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RESEARCH

Weight gain in smokers after quitting cigarettes: meta-analysis

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Abstract

Objective To describe weight gain and its variation in smokers who achieve prolonged abstinence for up to 12 months and who quit without treatment or use drugs to assist cessation.

Design Meta-analysis.

Data sources We searched the Central Register of Controlled Trials (CENTRAL) and trials listed in Cochrane reviews of smoking cessation interventions (nicotine replacement therapy, nicotinic partial agonists, antidepressants, and exercise) for randomised trials of first line treatments (nicotine replacement therapy, bupropion, and varenicline) and exercise that reported weight change. We also searched CENTRAL for trials of interventions for weight gain after cessation.

Review methods Trials were included if they recorded weight change from baseline to follow-up in abstinent smokers. We used a random effects inverse variance model to calculate the mean and 95% confidence intervals and the mean of the standard deviation for weight change from baseline to one, two, three, six, and 12 months after quitting. We explored subgroup differences using random effects meta-regression.

Results 62 studies were included. In untreated quitters, mean weight gain was 1.12 kg (95% confidence interval 0.76 to 1.47), 2.26 kg (1.98 to 2.54), 2.85 kg (2.42 to 3.28), 4.23 kg (3.69 to 4.77), and 4.67 kg (3.96 to 5.38) at one, two, three, six, and 12 months after quitting, respectively. Using the means and weighted standard deviations, we calculated that at 12 months after cessation, 16%, 37%, 34%, and 13% of untreated quitters lost weight, and gained less than 5 kg, gained 5-10 kg, and gained more than 10 kg, respectively. Estimates of weight gain were similar for people using different pharmacotherapies to support cessation. Estimates were also similar between people especially concerned about weight gain and those not concerned.

Conclusion Smoking cessation is associated with a mean increase of 4-5 kg in body weight after 12 months of abstinence, and most weight gain occurs within three months of quitting. Variation in weight change is large, with about 16% of quitters losing weight and 13% gaining more than 10 kg.

Introduction

Although smoking cessation results in considerable improvements in health, it is often accompanied by weight gain. The link between smoking and body weight has been known for many years. Cross sectional studies show that, on average, smokers weigh less than non-smokers, and former smokers weigh more than both smokers and non-smokers.[1] A large prospective study has shown that adolescents who initiate smoking gain less weight than their non-smoking peers.[2] Cohort studies also show that people who stop smoking gain weight.[1 3-8] Smoking cessation probably causes weight gain because nicotine (in cigarettes) is an appetite suppressant.[3] One of the most common and longlasting symptoms of tobacco withdrawal is increased appetite.[9] Furthermore, evidence suggests that nicotine increases the basal metabolic rate, and removal of this effect results in a decline in energy expenditure at a time when appetite is increased.[3]

Estimates of the amount of weight that smokers gain when quitting have varied. A large narrative systematic review[1] done over 20 years ago concluded that weight gain from smoking cessation was typically 2.9 kg, and this estimate or similar is often quoted in smoking cessation advice leaflets. However, the review did not describe the method of combining estimates, and could have provided an inaccurate estimate of weight gain for several reasons. Firstly, follow-up periods in the 41 prospective studies reviewed varied from two weeks to 40 years. Secondly, measures of both smoking and weight were often self reported, without validation. Thirdly, the definition of smoking cessation was often not clear and probably included people who were "point prevalent" abstinent at the time of follow-up.

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People who meet the definition of point prevalence abstinence will include those who have been continuously or intermittently abstinent for years, or those who have recently stopped only days or weeks before measurement. Point prevalence abstinence was more likely to have been used in the population based studies included in this review, such as the Framingham study,[10] because participants were not given a target quit date and followed from that point. A previous study has shown that the mean weight gain in studies measuring point prevalence abstinence was lower than those measuring weight change in continuous abstainers.[11]

We aimed to describe weight changes seen in smokers who were motivated to quit. Data in this study were derived from clinical trials of first line smoking cessation drugs and from trials of interventions designed to limit weight gain after cessation. We previously published a Cochrane review that examined the effectiveness of these interventions on preventing such weight gain in the short term and at six and 12 month follow-up in full detail.[12] The three treatments commonly used around the world are nicotine replacement therapy, bupropion, and varenicline. In brief, the Cochrane review showed that all three treatments reduced weight gain by 0.5 kg (nicotine replacement therapy), 1.1 kg (bupropion), and 0.4 kg (varenicline). There was no evidence that any of them reduced weight gain at one year, but the data were too imprecise to exclude effects of similar size. In the present study, rather than describing the effect of treatment on limiting weight gain, we described the weight change over time, and its variability between individuals for smokers who quit using these treatments, and for those who quit without using them, during the first 12 months of abstinence.

Methods

The aim of this study was to estimate the mean weight change, and the variation around the mean of that change, in smokers who presented for smoking cessation treatment and achieve abstinence. Most data were derived from clinical trials of first line interventions for smoking cessation, published in Cochrane reviews. The primary aim of most of the reviewed trials was to assess the effectiveness of the pharmacological interventions to assist quitting. These data and adverse event data were summarised in the relevant Cochrane reviews.[13-17] We used these trials to estimate mean weight change and its variation in untreated quitters (control arm data) and treated quitters (treatment arm data).

A second group of trials examined the effectiveness of specific interventions to prevent weight gain after cessation. Such trials typically enrolled smokers especially concerned about gaining weight and randomised them to standard support for smoking cessation or standard support plus an intervention to prevent weight gain. Here, we used data from the control groups only because some of these interventions were effective in reducing weight gain.[12] We used these data to estimate weight change in weight concerned smokers, because some authors have shown increased weight gain in this group.[18]

A third group of studies examined the effectiveness of exercise in promoting smoking cessation. A systematic review of randomised trials showed convincing evidence indicating that exercise suppresses cravings to smoke. Most trials of exercise in the Cochrane review on the effect of exercise on cessation did not report data for weight gain nor appeal to weight concerned smokers.[17] Nevertheless, exercise could reduce weight gain,[12] and we included only the control arms of these trials to estimate weight change in untreated quitters.

Search strategy and study selection

Trials included in this study were identified from our Cochrane review on interventions to prevent weight gain.[12] The search was updated in November 2011, and is reported in detail elsewhere. In brief, we searched the included lists of Cochrane reviews of smoking cessation interventions—nicotine replacement therapy (last search date, October 2007),[15] antidepressants (July 2009),[16] nicotine receptor partial agonists (October 2010),[13] and exercise interventions (July 2011)[17]—published in version 11 of the 2011 Cochrane Library. We updated the searches for nicotine replacement therapy, bupropion, varenicline, and exercise trials published since the last search date for each Cochrane review to November 2011 by searching the Cochrane CENTRAL register (Central Register of Controlled Trials) using a combination of smoking and treatment search terms. In addition, we searched the Cochrane Tobacco Addiction Group specialist register for interventions that specifically targeted weight gain after cessation in addition to smoking cessation (search date, November 2011), using a combination of smoking and weight related search terms.

For inclusion in our review, studies had to report or their authors had to supply data for weight change from baseline to at least one follow-up point in abstainers only. Almost all studies of nicotine replacement therapy, varenicline, bupropion, and exercise did not report weight data in either the title or abstract. Consequently, we assessed the full text of every study in the latest versions of the reviews of effectiveness of the four treatments for inclusion. For the update search, we obtained and read the full text of every trial, if the title or abstract made it apparent that it was a trial of one of these interventions. We contacted authors or sponsors (or both) if weight data were incompletely recorded or missing but it was clear that participants had been weighed. Likewise, we screened the full text of any trial in which the title or abstract clearly indicated that the intervention aimed to allay concern about weight gain after cessation or aimed to prevent such weight gain. Studies in foreign languages were translated into English.

Data extraction

Three authors (H-JA, AF, DL) extracted data, with each study having data extracted by two independent authors. Remaining differences were resolved by a fourth author (PA) extracting data and thereafter by consensus. We extracted the mean weight change (kg), standard deviation, and number of participants contributing to the mean from baseline to each given time point, in abstinent smokers only. Time points were calculated in reference to the target quit date. Time points were aggregated into months (weeks two to five=month one; weeks six to nine=month two; weeks 10-13=month three; weeks 22-26=month six; weeks 50-56=month 12.

