2.87, 0.27]
1.5 Naltrexone versus Placebo	1	157	Mean Difference (IV, Fixed, 95% CI)	-0.76 [-1.51, -0.01]
1.6 Naltrexone 25mg/day versus placebo	1	72	Mean Difference (IV, Fixed, 95% CI)	-1.2 [-2.10, -0.30]
2 Mean weight change (kg) at 6 months	2		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.1 Phenylpropanolamine versus Placebo	1	38	Mean Difference (IV, Fixed, 95% CI)	0.04 [-4.07, 4.15]
2.2 Ephedrine + caffine versus placebo	1	32	Mean Difference (IV, Fixed, 95% CI)	-0.70 [-2.72, 1.32]
3 Mean weight change (kg) at 12 months	2		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
3.1 Phenylpropanolamine versus placebo	1	38	Mean Difference (IV, Fixed, 95% CI)	-1.04 [-5.03, 2.95]

3.2 Ephedrine + Caffeine versus placebo	1	24	Mean Difference (IV, Fixed, 95% CI)	1.20 [-1.84, 4.24]

Comparison 3. Behavioural post cessation weight management interventions with/without pharmacotherapy versus control: smoking cessation

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Abstinence at end of treatment	4		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 Dietary and exercise advice versus no intervention	2	525	Risk Ratio (M-H, Fixed, 95% CI)	0.90 [0.76, 1.06]
1.2 Individual programme + advice versus no intervention	2	254	Risk Ratio (M-H, Fixed, 95% CI)	1.11 [0.84, 1.46]
1.3 Individual programme versus dietary + exercise advice	1	104	Risk Ratio (M-H, Fixed, 95% CI)	1.19 [0.78, 1.83]
1.4 VLCD + advice versus advice	1	287	Risk Ratio (M-H, Fixed, 95% CI)	1.40 [1.07, 1.85]
2 Abstinence at 6 months	3		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.1 Dietary and exercise advice versus no intervention	2	522	Risk Ratio (M-H, Fixed, 95% CI)	0.95 [0.72, 1.26]
2.2 Individual programme + advice versus no intervention	2	254	Risk Ratio (M-H, Fixed, 95% CI)	0.88 [0.54, 1.43]
2.3 Individual programme versus dietary + exercise advice	1	104	Risk Ratio (M-H, Fixed, 95% CI)	0.81 [0.40, 1.65]
3 Abstinence at 12 months	4		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
3.1 Dietary and exercise advice versus no intervention	2	522	Risk Ratio (M-H, Fixed, 95% CI)	0.66 [0.48, 0.90]
3.2 Individual programme + advice versus no intervention	2	254	Risk Ratio (M-H, Fixed, 95% CI)	0.79 [0.47, 1.33]
3.3 Individual programme versus dietary + exercise advice	1	104	Risk Ratio (M-H, Fixed, 95% CI)	0.96 [0.46, 2.02]
3.4 VLCD + advice versus advice	1	287	Risk Ratio (M-H, Fixed, 95% CI)	1.73 [1.10, 2.73]

Comparison 4. Behavioural post cessation weight management interventions including/not including exercise versus control: weight change

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean weight change (kg) at end of treatment	4		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
1.1 Dietary and exercise advice versus no intervention	2	140	Mean Difference (IV, Fixed, 95% CI)	-0.04 [-0.57, 0.50]

1.2 Individual programme + advice versus no intervention	2	90	Mean Difference (IV, Fixed, 95% CI)	-1.05 [-2.01, -0.09]
1.3 Individual programme versus dietary + exercise advice	1	47	Mean Difference (IV, Fixed, 95% CI)	-1.12 [-2.17, -0.07]
1.4 VLCD + advice versus advice	1	121	Mean Difference (IV, Fixed, 95% CI)	-3.7 [-4.82, -2.58]
2 Mean weight change (kg) at 12 months	4		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.1 Dietary and exercise advice versus no intervention	2	61	Mean Difference (IV, Fixed, 95% CI)	-0.21 [-2.28, 1.86]
2.2 Individual programme + advice versus no intervention	2	40	Mean Difference (IV, Fixed, 95% CI)	-2.58 [-5.11, -0.05]
2.3 Individual programme versus dietary + exercise advice	1	17	Mean Difference (IV, Fixed, 95% CI)	-2.49 [-5.51, 0.53]
2.4 VLCD + advice versus advice	1	62	Mean Difference (IV, Fixed, 95% CI)	-1.30 [-3.49, 0.89]

Comparison 5. CBT to accept moderate weight gain versus no behavioural weight advice: smoking cessation

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Abstinence at 6 months	1	147	Risk Ratio (M-H, Fixed, 95% CI)	1.81 [1.22, 2.70]
2 Abstinence at 12 months	1	147	Risk Ratio (M-H, Fixed, 95% CI)	2.43 [1.19, 4.95]

Comparison 6. CBT to accept moderate weight gain versus no behavioural weight advice: weight change

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean weight change (kg) at end of treatment	1	63	Mean Difference (IV, Fixed, 95% CI)	-1.1 [-1.82, -0.38]
2 Mean weight change (kg) at 6 months	1	29	Mean Difference (IV, Fixed, 95% CI)	-3.5 [-6.05, -0.95]
3 Mean weight change (kg) at 12 months	1	22	Mean Difference (IV, Fixed, 95% CI)	-5.20 [-9.28, -1.12]

Comparison 7. All types of antidepressant versus placebo for smoking cessation: weight change

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean weight change (kg) at end of treatment	7		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
1.1 Bupropion versus placebo	6	774	Mean Difference (IV, Fixed, 95% CI)	-1.11 [-1.47, -0.76]
1.2 Fluoxetine versus placebo	1	119	Mean Difference (IV, Fixed, 95% CI)	-1.3 [-1.91, -0.69]
2 Mean weight change (kg) at end of treatment: dose response	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.1 Bupropion: 300mg/day v 150mg/dayplacebo	1	44	Mean Difference (IV, Fixed, 95% CI)	-0.60 [-1.89, 0.69]
2.2 Bupropion: 300mg/day v 100mg/dayplacebo	1	37	Mean Difference (IV, Fixed, 95% CI)	-0.60 [-1.86, 0.66]
3 Mean weight change (kg) at 6 months	4	305	Mean Difference (IV, Fixed, 95% CI)	-0.19 [-1.10, 0.71]
3.1 Bupropion versus placebo	2	181	Mean Difference (IV, Fixed, 95% CI)	-0.58 [-2.16, 1.00]
3.2 Fluoxetine versus placebo	1	81	Mean Difference (IV, Fixed, 95% CI)	0.43 [-0.75, 1.61]
3.3 Fluoxetine + NRT versus placebo	1	43	Mean Difference (IV, Fixed, 95% CI)	-3.07 [-6.20, 0.06]
4 Mean weight change (kg) at 6 months: dose response	3		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
4.1 Bupropion: 300mg/day v 150mg/day	1	40	Mean Difference (IV, Fixed, 95% CI)	0.10 [-2.76, 2.96]
4.2 Bupropion: 300mg/day v 100mg/day	1	29	Mean Difference (IV, Fixed, 95% CI)	-2.10 [-6.22, 2.02]
4.3 Fluoxetine: 40mg v 20mg	1	34	Mean Difference (IV, Fixed, 95% CI)	0.47 [-1.82, 2.76]
4.4 Fluoxetine: 60mg v 30mg	1	49	Mean Difference (IV, Fixed, 95% CI)	3.00 [1.67, 4.33]
5 Mean weight change (kg) at 12 months	4		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
5.1 Bupropion versus placebo	4	252	Mean Difference (IV, Fixed, 95% CI)	-0.38 [0.00, 1.24]
6 Mean weight change (kg) at 12 months: dose response	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
6.1 Bupropion: 300mg/day v 150mg/day	1	33	Mean Difference (IV, Fixed, 95% CI)	0.20 [-4.81, 5.21]
6.2 Bupropion: 300mg/day v 100mg/day	1	24	Mean Difference (IV, Fixed, 95% CI)	-2.0 [-8.04, 4.04]

Comparison 8. Exercise interventions for smoking cessation: weight change

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

2 Mean weight change (kg) at 12 months	3	182	Mean Difference (IV, Fixed, 95% CI)	-2.07 [-3.78, -0.36]
2.1 Exercise + SC versus SC only	3	182	Mean Difference (IV, Fixed, 95% CI)	-2.07 [-3.78, -0.36]

Comparison 9. All types of NRT versus placebo for smoking cessation: weight change

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean weight change (kg) at end of treatment	19	2600	Mean Difference (IV, Fixed, 95% CI)	-0.69 [-0.88, -0.51]
1.1 Gum versus placebo	4	345	Mean Difference (IV, Fixed, 95% CI)	-0.58 [-1.02, -0.13]
1.2 Patch versus placebo	10	1619	Mean Difference (IV, Fixed, 95% CI)	-0.82 [-1.06, -0.58]
1.3 Inhaler versus placebo	2	111	Mean Difference (IV, Fixed, 95% CI)	-0.37 [-1.19, 0.45]
1.4 Sub-lingual tablet versus placebo	2	478	Mean Difference (IV, Fixed, 95% CI)	-0.48 [-0.99, 0.03]
1.5 Intranasal spray (+ patch) versus placebo	1	47	Mean Difference (IV, Fixed, 95% CI)	0.90 [-1.54, 3.34]
2 Mean weight change (kg) at end of treatment: patch v spray	1	154	Mean Difference (IV, Fixed, 95% CI)	-0.30 [-1.76, 1.16]
3 Mean weight change (kg) at end of treatment: dose response	4		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
3.1 4mg vs 2mg gum	1	161	Mean Difference (IV, Fixed, 95% CI)	-0.10 [-0.61, 0.41]
3.2 22mg vs 11mg patch	1	15	Mean Difference (IV, Fixed, 95% CI)	-0.40 [-2.65, 1.85]
3.3 44mg vs 22mg patch	1	24	Mean Difference (IV, Fixed, 95% CI)	-0.20 [-1.99, 1.59]
3.4 25mg patch vs 15mg patch- 8 week treatment course	1	497	Mean Difference (IV, Fixed, 95% CI)	0.40 [0.04, 0.76]
3.5 25mg patch vs 15mg patch- 22 weeks treatment	1	299	Mean Difference (IV, Fixed, 95% CI)	0.20 [-0.57, 0.97]
3.6 15x2mg gum vs 7x2mg gum	1	24	Mean Difference (IV, Fixed, 95% CI)	1.59 [-0.27, 3.45]
3.7 30x2mg gum vs 15x2mg gum	1	18	Mean Difference (IV, Fixed, 95% CI)	-0.27 [-1.83, 1.29]
4 Mean weight change (kg) at 6 months	9	771	Mean Difference (IV, Fixed, 95% CI)	-0.37 [-0.88, 0.14]
4.1 Gum versus placebo	2	103	Mean Difference (IV, Fixed, 95% CI)	-0.83 [-2.35, 0.69]
4.2 Patch versus placebo	2	115	Mean Difference (IV, Fixed, 95% CI)	-1.30 [-2.83, 0.22]
4.3 Patch (+ gum) versus placebo	1	72	Mean Difference (IV, Fixed, 95% CI)	-0.5 [-1.94, 0.94]
4.4 Patch (+ inhaler) versus placebo	1	95	Mean Difference (IV, Fixed, 95% CI)	0.40 [-0.77, 1.57]
4.5 Inhaler versus placebo	1	57	Mean Difference (IV, Fixed, 95% CI)	-0.60 [-1.98, 0.78]
4.6 Sub-lingual tablet versus placebo	2	329	Mean Difference (IV, Fixed, 95% CI)	-0.19 [-1.09, 0.72]
5 Mean weight change (kg) at 6 months: patch v spray	1	103	Mean Difference (IV, Fixed, 95% CI)	2.0 [-0.72, 4.72]
6 Mean weight change (kg) at 12 months	15	1334	Mean Difference (IV, Fixed, 95% CI)	-0.42 [-0.92, 0.08]

6.1 Gum versus placebo	1	49	Mean Difference (IV, Fixed, 95% CI)	-0.07 [-3.07, 2.93]
6.2 Patch versus placebo	4	641	Mean Difference (IV, Fixed, 95% CI)	-0.13 [-0.96, 0.70]
6.3 Patch (+ inhaler) versus placebo	1	67	Mean Difference (IV, Fixed, 95% CI)	-0.30 [-1.83, 1.23]
6.4 Patch (+ gum) versus placebo	1	62	Mean Difference (IV, Fixed, 95% CI)	-0.60 [-2.40, 1.20]
6.5 Intranasal spray versus placebo	2	79	Mean Difference (IV, Fixed, 95% CI)	-1.45 [-3.26, 0.35]
6.6 Intranasal spray (+ patch) versus placebo	1	43	Mean Difference (IV, Fixed, 95% CI)	-1.80 [-4.80, 1.20]
6.7 Inhaler versus placebo	2	90	Mean Difference (IV, Fixed, 95% CI)	-1.03 [-2.23, 0.17]
6.8 Sub-lingual tablet versus placebo	3	303	Mean Difference (IV, Fixed, 95% CI)	0.27 [-0.99, 1.54]
7 Mean weight change (kg) at 12 months: dose response	2		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
7.1 22mg patch vs 11mg	1	7	Mean Difference (IV, Fixed, 95% CI)	-3.90 [-10.74, 2.94]
7.2 44mg patch vs 11mg	1	12	Mean Difference (IV, Fixed, 95% CI)	-2.2 [-10.12, 5.72]
7.3 25mg patch vs 15mg- 8 week treatment course	1	198	Mean Difference (IV, Fixed, 95% CI)	0.60 [-0.43, 1.63]
7.4 25mg patch vs 15mg- 22 weeks treatment course	1	206	Mean Difference (IV, Fixed, 95% CI)	Not estimable
8 Mean weight change (kg) at 12 months: longer course vs. shorter	1	404	Mean Difference (IV, Fixed, 95% CI)	-0.24 [-0.97, 0.48]
8.1 22 weeks vs 8 weeks 25mg patch	1	222	Mean Difference (IV, Fixed, 95% CI)	-0.5 [-1.46, 0.46]
8.2 22 weeks vs 8 weeks 15mg patch	1	182	Mean Difference (IV, Fixed, 95% CI)	0.10 [-1.00, 1.20]

