Interventions for preventing weight gain after smoking cessation (Review)

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This is a reprint of a Cochrane review, prepared and maintained by The Cochrane Collaboration and published in *The Cochrane Library* 2012, Issue 1

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[Intervention Review]

Interventions for preventing weight gain after smoking cessation

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Editorial group: Cochrane Tobacco Addiction Group.
Publication status and date: New search for studies and content updated (no change to conclusions), published in Issue 1, 2012.
Review content assessed as up-to-date: 7 October 2011.

Citation: Farley AC, Hajek P, Lycett D, Aveyard P. Interventions for preventing weight gain after smoking cessation. *Cochrane Database of Systematic Reviews* 2012, Issue 1. Art. No.: CD006219. DOI: 10.1002/14651858.CD006219.pub3.

ABSTRACT

Background

Most people who stop smoking gain weight. There are some interventions that have been designed to reduce weight gain when stopping smoking. Some smoking cessation interventions may also limit weight gain although their effect on weight has not been reviewed.

Objectives

To systematically review the effect of: (1) Interventions targeting post-cessation weight gain on weight change and smoking cessation.

(2) Interventions designed to aid smoking cessation that may also plausibly affect weight on post-cessation weight change.

Search methods

Part 1 - We searched the Cochrane Tobacco Addiction Group's Specialized Register and CENTRAL in September 2011.

Part 2 - In addition we searched the included studies in the following "parent" Cochrane reviews: nicotine replacement therapy (NRT), antidepressants, nicotine receptor partial agonists, cannabinoid type 1 receptor antagonists and exercise interventions for smoking cessation published in Issue 9, 2011 of the Cochrane Library.

Selection criteria

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

Part 2 - We included trials that had been included in the selected parent Cochrane reviews if they had reported weight gain at any time point.

Data collection and analysis

We extracted data on baseline characteristics of the study population, intervention, outcome and study quality. Change in weight was expressed as difference in weight change from baseline to follow up between trial arms and was reported in abstinent smokers only. Abstinence from smoking was expressed as a risk ratio (RR). We used the most rigorous definition of abstinence available in each trial. Where appropriate, we performed meta-analysis using the inverse variance method for weight and Mantel-Haenszel method for smoking using a fixed-effect model.

Main results

Part 1: Some pharmacological interventions tested for limiting post cessation weight gain (PCWG) resulted in a significant reduction in WG at the end of treatment (dexfenfluramine (Mean difference (MD) -2.50 kg, 95% confidence interval (CI) -2.98 to -2.02, 1 study), phenylpropanolamine (MD -0.50 kg, 95% CI -0.80 to -0.20, N=3), naltrexone (MD -0.78 kg, 95% CI -1.52 to -0.05, N=2). There was no evidence that treatment reduced weight at 6 or 12 months (m). No pharmacological intervention significantly affected smoking cessation rates.

Weight management education only was associated with no reduction in PCWG at end of treatment (6 or 12m). However these interventions significantly reduced abstinence at 12m (Risk ratio (RR) 0.66, 95% CI 0.48 to 0.90, N=2). Personalised weight management support reduced PCWG at 12m (MD -2.58 kg, 95% CI -5.11 to -0.05, N=2) and was not associated with a significant reduction of abstinence at 12m (RR 0.74, 95% CI 0.39 to 1.43, N=2). A very low calorie diet (VLCD) significantly reduced PCWG at end of treatment (MD -3.70 kg, 95% CI -4.82 to -2.58, N=1), but not significantly so at 12m (MD -1.30 kg, 95% CI -3.49 to 0.89, N=1). The VLCD increased chances of abstinence at 12m (RR 1.73, 95% CI 1.10 to 2.73, N=1). There was no evidence that cognitive behavioural therapy to allay concern about weight gain (CBT) reduced PCWG, but there was some evidence of increased PCWG at 6m (MD 0.74, 95% CI 0.24 to 1.24). It was associated with improved abstinence at 6m (RR 1.83, 95% CI 1.07 to 3.13, N=2) but not at 12m (RR 1.25, 95% CI 0.83 to 1.86, N=2). However, there was significant statistical heterogeneity.

Part 2: We found no evidence that exercise interventions significantly reduced PCWG at end of treatment (MD -0.25 kg, 95% CI -0.78 to 0.29, N=4) however a significant reduction was found at 12m (MD -2.07 kg, 95% CI -3.78 to -0.36, N=3).

Both bupropion and fluoxetine limited PCWG at the end of treatment (bupropion MD -1.12 kg, 95% CI -1.47 to -0.77, N=7) (fluoxetine MD -0.99 kg, 95% CI -1.36 to -0.61, N=2). There was no evidence that the effect persisted at 6m (bupropion MD -0.58 kg, 95% CI -2.16 to 1.00, N=4), (fluoxetine MD -0.01 kg, 95% CI -1.11 to 1.10, N=2) or 12m (bupropion MD -0.38 kg, 95% CI -2.00 to 1.24, N=4). There were no data on WG at 12m for fluoxetine.

Overall, treatment with NRT attenuated PCWG at the end of treatment (MD -0.69 kg, 95% CI -0.88 to -0.51, N=19), with no strong evidence that the effect differed for the different forms of NRT. There was evidence of significant statistical heterogeneity caused by one study which reported a 4.3 kg reduction in PCWG due to NRT. With this study removed, the difference in weight change at end of treatment was -0.45 kg (95% CI -0.66 to -0.27, N=18). There was no evidence of an effect on PCWG at 12m (MD -0.42 kg, 95% CI -0.92 to 0.08, N=15).

We found evidence that varenicline significantly reduced PCWG at end of treatment (MD -0.41 kg, 95% CI -0.63 to -0.19, N=11), but this effect was not maintained at 6 or 12m. Three studies compared the effect of bupropion to varenicline. Participants taking bupropion gained significantly less weight at the end of treatment (-0.51 kg (95% CI -0.93 to -0.09 kg), N=3). Direct comparison showed no significant difference in PCWG between varenicline and NRT.

Authors' conclusions

Although some pharmacotherapies tested to limit PCWG show evidence of short-term success, other problems with them and the lack of data on long-term efficacy limits their use. Weight management education only, is not effective and may reduce abstinence. Personalised weight management support may be effective and not reduce abstinence, but there are too few data to be sure. One study showed a VLCD increased abstinence but did not prevent WG in the longer term. CBT to accept WG did not limit PCWG and may not promote abstinence in the long term. Exercise interventions significantly reduced weight in the long term, but not the short term. More studies are needed to clarify whether this is an effect of treatment or a chance finding. Bupropion, fluoxetine, NRT and varenicline reduce PCWG while using the medication. Although this effect was not maintained one year after stopping smoking, the evidence is insufficient to exclude a modest long-term effect. The data are not sufficient to make strong clinical recommendations for effective programmes to prevent weight gain after cessation.

PLAIN LANGUAGE SUMMARY

Interventions for preventing weight gain after smoking cessation

When giving up smoking, most people put on weight. Many smokers are concerned about this and say it may put them off making an attempt quit. Some studies show that weight gain also leads to people resuming smoking after an initially successful quit attempt. On the other hand, there are good reasons to believe that trying to limit weight gain may reduce the chance of stopping smoking. Several drug and behavioural programmes to limit post cessation weight gain have been tested. Of the drug treatments, naltrexone showed the most promise, but there were no data on its effects on weight once drug treatment stopped and there was not enough evidence to judge its effects on long term quitting. Weight management education alone did not limit weight gain and may undermine cessation. Weight management education with personalised support giving feedback on personal goals and a personal energy prescription limited weight gain and there was no evidence that it undermined cessation. Intermittent use of a VLCD improved cessation success and weight gain in the short term but not in the longer term.

Some smoking cessation treatments also limited weight gain. Bupropion, fluoxetine, NRT and varenicline all limited weight gain during treatment, however the effects on weight gain reduction were smaller after the treatment had stopped and there was insufficient evidence to be sure that these effects persisted in the long-term. There was some evidence to suggest that exercise reduced post cessation weight gain but more studies are needed to clarify whether this was a chance finding. The effects of all interventions were modest in relation to the average weight gain that follows stopping smoking.

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 percent 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. As well as gaining more weight, a large cohort study showed that 13% of women compared with 10% of men had a major weight gain greater than 13kg (Williamson 1991). Weight gain in people who sustained quitting for eight years has been shown to be 9kg (7kg above those who continued to smoke during this time), with 42% of people gaining over 10kg (Lycett 2011). This weight gain can have health consequences, with the incidence of diabetes being higher in smokers that quit smoking than continue with it, an effect that appeared to be explained by weight gain (Davey Smith 2005; Yeh 2010). Weight gain also reduces some of the benefits of quitting smoking on lung function (Chinn 2005).

Among smokers there is a high prevalence of concerns about post-cessation weight gain, and it has been cited as a primary reason for putting off quit attempts, especially in women (Clark 2004; Klesges 1989; Klesges 1992). Weight consciousness has been found to predict current smoking (Weekley 1992), and weight gain experienced during or after smoking cessation has been associated with relapse (Klesges 1988; Klesges 1989; Klesges 1992). However there is inconsistent evidence that fear of weight gain or actual weight gain after quitting does in fact lead to relapse. An equal number of studies show that it does (1 Copeland 2006; Pomerleau 2001; Meyers 1997; Clark 2006) and does not (Killen 1996; Hutter 2006; Mizes 1998; Fidler 2009), and methodological differences make it hard to draw a conclusion one way or the other.

Some smoking cessation 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 energy restriction or healthy 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 (Filozof 2004). 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 (1 Hall 1992) and that hunger increases urges to smoke in current smokers (Cheskin 2005). Additionally, early weight gain has also been found to be associated with successful cessation (Gritz 1988; Hall 1986; Hughes 1991). This suggests interventions that limit dietary intake may potentially reduce smoking cessation success and the adage that smokers should stop smoking first and then diet and not do these concurrently has become common in smoking cessation clinics.

There are a range of other treatments for smoking cessation that

have been developed independently of concerns about weight gain, with the sole aim of assisting smoking cessation. Some of these, such as nicotine replacement therapy, 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.

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

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, 6 and 12 months), and smoking cessation (at 6 and 12 months).

(ii) Part 2 - The effects of antidepressants, exercise, nicotine replacement therapy,varenicline and rimonabant on weight gain (at end of treatment, 6 and 12 months).

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 post cessation weight gain.
Part 2 - Smoking cessation interventions that are not designed primarily to limit post cessation weight gain but which might plausibly influence it, i.e. antidepressants, exercise, nicotine replacement therapy (NRT), rimonabant and varenicline.

Types of outcome measures

There are two primary outcome measures:
(i) Smoking status six months or more after quitting
(ii) Mean (SD) change in body weight (kg) from baseline to follow up in abstainers only.

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

Search methods for identification of studies

Part 1 - We searched the Cochrane Tobacco Addiction Group's Specialized Register of trials in September 2011, using the following search terms in title, abstract or keywords: food, calorie restrict*, intake, diet*, body mass index (BMI), Quetelet, waist-hip ratio (WHR), weight, body-weight, weight-changes. At the search date the specialized register included reports of trials indexed in MEDLINE to update 20110826, EMBASE to 2011 week 33, PsycINFO to 20110822 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.
Part 2 - We searched the following Cochrane reviews: Antidepressants for smoking cessation (latest search, Jul 2009) Hughes 2007, Exercise interventions for smoking cessation (latest search, July 2008) Ussher 2008, Nicotine replacement therapy for smoking cessation (latest search, Oct 2007) Stead 2008, Cannabinoid type

1 receptor antagonists (rimonabant) for smoking cessation (latest search, Jan 2011) Cahill 2011a and Nicotine receptor partial agonists for smoking cessation (latest search, Oct 2010) Cahill 2011b published in Issue 9 2011 of the Cochrane library. The text of 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. In addition we searched the Cochrane Central Register of Controlled Trials (CENTRAL) Issue 4, 2011 to identify trials relevant to the Part 2 reviews published since the last update. Thie following strategies were used:

(smoking OR smoking cessation OR Tobacco) AND (nicotine OR nicotine replacement therapy OR lozenge OR patch OR gum OR inhaler OR microtab OR nasal spray)

(smoking OR smoking cessation OR Tobacco) AND (antidepressant$ OR bupropion OR zyban)

(smoking OR smoking cessation OR Tobacco) AND (varenicline OR nicotine partial agonist OR champix OR chantix)

Data collection and analysis

Two people independently identified studies that fulfilled the inclusion criteria and extracted data. 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 or sponsors for clarification. If we were unable to successfully contact an author or sponsor, studies were excluded from the review.

For studies in Part 1, we extracted data on baseline characteristics, the intervention, smoking, weight data relevant to study quality. Where possible we extracted smoking outcomes as continuous biochemically confirmed abstinence, however we accepted less strict definitions if confirmed continuous abstinence was not available. We checked that, for smoking abstinence estimates, participants lost to follow up were coded as smokers and therefore all randomised participants were included in the denominator and if not we corrected abstinence rates for this. Abstinence rates and their corresponding risk ratio (95% CI) were reported at 6 and 12 months of follow up. For studies in Part 2, we extracted data on weight gain only.

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

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

SD = ($\sqrt{}$(n) x (upper limit - lower limit)) /standard error wide

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

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

SD=SE x $\sqrt{}$(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 weight were across participants. This was estimated in abstinent smokers from raw data that we have collected from a trial to prevent weight gain on smoking cessation (Parsons 2009) 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 have already been extracted on the participants, interventions and study quality in the Cochrane reviews included in Part 2 we extracted only data about weight gain. Weight data was extracted using the same approach as described in Part 1.

In some studies in Part 1 and 2, more than one trial arm had been compared with a control arm. Where appropriate, to create one comparison intervention arm we combined outcome data. For smoking we added together the numerator and denominator from each arm. Weight outcomes from more than one trial arm were calculated using the following formulas:

$Mean_c$ = ((Mean1*n1)+(Mean2*n2))/(n1+n2)

Standard deviation= $\sqrt{var_c}$

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

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

Key: $Mean_c$= Combined mean, sumsq=sum of squares

For studies in Part 1, we rated the potential for bias of included trials on methods of randomisation, allocation concealment and blinding following methods described in the Cochrane Handbook for Systematic Reviews of Interventions (Handbook 2005). This had already been performed for studies in Part 2 in the parent

reviews.