Study quality assessment

Although the data were derived from randomised controlled trials, weight gain was not considered by randomisation group, and therefore we treated the data as observational. As such, we based our assessment of quality on the framework proposed by Altman, a widely cited framework tailored to the assessment of descriptive cohort studies.[19] Study quality was mainly based on the assessment of smoking status and weight (table 1⇓). We assessed whether studies reported smoking abstinence as prolonged or continuous—that is, whether participants had sufficient time for weight gain to occur, or had point prevalence abstinence. In addition, a proportion of patients treated in clinics can claim abstinence even if they have not achieved it.

Biochemical validation would reduce the number of people falsely claiming abstinence, which would underestimate weight gain if such participants were included; therefore, we also extracted data regarding the use of biochemical validation. Finally, we examined whether studies reported how weight was assessed, and we categorised studies that obtained self reported weights, which are known to be subject to error,[20] from those studies in which people were weighed.

Data analysis

We combined data to describe weight change in quitters treated with varenicline, bupropion, or nicotine replacement therapy, and in those who were not given these treatments ("untreated quitters"). To estimate weight change in the untreated quitters, we combined data from the control group of trials of nicotine replacement therapy, varenicline, bupropion, and exercise for smoking cessation, and from the control group of trials of interventions to prevent or allay concerns about weight gain after cessation. Treated quitter groups included data from the active treatment arm of trials of nicotine replacement therapy, varenicline, and bupropion. We kept these groups separate because these pharmacotherapies could have a small effect on weight gain in the short term.[12] We combined studies with multiple treatment arms of the same pharmacotherapy (that is, testing different dose regimens or preparations). Control groups in which participants received one form of pharmacotherapy were not included in the meta-analysis for untreated quitters, but rather in the corresponding treatment group. We excluded treatment groups that received more than one pharmacotherapy.

We used a random effects inverse variance model to estimate a summary mean for weight change and 95% confidence intervals at months one, two, three, six, and 12 for each of the groups described above. The random effects model was chosen because of the high heterogeneity between trial estimates in each meta-analysis. The underlying assumption of a random effects model is that the true effect could vary between studies, based on characteristics of the study population or intervention. In this case, for example, the population mean might differ if participants are younger; healthier, by baseline body mass index or previous quit history; or if the study used a more intensive or longer intervention.

The studies in the meta-analysis were assumed to be a random sample of the relevant distribution of effects, and the combined effect estimated the mean effect of these different subpopulation means. We measured heterogeneity using the I^2 statistic. We also estimated the variation in weight change by calculating a weighted mean (according to the number participants in the study) of the standard deviations. Using z scores, we calculated the percentage of the quitting population who would be expected to lose weight, remain stable, gain less than 5 kg, gain 5-10 kg, or gain more than 10 kg over 12 months. We assumed that weight change after cessation is roughly normally distributed. We believe this assumption is reasonable; data from our trials suggest weight gain after cessation is normally distributed.[21 22] Also, other trials have reported means and standard deviations rather than medians and interquartile ranges, which they might have reported if data were skewed. We did all analyses using the Comprehensive Meta Analysis statistical program (version 2.2.50) and Stata (version 10).

Subgroup analyses

Owing to the heterogeneity present, we sought to identify subgroups with differing mean weight gain. We combined data from all studies at 12 month follow-up, using a random effects metaregression model with a binary predictor variable for weight concern. Twelve month data were used, because any effect of treatment on weight has not been shown to persist beyond this follow-up point.[12]

Sensitivity analyses

We evaluated the effect of study quality criteria on estimates of weight change in data from all studies combined at 12 month follow-up, using a random effects meta-regression model. We used binary predictor variables to assess whether the mean weight change differed in studies defining abstinence as point prevalence abstinence versus prolonged or continuous abstinence, and whether weight was measured at the clinic or elsewhere, at each follow-up point. It was not possible to test the effect of biochemical confirmation of abstinence, because all but one study confirmed abstinence biochemically.

Publication bias

Most trials assessed did not report weight gain, and it is possible that trials chose to report weight gain only if the gain was remarkably high. We constructed funnel plots for weight estimates for untreated patients and patients treated with nicotine replacement therapy, bupropion, and varenicline at three and 12 months to test for plot symmetry, in order to detect any publication bias.

Results

Included studies

Of 212 trials in the Cochrane reviews of nicotine replacement therapy, varenicline, bupropion, and exercise, 53 recorded weight change at one or more follow-ups (fig 1⇓). We also found another trial with weight data in the updated search. Of these 54 trials, three were excluded because all groups received some intervention that could affect weight gain. The search of online databases for studies aimed at preventing weight gain after cessation led to the full text search of 16 studies. Of these, 11 were included and an additional two were already found from searches of the Cochrane reviews. The three excluded trials all offered interventions that might limit weight gain to all participants. In total, we included 62 trials.

Description of studies and quality assessment

Studies often had eligible data from more than one trial arm (control and treatment arms), and some studies contributed data for more than one treatment. In total, 51 studies contributed weight change data in participants under control conditions (untreated quitters). Nine of these studies tested interventions to limit weight gain and largely recruited weight concerned smokers.[21 23-30] Data for weight gain in smokers taking nicotine replacement therapy (any preparation, any strength), bupropion (300 mg/day), and varenicline (2 mg/day) were collected from 34, 10, and 12 studies, respectively. Of the 62 included trials, 59 enrolled populations from North America, Europe, or Australia, and the remaining three[31-33] were conducted in east Asian countries (table 2⇓). One study[30] reported weight change at months three, six, and nine. Since this study was the only one with a nine month time point, we did not include the data at nine months. We could not extract data for weight gain by sex, because it was not presented in any study. Seven studies recruited women only.[23 25 29 30 35 36 86] One of these studies investigated exercise, and the remaining trials analysed interventions for weight gain after cessation. All other trials recruited both men and women.

Overall, studies were of high quality. Fifty one studies measured weight change in abstinent smokers, using the definition of prolonged abstinence or continuous abstinence from the first day of quitting. All but one of these studies validated abstinence biochemically.[37] Two other studies had definitions similar to the Russell standard criterion for prolonged abstinence and we counted them as such.[38] One study allowed participants to "slip up" for up to seven consecutive days,[39] and another[40] allowed patients to have up to three cigarettes per week but verified them as abstinent by carbon monoxide measurement. Eight studies[23 24 41-45] defined abstinence as biochemically validated point prevalence at seven days. One study[46] did not define abstinence.

Two studies used self reported weight[37 47] and 33 reported (or authors or sponsors confirmed) weighing participants. Twenty six studies did not report whether participants were weighed or data were self reported. We recorded weight assessment in these studies as unclear, although all studies but one[46] biochemically validated abstainers at follow-up (and therefore must have had a face-to-face meeting) and therefore probably measured participants' weight rather than using participants' self reported weight. No studies reported details of weight measurement such as validated scales or clothing requirements.

Effect on weight gain

Table 3⇓ and figures 2-8⇓⇓⇓⇓⇓⇓⇓ shows the means and 95% confidence intervals for weight change from baseline in treated and untreated smokers during the first 12 months of abstinence. In all groups, weight increased by about 1 kg per month for the first three months. Thereafter, the rate of increase reduced, leading to an estimated weight increase of about 4-5 kg at one year after cessation.

There were small differences in the estimates between different pharmacotherapies. We did not test for the significance of these differences because these data were available in the Cochrane review.[12] Table 3 shows weighted mean standard deviations, which indicated a large variation between participants. Using z scores, we calculated the percentage of the quitting population who would be expected to lose weight, remain stable, gain less than 5 kg, gain 5-10 kg, or gain more than 10 kg over 12 months (figs 9-11⇓⇓⇓). At 12 months, 16-21% of untreated participants lost weight, 35-38% gained less than 5 kg, 29-34% gained 5-10 kg, and 13-14% of participants gained more than 10 kg. These proportions were similar for participants who had used first line treatment for smoking cessation.

Subgroup analyses

We found no clear difference between the mean weight gain in studies that treated weight concerned smokers and those that treated the general population of smokers (table 4⇓). Therefore, the findings reported above and in table 3 include all data regardless of study participant selection for weight concern.

Sensitivity analyses and publication bias

Weight gain at 12 months was lower in trials that recorded abstinence as point prevalence, than in those that measured weight in prolonged or continuous abstainers, although this difference was not significant (3.80 kg (95% confidence interval 2.31 to 5.29) *v* 4.74 kg (4.33 to 5.16), P=0.14). We found no significant difference at all time points in weight gain between trials that measured weight at the clinic or when weight was reported otherwise. All studies reporting weight data at 12 months biochemically confirmed abstinence; therefore, sensitivity analysis by this study quality variable was not performed. No funnel plot showed evidence of asymmetry, providing good evidence that the trials represent a random selection of weight change estimates. Plots are available on request from the authors.