Comparison 10. Varenicline Tartate for smoking cessation: weight change

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean weight change (kg) at the end of treatment	6	1092	Mean Difference (IV, Fixed, 95% CI)	-0.23 [-0.58, 0.11]
2 1mg versus placebo end of treatment (oncken titrated + nontitrated arms	3	254	Mean Difference (IV, Fixed, 95% CI)	-0.12 [-0.68, 0.43]
3 Subgroup: 1mg titrated versus placebo end of treatment	1	60	Mean Difference (IV, Fixed, 95% CI)	0.74 [-0.95, 2.43]
4 Subgroup: 1mg nontitrated versus placebo end of treatment	3	208	Mean Difference (IV, Fixed, 95% CI)	-0.14 [-0.70, 0.43]
5 2mg versus placebo end of treatment	6	828	Mean Difference (IV, Fixed, 95% CI)	-0.29 [-0.65, 0.08]
6 Subgroup: 2mg titrated versus placebo end of treatment	4	609	Mean Difference (IV, Fixed, 95% CI)	-0.34 [-0.85, 0.18]

7 Subgroup: 2mg nontitrated daily versus placebo end of treatment	3	233	Mean Difference (IV, Fixed, 95% CI)	-0.21 [-0.71, 0.29]
8 24 week treatment versus 12 week treatment	1		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
8.1 Effects from baseline	1	726	Mean Difference (IV, Fixed, 95% CI)	-0.41 [-0.90, 0.08]
8.2 Effects from randomisation	1	726	Mean Difference (IV, Fixed, 95% CI)	-0.71 [-1.04, -0.38]

Comparison 11. Varenicline versus bupropion: weight change

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mean weight change (kg) at end of treatment	3	598	Mean Difference (IV, Fixed, 95% CI)	0.51 [0.09, 0.93]

Comparison 12. Varenicline v NRT: weight change

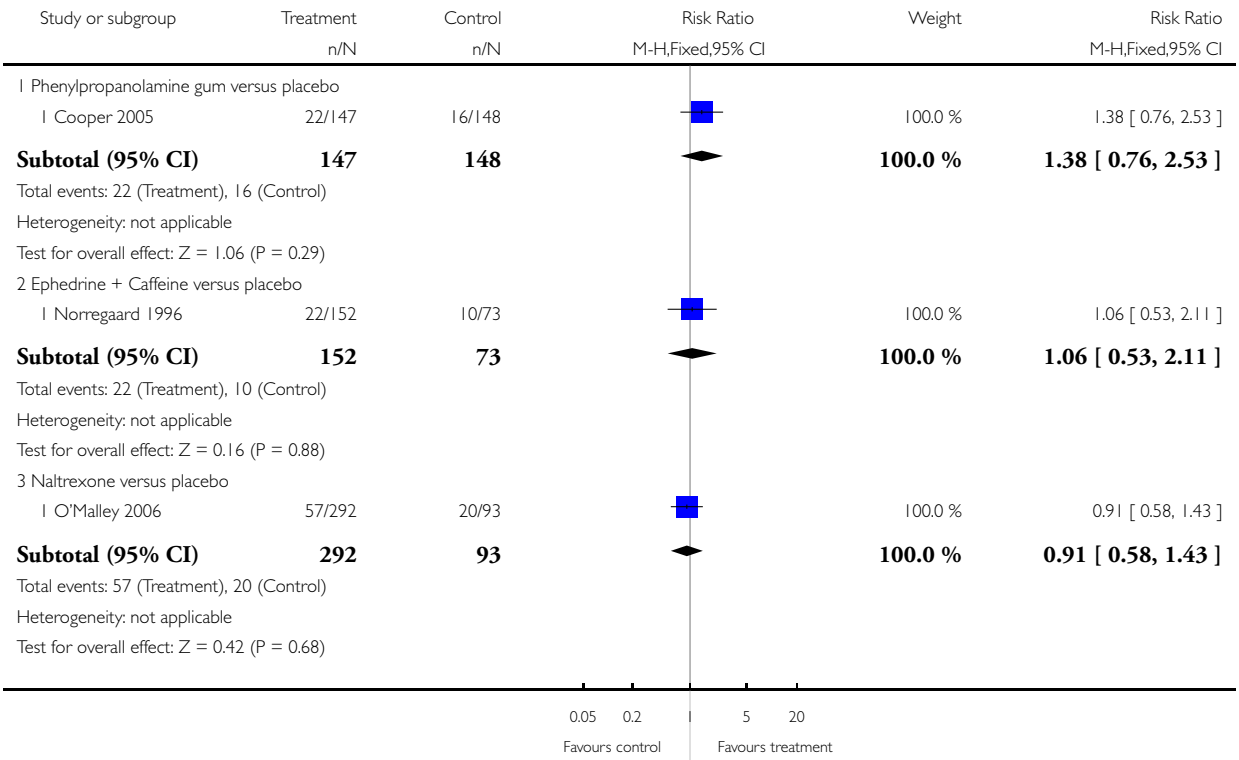
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 End of treatment	1	319	Mean Difference (IV, Fixed, 95% CI)	-0.05 [-0.58, 0.48]

Analysis 1.1. Comparison 1 Pharmacological interventions versus placebo for post-cessation weight control: smoking cessation, Outcome 1 Abstinence at 6 months.

Review: Interventions for preventing weight gain after smoking cessation

Comparison: 1 Pharmacological interventions versus placebo for post-cessation weight control: smoking cessation

Outcome: 1 Abstinence at 6 months

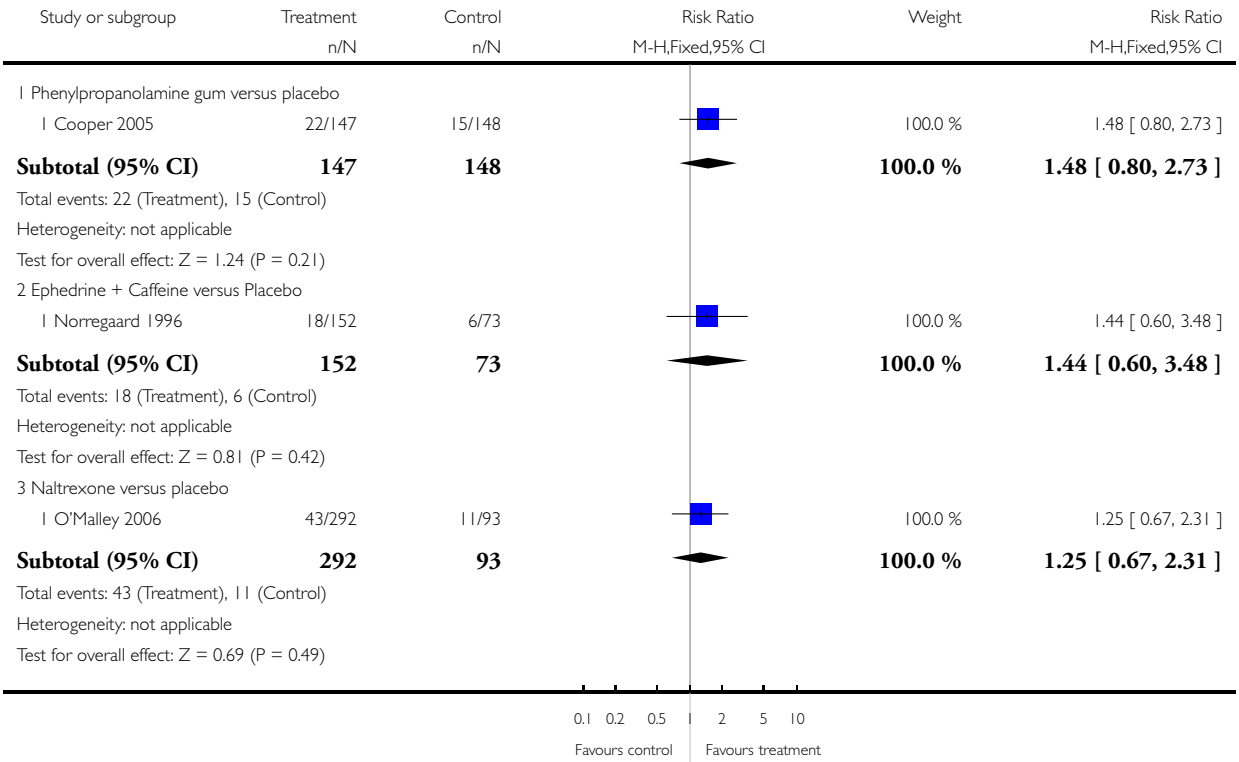


Analysis 1.2. Comparison 1 Pharmacological interventions versus placebo for post-cessation weight control: smoking cessation, Outcome 2 Abstinence at 12 months.

Review: Interventions for preventing weight gain after smoking cessation

Comparison: 1 Pharmacological interventions versus placebo for post-cessation weight control: smoking cessation

Outcome: 2 Abstinence at 12 months



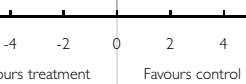
Analysis 2.1. Comparison 2 Pharmacological interventions versus placebo for post-cessation weight control: weight change, Outcome 1 Mean weight change (kg) at end of treatment.

Review: Interventions for preventing weight gain after smoking cessation

Comparison: 2 Pharmacological interventions versus placebo for post-cessation weight control: weight change

Outcome: 1 Mean weight change (kg) at end of treatment

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Dexfenfluramine versus placebo							
1 Spring 1995	18	1 (0.7)	15	3.5 (0.7)		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)							
2 Fluoxetine versus placebo							
1 Spring 1995	10	2.7 (0.5)	15	3.5 (0.7)		100.0 %	-0.80 [-1.27, -0.33]
Subtotal (95% CI)	**10**		**15**			**100.0 %**	**-0.80 [-1.27, -0.33]**
Heterogeneity: not applicable							
Test for overall effect: Z = 3.33 (P = 0.00086)							
3 Phenylpropanolamine versus Placebo							
1 Cooper 2005	16	0.59 (3.04)	22	1.81 (2.18)		3.0 %	-1.22 [-2.97, 0.53]
1 Klesges 1990	15	0.04 (1.07)	12	0.72 (1.04)		14.2 %	-0.68 [-1.48, 0.12]
1 Klesges 1995	19	0.34 (0.54)	28	0.78 (0.61)		82.8 %	-0.44 [-0.77, -0.11]
Subtotal (95% CI)	**50**		**62**			**100.0 %**	**-0.50 [-0.80, -0.20]**
Heterogeneity: Chi^2 = 0.97, df = 2 (P = 0.61); I^2 =0.0%							
Test for overall effect: Z = 3.23 (P = 0.0012)							
4 Ephedrine + Caffeine versus Placebo							
1 Norregaard 1996	27	0.2 (2.22)	13	1.5 (2.45)		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)							
5 Naltrexone versus Placebo							
1 O'Malley 2006	123	1.14 (1.94)	34	1.9 (1.98)		100.0 %	-0.76 [-1.51, -0.01]
Subtotal (95% CI)	**123**		**34**			**100.0 %**	**-0.76 [-1.51, -0.01]**
Heterogeneity: not applicable							
Test for overall effect: Z = 1.99 (P = 0.047)							
6 Naltrexone 25mg/day versus placebo							
1 O'Malley 2006	38	0.7 (1.91)	34	1.9 (1.98)		100.0 %	-1.20 [-2.10, -0.30]
Subtotal (95% CI)	**38**		**34**			**100.0 %**	**-1.20 [-2.10, -0.30]**
Heterogeneity: not applicable							
Test for overall effect: Z = 2.61 (P = 0.0090)							
Test for subgroup differences: Chi^2 = 49.64, df = 5 (P = 0.00), I^2 =90%							



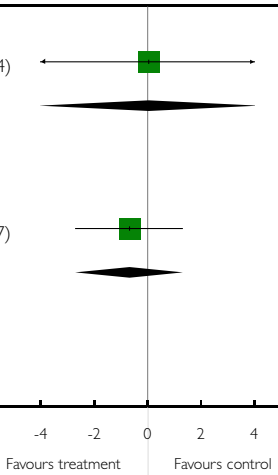
Analysis 2.2. Comparison 2 Pharmacological interventions versus placebo for post-cessation weight control: weight change, Outcome 2 Mean weight change (kg) at 6 months.

Review: Interventions for preventing weight gain after smoking cessation

Comparison: 2 Pharmacological interventions versus placebo for post-cessation weight control: weight change

Outcome: 2 Mean weight change (kg) at 6 months

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Phenylpropanolamine versus Placebo							
1 Cooper 2005	16	1.64 (6.36)	22	1.6 (6.4)		100.0 %	0.04 [-4.07, 4.15]
Subtotal (95% CI)	**16**		**22**			**100.0 %**	**0.04 [-4.07, 4.15]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.02 (P = 0.98)							
2 Ephedrine + caffine versus placebo							
1 Norregaard 1996	22	3.1 (2)	10	3.8 (2.97)		100.0 %	-0.70 [-2.72, 1.32]
Subtotal (95% CI)	**22**		**10**			**100.0 %**	**-0.70 [-2.72, 1.32]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.68 (P = 0.50)							
Test for subgroup differences: Chi^2 = 0.10, df = 1 (P = 0.75), I^2 =0.0%							



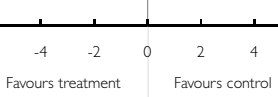
Analysis 2.3. Comparison 2 Pharmacological interventions versus placebo for post-cessation weight control: weight change, Outcome 3 Mean weight change (kg) at 12 months.

