

Interventions for smokeless tobacco use cessation (Review)

Ebbert J, Montori VM, Vickers-Douglas KS, Erwin PC, Dale LC, Stead LF



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TABLE OF CONTENTS

HEADER	1
ABSTRACT	1
PLAIN LANGUAGE SUMMARY	2
BACKGROUND	2
OBJECTIVES	3
METHODS	3
RESULTS	4
DISCUSSION	7
AUTHORS' CONCLUSIONS	8
ACKNOWLEDGEMENTS	8
REFERENCES	8
CHARACTERISTICS OF STUDIES	11
DATA AND ANALYSES	25
Analysis 1.1. Comparison 1 Pharmacotherapy: Bupropion versus placebo, Outcome 1 All tobacco abstinence at longest follow-up.	26
Analysis 2.1. Comparison 2 Pharmacotherapy: NRT versus placebo, Outcome 1 6 months or greater abstinence, strictest criteria.	27
Analysis 3.1. Comparison 3 Behavioral interventions, Outcome 1 Abstinence from all tobacco use (where reported) at 6 months or more.	28
Analysis 3.2. Comparison 3 Behavioral interventions, Outcome 2 Sensitivity analysis: Abstinence from smokeless tobacco use (where reported) at 6 months or more.	29
Analysis 3.3. Comparison 3 Behavioral interventions, Outcome 3 Subgroup analysis: Use of oral examination and feedback.	30
Analysis 3.4. Comparison 3 Behavioral interventions, Outcome 4 Subgroup analysis: Use of telephone support.	31
Analysis 3.5. Comparison 3 Behavioral interventions, Outcome 5 Subgroup analysis: Motivation.	32
Analysis 3.6. Comparison 3 Behavioral interventions, Outcome 6 Behavioural intervention +/- pharmacotherapy versus minimal contact. Long term cessation.	33
WHAT'S NEW	33
HISTORY	33
CONTRIBUTIONS OF AUTHORS	34
DECLARATIONS OF INTEREST	34
INDEX TERMS	34

[Intervention Review]

Interventions for smokeless tobacco use cessation

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ABSTRACT

Background

Use of smokeless tobacco (ST) can lead to nicotine addiction and long-term use can lead to health problems including periodontal disease and cancer.

Objectives

To assess the effects of behavioural and pharmacologic interventions for the treatment of ST use.

Search strategy

We searched the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, CINAHL, Web of Science, PsycINFO, Dissertation Abstracts Online, and Scopus. Date of last search: March, 2007.

Selection criteria

Randomized trials of behavioural or pharmacological interventions to help users of ST to quit with follow up of at least six months.

Data collection and analysis

Two authors independently extracted data.

Main results

Two trials of bupropion SR did not detect a benefit of treatment at six months or longer (Odds Ratio (OR) 0.86, 95% Confidence Interval (CI): 0.47 to 1.57). Four trials of nicotine patch did not detect a benefit (OR 1.16, 95% CI: 0.88 to 1.54), nor did two trials of nicotine gum (OR 0.98, 95% CI: 0.59 to 1.63). There was statistical heterogeneity among the results of 12 behavioural interventions included in the meta-analyses. Six trials showed significant benefits of intervention. In post-hoc subgroup analyses, behavioural interventions which include telephone counselling or an oral examination may increase abstinence rates more than interventions without these components.

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1

Authors' conclusions

Behavioural interventions should be used to help ST users to quit and telephone counselling or an oral examination may increase abstinence rates. Pharmacotherapies have not been shown to affect long-term abstinence.

PLAIN LANGUAGE SUMMARY

Are there ways to help people stop using smokeless tobacco

All of the included intervention studies have been conducted in the United States where ST includes ground tobacco (snuff) and chewing tobacco. Nicotine replacement therapy (patches or gum), and bupropion have not been shown to help people to stop using ST. Dentists and hygienists may help their patients to stop, especially when they show them the damage that ST causes in their mouths. Telephone counselling may assist ST users in quitting. More and larger studies are needed.

BACKGROUND

Smokeless tobacco (ST) is tobacco orally consumed and not burned. A variety of types of ST are consumed throughout the world and it is an important worldwide public health issue. In the United States, the principal types of ST are chewing tobacco (cut tobacco leaves) and snuff (moist ground tobacco). In Sweden, 'snus' (finely ground moist tobacco) is used. In India, ST contains tobacco leaf mixed with other ingredients, such as areca nut and lime (Critchley 2003). In Sudan, toombak is made from a fermented ground powdered tobacco mixed with sodium bicarbonate (Idris 1998).

In the United States in 2005, 7.7 million (3.2%) of Americans aged 12 or older were current (past month) ST users (US DHHS 2006). Although the rate of current cigarette smoking declined among U.S. young adults (aged 18 to 25 years) between 2002 and 2005, the rate of current ST use by young adults did not change significantly during that period. In India, it is estimated that 22% of males use ST solely and 8% use ST and smoked tobacco concomitantly (WHO 1997). Approximately 23% of Swedish men are reported to use snus (Foulds 2003). In Sudan, about 40% of males and 10% of females use toombak (Idris 1994).

Available literature suggests that adverse health consequences may vary by the type of ST use, which is strongly associated with geography (i.e., United States, Sweden, and India). According to the 1986 report of the U.S. Surgeon General, the use of ST products can lead to nicotine addiction (NIH 1986). ST consumed in the United States has been associated with periodontal disease (Ernster 1990; Fisher 2005), precancerous oral lesions (Mattson 1989), oral cancer (Stockwell 1986), and cancer of the kidney (

Goodman 1986; Muscat 1995), pancreas (Muscat 1997), and digestive system (Henley 2005). ST has been shown to act as a powerful autonomic and haemodynamic stimulus by increasing heart rate, blood pressure, and epinephrine levels (Wolk 2005), and has been associated with death from cardiovascular disease, cerebrovascular disease and cancer (Henley 2005). A recent systematic review concluded that betel quid and tobacco use in India are associated with substantial risks of oral cancer, but studies from the United States and Scandinavia do not show a statistically significant association between ST and oropharyngeal cancer (Critchley 2003). Studies have suggested that ST use during pregnancy is likely to be harmful to the foetus (England 2003; Gupta 2004; Gupta 2006).

Importantly, two of the world's largest cigarette manufacturers, Phillip Morris USA and R.J. Reynolds, have entered the ST market. Phillip Morris USA is test-marketing a ST product called 'Taboka' (PM USA 2006) and R.J. Reynolds has launched 'Camel Snus' (CTFK 2006). Both products have been designed to appeal to smokers with the presumed purpose of 'supporting' smoking quit attempts prompted by health concerns about smoking, clean indoor air policies and increased cigarette excise taxes (CTFK 2006). At the same time, ST is also increasingly being proposed as a harm reduction strategy for cigarette smokers (McNeill 2004; NIH 2006). Although the health risks of ST use are lower than those from smoked tobacco, concern exists that the promotion of ST use may lead to smokers using both products rather than quitting tobacco use altogether, and ex-smokers and never smokers initiating ST use. The impact of these factors on the prevalence of ST use remains unclear, but suggests an urgency for developing effective treatments for ST use.

Despite the widespread use of ST products and their potentially adverse health consequences, medical and oral health professionals have had a lack of evidence summaries or evidence-based guidelines to assist them in providing effective treatment for ST use. An expert review concluded that the evidence base for treating ST users was limited by small sample size and lack of control groups (Hatsukami 1997). Smokeless tobacco cessation guidelines for health professionals in England were published after the first version of the present review was published in 2004 (West 2004).

OBJECTIVES

To assess the effects of behavioural and pharmacotherapeutic interventions to treat ST use.

METHODS

Criteria for considering studies for this review

Types of studies

Randomized or pseudo-randomized controlled trials allocating smokeless tobacco users to an intervention or control, or to different interventions. We also included trials in which dentists or other healthcare providers were randomized to provide intervention or control, and trials in which the unit of randomization was the school, workplace or institution.

Types of participants

Users of any tobacco product that is placed in the mouth and not burned, including moist snuff, chewing tobacco and betel quid.

Types of interventions

Interventions could be pharmacological (including for example nicotine replacement therapy (NRT) and bupropion) or behavioural, and could be directed at individual ST users or at groups of users (for example, ST users visiting the dentist, attending school or working). The control condition could be usual care, a placebo, or any less intensive intervention.

Types of outcome measures

The preferred outcome for the meta-analysis was tobacco abstinence six months or more after the start of the intervention. If total tobacco abstinence was not reported, abstinence from ST alone was used. A secondary outcome was abstinence from all tobacco use. Trials with shorter follow up or without quit rates were

excluded. Biochemical validation of self-reported abstinence was not required, but validated rates were used where reported.

Search methods for identification of studies

We searched the following electronic retrieval systems and databases: the Cochrane Tobacco Addiction Group specialised register, the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, CINAHL, PsycINFO, Web of Science, Dissertation Abstracts Online, and Scopus in March 2007. Five further sources were also searched for a previous review (Ebbert 2003): Healthstar, ERIC, National Technical Information Service database, and Current Contents.

The following terms in the search strategy described the use of smokeless tobacco: chewing tobacco, oral tobacco, spit tobacco, snuff, smokeless tobacco, quid, chew and plug. The following terms described the interventions: behaviour modification; conditioning therapy; therapy, behaviour; therapy, conditioning; group therapy; cognitive therapy; counselling, behavioural intervention; pharmacotherapy; therapy and drug. The strategy also included the following Medical Subject Headings (MeSH): tobacco, smokeless; behaviour therapy; counselling; drug therapy. There were no language restrictions.

We scanned the reference lists of retrieved studies including review articles, conference proceedings and personal reference files. We asked content experts through electronic mail and telephone contact to identify unpublished randomized controlled trials (RCTs). We corresponded with experts in tobacco and ST use research.

Data collection and analysis

One author examined each title generated from the search and identified potentially eligible articles for which we obtained the abstracts. These were considered by two authors. For abstracts consistent with study eligibility, we obtained the full article text. Any difference of opinion about study inclusion would have been resolved by consensus.

We assessed study quality on one major criterion: appropriate separation between investigators deciding on participant inclusion and the process of random allocation to treatment or control (allocation concealment). Studies reporting an acceptable method of allocation concealment, for example central enrolment and allocation, or consecutively numbered sealed opaque envelopes, were rated A (adequate). Studies which did not give sufficient detail to assess quality were rated B (unclear). Studies reporting a method which did not allow allocation concealment (for example, allocation on the basis of patient record number), or where the procedure was not described, were rated C (inadequate). We conducted a sensitivity analysis of the effect of including trials classified as C in a meta-analysis. Other possible indicators of quality include:

blinding status of participants, investigators and outcome assessors; group similarity at baseline; equal treatment of groups during study conduct; completeness of follow up; analysis and conduct by the intention-to-treat principle; and use of a placebo or active intervention in the control group (Guyatt 1993). We did not formally assess the impact of differences in these criteria on the results. In the table 'Characteristics of Included Studies' we noted the use of biochemical validation, and reported differences in baseline characteristics, any co-interventions and the control intervention. If we were not able to extract data allowing an intention-to-treat analysis, this was recorded.