Smoking cessation outcome data are given based on the number of quitters in the treatment and control groups divided by the total number of participants receiving treatment 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. The I^2 statistic was used 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.

RESULTS

Description of studies

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

Interventions specifically designed to address post cessation weight gain

We found 16 trials which matched our inclusion criteria for the first part of the review. Two of these studies contributed data to both Parts 1 and 2 of the review (1 Cooper 2005; 1 Spring 1995). All studies recruited community volunteers who wanted to stop smoking and avoid weight gain. Nine studies recruited women only (1 Cooper 2005; 1 Copeland 2006; 1 Danielsson 1999; 1 Klesges 1990;1 Levine 2010 1 Perkins 2001; 1 Pirie 1992; 1 Spring 1995; 1 Spring 2004) and the remainder included smokers of both sexes (1 Hall 1992;1 Hankey 2009; 1 Klesges 1995; 1 Norregaard 1996; 1 O'Malley 2006; 1 Parsons 2009; 1 Toll 2010). Participants averaged 20-25 cigarettes per day with the exception of four studies where mean consumption was higher at between 26-32 (Hall 1992; 1 O'Malley 2006;1 Pirie 1992 and 1 Spring 1995). Mean baseline weight and/or body mass index (BMI) was reported in all but three studies (1 Klesges 1990; 1 Klesges 1995; 1 Toll 2010) and ranged between 64-76 kg/BMI 23-29.

Seven studies compared the effects of pharmacological interventions to placebo on smoking cessation and post cessation weight change. Pharmacological interventions included: 8.33 mg Phenylpropanolamine gum 16 pieces/day for 8 weeks (1 Cooper 2005), 9 pieces/day for 2 weeks (1 Klesges 1990) and up to 10 pieces/day for 4 weeks (1 Klesges 1995), 20 mg Ephedrine plus 200 mg caffeine 3/day for 12 weeks (1 Norregaard 1996), 100, 50 and 25 mg/day Naltrexone for 6 weeks (1 O'Malley 2006) and 30 mg/day Dexfenfluramine for 12 weeks (1 Spring 1995). This study also examined the efficacy of 40 mg/day of fluoxetine for preventing weight gain (1 Spring 1995). As the other fluoxetine studies were included in Part 2 of the reviews, this comparison is described in Part 2.

Six studies assessed the effects of multi component behavioural interventions to prevent weight gain added to usual smoking cessation support. In three studies the intervention consisted of education on weight management. This was education on healthy eating, increasing physical activity and behavioural change strategies such as self monitoring (Hall 1992;1 Hankey 2009; 1 Pirie 1992). Although, one study advised all participants to reduce energy intake by 100-300kcal/day depending on how much they smoked and increase activity to one hour of walking three times a week, this was general advice given to the group and no feedback was given. (1 Pirie 1992). One of these studies (1 Hankey 2009) gave advice appropriate to "stage of change". These have been classified as "weight management education" interventions. Three studies additionally included feedback on personal goals and a personal energy prescription (500kcal deficit of energy requirement calculated from age, gender, weight and activity level of individuals (Hall 1992; 1 Perkins 2001) or a 150-300kcal deficit based on individuals' food diaries (food was prepared and provided to participants in this study) (1 Spring 2004). These have been classified as "personalised weight management support" interventions. We considered the behavioural interventions to be compared to a "no weight intervention" arm, if participants received no intervention targeted at weight management (1 Pirie 1992) or if the control arm included minimal weight intervention given to appease the participants (1 Hall 1992, good nutrition and exercise information pack not aimed at post cessation weight gain given to participants, 1 Spring 2004, last session (Wk16) spent talking about weight loss strategies, 75/107 randomised participants attended) rather than a specifically designed to have an effect.

One study tested the efficacy of a very low calorie diet (VLCD). In this study, participants in the intervention and control group both received the weight management education as well as usual smoking cessation support. Both groups were also advised to follow a 1600kcal diet, while the intervention group received two, two week blocks of a VLCD provided free of charge. Treatment took place in a specialist obesity treatment centre (1 Danielsson 1999).

Cognitive behavioral therapy (CBT) to address concern about weight gain is aimed at ameliorating concern and promoting abstinence, not at reducing weight gain as such, but we included these studies. 1 Perkins 2001 tested the effect of CBT to promote acceptance of modest weight gain added to standard smoking cessation counselling compared to usual smoking cessation support only. 1 Levine 2010 tested the effect of CBT and bupropion separately and in combination added to standard smoking cessation counselling.

1 Spring 2004 tested whether it was better to quit first then ad-

dress weight gain or whether the two could occur concurrently. In this study participants, all participants received 16 weeks of smoking cessation support (target quit day,week 5) and in addition were randomised to a concurrent personalised weight management support programme (weeks 1-8) or personalised weight management support programme sequential to quitting (weeks 9-16). In the third arm participants did not receive a personalised weight management support programme but the final session focused on weight management education. 75/107 participants enrolled in the control arm were present for the final session.

Finally, one study compared the effect of group to individual relapse prevention follow up sessions on smoking cessation and weight change after a 2 week smoking cessation programme (1 Copeland 2006). As there was no control group without the weight advice, the study is not included in the meta analyses below.

Smoking cessation therapy was provided for all participants in all studies of pharmacological and behavioural interventions. The duration, number and format 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 including the following components: cognitive behavioural skills such as anticipating and planning for high risk situations, coping skills, relapse prevention and benefits of quitting smoking. In four studies all participants were also supplied with NRT (1 Copeland 2006; 1 Danielsson 1999;1 Hankey 2009;1 O'Malley 2006) and in 1 Pirie 1992 two of the four comparison arms received NRT.

Nine studies (1 Cooper 2005; 1 Copeland 2006; 1 Danielsson 1999; Hall 1992;1 Hankey 2009; 1 Norregaard 1996; 1 Perkins 2001; 1 Pirie 1992; 1 Spring 2004) reported smoking as an outcome at six and/or 12 months. Smoking was either recorded as point prevalence (1 Cooper 2005, 1 Hall 1992) or prolonged or continuous abstinence (all others). Continuous abstinence was defined as 'not a single puff since quit date'. Definitions of prolonged abstinence varied, but mainly allowed for a grace period for the two first weeks after quit day or for small lapses that did not lead to full relapse. All studies apart from one (1 O'Malley 2006) reported biochemically confirmed rates. All 15 studies reported weight gain as an outcome at end of treatment, and some reported weight at six and/or 12 months.

Interventions not specifically designed to address post cessation weight gain

We found 53 individual trials from the lists of included studies in the parent reviews which matched our inclusion criteria for the second part of the review and had extractable data. Two of these studies also contributed data to the first part of the review (2 NRT Cooper 2005;2 NRT Pirie 1992). We included 4/11 exercise studies, 12/67 antidepressant studies (2 AD Gonzales 2006; 2 AD Jorenby 2006; 2 AD Nides 2006 also appear in varenicline list), 28/133 nicotine replacement therapy studies, and 12/15 varenicline studies. We were unable to obtain published or unpublished data from the authors of any studies in the cannabinoid receptor antagonists parent review. One additional study was identified through the update search (2 NRT Pack 2008). Participants were adult smokers who were typically volunteers from the community (although some 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 20-30 cigarettes per day. Twenty three studies reported baseline weight/BMI which was within healthy weight to slightly overweight (with mean BMI of 24-25 or mean weight no greater than 85 kg) the remaining 33 studies did not report baseline weight or BMI. As these were populations intent on smoking cessation only, they are likely to be smokers of typical body weight. One study, recruited participants based on cigarette consumption, smoking an average of 17-18 (2 NRT Shiffman 2002A) and 25-26 (2 NRT Shiffman 2002B) cigarettes per day.

Twelve studies from the antidepressant parent review were included in this review, three of which compared bupropion to varenicline as well as 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, ten 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 Piper 2007; 2 AD Rigotti 2006; 2 AD Simon 2004;2 AD Simon 2009; 2 AD Uyar 2007; 2 AD Zellweger 2005) and two studies compare fluoxetine to placebo (2 AD Niaura 2002; 2 AD Saules 2004). 2 AD Saules 2004 tested fluoxetine versus placebo, but both intervention and control arms used NRT, but we included it in the analyses with other fluoxetine versus placebo studies. One other study examined the efficacy of fluoxetine versus placebo (1 Spring 1995). It was not included in the parent Cochrane review because smoking cessation at 6 months was not reported, but was identified and included here.

All bupropion studies administered 300 mg/day and 2 AD Hurt 1997 also included a 100 mg/day and 150 mg/day arm. For the main comparison, the 300 mg/day arm is used for the Hurt study and the lower dose arms are used to compare to the standard 300 mg/day treatment to the lower dose arms . Two fluoxetine studies compared two dosing levels (30 mg & 60 mg/day (2 AD Niaura 2002) and 20 mg & 40 mg/day (2 AD Saules 2004)) which were combined for the main comparison and the lower doses and higher doses were compared in a separate comparison to examine for a dose dependent effect. One other study examined 40 mg fluoxetine versus placebo (1 Spring 1995). The treatment period for all antidepressant studies ranged from seven weeks to 14 weeks with a run in to quit day of one to four weeks.

Four studies provided data from the exercise interventions parent review. In all four studies, participants in the treatment arm received an exercise component in parallel with cognitive behavioural treatment for smoking cessation, which was supplemented with nicotine replacement therapy in 2 EX Ussher 2003

and 2 EX Bize 2010. The exercise component included supervised exercise in three studies. 2 EX Marcus 1999 tested three supervised exercise sessions/week for 12 weeks, 30-40 mins resting heart rate plus 60-85% heart reserve, 2 EX Marcus 2005 tested one supervised, four unsupervised exercise sessions/week for eight weeks, at least 30 minutes at resting heart rate plus 45-59% heart reserve and 2 EX Bize 2010 tested moderate-intensity (40-60% of maximal aerobic power) group-based cardiovascular (CV) activity under the supervision of a trained monitor for 45 minutes weekly for nine weeks. In contrast, 2 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 regimes (11 mg, 22 mg and 44 mg) (2 NRT Dale 1995) which has been included in a separate comparison. Dosing regimes in the nine 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 higher doses.

Five studies provided data on weight change whilst using NRT 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 studies, participants used 2 mg with ad libitum dosing instructions (2 NRT Hjalmarson 1984, 1 Pirie 1992). One study asked participants to chew 10-12 pieces daily (1 Cooper 2005). In 2 NRT Gross 1995, participants were given 2 mg gum but then randomised to instruction to chew seven, 15, or 30 pieces daily. 2 NRT Garvey 2000 randomised smokers to placebo, 9-15 pieces of 2 mg gum, or 9-15 pieces of 4 mg gum. Treatment length varied from eight weeks to one year, with a median of 12 weeks.

There were two placebo controlled studies of nicotine nasal spray up to 40 mg/day (2 NRT Hjalmarson 1994; 2 NRT Sutherland 1992). There were two placebo controlled study of up to 6 months usage 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) versus inhaler alone (and this was therefore included in the patch versus placebo comparison), one placebo controlled study of nicotine patch added to nicotine gum (2 NRT Puska 1995) versus gum alone and this was included in the patch versus placebo condition. The median length of treatment for all NRT studies was 12 weeks (range 4-52). 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).

One study directly compared the effectiveness of nicotine lozenge with nicotine gum (2 NRT Pack 2008) and one study directly compared nicotine patch to nicotine spray (2 NRT Lerman 2004). Three studies allowed direct comparisons between different NRT doses (2 NRT CEASE 1999; 2 NRT Dale 1995; 2 NRT Gross 1995).

Twelve studies in the nicotine receptor antagonist parent review reported weight change when using varenicline. Eleven studies were placebo controlled and included a 2 mg/daily arm, 2 VA Nakamura 2007, 2 VA Nides 2006 and 2 VA Oncken 2006 also randomised participants to 0.3 mg and/or 1 mg/daily with or without titration. We compared these lower doses to higher doses in a comparison of dose response.

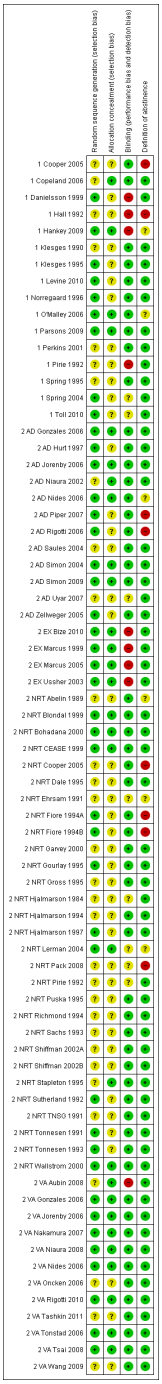
One study compared 2 mg/daily varenicline to a 21 mg patch tapering to 7 mg (2 VA Aubin 2008). As mentioned above, 2 VA Gonzales 2006; 2 VA Jorenby 2006; 2 VA Nides 2006 also compared varenicline with bupropion. Two of the twelve studies were phase II trials (2 VA Nides 2006; 2 VA Oncken 2006). The treatment phase lasted for 12 weeks in six 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 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 randomised to an additional 12 weeks of varenicline or placebo and the effect of an extra 12 weeks of treatment is explored in a separate comparison. This was combined with the other studies where the 12 weeks of varenicline/placebo was given in the first 12 weeks of abstinence, not the second. 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. Definition of abstinence varied between studies as in the first part of the review and is noted in the table of characteristics of included studies. In most studies, all participants received some form of smoking cessation behavioural support in addition to the pharmacotherapy/exercise therapy and details are outlined in the table of characteristics of included studies. Some of the end of treatment data and longer term follow-up data were received through personal communication with authors and this is also noted in characteristics of included studies.

