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

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Executive summary

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Executive summary

Background

Approximately 25% of adults in the UK are smokers. Smoking is associated with numerous diseases, including cancer and heart disease, and smokers have reduced life expectancy. Nicotine in cigarettes renders them addictive so that smokers generally find it extremely difficult to give up their habit. Most smokers (around 70%) say they would like to stop but some express an unwillingness or inability to do so in the near future. Nicotine replacement therapy (NRT) attempts to substitute the nicotine obtained from smoking with that derived from gum, inhaler or patch, so that smokers are enabled to quit smoking and then gradually become independent of nicotine.

Some nicotine replacement therapies that were previously licensed in the UK for abrupt quitting from smoking have recently been granted a new licensed indication called 'cut down to stop' or 'cut down to quit' (CDTQ). This aims at smokers who express unwillingness or inability to stop smoking in the short term by enabling them gradually to cut down their smoking over an extended period while supported by NRT so that they may eventually become able and willing to attempt to quit altogether. Thus the CDTQ stratagem involves more prolonged support with NRT than the previously licensed indication for an abrupt quit attempt and by definition targets a different population of smokers.

Objective

The primary objective of this assessment report was to examine the effectiveness and cost-effectiveness of NRT for CDTQ smoking.

Method

Searches of bibliographic databases and contact with experts and industry were undertaken in order to identify relevant systematic reviews, randomised controlled trials (RCTs) and existing economic analyses of CDTQ. Searches were carried out in July 2006. Evidence from RCTs was included in the report if the population consisted of smokers who declared an inability or unwillingness to attempt to quit smoking in the short term, if the intervention encompassed a cut-down smoking programme supported by NRT and if the comparator was a cut-down programme with placebo or other support.

Systematic reviews were included if at least one electronic database had been searched and if RCTs documenting quit rates in smoking reduction programmes with NRT were reviewed. Economic studies were included if they encompassed cost-effectiveness or cost–utility analysis of CDTQ programme(s).

A systematic review of RCTs was performed that included meta-analyses of smoking outcomes and analyses of individual patient data.

The outcome taken as an indicator of success was the proportion of smokers who sustained continuous abstinence from smoking. Various measures for this outcome have been used, and these encompass different durations of continuous abstinence. The measures reviewed were:
(1) a defined period of sustained abstinence that starts within the first 6 weeks of NRT treatment (the measure used in most RCTs); and (2) at least 6 months' continuous abstinence that starts at any time within the NRT treatment period (a measure that can be calculated from individual patient data in the RCTs).

A decision analytical model was constructed to estimate the cost-effectiveness of CDTQ from the NHS perspective. CDTQ was considered as a choice option for individual smokers and also as a policy option.

Results

Effectiveness

No systematic reviews of the effectiveness of CDTQ were identified. No RCTs specifically addressing CDTQ were identified. Seven randomised placebo-controlled trials satisfied the inclusion criteria; six of these were industry sponsored. The RCTs were primarily designed to investigate the effectiveness of a smoking ▶

reduction programme. Sustained smoking cessation was only reported as a secondary outcome in these trials and required commencement of cessation within the first 6 weeks of treatment.

In four RCTs smokers received NRT gum or placebo, in two NRT inhalator or placebo and in one placebo-controlled RCT smokers exercised free choice of the type of NRT they received.

Meta-analyses of the study level results for sustained abstinence from smoking, point prevalence of smoking abstinence, sustained smoking reduction and point prevalence of smoking reduction demonstrated statistically significant superiority of NRT compared with placebo for all four outcomes. The proportion of participants who achieved sustained abstinence commencing within the first 6 weeks of treatment was meagre (about 2% of those in receipt of NRT). This is not surprising given that it is inherently unlikely that smokers who had expressed unwillingness or inability to quit in the short term would stop within 6 weeks. Therefore, individual patient data from unpublished reports of five RCTs were used to calculate sustained abstinence of at least 6 months starting at any time during the treatment period (generally 12 months). Using this more realistic criterion for sustained abstinence, meta-analysis indicated statistically significant superiority of NRT versus placebo [relative risk 2.06, 95% confidence interval (CI) 1.34 to 3.15]. The proportions achieving this outcome across all five RCTs were 6.75% (95% CI 5.3 to 8.56%) of participants in receipt of NRT and 3.29% (95% CI 2.56 to 4.21%) of those receiving placebo. The number-needed-to-treat was 29. This measure of sustained abstinence was used for economic modelling.

No significant treatment-related adverse events were reported in the trials and minor events were similar in frequency and type to those in previously reported studies of NRT. None of the included studies reported health-related quality of life measures for abstainers from smoking.