Discussion

Our meta-analysis has shown that abstinent smokers gain a mean weight of 4-5 kg after 12 months of abstinence. However, we have found substantial variation in weight gain, indicating that this mean value does not reflect many people who give up smoking. We estimated that at 12 months, 16-21% of participants lost weight and 13-14% gained more than 10 kg.

Although weight gain after smoking cessation is widely recognised, this meta-analysis provides clinicians and patients with a more robust and detailed description of the first 12 months of weight change after cessation. The finding of a mean weight gain of 4.7 kg in untreated quitters at one year after smoking cessation is substantially higher than the 2.9 kg often quoted in smoking cessation advice leaflets, which stemmed from a previous review.[1] Moreover, this mean weight gain is greater than the 2.3 kg gain that female smokers report being willing to tolerate, on average, before embarking on a quit attempt.[48]

This review reports on variation in weight gain, which is rarely described or discussed in the literature, and has clinical implications. Some people are either destined or able to prevent weight gain without intervention, whereas others seem likely to gain enough weight that puts them at increased risk of diabetes, among other complications.[49] In practice, doctors could detect people gaining excessive weight and intervene early to prevent this.

We were unable to show a significant difference between weight change estimates in point prevalence abstainers and prolonged or continuous abstainers, and therefore, we combined all estimates at each time point regardless of abstinence definition. This may be because the data were derived from clinical trials, in which participants were all given the same target quit date, and therefore many point prevalence abstainers were also prolonged abstainers.[50] However, the point estimate did indicate a smaller weight change in point prevalence abstainers and it is possible that this difference was the case in our analysis, although it was not sufficiently powered to detect statistical significance.

Most trials aimed at preventing weight gain typically enrolled weight concerned women, but did not provide clear evidence that this group were at risk of greater weight gain. This result might seem surprising, since people concerned about weight may have experienced excessive weight gain in previous quit attempts, and excessive gain is associated with greater weight gain in a current quit attempt.[51] However, the association between weight concerns and weight gain after cessation is unclear.[18 52 53] Furthermore, nearly all such trials recruited exclusively women, whereas trials appealing to the general population were all mixed sex. Consequently, the data were inevitably confounded and also not precise enough to exclude a difference between weight concerned populations and populations not specifically concerned about weight gain.

Our estimates provided the difference between starting weight and weight up to one year later. The mean weight of a population is likely to increase over one year independently of a smoking cessation attempt.[54] The Lung Health Study showed that continuing smokers gain on average of 0.3 kg/year for men and 0.5 kg/year for women.[55] Another study[7] estimated a gain of about 0.3 kg/year for both sexes, meaning that roughly 4.3 kg

of the mean weight gain at 12 months in our analysis was due to cessation (table 3).

These data relate only to weight gain in people who achieve and maintain abstinence, but provide no evidence on what happens to weight in smokers who are abstinent and then relapse or in continuing smokers who never achieve abstinence. For smokers who gain weight on cessation, available data suggest that they lose weight again if they relapse to smoking,[56] although few studies have reported data for weight gain in those who relapse. An incremental weight gain would be important because many people repeatedly attempt to quit. Furthermore, because few trials followed participants beyond one year, we cannot report here on weight gain beyond this time point. Evidence is conflicting as to whether weight continues to increase beyond the first year after cessation.[55 57-59]

We limited our review to randomised controlled trials for smoking cessation, pharmacotherapy use, exercise, and interventions aiming to prevent weight gain. The validity of data for weight gain after cessation depends on accurate timing of the start of abstinence, the validity of recording of abstinence, and frequent follow-up. Most of the trials we reviewed show these features but few observational studies do. We also limited our review to trials in the Cochrane reviews of first line treatment, which led to the exclusion of a few other trials, chiefly the Lung Health Study.[55] However, estimates of the effect of cessation on weight gain at one year from the Lung Health Study were similar to our estimates, and there was no reason to presume that using data from only randomised controlled trials created a bias.

Limitations

These data were derived from smokers treated in clinics for tobacco dependence. Such groups are usually more dependent and heavier smokers than the general population of smokers. There is conflicting evidence that heaviness of smoking relates to weight gain,[4] with different studies reporting that heavier smokers gain more weight, or that moderate smokers gain most weight. Smokers seeking treatment could differ from those who quit on their own in other ways. Most people do not attend smoking cessation clinics or consult their doctor for help until they have tried and failed to stop smoking themselves. Their previous failure to accomplish one goal, smoking cessation, could reflect on their ability to limit weight gain after cessation. This theory is speculative, however. The differences between the population enrolled in clinical treatment and smokers quitting without clinical help could be related to weight gain after cessation. A systematic review of population based studies, taking careful account of the assessment of continuing abstinence, would be needed to assess weight gain after smoking cessation in the general population. Therefore, our review data are directly relevant to clinicians who only treat smokers who present for help with cessation.

Weight gain was reported in only 25% of the smoking cessation trials considered for inclusion. It was not possible to determine whether those studies reporting weight were a biased sample of all smoking cessation trials, although we found no evidence of bias on the funnel plot. Trials that aimed to prevent weight gain after cessation reported weight change as a primary outcome, and we observed no difference in weight gain between these trials and the treatment trials, in which only a minority reported weight gain.

Different studies, and therefore different study participants, contributed data to the meta-analyses at each time point and we noted heterogeneity in most analyses. We therefore cannot interpret mean weight change across different time points as a trajectory. Studies would need to report individual weight gain trajectories, rather than cross sectional means, for us to summarise these changes. Large weight gain might lead to intentional relapse to smoking, which would mean that people who put on large amounts of weight early in their quit attempt and relapse were not represented by our data. However, data are conflicting for the association between weight gain and probability of relapse.[51 60-68]

Conclusions

Previous reports have underestimated the average amount of weight gained when people stop smoking. In clinic treated smokers, the population mean is about 4-5 kg after 1 year. Weight gain is greatest during the first three months of quitting (average monthly weight gain of about 1 kg), after which the rate of increase declines. However, we saw a large variation around the population mean. At 12 months, about 16-21% of participants lost weight and 13-14% gained more than 10 kg.

Weight gain is important because weight concern is widespread among smokers and could deter some from trying to quit. Gaining weight after cessation limits some of the health benefits of quitting and is associated with an increased risk of health problems.[69-73] So far, interventions have had a limited effect on preventing weight gain.[12] These data suggest that doctors might usefully give patients a range of expected weight gain, although further research should identify the subgroups most at risk of gaining weight and clarify the optimum content and timing of interventions to prevent weight gain after cessation.

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Data sharing: No additional data available.

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What is already known on this topic

Smoking cessation is often followed by an increase in bodyweight, but estimates vary and are not well grounded

What this study adds

Smoking cessation is associated with a mean increase in body weight of about 4-5 kg after 1 year, with most weight gain occurring within three months of quitting

Changes in body weight vary widely, with around 16% of quitters losing weight and 13% gaining more than 10 kg

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Tables

Table 1| Application of Altman's criteria for judging the quality of studies on outcome

Criterion	Altman criteria	How applied in this review
Sample of patients	Inclusion criteria defined, sample selection explained, adequate description of diagnostic criteria, clinical and demographic characteristics fully described, representative, assembled at common (usually early) point in course of disease, complete (all eligible patients included)	All cohorts included smokers wanting to quit, assembled before quit day and with time measured from quit day. Population categorised by type of abstinence measure (that is, prolonged or continuous, point prevalence and biochemically confirmed or not).
Follow-up of patients	Sufficiently long	Followed at 1, 2, 3, 6, and 12 months
Outcome	Objective, unbiased (for example, assessment blinded to prognostic information), fully defined, appropriate, known for all or high proportion of patients	Self reported weight, measured weight, presumed measured, and unclear
Analysis	Continuous predictor variable analysed appropriately, statistical adjustment for all important prognostic factors	Not applicable. The aim of the study was not to assess the effect of a particular prognostic factor but to record the outcome in all who were abstinent
Treatment subsequent to inclusion in cohort	Fully described, treatment standardised or randomised	Recorded pharmacological treatment received or no active treatment to prevent weight gain