Review: Interventions for preventing weight gain after smoking cessation

Comparison: 2 Pharmacological interventions versus placebo for post-cessation weight control: weight change

Outcome: 3 Mean weight change (kg) at 12 months

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Phenylpropanolamine versus placebo							
1 Cooper 2005	16	0.82 (7.14)	22	1.86 (4.58)		100.0 %	-1.04 [-5.03, 2.95]
Subtotal (95% CI)	**16**		**22**			**100.0 %**	**-1.04 [-5.03, 2.95]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.51 (P = 0.61)							
2 Ephedrine + Caffeine versus placebo							
1 Norregaard 1996	18	5.9 (3.56)	6	4.7 (3.19)		100.0 %	1.20 [-1.84, 4.24]
Subtotal (95% CI)	**18**		**6**			**100.0 %**	**1.20 [-1.84, 4.24]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.77 (P = 0.44)							
Test for subgroup differences: Chi^2 = 0.77, df = 1 (P = 0.38), I^2 =0.0%							

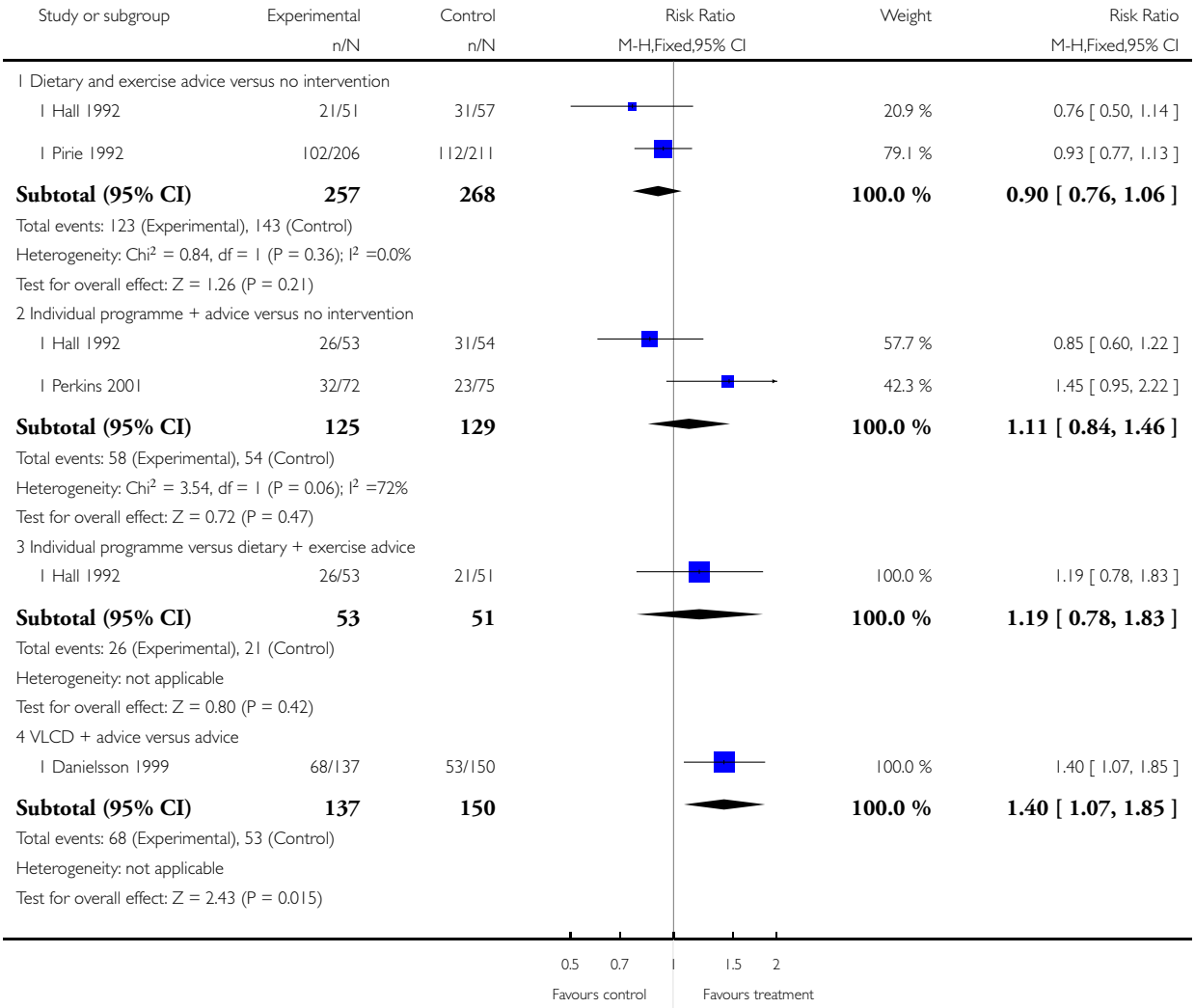


Analysis 3.1. Comparison 3 Behavioural post cessation weight management interventions with/without pharmacotherapy versus control: smoking cessation, Outcome 1 Abstinence at end of treatment.

Review: Interventions for preventing weight gain after smoking cessation

Comparison: 3 Behavioural post cessation weight management interventions with/without pharmacotherapy versus control: smoking cessation

Outcome: 1 Abstinence at end of treatment

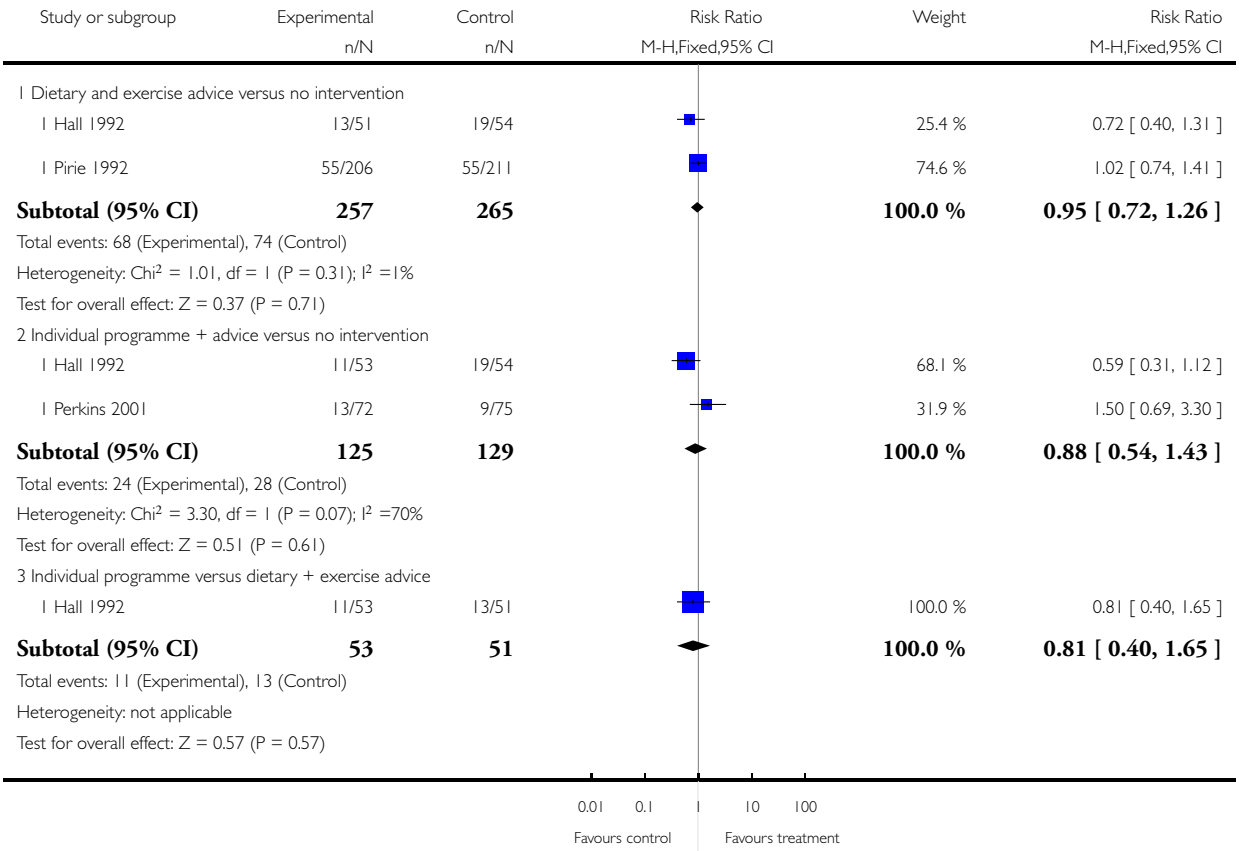


Analysis 3.2. Comparison 3 Behavioural post cessation weight management interventions with/without pharmacotherapy versus control: smoking cessation, Outcome 2 Abstinence at 6 months.

Review: Interventions for preventing weight gain after smoking cessation

Comparison: 3 Behavioural post cessation weight management interventions with/without pharmacotherapy versus control: smoking cessation

Outcome: 2 Abstinence at 6 months



Analysis 3.3. Comparison 3 Behavioural post cessation weight management interventions with/without pharmacotherapy versus control: smoking cessation, Outcome 3 Abstinence at 12 months.

Review: Interventions for preventing weight gain after smoking cessation

Comparison: 3 Behavioural post cessation weight management interventions with/without pharmacotherapy versus control: smoking cessation

Outcome: 3 Abstinence at 12 months

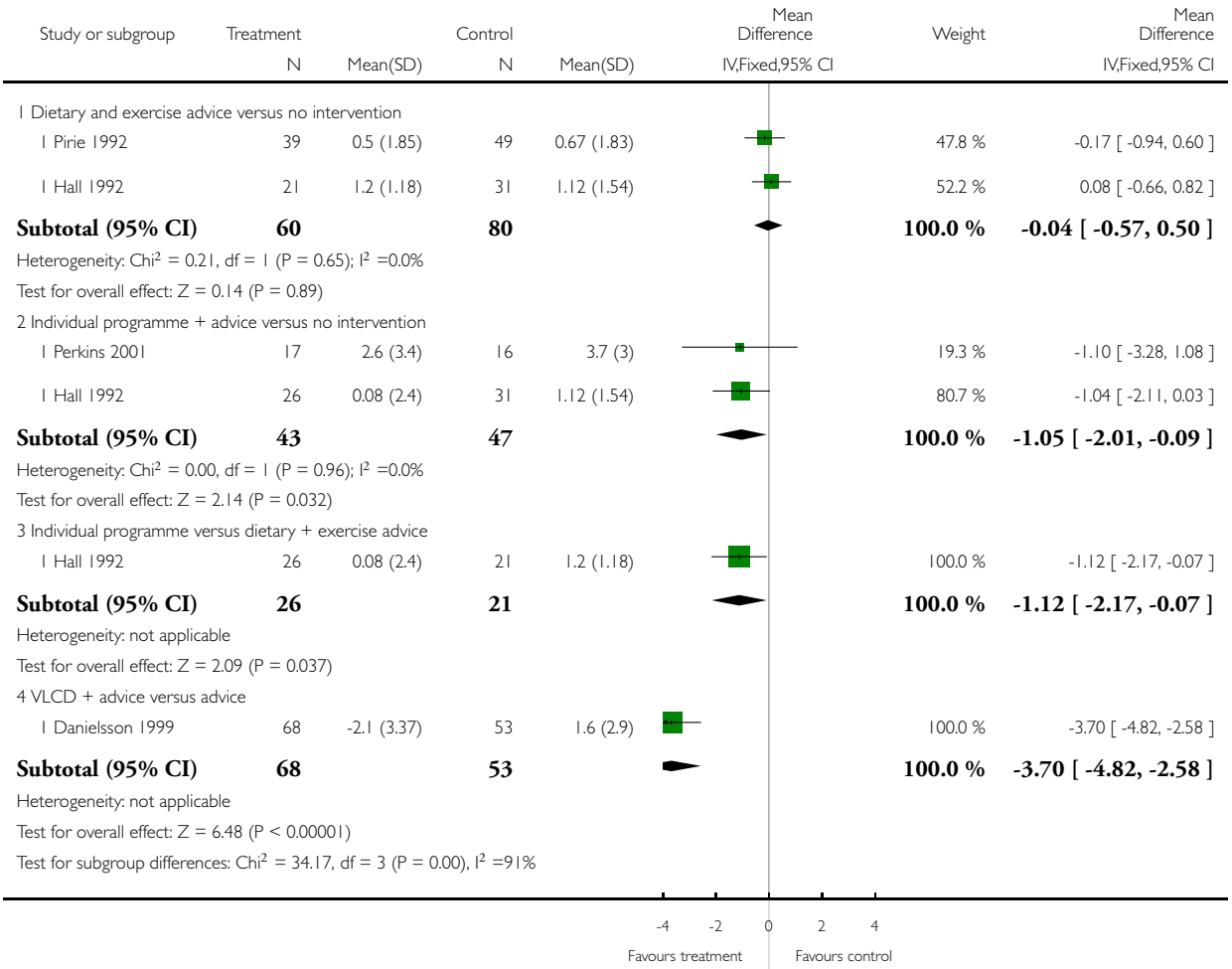
Study or subgroup	Experimental n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Dietary and exercise advice versus no intervention					
1 Hall 1992	11/51	19/54		24.0 %	0.61 [0.32, 1.16]
1 Pirie 1992	39/206	59/211		76.0 %	0.68 [0.47, 0.97]
Subtotal (95% CI)	**257**	**265**		**100.0 %**	**0.66 [0.48, 0.90]**
Total events: 50 (Experimental), 78 (Control)					
Heterogeneity: Chi^2 = 0.07, df = 1 (P = 0.79); I^2 =0.0%					
Test for overall effect: Z = 2.61 (P = 0.0092)					
2 Individual programme + advice versus no intervention					
1 Hall 1992	11/53	19/54		73.3 %	0.59 [0.31, 1.12]
1 Perkins 2001	9/72	7/75		26.7 %	1.34 [0.53, 3.41]
Subtotal (95% CI)	**125**	**129**		**100.0 %**	**0.79 [0.47, 1.33]**
Total events: 20 (Experimental), 26 (Control)					
Heterogeneity: Chi^2 = 2.03, df = 1 (P = 0.15); I^2 =51%					
Test for overall effect: Z = 0.89 (P = 0.37)					
3 Individual programme versus dietary + exercise advice					
1 Hall 1992	11/53	11/51		100.0 %	0.96 [0.46, 2.02]
Subtotal (95% CI)	**53**	**51**		**100.0 %**	**0.96 [0.46, 2.02]**
Total events: 11 (Experimental), 11 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 0.10 (P = 0.92)					
4 VLCD + advice versus advice					
1 Danielsson 1999	38/137	24/150		100.0 %	1.73 [1.10, 2.73]
Subtotal (95% CI)	**137**	**150**		**100.0 %**	**1.73 [1.10, 2.73]**
Total events: 38 (Experimental), 24 (Control)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.37 (P = 0.018)					

Analysis 4.1. Comparison 4 Behavioural post cessation weight management interventions including/not including exercise versus control: weight change, Outcome 1 Mean weight change (kg) at end of treatment.