Cost-effectiveness analysis

No existing economic analyses of CDTQ were identified. A *de novo* decision analytic model was constructed to estimate the cost-effectiveness of making CDTQ with NRT available for smokers unwilling or unable to attempt an abrupt quit. The outcome measure was expected quality-adjusted life-years (QALYs). The model also took account of the possibility that some smokers willing to attempt abrupt quitting might instead switch to CDTQ. Smokers leaking from abrupt quit to CDTQ were assumed either to experience a 'CDTQ-success rate' or to retain the abstinence success rate of abrupt quitters.

The model compared three CDTQ NRT options (over-the-counter NRT; brief advice + NRT repeat prescriptions; smokers' clinic with individual or group counselling + repeat NRT prescriptions) with no quit attempt, attempt without NRT, abrupt quit attempt with NRT in any of three options (over-the-counter NRT; brief advice + NRT repeat prescriptions; smokers' clinic with individual or group counselling + NRT repeat prescriptions). A smoker may thus switch to any one of three CDTQ modes from any of five other behaviours (no quit attempt, quit attempt without NRT, abrupt quit attempt with NRT in any of three available modes). Further analyses compared each CDTQ option with a mix of no quit attempt and corresponding abrupt quit option. Lastly, a 'full analysis' compared a range of CDTQ options with the full mix of non-CDTQ options.

CDTQ success rate was based on trials in which behavioural support was variously described as minimal or moderate (at least eight scheduled clinic visits). In a real-world setting this corresponds more closely to 'smokers' clinic' than to 'brief advice plus repeat prescription'.

Model results suggest that CDTQ with NRT delivers incremental cost-effectiveness ratios (ICERs) ranging from approximately £1500/QALY to approximately £7700/QALY depending on the age at which smoking cessation was achieved and the modes of CDTQ delivery.

Assuming applicability to a single population, CDTQ was not cost-effective compared with abrupt quitting.

If CDTQ with NRT were to be offered on the NHS as a matter of policy, the base-case results suggest that it would only be effective and cost-effective if a substantial majority of the people attempting CDTQ with NRT were those who would otherwise make no attempt to quit. This result is robust to considerable variation in the forms of CDTQ with NRT offered, and to the assumptions about QALY gained per quit success.

However, incremental cost-effectiveness ratio values are sensitive to assumptions about success ▶

rates for different methods of attempting to quit smoking. The base case assumes that willing abrupt quitters who switch to CDTQ have the same success rate in CDTQ as smokers who are unwilling to try abrupt quit. If it is assumed that smokers who might otherwise try abrupt quitting and undertake CDTQ instead retain a fixed success rate (i.e. the same success rate in CDTQ as in abrupt quit), then all forms of CDTQ provision appear to be cost-effective. This assumes that success rate is more strongly related to characteristics of smokers than to the particular nature of the NRT intervention.

Conclusion

Meta-analysis of RCT evidence of quit rates in NRT-supported smoking reduction studies indicates that NRT is an effective intervention in achieving sustained smoking abstinence for smokers who declare unwillingness or inability to attempt an abrupt quit. The 12-month sustained abstinence success rate in this population (approximately 5.3% with NRT versus approximately 2.6% with placebo) is considerably less than that documented for an abrupt quit NRT regime in smokers willing to attempt an abrupt quit with NRT (which according to other systematic reviews is approximately 16% with NRT versus 10% with placebo).

Most of the evidence of effectiveness of CDTQ in this report came from trials that required considerable patient–investigator contact. Therefore, for CDTQ with NRT to generate similar abstinence rates for this recalcitrant population in a real-world setting would probably require a similar mode of delivery.

Decision analytic modelling based on reasonable assumptions about costs, benefits and success rates suggests that CDTQ is highly cost-effective compared with no quit attempt. CDTQ remains cost-effective if dilution from abrupt quitting forms a small proportion of CDTQ attempts. In an alternative analysis in which smokers who switch from an abrupt quit to CDTQ retain the success rate of abrupt quitters, all forms of CDTQ appear cost-effective.

Recommendations for further research

Randomised trials in recalcitrant smokers allowing head-to-head comparison of CDTQ delivered with various NRT modalities (e.g. inhalator, nasal spray, lozenge, gum, patch) would be informative. Research is also 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.

Publication

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NIHR Health Technology Assessment Programme

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The research findings from the HTA Programme directly influence decision-making bodies such as the National Institute for Health and Clinical Excellence (NICE) and the National Screening Committee (NSC). HTA findings also help to improve the quality of clinical practice in the NHS indirectly in that they form a key component of the 'National Knowledge Service'.

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First is the commissioned route. Suggestions for research are actively sought from people working in the NHS, the public and consumer groups and professional bodies such as royal colleges and NHS trusts. These suggestions are carefully prioritised by panels of independent experts (including NHS service users). The HTA Programme then commissions the research by competitive tender.

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The research reported in this issue of the journal was commissioned by the HTA Programme as project number 06/09/01. The contractual start date was in May 2006. The draft report began editorial review in March 2007 and was accepted for publication in June 2007. As the funder, by devising a commissioning brief, the HTA Programme specified the research question and study design. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

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