

EXECUTIVE SUMMARY

Cut Down to Quit with Nicotine Replacement Therapies (NRT) in Smoking Cessation: Systematic review of effectiveness and economic analysis

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 (~70%) say they would like to stop but some express an unwillingness or inability to do so in the near future. Nicotine replacement therapies attempt 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.

Nicotine replacement therapies that were previously licensed for abrupt quitting from smoking have recently been granted a new licensed indication called “cut down to stop”, “nicotine assisted reduction 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 to gradually 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. 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 the newly licensed indication of NRT for “cut down to quit” smoking.

Method

Bibliographic data-bases, contact with experts and industry were undertaken in order to identify relevant systematic reviews, randomised controlled trials and existing economic analyses of CDTQ. RCTs were included if the population consisted of smokers that 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 for success of the intervention was the proportion of smokers that sustained continuous abstinence from smoking. Various measures for this outcome can be used, and they may encompass different durations of continuous abstinence; the measures reviewed were: a) a defined period of sustained abstinence that starts within the first six weeks of NRT-treatment; b) at least six months continuous abstinence that starts at any time within the NRT treatment period.

A decision analytical model was constructed to estimate the cost-effectiveness of CDTQ from an 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. Seven randomised placebo controlled trials satisfied the inclusion criteria; six of these were industry-sponsored. None of the RCTs were primarily designed to investigate effectiveness of a smoking reduction programme in terms of sustained smoking cessation. This was only reported as a secondary outcome and required commencement of cessation within the first six weeks of treatment.

In five RCTs smokers received NRT gum or placebo, in two NRT inhaler or placebo and in one smokers exercised free-choice of NRT or placebo type.

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 relative to placebo for all four outcomes. In the studies sustained abstinence was defined as abstinence starting within the first six weeks of study. The proportion of participants that achieved sustained abstinence defined in this way was meagre (about 2% of those in receipt of NRT). Even with NRT support it appeared inherently unlikely that smokers who had expressed unwillingness or inability to quit in the short-term would stop within six weeks. We therefore used individual patient data from unpublished reports of five RCTs to calculate sustained abstinence of at least six months starting at any time during the treatment period (generally 12 months). Using this more relaxed criterion for sustained abstinence, meta-analysis indicated statistically significant superiority of NRT vs. placebo (relative risk 2.06, 95% 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 more relaxed measure for sustained abstinence was used for economic modelling.

No significant treatment-related adverse events were reported in these trials and minor events tallied in frequency and type with 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 to either 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; NRT brief advice + repeat prescriptions; smokers’ clinic with individual or group counselling + repeat prescriptions) with no quit attempt, attempt without NRT, abrupt quit attempt with NRT in any of three options (over the counter NRT; NRT brief advice + repeat prescriptions; smokers’ clinic with individual or group counselling + 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 is a highly cost-effective option compared to no quit attempt. Incremental cost effectiveness ratios (ICERs) ranged from ~£1500/QALY to ~£7,700/QALY depending on age at which smoking cessation was achieved and the modes of CDTQ delivery. Compared to abrupt quitting, assuming applicability to a single population, CDTQ was not cost-effective. If CDTQ with NRT were to be offered on the NHS as a matter of policy, these base case results suggest 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 assumption about QALY gained per quit success. However, the results are highly 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 undertake CDTQ instead while retaining a fixed success rate, 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

RCT evidence indicates that CDTQ with NRT is an effective intervention in achieving sustained smoking abstinence for smokers who declare unwillingness or inability to attempt an abrupt quit. The twelve month success rate in this population (~5.3%) is considerably less than that documented for an abrupt quit NRT regime in smokers willing to attempt an abrupt quit with NRT (~15.5%). For CDTQ with NRT to

generate this success rate in a real world setting would probably require a “counselling” mode of delivery.

Decision analytic modelling based on reasonable assumptions about costs, benefits and success rates suggests that CDTQ is highly cost-effective compared to no quit attempt but not compared to abrupt quitting. CDTQ remains cost-effective if dilution from abrupt quitting forms a small proportion of CDTQ attempts. In an alternative analysis in which smokers that switch from an abrupt quit to CDTQ retain the success rate of abrupt quitters then all forms of CDTQ appear cost-effective.