Risk of bias in included studies

We extracted information about randomisation, allocation concealment, blinding and measurement of abstinence and assessed the potential for bias in each domain (Figure 1). No studies were found to have used biased methods of randomisation or allocation concealment however a large proportion of studies didn't report the method of generating the random allocation sequence (31/72 studies) or allocation concealment (44/72 studies) in enough detail for likelihood of bias to be assessed. As the majority of these studies were published before the CONSORT statement guidelines were issued, it is likely that this is due to lack of reporting rather than bias. Given the nature of the behavioural interventions and exercise interventions, blinding was not possible for these studies and therefore there was some potential for 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 a further two studies. 1 Norregaard 1996 found that 68% of the treatment group and 63% of the placebo group had correctly guessed their allocation to active or placebo NRT and 2 NRT Tonnesen 1993 46% on active treatment and 58% on placebo treatment guessed correctly, indicating guessing was no better than chance. A more serious potential for bias concerns the weight management interventions in the group of 'behavioural treatment' studies. Six out of the seven 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. Six studies out of all included in the review measured weight change in abstinent participants measured using point prevalence criteria. This was defined as being abstinent at the time of follow up in one study (1 Cooper 2005/2 NRT Cooper 2005) and abstinent for seven days previous to follow up in the remaining five studies (1 Hall 1992; 2 AD Piper 2007; 2 AD Rigotti 2006; 2 NRT Fiore 1994A; 2 NRT Fiore 1994B). Whether abstinence was biochemically validated or unvalidated, this was deemed as demonstrating a high risk of bias as smoking prior to the seven day period would reduce potential weight gain. Six studies were rated as being unclear in terms of bias introduced by abstinence measurement. This was because in three studies abstinence was measured as prolonged or continuous (i.e. participants need to be completely abstinent from two weeks after their quit day or from their quit day, respectively) but was not biochemically validated (1 O'Malley 2006; 2 AD Nides 2006/2 VA Nides 2006; 2 NRT Lerman 2004), in two study the definition of abstinence was not reported (1 Hankey 2009; 2 NRT Ehrsam 1991) and in one study although participants were only counted as abstinent if their exhaled CO levels were below 11 ppm at follow up, they were able to smoke up to three cigarettes per week (2 NRT Abelin 1989).

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



Effects of interventions

Effect of pharmacological interventions to prevent post cessation weight gain on weight and smoking cessation

There was evidence that dexfenfluramine (mean difference (MD) -2.50 to 95% confidence interval (CI) -2.98 to -2.02), one study), phenylpropanolamine (PPA) (MD -0.50 kg, 95% CI -0.80 to -0.20, three studies) and naltrexone (MD -0.78 kg, 95% CI -1.52 to -0.05, two studies) reduced weight gain at the end of treatment (Analysis 1.1) but no evidence that ephedrine and caffeine (MD -1.30 kg, 95% CI -2.87 to 0.27 kg, one study) or chromium (MD -0.81 kg, 95% CI -3.05 to 1.43, one study) did so. No pharmacological intervention significantly reduced weight gain at six or 12 months, but this was examined only for chromium, ephedrine and caffeine, and PPA. (Analysis 1.2 and Analysis 1.3). There was no evidence that these pharmacological interventions either increased or decreased quit rates at six or 12 months, but the wide confidence intervals mean the estimates were imprecise (Analysis 2.1; Analysis 2.2).

Effect of behavioural interventions to prevent post cessation weight gain on weight and smoking cessation

There was no evidence at any follow up that weight management education alone reduced weight gain (At EOT MD -0.04 kg, 95% CI -0.57 to 0.50, two studies; at 6 months MD 0.89 kg, 95% CI -0.78 to 2.55, two studies; and 12 months MD -0.21 kg, 95% CI -2.28 to 1.86, two studies (Analysis 3.1; Analysis 3.2; Analysis 3.3)). Interventions providing weight management education only compared with no intervention showed no difference in quit rate at six months (RR 1.02, 95% CI 0.80 to 1.31, three studies, Analysis 4.1). At 12 months, however, the intervention significantly reduced success in quitting (RR 0.66, 95% CI 0.48 to 0.90, two studies, Analysis 4.2).

Personalised weight management support programmes significantly reduced weight gain at end of treatment (MD -1.11 kg, 95% CI -1.93 to -0.29, 3 studies, Analysis 3.1) and this effect was strengthened at 12 months (MD -2.58 kg, 95% CI -5.11 to -0.05), two studies, Analysis 3.3). However, one study (1 Spring 2004) provided data at six months and showed no difference in weight change between a personalised weight management support programme and no intervention (MD 0.40 kg, 95% CI -2.54 to 3.34, Analysis 3.2). The within study comparison from 1 Hall 1992 suggested that personalised weight management support is more effective than weight management education only at end of treatment (-MD 1.12 kg, 95% CI -2.17 to -0.07, Analysis 3.1) and at 12 months (MD -2.49 kg, 95% CI -5.51 to 0.53, Analysis 3.3). Personalised weight management support had no effect on quit rate at six months (RR 0.88, 95% CI 0.54 to 1.43, two studies, Analysis 4.1) or at 12 months (RR 0.79, 95% CI 0.47 to 1.33, two studies, Analysis 4.2) although confidence intervals were wide..

The single study (1 Danielsson 1999) that incorporated an intermittent very low calorie diet into a weight management education intervention showed a significant reduced weight gain at end of treatment (MD -3.70 kg, 95% CI -4.82 to -2.58, Analysis 3.1). At 12 months the effect was smaller and not significant (MD -1.30 kg, 95% CI -3.49 to 0.89, Analysis 3.3). This intervention was associated with a significant improvement in abstinence at 12 months (RR 1.73, 95% CI 1.10 to 2.73, Analysis 4.2).

Effect of CBT to accept post cessation weight gain on weight and smoking cessation

There was mixed evidence for the effect of CBT to reduce weight gain concerns showing no reduction in weight gain at end of treatment (MD -0.18 kg, 95% CI -0.56 to 0.20, two studies, I^2 92%, Analysis 6.1) or at 12 months (MD 0.13 kg, 95% CI -0.72, 0.98, two studies, I^2 71%, Analysis 6.3). However, there was evidence of significantly increased weight in the CBT group at 6 months (MD 0.74 kg, 95% CI 0.24 to 1.24, 2 studies, I^2 82%, Analysis 6.2). CBT significantly increased the quit rate at 6 months (RR 1.70, 95% CI 1.13 to 2.56, 2 studies, I^2 57%, Analysis 5.1) but not at 12 months (RR 1.25, 95% CI 0.83 to 1.86, 2 studies, I^2 26%, Analysis 5.2). One study (1 Levine 2010) tested CBT added to treatment with bupropion (300 mg/day), and found no evidence of reduced weight gain or increased abstinence in those who received CBT and bupropion treatment compared to those who received bupropion treatment with no additional CBT for weight concerns. (Analysis 4.1; Analysis 4.2; Analysis 3.1; Analysis 3.2; Analysis 3.3). However, there was evidence of significantly increased weight gain at six months (MD 0.86 kg, 95% CI 0.30 to 1.42 kg, 1 study). There was significant statistical heterogeneity when combining studies as the effects seen in each study differed markedly, with 1 Perkins 2001 finding a significant effect of CBT on weight reduction at end of treatment, six and 12 months and increased quit rates at six months and 1 Levine 2010 finding no such effects at any time point, but finding significant weight gain in the CBT arm at six months.

Effect of antidepressants on post cessation weight gain

Bupropion (300 mg/day) limited post cessation weight gain compared with placebo at the end of treatment (MD -1.12 kg, 95% CI -1.47 to -0.77, seven studies, Analysis 7.1). At six and 12 months

the reduction in weight was lower than at end of treatment and it was not significant (MD -0.87 kg, 95% CI -2.21 to 0.47, four studies, Analysis 7.3 and MD -0.38 kg, 95% CI -2.00 to 1.24, four studies, Analysis 7.5). There was no evidence of a dose dependent response for bupropion at end of treatment, six or 12 months (Analysis 7.2, Analysis 7.4, Analysis 7.6).

Fluoxetine reduced weight gain at end of treatment (MD -0.99 kg, 95% CI -1.36 to -0.61, two studies, Analysis 7.1). At six months, the effect was smaller and not significant (MD -0.19 kg, 95% CI -1.10 to 0.71, two studies, Analysis 7.3), Two studies of fluoxetine randomised participants to higher and lower doses as well as to placebo (2 AD Niaura 2002 to 60 mg and 30 mg and 2 AD Saules 2004 to 40 mg or 20 mg). There was no evidence that higher doses were more effective at six months and in fact people randomised to 60 mg had significantly greater weight gain at six months than people randomised to 30 mg, an effect not seen in the 40 mg versus 20 mg comparison (Analysis 7.4).

Effect of exercise interventions on post cessation weight gain

Neither individual nor pooled data for the three trials of exercise programmes showed any reduction in weight gain at the end of the programme (Analysis 8.1), with a summary estimated mean difference of -0.25 kg (95% CI -0.78 to 0.29). However, three studies provided data at 12 months follow up which when pooled showed a significant reduction in weight gain favouring treatment (Analysis 8.2), with a summary estimate of -2.07 kg (95% CI -3.78 to -0.36).

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

Participants taking any type of NRT gained less weight than placebo referents at the end of treatment (MD -0.69 kg, 95% CI -0.88 to -0.51, 19 studies, I^2=82%). Statistical heterogeneity was due to one study 2 NRT Abelin 1989 which showed a 4.3 kg difference between weight gain in the treatment and control arm. When this study was removed, statistical heterogeneity reduced to 0% and the overall estimate decreased but remained statistically significant (MD -0.46 kg, 95% CI -0.66 to -0.27, Analysis 9.1). Estimates of difference in weight gain for different types of NRT were similar: gum MD -0.58 kg (95% CI -1.02 to -0.13.4 studies), patch (without Abelin 1989) MD -0.45 kg (95% CI -0.70 to -0.20, 10 studies), inhaler MD -0.37 kg (95% CI -1.19 to 0.45, two studies), sublingual tablet MD -0.48 kg (95% CI -0.99 to 0.03, 2 studies), intranasal spray (+ patch) MD 0.90 kg (95% CI -1.54 to 3.34, one study). There was some evidence that there was less weight gain at the end of treatment in participants using the lozenge compared to those using patch (MD -2.45 [-4.43, -0.47], 1 study), although this difference didn't remain in the long term. Overall, weight gain was less for those taking NRT at six and 12 months although not significantly (MD -0.37 kg, 95% CI -0.88 to 0.14, 9 studies Analysis 9.5 and MD -0.42 kg, 95% CI -0.92 to 0.08, 15 studies, Analysis 9.8). 2 NRT Lerman 2004 compared patch to spray and found no significant difference in weight gain at end of treatment or six months (Analysis 9.2; Analysis 9.5).

Longer courses of NRT with 15 mg or 25 mg patches were not associated with reduced weight gain at 12 months Analysis 9.11. 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 mg, 22 mg and 11 mg patches to placebo, 2 NRT CEASE 1999 compared 25 mg and 15 mg patches to placebo, and 2 NRT Gross 1995 compared different numbers of 2 mg NRT gum per day. There was no significant dose dependent difference in weight gain at the end of treatment (Analysis 9.4) or at 12 months (Analysis 9.10).

Effect of rimonabant on post cessation weight gain

We were unable to obtain mean weight change data with confidence intervals for rimonabant on post cessation weight gain. All weight related findings that have been reported have been summarised by the parent Cochrane review (Cahill 2011a) which indicates that rimonabant may reduce weight gain during treatment by a small amount. However, the FDA did not authorise the use of rimonabant and the European Medicines Agency and Food and Drug Administration have withdrawn marketing authorisation because they concluded the benefits of rimonabant did not outweigh the risks.

Effect of varenicline on post cessation weight gain

There was no evidence that 1 mg of varenicline reduced weight gain more than placebo (MD -0.12 kg, 95% CI -0.68 to 0.43, three studies) but there was evidence that 2 mg daily did reduce weight gain (MD -0.41 kg, 95% CI -0.63 to -0.19, 11 studies) (Analysis 10.1). Only one study provided data at six months, showing no evidence of effect (MD 0.41 kg, 95% CI -0.79 to 1.61, Analysis 10.2) and two studies at 12 months, also showing no evidence of an effect (MD 1.11 kg, 95% CI -0.75 to 2.98, Analysis 10.3).

Three studies compared treatment with bupropion to varenicline. Participants taking varenicline gained significantly more weight at the end of treatment (MD 0.51 kg, 95% CI 0.09 to 0.93, Analysis 11.1). There was no evidence that weight gain differed in the one trial of varenicline versus NRT (2 VA Aubin 2008, Analysis 12.1).

DISCUSSION

Since the first version of this review was published in 2009, we have found five additional trials and received data from the authors of a further trial fitting criteria for part 1, and there are now 16 trials of interventions specifically designed to limit post cessation

weight gain. Although a range of pharmacological interventions were tested, none showed evidence that weight gain was prevented in the longer term. Behavioural interventions were more promising. Personalised weight management support, which included weight management education with both feedback on personal goals and a personal energy prescription, showed reduced weight gain at one year, but the estimate of effect was very imprecise covering both substantial benefit and a clinically irrelevant benefit. There was no evidence that detailed weight management education without personalised assessment, planning and feedback reduced weight gain and at least some evidence that this may have reduced smoking cessation rates. The earlier version of this review suggested that CBT to accept moderate weight gain increased abstinence, and limited long term post cessation weight gain however, a subsequently published trial was not as promising. When the two trials were combined, although smoking cessation rates were still significantly increased at six months, there was a significant increase in weight gain at six months, and no effects on either weight or quitting at 12 months. However, statistical heterogeneity was high. Eight new trials were identified during the update that fitted the criteria for Part 2 of this review (three bupropion studies, four varenicline studies and an NRT study that compare lozenge to gum preparations). In total, we examined evidence for five different interventions used to support smoking cessation that might incidentally reduce weight gain on cessation. There was strong evidence that four of these, NRT, bupropion, fluoxetine, and varenicline all reduced weight gain by about 0.5 kg (NRT and varenicline) and about 1 kg (fluoxetine and bupropion) by the end of the usual treatment period. A few of the trials recorded weight at later follow ups, and there was no evidence that these pharmacotherapies attenuated weight gain when assessed then but there is insufficient evidence to exclude an effect. There was some evidence that nicotine nasal spray did so at one year and it is perhaps notable that spray was available for the whole year for participants in these trials. One behavioural intervention, exercise to assist smoking cessation, showed no evidence that it reduced weight gain during the exercise programme but, perhaps surprisingly given this finding, there was evidence of reduced weight gain at one year.

