'Cut down to quit' with nicotine replacement therapies in smoking cessation: a systematic review of effectiveness and economic analysis

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CRD summary
This review evaluated the effectiveness of nicotine replacement therapy (NRT) in achieving smoking abstinence for smokers unwilling or unable to quit abruptly. The authors concluded that NRT was an effective intervention in achieving smoking abstinence for smokers who were unwilling or unable to attempt an abrupt quit. The authors’ conclusions reflected the evidence presented and were likely to be reliable.

Authors’ objectives
To assess the effectiveness of ‘cut down to quit’ (CDQT) smoking (gradually cutting down smoking over an extended period of time) using nicotine replacement therapy (NRT).

Searching
The Cochrane Library (2006, issue 2), MEDLINE, EMBASE, CINAHL, PsycINFO and the Science Citation Index were searched from 1992 until 2006 to identify relevant studies written in any language. Search terms were reported. Research registries, citations of relevant studies and reviews, licensing authority and pharmaceutical industry documents were searched. Subject-matter experts and the pharmaceutical industry were contacted in order to identify additional studies.

Study selection
Eligible for inclusion in the review were randomised controlled trials (RCTs) comparing NRT (gum or inhalator alone or as part of a combination therapy) with placebo, no treatment, non-NRT drugs for smoking cessation or psychological interventions (such as motivational support). Participants were smokers who were currently unwilling or unable to quit abruptly. Characteristics of participants such as average age (42-46 years), proportion of female participants (45 per cent to 65 per cent), average cigarette consumption (24-30 cigarettes per day), average exhaled concentration of carbon monoxide (CO) in parts per million (ppm) (26-30 ppm) and intensity of physical dependence on nicotine as measured by Fagerstorm scores (5.4 to 6.6), were similar in all studies. The primary outcomes of interest were stated to be sustained abstinence, point prevalence abstinence, sustained reduction and point prevalence reduction in smoking, but sustained abstinence from smoking was used as the main indicator of success of NRT. Other outcomes of interest included health related quality of life (HRQoL), reduction in smoking and adverse events. Two reviewers selected studies for inclusion in the review, with any disagreements resolved by discussion and the involvement of a third reviewer if necessary.

Smoking reduction required self-reported decrease in cigarette consumption of ≥50 per cent relative to baseline, which was validated (except one study) by a reduction in exhaled CO relative to baseline. Smoking cessation was validated by an exhaled concentration of CO of less than 10 ppm.

Assessment of study quality
Study quality was assessed using guidelines proposed by the NHS Centre for Reviews and Dissemination (CRD) Report Number 4, which included assessment of randomisation, allocation concealment, similarity of groups at baseline, blinding and intention to treat (ITT) analysis. It was unclear whether the quality of individual patient data was assessed. Quality was assessed by one reviewer and independently checked for agreement by a second reviewer. Disagreements were resolved by discussion and the involvement of a third reviewer if necessary.

Data extraction
Data was extracted in order to calculate relative risks (RR) or hazard ratios (HRs) with 95% confidence intervals (CI). For studies where individual patient data (IPD) was available, rate of sustained abstinence for at least six months was calculated. Data extraction was performed by one reviewer and independently checked for accuracy by a second reviewer. Disagreements were resolved by discussion and the involvement of a third reviewer if necessary.
Methods of synthesis
Studies were combined in a meta-analysis using a fixed-effect model. IPD were synthesised for some outcomes and study level data for others. Heterogeneity was assessed using the $X^2$. Where possible, pre-specified subgroup analyses were performed to assess the difference in effectiveness between different participant groups or interventions.

Results of the review
Seven RCTs (n=3,156) were included in the review. In all studies NRT was compared with placebo. Sample sizes ranged from 193 to 923. Five RCTs (n=1,833) had IPD. All studies were assessed to be of high quality.

Results of several outcomes were reported (see full report) however, the main clinical outcome of interest was sustained abstinence from smoking. In the IPD meta-analysis (five RCTs, n=1,833), NRT (gum and inhalator) NRT was found to be statistically significantly superior to placebo for sustained abstinence for at least six months (RR 2.06, 96% CI: 1.34, 3.15, p-value not given). Gum alone (four RCTs, n=1,404) was also found to be statistically significantly superior to placebo for sustained abstinence for at least six months (RR 2.59, 95% CI: 1.60, 4.60, p-value not given). However, inhalator alone (one RCT, n=429) was not statistically different to placebo (RR 1.00, 95% CI: 0.41, 2.44, p-value not given).

It appeared that there was no statistically significant heterogeneity in any of the meta-analyses. The proportion of patients in the NRT arm who sustained abstinence for at least six months was 6.75 per cent (range 3.2 per cent to 10.2 per cent) and in the placebo arm 3.29 per cent (range 1.1 per cent to 4.7 per cent). The number needed to treat (NNT) was 29. Meta-analyses of study level results revealed that NRT was superior to placebo for all four primary outcomes: point prevalence of abstinence and sustained abstinence, sustained and point prevalence of smoking reduction (see full report for further details). No serious treatment-related adverse events were reported in any of the trials. Minor treatment related adverse events were similar in frequency and type to those in previously reported studies of NRT.

Authors' conclusions
NRT is an effective intervention to achieve smoking abstinence for smokers who declared unwillingness or inability to attempt an abrupt quit.

CRD commentary
This review addressed a clear research question and was supported by detailed inclusion criteria. The search strategy was comprehensive and included studies in languages other than English, and attempts were made to identify unpublished material, thus reducing the possibility of publication and language bias. The criteria used to assess validity were appropriate for the study design. Adequate details of primary studies were provided and it was appropriate that a meta-analysis was performed. Although IPD was used to derive the main outcome of sustained abstinence, smoking cessation was not a primary outcome of any of the included trials. This was a well conducted review with sufficient attempts to minimise errors and bias. The authors' conclusions reflected the evidence presented and were likely to be reliable.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: Randomised trials in recalcitrant smokers allowing head-to-head comparison of CDTQ delivered with various NRT modalities (such as inhalator, nasal spray, lozenges, gum and patch) would be more informative than placebo-controlled trials. Research was needed into the best ways of implementing a CDTQ strategy and integrating this with abrupt quit options in the context of all UK smoking services.

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