Two authors independently extracted data about participants, interventions, outcomes, and methodological quality. Any discrepancies in extracted data were resolved by consensus.

We extracted data on the numbers of users quit at the longest follow up, using the strictest definition of abstinence reported. We selected continuous or prolonged abstinence in preference to point prevalence where both were reported. If biochemical validation was used we selected validated rates. Participants who were randomized but dropped out or were lost to follow up were assumed to be continuing users.

We used odds ratios (ORs) to represent the point estimate of the magnitude of association between intervention exposure and treatment outcomes, and 95% confidence intervals (CIs) to represent the precision around this point estimate. An OR greater than one indicates that the odds of quitting were higher in the intervention group than in the control group.

We pooled results of studies when it was clinically and statistically appropriate to combine them. We did not combine pharmacotherapy and behavioural interventions. We conducted meta-analyses using a fixed-effect model, unless there was evidence of between-study heterogeneity (Fleiss 1993). Heterogeneity was quantified using the I^2 statistic (Higgins 2003). This describes the percentage of the variability in effect estimates that is due to heterogeneity rather than sampling error (chance). Values over 50% suggest moderate heterogeneity. Where heterogeneity was higher than this we explored possible explanations, avoided estimating a pooled effect or considered the results of a random effects model.

For the pharmacological interventions, we hypothesized that nicotine replacement therapy (NRT) would lead to different outcomes compared with non-NRT pharmacotherapies (i.e., bupropion). Underlying this hypothesis is the difference in the mechanisms of action between the two forms of treatment (Fiore 2000). Thus, we pooled the pharmacological trials assessing the treatment effect of NRT separately from those assessing the treatment effect of non-nicotine therapy.

We hypothesized that the intensity of the behavioural interventions in terms of frequency and/or time of contacts with a health professional or study investigator would lead to different outcomes. We anticipated that longer and more frequent contacts would increase abstinence rates compared to shorter and less frequent contacts. We also hypothesized that the behavioural inter-

ventions involving recruitment of individual ST users would be associated with higher abstinence rates for intervention compared to control than those recruiting ST users at the organizational level. This was based upon the presumption that ST users receiving interventions at the organizational level (e.g., dental practice or athletic teams) may receive interventions although they are not actively seeking treatment for ST use, which will potentially lead to lower abstinence rates in this group. Notably, two trials randomized individuals not actively seeking treatment (Cigrang 2002; Stevens 1995).

RESULTS

Description of studies

See: [Characteristics of included studies](#); [Characteristics of excluded studies](#).

We identified 20 trials that met the inclusion criteria (Boyle 1992; Boyle 2004; Cigrang 2002; Cummings 1995; Dale 2002; Dale 2007; Ebbert 2007; Gansky 2005; Hatsukami 1996; Hatsukami 2000; Howard-Pitney 1999; Severson 1998; Severson 2000; Severson 2006; Severson 2007a; Severson 2007b; Stevens 1995; Stotts 2003; Walsh 1999; Walsh 2003). Of the 20 trials, eight assessed the effect of pharmacological interventions for ST use (Boyle 1992; Dale 2002; Dale 2007; Ebbert 2007; Hatsukami 1996; Hatsukami 2000; Howard-Pitney 1999; Stotts 2003) and 14 studied the effect of behavioural interventions for ST use (Boyle 2004; Cigrang 2002; Cummings 1995; Gansky 2005; Hatsukami 1996; Severson 1998; Severson 2000; Severson 2006; Severson 2007a; Severson 2007b; Stevens 1995; Stotts 2003; Walsh 1999; Walsh 2003). These totals include one study that assessed both nicotine gum and a minimal contact or intensive behavioural intervention in a factorial design (Hatsukami 1996), and one that compared a minimal intervention to an intensive behavioural intervention with either active or placebo nicotine patches (Stotts 2003).

Pharmacological interventions

Eight randomized controlled trials (RCTs) randomized 1635 subjects to pharmacotherapy or placebo. The efficacy of bupropion SR (sustained-release) given for 12 weeks was assessed in a pilot study (Dale 2002) and a multicenter trial (Dale 2007). Four studies assessed the efficacy of nicotine patch therapy (Hatsukami 2000; Howard-Pitney 1999; Stotts 2003; Ebbert 2007), and two studies assessed the efficacy of nicotine gum for ST users (Boyle 1992; Hatsukami 1996).

Both the treatment and control groups received the same behavioural interventions. Brief individual counselling at clinic visits was provided in four (Hatsukami 2000; Dale 2002; Dale 2007; Ebbert 2007), pharmacist advice and telephone support in one (

Howard-Pitney 1999), a group programme in one (Boyle 1992), and a six-week group programme with additional telephone support in a trial in adolescents (Stotts 2003). One compared a group programme to a minimal contact condition in a factorial design (Hatsukami 1996). One tested mint snuff as an ST substitute in a factorial design (Hatsukami 2000); there was no evidence of a benefit, and these arms were collapsed in the analysis.

The bupropion SR studies used a dose of 150 mg by mouth once a day for three days and then increased the dose to 150 mg twice a day (Dale 2002; Dale 2007). One nicotine patch study used 15 mg patches for six weeks (Howard-Pitney 1999); the second used 21 mg patches with a tapering schedule for a total of 10 weeks (Hatsukami 2000), and a third, in adolescents, tailored patch dose to baseline cotinine, using either 21 mg or 14 mg, both tapered over a six-week period (Stotts 2003). One nicotine patch study randomized subjects to doses of 21, 42 and 63 mg per day compared to placebo, and the 21 mg and placebo arms were compared for analysis (Ebbert 2007). One nicotine gum trial instructed enrolled ST users to attempt a target daily dose of 12 pieces of 2 mg nicotine gum per day (Boyle 1992). The other nicotine gum study instructed ST users to use at least six pieces of 2 mg nicotine gum a day for one month and then gradually reduce use (Hatsukami 1996).

Behavioural interventions

Five RCTs randomized 2670 ST users at the organizational level. One study (Severson 1998) randomly allocated 75 dental practices to receive a workshop for their dental health professionals to develop skills in the identification and counselling of ST users or to provide usual care. One study (Cummings 1995) analyzed data from the Working Well Trial that randomized energy-related worksites to receive either employee-targeted intense interventions based upon the Social Learning Theory (Bandura 1986) and the Transtheoretical Model of Change (DiClemente 1998), or minimal interventions consisting of mailings and posters displayed in the workplace. Three of the organizational level trials were targeted at athletes. A trial in college athletes (Walsh 1999) randomized 16 campuses to receive either a behavioural intervention based upon the Health Belief Model (Rosenstock 1988) and the Social Learning Theory (Bandura 1986), or no intervention. A trial in high school athletes (Walsh 2003) randomized 44 schools either to an intervention, including oral screening, a peer-led discussion, small group cessation counselling and a phone call on quit date, or to a control condition. A trial in college baseball athletes randomized 52 colleges to an intervention based on the diffusion of innovation theory (Rogers 1983) and cognitive social learning theory which included a videoconference, an oral-cancer screening examination, a certified athletic trainer (ATC)-facilitated discussion, and a peer-led component (Gansky 2005). None of the studies randomized by organization selected ST users according to their motivation to quit.

Eight RCTs randomized 5677 ST users at the individual level. One study allocated ST users attending a routine dental visit to

a multicomponent intervention consisting of feedback on oral lesions and advice to quit from both hygienist and dentist, as well as self-help materials and a follow-up call from a counsellor. The control group received usual care which may have included advice to quit (Stevens 1995). Participants were not selected according to motivation to quit. Two studies assessed the impact of adding components to a minimal self-help intervention. One tested a hand-held device for programming gradual reduction, as an adjunct to self-help materials and support (Severson 2000). Due to problems with the prototype device, people whose machine failed twice or more were excluded from the reported analysis, and we have not included it in the meta-analysis. A second study by the same group compared telephone support with self-help written materials alone (Severson 2007a). One study assessed the efficacy of telephone-based counselling for ST users compared to self-help materials alone (Boyle 2004). A study in high school adolescents, also included in the pharmacotherapy section, randomized a behavioural intervention of six weekly group sessions with a health educator, plus stage-based follow-up telephone counselling (Stotts 2003). The control group had five to ten minutes of counselling and a single telephone call. A pilot study in personnel on active military service recruited self-identified ST users at a health screening, unselected for motivation to quit. Members of the intervention group were telephoned and asked if they wished to receive self-help materials and to have further support calls, using a motivational interviewing approach (Cigrang 2002). Based upon these promising preliminary results, a similar study was conducted with a larger sample of military recruits (Severson 2006). One study assessed the efficacy of a web-based intervention randomizing ST users to a basic or enhanced version (Severson 2007b).

Risk of bias in included studies

Pharmacological interventions

All eight randomized controlled trials (RCTs) assessing pharmacological interventions were placebo-controlled. Three studies assessed the efficacy of the blinding procedure by having participants guess their treatment assignment, suggesting that blinding was adequate in one (Dale 2007), and inadequate in another (Ebbert 2007), while the third did not report the results (Hatsukami 2000). Four studies followed patients for six months (Boyle 1992; Howard-Pitney 1999; Dale 2002; Ebbert 2007) and four for 12 months (Hatsukami 1996; Hatsukami 2000; Stotts 2003; Dale 2007). Five studies assessed continuous abstinence (Hatsukami 1996; Hatsukami 2000; Dale 2002; Dale 2007; Ebbert 2007) but one of them (Hatsukami 1996) did not tabulate that outcome, so point prevalence is used in the meta-analysis. The remaining studies only reported point prevalence quit rates at longest follow up (Boyle 1992; Howard-Pitney 1999; Stotts 2003). All eight studies used biochemical confirmation of tobacco abstinence using tobacco alkaloid measurements (cotinine, anabasine or anatabine). For studies determining abstinence from all tobacco products,

carbon monoxide measurements were used to determine abstinence from smoked tobacco. Three studies reported abstinence from smokeless tobacco only (Hatsukami 1996; Hatsukami 2000; Howard-Pitney 1999). Since validation was also required, other forms of regular tobacco use would have been detected, but infrequent smokers might have been included as quitters.

Behavioural interventions

Across the behavioural studies, no co-interventions were apparent except for one RCT in which the intervention group was offered nicotine gum, although less than 10% of participants reportedly used it (Walsh 1999). Two studies mentioned allocation concealment in the randomization procedure (Cummings 1995; Gansky 2005). One study did not use an appropriate method of allocation concealment (Stevens 1995). Eligibility was assessed by a receptionist on the basis of a questionnaire given to all clinic attendees, with allocation on the basis of clinic record number. This method has the potential for selection bias, although allocation was not conducted by the person providing the intervention. We tested the sensitivity of the results to the inclusion of this study.