Pharmacotherapy to limit weight gain

To date, six pharmacological interventions (phenylpropanolamine (PPA), ephedrine + caffeine, naltrexone, dexfenfluramine, fluoxetine and chromium) have been combined with standard smoking cessation treatment to test their effect on post cessation weight gain compared with smoking cessation treatment alone. None have shown evidence of a long-term effect on weight gain and therefore none can be recommended for use in clinical practice. There was however promising evidence that PPA, dexfenfluramine, and naltrexone prevent weight gain in the short term. Dexfenfluramine has been withdrawn from use because it causes serious problems and the dose of PPA allowed for use is lower than the dose tested in these trials. Naltrexone, which is used in treatment of other substance use dependence, is promising, although the effect on weight gain is modest.

Behavioural programmes to limit weight gain

English smoking cessation guidelines from NICE make no specific recommendations about preventing post cessation weight gain, while US guidance recommends either bupropion, NRT, or exercise as interventions. A common perception is that concurrent behavioural treatment for smoking and weight undermines smoking cessation and advice is to establish smoking cessation before tackling weight (McEwan 2006). Some of the reason for this is the evidence from laboratory studies which show increased urges to smoke during periods of food restriction (Cheskin 2005, Leeman 2010). With one possible exception, our review revealed no evidence to reinforce this fear.

US guidelines do not discuss the role of dietary interventions, which are the mainstay of weight control interventions in other contexts. Our review suggested that weight management programmes did not generally undermine smoking cessation. At six months no interventions showed strong evidence that cessation was reduced and at 12 months, only one intervention did. This was weight management education without personalised support. Given there was no evidence that cessation was undermined at six months, these data are hard to interpret. Nevertheless there was no evidence that this kind of non personalised weight management education reduced weight gain and such general advice cannot be recommended. The other similar but more intensive personalised weight management support programmes look the most promising of all interventions we reviewed, but the effect estimate is imprecise and requires confirmation. These interventions differed but all included personal goal setting, monitoring and feedback on progress. Other elements that may have contributed to success were degree of personalised energy restriction, or providing food to help with adherence. Although it would be possible to manipulate one element at a time, the commonalities of these data with those in the weight loss field suggest that all elements are likely to be important ingredients in the success of the intervention. It is also worth noting that the point estimates for abstinence both suggested that cessation was less likely in those receiving this intervention, though not significantly so. Further trials of this approach are required for confirmation. The other dietary approach that showed distinct promise was the VLCD. There was evidence that use early on in cessation increased abstinence in the long-term and clear evidence of a short-term reduction in weight gain and non-significant evidence of a reduction in weight at one year. In this study, the control arm was advised to adhere to a 1600kcal/day diet, which creates an energy deficit, therefore this may have masked the full effect of the VLCD in the intervention arm. However, this was one trial that advertised for participants and whether

this kind of demanding intervention would be popular with many people trying to stop smoking remains to be seen.

Physical activity or exercise programmes were included in Part 2 of our review because they were aimed at increasing cessation. There is strong evidence that exercise reduces cravings to smoke. (Taylor 2007). In most trials of interventions in weight management, the difference between intervention and control is most marked at end of treatment and declines over follow up. In this context, it is puzzling that there was no evidence of effectiveness of exercise on weight at end of programme, but there was at 12 month follow up. This might either represent a chance finding or reflect the fact that the programme encouraged people to go on exercising after it had finished. Further evidence is required before we can be confident that physical activity programmes provide an effective intervention.

There is a caveat regarding the open label design of the above behavioural intervention studies. With the exception of 1 Hall 1992, they all enrolled women who had problems with weight gain on cessation and were therefore looking to be enrolled in weight control programmes. Such participants may have been more likely to default from the control programme than when allocated the active intervention that they presumably wanted, especially in studies such as 1 Danielsson 1999 and 1 Spring 2004 where this included free meals. The open label design is unavoidable in this field, but it is important to note that it could bias the smoking abstinence results in favour of the intervention. Another possible explanation of the positive result of the very low calorie diet is that it induced ketosis, which may have suppressed hunger (Johnstone 2008) and nicotine withdrawal.

Reducing fears about weight gain through CBT

CBT to address weight gain concerns increased weight and improved quit rates at six months, but there was no evidence of any effect at 12 months. The results of the two studies that have tested this approach varied significantly. Thus, further trials of this intervention are required before it can be recommended as a treatment programme for weight concerned smokers wanting to stop smoking.

Pharmacotherapy for smoking cessation

We found evidence that antidepressants, nicotine replacement therapy, and varenicline attenuate weight gain during the treatment phase, however there was insufficient evidence that the effect persisted in the longer term. The evidence suggested that for antidepressants, fluoxetine and bupropion, and for varenicline, the weight of those allocated to active intervention was the same as that for placebo in the longer term. The picture was more complicated for long term effects of NRT. The strongest effect at 12 months was seen in trials of nasal spray and inhaler, however in these trials participants were allowed to use the NRT preparation for up to a year. Taking these data together, they seem to indicate that the effect of pharmacotherapies is seen during treatment and that those who use pharmacotherapy catch up with accelerated weight gain once treatment is withdrawn. Data from within trials, 2 NRT Sutherland 1992, and an observational study (Hajek 1988) strengthens the conclusion that the possible long-term effect of NRT depends upon long-term use. The difference in weight between long-term users and non-users was several kilograms in these studies, but little is known regarding possible adverse effects of long term use of NRT. Although we found no dose response effects in trials where participants were randomised to a higher or lower dose of NRT, there is preliminary data from records of NRT actually consumed that weight gain is associated with the dose of NRT used (Ferguson 2011).

Methodological considerations

Several features of our review merit comment. First, we encountered studies of fluoxetine in Part 1 and Part 2 of the review. The study of fluoxetine in Part 1 was excluded from the parent Cochrane review because it did not incorporate at least a six-month follow up. It was included in the Part 1 search because the aim was to reduce weight gain. This means that it is possible that we did not include some other studies of fluoxetine that were not specifically aimed at reducing weight gain and did not incorporate a six- or 12-month follow up. There is no reason to imagine that excluding them would create a bias, however. Second, in this update but not in the original version of our review, we added 2 VA Tonstad 2006 to our main analysis of the effect of varenicline on weight gain. In this trial, participants had taken 12 weeks of varenicline before the abstinent participants were randomised to a further 12 weeks or placebo. Thus this study examines weight gain in months three to six of a quit attempt, not months zero to three as in the other studies. We could see no strong reason to imagine that this would bias the analysis. Weight gain is less rapid in months three to six (O'Hara 1998) so, if anything, it is likely that taking varenicline would prevent less weight gain during this later period than during the former. However, the statistical significance of the result is sensitive to whether the Tonstad study is included or excluded from the meta-analysis.

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

As noted in the introduction, the data here relate to weight gain in abstinent smokers only. It is practically difficult to follow up non-abstinent smokers as they have no motive to attend smoking

cessation clinics and thus authors do not usually provide data on continuing smokers. However, most people gain weight on cessation and most people make repeated attempts to quit. It is possible that this leads to incremental weight gain and it would be useful if data could be collected on this.

AUTHORS' CONCLUSIONS

Implications for practice

- Weight management education may reduce abstinence and is not effective at controlling weight and should not be used.

- Personalised weight management support programmes, incorporating both feedback on personal goals and a personal energy prescription may reduce weight gain and there is no strong evidence they reduce abstinence. Further research is required to examine whether these effects can be replicated, and if the effect can be generalised to all smokers, not just those specifically concerned about gaining weight. Until then they should be used cautiously, ideally in research.

- Very low calorie diets may increase abstinence and prevent weight gain in the short-term at least, but these conclusions are based on a single trial only.

- The evidence showed that CBT to allay concerns about weight gain does not reduce weight gain or increase abstinence in the long term. There was significant heterogeneity between the findings of two studies of this approach.

- There is mixed evidence that exercise limits post cessation weight gain but further research is required to show conclusively that it is beneficial.

- Nicotine replacement therapy, bupropion, fluoxetine and varenicline all reduce weight gain in the short term, but patients need to be told that it is unclear whether they reduce weight gain in the long term.

- The long-term effect of all combined smoking cessation and weight control interventions on weight gain is small at best, less than 1 kg, compared with the weight gain at one year (about 5 kg) and is of borderline clinical relevance. The only possible exceptions are personalised dietary and exercise interventions which may reduce this weight gain by half.

Implications for research

- It is important to know whether the effects of personalised weight management support programmes and very low calorie diets can be replicated and if the effect is confirmed, whether it can be generalised to all smokers trying to stop or whether the effect is specific to smokers concerned about weight gain.

- Further studies of CBT to reduce weight concerns are required to clarify its effect on weight gain and smoking cessation, as the two studies carried out to date vary significantly in their estimation of effect and there was some evidence of increased weight gain at six months.

- Further studies of exercise interventions are needed. The finding that an intervention aimed at increasing exercise levels had no effect initially but somehow affected weight on year later seems counterintuitive as adherence to exercise regimes usually decline rather than increase with time.

- Future trials of interventions for limiting post cessation weight gain should report mean weight change, standard deviation for the weight change and the number contributing to the mean in biochemically confirmed continuous or prolonged abstinent participants only rather than in those abstinent for only one week. Weight change in those who continue to smoke should be reported separately.

- Trials of current and future pharmacotherapies for smoking cessation should measure weight change, reporting mean weight change, standard deviation of the change and numbers contributing to the mean, separating abstinent from smoking participants as described above.

ACKNOWLEDGEMENTS

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

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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 64-66kg
Interventions	1. Phenylpropanolamine (PPA) gum 8.33mg 16 pieces/d 8w, 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 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

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Methods not described
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	Low risk	All group facilitators and participants were blind to treatment conditions
Definition of abstinence	High risk	Weight measured in self report point prevalent abstainers

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

1 Copeland 2006 (*Continued*)

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. Randomised to follow up in either individual or group format: Six follow up relapse prevention sessions including psychological, dietary, and exercise components over 38 weeks
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

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Low risk	"Statisticians generated the random assignment sequence for follow up condition"
Blinding (performance bias and detection bias) All outcomes	Low risk	"Therapists were blind to participant follow-up treatment condition assignment until the last meeting of the cessation program."
Definition of abstinence	Low risk	Weight measured in biochemically validated continuous abstainers

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

1 Danielsson 1999 (*Continued*)

Notes	Prolonged abstinence defined as "completely and continuously stopped from week 2 onwards"	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Open consecutive randomisation (in the order their questionnaires were received at the clinic)
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Definition of abstinence	Low risk	Weight measured in biochemically validated prolonged abstainers

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, daily weight monitoring, individual energy prescription to result in 2lb/week weight loss if weight was gained(based on weight, age, gender, activity level), healthy eating advice and behavioural advice to manage triggers for uncontrolled eating (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 I thought we did use this to compare individual with general (nutritional, exercise and behavioural eduction delivered in group sessions)
Risk of bias	

1 Hall 1992 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Method not described
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Definition of abstinence	High risk	Weight measured in biochemically validated point prevalent abstainers

1 Hankey 2009

Methods	Country: Scotland Recruitment: Smokers at a smoking cessation clinic
Participants	138 smokers, 75.4% female, av baseline weight 76.2 (18.1) kg, av age 50yrs, av BMI 28.2 (5.5), av CPD, 25.2 (12.6)
Interventions	(1) 24wk dietary stage of change based interventions focusing advice and self monitoring of physical activity (ppts given pedometers), portion control, fruit and vegetable intake and fat intake for 4 weeks post quit. Also included bolster session at weeks 8, 12, 16 and 20 post quit. No individual targets set (2) No dietary intervention Both conditions were embedded within a smoking cessation clinic that followed the Maudsley model
Outcomes	1. Abstience at 6m (validation: CO monitoring). Definition of abstinence or CO level not given 2. Mean (SD) weight change (KG) in abstainers at end of treatment and 12 months
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	computer generated
Allocation concealment (selection bias)	Low risk	Randomisation carried out via an interactive voice response system

1 Hankey 2009 (*Continued*)

Blinding (performance bias and detection bias) All outcomes	High risk	Not possible
Definition of abstinence	Unclear risk	Definitions of abstinence and biochemical verification not given

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	1. 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

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method not described
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind
Definition of abstinence	Low risk	Weight measured in biochemically validated continuous abstainers

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	1. 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

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Independent randomisation
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	Low risk	"Neither the investigators nor the subjects knew which gum contained the active ingredients"
Definition of abstinence	Low risk	Weight measured in biochemically validated continuous abstainers

1 Levine 2010

Methods	Country: USA Recruitment: community volunteers
Participants	349 weight concerned women smokers, aged between 18-65yrs,motivated to quit smoking, av 20.7cpd, av age 42
Interventions	1. weight concerns CBT + bupropion 300mg/day2. weight concerns CBT + placebo3. Standard cessation counselling + bupropion 300mg/day 4. Standard cessation counselling + placebo CBT was delivered weekly for Buproprion/placebo was taken for 26 wks
Outcomes	1. Prolonged abstinence at end of treatment and 6m (Validatio: CO </= 8ppm, or urinary cotinine <15µg/L) 2. Mean (SD) weight change (kg) at 12w, 6m and 12m
Notes	

1 Levine 2010 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Block randomisation sequence
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind
Definition of abstinence	Low risk	Weight measured in biochemically validated prolonged abstainers

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). 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		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Minimisation
Allocation concealment (selection bias)	Unclear risk	Not described

1 Norregaard 1996 (*Continued*)

Blinding (performance bias and detection bias) All outcomes	Low risk	"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 ($p < 0.001$)"
Definition of abstinence	Low risk	Weight measured in biochemically validated prolonged abstainers

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 behavioral support (1x45mins, 5x15mins)
Outcomes	1. Mean (SD) weight change (kg) in continuous abstainers at end of treatment (validation: exhaled CO<10ppm)
Notes	Arms 1-3 combined for the main comparison No 6 month follow up data

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Block randomisation, stratified by sex after the first 150 participants
Allocation concealment (selection bias)	Low risk	Random sequence was provided to the pharmacist, who assigned participants
Blinding (performance bias and detection bias) All outcomes	Low risk	All were blinded to the treatment assignment
Definition of abstinence	Unclear risk	Weight measured in continuous abstainers, validation unclear

