Relapse prevention in UK stop smoking services: current practice, systematic reviews of effectiveness and cost-effectiveness analysis

CRD summary
This review concluded that relapse prevention interventions were expected to be effective and cost-effective if incorporated into routine treatment within National Health Service stop smoking services. This was a generally well-conducted review. The variable quality of the included studies should be borne in mind when considering the reliability of the conclusions.

Authors' objectives
To assess the effectiveness and cost-effectiveness of relapse prevention in National Health Service (NHS) Stop Smoking Services. This abstract critically appraises only the effectiveness aspect of the review.

Searching
The Cochrane Tobacco Addiction Group's register of trials was searched from 2004 to July 2008 along with MEDLINE, EMBASE, PsycINFO, Cochrane Central Register of Controlled Trials (CENTRAL), Science Citation Index and Social Science Citation Index. Abstracts of the annual meeting of the Society for Research on Nicotine and Tobacco were searched and authors were contacted where appropriate. References of identified studies were checked. Search strategies were reported in full. There were no language restrictions. Trials from a previous Cochrane review (see Other Publications of Related Interest) were included with two exceptions.

Study selection
Randomised controlled trials (RCTs) with a minimum of six months follow-up post-randomisation were eligible for inclusion if they enrolled smokers or people who had recently smoked and were now abstinent. Participants could have quit smoking on their own, be undergoing enforced abstinence or be smokers who were participating in treatment programmes. Trials were required to assess interventions that were intended to prevent relapse to smoking; these could include pharmacological interventions or behavioural interventions (group meetings, face-to-face sessions, written or other materials and proactive or reactive telephone support). Relevant comparators were no intervention, a shorter or less intensive intervention or an intervention not oriented towards relapse prevention. The primary outcome was abstinence from smoking, preferably recorded as continuous abstinence; point prevalence abstinence was used instead where necessary; main outcomes were these measures at long-term follow-up (12 to 18 months).

The included studies assessed a large number of different interventions provided in a range of settings to groups that included people who had achieved abstinence with and without assistance and with enforced abstinence. Most studies were conducted in USA; others were in UK, Germany, Spain, Belgium, Canada, Japan, Australia and in multiple countries. Some studies enrolled only pregnant or post-partum women. Measures of abstinence included carbon monoxide, saliva thiocyanate, urinary or saliva cotinine and self-report.

Two reviewers independently assessed the studies for inclusion. Differences were resolved through discussion with additional reviewers.

Assessment of study quality
The studies were assessed for validity using the Cochrane risk of bias assessment tool to assess randomisation, allocation concealment, blinding, assessment of incomplete data, baseline comparability and adequate description of interventions.

The authors did not state how many reviewers performed the quality assessment.

Data extraction
Two reviewers independently extracted data including abstinence at one to three months (short term), six to nine months (medium term) and 12 to 18 months (long term) using a prespecified form. For trials that enrolling pregnant or
post-partum women, abstinence at delivery or last follow-up prior to this was extracted. Categories were reported for participants (smokers or abstinent smokers) and intervention type (behavioural or pharmacological and subdivisions of these categories). Disagreements were resolved through discussion. Authors were contacted to obtain missing data where possible.

**Methods of synthesis**
The studies were combined using a DerSimonian and Laird random-effects model to calculate pooled odds ratios (OR) with 95% confidence intervals (CIs). It appeared that some analyses were carried out using a Mantel-Haenszel fixed-effect model. Numbers needed to treat (NNT) were calculated for statistically significant comparisons. Statistical heterogeneity was assessed using the I^2 statistic and where this exceeded 80% meta-analysis was not performed. Where trials contained multiple intervention groups, pairwise comparisons between each active intervention and control were conducted with the non-control group divided by the number of comparisons in order to prevent double counting. Publication bias was assessed using funnel plot analysis. The single cluster-randomised trial was assessed as having minimal impact of clustering and was analysed with the rest of the trials.