All behavioural intervention studies assessed point prevalence abstinence. Six used point prevalence abstinence at final follow up (Cummings 1995; Severson 2000; Severson 2006; Severson 2007a; Stotts 2003; Walsh 1999), and four required self-reported point prevalence abstinence at both an interim and final follow up (Cigrang 2002; Severson 1998; Stevens 1995; Walsh 2003). Three reported both point prevalence and repeated point prevalence (Severson 2007a; Severson 2007b; Boyle 2004) and the repeated point prevalence was used for the meta-analysis. Four had final follow up at six months (Cigrang 2002; Severson 2000; Boyle 2004; Severson 2007b), six at 12 months (Gansky 2005; Severson 1998; Stevens 1995; Stotts 2003; Walsh 1999; Walsh 2003), and one at two years (Cummings 1995). We used 12 month outcomes for one study that also had 18 month follow up, because loss to follow up had increased at the later time point (Severson 2007a). Only one trial reported using biochemical validation of self-reported quitting (Stotts 2003). One attempted to obtain saliva samples, but due to low compliance based their results on self report only (Stevens 1995). One obtained samples but did not analyze them, as a method for increasing accuracy of self report (Walsh 1999). Six reported smokeless tobacco cessation only (Cigrang 2002; Cummings 1995; Gansky 2005; Severson 2000; Severson 2006; Walsh 2003), three reported all tobacco use cessation (Boyle 2004; Severson 1998; Severson 2007a) and three reported both smokeless and all tobacco use cessation (Severson 2007b; Stevens 1995; Stotts 2003). The results of the meta-analysis are not affected by choice of outcome in these trials, although quit rates were lower for all tobacco use than for ST alone.

Randomization at the organizational level and analysis of outcomes at the individual level may lead to errors in estimated confidence intervals (Altman 1997). All the studies using cluster randomization used appropriate methods of analysis and reporting, using cluster level averages (Cummings 1995; Walsh 1999), odds

ratios adjusted for clustered responses (Gansky 2005; Walsh 2003), or reported low levels of intraclass correlation and non-significant practice effects (Stevens 1995).

Effects of interventions

Pharmacological interventions

Bupropion

The two bupropion studies with six months or longer follow up observed no effect on continuous all-tobacco abstinence, but with wide confidence intervals (CIs) (Dale 2002; Dale 2007; Odds ratio (OR) 0.86, 95% CI: 0.47 to 1.57, $I^2 = 0\%$).

NRT

This estimate combines ST abstinence and tobacco abstinence, although all the studies included tobacco alkaloid data that would have considered recent tobacco users as treatment failures. For the study that randomized patients to three different doses of nicotine patches (Ebbert 2007), we used the comparison between the 21 mg patch and placebo. We did not find evidence of heterogeneity among randomized controlled trials (RCTs) testing nicotine patch therapy, among RCTs testing nicotine gum therapy, nor among all RCTs of nicotine replacement therapy (NRT). These trials, however, were small, and confidence intervals wide. At six months or longer, neither nicotine patch (four trials, 1032 participants, OR 1.16, 95% CI: 0.88 to 1.54, $I^2 = 29\%$) nor nicotine gum (two trials, 310 participants, OR 0.98, 95% CI: 0.59 to 1.63, $I^2 = 0\%$) was seen to increase abstinence rates. In the trial of nicotine patch for adolescent ST users (Stotts 2003) the quit rates were twice as high in the placebo group, although the difference did not reach statistical significance.

Behavioural interventions

There was evidence of heterogeneity among the 12 trials eligible for the meta-analysis ($I^2 = 71\%$). Excluding the trial that used a potentially biased method for treatment allocation (Stevens 1995) did not affect this. Six of the trials showed a significant effect of behavioural intervention (Boyle 2004; Severson 1998; Severson 1998; Severson 2006; Severson 2007b; Walsh 2003), four showed non-significant trends towards benefit (Cigrang 2002; Severson 2007a; Stevens 1995; Stotts 2003) and two showed no evidence of an effect (Cummings 1995; Gansky 2005).

The subgroup of seven studies which randomized individuals had no evidence of heterogeneity ($I^2 = 0\%$) and the pooled effect was significant (OR 1.76, 95% CI 1.49 to 2.08). Heterogeneity remained evident ($I^2 = 84\%$) among the five trials that randomized by organization (Cummings 1995; Gansky 2005; Severson 1998; Walsh 1999; Walsh 2003), because of the lack of benefit detected in Cummings 1995 and Gansky 2005.

A sensitivity analysis preferring ST abstinence over all tobacco abstinence where trials reported both outcomes did not alter the findings.

We further explored the heterogeneity by grouping the twelve trials according to whether or not the intervention included an oral

examination component with direct feedback to patients regarding ST-induced mucosal changes. In contrast to the previous version of this review, both subgroups remained strongly heterogeneous. Amongst the five trials including an oral examination $I^2 = 79\%$, with [Gansky 2005](#) once again the outlier. The pooled effect using a random-effects (RE) model was significant (RE OR 1.92, 95% CI, 1.14 to 3.23). When this study is excluded from the subgroup, almost no heterogeneity is observed, fixed-effect and random-effects models giving similar estimates (RE OR 2.38, 95% CI 1.75 to 3.23). Gansky and colleagues suggested that the lack of effect in their trial could have been due to a 'spill-over' effect due to contact between the athletic trainers in the different groups, but any conclusions about the effect of oral examinations have to be cautious. There was also substantial heterogeneity among the seven studies without an oral examination component ([Boyle 2004](#); [Cigrang 2002](#); [Cummings 1995](#); [Severson 2006](#); [Severson 2007a](#); [Severson 2007b](#); [Stotts 2003](#)), $I^2 = 61\%$. The pooled effect in this subgroup, using a random-effects model, was significant (RE OR 1.59, 95% CI 1.21 to 2.09) but was smaller than for the subgroup in which there was an oral examination.

In a further subgroup analysis we distinguished between eight studies in which telephone support formed part of the intervention ([Boyle 2004](#); [Cigrang 2002](#); [Severson 1998](#); [Severson 2006](#); [Severson 2007a](#); [Stevens 1995](#); [Walsh 1999](#); [Walsh 2003](#)) and three where it did not ([Cummings 1995](#); [Gansky 2005](#); [Severson 2007b](#)). A trial where brief phone support was included in the control condition but not the intervention ([Stotts 2003](#)) was kept separate. Heterogeneity within the telephone support subgroup was low and the odds ratio higher and significant (RE OR 2.09, 95% CI 1.68 to 2.61, $I^2 = 24\%$). Heterogeneity remained in the subgroup testing interventions without telephone support, and the effect was not significant when a random-effects model was used (RE OR 1.18, 95% CI: 0.81 to 1.73, $I^2 = 78\%$).

We also considered whether or not selection of participants interested in quitting influenced treatment effect. Neither [Cigrang 2002](#), [Severson 2006](#) nor any of the cluster randomized trials selected only motivated quitters. Heterogeneity persisted in this subgroup. In the subgroup of four trials recruiting only ST users interested in stopping ([Boyle 2004](#); [Severson 2007a](#); [Severson 2007b](#); [Stotts 2003](#)) there was no evidence of heterogeneity and a significant pooled effect (OR 1.47, 95% CI 1.10 to 1.95).

One further behavioural study was not included in the meta-analysis because two active interventions were compared, and because technical problems with the device for scheduling gradual cessation led to a high drop out rate in that condition, so that an intention-to-treat analysis was not used. No significant difference was detected between the conditions ([Severson 2000](#)). At six months, the self-reported ST abstinence rate was 27.6% (21/76) in the hand-held device group and 30.2% (29/96) in the manual and video group.

One trial ([Hatsukami 1996](#)) failed to detect a difference between

more intense and less intense behavioural interventions in a 2x2 study of nicotine gum and behavioural interventions (OR 1.48, 95% CI: 0.80 to 2.73).

No effort was made to perform a quantitative synthesis of the incidence of adverse events reported with the different interventions. One study reported a higher rate of skin reactions and nausea associated with the nicotine patch, but found no difference in the number of people who stopped treatment due to side effects ([Howard-Pitney 1999](#)). One study reported the loss of two subjects due to headache and gastro-intestinal distress associated with nicotine gum use ([Boyle 1992](#)). Sleep disturbance was more common among patients on active bupropion SR ([Dale 2007](#)).

DISCUSSION

This systematic review provides evidence from randomized controlled trials enrolling 9982 ST users testing pharmacological and behavioural interventions to treat smokeless tobacco (ST) use. Meta-analyses suggest that behavioural interventions can be effective for ST users, although interventions do not show consistent effects. Among the behavioural interventions, the use of telephone counselling or an oral examination may be associated with the greatest treatment effect.

Bupropion SR has not been shown to be effective for increasing tobacco abstinence among ST users beyond six months. Evidence of the efficacy of the nicotine patch or nicotine gum for increasing long-term abstinence rates is inconclusive. The findings for bupropion SR and nicotine replacement therapy (gum, patch) have wide confidence intervals and are consistent with either an increase or decrease in the abstinence rates.

We found evidence of heterogeneity among the behavioural interventions, with some trials showing a statistically and clinically significant effect, some with non-significant trends and two with very similar intervention and control quit rates and relatively narrow confidence intervals ([Cummings 1995](#); [Gansky 2005](#)). In seeking to explain the heterogeneity we considered subgroups based on trial design and intervention characteristics. These included whether or not the studies were individually randomized, or recruited only participants motivated to quit, or whether the intervention included an oral examination or telephone support. Categorization by use of telephone support had low levels of subgroup heterogeneity, but this was a post hoc analysis, and the two studies with similarly small effect sizes that did not use telephone support as part of the intervention had many other differences. One was a population-based intervention in worksites, based on self-help materials ([Cummings 1995](#)), and the other enrolled college athletes and included an oral examination and offer of counselling ([Gansky 2005](#)). In the earlier version of this review ([Ebbert 2004](#)) we suggested that interventions including oral examination and feedback were more effective. In this update such an effect was

only evident after excluding Gansky 2005 from the oral examination subgroup. The authors of that study proposed that the lack of a significant treatment effect might have been due to a 'spill-over' effect from the intervention group to the control, thus washing out any potential treatment effect. The authors support this hypothesis through previously unpublished findings, and the suggestion that Californian athletic trainers are a closely-knit group. One year earlier, a survey of athletic trainers found that 14% provided tobacco cessation counselling. During the study period, a similar survey observed that 30% reported providing tobacco cessation counselling. Because of unexplained heterogeneity, pooled estimates do not provide a reliable guide to treatment effects, but even with the use of random-effects models for pooling, effects remained statistically significant in all subgroups that had significant effects in fixed-effect analyses.

The inference of the effect size of behavioural interventions for increasing ST abstinence rates is weakened by the limited methodological quality of some of these trials, including loss to follow up and potential baseline differences between the groups. We cannot exclude the possibility that publication bias is also impacting on our results.