Review: Interventions for preventing weight gain after smoking cessation

Comparison: 4 Behavioural post cessation weight management interventions including/not including exercise versus control: weight change

Outcome: 1 Mean weight change (kg) at end of treatment

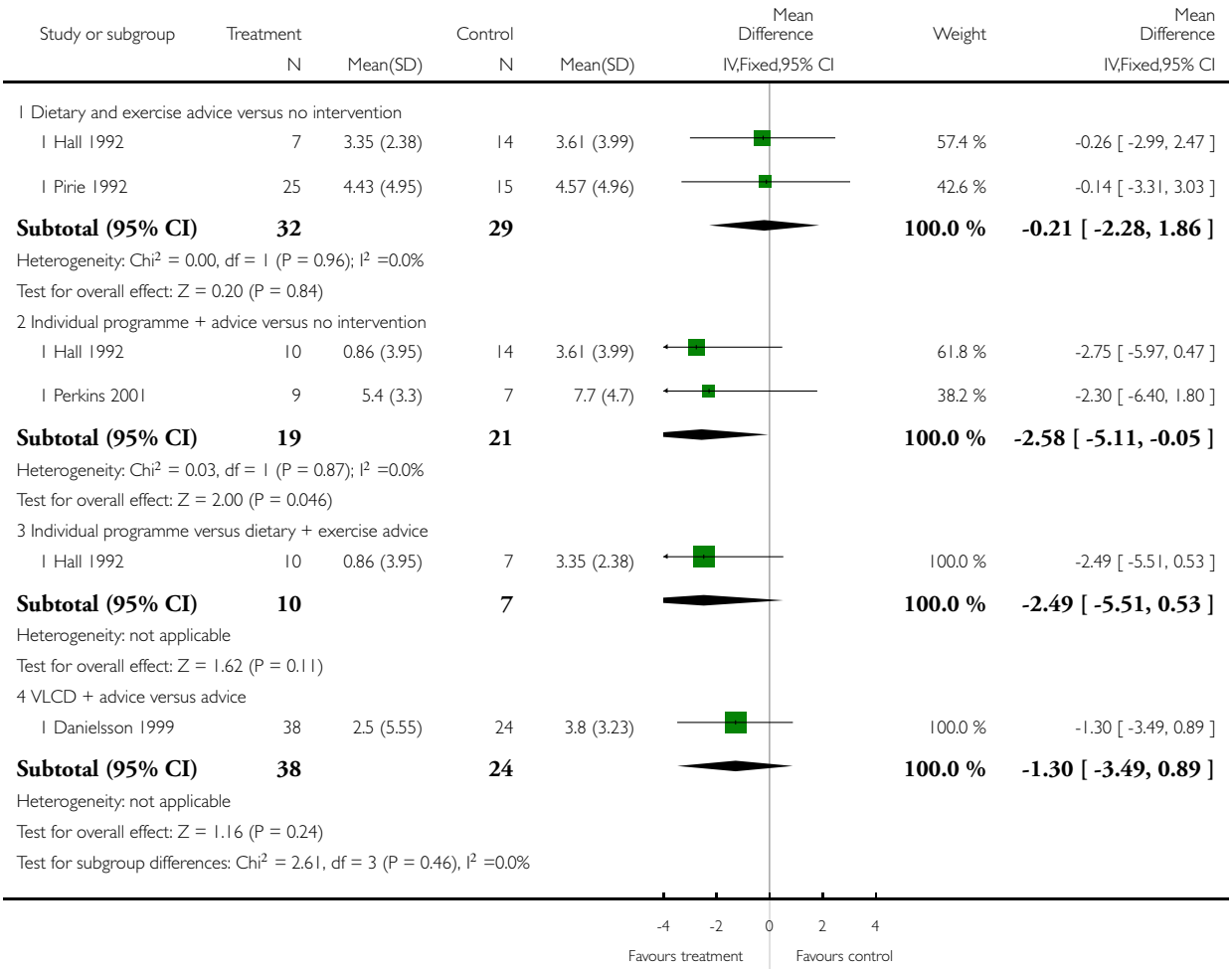


Analysis 4.2. Comparison 4 Behavioural post cessation weight management interventions including/not including exercise versus control: weight change, Outcome 2 Mean weight change (kg) at 12 months.

Review: Interventions for preventing weight gain after smoking cessation

Comparison: 4 Behavioural post cessation weight management interventions including/not including exercise versus control: weight change

Outcome: 2 Mean weight change (kg) at 12 months



Analysis 5.1. Comparison 5 CBT to accept moderate weight gain versus no behavioural weight advice: smoking cessation, Outcome 1 Abstinence at 6 months.

Review: Interventions for preventing weight gain after smoking cessation

Comparison: 5 CBT to accept moderate weight gain versus no behavioural weight advice: smoking cessation

Outcome: 1 Abstinence at 6 months

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Perkins 2001	40/72	23/75		100.0 %	1.81 [1.22, 2.70]
Total (95% CI)	**72**	**75**		**100.0 %**	**1.81 [1.22, 2.70]**

Total events: 40 (Treatment), 23 (Control)
Heterogeneity: not applicable
Test for overall effect: Z = 2.93 (P = 0.0034)
Test for subgroup differences: Not applicable

Analysis 5.2. Comparison 5 CBT to accept moderate weight gain versus no behavioural weight advice: smoking cessation, Outcome 2 Abstinence at 12 months.

Review: Interventions for preventing weight gain after smoking cessation

Comparison: 5 CBT to accept moderate weight gain versus no behavioural weight advice: smoking cessation

Outcome: 2 Abstinence at 12 months

Study or subgroup	Treatment n/N	Control n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Perkins 2001	21/72	9/75		100.0 %	2.43 [1.19, 4.95]
Total (95% CI)	**72**	**75**		**100.0 %**	**2.43 [1.19, 4.95]**

Total events: 21 (Treatment), 9 (Control)
Heterogeneity: not applicable
Test for overall effect: Z = 2.45 (P = 0.014)
Test for subgroup differences: Not applicable

Analysis 6.1. Comparison 6 CBT to accept moderate weight gain versus no behavioural weight advice: weight change, Outcome 1 Mean weight change (kg) at end of treatment.

Review: Interventions for preventing weight gain after smoking cessation

Comparison: 6 CBT to accept moderate weight gain versus no behavioural weight advice: weight change

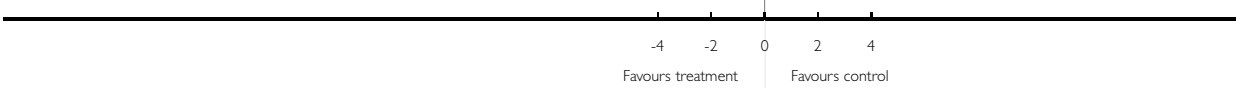
Outcome: 1 Mean weight change (kg) at end of treatment

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Perkins 2001	40	1.1 (1.4)	23	2.2 (1.4)		100.0 %	-1.10 [-1.82, -0.38]
Total (95% CI)	**40**		**23**			**100.0 %**	**-1.10 [-1.82, -0.38]**

Heterogeneity: not applicable

Test for overall effect: Z = 3.00 (P = 0.0027)

Test for subgroup differences: Not applicable



Analysis 6.2. Comparison 6 CBT to accept moderate weight gain versus no behavioural weight advice: weight change, Outcome 2 Mean weight change (kg) at 6 months.

Review: Interventions for preventing weight gain after smoking cessation

Comparison: 6 CBT to accept moderate weight gain versus no behavioural weight advice: weight change

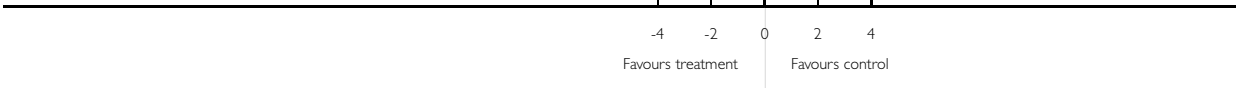
Outcome: 2 Mean weight change (kg) at 6 months

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Perkins 2001	20	2.9 (2.6)	9	6.4 (3.5)		100.0 %	-3.50 [-6.05, -0.95]
Total (95% CI)	**20**		**9**			**100.0 %**	**-3.50 [-6.05, -0.95]**

Heterogeneity: not applicable

Test for overall effect: Z = 2.69 (P = 0.0073)

Test for subgroup differences: Not applicable



Analysis 6.3. Comparison 6 CBT to accept moderate weight gain versus no behavioural weight advice: weight change, Outcome 3 Mean weight change (kg) at 12 months.

Review: Interventions for preventing weight gain after smoking cessation

Comparison: 6 CBT to accept moderate weight gain versus no behavioural weight advice: weight change

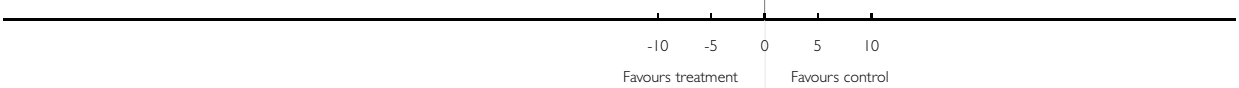
Outcome: 3 Mean weight change (kg) at 12 months

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Perkins 2001	15	2.5 (4.2)	7	7.7 (4.7)		100.0 %	-5.20 [-9.28, -1.12]
Total (95% CI)	**15**		**7**			**100.0 %**	**-5.20 [-9.28, -1.12]**

Heterogeneity: not applicable

Test for overall effect: Z = 2.50 (P = 0.012)

Test for subgroup differences: Not applicable



Analysis 7.1. Comparison 7 All types of antidepressant versus placebo for smoking cessation: weight change, Outcome 1 Mean weight change (kg) at end of treatment.

Review: Interventions for preventing weight gain after smoking cessation

Comparison: 7 All types of antidepressant versus placebo for smoking cessation: weight change

Outcome: 1 Mean weight change (kg) at end of treatment

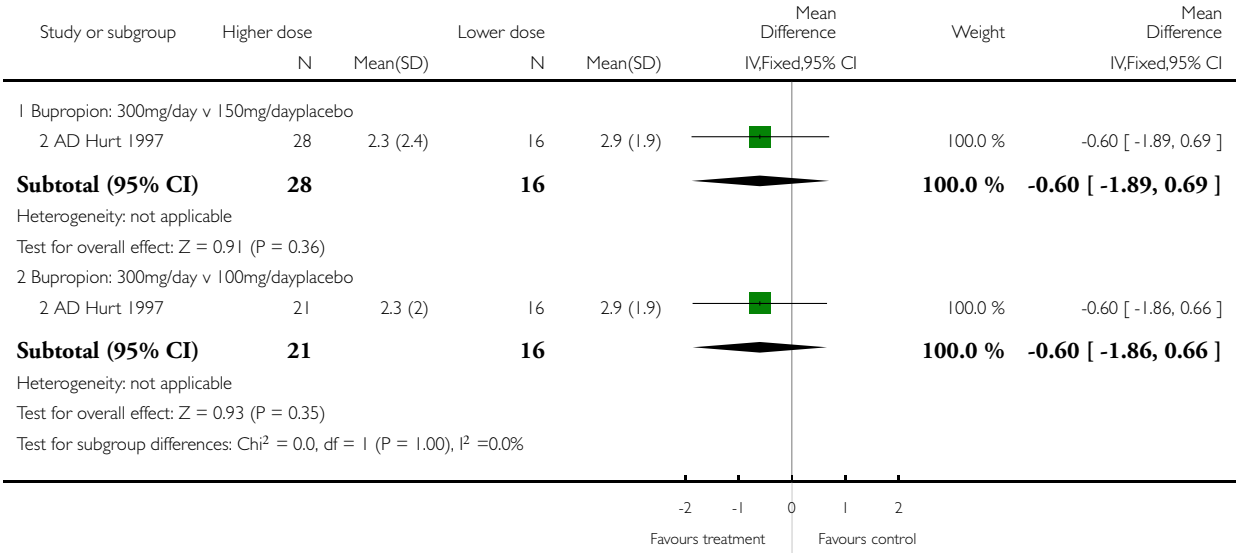
Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Bupropion versus placebo							
2 AD Nides 2006	22	1.68 (1.92)	10	4 (2.18)		5.2 %	-2.32 [-3.89, -0.75]
2 AD Hurt 1997	38	1.5 (2)	16	2.9 (1.9)		10.0 %	-1.40 [-2.53, -0.27]
2 AD Jorenby 2006	102	1.88 (3.4)	60	3.15 (4.1)		8.4 %	-1.27 [-2.50, -0.04]
2 AD Rigotti 2006	31	1.2 (3.9)	25	2.4 (3.6)		3.3 %	-1.20 [-3.17, 0.77]
2 AD Zellweger 2005	248	1.32 (1.8)	66	2.32 (1.64)		61.6 %	-1.00 [-1.45, -0.55]
2 AD Gonzales 2006	95	2.12 (1.8)	61	2.92 (3.94)		11.5 %	-0.80 [-1.85, 0.25]
Subtotal (95% CI)	**536**		**238**			**100.0 %**	**-1.11 [-1.47, -0.76]**
Heterogeneity: Chi^2 = 3.16, df = 5 (P = 0.68); I^2 =0.0%							
Test for overall effect: Z = 6.12 (P < 0.00001)							
2 Fluoxetine versus placebo							
2 AD Niaura 2002	73	1.3 (1.4)	46	2.6 (1.8)		100.0 %	-1.30 [-1.91, -0.69]
Subtotal (95% CI)	**73**		**46**			**100.0 %**	**-1.30 [-1.91, -0.69]**
Heterogeneity: not applicable							
Test for overall effect: Z = 4.17 (P = 0.000031)							
Test for subgroup differences: Chi^2 = 0.26, df = 1 (P = 0.61), I^2 =0.0%							

Analysis 7.2. Comparison 7 All types of antidepressant versus placebo for smoking cessation: weight change, Outcome 2 Mean weight change (kg) at end of treatment: dose response.