1 Parsons 2009

Methods	Country: UK Recruitment: community volunteers
Participants	143 smokers, 63% female, av age 45.5 (12.4) years, av baseline weight 75.1 (17.8) kg, av 20(8) CPD
Interventions	1. St John's Wort ((Jarsin preparation (LI 160, Lichtwer Pharma, Berlin, Germany), standard hypericin content 0.12% - 0.28%)) 900mg daily and chromium polynicotinate 400micrograms daily for 14w 2. SJW active, Chromium placebo 3. SJW placebo, Chromium active 4. SJW placebo, Chromium placebo All participants received 7w of behavioural counselling with TQD coinciding with the 3rd visit
Outcomes	1. Prolonged abstinence at end of treatment (validated: CO<10ppm) and 6m (self report) 2. Mean (SD) weight change (kg) in prolonged abstainers at end of treatment and 6m
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	independent statistician prepared an excel spreadsheet using Stata to generate two lists of randomly sequenced blocks of 2, 4, or 6, which were passed to the medication packing company
Allocation concealment (selection bias)	Low risk	Lists were used to package together medication of SJW or placebo and CR or placebo, which were allocated in sequence to participants in clinic.
Blinding (performance bias and detection bias) All outcomes	Low risk	Participants, therapists, and outcome assessors were blind to the treatment allocation.
Definition of abstinence	Low risk	Weight measured in biochemically validated prolonged abstainers

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 gain, with a 500kcal deficit of the energy required to maintain baseline weight. behavioural support (stimulus control techniques), self monitoring and constructive feedback. 10x 90min sessions over 7 weeks2. 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 CB 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

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	After a sufficient number of participants to form a group recruited, group assigned to a treatment condition
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	Low risk	"Participants did not learn of their treatment condition assignment until the first treatment session, after all baseline information had been received"
Definition of abstinence	Low risk	Weight measured in biochemically validated continuous abstainers

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 (general calorie restriction 100-300kcal based on cigarette consumption, increased exercise to 1hour daily walking, encouraged to self monitor, acceptance of weight gain) 2. Group SC therapy only

1 Pirie 1992 (*Continued*)

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

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method not stated
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	High risk	Not possible due to nature of the interventions
Definition of abstinence	Low risk	Weight measured in biochemically validated continuous abstainers

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 support for first 4w and fortnightly support for remaining 8w
Outcomes	1. 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

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**

1 Spring 1995 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	Method not stated
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	Low risk	"All subjects received identical packets of three pills"
Definition of abstinence	Low risk	Weight measured in biochemically validated prolonged abstainers

1 Spring 2004

Methods	Country: USA Recruitment: community volunteers
Participants	315 mildly weight concerned women, av age 42.7 (10.3) yrs, av 20.3 (9.5) CPD, av BMI 27.4 (7.6)
Interventions	1. Early diet group. Diet during 1-8w of treatment programme (Pre-packaged Nutri/system foods: high-carbohydrate, low-fat, balanced diet based on baseline precessation energy intake from food diaries minus 150 kcal per day). Ppts led on a 30 minute walk after the treatment programme session 2. Late diet group. Diet during 9-16w of treatment programme 3. Control. Final smoking cessation group session focused on weight loss strategies All participants received 16 weekly cognitive behavioural smoking cessation group support sessions
Outcomes	1. Mean (SD) weight change (kg) at end of treatment and 6m in continuous abstainers (validation: CO</=10ppm)
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Block randomisation
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	Unclear risk	not applicable

1 Spring 2004 (*Continued*)

Definition of abstinence	Low risk	Weight measured in biochemically validated continuous abstainers

1 Toll 2010

Methods	Country: USA Recruitment: community volunteers
Participants	127 weight concerned smokers, 28.5% males, mean BMI 28.4±6.16, mean 25.5±10.76 expired CO,
Interventions	(1) 25-mg naltrexone daily beginning the week before quitting continuing until 26w (2) placebo All ppts received 21mg patches 6wks and then 14mg 2wks, starting on quit day. All received CBT for weight concerns weekly for 4 wks, bimonthly twice and then monthly
Outcomes	1. Point prevalence abstinence at end of treatment (26w) 2. Mean (SD) weight change (kg) at end of treatment (26w) in continuous abstainers (validation: CO <10ppm)
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Block stratified for gender, sequence provided by author and given to pharmacist
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not described
Definition of abstinence	Low risk	Weight measured in biochemically validated continuous abstainers

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

2 AD Gonzales 2006 (*Continued*)

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

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Randomization: computer generated sequence 1:1:1
Allocation concealment (selection bias)	Low risk	Participants were randomised according to a predefined central computer sequence
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind
Definition of abstinence	Low risk	Weight measured in biochemically validated continuous abstainers

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 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)

2 AD Hurt 1997 (*Continued*)

Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Stratified by site, method not specified
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind
Definition of abstinence	Low risk	Weight measured in biochemically validated continuous abstainers

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 change (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		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Centralised, computer-generated
Allocation concealment (selection bias)	Low risk	"SItes used an electronic system to assign participants to treatment"

2 AD Jorenby 2006 (*Continued*)

Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind
Definition of abstinence	Low risk	Weight measured in biochemically validated prolonged abstainers

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 arms: 9 sessions (60-90 mins) individual CBT. Included coping skills, stimulus control techniques and relapse prevention
Outcomes	Mean (SD) weight change (kg) in continuous abstainers at end of treatment (Validation: CO less than 8ppm and salivary cotinine less than 20ng/ml)
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method not stated
Allocation concealment (selection bias)	Low risk	Not described
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind
Definition of abstinence	Low risk	Weight measured in biochemically validated continuous abstainers

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
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 change (kg) in continuous abstainers at end of treatment (validation: CO</= 10ppm) (email communication)
Notes	Continuous abstinence defined as self reported quit from target quit day with biochemical validation. Arms 1-3 and 5 in main comparison (same study as 3 VA Nides 2006)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated list
Allocation concealment (selection bias)	Low risk	"Investigators assigned medication to subjects in numerical order of acceptance into the study" from computer generated list
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind
Definition of abstinence	Unclear risk	Weight measured in self report prolonged abstainers

2 AD Piper 2007

Methods	Setting: USA Recruitment: volunteers
Participants	608 smokers of 10 CPD; 58% F, av. age 42, av CPD 22, no details of depression history
Interventions	1. Nicotine gum (4 mg) and bupropion (300 mg) 2. Placebo gum and bupropion 3. Double placebo All arms: 3x 10 min counselling over 3 weeks

2 AD Piper 2007 (*Continued*)

Outcomes	1. Mean (SD) weight change (kg) in point prevalent abstainers at end of treatment (data from email communication) (validation: CO<10ppm)	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Block randomisation
Allocation concealment (selection bias)	Unclear risk	methods not stated
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind
Definition of abstinence	High risk	Weight measured in biochemically validated point prevalent abstainers

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 change (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		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated stratified

2 AD Rigotti 2006 (*Continued*)

Allocation concealment (selection bias)	Unclear risk	"The study pharmacist used the computer generated sequence, concealed from enrolment staff, to assign participants to study arm."
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind
Definition of abstinence	High risk	Weight measured in biochemically validated point prevalent abstainers

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 6 sessions.
Outcomes	Mean (SD) weight change (kg) in continuous abstainers at 6 months (email communication) (Validation: CO<10ppm)
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind
Definition of abstinence	Low risk	Weight measured in biochemically validated continuous abstainers

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

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated
Allocation concealment (selection bias)	Low risk	Participants allocated according to computer generated list
Blinding (performance bias and detection bias) All outcomes	Low risk	"All study personnel engaged in providing interventions to participants were blinded to treatment assignment"
Definition of abstinence	Low risk	Weight measured in biochemically validated continuous abstainers

2 AD Simon 2009

Methods	Setting: San Francisco Veterans Affairs Medical Center, USA Recruitment: hospitalised volunteers
Participants	85 inpatient smokers, 3.5% female, av age 56 yrs, av BMI 27.5, av CPD 16
Interventions	1. Bupropion 300 mg for 7w 2. Placebo All ppts received Individual cognitive behavioural 30-60 min during hospital stay + 5 phone calls at w1, w3, w5, w8, w12, recycling encouraged.
Outcomes	Mean (SD) weight change (kg) in continuous abstainers at 6m (data from email communication) Validation: saliva cotinine <15 ng/ml

2 AD Simon 2009 (*Continued*)

Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	used a computer algorithm to generate a random list of treatment assignments
Allocation concealment (selection bias)	Low risk	All study personnel engaged in providing interventions to participants were blinded to treatment assignment.
Blinding (performance bias and detection bias) All outcomes	Low risk	All study personnel engaged in providing interventions to participants were blinded to treatment assignment.
Definition of abstinence	Low risk	Weight measured in biochemically validated continuous abstainers

2 AD Uyar 2007

Methods	Setting: cessation clinic, Turkey Recruitment: cessation clinic patients
Participants	131 smokers; 81% M, av. age 36, av baseline weight 70-75kg, av ftnd score 3.9-4.8
Interventions	1. Bupropion 300mg for 7 weeks (150 mg daily for the first 3 days, then 150 mg twice daily for 6 weeks) 2. Nicotine patch 21mg for 6 weeks incl tapering 3. Advice and follow up only All arms: Brief counselling and booklet on consequences of smoking with follow up for 24 weeks
Outcomes	Mean (SD) weight change (kg) in continuous abstainers at 24 weeks (data from email communication) Validation: CO levels <10 ppm
Notes	
Risk of bias	
Bias	**Authors' judgement**	**Support for judgement**

2 AD Uyar 2007 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not described
Definition of abstinence	Low risk	Weight measured in biochemically validated continuous abstainers

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 change (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

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	3:1 ratio
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind

2 AD Zellweger 2005 (*Continued*)

Definition of abstinence	Low risk	Weight measured in biochemically validated prolonged abstainers

2 EX Bize 2010

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	1. Intervention: moderate-intensity group-based CV activity, 45 mins, weekly for 9 weeks + 15 mins cessation counselling for 9 weeks (including NRT prescription) 2. Control: 9 weeks of 15 mins per week cessation counselling (including NRT prescription) + Health Education for equal time as exercise intervention (not exercise) Exercise started 5 weeks before quit date
Outcomes	Mean (SD) weight change (kg) in continuous abstainers at end of treatment and 12m (Validation: CO <10ppm)
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Remotely and randomly generated by a computer.
Allocation concealment (selection bias)	Low risk	Secured by means of sealed envelopes
Blinding (performance bias and detection bias) All outcomes	High risk	Not possible
Definition of abstinence	Low risk	Weight measured in biochemically validated continuous abstainers

2 EX Marcus 1999

Methods	Country: USA Recruitment: not described
Participants	20 women, av age 39, av CPD 28, av BMI 24-27.

2 EX Marcus 1999 (*Continued*)

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 change (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		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer generated
Allocation concealment (selection bias)	Low risk	"randomisation code for group assignment was generated by a computer code"
Blinding (performance bias and detection bias) All outcomes	High risk	Not possible
Definition of abstinence	Low risk	Weight measured in biochemically validated continuous abstainers

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 change (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	

2 EX Marcus 2005 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated
Allocation concealment (selection bias)	Low risk	"Group assignment was based on a randomisation code generated by a computer software program"
Blinding (performance bias and detection bias) All outcomes	High risk	Not possible
Definition of abstinence	Low risk	Weight measured in biochemically validated continuous abstainers

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). 2. Cessation programme as 1. once/week for 7 weeks + brief health education once/week for 7 weeks
Outcomes	Mean (SD) weight change (kg) in continuous abstainers at end of treatment
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer generated
Allocation concealment (selection bias)	Low risk	Allocated in order of attendance
Blinding (performance bias and detection bias) All outcomes	High risk	Not possible
Definition of abstinence	Low risk	Weight measured in biochemically validated continuous abstainers

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 prolonged abstainers at end of treatment (Validation: CO content 0-11ppm)
Notes	Abstainence defined as participants who smoked 0-3 cigarettes per week with validation

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method not stated
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind
Definition of abstinence	Unclear risk	Participants were allowed to smoke up to 3 cigarettes per week

2 NRT Blondal 1999

Methods	Country: Iceland Recruitment: community volunteers
Participants	237 smokers 67% F, 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 change (kg) in continuous abstainers at end of treatment (email communication) and 12m (email communication) (Validation: CO<11ppm)
Notes	

Risk of bias

2 NRT Blondal 1999 (*Continued*)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated code at pharmacy
Allocation concealment (selection bias)	Low risk	"participants allocated their treatment by generated randomisation code at a local pharmacy"
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind
Definition of abstinence	Low risk	Weight measured in biochemically validated continuous abstainers

2 NRT Bohadana 2000

Methods	Country: France Recruitment: community volunteers
Participants	400 smokers, 18-70 yrs, 51% F, 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 change (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 two weeks

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated code
Allocation concealment (selection bias)	Low risk	"sealed randomisation envelopes were provided for each subject and were held by the hospital pharmacy, which was responsible for dispensing medication"
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind

Definition of abstinence	Low risk	Weight measured in biochemically validated prolonged abstainers

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 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 report from 2w Doses and durations collapsed in main analyses.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Stratified only by centre
Allocation concealment (selection bias)	Low risk	"A computer-generated allocation list was prepared centrally and allocated subjects to treatment numbers"
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind
Definition of abstinence	Low risk	Weight measured in biochemically validated prolonged abstainers

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 8w, 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 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 Although these treatments are specifically tested for their effect on smoking and on weight gain the NRT arm is included in the second part of the review as it is included in the parent Cochrane review

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method not stated
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	Low risk	All group facilitators and participants were blind to treatment conditions
Definition of abstinence	High risk	Weight measured in biochemically validated point prevalent abstainers

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 change (kg) in continuous abstainers at end of treatment (email communication) and 12m (email communication) (Validation: Blood cotinine)	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method not stated
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind
Definition of abstinence	Low risk	Weight measured in biochemically validated continuous abstainers

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

2 NRT Ehrsam 1991 (*Continued*)

Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not described
Definition of abstinence	Unclear risk	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 (Kg) in point prevalence abstainers at end of treatment (email communication) (Validation: CO <10ppm)
Notes	Point prevalence abstinence was defined as validated self report abstinence for 7 days prior to measurement. Different participants to Fiore 1994B added in separately in the main comparison

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Pregenerated computer sequence
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind
Definition of abstinence	High risk	Weight measured in biochemically validated point prevalent abstainers

2 NRT Fiore 1994B

Methods	Country: USA Recruitment: community volunteers
Participants	112 smokers, av age 43-45yrs, av weight 72-73kg

2 NRT Fiore 1994B (*Continued*)

Interventions	1. Nicotine patch (22mg/24hr, 6 wks incl weaning) 2. Placebo patch All participants received x8 weekly 10-20 min individual counselling
Outcomes	Mean (SD) weight change (kg) in point prevalence abstainers at end of treatment (email communication) (Validation: CO <10ppm)
Notes	Point prevalence abstinence was defined as validated self report abstinence for 7 days prior to measurement. Different participants to Fiore 1994A added in separately in the main comparison

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Pregenerated computer sequence
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind
Definition of abstinence	High risk	Weight measured in biochemically validated point prevalent abstainers

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.