AUTHORS' CONCLUSIONS

Implications for practice

- 1) Behavioural interventions appear to be effective for increasing tobacco abstinence rates among smokeless tobacco (ST) users.
- 2) Behavioural interventions which include telephone support or an oral examination with feedback may be effective for increasing tobacco abstinence rates among ST users. These estimates combine

both population-based interventions and individuals self-selecting for treatment. These analyses, however, are based on post hoc subgroups and should be interpreted with caution.

- 3) Evidence for the effectiveness of bupropion SR and nicotine replacement therapy (NRT) for the treatment of ST use is inconclusive. The evidence for the use of these pharmacotherapies is insufficient to provide clear guidelines for practice. These interventions have not been shown to have the effects expected from them.

Implications for research

Further research is required in several areas:

- 1) Studies to deconstruct behavioural interventions to identify effective core components such as telephone counselling or oral examinations with feedback.
- 2) Comparisons of different NRT doses, forms, and durations of therapy.
- 4) Combination therapies using both non-nicotine pharmacotherapy and NRT.
- 5) The influence of different types of ST (snuff, chew, betel quid) on abstinence outcomes.
- 6) Effective treatments for adolescents who use ST.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Boyle 1992

Methods	Country: USA Recruitment: community volunteers Randomization: individual, computer-generated code
Participants	100 adult moist snuff/ chewing tobacco users (1 also smoker) Av. age 32 Av 11 dips/day (4-26)
Interventions	Pharmacotherapy: NRT 1. Nicotine gum 2 mg for 6w, target dose 12 pieces/day 2. Placebo gum All participants given S-H manual and attended 4 weekly group meetings covering education/ self-monitoring/ coping skills/ group social support, 20-60 mins, 4-10/group.
Outcomes	PP abstinence, all tobacco use, 6m Verification: tobacco alkaloids (salivary cotinine, anabasine and anatabine in urine < 2.0 ng/ml)
Notes	For success, required to have attended all meetings Groups not equal at baseline - active gum group had higher cotinine levels

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	Adequate

Boyle 2004

Methods	Country: USA Recruitment: advertisement in health plan newsletter and community media Randomization: individual, computer-generated sequence
Participants	221 male moist snuff users (92% used daily), not regular users of other types of tobacco, interested in quitting Av. age 36, av.uses/day 7.9
Interventions	Behavioural therapy 1. S-H materials 2. S-H material + proactive telephone counselling. Initial call 4 days after S-H material mailing. Subsequent calls were negotiated and placed an emphasis on support, problem-solving, and use of cognitive-behavioral strategies including monitoring tobacco behavior patterns, goal setting, finding alternative coping options, and planning for high-risk situations or cues associated with tobacco use.

Boyle 2004 (Continued)

Outcomes	PP abstinence, all tobacco use, 6m Verification: none	
Notes	New study for 2007 update	
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Allocation concealment?	Unclear	Unclear

Cigrang 2002

Methods	Country: USA Recruitment: active military at preventive visit Randomization: individual, method not stated	
Participants	60 adult male ST users, not selected for motivation to quit. (smoking status not specified)	
Interventions	Behavioural therapy 1. Invited to receive mailed manual and video during a telephone call using a motivational interviewing style. Two further 10 min support calls after receipt of materials and on quit date 2. Usual care control, given information on how to sign up for an 8w cessation class	
Outcomes	Prolonged abstinence at 6m (7 day PP at 3m and 6m) Verification: none	
Notes		
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Allocation concealment?	Unclear	B - Unclear

Cummings 1995

Methods	Country: USA Recruitment: companies as part of Working Well trial Randomization: by company, matched pairs randomly allocated	
Participants	733 ST users in 39 energy related worksites av. age 36, results for males only (99% of total) reported. 19% smokers.	
Interventions	Behavioural therapy 1. Stage-matched ST information, S-H manual and video, ST poster with self-test at worksite, community resources. Intervention over 2 yrs	

Cummings 1995 (Continued)

	2. Mailings of printed materials to worksite (10 over 2 yrs), ST poster at worksite	
Outcomes	PP abstinence, ST use, 2 yrs. Verification: none	
Notes	Results based on cohort completing 2 yr follow up.	
Risk of bias		
Item	Authors' judgement	Description
Allocation concealment?	Yes	Adequate

Dale 2002

Methods	Country: USA Recruitment: media Randomization: individual, method not described. Double blind	
Participants	68 ST users (smokers excluded) 67/68 male, av.age 37	
Interventions	Pharmacotherapy: bupropion 1. Bupropion 300 mg 12w 2. Placebo All received 10 min behavioral intervention at each study visit (10 during treatment phase)	
Outcomes	Continuous abstinence, all tobacco use, 24w. (PP also reported, also 12w) Verification: urine cotinine	
Notes	1 withdrawal in bupropion group due to generalized rash.	
Risk of bias		
Item	Authors' judgement	Description
Allocation concealment?	Yes	Adequate

Dale 2007

Methods	Country: USA Recruitment: media, community volunteers Randomization: Individual, computer-generated, blinded	
Participants	225 male snuff/chewing tobacco users (3 current smokers), av.age 38	

Dale 2007 (Continued)

Interventions	Pharmacotherapy: bupropion 1. Bupropion 300 mg (150 mg by mouth twice per day) for 12w 2. Placebo. All subjects received oral exam and 16 behavioral counseling sessions during treatment and follow-up period	
Outcomes	Continuous, all tobacco abstinence at 24w and 52w. (PP & prolonged also reported, also 24w) Verification: urine tobacco alkaloids	
Notes	New study for 2007 update More sleep disturbance noted with bupropion (31% vs. 13%; P = 0.002)	
Risk of bias		
Item	Authors' judgement	Description
Allocation concealment?	Yes	Adequate

Ebbert 2007

Methods	Country: USA Recruitment: media, community volunteers Randomization: Individual	
Participants	42 male snuff users using at least 3 cans/pouches ST/week (smokers excluded) av.age 34-38	
Interventions	Pharmacotherapy: nicotine patch. 1. 63 mg patch 2. 42 mg patch 3. 21 mg patch 4. Placebo All subjects received behavioural counselling during the treatment phase	
Outcomes	Continuous all tobacco abstinence at 6m (PP also reported). Verification: urine tobacco alkaloids	
Notes	New study for 2007 update 21 mg dose used in MA 42 mg 3/11 (27%), 63 mg 4/10 (40%)	
Risk of bias		
Item	Authors' judgement	Description
Allocation concealment?	Yes	Adequate

Gansky 2005

Methods	Country: USA Recruitment: Contacted athletic trainers (ATCs) at California colleges Randomization: Schools stratified by tertiles of baseline ST use then within strata colleges were randomized to intervention or control group, so allocation concealed until after baseline data collection	
Participants	College baseball athletes who used ST (285 intervention, 352 control 30-day users, includes 206 30-day smokers)	
Interventions	Based upon the innovation theory and social learning theory. 1. 3hr video conference for ATCs/ dentists/ hygienists, follow-up newsletter for ATCs 2. Dental component: dentists/hygienists provided oral cancer screening, advised ST users to stop, identified oral lesions, provided S-H guide, offered single 10-15 min individual counselling session focusing on ST addiction, set a quit date, developing a plan, training in action and thinking skills to get ready to quit and to prevent relapse. 3. ATC follow up and referral: follow up by ATC on quit date and 3 booster sessions 1w apart. 4. Peer-led component: 50-60 min education meeting with included 3 components: 2 videos and slides of facial disfigurement. Control: usual anti-tobacco education	
Outcomes	30-day PP ST abstinence at 12m Verification: None	
Notes	New study for 2007 update Intraclass correlation: 0.0197. 24% loss to follow-up not broken down by study arm.	
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Allocation concealment?	Unclear	Unclear

Hatsukami 1996

Methods	Country: USA Recruitment: media Randomization: individual, method not stated. code for gum allocation kept by a third party	
Participants	210 ST users, not regular smokers all male, av age 31	
Interventions	Pharmacotherapy: NRT crossed in factorial design with behaviour therapy variants 1. 2 mg nicotine gum for 8w. At least 6 pieces/day initially then decrease. Option to use for 3rd month 2. Placebo Group behaviour therapy: 8 x 45-60 min sessions over 10w. Minimal contact: 4 brief sessions with nurse, S-H booklet.	
Outcomes	PP abstinence, ST use, 12m. Verification: : salivary cotinine <=20ng/ml and CO < 8ppm at all follow ups	

Hatsukami 1996 (Continued)

Notes	Continuous abstinence rates not tabulated, shown in survival curves.	
Risk of bias		
Item	Authors' judgement	Description
Allocation concealment?	Yes	Adequate

Hatsukami 2000

Methods	Country: USA Recruitment: media Randomization: individual, method not stated	
Participants	402 ST users, not regular smokers 99% male, av age 31	
Interventions	Pharmacotherapy: NRT 1. 21 mg nicotine patch for 10w incl tapering period 2. Placebo A second component, mint snuff was also tested in a factorial design. All received 10 min individual counselling at 8 clinic visits. Some end of treatment quitters assigned to more intensive follow up, but this was not intended as a treatment component.	
Outcomes	Continuous abstinence, ST use, 62w. (Also PP). Verification: salivary cotinine <15ng/ml at all follow ups	
Notes	No evidence of any effect of mint snuff, and no interaction with NRT. Quit rates for any tobacco use were reported to be lower and not significantly different between conditions. Rates not given so ST quit rates used in MA	
Risk of bias		
Item	Authors' judgement	Description
Allocation concealment?	Unclear	Unclear

Howard-Pitney 1999

Methods	Country: USA Recruitment: media Randomization: individual, sequential distribution from computer-randomized blinded list	
Participants	410 ST users >=18. 5% also smoked 99% male, av age 36	

Howard-Pitney 1999 (Continued)

Interventions	Pharmacotherapy: NRT 1. 15 mg nicotine patch for 6 weeks 2. Placebo All received 2 sessions with pharmacist at baseline and at 4w, S-H materials and telephone support at 48 hours and 10 days post target quit date	
Outcomes	PP abstinence, ST use, 6m Verification: : salivary cotinine <20ng/ml at 6m	
Notes	8 active & 14 placebo patch discontinued due to serious side effects.	
Risk of bias		
Item	Authors' judgement	Description
Allocation concealment?	Yes	Adequate

Severson 1998

Methods	Country: USA Recruitment: ST users at dental hygiene visits Randomization: by dental practice, method not stated	
Participants	633 ST users in 75 dental practices, not selected for motivation, no demographic details	
Interventions	Behavioural therapy 1. Usual dental care and office intervention (oral examination, advice to quit, quit date setting), S-H materials (pamphlets and oral replacement, video), telephone support (1 call) 2. Usual dental care	
Outcomes	Multiple PP (3m & 12m), all tobacco Verification: : none	
Notes	There were differences in groups at baseline. Intraclass correlation was low.	
Risk of bias		
Item	Authors' judgement	Description
Allocation concealment?	Unclear	Unclear

Severson 2000

Methods	Country: USA Recruitment: media Randomization: individual, method not stated
Participants	198 ST users >=18, motivated to quit. 4% also smoked 98% male, av age 39
Interventions	Behavioural therapy 1. Computerized ST gradual reduction and telephone support (1-3 calls, 10-20 min, quit date setting) 2. S-H manual , S-H video and telephone support (1-3 calls, 10-20 min, quit date setting)
Outcomes	PP abstinence, ST and cigs, 6m. Verification: none
Notes	Not used in meta-analysis Excludes people quitting prior to intervention, and with >2 equipment failures with computer for gradual reduction.