**Results of the review**
Fifteen RCTs identified by this review and 39 studies from the previous Cochrane review gave a total of 54 RCTs. Thirty-six studies (13 newly identified) randomised newly abstinent smokers and 18 studies (two newly identified) randomised existing smokers. All studies adequately described the interventions and most of them by far had baseline comparability of groups. Most trials did not clearly report adequate allocation concealment and method of sequence generation for randomisation or blinding.

Self-help behavioural interventions delivered to individuals who had achieved abstinence without assistance were effective at preventing relapse to smoking at long-term follow-up (OR 1.52, 95% CI 1.15 to 2.01, I^2=0%, NNT=14; three RCTs). None of the behavioural interventions in assisted or enforced abstinence showed effectiveness beyond the short term.

Also effective were several types of pharmacotherapy. Bupropion was effective at long-term follow-up (OR 1.49, 95% CI 1.10 to 2.01, I^2=0%, NNT=11; four RCTs) and nicotine replacement therapy at both medium (OR 1.56, 95% CI 1.16 to 2.11, I^2=37%, NNT=14; four RCTs) and long-term follow-up (OR 1.33, 95% CI 1.08 to 1.63, I^2=0%, NNT=20; four RCTs). One RCT indicated effectiveness of varenicline at short and medium term follow-up (short term OR 2.54, 95% CI 1.93 to 3.36, NNT=6; medium term OR 1.40, 95% CI 1.12 to 1.76, NNT=12). One RCT indicated effectiveness of rimonabant (short term OR 1.67, 95% CI 1.14 to 2.46 and medium term OR 1.48, 95% CI 1.14 to 1.93; NNTs not reported).

Interventions in pregnant and postpartum women did not appear to be effective, with the exception of one large RCT that indicated long-term effectiveness of individual behavioural counselling (OR 1.38, 95% CI 1.05 to 1.82).

There was little evidence of the effectiveness of any intervention in trials that enrolled current smokers, with the exception of bupropion.

Full results of all the analyses were reported.

**Cost information**
An economic analysis found that relapse prevention interventions were highly cost-effective. Bupropion was associated with an incremental increase of 0.07 quality adjusted life years (QALYs) and a saving of £68 by the NHS. Nicotine replacement therapy was associated with an increase of 0.04 QALY at a cost of £12. Varenicline had a similar impact on QALYs, but at nearly seven times the cost of nicotine replacement therapy.

**Authors’ conclusions**
Relapse prevention interventions are expected to be effective and cost-effective if incorporated into routine treatment within NHS stop smoking services.

**CRD commentary**
The review question was clear and supported by explicit inclusion criteria. The authors searched a wide range of...
databases and other sources without language restrictions, which reduced the chances that relevant studies were omitted and selection biases introduced. The authors reported that they used methods designed to reduce bias and error in study selection and data extraction, but not in the validity assessment. The validity assessment used relevant criteria and the results were fully reported. However, these results were not apparently used to inform the synthesis despite the variable results of the appraisal. The synthesis appeared to use appropriate methods and included an assessment of heterogeneity.

This was a generally well-conducted review. The variable quality of the included studies should be borne in mind when considering the reliability of the conclusions.

Implications of the review for practice and research

Practice: The authors stated that if relapse prevention interventions were to be incorporated into the NHS stop smoking services then guidance would be required to encourage adoption of the most effective interventions and incentives needed to be provided to focus on sustaining quit attempts beyond currently monitored four-week targets.

Research: The authors made multiple recommendations for further research. Briefly these comprised: placebo RCTs of interventions as an extension to current NHS services; acceptability studies of extended pharmacotherapy use (bupropion in particular); assessment of the impact of adjunctive behavioural therapy in the early stages of nicotine replacement quit attempts; confirmation of the different relapse rate trajectories observed for bupropion, varenicline and nicotine replacement. Recommendations for RCTs of behavioural interventions for relapse prevention in smokers who had achieved abstinence unsupported or through NHS stop smoking services were made, along with the need for research to refine particular interventions. Some methodological standardisation requirements were identified.

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Other publications of related interest


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