Nicotine replacement therapy to improve quit rates

Matrix Insight, in collaboration with Imperial College London, Kings College London and Bazian Ltd, were commissioned by Health England to undertake a research study to develop and apply a method for prioritising investments in preventative interventions for England. Seventeen preventative health interventions were included in the study. Each intervention was evaluated in terms of the following criteria: reach; inequality score; cost-effectiveness; and affordability. This report presents the results of the analysis for one of the interventions: nicotine replacement therapy to improve quit rates. The full report of the study is available from the ***H.E.L.P.*** website.

Summary

Description of the intervention
Nicotine replacement therapy comprises GP advice and prescriptions (baseline visit plus six prescriptions spread over approximately 12 weeks) and drug provision (Wang et al, 2008).

Criteria	Measure	Value	Certainty
1. Reach			
Percentage of population affected by the condition and that could potentially benefit from the intervention.	Adult smokers who would like to quit as a percentage of the population aged 15 and above in England (Healthcare Commission 2007; Office for National Statistics, 2009)	12.82%	★★★
2. Inequality score			
Ratio of the percentage of disadvantaged population to the percentage of the general population that could potentially benefit from the intervention.	Ratio of percentage of adult smokers attempting to quit in routine and manual occupations to percentage of smokers attempting to quit in the general population (Office for National Statistics, 2009)	1.47	★★
3. Cost-effectiveness			
Cost of the intervention per QALY gained (in £2007/08)	See cost-effectiveness	£2,388	★★
Net cost of the intervention per QALY gained (in £2007/08)	See cost-effectiveness	-£933	★★
Timing of benefits	QALY gain and cost savings are estimated to occur in the long-run (5 years or more after the intervention).		
4. Affordability			
Total cost of implementing the intervention at the national level	Multiple of eligible individuals and unit cost of the intervention	Between £100 million and £1 billion	★★★

Key to certainty grading scales

★ Low quality evidence
★★ Medium quality evidence
★★★ High quality evidence

Box 1. Cost per QALY gained

A quality adjusted life year (QALY) is a simple way of combining quality of life with length of life.
One QALY is equivalent to one year in full health. The cost per QALY gained is therefore the cost of achieving one extra year of full health. Its calculation is based on the following formula:

$$cost\ per\ QALY\ gained = \frac{incremental\ cost\ of\ intervention}{QALYs\ gained}$$

The net cost per QALY gained is the cost per QALY considering the incremental cost of the intervention as well as the cost saved through health treatment avoided. Its calculation is based on the following formula:

$$net\ cost\ per\ QALY\ gained = \frac{incremental\ cost\ of\ intervention - cost\ savings}{QALYs\ gained}$$

Cost effectiveness

Cost. Nicotine replacement therapy to improve quit rates cost £57.3 per person more on average than attempting to quit with no smoking cessation therapy (£2007/08).

Effect. Compared to no drug prescription, nicotine replacement therapy increases the quit rate among those who attempt to quit by 1.86 per cent. This effect was obtained from a review undertaken to identify evidence on the effectiveness and cost-effectiveness of smoking cessation interventions.

Benefits. The benefits of the intervention derive from stopping individuals smoking. Two types of benefits are considered: QALYs and health care cost savings. [1] Based on the QALYs gained and the health care cost savings of quitting smoking, a 1.86 per cent increase in the quit rate is associated with the following benefits:

- An additional 0.024 QALYs per person
- Cost savings of £79.7 per person (£2007/08)

Please refer to decision model for details on how the QALY gain and cost savings were calculated.