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	Unclear

Severson 2006

Methods	Country: USA Recruitment: Participants identified through the annual dental visits to one of 24 military dental clinics
Participants	785 ST users
Interventions	Behavioural intervention 1. Telephone counselling by a trained cessation counsellor and offered assistance in quitting ST use + mailed videotape & S-H guide + 2 additional counselling calls coinciding with receipt of the mailed materials and ST quit date 2. Usual care cessation strategies offered at each military base
Outcomes	PP at 6m (ST use) Verification: none
Notes	New study for 2007 update, based on conference abstract

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	Unclear

Severson 2007a

Methods	Country: USA Recruitment: media Randomization: individual, method not stated	
Participants	1069 ST users >=15 yrs, willing to quit all tobacco use. 5.7% also smoked 97% male, av age 39 (range 17-82)	
Interventions	Behavioural therapy 1. Manual-only: S-H manual (60pp) 2. Assisted S-H: telephone support (2 calls 10-15 min with quit date setting and withdrawal management), S-H manual (60pp), S-H video (20 mins)	
Outcomes	PP abstinence (all tobacco) at 12m Verification: none	
Notes	First included as Severson 2000b with 12m data from an abstract	
<i>Risk of bias</i>		
Item	Authors' judgement	Description
Allocation concealment?	Unclear	Unclear

Severson 2007b

Methods	Country: USA Recruitment: Targeted mailings, press releases to print and broadcast media, web-links, paid advertising in newspapers and magazines Randomization: Individual	
Participants	2523 ST users who had used ST for at least 1yr and used at least one tin/week interested in quitting, at least 18 yrs of age, a resident of US or Canada, had an email address checked weekly, and will to provide contact information.	
Interventions	Web-based behavioural therapy 1. Basic website: static textual format including the 'Enough Snuff' pocket guide for quitting, a resource section, and links 2. Enhanced: personal quitting assistant (guided, interactive programme), printable resources, links to other websites, two web forums ('Talk with Others' and 'Ask an Expert'), a planning to quit module, and a staying quit module	
Outcomes	PP/Repeated PP (ST & all tobacco) via online surveys or phone for non-respondents at 3m, 6m Verification: none	
Notes	New study for 2007 update, based on conference abstract	
<i>Risk of bias</i>		
Item	Authors' judgement	Description

Severson 2007b (Continued)

Allocation concealment?	Yes	Adequate
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Stevens 1995

Methods	Country: USA, 11 dental clinics Recruitment: at dental hygiene visit, unselected for motivation to quit Randomization: pseudo-random assignment by clinic record number at 8 clinics. At 3 others, all users enrolled.
Participants	518 male ST users (30% also smoked) Intervention from hygienists and dentists with 2 hr training.
Interventions	Behavioural therapy 1. Oral examination with feedback, advice to quit from hygienist and dentist, S-H manual, quit kit, video, quit date, telephone call from counsellor, free helpline, 6 newsletters. 2. Usual care
Outcomes	Abstinence at 12m (2 PP, 3m and 12m), ST only and all tobacco Verification: salivary cotinine, but low compliance so only self-report data given in paper
Notes	Allocation not concealed, but not conducted by therapist. Potential for recruitment bias. Also 3 clinics assessed usual care for 3m then provided intervention. Pre-intervention results not included here

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	No	Inadequate

Stotts 2003

Methods	Country: USA, 41 high schools Recruitment: volunteers motivated to quit Randomization: computer-generated random code, Participants not blinded to usual care or pharmacotherapy group after allocation, but blinding maintained for active/placebo groups
Participants	303 male ST users aged 14-19. 185 returned consent forms and received interventions, intention to treat analysis used. Av age of consenting participants 17, 80-90% used snuff, 65.6%-81.0% used cigarettes (frequency not stated)
Interventions	Both pharmacotherapy and behavioural therapy All participants offered oral screening 1. Nicotine patch: patch dose tailored to baseline cotinine, >150ng/ml received 21 mg initially, otherwise 14 mg, then tapered, 6w treatment. 6w behavioural intervention, 50 min group sessions with a health educator. Quit date at 3-4w, 1w supply of patches at a time. Stage-based proactive counselling at 2w, 4w, 8w, 3m, 6m, 12m. Free helpline, newsletter.

Stotts 2003 (Continued)

	2. Placebo patch and same behavioural therapy (active & placebo groups attended same sessions; participants and educators blinded). 3. Minimal intervention control; 5-10 min counselling, 1 phone call 2w later.	
Outcomes	Abstinence at 12m Snuff/chew/any spit/cigarette and all tobacco reported. All tobacco used in analyses Verification: salivary cotinine	
Notes	1+2 vs 3 for behavioural section. No evidence of benefit of NRT so this is more conservative than 2 vs 3. Randomization preceded consent, and there was a higher dropout rate in the control group (who knew they would not get chance of NRT). Therefore the intention to treat analysis might underestimate quit rates in the control group, and not be conservative. Baseline tobacco use was not reported for those who did not enrol, but was lower in placebo group. Incentives offered for attendance and assessment.	
Risk of bias		
Item	Authors' judgement	Description
Allocation concealment?	Yes	Adequate

Walsh 1999

Methods	Country: USA Recruitment: rural colleges with baseball and football teams Randomization: by college, matched for baseline ST use and one of pair assigned to intervention. Method not stated	
Participants	360 college athletes on 16 campuses, <2% were current smokers	
Interventions	Behavioural therapy 1. Oral examination with feedback, photos of ST effects, advice to quit, S-H manual, optional brief counselling (15-20 min, quit date, triggers, withdrawal), optional nicotine gum, optional telephone counselling (2 calls, 5-10 min) 2. Oral examination only	
Outcomes	PP abstinence, ST use, 12m. Verification: salivary cotinine used as 'bogus pipeline' (i.e. samples not tested), not to correct self reports	
Notes	3/24 who used nicotine gum quit	
Risk of bias		
Item	Authors' judgement	Description
Allocation concealment?	No	Inadequate

Walsh 2003

Methods	Country: USA, 44 high schools Recruitment: Randomly selected rural high schools Randomization: by school, stratified on number and size of baseball teams and prevalence of ST use. Method not stated
Participants	Subgroup of 307 ST users among 1084 baseball athletes in 44 high schools (Study also included a prevention component, not assessed in this review)
Interventions	Behavioural therapy 1. Peer-led component: interactive, peer-led team directing education with a videotape and discussion (10-15 min), a slide presentation (20-30 min) and a small-group discussion on tobacco industry advertising (10 min). Dental component: an oral cancer screening exam performed by a dentist or a dental hygienist with advice to quit, a S-H guide, tobacco cessation counselling in small groups (15 min), and a telephone call on the quit date (5-10 min). Theoretical basis: cognitive social learning theory 2. No intervention
Outcomes	Abstinence at 1m and 12m. Verification: none.
Notes	Subgroup analysis of 1084 high school baseball players. Potential for random error based upon subgroup analysis.

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Unclear	Unclear

MA: meta-analysis

m: month(s)

min: minute(s)

PP: point prevalence

S-H: self-help

ST: smokeless tobacco/spit tobacco.

w: week.

Characteristics of excluded studies [ordered by study ID]

Chakravorty 1992	Follow up only 1m. School-based intervention comparing oral replacement (non-tobacco herbal snuff ('Mintsuff') or chewing gum for 1m) and lecture on ST health risks and benefits of quitting to a lecture-only condition.
Croucher 2003	Small feasibility study of interventions to reduce ST use. Moist snuff users (N=40 males) were randomly assigned to 4 mg nicotine gum, non-tobacco mint snuff, brand switching, or elimination of ST use in specific situations.

(Continued)

	Abstinence at 26w was a secondary outcome, not reported by treatment group.
Glover 1994	Follow up only 4-8w. Interventions differed only on amount of contact with supervisor. Primarily a process evaluation of use of materials.
Glover 2002	Follow up only 3m. Trial of bupropion SR in 70 male ST users
Greene 1994	Not randomized
Gupta 1986	Not randomized
Hatsukami 2003	Pilot study. Abstinence rates not reported by treatment group. Only 10 participants in each of 4 arms.
Klesges 2006	Subgroup receiving the smokeless tobacco cessation intervention not separated from overall group. Unable to determine the number in the control group and data unavailable.
McChargue 2002	Short-term study of withdrawal symptoms
Vigg 2003	Follow up only 8w
Williams 1995	Follow up only 3m. College-based trial of S-H quit manual with peer interaction. Compared 4 assessment sessions to 2 sessions.

m: month(s)

S-H: self-help

w: week(s)

DATA AND ANALYSES

Comparison 1. Pharmacotherapy: Bupropion versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 All tobacco abstinence at longest follow-up	2		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
1.1 6 months or greater continuous abstinence	2	293	Odds Ratio (M-H, Fixed, 95% CI)	0.86 [0.47, 1.57]

Comparison 2. Pharmacotherapy: NRT versus placebo

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 6 months or greater abstinence, strictest criteria	6	1341	Odds Ratio (M-H, Fixed, 95% CI)	1.12 [0.87, 1.43]
1.1 Nicotine Patch	4	1031	Odds Ratio (M-H, Fixed, 95% CI)	1.16 [0.88, 1.54]
1.2 Nicotine Gum	2	310	Odds Ratio (M-H, Fixed, 95% CI)	0.98 [0.59, 1.63]

Comparison 3. Behavioral interventions

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Abstinence from all tobacco use (where reported) at 6 months or more	12	8149	Odds Ratio (M-H, Fixed, 95% CI)	1.59 [1.40, 1.80]
1.1 Randomisation by organisation	5	2670	Odds Ratio (M-H, Fixed, 95% CI)	1.38 [1.15, 1.67]
1.2 Individual randomisation	7	5479	Odds Ratio (M-H, Fixed, 95% CI)	1.76 [1.49, 2.08]
2 Sensitivity analysis: Abstinence from smokeless tobacco use (where reported) at 6 months or more	12	8149	Odds Ratio (M-H, Fixed, 95% CI)	1.61 [1.43, 1.82]
2.1 All tobacco use	4	4446	Odds Ratio (M-H, Fixed, 95% CI)	1.72 [1.41, 2.09]
2.2 Smokeless tobacco use	8	3703	Odds Ratio (M-H, Fixed, 95% CI)	1.55 [1.33, 1.81]
3 Subgroup analysis: Use of oral examination and feedback	12		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
3.1 Intervention included oral examination and feedback	5	2455	Odds Ratio (M-H, Random, 95% CI)	1.92 [1.14, 3.23]
3.2 Oral examination not part of the intervention	7	5694	Odds Ratio (M-H, Random, 95% CI)	1.59 [1.21, 2.09]