Table 2| Study description and quality variables

Trial	Aim of treatment	Weight change follow-up points	Region	Abstinence	Biochemical validation	Weight measurement	Treatment*	Patients (no) at baseline	Women at baseline (%)	Mean age at baseline (years)	Mean smoking intake at baseline (cigarettes/day)
Abelin et al 1989[40]	SC	Month 3	Europe	PA	Yes	NR	NRT	99	42	41 (10)	28 (10)
							Control	100	72	43 (11)	27 (11)
Aubin et al 2008[74]	SC	Month 3	Europe	PA	Yes	Clinic weighed	Varenicline	376	52	43 (11)	23
							NRT	370	50	43 (12)	22
Blondal et al 1999[75]	SC	Months 6, 12	Europe	CA	Yes	NR	NRT	240	71	42	29 (1)
Bohadana et al 2000[76]	SC	Months 6, 12	Europe	PA	Yes	NR	NRT	400	51	37 (9)	25 (10)
Cooper et al 2005[23]	SC and PCWGP	Months 2, 6, 12	USA	PP	Yes	Clinic weighed	NRT	148	100	38 (11)	23 (8)
							Control	148	100	39 (10)	23 (8)
Dale et al 1995[77]	SC	Months 2, 12	USA	CA	Yes	Clinic weighed	NRT	52	56	48 (12)†	26 (11)†
Ehrsam et al 1991[46]	SC	Month 2	Europe	NR	NR	Clinic weighed	NRT	56	NR	NR	22 (7)
							Control	56	NR	NR	24 (7)
Fiore et al 1994a[41]	SC	Month 2	USA	PP	Yes	NR	NRT	44	57	43 (10)	28 (8)
							Control	43	56	43 (9)	30 (10)
Fiore et al 1994b[41]	SC	Month 2	USA	PP	Yes	NR	NRT	57	68	43 (9)	30 (10)
							Control	55	67	44 (11)	31 (10)
Garvey et al 2000[39]	SC	Month 1	USA	PA	Yes	Clinic weighed	NRT	405	49	41 (12)	24 (11)
							Control	203	51	40 (12)	23 (11)
Gonzales et al 2006[78]	SC	Month 3	USA	PA	Yes	Clinic weighed	Varenicline	352	40	43 (12)	21 (10)
							Bupropion	329	42	42 (12)	21 (9)
							Control	344	45	43 (12)	22 (10)
Gourlay et al 1995[79]	SC	Month 3	Australia	CA	Yes	NR	NRT	315	58	41 (11)	28 (10)
							Control	314	57	42 (10)	27 (9)
Gross et al 1995[80]	SC	Month 3	USA	CA	Yes	Clinic weighed	NRT	132	51	42 (10)	33 (11)
							Control	46			
Hall et al 1992[24]	SC and PCWGP	Months 2, 12	USA	PP	Yes	Clinic weighed	Control	54	27	39 (9)	32 (12)
Hjalmarson et al 1984[81]	SC	Month 6	Europe	CA	Yes	NR	NRT	106	46	43 (11)	24 (10)
							Control	100	56	41 (14)	24 (10)
Hjalmarson et al 1994[82]	SC	Month 12	Europe	CA	Yes	Clinic weighed	NRT	125	42	45 (12)	21 (6)
							Control	123	57	45 (12)	22 (8)
Hjalmarson et al 1997[83]	SC	Months 1, 2, 3, 6, 12	Europe	CA	Yes	NR	NRT	123	38	48 (11)	22 (8)
							Control	124	64	47 (10)	21 (8)
Hurt et al 1997[84]	SC	Months 2, 6, 12	USA	CA	Yes	NR	Bupropion	156	51	45 (12)	27 (11)
							Control	153	55	43 (11)	27 (9)
Jorenby et al 2006[85]	SC	Month 3	USA	CA	Yes	NR	Varenicline	344	45	45 (11)	23 (10)
							Bupropion	342	40	43 (12)	22 (9)
							Control	341	41	42 (12)	22 (9)
Klesges et al 1990[86]	SC and PCWGP	Month 1	USA	CA	Yes	NR	Control	20	100	28 (8)†	22 (10)†
Klesges et al 1995[34]	SC and PCWGP	Month 1	USA	CA	Yes	Clinic weighed	Control	55	NR	NR	NR
Lerman et al 2004[37]	SC	Months 2, 6	USA	CA	No	Self reported	NRT	299	54	46 (11)	21 (11)
Levine et al 2010[25]	SC and PCWGP	Months 3, 6, 12	USA	PA	Yes	Clinic weighed	Bupropion	89	100	41 (11)	20 (7)
							Control	67	100	42 (10)	22 (9)

Table 2 (continued)

Trial	Aim of treatment	Weight change follow-up points	Region	Abstinence	Biochemical validation	Weight measurement	Treatment*	Patients (no) at baseline	Women at baseline (%)	Mean age at baseline (years)	Mean smoking intake at baseline (cigarettes/day)
Marcus et al 1999[35]	SC	Months 3, 12	USA	CA	Yes	Clinic weighed	Control	147	100	40 (9)	22 (9)
Nakamura et al 2007[31]	SC	Month 3	Asia	PA	Yes	Clinic weighed	Varenicline	130	21	40 (12)	24 (10)
							Control	129	24	40 (12)	23 (9)
Niaura et al 2002[87]	SC	Month 2	USA	CA	Yes	Clinic weighed	Control	333	61	41 (10)	27 (11)
Niaura et al 2008[88]	SC	Month 3	USA	PA	Yes	Clinic weighed	Varenicline	157	50	42 (11)	22
							Control	155	47	42 (12)	22
Nides et al 2006[89]	SC	Month 2	USA	PA	Yes	Clinic weighed	Varenicline	127	50	42 (11)	19 (7)
							Bupropion	128	55	41 (11)	20 (7)
							Control	123	51	42 (10)	22 (8)
Norregaard et al 1996[26]	SC and PCWGP	Months 2, 3, 6, 12	Europe	CA	Yes	Clinic weighed	Control	73	65	39	20
O'Malley et al 2006[27]	SC and PCWGP	Month 2	USA	CA	Yes	Clinic weighed	Control	93	46	46 (11)	27 (11)
Oncken et al 2006[90]	SC	Month 2	USA	PA	Yes	Clinic weighed	Varenicline	259	51	43 (10)	21 (9)
							Control	129	48	43 (9)	20 (7)
Pack et al 2008[42]	SC	Month 2, 6, 12	USA	PP	Yes	NR	NRT	408	56	43 (12)	23 (10)
Parsons et al 2009[21]	SC and PCWGP	Months 1, 6	Europe	PA	Yes	Clinic weighed	Control	35	71	49 (13)	22 (12)
Perkins et al 2001[28]	SC and PCWGP	Months 1, 6, 12	USA	CA	Yes	Clinic weighed	Control	75	100	46 (10)	26 (5)
Piper et al 2007[43]	SC	Month 2	USA	PP	Yes	Clinic weighed	Bupropion	224	60	42 (11)	23 (11)
							Control	156	60	42 (11)	22 (10)
Pirie et al 1992[29]	SC and PCWGP	Months 1, 6, 12	USA	CA	Yes	Clinic weighed	NRT	108	100	42 (9)	27 (12)
							Control	103	100	42 (9)	26 (12)
Puska et al 1995[91]	SC	Months 6, 12	Europe	PA	Yes	NR	NRT	300	43	40 (9)	21 (9)
Richmond et al 1994[92]	SC	Months 3, 6, 12	Australia	PA	Yes	NR	NRT	153	NR	NR	NR
							Control	152	NR	NR	NR
Rigotti et al 2006[44]	SC	Months 3, 12	USA	PP	Yes	NR	Bupropion	124	31	57 (10)	23 (14)
							Control	124	31	55 (10)	21 (11)
Rigotti et al 2010[93]	SC	Months 3, 12	Worldwide	CA	Yes	Clinic weighed	Varenicline	355	25	57 (9)	22
							Control	359	18	56 (8)	23
Sachs et al 1993[94]	SC	Month 6	USA	CA	Yes	NR	NRT	113	59	48 (11)	27 (9)
							Control	107	59	48 (11)	29 (11)
Saules et al 2004[95]	SC	Month 6	USA	CA	Yes	NR	NRT	48	52	41	NR
Shiffman et al 2002a[96]	SC	Months 3, 6, 12	USA Europe	CA	Yes	Clinic weighed	NRT	459	57	41 (12)	18 (8)
							Control	458	60	40 (12)	17 (9)
Shiffman et al 2002b[96]	SC	Months 3, 6, 12	USA-Europe	CA	Yes	Clinic weighed	NRT	450	57	44 (12)	26 (11)
							Control	451	53	45 (12)	27 (10)
Simon et al 2004[97]	SC	Month 12	USA	CA	Yes	Unclear	NRT	123	16	49 (11)	23 (11)
Simon et al 2009[98]	SC	Month 6, 12	USA	CA	Yes	NR	Bupropion	42	7	55 (8)	16 (11)
							Control	43	0	57 (7)	16 (9)
Spring et al 1995[36]	SC and PCWGP	Month 3	USA	PA	Yes	Clinic weighed	Control	48	100	41 (11)	27 (12)