Review: Interventions for preventing weight gain after smoking cessation

Comparison: 7 All types of antidepressant versus placebo for smoking cessation: weight change

Outcome: 2 Mean weight change (kg) at end of treatment: dose response

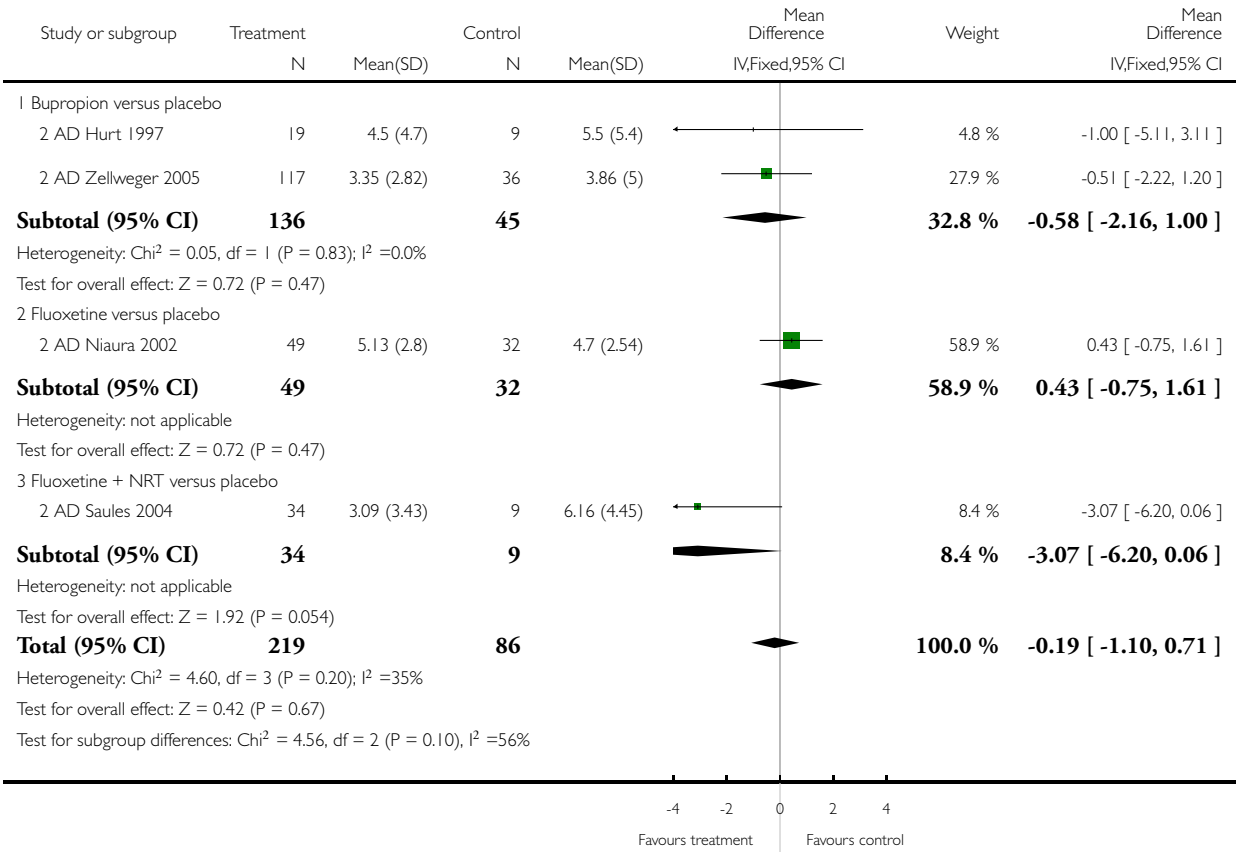


Analysis 7.3. Comparison 7 All types of antidepressant versus placebo for smoking cessation: weight change, Outcome 3 Mean weight change (kg) at 6 months.

Review: Interventions for preventing weight gain after smoking cessation

Comparison: 7 All types of antidepressant versus placebo for smoking cessation: weight change

Outcome: 3 Mean weight change (kg) at 6 months

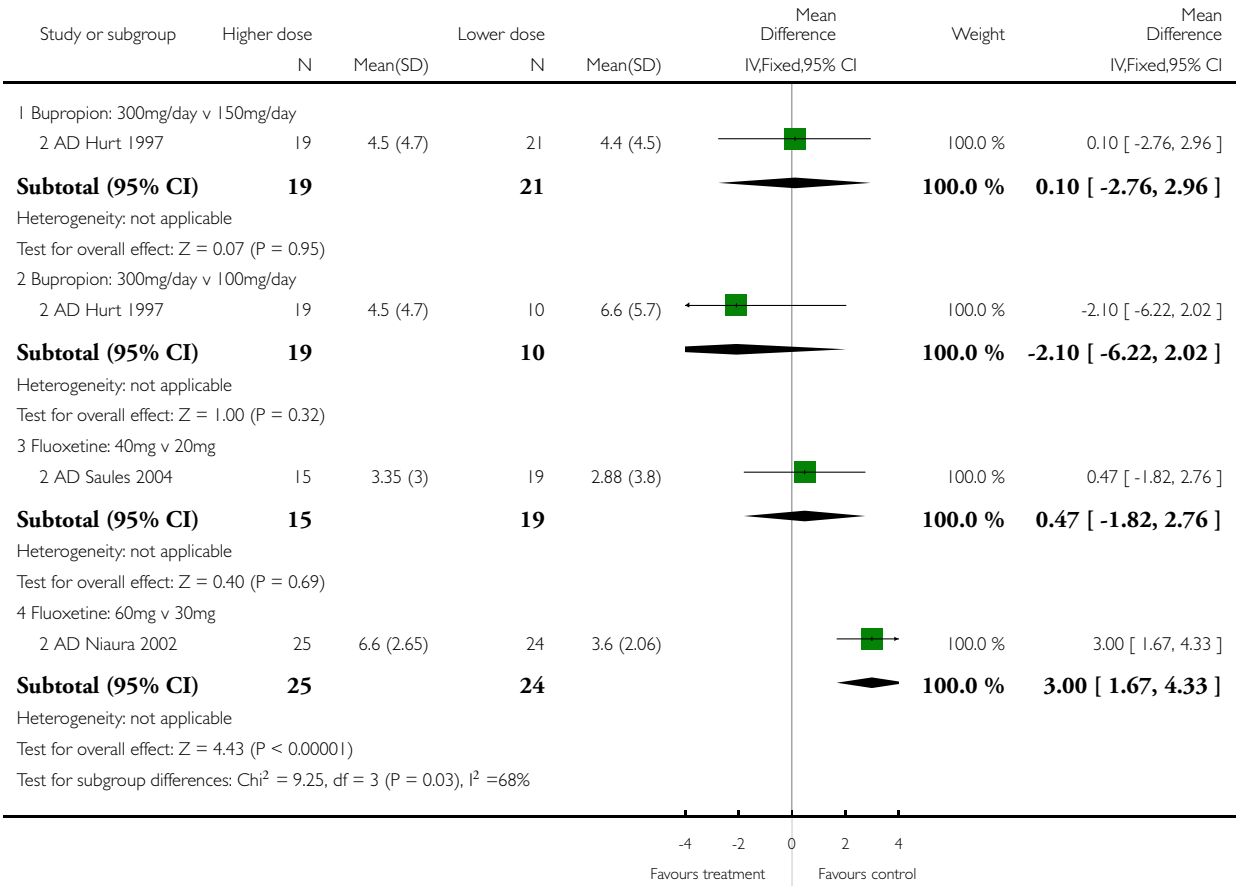


Analysis 7.4. Comparison 7 All types of antidepressant versus placebo for smoking cessation: weight change, Outcome 4 Mean weight change (kg) at 6 months: dose response.

Review: Interventions for preventing weight gain after smoking cessation

Comparison: 7 All types of antidepressant versus placebo for smoking cessation: weight change

Outcome: 4 Mean weight change (kg) at 6 months: dose response



Analysis 7.5. Comparison 7 All types of antidepressant versus placebo for smoking cessation: weight change, Outcome 5 Mean weight change (kg) at 12 months.

Review: Interventions for preventing weight gain after smoking cessation

Comparison: 7 All types of antidepressant versus placebo for smoking cessation: weight change

Outcome: 5 Mean weight change (kg) at 12 months

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Bupropion versus placebo							
2 AD Rigotti 2006	20	5.6 (8.2)	15	6.9 (5.2)		13.2 %	-1.30 [-5.75, 3.15]
2 AD Zellweger 2005	117	4.15 (4.18)	36	4.45 (6.12)		57.1 %	-0.30 [-2.44, 1.84]
2 AD Simon 2004	17	2.72 (6.7)	23	2.94 (3.86)		20.7 %	-0.22 [-3.77, 3.33]
2 AD Hurt 1997	16	6.1 (7.9)	8	6 (5.4)		9.0 %	0.10 [-5.28, 5.48]
Subtotal (95% CI)	**170**		**82**			**100.0 %**	**-0.38 [-2.00, 1.24]**

Heterogeneity: $Chi^2 = 0.21$, df = 3 (P = 0.98); $I^2 = 0.0\%$

Test for overall effect: Z = 0.46 (P = 0.65)

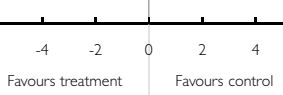
Analysis 7.6. Comparison 7 All types of antidepressant versus placebo for smoking cessation: weight change, Outcome 6 Mean weight change (kg) at 12 months: dose response.

Review: Interventions for preventing weight gain after smoking cessation

Comparison: 7 All types of antidepressant versus placebo for smoking cessation: weight change

Outcome: 6 Mean weight change (kg) at 12 months: dose response

Study or subgroup	Higher dose N	Mean(SD)	Lower dose N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Bupropion: 300mg/day v 150mg/day							
2 AD Hurt 1997	16	6.1 (7.9)	17	5.9 (6.7)		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)							
2 Bupropion: 300mg/day v 100mg/day							
2 AD Hurt 1997	16	6.1 (7.9)	8	8.1 (6.7)		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: Chi^2 = 0.30, df = 1 (P = 0.58), I^2 =0.0%							



Analysis 8.1. Comparison 8 Exercise interventions for smoking cessation: weight change, Outcome 1 Mean weight change (kg) at end of treatment.

Review: Interventions for preventing weight gain after smoking cessation

Comparison: 8 Exercise interventions for smoking cessation: weight change

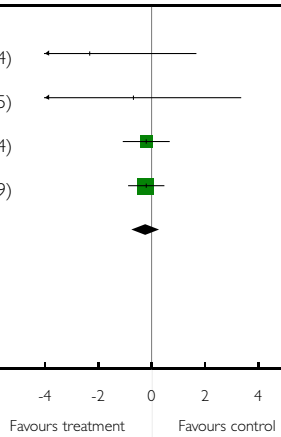
Outcome: 1 Mean weight change (kg) at end of treatment

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Exercise + SC versus SC only							
2 EX Marcus 1999	24	3.03 (3.45)	13	5.36 (6.94)		1.8 %	-2.33 [-6.35, 1.69]
2 EX Marcus 2005	12	3.86 (5.66)	16	4.56 (5.05)		1.7 %	-0.70 [-4.75, 3.35]
2 EX Cornuz 2007	107	2.5 (4.14)	115	2.7 (2.14)		36.9 %	-0.20 [-1.08, 0.68]
2 EX Ussher 2003	61	1.8 (1.9)	56	2 (1.9)		59.6 %	-0.20 [-0.89, 0.49]
Total (95% CI)	**204**		**200**			**100.0 %**	**-0.25 [-0.78, 0.29]**

Heterogeneity: Chi^2 = 1.11, df = 3 (P = 0.77); I^2 =0.0%

Test for overall effect: Z = 0.91 (P = 0.36)

Test for subgroup differences: Not applicable



Analysis 8.2. Comparison 8 Exercise interventions for smoking cessation: weight change, Outcome 2 Mean weight change (kg) at 12 months.

Review: Interventions for preventing weight gain after smoking cessation

Comparison: 8 Exercise interventions for smoking cessation: weight change

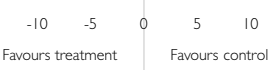
Outcome: 2 Mean weight change (kg) at 12 months

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Exercise + SC versus SC only							
2 EX Cornuz 2007	59	4.4 (6.91)	70	6.2 (4.18)		71.8 %	-1.80 [-3.82, 0.22]
2 EX Marcus 1999	15	8.92 (8.9)	6	5.76 (12.6)		2.4 %	3.16 [-7.88, 14.20]
2 EX Ussher 2003	14	3.9 (5.3)	18	7.2 (4.1)		25.8 %	-3.30 [-6.66, 0.06]
Total (95% CI)	**88**		**94**			**100.0 %**	**-2.07 [-3.78, -0.36]**

Heterogeneity: Chi^2 = 1.45, df = 2 (P = 0.49); I^2 =0.0%

Test for overall effect: Z = 2.37 (P = 0.018)

Test for subgroup differences: Not applicable



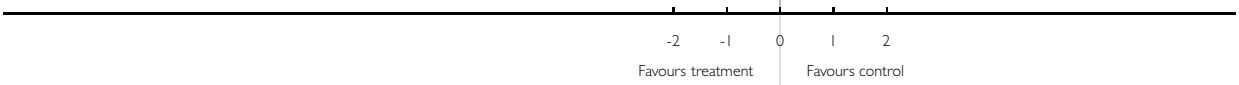
Analysis 9.1. Comparison 9 All types of NRT versus placebo for smoking cessation: weight change, Outcome 1 Mean weight change (kg) at end of treatment.