2 NRT Garvey 2000 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method not stated, stratified by high- and low-dependence
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind
Definition of abstinence	Low risk	Weight measured in biochemically validated prolonged abstainers

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
Interventions	1. Nicotine patch 30cm2 (21mg/24 hr) for 4 wks, 20cm2 (14mg/24 hr) for 4 wks, 10cm2 (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		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Treatments were randomly allocated to study numbers by using a 1:1 ratio within blocks of 10
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind

2 NRT Gourlay 1995 (*Continued*)

Definition of abstinence	Low risk	Weight measured in biochemically validated continuous abstainers

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 randomised 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		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method not stated
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	Low risk	Not possible
Definition of abstinence	Low risk	Weight measured in biochemically validated prolonged abstainers

2 NRT Hjalmarson 1984

Methods	Country: Sweden Recruitment: smoking cessation clinic	
Participants	206 smokers, 56% female, av.age 42, av. CPD 24	

2 NRT Hjalmarson 1984 (*Continued*)

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 6 wks	
Outcomes	Mean (SD) weight gain (kg) in continuous abstainers at 6 months (email communication) (Validation: CO<10ppm)	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Randomized by therapy group.
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Unclear if enroller blind, but therapists blind
Definition of abstinence	Low risk	Weight measured in biochemically validated continuous abstainers

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 x8 45-60 min group sessions over 6 wks with clinical psychologist	
Outcomes	Mean (SD) weight change (kg) in continuous abstainers at 12m (Validation: CO<10ppm)	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**

2 NRT Hjalmarson 1994 (*Continued*)

Random sequence generation (selection bias)	Unclear risk	Method not described
Allocation concealment (selection bias)	Unclear risk	Treatment allocater not blinded if more than 1 participant from the same household so that they could be given same medication
Blinding (performance bias and detection bias) All outcomes	Low risk	Therapists and participants
Definition of abstinence	Low risk	Weight measured in biochemically validated continuous abstainers

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 12 months (Validation: CO<10ppm)
Notes	Prolonged abstainers defined as validated self reported abstinence from week 2

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Participants assigned a number on attending first group session. Numbers on a list randomising to medication. Participants from the same household randomised to same treatment
Allocation concealment (selection bias)	Unclear risk	Treatment allocater not blinded if more than 1 participant from the same household so that they could be given same medication

2 NRT Hjalmarson 1997 (*Continued*)

Blinding (performance bias and detection bias) All outcomes	Low risk	Participant and therapist blinded
Definition of abstinence	Low risk	Weight measured in biochemically validated prolonged abstainers

2 NRT Lerman 2004

Methods	Country: USA Recruitment: community volunteers and referrals
Participants	350 smokers (includes 51 who withdrew before treatment) 54% F, 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	For prolonged abstinence, relapse was defined as 7 consecutive days of smoking at any point during follow-up period

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated, operated by data manager.
Allocation concealment (selection bias)	Low risk	After allocation only outcome assessors blind
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not described
Definition of abstinence	Unclear risk	Weight measured in self report continuous abstainers

2 NRT Pack 2008

Methods	Country: USA Recruitment: community volunteers 2x2 factorial design
Participants	408 smokers, 56%F, ave age 40-44yrs, ave CPD 22-24
Interventions	1. Nicotine lozenge + 4 calls from Wisconsin Tobacco Quit Line 2. Nicotine gum + 4 calls from Wisconsin Tobacco Quit Line 3. Nicotine lozenge + Self help brochure 4. Nicotine gum + Self help brochure Participants were treated with 8w of NRT. F/U at 8wks, 6m and 12m
Outcomes	Mean (SD) weight change (kg) in 7-day point prevalence abstainers at end of treatment, 6m, 12m
Notes	Weight data from arms 1&2 and 3&4 were combined for the analysis

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not described
Definition of abstinence	High risk	Weight measured in CO validated point prevalent abstainers

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 8w 2. Group therapy plus weight control programme 8w 3. Group therapy plus nicotine gum 8w 4. Group therapy plus weight control programme and nicotine gum 8w Gum type: 2mg ad lib 8 week treatment period + 3 months supply
Outcomes	Mean (SD) weight change (kg) in continuous abstainers end of treatment, 6 and 12m (Validation: expired CO <=10ppm)

2 NRT Pirie 1992 (*Continued*)

Notes	Group 3 compared with group 1. Group 1, 3 and 4 compared in first part of review	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Not described
Definition of abstinence	Low risk	Weight measured in biochemically validated continuous abstainers

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 change (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 week 1	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind

2 NRT Puska 1995 (*Continued*)

Definition of abstinence	Low risk	Weight measured in biochemically validated prolonged abstainers

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 change (kg) in prolonged abstainers at end of treatment (email communication), 6 months (email communication) and 12 months (email communication) (Validation: CO</=10ppm)
Notes	Prolonged abstainers were defined as continuous abstinence for a sustained period preceding the assessment point at 12 months

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind
Definition of abstinence	Low risk	Weight measured in biochemically validated prolonged abstainers

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

2 NRT Sachs 1993 (*Continued*)

Outcomes	Mean (SD) weight change (kg) in continuous abstainers at 6m (Validation: CO <10ppm)	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method not stated
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind
Definition of abstinence	Low risk	Weight measured in biochemically validated continuous abstainers

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 All participants received brief advice at 4 visits.	
Outcomes	Mean (SD) weight change (kg) in prolonged abstainers at end of treatment (email communication), 6 (email communication) and 12 months (email communication) (Validation: CO<=10ppm)	
Notes	Prolonged abstinence defined as sustained from 2 wks, no slips allowed	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method not stated
Allocation concealment (selection bias)	Unclear risk	Not described

2 NRT Shiffman 2002A (*Continued*)

Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind
Definition of abstinence	Low risk	Weight measured in biochemically validated prolonged abstainers

2 NRT Shiffman 2002B

Methods	Country: USA & UK (15 sites) Recruitment: community volunteers, high dependence (time to first 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 change (kg) in prolonged abstainers at end of treatment (email communication), 6 (email communication) and 12 months (email communication) (Validation: CO<=10ppm)
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method not stated
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind
Definition of abstinence	Low risk	Weight measured in biochemically validated prolonged abstainers

2 NRT Stapleton 1995

Methods	Country: UK Recruitment: General practice patients
Participants	1200 smokers Av. CPD 23-4, av weight 71-72kg

2 NRT Stapleton 1995 (*Continued*)

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 randomised 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 week 2. The dose increase after 1 wk did not affect cessation, 1+2 vs 3 in main comparison

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Computer-generated list
Allocation concealment (selection bias)	Low risk	"Study subjects were assigned a treatment according to a computer generated list compiled in blocks of six"
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind
Definition of abstinence	Low risk	Weight measured in biochemically validated prolonged abstainers

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)

2 NRT Sutherland 1992 (*Continued*)

Notes	Prolonged abstinence defined as validated self reported no smoking from the start of the last week of group treatment to the 12 months follow up	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Drew card with A or P for active or placebo allocation
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	Low risk	"Subjects and therapist were blind to spray assignment"
Definition of abstinence	Low risk	Weight measured in biochemically validated prolonged abstainers

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 (6w) (Validation: CO <9ppm)	
Notes	2 trials pooled and data relating to a 7mg patch group used in only 1 trial omitted	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Method not stated
Allocation concealment (selection bias)	Unclear risk	Not described

2 NRT TNSG 1991 (*Continued*)

Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind
Definition of abstinence	Low risk	Weight measured in biochemically validated continuous abstainers

2 NRT Tonnesen 1991

Methods	Country: Denmark Recruitment: community volunteers
Participants	289 smokers 70% F, 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 change (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 week of quitting

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	According to a computer generated randomisation code
Allocation concealment (selection bias)	Unclear risk	"packages labelled with consecutive numbers from computer-generated random code"
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind
Definition of abstinence	Low risk	Weight measured in biochemically validated prolonged abstainers

2 NRT Tonnesen 1993

Methods	Country: Denmark Recruitment: community volunteers
Participants	286 smokers, av CPD 20 60% F, 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 change (kg) in continuous abstainers at end of treatment (email communication) and 12m (email communication) (Validation: expired CO<10ppm)
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated randomisation code
Allocation concealment (selection bias)	Unclear risk	"participants were randomly assigned according to code generated by a computer"
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind
Definition of abstinence	Low risk	Weight measured in biochemically validated continuous abstainers

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 12 months (Validation: CO<10ppm)

2 NRT Wallstrom 2000 (*Continued*)

Notes	Prolonged abstinence defined as complete abstinence from wk 2	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer assignment
Allocation concealment (selection bias)	Low risk	"Subjects were randomised to receive either active or placebo treatment using a computer program"
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind
Definition of abstinence	Low risk	Weight measured in biochemically validated prolonged abstainers

2 VA Aubin 2008

Methods	Country: Belgium, France, Netherlands, UK, USA Recruitment: smoking cessation clinics or community volunteers
Participants	Healthy adults, Mean age 42.9yr, 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) 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 week 9.
Risk of bias	

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Central computer-generated sequence.
Allocation concealment (selection bias)	Low risk	Central allocation

2 VA Aubin 2008 (*Continued*)

Blinding (performance bias and detection bias) All outcomes	High risk	Open label design
Definition of abstinence	Low risk	Weight measured in biochemically validated prolonged abstainers

2 VA Gonzales 2006

Methods	Country: USA Recruitment: community volunteers
Participants	1025 smokers 55% F (Placebo), 48% F (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 1 compared with 3 (same study as 3 AD Gonzales)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer generated sequence 1:1:1
Allocation concealment (selection bias)	Low risk	Participants were randomised according to a predefined central computer sequence
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind
Definition of abstinence	Low risk	Weight measured in biochemically validated prolonged abstainers

2 VA Jorenby 2006

Methods	Country: USA, multicentre 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 change (kg) in prolonged abstainers at end of treatment (validation: CO < 10ppm)
Notes	Prolonged abstinence defined as validated abstinence w 9-12. Arm 1 and 3 in main comparison

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Centralised, computer-generated
Allocation concealment (selection bias)	Low risk	"SItes used an electronic system to assign participants to treatment"
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind
Definition of abstinence	Low risk	Weight measured in biochemically validated prolonged abstainers

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 Fagerstrom score 5.6
Interventions	1. Varenicline 0.25mg x 2/day 12w 2. Varenicline 0.50mg x 2/day 12w 3. Varenicline 1.00mg x 2/day 12w 4. Placebo tablet x 2/day 12w

2 VA Nakamura 2007 (*Continued*)

	All participants received S-H booklet *Clearing the Air* at baseline, + brief counselling (= <10 mins) at each clinic visit	
Outcomes	Mean (SD) weight change (kg) in prolonged abstainers at end of treatment (validation: CO <=10ppm)	
Notes	Prolonged abstinence defined as continuous abstinence during weeks 9-12	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated random number lists
Allocation concealment (selection bias)	Low risk	'randomised to 1 of the 4 treatment groups in a 1:1:1:1 ratio using a central procedure'
Blinding (performance bias and detection bias) All outcomes	Low risk	'double-blinding of subjects and investigators was maintained throughout the study'
Definition of abstinence	Low risk	Weight measured in biochemically validated prolonged abstainers

2 VA Niaura 2008

Methods	Country: USA Setting: 5 research centres	
Participants	320 healthy adult volunteers, aged 18-65, smoking >=10cpd. 52% M, 91% white, mean age 42, mean CPD 22, mean Fagerström score 5.4	
Interventions	(1) Varenicline tartrate 12w (Week 1: titrated from 0.5 to 1.0 mg/day) followed by a self-regulated flexible schedule (Weeks 2-12: 0.5-2.0 mg/day). (2) Placebo	
Outcomes	Mean (SD) weight change (kg) in continuous abstainers at end of treatment (12w). (Validation: CO</=10ppm)	
Notes	Continuous abstinence defined as self report abstinence weeks 4-12 with biochemical validation	
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**

2 VA Niaura 2008 (*Continued*)

Random sequence generation (selection bias)	Low risk	randomly permuted blocks and a pseudo-random number generator
Allocation concealment (selection bias)	Low risk	participants were assigned in a 1:1 ratio to varenicline treatment or placebo in the numerical order that they were accepted to the study
Blinding (performance bias and detection bias) All outcomes	Low risk	double blind
Definition of abstinence	Low risk	Weight measured in biochemically validated continuous abstainers

2 VA 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
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 change (kg) in continuous abstainers at end of treatment (validation: CO</= 10ppm) (email communication)
Notes	Continuous abstinence defined as self reported quit from target quit day with biochemical validation. Arms 1-3 and 5 in main comparison (same study as 3 AD Nides 2006)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated list
Allocation concealment (selection bias)	Low risk	"Investigators assigned medication to subjects in numerical order of acceptance into the study" from computer generated list"

2 VA Nides 2006 (*Continued*)

Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind
Definition of abstinence	Low risk	Weight measured in biochemically validated continuous abstainers

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 change (kg) in continuous abstainers at end of treatment (validation: CO <= 10ppm)
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Not described
Allocation concealment (selection bias)	Unclear risk	Not described
Blinding (performance bias and detection bias) All outcomes	Low risk	"Subjects and investigators were blinded to the study drug treatment assignment"
Definition of abstinence	Low risk	Weight measured in biochemically validated continuous abstainers