Table 2 (continued)

Trial	Aim of treatment	Weight change follow-up points	Region	Abstinence	Biochemical validation	Weight measurement	Treatment*	Patients (no) at baseline	Women at baseline (%)	Mean age at baseline (years)	Mean smoking intake at baseline (cigarettes/day)
Spring et al 2004[30]	SC and PCWGP	Months 3, 6	USA	PA	Yes	Clinic weighed	Control	107	100	43 (11)	20 (9)
Stapleton et al 1995[99]	SC	Months 3, 12	Europe	CA	Yes	NR	NRT	800	58	40 (10)	24 (7)
							Control	400	55	42 (10)	24 (8)
Sutherland et al 1992[100]	SC	Month 12	Europe	PA	Yes	Clinic weighed	NRT	116	63	39 (9)	25 (10)
							Control	111	66	40 (10)	27 (10)
Tashkin et al 2011[101]	SC	Months 3, 12	USA-Europe	PA	Yes	NR	Varenicline	248	37	57 (9)	25 (11)
							Control	251	38	57 (9)	24
Toll et al 2010[45]	SC and PCWGP	Months 1, 6	USA	PP	Yes	Clinic weighed	NRT	85	72	46 (11)	22 (9)
Tonnesen et al 1991[102]	SC	Months 3, 12	Europe	PA	Yes	NR	NRT	145	69	45	21
							Control	144	70	45	22
Tonnesen et al 1993[103]	SC	Months 3, 12	Europe	PA	Yes	NR	NRT	145	63	39 (12)	20 (6)
							Control	141	60	39 (14)	20 (7)
Tonnesen et al 1999[104]	SC	Months 2, 6, 12	Europe	CA	Yes	NR	NRT	2861	51	41 (10)	27 (10)
							Control	714	48	41 (10)	27 (10)
Tonstad et al 2006[105]	SC	Month 6	USA-Canada-Europe	CA	Yes	Clinic weighed	Varenicline	1927	51	44 (11)	22 (8)
Transdermal Nicotine Study Group 1991[106]	SC	Month 2	USA	CA	Yes	NR	NRT	664	70	42 (10)	31 (10)
							Control	271	60	43 (10)	31 (11)
Tsai et al 2007[32]	SC	Month 3	Asia	PA	Yes	Clinic weighed	Varenicline	126	19	40 (9)	23
							Control	124	7	41 (11)	23
Uyar et al 2007[47]	SC	Month 6	Europe	CA	Yes	Self-reported	Bupropion	50	12	36 (11)	NR
							NRT	50	20	36 (13)	NR
							Control	31	30	36 (11)	NR
Wallstrom et al 2000[107]	SC	Month 12	Europe	CA	Yes	NR	NRT	123	63	45 (12)	18 (5)
							Control	124	59	45 (11)	21 (7)
Wang et al 2009[33]	SC	Months 3, 12	Asia	PA	Yes	Clinic weighed	Varenicline	165	4	39	20
							Control	168	3	39	21
Zellweger et al 2005[108]	SC	Months 2, 12	Europe	PA	Yes	NR	Bupropion	517	64	40 (9)	22 (8)
							Control	170	64	40 (9)	24 (9)

SC=smoking cessation; PCWGP=postcessation weight gain; NRT=nicotine replacement therapy; NR=not reported; PA=prolonged abstinence; CA=continuous abstinence; PP=point prevalence abstinence. For the Shiffman studies, smokers were stratified and received two different treatments on the basis of nicotine dependence level (separated in “a” and “b” groups). For the Fiore studies, “a” and “b” refer to two separate studies reported in the same article.

*Control=data taken from placebo arms of pharmacotherapy trials and control arms of behavioural interventions. Only included if participants did not receive any intervention that could have affected weight (for example, nicotinic replacement therapy, exercise, dietary advice).

†Whole study population analysed.

Table 3| Meta-analysis of combined data for weight change from baseline, by treated and untreated quitter groups

Time after target quit day	Mean (95% CI) change in weight (kg)*	Weighted mean standard deviation†	I^2 (%)	No of participants	No of studies
Untreated quitters (weight concerned and non-weight concerned)					
Month 1	1.12 (0.76 to 1.47)	1.41	57	135	6
Month 2	2.26 (1.98 to 2.54)	1.94	64	556	16
Month 3	2.85 (2.42 to 3.28)	2.79	84	776	25
Month 6	4.23 (3.69 to 4.77)	4.21	52	409	18
Month 12	4.67 (3.96 to 5.38)	4.72	69	514	25
Quitters treated with nicotine replacement therapy					
Month 1	0.96 (0.70 to 1.23)	1.65	51	257	4
Month 2	2.00 (1.72 to 2.27)	2.64	65	1174	10
Month 3	2.29 (1.68 to 2.89)	2.52	93	899	11
Month 6	3.65 (3.17 to 4.12)	4.04	76	1121	17
Month 12	4.86 (4.34 to 5.38)	4.53	71	1138	19
Quitters treated with bupropion (300 mg/day)					
Month 1	Not determined	Not determined	Not determined	Not determined	Not determined
Month 2	1.36 (1.16 to 1.56)	2.63	0	377	4
Month 3	2.31 (1.42 to 3.21)	2.87	77	244	4
Month 6	2.71 (0.84 to 4.59)	5.70	61	48	4
Month 12	4.08 (3.44 to 4.71)	4.86	0	183	5
Quitters treated with varenicline (2 mg/day)					
Month 1	Not determined	Not determined	Not determined	Not determined	Not determined
Month 2	2.19 (1.62 to 2.77)	3.51	0	127	2
Month 3	2.12 (1.74 to 2.50)	2.67	81	1052	9
Month 6	4.03 (3.66 to 4.40)	3.30	0	301	1
Month 12	4.17 (1.64 to 6.71)	5.31	91	174	3

*Calculated from random effects meta-analysis, which assumes that there are several different underlying true values for weight change, depending on population.
†Mean of the standard deviations for each study contributing data to time point mean, weighted by the number of participants contributing data to each mean. This value gives the standard deviation in weight gain for all participants within the study populations as a whole.

Table 4| **Subgroup analyses for untreated quitters, by time point**

	Mean (95% CI)	I^2 (%)	No of studies	P
1 months after cessation				
Weight concerned	0.81 (0.61 to 1.02)	0	2	0.04
Not selected for weight concern	1.46 (1.08 to 1.84)	0	4	
2 months after cessation				
Weight concerned	1.58 (1.21 to 1.96)	26	3	0.01
Not selected for weight concern	2.46 (2.25 to 2.69)	24	13	
3 months after cessation				
Weight concerned	3.24 (2.51 to 3.98)	54	5	0.38
Not selected for weight concern	2.77 (2.29 to 3.24)	83	20	
6 months after cessation				
Weight concerned	4.71 (3.47 to 5.95)	55	7	0.14
Not selected for weight concern	4.06 (3.49 to 4.65)	51	11	
12 months after cessation				
Weight concerned	4.22 (2.71 to 5.73)	50	6	0.96
Not selected for weight concern	4.79 (3.98 to 5.60)	73	19	