Review: Interventions for preventing weight gain after smoking cessation

Comparison: 9 All types of NRT versus placebo for smoking cessation: weight change

Outcome: 1 Mean weight change (kg) at end of treatment

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Gum versus placebo							
2 NRT Cooper 2005	24	2.19 (4.14)	22	3.6 (3.82)		0.7 %	-1.41 [-3.71, 0.89]
2 NRT Pirie 1992	34	0.49 (1.82)	15	1.1 (1.81)		2.9 %	-0.61 [-1.71, 0.49]
2 NRT Garvey 2000	161	0.95 (1.6)	47	1.5 (1.65)		12.5 %	-0.55 [-1.08, -0.02]
2 NRT Gross 1995	35	2.07 (2.26)	7	2.49 (1.54)		1.9 %	-0.42 [-1.78, 0.94]
Subtotal (95% CI)	**254**		**91**			**17.9 %**	**-0.58 [-1.02, -0.13]**
Heterogeneity: Chi² = 0.57, df = 3 (P = 0.90); I² =0.0%							
Test for overall effect: Z = 2.55 (P = 0.011)							
2 Patch versus placebo							
2 NRT Abelin 1989	72	0.1 (1.8)	45	4.4 (2.2)		6.0 %	-4.30 [-5.07, -3.53]
2 NRT Ehrsam 1991	22	1.23 (1.7)	11	1.9 (1.5)		2.7 %	-0.67 [-1.81, 0.47]
2 NRT TNSG 1991	332	2 (1.9)	68	2.6 (1.5)		20.9 %	-0.60 [-1.01, -0.19]
2 NRT Fiore 1994A	26	2.6 (1.8)	17	3.2 (2.6)		1.8 %	-0.60 [-2.02, 0.82]
2 NRT Richmond 1994	55	2.62 (2.68)	22	3.15 (3.63)		1.3 %	-0.53 [-2.20, 1.14]
2 NRT CEASE 1999	497	1.7 (2.1)	147	2.2 (2.3)		20.5 %	-0.50 [-0.92, -0.08]
2 NRT Fiore 1994B	21	2.6 (1.91)	11	2.8 (1.56)		2.3 %	-0.20 [-1.43, 1.03]
2 NRT Gourlay 1995	21	1.9 (3.1)	6	1.9 (3.1)		0.4 %	0.0 [-2.81, 2.81]
2 NRT Tonnesen 1991	43	2.6 (2.1)	7	2.5 (1.9)		1.5 %	0.10 [-1.44, 1.64]
2 NRT Stapleton 1995	155	3.1 (2.9)	41	2.8 (2.3)		5.0 %	0.30 [-0.54, 1.14]
Subtotal (95% CI)	**1244**		**375**			**62.5 %**	**-0.82 [-1.06, -0.58]**
Heterogeneity: Chi² = 92.55, df = 9 (P<0.00001); I² =90%							
Test for overall effect: Z = 6.74 (P < 0.00001)							
3 Inhaler versus placebo							
2 NRT Tonnesen 1993	36	3.3 (2)	18	3.8 (1.9)		3.0 %	-0.50 [-1.59, 0.59]
2 NRT Hjalmarson 1997	35	1.7 (1.6)	22	1.9 (2.7)		2.3 %	-0.20 [-1.45, 1.05]
Subtotal (95% CI)	**71**		**40**			**5.2 %**	**-0.37 [-1.19, 0.45]**
Heterogeneity: Chi² = 0.13, df = 1 (P = 0.72); I² =0.0%							



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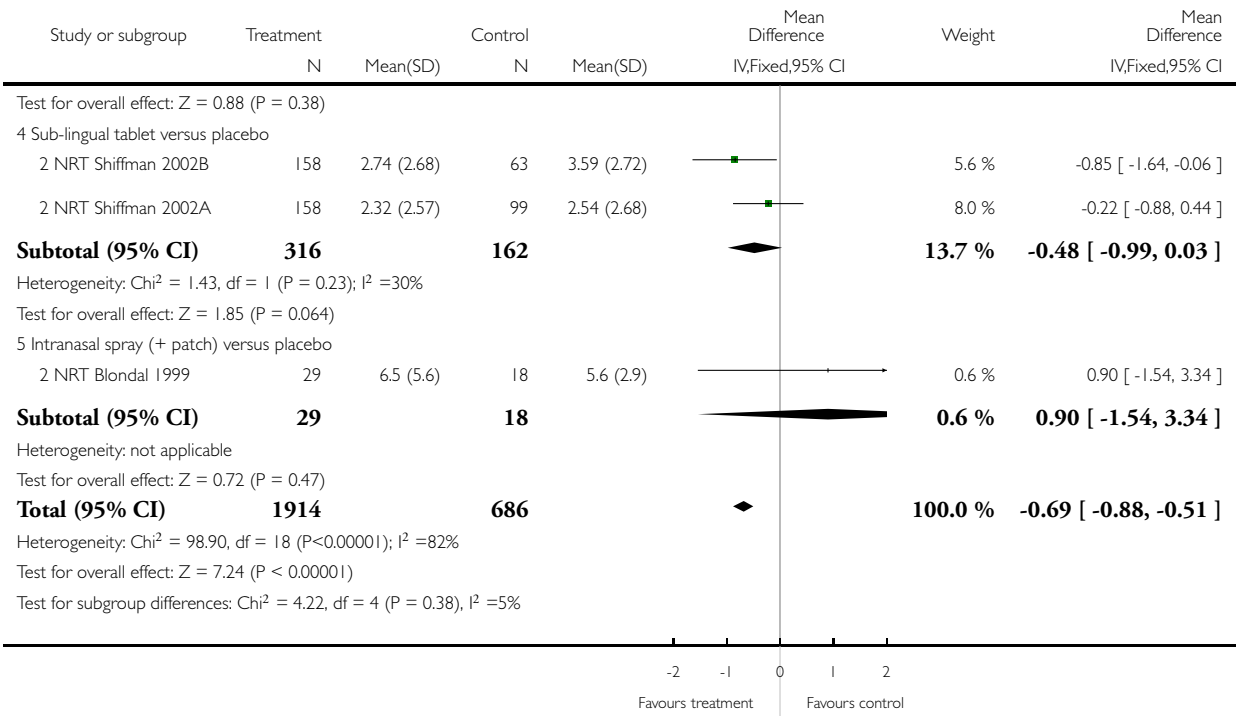


Analysis 9.2. Comparison 9 All types of NRT versus placebo for smoking cessation: weight change, Outcome 2 Mean weight change (kg) at end of treatment: patch v spray.

Review: Interventions for preventing weight gain after smoking cessation

Comparison: 9 All types of NRT versus placebo for smoking cessation: weight change

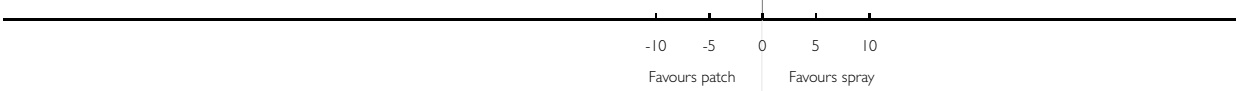
Outcome: 2 Mean weight change (kg) at end of treatment: patch v spray

Study or subgroup	Patch N	Mean(SD)	Spray N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
2 NRT Lerman 2004	82	1.5 (4.4)	72	1.8 (4.8)		100.0 %	-0.30 [-1.76, 1.16]
Total (95% CI)	**82**		**72**			**100.0 %**	**-0.30 [-1.76, 1.16]**

Heterogeneity: not applicable

Test for overall effect: Z = 0.40 (P = 0.69)

Test for subgroup differences: Not applicable

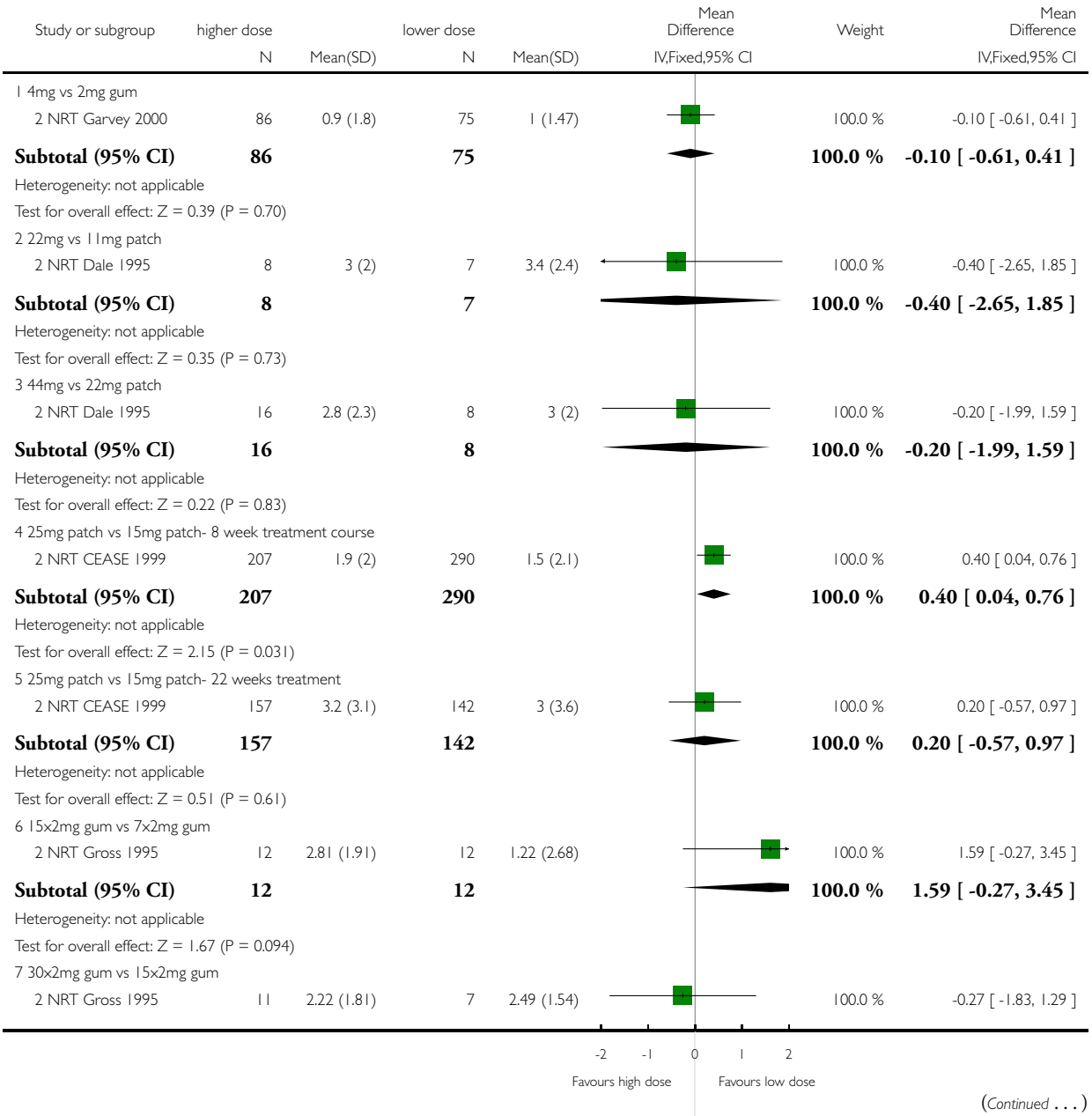


Analysis 9.3. Comparison 9 All types of NRT versus placebo for smoking cessation: weight change, Outcome 3 Mean weight change (kg) at end of treatment: dose response.

Review: Interventions for preventing weight gain after smoking cessation

Comparison: 9 All types of NRT versus placebo for smoking cessation: weight change

Outcome: 3 Mean weight change (kg) at end of treatment: dose response



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Study or subgroup	higher dose N	Mean(SD)	lower dose N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Subtotal (95% CI)	**11**		**7**			**100.0 %**	**-0.27 [-1.83, 1.29]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.34 (P = 0.74)							
Test for subgroup differences: Chi^2 = 5.44, df = 6 (P = 0.49), I^2 =0.0%							

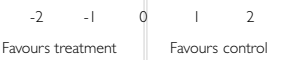
Analysis 9.4. Comparison 9 All types of NRT versus placebo for smoking cessation: weight change, Outcome 4 Mean weight change (kg) at 6 months.

Review: Interventions for preventing weight gain after smoking cessation

Comparison: 9 All types of NRT versus placebo for smoking cessation: weight change

Outcome: 4 Mean weight change (kg) at 6 months

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Gum versus placebo							
2 NRT Hjalmarson 1984	36	1.34 (3.6)	18	2.58 (3.2)		7.3 %	-1.24 [-3.13, 0.65]
2 NRT Pirie 1992	34	3.61 (4.18)	15	3.7 (4.18)		4.1 %	-0.09 [-2.63, 2.45]
Subtotal (95% CI)	**70**		**33**			**11.4 %**	**-0.83 [-2.35, 0.69]**
Heterogeneity: Chi^2 = 0.51, df = 1 (P = 0.48); I^2 =0.0%							
Test for overall effect: Z = 1.07 (P = 0.28)							
2 Patch versus placebo							
2 NRT Sachs 1993	38	4.3 (3.5)	13	5.8 (2.8)		7.4 %	-1.50 [-3.39, 0.39]
2 NRT Richmond 1994	45	3.16 (4.84)	19	4.09 (4.87)		3.8 %	-0.93 [-3.54, 1.68]
Subtotal (95% CI)	**83**		**32**			**11.2 %**	**-1.30 [-2.83, 0.22]**
Heterogeneity: Chi^2 = 0.12, df = 1 (P = 0.73); I^2 =0.0%							
Test for overall effect: Z = 1.67 (P = 0.094)							
3 Patch (+ gum) versus placebo							
2 NRT Puska 1995	41	3.8 (3.3)	31	4.3 (2.9)		12.7 %	-0.50 [-1.94, 0.94]



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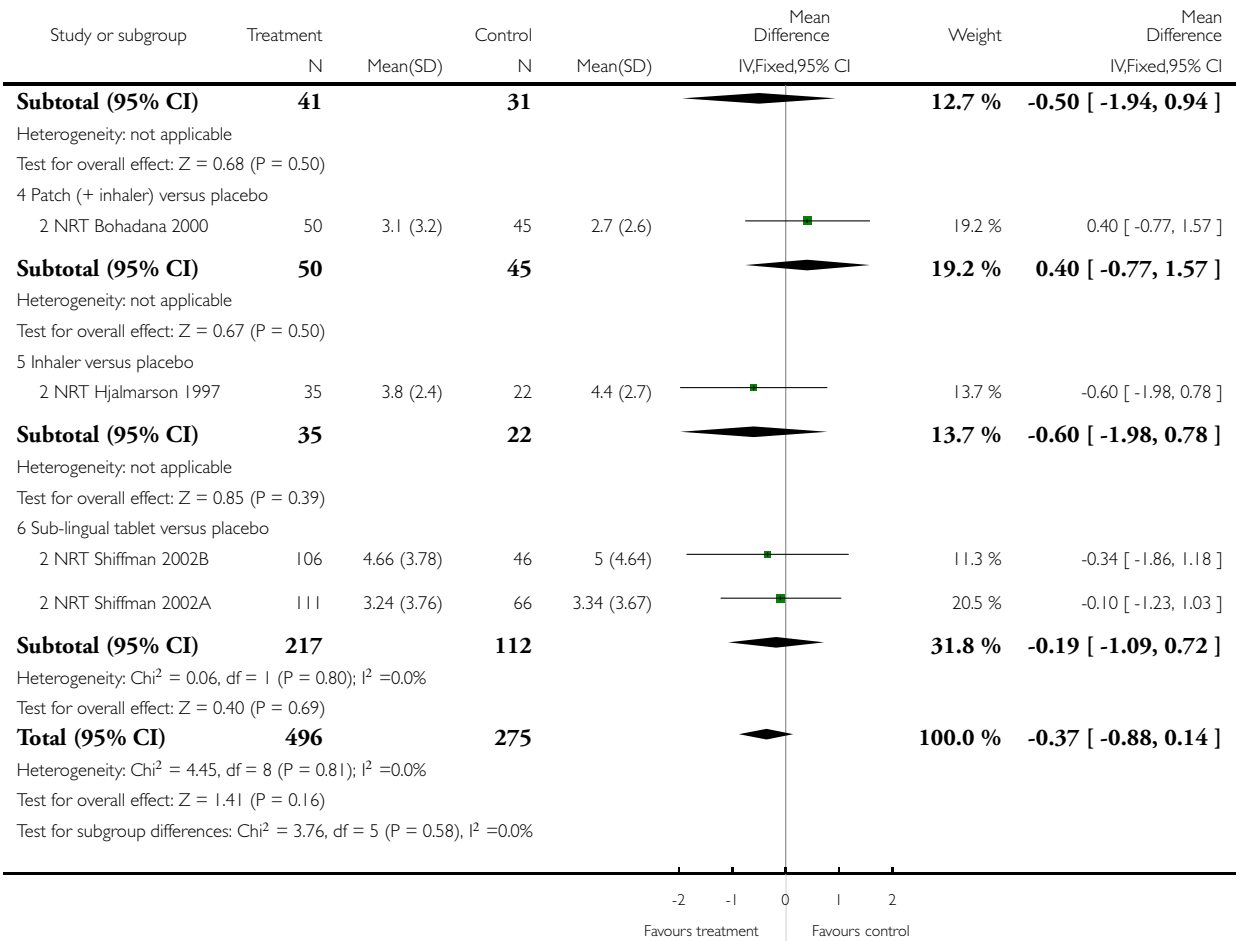


Analysis 9.5. Comparison 9 All types of NRT versus placebo for smoking cessation: weight change, Outcome 5 Mean weight change (kg) at 6 months: patch v spray.