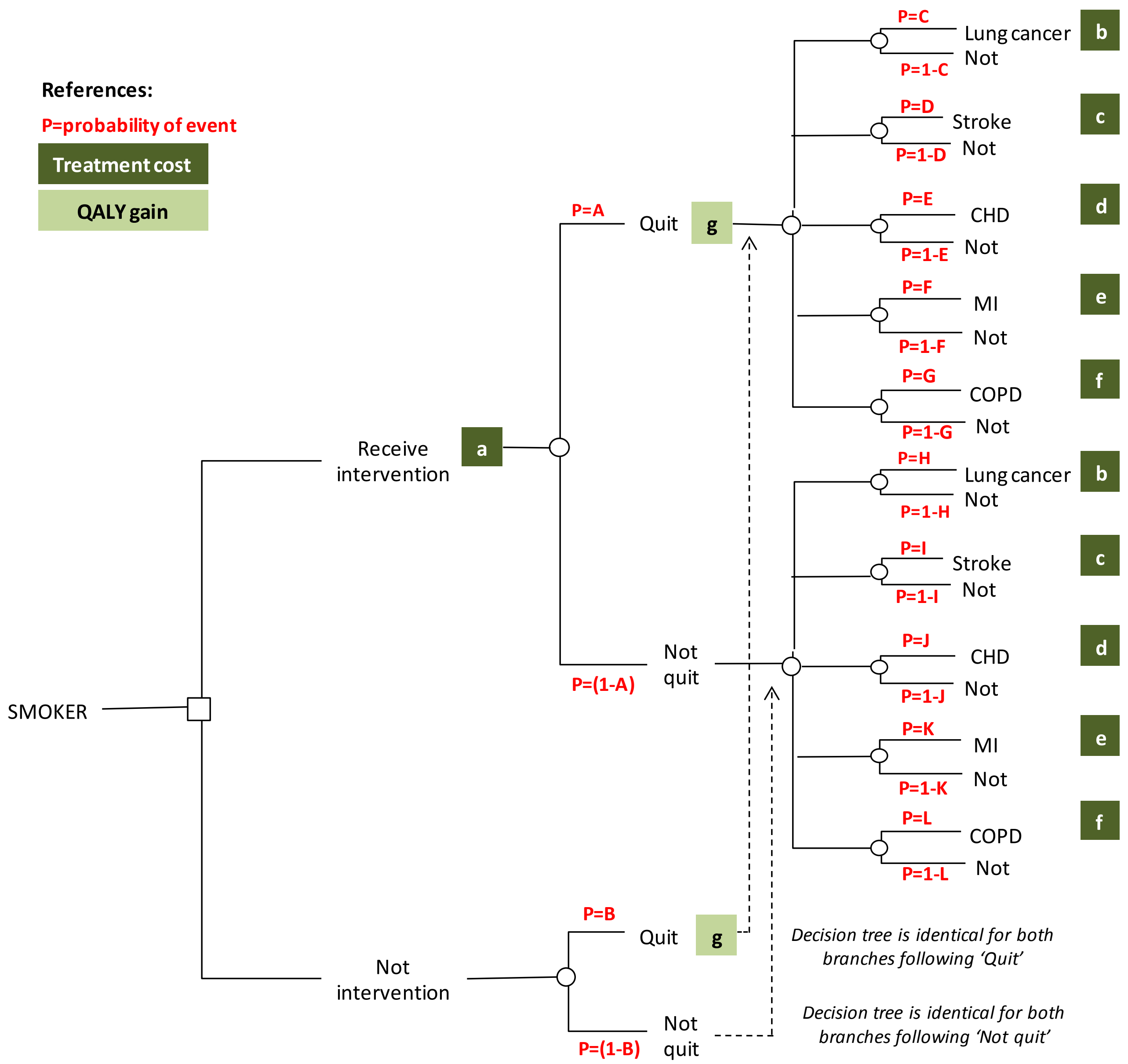
[1] Cost associated with increased life expectancy resulting from the intervention –such as pensions and health care costs– are not included in the analysis.

Decision model

An economic model was built to estimate the cost-effectiveness of the intervention. The model estimates the QALY gain and cost savings associated with the intervention. Figure 1 illustrates the structure of the model, which is based on the following assumptions:

- The effect of the intervention is given by a change in the chances of an individual's quitting smoking.
- Individuals receiving the intervention are assumed to be 45 years old on average.
- Smoking is assumed to be associated with five diseases: lung cancer, stroke, coronary heart diseases (CHD), myocardial infarction (MI) and chronic obstructive pulmonary disease (COPD). These diseases have impacts in terms of quality of life and health care costs.
- The probabilities of experiencing these diseases vary for smokers and former smokers. Former smokers have reduced probabilities of experiencing the diseases. Thus, quitting smoking reduces the probability of experiencing these diseases and produces corresponding improvements in quality of life and health care cost savings.