2 VA Rigotti 2010

Methods	Country: 15 countries in Europe, Asia, Americas Setting: 39 research centres
Participants	714 adult smokers, aged 35-75, smoking at least 10cpd, with stable CVD and motivated to quit. 79% male, 80% white, mean CPD 22, mean Fagerström 5.6
Interventions	1. Varenicline 1.0 mg 2/d for 12 wks, preceded by 1wk titrated dose. 2. Placebo tablets as above. Both groups received brief (10mins) counselling at weekly clinic visits throughout treatment phase, and phone call 3d post-TQD
Outcomes	Mean (SD) weight change (kg) in week 9-12 continuous abstainers at end of treatment (12w) and 12 months (12m) (Validation: expired CO</=10 ppm).
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	The study sponsor conducted the randomization centrally using a computer generated list that prespecified the order of treatment allocation
Allocation concealment (selection bias)	Low risk	see above
Blinding (performance bias and detection bias) All outcomes	Low risk	Double-blind (participants and study implementation). Cardiovascular outcomes "were reviewed separately and adjudicated under blinded conditions by an independent event committee made up of 3 board-certified cardiologists"
Definition of abstinence	Low risk	Weight measured in biochemically validated prolonged abstainers from 9 weeks

2 VA Tashkin 2011

Methods	Country: USA (17 centres), Spain (3 centres), France (4 centres), Italy (3 centres) Setting: 27 research centres.
Participants	504 adult smokers with mild-to-moderate COPD, aged 35+, smoking 10+ CPD, motivated to quit; allocated to varenicline (250), or placebo (254). 62% male, mean age 57, CPD 24-25, Fagerström score 5.9-6.2., av BMI 26.6 (SD5.5)

2 VA Tashkin 2011 (*Continued*)

Interventions	1. Varenicline 1.0 mg 2/d for 12 wks, preceded by 1wk titrated dose. 2. Placebo tablets as above. Both groups received SC educational booklet, + brief (10mins) counselling at weekly clinic visits throughout treatment phase, and phone call 3d post-TQD
Outcomes	Mean (SD) weight change at in continuous abstainers end of treatment (12w) and 12m (Validation: CO</=10ppm)
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Methods not described
Allocation concealment (selection bias)	Unclear risk	Methods not described
Blinding (performance bias and detection bias) All outcomes	Low risk	double blind
Definition of abstinence	Low risk	Weight measured in biochemically validated prolonged abstainers from week 9

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 regime Participants had already received 12w of varenicline. All participants received brief counselling (<=10 mins) at each clinic visit throughout treatment phase (wks 13-24). Treatment phase clinic visits were at wks 13, 14, 16, 20 and 24
Outcomes	Mean (SD) weight change (kg) in continuous abstainers at 6 months (validation: CO <=10ppm)
Notes	Continuous abstinence was defined as validated complete abstinence during week 13-24

2 VA Tonstad 2006 (*Continued*)

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Computer-generated lists stratified by centre, x4 random block design
Allocation concealment (selection bias)	Low risk	computer generated sequence used for allocation of participants
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind
Definition of abstinence	Low risk	Weight measured in biochemically validated prolonged abstainers from week 13

2 VA Tsai 2008

Methods	Country: Taiwan and Korea Recruitment: community volunteers
Participants	250 healthy adult volunteers, motivated to quit, aged 18 to 75; allocated to varenicline (126), or placebo (124). 11% female, av age 40.3, BMI >15 or <38 or weight >45.5 kg, av CPD 24
Interventions	1. Varenicline 1.0mg x 2/day 12w 1st w titrated 2. Placebo tablet x 2/day 12w All participants received a smoking cessation booklet *Clearing the Air* at baseline + brief counselling (=<10 mins) at each clinic visit
Outcomes	Mean (SD) weight change (kg) in prolonged abstainers at end of treatment (validated: CO <=10ppm)
Notes	Prolonged abstinence is defined as validated complete abstinence during weeks 9-12

Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Low risk	Permutated blocks (block=4)
Allocation concealment (selection bias)	Low risk	web- and telephone-based assignment
Blinding (performance bias and detection bias)	Low risk	Subjects, investigators, study staff and sponsor personnel blind to treatment

2 VA Tsai 2008 (*Continued*)

All outcomes		
Definition of abstinence	Low risk	Weight measured in biochemically validated prolonged abstainers

2 VA Wang 2009

Methods	Setting: Not described Country: China (10 sites), Singapore (3 sites), Thailand (2 sites)	
Participants	333 healthy adult volunteers, aged 18 to 75;97% male, mean age 39, BMI >15 and <38 or weight >45.5 kg, mean CPD 20, mean Fagerström score 5.4	
Interventions	1. Varenicline 1.0mg x 2/day 2. Placebo tablet x 2/day Treatment period 12 wks, 1st wk titrated dosage. All participants received a smoking cessation booklet at baseline, + brief counselling (10 mins) at each clinic visit, except for wks 5 and 7, when counselling was conducted by phone.	
Outcomes	Mean (SD) weight change (kg) in continuous abstainers at end of treatment (12w) and 6 months (Validation: CO</=10ppm)	
Notes		
Risk of bias		
Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	eligible subjects were randomised in a 1:1 ratio
Allocation concealment (selection bias)	Unclear risk	not described
Blinding (performance bias and detection bias) All outcomes	Low risk	double blind
Definition of abstinence	Low risk	Weight measured in biochemically validated prolonged abstainers from week 9

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

Study	Reason for exclusion
1 Ames 2007	Not an intervention designed specifically to tackle post cessation weight gain
1 Chaney 2008	Exercise intervention excluded by parent cochrane review
1 Hughes 1997	Effect of NRT on post cessation weight gain, not identified in NRT parent review
1 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 King 2006	Weight only measured at end of 1 month (2 month intervention)
1 Lagrue 1994	Intervention on overweight patients only
1 Leischow 1992	Unable to obtain full data
1 Love 2011	Patients not randomised
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 Spring 1991	Unable to obtain data
1 Toll 2008	Participants not randomised to experimental or control conditions
1 Wilcox 2010	Uncontrolled trial
2 AD Ahluwalia 2002	Unable to obtain full data
2 AD Aubin 2004	Unable to obtain full data
2 AD Berlin 1995	No weight data
2 AD Blondal 1999	No weight data
2 AD Brown 2006	No weight data
2 AD Cinciripini 05	No weight data
2 AD Collins 2004	No weight data

(*Continued*)

2 AD Covey 2002	No weight data
2 AD Covey 2007	All participants received 8 weeks of open label bupropion and NRT
2 AD Da Costa 2002	No weight data
2 AD Dalsgareth 2004	Unable to obtain full data
2 AD Evins 2001	Unable to obtain full data
2 AD Evins 2005	No weight data
2 AD Evins 2006	No weight data
2 AD Evins 2008	less than 6 months follow up
2 AD Ferry 1992	No weight data
2 AD Ferry 1994	No weight data
2 AD George 2002	No weight data
2 AD GlaxoSmithK SMK20001	No weight data
2 AD Gonzales 2001	No weight data
2 AD Haggsträm 2006	No weight data
2 AD Hall 1998	No weight data
2 AD Hall 2002	No weight data
2 AD Hall 2004	No weight data
2 AD Hatsukami 2004	No weight data
2 AD Hays 2001	Unable to obtain full data
2 AD Hertzberg 2001	No weight data
2 AD Holt 2005	No weight data
2 AD Hurt 2003	No weight data
2 AD Killen 2000	No weight data

(*Continued*)

2 AD Killen 2004	No weight data
2 AD Killen 2006	No weight data
2 AD Myles 2004	No weight data
2 AD Piper 2004	No weight data
2 AD Piper 2009	No weight data
2 AD Prochazka 1998	No weight data
2 AD Prochazka 2004	No weight data
2 AD Rovina 2009	No weight data
2 AD Selby 2003	No weight data
2 AD Swan 2003	No weight data
2 AD Tashkin 2001	No weight data
2 AD 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 AD Wagena 2005	No weight data
2 EX Hill 1985	No weight data
2 EX Hill 1993	No weight data
2 EX Kinnunen 2008	Unable to get data
2 EX Marcus 1991	No weight data
2 EX Marcus 1995	No weight data
2 EX Martin 1997	No weight data
2 EX Prapavessis 2007	Unable to get data
2 EX Russell 1988	No weight data
2 EX Taylor	No weight data

(*Continued*)

2 NRT Ahluwalia 1998	No weight data
2 NRT Ahluwalia 2006	No weight data
2 NRT Areechon 1988	No weight data
2 NRT Blondal 1989	No weight data
2 NRT Blondal 1997	Unable to obtain full data
2 NRT Bolin 1999	No weight data
2 NRT Br Thor Soc 83	No weight data
2 NRT Buchkremer 88	No weight data
2 NRT Bullen 2010	Participants took medication before quit day
2 NRT Campbell 1987	No weight data
2 NRT Campbell 1991	No weight data
2 NRT Campbell 1996	No weight data
2 NRT Cinciripini 96	No weight data
2 NRT Clavel 1985	No weight data
2 NRT Clavel-Cha '92	No weight data
2 NRT Croghan 2003	No weight data
2 NRT Croghan 2007	No weight data
2 NRT Daughton 1991	No weight data
2 NRT Daughton 1998	No weight data
2 NRT Dautzenberg 01	No weight data
2 NRT Davidson 1998	No weight data
2 NRT Etter 2009	Participants took medication before the quit date
2 NRT Fagerstrom 82	No weight data

(*Continued*)

2 NRT Fagerstrom 84	No weight data
2 NRT Fee 1982	No weight data
2 NRT Fortmann 1995	No weight data
2 NRT Garcia 1989	No weight data
2 NRT Gilbert 1989	No weight data
2 NRT Glavas 2003a	No weight data
2 NRT Glavas 2003b	No weight data
2 NRT Glover 2002	Unable to obtain full data
2 NRT Goldstein 1989	No weight data
2 NRT Hall 1985	No weight data
2 NRT Hall 1987	No weight data
2 NRT Hall 1996	No weight data
2 NRT Hand 2002	No weight data
2 NRT Harackiewicz 1988	No weight data
2 NRT Hatsukami 2007	Less than 6 months follow up
2 NRT Hays 1999	No weight data
2 NRT Herrera 1995	No weight data
2 NRT Hilleman 1994	No weight data
2 NRT Huber 1988	No weight data
2 NRT Hughes 1989	No weight data
2 NRT Hughes 1990	No weight data
2 NRT Hughes 1991	No weight data
2 NRT Hughes 1999	No weight data

(*Continued*)

2 NRT Hughes 2003	No weight data
2 NRT Hurt 1990	No weight data
2 NRT Hurt 1994	No weight data
2 NRT ICRF 2007	No weight data
2 NRT Jamrozik 1984	No weight data
2 NRT Jarvis 1982	No weight data
2 NRT Jensen 1991	No weight data
2 NRT Jorenby 1995	No weight data
2 NRT Jorenby 1999	Unable to obtain full data
2 NRT Joseph 1996	No weight data
2 NRT Kalman 2006	No weight data
2 NRT Killen 1984	No weight data
2 NRT Killen 1990	No weight data
2 NRT Killen 1997	No weight data
2 NRT Killen 1999	Unable to obtain full data
2 NRT Kornitzer 1987	Unable to obtain full data
2 NRT Kornitzer 1995	No weight data
2 NRT Kralikova 2002	No weight data
2 NRT Kralikova 2009	Participants could reduce smoking or quit smoking
2 NRT Leischow 1996	No weight data
2 NRT Leischow 1999	No weight data
2 NRT Leischow 2004	No weight data
2 NRT Lewis 1998	No weight data
2 NRT Llivina 1988	No weight data

(*Continued*)

2 NRT Malcolm 1980	No weight data
2 NRT Marshall 1985	No weight data
2 NRT McGovern 1992	No weight data
2 NRT Molyneux 2003	No weight data
2 NRT Moolchan 2005	No weight data
2 NRT Mori 1992	No weight data
2 NRT Muller 1990	No weight data
2 NRT Nakamura 1990	No weight data
2 NRT Nebot 1992	No weight data
2 NRT Niaura 1994	No weight data
2 NRT Niaura 1999	No weight data
2 NRT Ockene 1991	No weight data
2 NRT Oncken 2007	No weight data
2 NRT Otero 2006	No weight data
2 NRT Page 1986	No weight data
2 NRT Paoletti 1996	No weight data
2 NRT Peng 2007	Less than 6 months follow up
2 NRT Perng 1998	No weight data
2 NRT Piper 2007	No weight data
2 NRT Puska 1979	No weight data
2 NRT Richmond 1993	No weight data
2 NRT Rose 1994	No weight data
2 NRT Rose 1998	No weight data

(*Continued*)

2 NRT Rose 2006	No weight data
2 NRT Rose 2009	Participants took medication before quit day
2 NRT Roto 1987	Unable to obtain full data
2 NRT Russell 1983	No weight data
2 NRT Schneider '85A	No weight data
2 NRT Schneider '85B	No weight data
2 NRT Schneider 1995	No weight data
2 NRT Schneider 1996	No weight data
2 NRT Schnoll 2010	No weight data
2 NRT Schuurmans 04	No weight data
2 NRT Segnan 1991	No weight data
2 NRT Shiffman 2009	Not abrupt quitting
2 NRT Sonderskov 97	No weight data
2 NRT Stapleton 2011	Less than 6 months follow up
2 NRT Tonnesen 1988	No weight data
2 NRT Tonnesen 2000	No weight data
2 NRT Tonnesen 2006	No weight data
2 NRT Veaugh-Geiss 2010	No weight data
2 NRT Villa 1999	No weight data
2 NRT Westman 1993	No weight data
2 NRT Wisborg 2000	No weight data
2 NRT Wong 1999	No weight data
2 NRT Zelman 1992	No weight data
2 RM STRATUS-EU 2006	Unable to obtain data

(*Continued*)

2 RM STRATUS-US 2006	Unable to obtain data
2 RM STRATUS-WW 2005	Unable to obtain data
2 VA Hajek 2011	Participants took medication before quit day
2 VA Tsukahara 2010	No weight data for abstainers
2 VA Williams 2007	No weight data
VA Carson 2010	Less than 6 months follow up