Review: Interventions for preventing weight gain after smoking cessation

Comparison: 9 All types of NRT versus placebo for smoking cessation: weight change

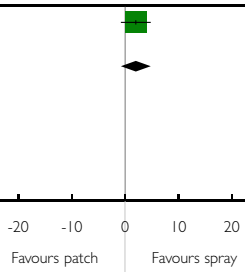
Outcome: 5 Mean weight change (kg) at 6 months: patch v spray

Study or subgroup	Patch N	Mean(SD)	Spray N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
2 NRT Lerman 2004	53	4.8 (6)	50	2.8 (7.9)		100.0 %	2.00 [-0.72, 4.72]
Total (95% CI)	**53**		**50**			**100.0 %**	**2.00 [-0.72, 4.72]**

Heterogeneity: not applicable

Test for overall effect: Z = 1.44 (P = 0.15)

Test for subgroup differences: Not applicable

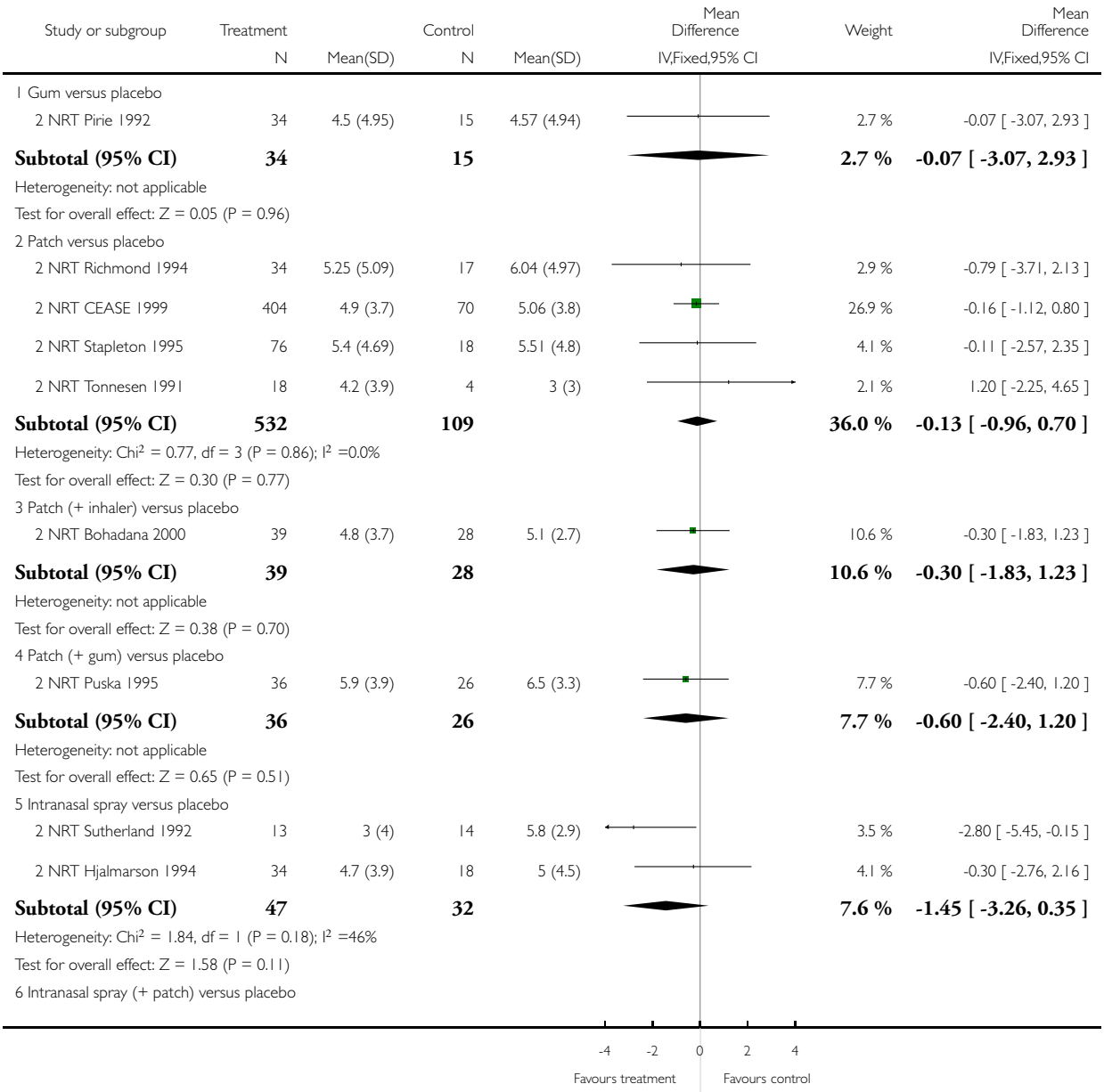


Analysis 9.6. Comparison 9 All types of NRT versus placebo for smoking cessation: weight change, Outcome 6 Mean weight change (kg) at 12 months.

Review: Interventions for preventing weight gain after smoking cessation

Comparison: 9 All types of NRT versus placebo for smoking cessation: weight change

Outcome: 6 Mean weight change (kg) at 12 months



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Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
2 NRT Blondal 1999	29	6.5 (5.6)	14	8.3 (4.2)		2.8 %	-1.80 [-4.80, 1.20]
Subtotal (95% CI)	**29**		**14**			**2.8 %**	**-1.80 [-4.80, 1.20]**
Heterogeneity: not applicable							
Test for overall effect: Z = 1.18 (P = 0.24)							
7 Inhaler versus placebo							
2 NRT Hjalmarson 1997	35	4.5 (2.9)	22	5.6 (2.2)		14.0 %	-1.10 [-2.43, 0.23]
2 NRT Tonnesen 1993	24	4.4 (5.3)	9	5.1 (2.8)		3.2 %	-0.70 [-3.50, 2.10]
Subtotal (95% CI)	**59**		**31**			**17.2 %**	**-1.03 [-2.23, 0.17]**
Heterogeneity: Chi^2 = 0.06, df = 1 (P = 0.80); I^2 =0.0%							
Test for overall effect: Z = 1.67 (P = 0.094)							
8 Sub-lingual tablet versus placebo							
2 NRT Wallstrom 2000	45	5.37 (3.5)	37	5.8 (6)		5.2 %	-0.43 [-2.62, 1.76]
2 NRT Shiffman 2002B	67	6.61 (5.76)	28	7.01 (7.22)		2.7 %	-0.40 [-3.41, 2.61]
2 NRT Shiffman 2002A	82	4.8 (5.52)	44	3.8 (4.62)		7.5 %	1.00 [-0.81, 2.81]
Subtotal (95% CI)	**194**		**109**			**15.5 %**	**0.27 [-0.99, 1.54]**
Heterogeneity: Chi^2 = 1.21, df = 2 (P = 0.55); I^2 =0.0%							
Test for overall effect: Z = 0.42 (P = 0.67)							
Total (95% CI)	**970**		**364**			**100.0 %**	**-0.42 [-0.92, 0.08]**
Heterogeneity: Chi^2 = 8.68, df = 14 (P = 0.85); I^2 =0.0%							
Test for overall effect: Z = 1.65 (P = 0.098)							
Test for subgroup differences: Chi^2 = 4.80, df = 7 (P = 0.68), I^2 =0.0%							

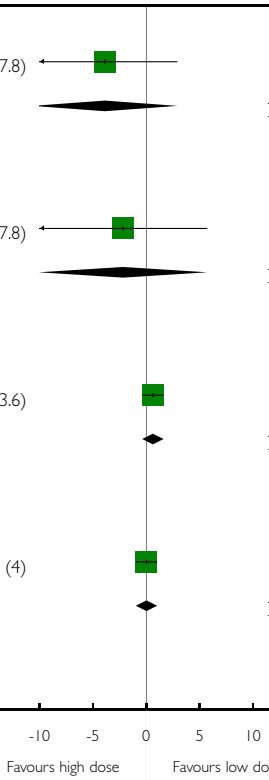
Analysis 9.7. Comparison 9 All types of NRT versus placebo for smoking cessation: weight change, Outcome 7 Mean weight change (kg) at 12 months: dose response.

Review: Interventions for preventing weight gain after smoking cessation

Comparison: 9 All types of NRT versus placebo for smoking cessation: weight change

Outcome: 7 Mean weight change (kg) at 12 months: dose response

Study or subgroup	High dose patch N	Mean(SD)	Low dose patch N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 22mg patch vs 11mg							
2 NRT Dale 1995	2	4.6 (0.1)	5	8.5 (7.8)		100.0 %	-3.90 [-10.74, 2.94]
Subtotal (95% CI)	**2**		**5**			**100.0 %**	**-3.90 [-10.74, 2.94]**
Heterogeneity: not applicable							
Test for overall effect: Z = 1.12 (P = 0.26)							
2 44mg patch vs 11mg							
2 NRT Dale 1995	7	6.3 (5.4)	5	8.5 (7.8)		100.0 %	-2.20 [-10.12, 5.72]
Subtotal (95% CI)	**7**		**5**			**100.0 %**	**-2.20 [-10.12, 5.72]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.54 (P = 0.59)							
3 25mg patch vs 15mg- 8 week treatment course							
2 NRT CEASE 1999	114	5.3 (3.7)	84	4.7 (3.6)		100.0 %	0.60 [-0.43, 1.63]
Subtotal (95% CI)	**114**		**84**			**100.0 %**	**0.60 [-0.43, 1.63]**
Heterogeneity: not applicable							
Test for overall effect: Z = 1.15 (P = 0.25)							
4 25mg patch vs 15mg- 22 weeks treatment course							
2 NRT CEASE 1999	108	4.8 (3.6)	98	4.8 (4)		100.0 %	0.0 [-1.04, 1.04]
Subtotal (95% CI)	**108**		**98**			**100.0 %**	**0.0 [-1.04, 1.04]**
Heterogeneity: not applicable							
Test for overall effect: Z = 0.0 (P = 1.0)							

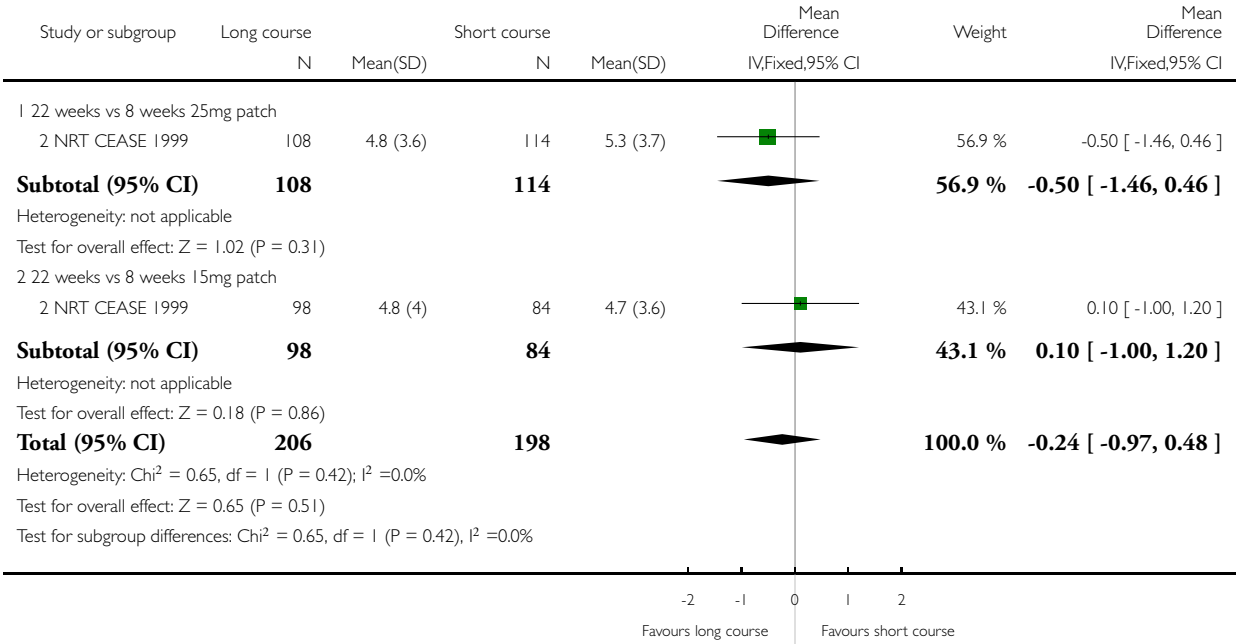


Analysis 9.8. Comparison 9 All types of NRT versus placebo for smoking cessation: weight change, Outcome 8 Mean weight change (kg) at 12 months: longer course vs. shorter.