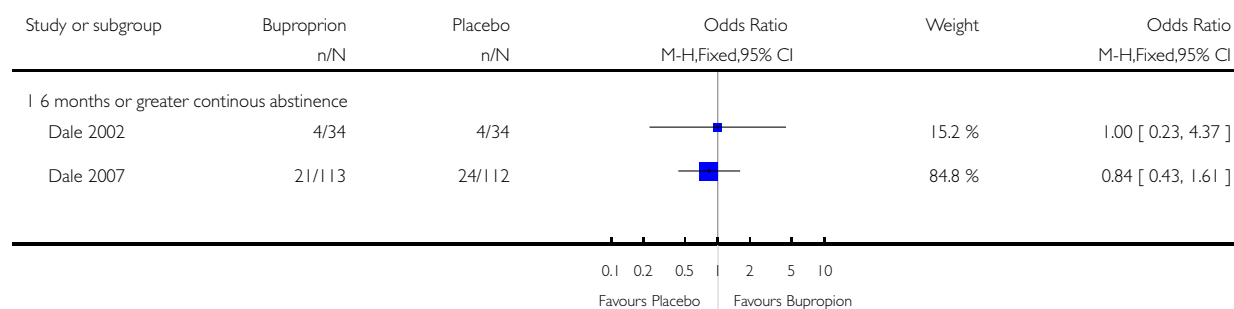
4 Subgroup analysis: Use of telephone support	12		Odds Ratio (M-H, Random, 95% CI)	Subtotals only
4.1 Telephone support for intervention, not for control	8	3953	Odds Ratio (M-H, Random, 95% CI)	2.09 [1.68, 2.61]
4.2 No telephone support for either condition	3	3893	Odds Ratio (M-H, Random, 95% CI)	1.18 [0.81, 1.73]
4.3 Telephone support for control group only	1	303	Odds Ratio (M-H, Random, 95% CI)	1.29 [0.54, 3.05]
5 Subgroup analysis: Motivation	12		Odds Ratio (M-H, Fixed, 95% CI)	Subtotals only
5.1 Motivated	4	4116	Odds Ratio (M-H, Fixed, 95% CI)	1.60 [1.32, 1.95]
5.2 Not selected by motivation	8	4033	Odds Ratio (M-H, Fixed, 95% CI)	1.58 [1.35, 1.85]
6 Behavioural intervention +/- pharmacotherapy versus minimal contact. Long term cessation	1	210	Odds Ratio (M-H, Fixed, 95% CI)	1.48 [0.80, 2.73]
6.1 Nicotine gum	1	106	Odds Ratio (M-H, Fixed, 95% CI)	2.46 [0.99, 6.12]
6.2 Placebo gum	1	104	Odds Ratio (M-H, Fixed, 95% CI)	0.91 [0.38, 2.18]

Analysis 1.1. Comparison 1 Pharmacotherapy: Bupropion versus placebo, Outcome 1 All tobacco abstinence at longest follow-up.

Review: Interventions for smokeless tobacco use cessation

Comparison: 1 Pharmacotherapy: Bupropion versus placebo

Outcome: 1 All tobacco abstinence at longest follow-up

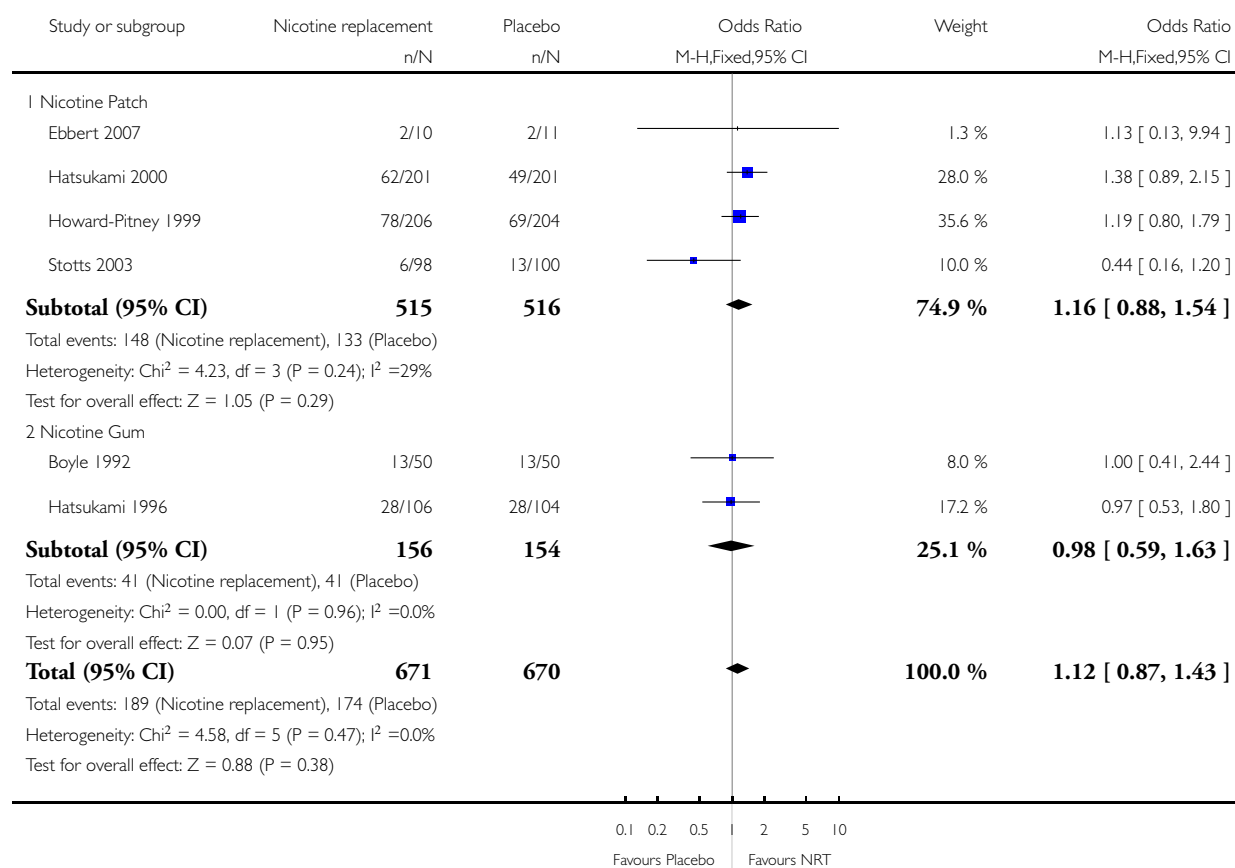


Analysis 2.1. Comparison 2 Pharmacotherapy: NRT versus placebo, Outcome 1 6 months or greater abstinence, strictest criteria.

Review: Interventions for smokeless tobacco use cessation

Comparison: 2 Pharmacotherapy: NRT versus placebo

Outcome: 1 6 months or greater abstinence, strictest criteria

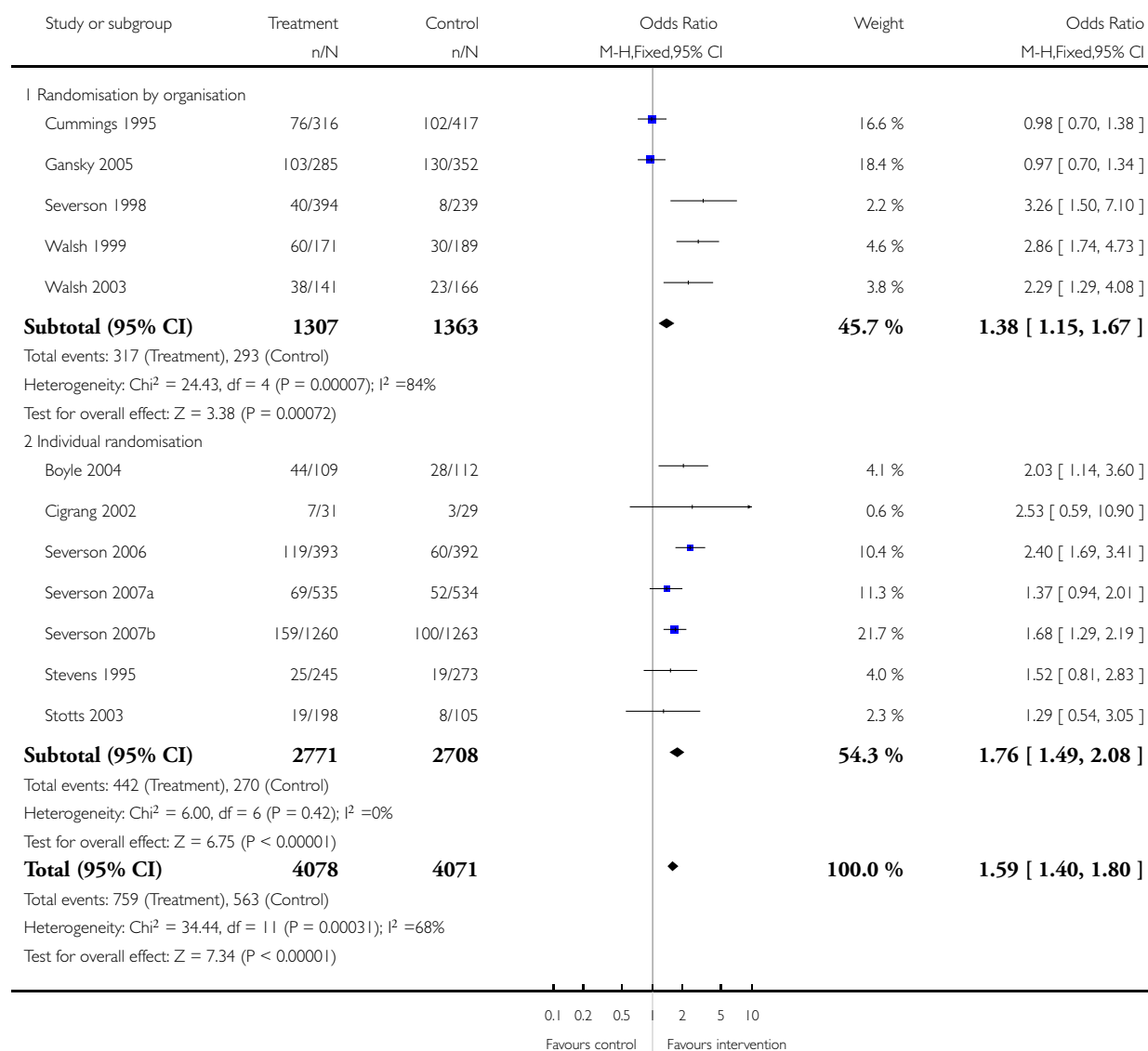


Analysis 3.1. Comparison 3 Behavioral interventions, Outcome 1 Abstinence from all tobacco use (where reported) at 6 months or more.