DATA AND ANALYSES

Comparison 1. 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	8		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 Phenylpropanolamine versus Placebo	3	112	Mean Difference (IV, Fixed, 95% CI)	-0.50 [-0.80, -0.20]
1.3 Ephedrine + Caffeine versus Placebo	1	40	Mean Difference (IV, Fixed, 95% CI)	-1.30 [-2.87, 0.27]
1.4 Naltrexone versus Placebo	2	179	Mean Difference (IV, Fixed, 95% CI)	-0.78 [-1.52, -0.05]
1.5 Chromium versus placebo	1	15	Mean Difference (IV, Fixed, 95% CI)	-0.81 [-3.05, 1.43]
2 Mean weight change (kg) at 6 months	3		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
2.1 Phenylpropanolamine versus Placebo	1	38	Mean Difference (IV, Fixed, 95% CI)	-2.06 [-5.56, 1.44]
2.2 Ephedrine + caffeine versus placebo	1	32	Mean Difference (IV, Fixed, 95% CI)	-0.70 [-2.72, 1.32]
2.3 Chromium versus placebo	1	9	Mean Difference (IV, Fixed, 95% CI)	-3.87 [-12.01, 4.27]
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 2. 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	5		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	2	557	Risk Ratio (M-H, Fixed, 95% CI)	1.01 [0.72, 1.43]
1.4 Chromium versus placebo	1	143	Risk Ratio (M-H, Fixed, 95% CI)	0.48 [0.12, 1.84]
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 3. Behavioural weight management interventions versus advice or no intervention: 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	5		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
1.1 Weight management education versus no weight intervention	2	140	Mean Difference (IV, Fixed, 95% CI)	-0.04 [-0.57, 0.50]
1.2 Personalised weight management support versus no weight intervention	3	121	Mean Difference (IV, Fixed, 95% CI)	-1.11 [-1.93, -0.29]
1.3 Personalised weight management support versus weight management education	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]
1.5 Early versus late personalised weight management support	1	41	Mean Difference (IV, Fixed, 95% CI)	1.4 [-1.32, 4.12]
2 Mean weight change (kg) at 6 months	3	118	Mean Difference (IV, Fixed, 95% CI)	1.59 [0.33, 2.86]
2.1 Weight management education verses no weight intervention	2	81	Mean Difference (IV, Fixed, 95% CI)	0.89 [-0.78, 2.55]
2.2 Personalised weight management support versus no weight intervention	1	15	Mean Difference (IV, Fixed, 95% CI)	0.40 [-2.54, 3.34]
2.3 Early versus late personalised weight management support	1	22	Mean Difference (IV, Fixed, 95% CI)	4.2 [1.63, 6.77]
3 Mean weight change (kg) at 12 months	4		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
3.1 Weight management education versus no weight intervention	2	61	Mean Difference (IV, Fixed, 95% CI)	-0.21 [-2.28, 1.86]
3.2 Personalised weight management support versus no weight intervention	2	40	Mean Difference (IV, Fixed, 95% CI)	-2.58 [-5.11, -0.05]
3.3 Personalised weight management support versus weight management education	1	17	Mean Difference (IV, Fixed, 95% CI)	-2.49 [-5.51, 0.53]

3.4 VLCD + advice versus advice	1	62	Mean Difference (IV, Fixed, 95% CI)	-1.30 [-3.49, 0.89]

Comparison 4. Behavioural weight management interventions versus advice or no intervention: smoking cessation

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Abstinence at 6 months	4		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 Weight management education versus no intervention	3	660	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.80, 1.31]
1.2 Personalised weight management support versus no intervention	2	254	Risk Ratio (M-H, Fixed, 95% CI)	0.88 [0.54, 1.43]
1.3 Personalised weight management support versus weight management education	1	104	Risk Ratio (M-H, Fixed, 95% CI)	0.81 [0.40, 1.65]
2 Abstinence at 12 months	4		Risk Ratio (M-H, Fixed, 95% CI)	Subtotals only
2.1 Weight management education versus no intervention	2	522	Risk Ratio (M-H, Fixed, 95% CI)	0.66 [0.48, 0.90]
2.2 Personalised weight management support versus no intervention	2	254	Risk Ratio (M-H, Fixed, 95% CI)	0.79 [0.47, 1.33]
2.3 Personalised weight management support versus weight management education	1	104	Risk Ratio (M-H, Fixed, 95% CI)	0.96 [0.46, 2.02]
2.4 VLCD + advice versus advice	1	287	Risk Ratio (M-H, Fixed, 95% CI)	1.73 [1.10, 2.73]

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	2	496	Odds Ratio (M-H, Fixed, 95% CI)	1.70 [1.13, 2.56]
1.1 No additional pharmacotherapy treatment	2	301	Odds Ratio (M-H, Fixed, 95% CI)	1.83 [1.07, 3.13]
1.2 With bupropion	1	195	Odds Ratio (M-H, Fixed, 95% CI)	1.53 [0.81, 2.89]
2 Abstinence at 12 months	2	496	Risk Ratio (M-H, Fixed, 95% CI)	1.25 [0.83, 1.86]
2.1 No additional pharmacotherapy	2	301	Risk Ratio (M-H, Fixed, 95% CI)	1.51 [0.81, 2.79]
2.2 With bupropion	1	195	Risk Ratio (M-H, Fixed, 95% CI)	1.06 [0.62, 1.81]

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	2	164	Mean Difference (IV, Fixed, 95% CI)	-0.18 [-0.56, 0.20]
1.1 With no additional pharmacotherapy	2	105	Mean Difference (IV, Fixed, 95% CI)	-0.01 [-0.57, 0.55]
1.2 With bupropion	1	59	Mean Difference (IV, Fixed, 95% CI)	-0.33 [-0.86, 0.20]
2 Mean weight change (kg) at 6 months	2	101	Mean Difference (IV, Fixed, 95% CI)	0.74 [0.24, 1.24]
2.1 With no additional pharmacotherapy	2	55	Mean Difference (IV, Fixed, 95% CI)	0.31 [-0.75, 1.37]
2.2 With bupropion	1	46	Mean Difference (IV, Fixed, 95% CI)	0.86 [0.30, 1.42]
3 Mean weight change (kg) at 12 months	2	76	Mean Difference (IV, Fixed, 95% CI)	0.13 [-0.72, 0.98]
3.1 With no additional pharmacotherapy	2	44	Mean Difference (IV, Fixed, 95% CI)	-0.82 [-2.68, 1.04]
3.2 With bupropion	1	32	Mean Difference (IV, Fixed, 95% CI)	0.38 [-0.57, 1.33]

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	9		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
1.1 Bupropion versus placebo	7	869	Mean Difference (IV, Fixed, 95% CI)	-1.12 [-1.47, -0.77]
1.2 Fluoxetine versus placebo	2	144	Mean Difference (IV, Fixed, 95% CI)	-0.99 [-1.36, -0.61]
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/day placebo	1	44	Mean Difference (IV, Fixed, 95% CI)	-0.60 [-1.89, 0.69]
2.2 Bupropion: 300mg/day v 100mg/day placebo	1	37	Mean Difference (IV, Fixed, 95% CI)	-0.60 [-1.86, 0.66]
3 Mean weight change (kg) at 6 months	6		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
3.1 Bupropion versus placebo	4	218	Mean Difference (IV, Fixed, 95% CI)	-0.87 [-2.21, 0.47]
3.2 Fluoxetine versus placebo	2	124	Mean Difference (IV, Fixed, 95% CI)	-0.01 [-1.11, 1.10]
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 versus no exercise 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 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: lozenge v gum	1	54	Mean Difference (IV, Fixed, 95% CI)	-2.45 [-4.43, -0.47]
4 Mean weight change (kg) at end of treatment: dose response	4	1038	Mean Difference (IV, Fixed, 95% CI)	0.22 [-0.04, 0.48]
4.1 4mg vs 2mg gum	1	161	Mean Difference (IV, Fixed, 95% CI)	-0.10 [-0.61, 0.41]
4.2 22mg vs 11mg patch	1	15	Mean Difference (IV, Fixed, 95% CI)	-0.40 [-2.65, 1.85]

4.3 44mg vs 22mg patch	1	24	Mean Difference (IV, Fixed, 95% CI)	-0.20 [-1.99, 1.59]
4.4 25mg patch vs 15mg patch- 8 week treatment course	1	497	Mean Difference (IV, Fixed, 95% CI)	0.40 [0.04, 0.76]
4.5 25mg patch vs 15mg patch- 22 weeks treatment	1	299	Mean Difference (IV, Fixed, 95% CI)	0.20 [-0.57, 0.97]
4.6 15x2mg gum vs 7x2mg gum	1	24	Mean Difference (IV, Fixed, 95% CI)	1.59 [-0.27, 3.45]
4.7 30x2mg gum vs 15x2mg gum	1	18	Mean Difference (IV, Fixed, 95% CI)	-0.27 [-1.83, 1.29]
5 Mean weight change (kg) at 6 months	9	771	Mean Difference (IV, Fixed, 95% CI)	-0.37 [-0.88, 0.14]
5.1 Gum versus placebo	2	103	Mean Difference (IV, Fixed, 95% CI)	-0.83 [-2.35, 0.69]
5.2 Patch versus placebo	4	282	Mean Difference (IV, Fixed, 95% CI)	-0.31 [-1.09, 0.47]
5.3 Inhaler versus placebo	1	57	Mean Difference (IV, Fixed, 95% CI)	-0.60 [-1.98, 0.78]
5.4 Sub-lingual tablet versus placebo	2	329	Mean Difference (IV, Fixed, 95% CI)	-0.19 [-1.09, 0.72]
6 Mean weight change (kg) at 6 months: patch v spray	1	103	Mean Difference (IV, Fixed, 95% CI)	2.0 [-0.72, 4.72]
7 Mean weight change (kg) at 6 months: lozenge v gum	1	40	Mean Difference (IV, Fixed, 95% CI)	-2.35 [-5.34, 0.64]
8 Mean weight change (kg) at 12 months	15	1334	Mean Difference (IV, Fixed, 95% CI)	-0.42 [-0.92, 0.08]
8.1 Gum versus placebo	1	49	Mean Difference (IV, Fixed, 95% CI)	-0.07 [-3.07, 2.93]
8.2 Patch versus placebo	6	770	Mean Difference (IV, Fixed, 95% CI)	-0.23 [-0.90, 0.45]
8.3 Intranasal spray versus placebo	3	122	Mean Difference (IV, Fixed, 95% CI)	-1.55 [-3.09, -0.00]
8.4 Inhaler versus placebo	2	90	Mean Difference (IV, Fixed, 95% CI)	-1.03 [-2.23, 0.17]
8.5 Sub-lingual tablet versus placebo	3	303	Mean Difference (IV, Fixed, 95% CI)	0.27 [-0.99, 1.54]
9 Mean weight change (kg) at 12 months: lozenge v gum	1	33	Mean Difference (IV, Fixed, 95% CI)	-3.31 [-9.77, 3.15]
10 Mean weight change (kg) at 12 months: dose response	2	423	Mean Difference (IV, Fixed, 95% CI)	0.24 [-0.49, 0.96]
10.1 22mg patch vs 11mg	1	7	Mean Difference (IV, Fixed, 95% CI)	-3.90 [-10.74, 2.94]
10.2 44mg patch vs 11mg	1	12	Mean Difference (IV, Fixed, 95% CI)	-2.2 [-10.12, 5.72]
10.3 25mg patch vs 15mg- 8 week treatment course	1	198	Mean Difference (IV, Fixed, 95% CI)	0.60 [-0.43, 1.63]
10.4 25mg patch vs 15mg- 22 weeks treatment course	1	206	Mean Difference (IV, Fixed, 95% CI)	0.0 [-1.04, 1.04]
11 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]
11.1 22 weeks vs 8 weeks 25mg patch	1	222	Mean Difference (IV, Fixed, 95% CI)	-0.5 [-1.46, 0.46]
11.2 22 weeks vs 8 weeks 15mg patch	1	182	Mean Difference (IV, Fixed, 95% CI)	0.10 [-1.00, 1.20]

Comparison 10. Varenicline 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	11		Mean Difference (IV, Fixed, 95% CI)	Subtotals only
1.1 1mg versus placebo	3	254	Mean Difference (IV, Fixed, 95% CI)	-0.12 [-0.68, 0.43]
1.2 2mg versus placebo	11	2008	Mean Difference (IV, Fixed, 95% CI)	-0.41 [-0.63, -0.19]
2 Mean weight change (kg) at 6 months	1	105	Mean Difference (IV, Fixed, 95% CI)	0.41 [-0.79, 1.61]
3 Mean weight change (kg) at 12 months	2	151	Mean Difference (IV, Fixed, 95% CI)	1.11 [-0.75, 2.98]

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 versus NRT: 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	319	Mean Difference (IV, Fixed, 95% CI)	-0.05 [-0.58, 0.48]

WHAT'S NEW

Last assessed as up-to-date: 7 October 2011.

Date	Event	Description
23 November 2011	New citation required but conclusions have not changed	Change of name for one author (Amanda Parsons is now Amanda Farley), one new author added (DL), and two authors of previous version removed (see Contributions of Authors)

(*Continued*)

23 November 2011	New search has been performed	Twelve additional studies added. Conclusions largely unchanged

HISTORY

Protocol first published: Issue 4, 2006

Review first published: Issue 1, 2009

Date	Event	Description
24 April 2008	Amended	Converted to new review format.
14 July 2006	New citation required and major changes	Substantive amendment

CONTRIBUTIONS OF AUTHORS

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

DECLARATIONS OF INTEREST

Paul Aveyard and Amanda Parsons are authors of a study included in this review testing the effect of St John's wort and chromium supplements on smoking cessation and post cessation weight gain. The trial was funded by Cancer Research UK and the supplements were bought from the manufacturer. Paul Aveyard has done consultancy work for pharmaceutical and biotechnology companies that has led to payments to him and his institution. This includes work for companies providing smoking cessation medication, including McNeil, Xenova and Pfizer.

SOURCES OF SUPPORT

Internal sources

- University of Birmingham, UK.

Paid the salary of Amanda Parsons, Jennie Inglis and Paul Aveyard
Mujahed Sharim studied for a masters in public health at the University and completed part of the work as part of his masters project

- UKCTCS, UK.

Paid the doctoral stipend of Deborah Lycett and contributed to the salaries of Amanda Parsons and Paul Aveyard. The UK Centre for Tobacco Control Studies is a UKCRC Public Health Research: Centre of Excellence. Funding from British Heart Foundation, Cancer Research UK, Economic and Social Research Council, Medical Research Council, and the National Institute of Health Research, under the auspices of the UK Clinical Research Collaboration, is gratefully acknowledged.

- Queen Mary's University of London, UK.

Paid the salary of Peter Hajek

- National Institute of Health Research, UK.

Contributed to the salary of Paul Aveyard

External sources

- No sources of support supplied

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]; Randomized Controlled Trials as Topic; Smoking Cessation [*methods]

MeSH check words

Female; Humans; Male