Review: Interventions for preventing weight gain after smoking cessation

Comparison: 9 All types of NRT versus placebo for smoking cessation: weight change

Outcome: 8 Mean weight change (kg) at 12 months: longer course vs. shorter



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

Review: Interventions for preventing weight gain after smoking cessation

Comparison: 10 Varenicline Tartate for smoking cessation: weight change

Outcome: 1 Mean weight change (kg) at the end of treatment

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
2 VA Nides 2006	53	2.15 (4)	10	4 (2.28)		3.7 %	-1.85 [-3.63, -0.07]
2 VA Oncken 2006	197	2.62 (3.72)	14	2.14 (2.36)		6.6 %	0.48 [-0.86, 1.82]
2 VA Jorenby 2006	151	2.89 (2.94)	60	3.15 (4.11)		9.1 %	-0.26 [-1.40, 0.88]
2 VA Gonzales 2006	155	2.37 (2.76)	61	2.92 (3.94)		10.1 %	-0.55 [-1.63, 0.53]
2 VA Tsai 2008	75	1.29 (2.42)	40	1.59 (1.7)		20.4 %	-0.30 [-1.06, 0.46]
2 VA Nakamura 2007	225	1.37 (1.71)	51	1.48 (1.57)		50.1 %	-0.11 [-0.60, 0.38]
Total (95% CI)	**856**		**236**			**100.0 %**	**-0.23 [-0.58, 0.11]**

Heterogeneity: Chi^2 = 4.88, df = 5 (P = 0.43); I^2 =0.0%

Test for overall effect: Z = 1.33 (P = 0.18)

Test for subgroup differences: Not applicable

Analysis 10.2. Comparison 10 Varenicline Tartate for smoking cessation: weight change, Outcome 2 1mg versus placebo end of treatment (oncken titrated + nontitrated arms.

Review: Interventions for preventing weight gain after smoking cessation

Comparison: 10 Varenicline Tartate for smoking cessation: weight change

Outcome: 2 1mg versus placebo end of treatment (oncken titrated + nontitrated arms

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
2 VA Nides 2006	14	2.14 (2.28)	10	4 (2.28)		9.0 %	-1.86 [-3.71, -0.01]
2 VA Nakamura 2007	71	1.38 (2.02)	51	1.48 (1.57)		76.1 %	-0.10 [-0.74, 0.54]
2 VA Oncken 2006	94	2.94 (3.65)	14	2.14 (2.36)		14.9 %	0.80 [-0.64, 2.24]
Total (95% CI)	**179**		**75**			**100.0 %**	**-0.12 [-0.68, 0.43]**

Heterogeneity: $Chi^2 = 4.97$, df = 2 (P = 0.08); $I^2 = 60\%$

Test for overall effect: Z = 0.44 (P = 0.66)

Test for subgroup differences: Not applicable

Analysis 10.3. Comparison 10 Varenicline Tartate for smoking cessation: weight change, Outcome 3 Subgroup: 1mg titrated versus placebo end of treatment.

Review: Interventions for preventing weight gain after smoking cessation

Comparison: 10 Varenicline Tartate for smoking cessation: weight change

Outcome: 3 Subgroup: 1mg titrated versus placebo end of treatment

Study or subgroup	Experimental N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
2 VA Oncken 2006	46	2.88 (4)	14	2.14 (2.36)		100.0 %	0.74 [-0.95, 2.43]
Total (95% CI)	**46**		**14**			**100.0 %**	**0.74 [-0.95, 2.43]**

Heterogeneity: not applicable

Test for overall effect: Z = 0.86 (P = 0.39)

Test for subgroup differences: Not applicable

Analysis 10.4. Comparison 10 Varenicline Tartate for smoking cessation: weight change, Outcome 4 Subgroup: 1mg nontitrated versus placebo end of treatment.

Review: Interventions for preventing weight gain after smoking cessation

Comparison: 10 Varenicline Tartate for smoking cessation: weight change

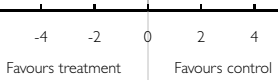
Outcome: 4 Subgroup: 1mg nontitrated versus placebo end of treatment

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
2 VA Nides 2006	14	2.14 (2.28)	10	4 (2.28)		9.2 %	-1.86 [-3.71, -0.01]
2 VA Nakamura 2007	71	1.38 (2.02)	51	1.48 (1.57)		77.7 %	-0.10 [-0.74, 0.54]
2 VA Oncken 2006	48	3 (3.33)	14	2.14 (2.36)		13.1 %	0.86 [-0.69, 2.41]
Total (95% CI)	**133**		**75**			**100.0 %**	**-0.14 [-0.70, 0.43]**

Heterogeneity: Chi^2 = 4.92, df = 2 (P = 0.09); I^2 =59%

Test for overall effect: Z = 0.48 (P = 0.63)

Test for subgroup differences: Not applicable



Analysis 10.5. Comparison 10 Varenicline Tartate for smoking cessation: weight change, Outcome 5 2mg versus placebo end of treatment.

Review: Interventions for preventing weight gain after smoking cessation

Comparison: 10 Varenicline Tartate for smoking cessation: weight change

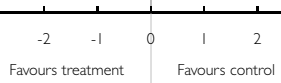
Outcome: 5 2mg versus placebo end of treatment

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
2 VA Nides 2006	24	1.96 (2.3)	10	4 (2.28)		4.6 %	-2.04 [-3.73, -0.35]
2 VA Gonzales 2006	155	2.37 (2.76)	61	2.92 (3.94)		11.3 %	-0.55 [-1.63, 0.53]
2 VA Tsai 2008	75	1.29 (2.42)	40	1.59 (1.7)		22.8 %	-0.30 [-1.06, 0.46]
2 VA Jorenby 2006	151	2.89 (2.94)	60	3.15 (4.11)		10.1 %	-0.26 [-1.40, 0.88]
2 VA Nakamura 2007	84	1.37 (1.55)	51	1.48 (1.57)		44.6 %	-0.11 [-0.65, 0.43]
2 VA Oncken 2006	103	2.34 (3.77)	14	2.14 (2.36)		6.4 %	0.20 [-1.23, 1.63]
Total (95% CI)	**592**		**236**			**100.0 %**	**-0.29 [-0.65, 0.08]**

Heterogeneity: $Chi^2 = 5.23$, df = 5 (P = 0.39); $I^2 = 4\%$

Test for overall effect: Z = 1.55 (P = 0.12)

Test for subgroup differences: Not applicable



Analysis 10.6. Comparison 10 Varenicline Tartate for smoking cessation: weight change, Outcome 6 Subgroup: 2mg titrated versus placebo end of treatment.

Review: Interventions for preventing weight gain after smoking cessation

Comparison: 10 Varenicline Tartate for smoking cessation: weight change

Outcome: 6 Subgroup: 2mg titrated versus placebo end of treatment

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
2 VA Gonzales 2006	155	2.37 (2.76)	61	2.92 (3.94)		22.7 %	-0.55 [-1.63, 0.53]
2 VA Tsai 2008	75	1.29 (2.42)	40	1.59 (1.7)		45.9 %	-0.30 [-1.06, 0.46]
2 VA Jorenby 2006	151	2.89 (2.95)	60	3.15 (4.11)		20.4 %	-0.26 [-1.40, 0.88]
2 VA Oncken 2006	53	1.92 (3.49)	14	2.14 (2.36)		11.0 %	-0.22 [-1.77, 1.33]
Total (95% CI)	**434**		**175**			**100.0 %**	**-0.34 [-0.85, 0.18]**

Heterogeneity: $Chi^2 = 0.20$, df = 3 (P = 0.98); $I^2 = 0.0\%$

Test for overall effect: Z = 1.29 (P = 0.20)

Test for subgroup differences: Not applicable

Analysis 10.7. Comparison 10 Varenicline Tartate for smoking cessation: weight change, Outcome 7 Subgroup: 2mg nontitrated daily versus placebo end of treatment.

Review: Interventions for preventing weight gain after smoking cessation

Comparison: 10 Varenicline Tartate for smoking cessation: weight change

Outcome: 7 Subgroup: 2mg nontitrated daily versus placebo end of treatment

Study or subgroup	Treatment N	Mean(SD)	Control N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
2 VA Nides 2006	24	1.96 (2.3)	10	4 (2.28)		8.7 %	-2.04 [-3.73, -0.35]
2 VA Nakamura 2007	84	1.37 (1.57)	51	1.48 (1.57)		82.5 %	-0.11 [-0.66, 0.44]
2 VA Oncken 2006	50	2.79 (4.03)	14	2.14 (2.36)		8.9 %	0.65 [-1.02, 2.32]
Total (95% CI)	**158**		**75**			**100.0 %**	**-0.21 [-0.71, 0.29]**

Heterogeneity: Chi^2 = 5.68, df = 2 (P = 0.06); I^2 =65%

Test for overall effect: Z = 0.83 (P = 0.41)

Test for subgroup differences: Not applicable

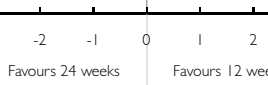
Analysis 10.8. Comparison 10 Varenicline Tartate for smoking cessation: weight change, Outcome 8 24 week treatment versus 12 week treatment.

Review: Interventions for preventing weight gain after smoking cessation

Comparison: 10 Varenicline Tartate for smoking cessation: weight change

Outcome: 8 24 week treatment versus 12 week treatment

Study or subgroup	24 weeks treatment N	Mean(SD)	12 weeks treatment N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
1 Effects from baseline							
2 VA Tonstad 2006	425	3.62 (3.29)	301	4.03 (3.3)		100.0 %	-0.41 [-0.90, 0.08]
Subtotal (95% CI)	**425**		**301**			**100.0 %**	**-0.41 [-0.90, 0.08]**
Heterogeneity: not applicable							
Test for overall effect: Z = 1.65 (P = 0.099)							
2 Effects from randomisation							
2 VA Tonstad 2006	425	0.8 (2.13)	301	1.51 (2.31)		100.0 %	-0.71 [-1.04, -0.38]
Subtotal (95% CI)	**425**		**301**			**100.0 %**	**-0.71 [-1.04, -0.38]**
Heterogeneity: not applicable							
Test for overall effect: Z = 4.21 (P = 0.000025)							



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

Review: Interventions for preventing weight gain after smoking cessation

Comparison: 11 Varenicline versus bupropion: weight change

Outcome: 1 Mean weight change (kg) at end of treatment

Study or subgroup	Varenicline N	Mean(SD)	Bupropion N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
2 AD Gonzales 2006	155	2.37 (2.76)	95	2.12 (1.8)		54.4 %	0.25 [-0.32, 0.82]
2 AD Nides 2006	24	1.96 (2.3)	22	1.68 (1.92)		11.7 %	0.28 [-0.94, 1.50]
2 AD Jorenby 2006	151	2.89 (2.94)	151	1.88 (3.4)		33.9 %	1.01 [0.29, 1.73]
Total (95% CI)	**330**		**268**			**100.0 %**	**0.51 [0.09, 0.93]**

Heterogeneity: Chi^2 = 2.82, df = 2 (P = 0.24); I^2 =29%

Test for overall effect: Z = 2.40 (P = 0.016)

Test for subgroup differences: Not applicable

Analysis 12.1. Comparison 12 Varenicline v NRT: weight change, Outcome 1 End of treatment.

Review: Interventions for preventing weight gain after smoking cessation

Comparison: 12 Varenicline v NRT: weight change

Outcome: 1 End of treatment

Study or subgroup	Varenicline N	Mean(SD)	Nicotine patch N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
2 VA Aubin 2008	188	2.02 (2.5)	131	2.07 (2.3)		100.0 %	-0.05 [-0.58, 0.48]
Total (95% CI)	**188**		**131**			**100.0 %**	**-0.05 [-0.58, 0.48]**

Heterogeneity: not applicable

Test for overall effect: Z = 0.18 (P = 0.85)

Test for subgroup differences: Not applicable

FEEDBACK

Reporting of adverse events, 4 May 2009

Summary

Adverse events of the interventions discussed should be fully reported in the review.

Reply

We agree that it is important, and recognise that it is Cochrane policy, to report adverse events (AEs) of interventions included within a Cochrane review. Only three of the pharmacological studies and one behavioural study included in the first part of our review reported AEs. One pharmacological study also reported details of drop-outs due to AEs. We also discussed the fact that two of the most effective drugs for limiting weight gain (dexfenfluramine and PPA) are withdrawn or restricted from UK and US markets because of adverse events.

The second part of the review was based on "parent" Cochrane reviews that had already reported AEs associated with the reviewed drugs.

At the next update, we plan to include AE reports in the first part of the review. We will also amend the Methods section to cover the collection and reporting of AE data, and will direct the reader to the "parent" reviews for coverage of AEs associated with the relevant smoking cessation pharmacotherapies in the second part of the review.

Contributors

Comment by Dr Andrew Herxheimer; reply by Amanda Parsons and Paul Aveyard.
Feedback Editor Tim Lancaster.

WHAT'S NEW

Last assessed as up-to-date: 6 November 2008.

Date	Event	Description
14 July 2009	Feedback has been incorporated	Feedback added

HISTORY

Protocol first published: Issue 4, 2006

Review first published: Issue 1, 2009

Date	Event	Description
4 December 2008	Amended	Error in Background section corrected, corresponding citations revised
1 September 2008	Amended	Converted to new review format.

CONTRIBUTIONS OF AUTHORS

MS carried out searches for the first part of the review and AP, MS and JI independently identified relevant studies and extracted data. AP drafted the review. PA and PH gave conceptual and editorial support.

DECLARATIONS OF INTEREST

Paul Aveyard and Amanda Parsons have recently conducted a pilot trial testing the effects of chromium supplements on 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

External sources

- Barts and The London - Queen Mary's School of Medicine and Dentistry, UK.

Paid the salary of Peter Hajek

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Secondary objectives, time of outcome measurement, Cochrane reviews we have inspected.

INDEX TERMS

Medical Subject Headings (MeSH)

*Weight Gain [drug effects]; Antidepressive Agents [therapeutic use]; Benzazepines [administration & dosage]; Exercise; Nicotine [administration & dosage]; Nicotinic Agonists [administration & dosage]; Piperidines [administration & dosage]; Pyrazoles [administration & dosage]; Quinoxalines [administration & dosage]; Smoking Cessation [*methods]

MeSH check words

Female; Humans; Male