Review: Interventions for smokeless tobacco use cessation

Comparison: 3 Behavioral interventions

Outcome: 1 Abstinence from all tobacco use (where reported) at 6 months or more

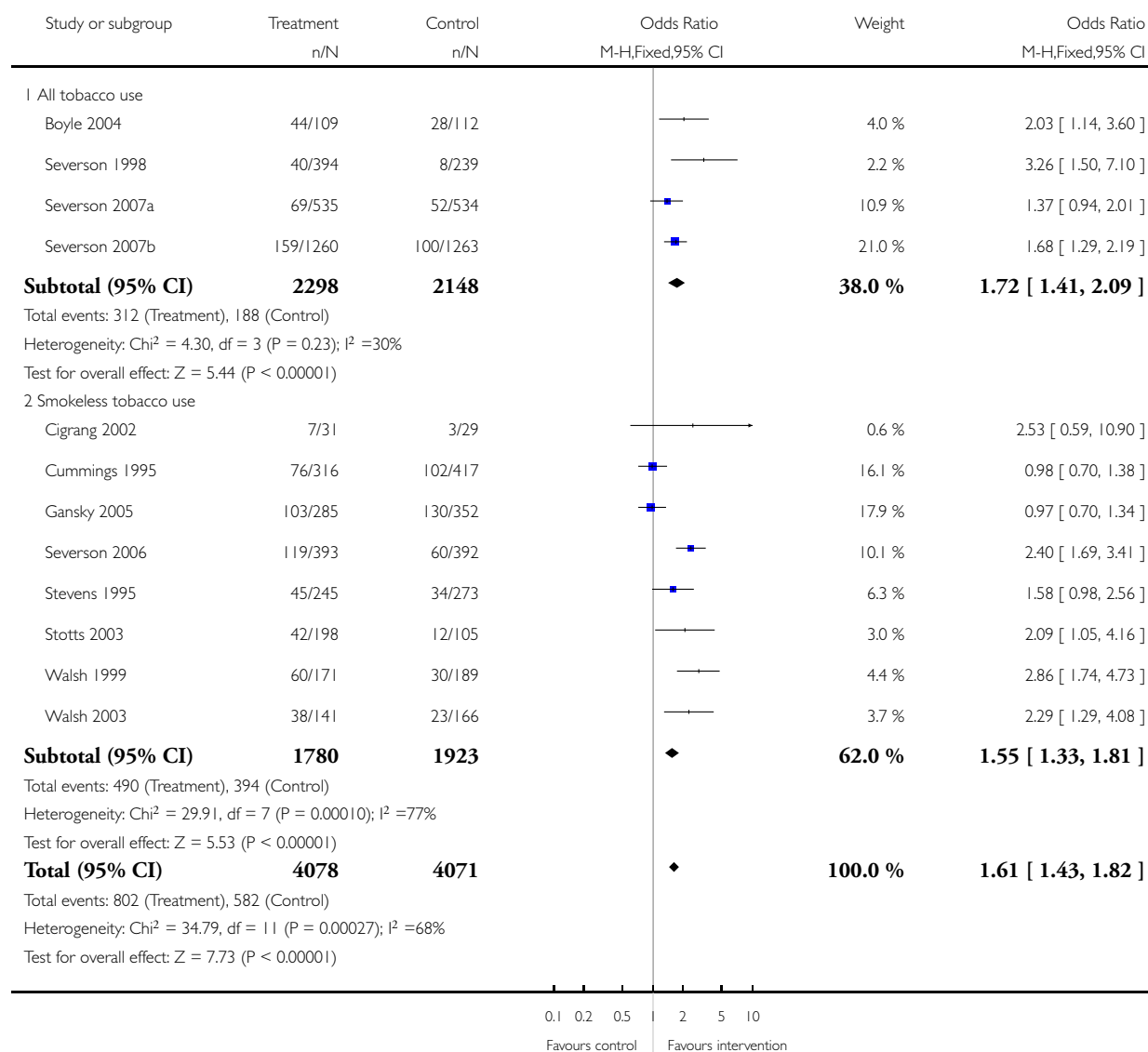


Analysis 3.2. Comparison 3 Behavioral interventions, Outcome 2 Sensitivity analysis: Abstinence from smokeless tobacco use (where reported) at 6 months or more.

Review: Interventions for smokeless tobacco use cessation

Comparison: 3 Behavioral interventions

Outcome: 2 Sensitivity analysis: Abstinence from smokeless tobacco use (where reported) at 6 months or more

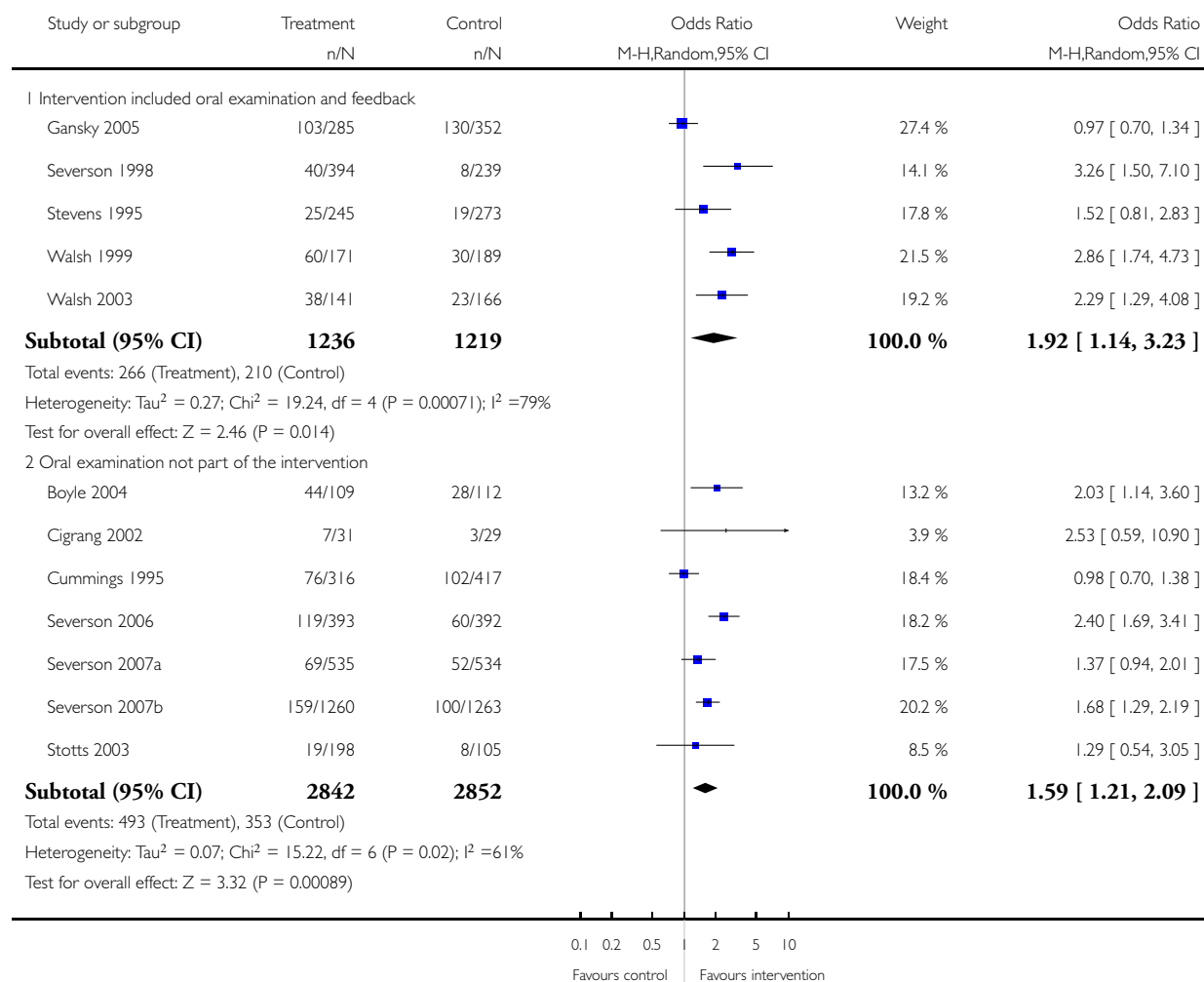


Analysis 3.3. Comparison 3 Behavioral interventions, Outcome 3 Subgroup analysis: Use of oral examination and feedback.