Figures

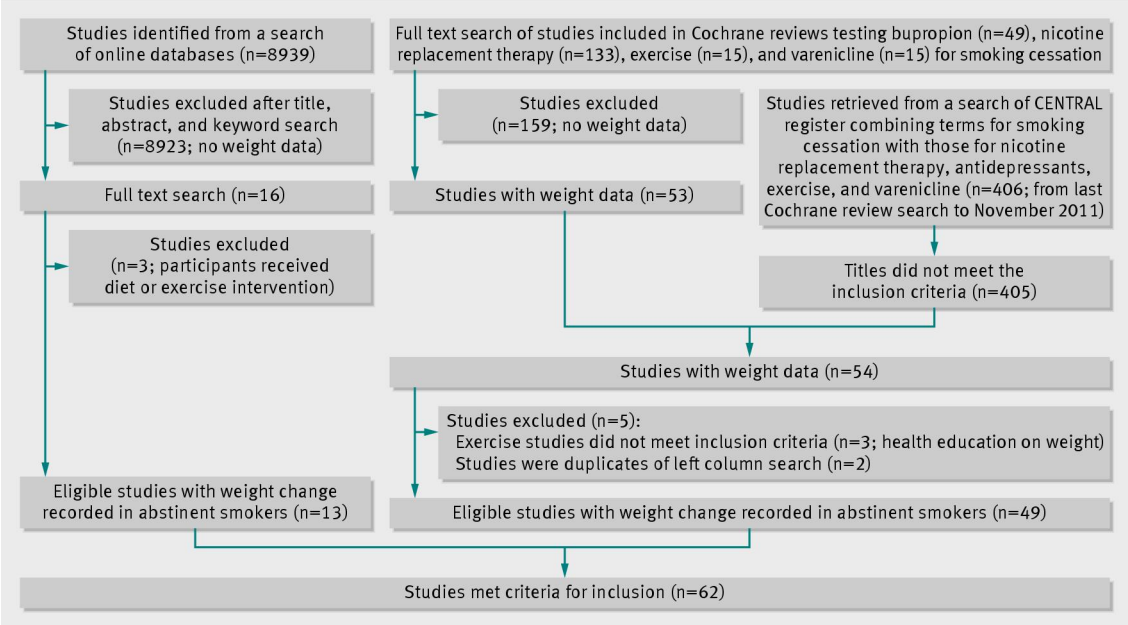

Fig 1 Study selection for inclusion in meta-analysis

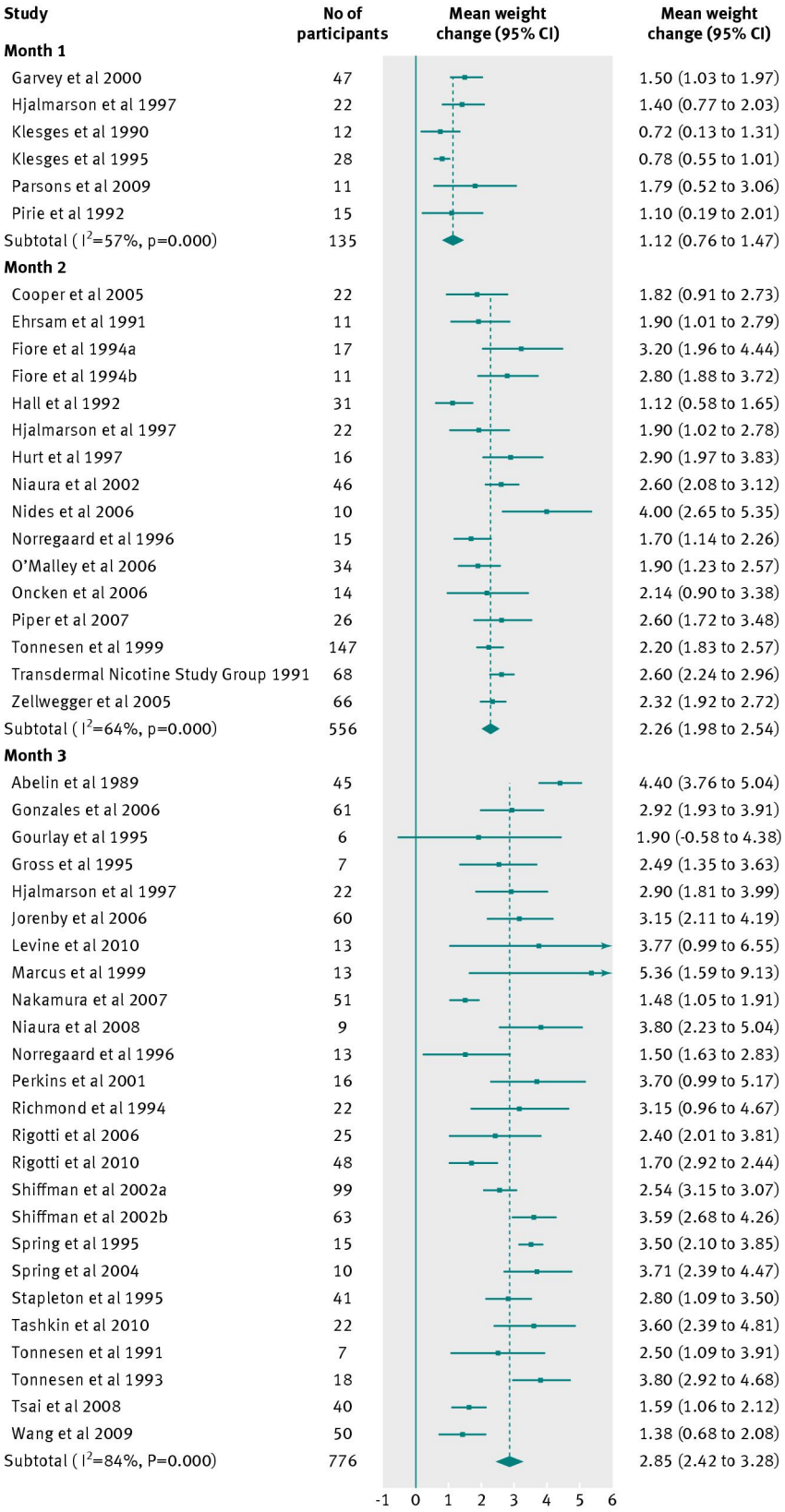

Fig 2 Meta-analyses of mean (95% CI) change in weight (kg) from baseline to one, two, and three month follow-up in abstinent untreated smokers. For the Shiffman studies, smokers were stratified and received two different treatments on the basis of nicotine dependence level (separated in "a" and "b" groups). For the Fiore studies, "a" and "b" refer to two separate studies reported in the same article