Figure 1. Smoking cessation model



Unless stated otherwise, the analysis was undertaken in accordance with H.M. Treasury's Green Book (HM Treasury, 2003). Specifically:

- Any costs and effects incurred more than one year after the intervention were discounted at 3.5%.
- Where necessary monetary values were converted in 2007/8 prices using Gross Domestic Product (GDP) deflators (HM Treasury, 2008).
- Where necessary monetary values were converted into pounds sterling using: www.x-rates.com

The model draws the following estimates from the literature:

- The unit cost of the intervention (Table 1).
- The effect of the intervention on people's smoking behaviour (Table 1).
- The probabilities that those who smoke experience diseases (Table 2).
- The probabilities that those who don't smoke experience diseases (Table 2).
- The impact of experiencing diseases on quality of life, measured in QALYs (Table 3).
- The impact of experiencing diseases on health care treatment costs (Table 3).

Table 1. Intervention costs and effects (monetary values in £2007/08)

Ref	Description	Value	Calculation and source
a	Cost of intervention	£57.3	Cost estimate calculated by Wang et al (2008). Includes GP advice/prescriptions (baseline visit plus six prescriptions spread over approximately 12 weeks) and drug provision (NRT provision plus pharmacy prescription charge).
A	P(if intervention, 12-month quit)	0.0186	This is the net effect of the intervention on those who attempt. It was calculated based on data provided by Wang et al (2008) as the difference between the quit rate among those who attempt an abrupt quit with NRT prescription only (0.0586) and the quit rate among those who attempt to quit with no NRT (0.04). The latter is assumed as the background quit rate, and thus subtracted from the quit rate associated with the intervention to obtain the net effect of the intervention. The reported quit rate associated with the intervention assumes a 21% relapse rate between 6 and 12 months' abstinence. The 21% relapse rate from 6 to 12 months was derived from the meta-analysis of 12 studies conducted by Stapleton and Stapleton (1998). See evidence review for additional details.
B	P(if no intervention, 12-month quit)	0.0000	Given that the effect of the intervention measures incremental quit rate, the probability of quitting for those not receiving the intervention is assumed zero.

Table 2. Transition probabilities

<table>
<tr><th>Ref</th><th>Description</th><th>Value</th><th>Calculation and source</th></tr>
<tr><td colspan="4">The probability of contracting the disease for (former) smokers was assumed to be equivalent to the average prevalence of the disease among (former) smokers. These were calculated for three different age groups: 55 to 64, 65 to 74, and 75 and older. The following formula was used in the calculation:

$$D = \frac{x}{t} \cdot D_x \cdot RR_x + \frac{y}{t} \cdot D_x \cdot RR_y + \frac{z}{t} \cdot D_x \cdot RR_z$$

where: D = prevalence of disease; RR = relative risk of contracting the disease; x = non-smokers; y = former smokers; z = smokers.; and t = total population.</td></tr>
<tr><td>C</td><td>P(if smoker, lung cancer) by age group</td><td>0.0045
0.0297
0.0329</td><td rowspan="2">These were obtained by applying the following parameters to the above formula:
• Prevalence of the disease in the total population by age group (D=0.0015; D=0.008; D=0.008).
• Relative risk of lung cancer among men (RR smokers=1; RR former smokers=0.44; RR non-smokers=0.03) and women (RR smokers=1; RR former smokers=0.21; RR non-smokers=0.05).
• Proportion of smokers in the general population by age group (z/t=0.195; z/t= 0.116; z/t=0.08).
• Proportion of former smokers in the general population by age group (y/t=0.367; y/t=0.419; y/t=0.469).
All data refers to the UK (Flack et al, 2007).</td></tr>
<tr><td>H</td><td>P(if former smoker, lung) cancer) by age group</td><td>0.0014
0.0087
0.0095</td></tr>
<tr><td>D</td><td>P(if smoker, stroke) by age group</td><td>0.0272
0.0961
0.1684</td><td rowspan="2">These were obtained by applying the following parameters to the above formula:
• Prevalence of the disease in the total population aged 65 to 74 years old (D=0.022; D=0.076; D=0.133).
• Relative risk of stroke (RR smokers=1.37; RR former smokers=1.11; RR non-smokers=1).
• Proportion of smokers in the general population by age group (z/t=0.195; z/t= 0.116; z/t=0.08).
• Proportion of former smokers in the general population by age group (y/t=0.367; y/t=0.419; y/t=0.469).
All data refers to the UK (Flack et al, 2007).</td></tr>
<tr><td>I</td><td>P(if former smoker, stroke) by age group</td><td>0.0220
0.0778
0.1365</td></tr>
<tr><td>E</td><td>P(if smoker, CHD) by age group</td><td>0.2149
0.4564
0.5771</td><td>These were obtained by applying the following parameters to the above formula:
• Prevalence of the disease in the total population aged 65 to 74 years old (D=0.111; D=0.215; D=0.264).
• Relative risk of CHD (RR smokers=3.12; RR former smokers=1.55; RR non-smokers=1).</td></tr>
</table>