Review: Interventions for smokeless tobacco use cessation

Comparison: 3 Behavioral interventions

Outcome: 3 Subgroup analysis: Use of oral examination and feedback

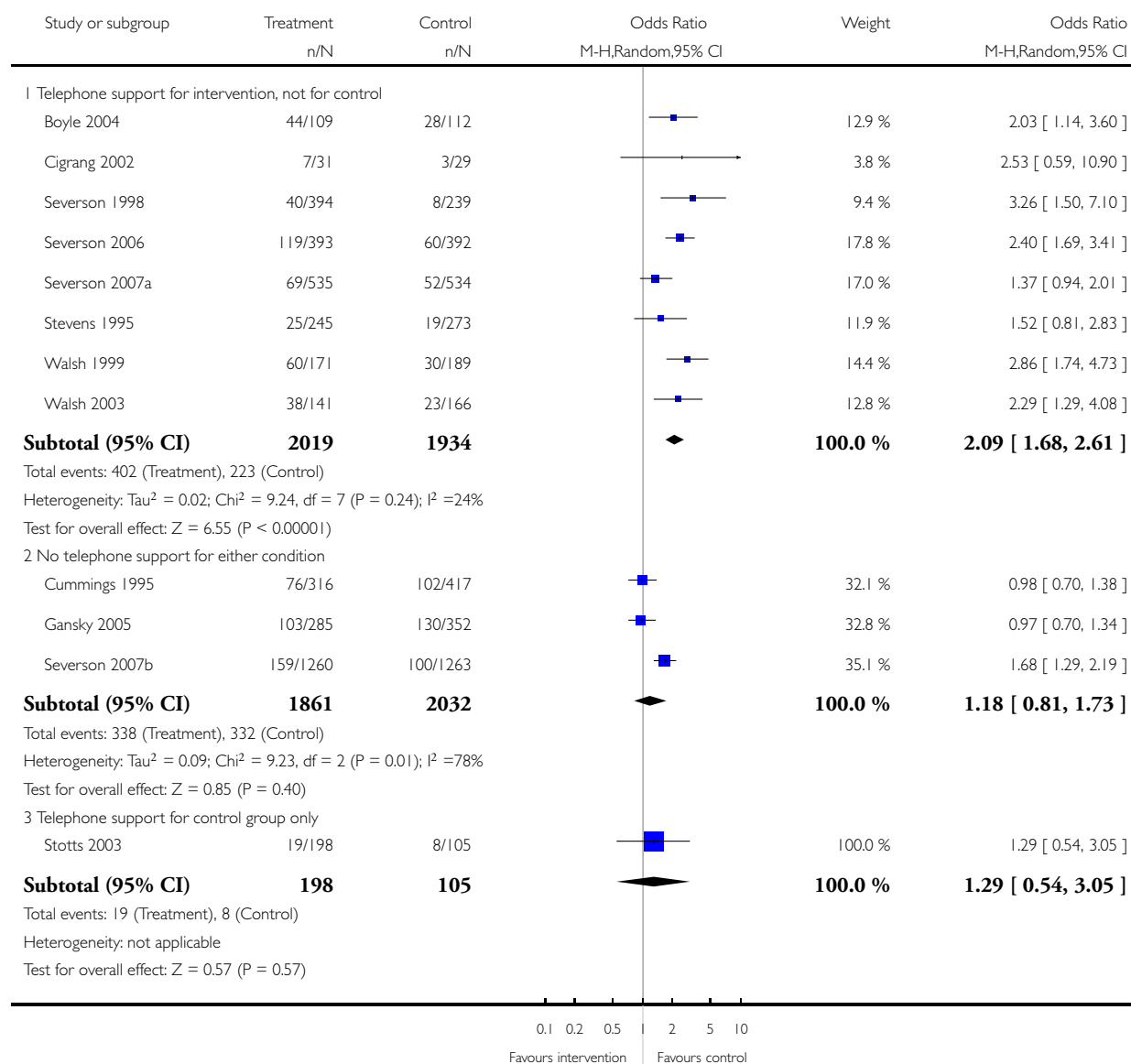


Analysis 3.4. Comparison 3 Behavioral interventions, Outcome 4 Subgroup analysis: Use of telephone support.

Review: Interventions for smokeless tobacco use cessation

Comparison: 3 Behavioral interventions

Outcome: 4 Subgroup analysis: Use of telephone support

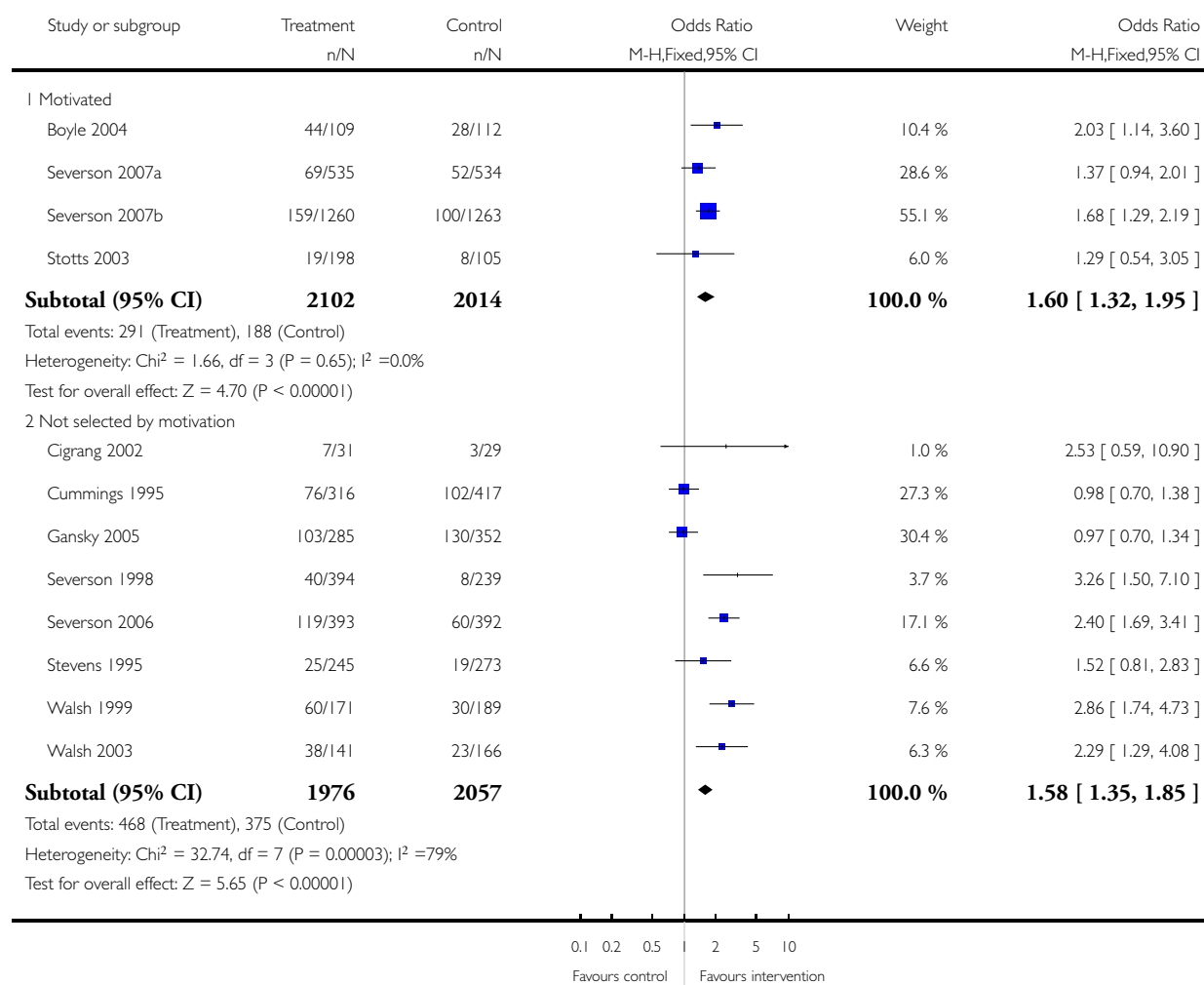


Analysis 3.5. Comparison 3 Behavioral interventions, Outcome 5 Subgroup analysis: Motivation.

Review: Interventions for smokeless tobacco use cessation

Comparison: 3 Behavioral interventions

Outcome: 5 Subgroup analysis: Motivation

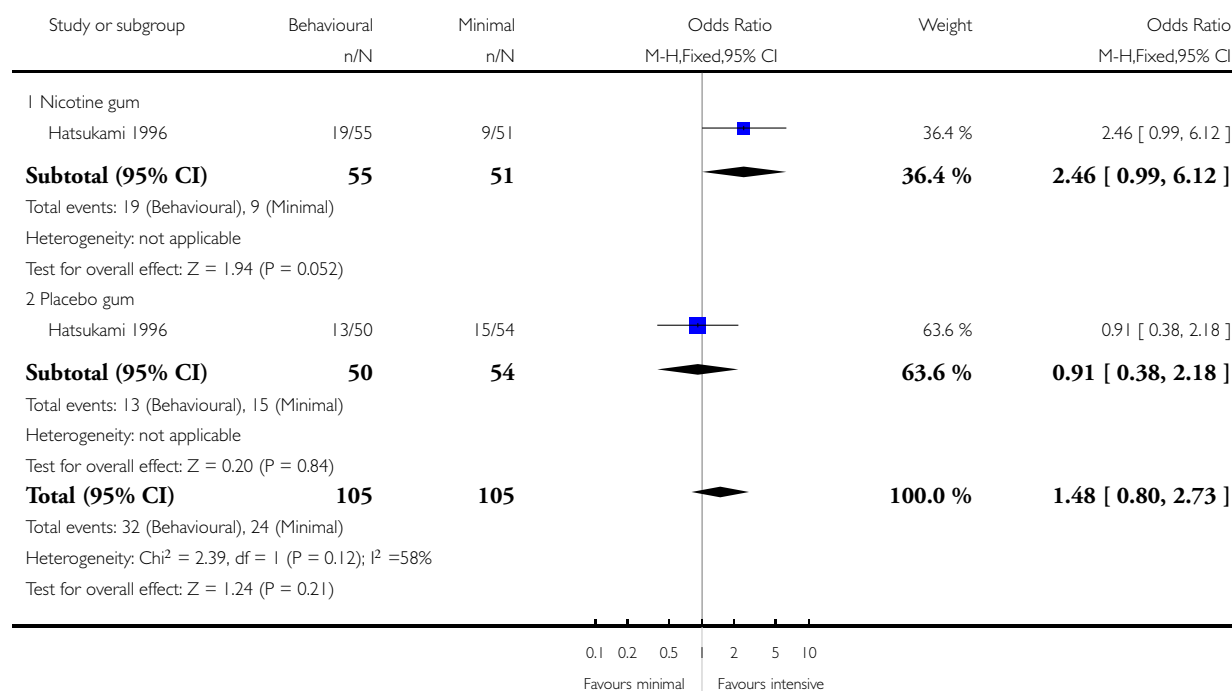


Analysis 3.6. Comparison 3 Behavioral interventions, Outcome 6 Behavioural intervention +/- pharmacotherapy versus minimal contact. Long term cessation.

Review: Interventions for smokeless tobacco use cessation

Comparison: 3 Behavioral interventions

Outcome: 6 Behavioural intervention +/- pharmacotherapy versus minimal contact. Long term cessation



WHAT'S NEW

Last assessed as up-to-date: 19 July 2007.

28 October 2008	Amended	Converted to new review format.
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HISTORY

Protocol first published: Issue 3, 2003

Review first published: Issue 3, 2004

CONTRIBUTIONS OF AUTHORS

JE conceived, designed, and coordinated the review. He was in charge of data collection and worked with PJE to develop search strategies. He assisted LS in entering data into RevMan and was involved in the interpretation and data analysis. He principally authored the review.

LC assisted in the data collection and interpretation. She screened search results and helped organize, appraise, and abstract data from retrieved papers. She wrote to the authors of papers for additional information and queried experts in the field for unpublished work. She assisted in the writing of the review and provided critical feedback.

VM helped conceive, design, and coordinate the review. He was involved with interpretation of the data and writing of the review.

KS was involved with the interpretation of the data and provided a methodological and clinical perspective of the behavioral interventions.

PE developed the search strategies and completed all of the searches.

LD assisted with data interpretation, oversaw the project, and provided methodological and clinical perspectives on the pharmacotherapy trials.

LS managed the data for the review and entered data into RevMan. She interpreted the data and contributed to the text.

DECLARATIONS OF INTEREST

LD and JE are involved in trials of bupropion SR and high dose nicotine patch therapy for the treatment of ST use. LD has received research support from Glaxo Wellcome, Inc., McNeil Consumer Products Company, Elan Pharmaceutical Research, and Lederle Laboratories.

INDEX TERMS

Medical Subject Headings (MeSH)

*Tobacco, Smokeless; Bupropion [therapeutic use]; Chewing Gum; Counseling; Nicotine [therapeutic use]; Nicotinic Agonists [therapeutic use]; Randomized Controlled Trials as Topic; Tobacco Use Cessation [*methods]

MeSH check words

Humans