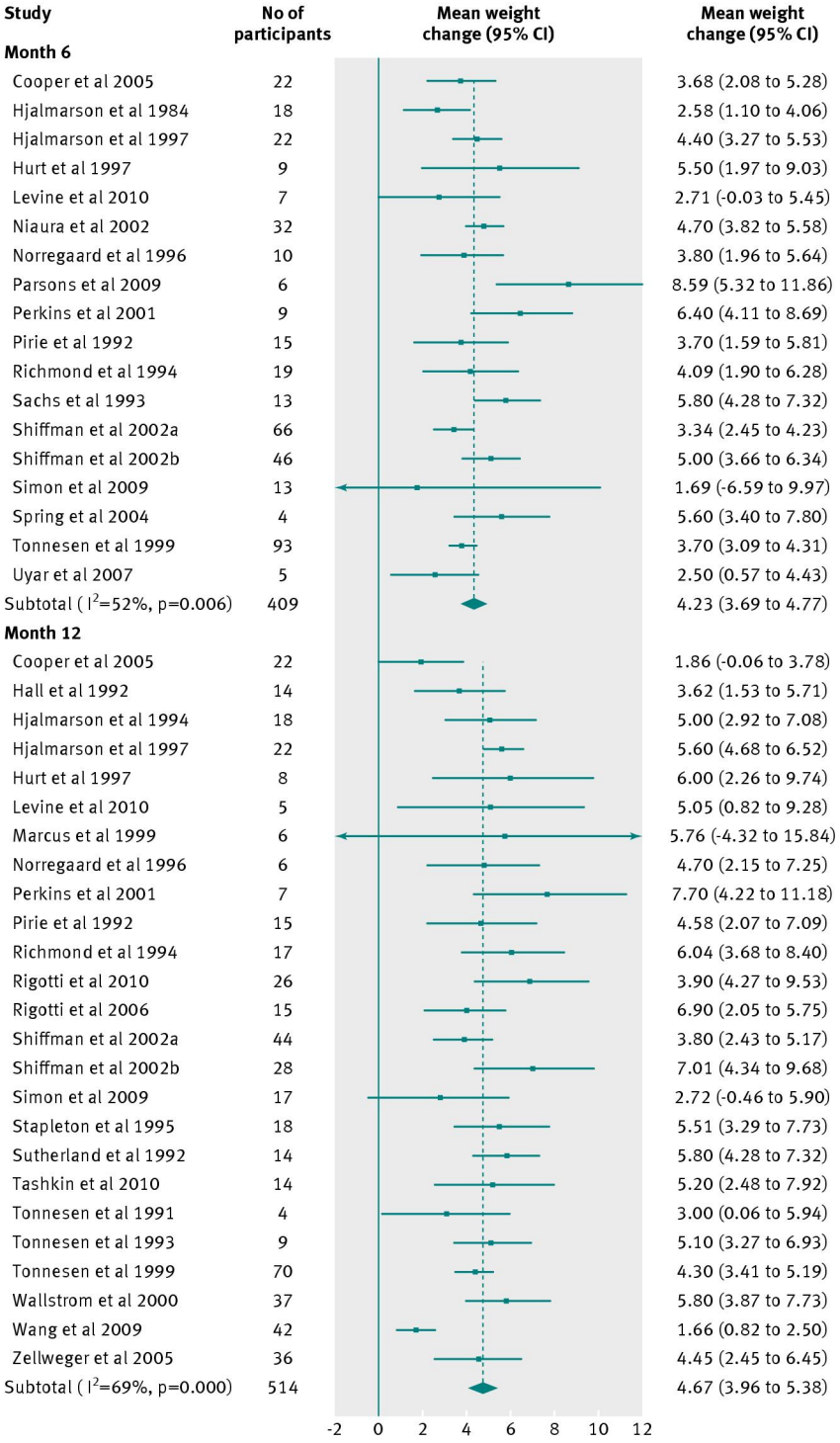

Fig 3 Meta-analyses of mean (95% CI) change in weight (kg) from baseline to six and 12 month follow-up in abstinent untreated smokers. For the Shiffman studies, smokers were stratified and received two different treatments on the basis of nicotine dependence level (separated in “a” and “b” groups)

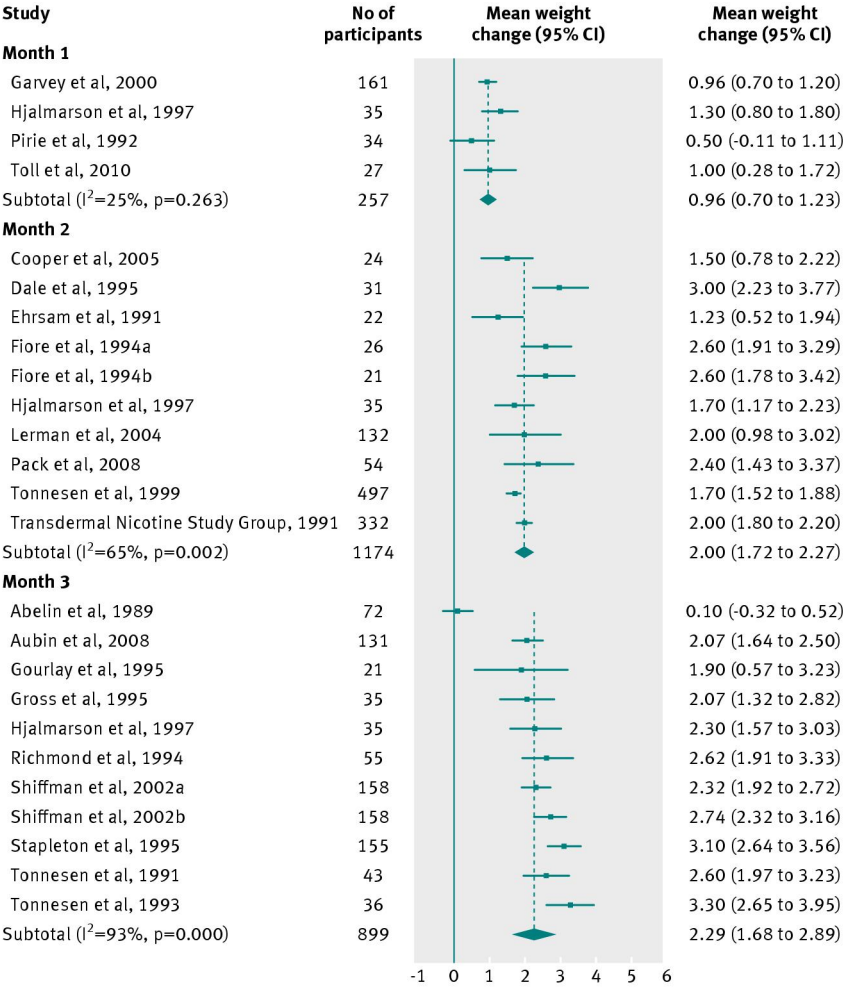

Fig 4 Meta-analyses of mean (95% CI) change in weight (kg) from baseline to one, two, and three month follow-up in abstinent smokers treated with nicotine replacement therapy (any dose, any regimen). For the Shiffman studies, smokers were stratified and received two different treatments on the basis of nicotine dependence level (separated in “a” and “b” groups). For the Fiore studies, “a” and “b” refer to two separate studies reported in the same article

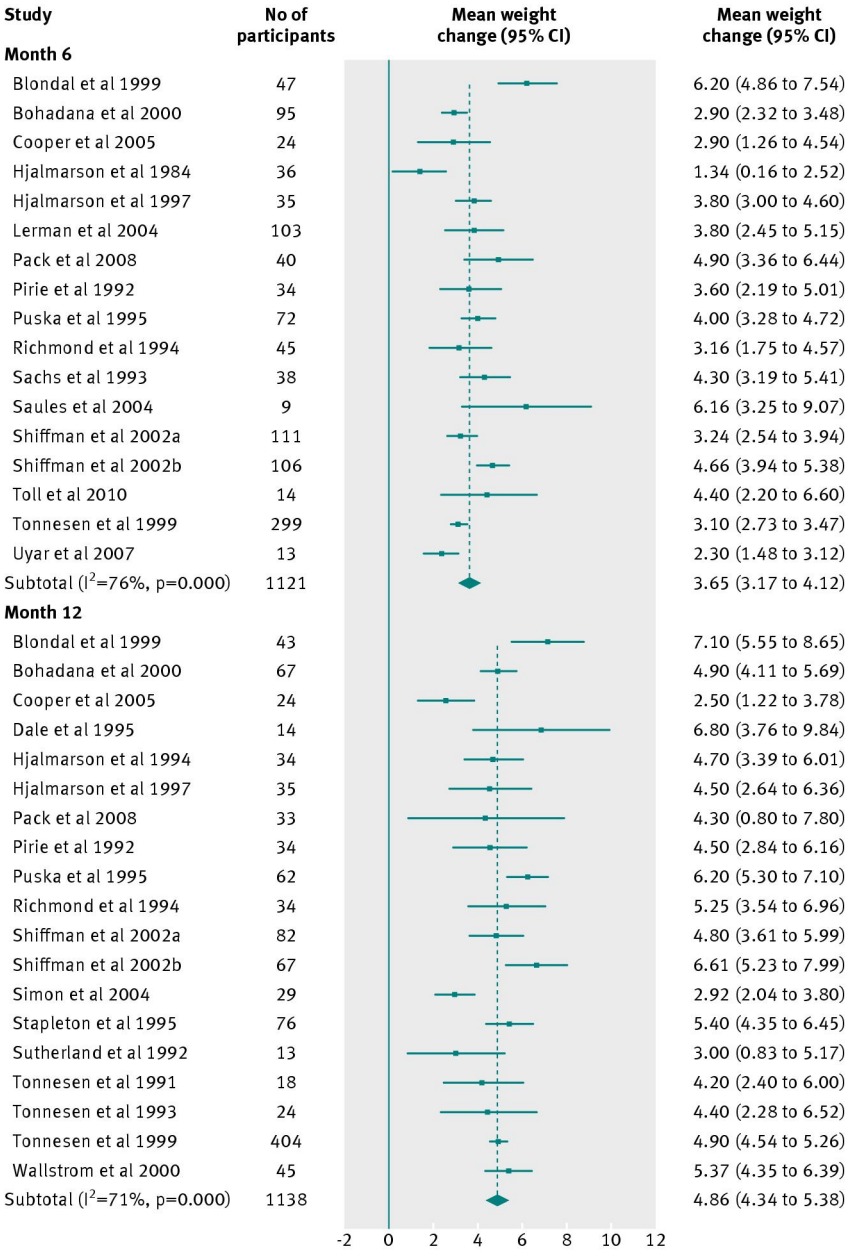

Fig 5 Meta-analyses of mean (95% CI) change n weight (kg) from baseline to six and 12 month follow-up in abstinent smokers treated with nicotine replacement therapy (any dose, any regimen). For the Shiffman studies, smokers were stratified and received two different treatments on the basis of nicotine dependence level (separated in “a” and “b” groups)