<table>
<tr><th>Ref</th><th>Description</th><th>Value</th><th>Calculation and source</th></tr>
<tr><td>J</td><td>P(if former smoker, CHD) by age group</td><td>0.1068
0.2267
0.2867</td><td>• Proportion of smokers in the general population by age group (z/t=0.195; z/t= 0.116; z/t=0.08).
• Proportion of former smokers in the general population by age group (y/t=0.367; y/t=0.419; y/t=0.469).
All data refers to the UK (Flack et al, 2007).</td></tr>
<tr><td>F</td><td>P(if smoker, myocardial infarction) by age group</td><td>0.0854
0.1644
0.1694</td><td rowspan="2">These were obtained by applying the following parameters to the above formula:
• Prevalence of the disease in the total population aged 65 to 74 years old (D=0.067; D=0.121; D=0.121).
• Relative risk of MI among men (RR smokers=1.6; RR former smokers=1.11; RR non-smokers=1) and women (RR smokers=2.76; RR former smokers=1.05; RR non-smokers=1).
• Proportion of smokers in the general population by age group (z/t=0.195; z/t= 0.116; z/t=0.08).
• Proportion of former smokers in the general population by age group (y/t=0.367; y/t=0.419; y/t=0.469).
All data refers to the UK (Flack et al, 2007).</td></tr>
<tr><td>K</td><td>P(if former smoker, myocardial infarction) by age group</td><td>0.0592
0.1141
0.1175</td></tr>
<tr><td>G</td><td>P(if smoker, COPD) by age group</td><td>0.0114
0.0578
0.1152</td><td rowspan="2">These were obtained by applying the following parameters to the above formula:
• Prevalence of the disease in the total population aged 65 to 74 years old (D=0.01; D=0.05; D=0.10).
• Relative risk of COPD among men (RR smokers=1; RR former smokers=0.84; RR non-smokers=0.68) and women (RR smokers=1; RR former smokers=0.96; RR non-smokers=0.92).
• Proportion of smokers in the general population by age group (z/t=0.195; z/t= 0.116; z/t=0.08).
• Proportion of former smokers in the general population by age group (y/t=0.367; y/t=0.419; y/t=0.469).
All data refers to the UK (Flack et al, 2007).</td></tr>
<tr><td>L</td><td>P(if former smoker, COPD) by age group</td><td>0.0103
0.0519
0.1034</td></tr>
</table>

Table 3. Associated outcomes (monetary values in £2007/08)