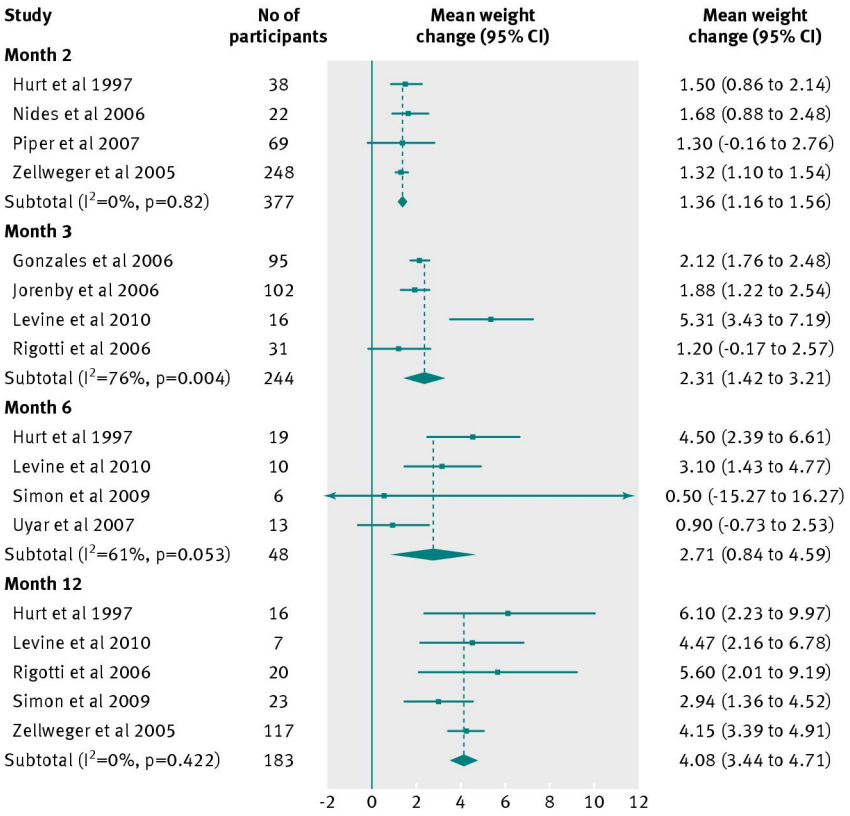

Fig 6 Meta-analyses of mean (95% CI) change in weight (kg) from baseline to two, three, six, and 12 month follow-up in abstinent smokers treated with bupropion (300 mg/day)

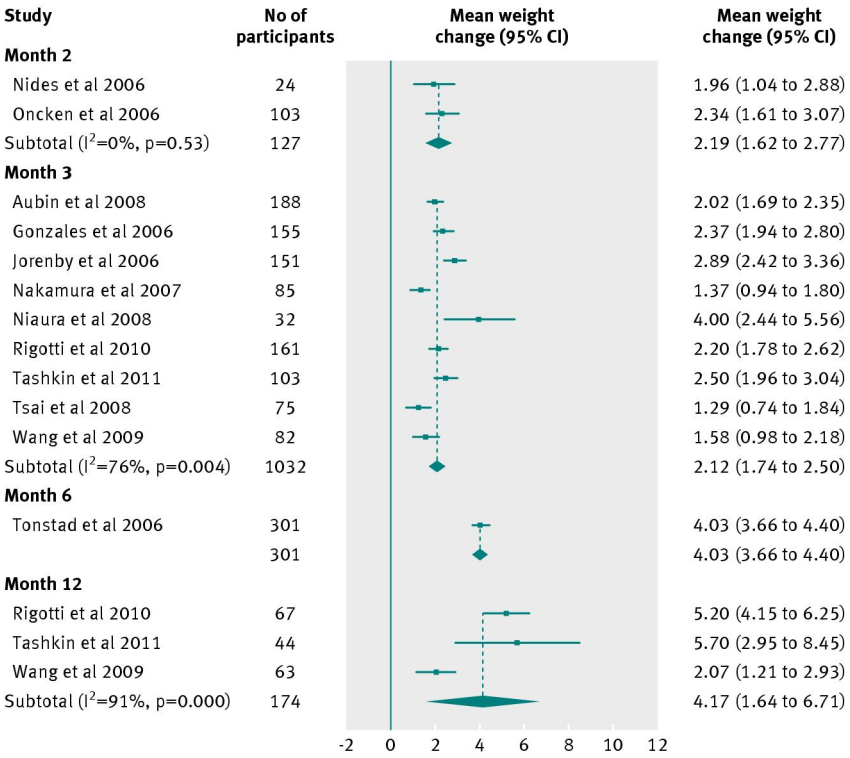

Fig 7 Meta-analyses of mean (95% CI) change in weight (kg) from baseline to two, three, and 12 month follow-up in abstinent smokers treated with varenicline (2 mg/day)

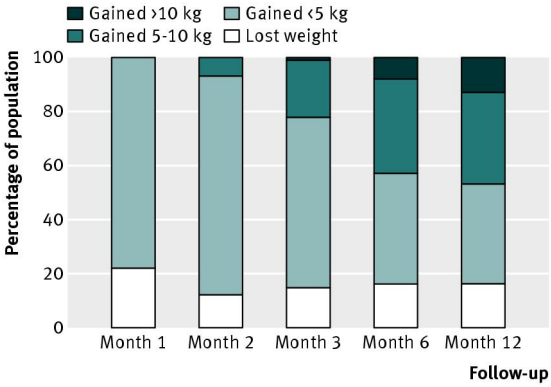

Fig 8 Percentage of untreated quitting population who would be expected to lose weight, gain <5 kg, gain 5-10 kg, or gain >10 kg over 12 months

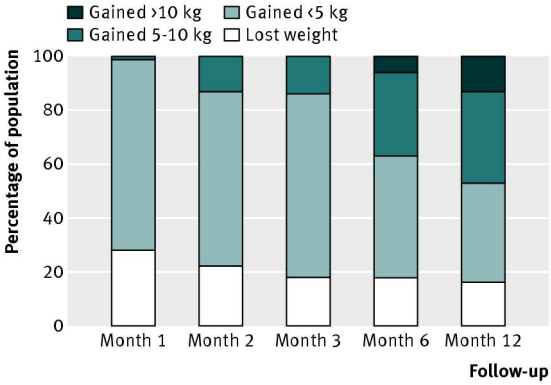

Fig 9 Percentage of quitting population treated with nicotine replacement therapy who would be expected to lose weight, gain <5 kg, gain 5-10 kg, or gain >10 kg over 12 months

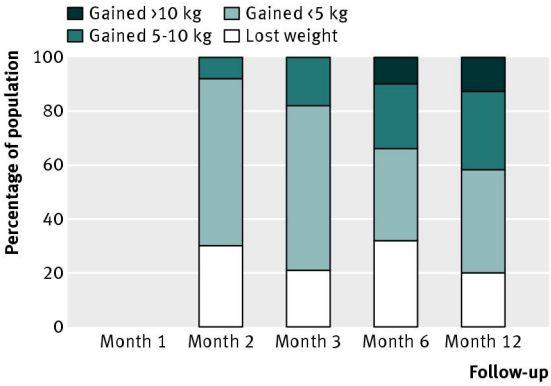

Fig 10 Percentage of quitting population treated with bupropion who would be expected to lose weight, gain <5 kg, gain 5-10 kg, or gain >10 kg over 12 months

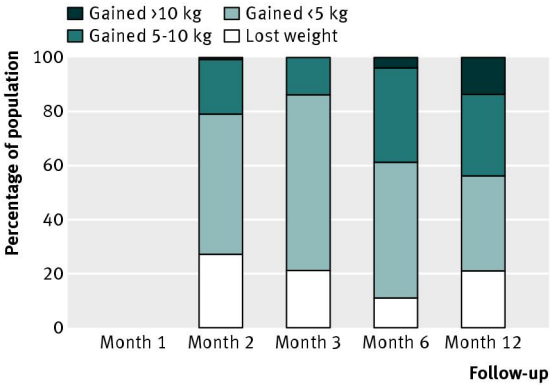

Fig 11 Percentage of quitting population treated with varenicline who would be expected to lose weight, gain <5 kg, gain 5-10 kg, or gain >10 kg over 12 months