Ref	Outcome	Value	Calculation and source
All lifetime treatment cost calculations were based on the present value of the annual treatment cost through the expected duration of the disease. The duration of the disease was assumed to be given by the difference between the average onset and mortality ages for the disease. Three possible onset ages were considered: 60, 70 and 80 years old. Total treatment costs were discounted to the age of individuals receiving the intervention, which was assumed 45 years old, at a 3.5% annual rate.			
b	Lung cancer treatment cost by onset age of disease	£4,923 £3,490 £2,474	The annual treatment of lung cancer cost was estimated by Flack et al (2007) at £5,742 (in £2007/08). The mortality age was assumed to be equal to that for colon cancer and to increase with the onset age of the disease. As reported by Matrix (2006), the mortality ages assumed are: 64, 74 and 86 years old.
c	Stroke treatment cost by onset age of disease	£4,905 £2,101 £2,187	The annual treatment cost was estimated by Matrix (2006) at £2,194 (in £2007/08) based on data from the Department of Health. The average mortality was assumed to increase with the onset age of the disease. As reported by Matrix (2006), the mortality ages assumed are: 64, 72 and 84 years old.
d	CHD treatment cost by onset age of disease	£7,182 £4,547 £2,809	The annual treatment cost was estimated by Matrix (2006) at £1,511 (in £2007/08) based on data from the British Heart Foundation. The average mortality was assumed to increase with the onset age of the disease. As reported by Matrix (2006), the mortality ages assumed are: 72, 78 and 87 years old.
e	Myocardial infarction treatment cost by onset age of disease	£10,790 £6,831 £4,221	The annual treatment cost was estimated by Flack et al (2007) at £2,270 (in £2007/08) based on data from the Department of Health and the Health and Social Care Information Centre. The mortality age was assumed to be equal to that for CHD and to increase with the onset age of the disease. As reported by Matrix (2006), the mortality ages assumed are: 72, 78 and 87 years old.
f	COPD treatment cost by onset age of disease	£4,594 £2,908 £1,797	The annual treatment cost was estimated by Flack et al (2007) at £967 (in £2007/08) based on data from the National Clinical Guideline on Management of COPD. The mortality age was assumed to be equal to that for CHD and to increase with the onset age of the disease. As reported by Matrix (2006), the mortality ages assumed are: 72, 78 and 87 years old.
g	QALYs: 12 month quit	1.29	This is the number of QALYs gained associated with lifetime quitting based on the number of quitters at 12 months. It was estimated by Fiscella and Franks (1996) using the results from the Healthy People 2000 Years of Healthy Life research project (US). It implicitly assumes a 35% relapse rate.

Effectiveness evidence

A literature review was undertaken by Bazian to identify evidence on the effectiveness and cost-effectiveness of nicotine replacement therapy to improve quit rates. Further details are available on the evidence methods page of the ***H.E.L.P.*** website.

The review of the evidence on the effectiveness of nicotine replacement therapy to improve quit rates identified one review of studies. Table 4 provides the following details of the studies identified:

- Population
- Intervention
- Results

The review of the evidence on the cost-effectiveness of nicotine replacement therapy to improve quit rates identified one review of studies. Table 5 provides the following details of the studies identified:

- Population, intervention and model
- Perspective, discounting, inflation, cost year
- Utility/benefit
- Unit costs
- Efficiency

Table 6 and Table 7 provide a quality assessment of the effectiveness and cost-effectiveness studies. Further details are available on the quality appraisal methods page.

The following criteria were applied to select effectiveness evidence for undertaking the economic analysis:

- Location. Studies from the UK were preferred over studies from other locations.
- Population. Studies applied to the general population were preferred over studies applied to restricted population groups (e.g. pregnant women; individuals from specific communities/nationalities).
- Counterfactual. Studies for which the counterfactual intervention was ‘usual care’ or ‘do nothing’ in a UK setting were preferred over studies for which the counterfactual was different from ‘usual care’ or ‘do nothing’.
- Method. Studies using more rigorous design methods (e.g. randomised control trials or quasi experimental designs with regression models controlling for confounders) were preferred over studies using less rigorous design methods (e.g. before-after studies or simple correlation analysis).

Table 4. Effectiveness of nicotine replacement therapy to improve quit rates

Study reference	Population	Intervention	Results
Extract effectiveness results from p. 18 of HTA 'sustained abstinence outcomes based on IPD' as this MA was used in the cost-effectiveness modelling of cut-down- to-quit (CDTQ) programmes.			
Wang et al, 2008 ▪ systematic review	Smokers who are currently unable or unwilling to quit abruptly	*Intervention* ▪ NRT with gum or inhalator alone or as part of combination therapy (e.g. motivational support); results are reported with gum/inhalator combined and with each separately *Control* ▪ Placebo or no treatment, non-NRT drugs for smoking cessation, psychological interventions (motivational support) for quitting	Sustained abstinence for at least 6 months: 6.75% with intervention vs. 3.29% with control; RR 2.06 (95% CI 1.34 to 3.15)

Table 5. Cost-effectiveness of nicotine replacement therapy to improve quit rates

Study reference	Population, intervention and model	Perspective, discounting, inflation, cost year	Utility/benefit	Unit costs	Efficiency
HTA: 'Cut down to Quit' with NRT performed a systematic review of effectiveness and cost-effectiveness studies. No existing economic analyses of CDTQ were identified, so reviewers performed a de novo decision analytic model to estimate CE of making CDTQ with NRT available for smokers who were unwilling or unable to attempt an abrupt quit. Quit rates in the model are based on meta-analysis of patient-level data from 5 studies (these are extracted in the effectiveness sheet). This is a complex decision tree model with different base cases, several levels of complexity and assumptions. We report results from one aspect of the simple analysis, where the effects of a single smoker changing their intended pattern of smoking was considered (table 18)					
Wang et al, 2008 ▪ systematic review	Cut Down to Quit (licensed indication for NRTs in the UK) vs. placebo essentially indistinguishable in appearance and taste/smell from the NRT intervention. Decision tree model to assess cost-effectiveness of making NRT available in the context of a CDTQ programme. Details of decision tree - figure 14. p. 36 of HTA. Only therapy modelled was NRT - changes in habits of smokers using other therapies was not considered. Full range option: individual may or may not attempt to quit smoking, and if an attempt is made, this may be with or without NRT.	▪ Health sector perspective ▪ No adjustment for inflation ▪ QALY gain by age group discounted at 3.5% ▪ Cost year: GBP2006	Total QALYs gained by quitting (assumes LYGs occur at the end of life and a population average utility of 0.755 for >65 years) - discounted values (undiscounted): Age at quitting: ▪ <35: 2.22 (8.44) ▪ 35-45: 2.58 (7.36) ▪ 45-54: 2.14 (4.47) ▪ 55-64: 0.99 (1.455)	Total £104.96 *Breakdown* GP visits Initial visit (1@ £2.24 per minute) £6.72 scheduled scripts (6.3 of 10 collected) @ £2.24 =£14.11 Total £20.83 Follow-up drug provision for a year £84.12 Costs for different choices for individual smokers No attempt: 0 CDTQ with NRT OTC: 0 CDTQ prescription only: 104.96 CDTQ individual counselling: 153.79 CDTQ group counselling: 128.27	Cost per effect £7661/quit No attempt change to CDTQ prescription only (table 18 HTA) ▪ <35 years: £3451 ▪ 35-44 years: £2970 ▪ 45-54 years: £3580 ▪ 55-64 years: £7739

Study reference	Population, intervention and model	Perspective, discounting, inflation, cost year	Utility/benefit	Unit costs	Efficiency
	For attempts made with NRT, these could be abrupt or CDTQ and within each of these using: ▪ OTC NRT ▪ Prescription NRT ▪ A smoker's clinic (prescription NRT plus behavioural support) Outcome measure was expected lifetime QALYs; long time quitter was taken to be 12 months' sustained abstinence from smoking. Relapse could occur in successful long-term quitters after a number of years. Relapse rate of 21% between 6 and 12 months was applied. Estimation of cost-effectiveness was undertaken with differing levels of complexity: ▪ 'simple analysis': single smoker comparing each CDTQ option with each non-CDTQ option				

Study reference	Population, intervention and model	Perspective, discounting, inflation, cost year	Utility/benefit	Unit costs	Efficiency
	▪ 'mixed analysis' comparing single CDTQ option with mix of 'no attempt' and corresponding abrupt quit option ▪ 'full analysis' comparing a range of CDTQ options with full mix of non-CDTQ options Base case assumes that lower success rate for CDTQ compared with abrupt quit applies to all CDTQ attempts. The simple analysis (some results presented here) considered a single smoker considering joining a CTDQ programme.				

Table 6. Quality assessment for meta-analysis studies

Study reference	QA for meta-analysis			Score	Grading (++ 3; + 2; -1)
	Search and inclusion criteria?	Quant data each study?	Assessment of quality data?		
Wang et al, 2008	Yes	Yes	Yes	3	++

Table 7. Quality assessment for economic studies

Study reference	QA for economic studies						Score	Grading (++ 4-6; + 3; -0-2)
	All costs of intervention included?	Market values used for costs?	Perspective reported?	Sensitivity analysis?	Reports base year adopted?	Effectiveness data from RCT or MA?		
Wang et al, 2008	Yes	Don't know	Yes	Yes	Yes	Yes	5	++

References

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