Cost-effectiveness of e-cigarettes compared with nicotine replacement therapy in stop smoking services in England (TEC study): a randomised controlled trial

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# Abstract

Aim

To evaluate the cost-effectiveness of e-cigarettes as a smoking cessation aid used in routine stop smoking services in England.

Design

Cost-effectiveness analysis was performed from the National Health Service (NHS) and Personal Social Services (PSS) perspective for 12 months period and lifetime. Costs, including that of both treatments, other smoking cessation help and healthcare services, and health benefits, estimated from EQ-5D-5L and measured in quality-adjusted life years (QALYs), for the 12-month analysis, came from a randomised controlled trial. Lifetime analysis was model-based with input from both trial data and published secondary data sources. Cost-effectiveness was measured by an incremental cost-effectiveness ratio (ICER).

Setting

Three Stop-Smoking Service sites in England

Participants

Adult smokers (n=886) who sought help to quit in the participating sites

Intervention and comparator

An e-cigarette (EC) starter kit versus provision of nicotine replacement therapy (NRT) for up to three months, both with standard behavioural support. A total of 886 participants were randomised (439 in EC arm, 447 in NRT arm). Excluding one death in each arm, the one-year quit rate was 18.0% and 9.9%, respectively.

Measurements

Cost of treatments was estimated from treatment log. Costs of other smoking cessation help and healthcare services, and EQ-5D-5L were collected at baseline, six- and 12-month follow-ups. Incremental costs and incremental QALYs were estimated using regression adjusting for baseline covariates and their respective baseline values.

Findings

The ICER was £1,100 per QALY gained at the 12 months after quit date (87% probability below £20,000/QALY). Markov model estimated the lifetime ICER of EC to be £65 per QALY (85% probability below £20,000/QALY).

Conclusion

Using e-cigarettes as a smoking cessation aid with standard behavioural support in stop-smoking services in England is likely to be more cost-effective than using nicotine replacement therapy in the same setting.

Key words

e-cigarette; cost-effectiveness; smoking cessation; nicotine replacement therapy; life-time modelling; Markov model; stop smoking services; economic evaluation

# Introduction

In Great Britain, the prevalence of e-cigarette (EC) use in adults is approximately 6% of the adult population in 2017 [1]. The policy on EC varies internationally, and whether or not it should be promoted as a way to quit smoking remains a controversial issue [2].

The UK National Institute for Health and Care Excellence (NICE) guidance for Stop-Smoking Service (SSS) currently advises that ‘people who smoke should not be discouraged from switching to e-cigarettes, and as a result continue to smoke’ [3]. The evidence base is still developing and further research on effectiveness and cost-effectiveness of EC is needed to inform policy.

We conducted a two-group, pragmatic, multi-centre, individually randomised controlled trial (RCT) comparing EC with nicotine replacement therapy (NRT) within the English SSS (National Research Ethics Service approval 14/LO/2235). The protocol has been published previously [4] and the CO-validated 12-month sustained abstinence rate was 9.9% (SE 1.4%) in the NRT arm and 18.0% (SE 1.7%) in the EC arm [5]. The project has been published in full in Health Technology Assessment [6]. Here we present the analyses 1) to evaluate 12-month cost-effectiveness of EC comparing with NRT from a National Health Service (NHS) and Personal Social Services (PSS) perspective; 2) to observe if the participants spend more on smoking cessation due to EC; 3) to estimate lifetime cost-effectiveness of EC comparing with NRT from a NHS/PSS perspective.

# Methods

## Trial design

### Intervention and comparator

All participants were offered six weekly behavioural support sessions at their SSS as per standard practice, with the second session on the target quit date (TQD).

Participants in the NRT arm, the comparator, could choose two products and were free to switch products. The trial sites provided NRT products either directly or through a letter of recommendation (LOR) to use in local pharmacies (Details see supporting information). Direct provision was free of charge, while LOR imposed a prescription charge upon redeeming if not exempted. Supplies were provided for up to 3 months, as per usual practice and could be obtained through GP prescription after that.

The EC arm, the intervention, was provided with the ‘One Kit’ device and a 30ml bottle of e-liquid (18mg/ml nicotine). Due to the discontinuation of the original product, the One Kit 2016 was given to a small group of participants entering the trial at a later time (Device details see supporting information). Participants were instructed to obtain further e-liquid supplies themselves and advised on possible channels of purchase. Information sheets on how to operate the EC were also provided. One additional 10ml bottle of e-liquid could be requested if required.

The initiation of NRT or EC use started immediately after randomisation on TQD.

### Participants

Participants were recruited from three SSS sites in England. Smokers aged 18 or over, who sought help to quit and were able to read/write/understand English, were eligible for the trial. Those who were pregnant or breastfeeding, had a strong preference to use or not to use NRT or EC in their quit attempt, or were currently enrolled in other interventional research or currently using NRT or EC, were excluded. Written informed consent was obtained at baseline.

From May 2015 to January 2017, 886 participants were randomised (447 in the NRT arm and 439 in the EC arm). The median age was 41 (IQR: 33 to 51) in the NRT arm and 41 (IQR: 33 to 53) in the EC arm. Male represented 52% (228/439) of the EC arm and 52% (233/447) of the NRT arm. One death occurred before 6-month follow-up in the NRT arm and one death occurred before 12-month follow-up in the EC arm.

### Blinding

It was not possible to mask the allocation when conducting the cost-effectiveness analysis. However, the data were not accessed by the health economists before data lock, and the smoking cessation outcome data were only made available as an input to the model-based secondary analysis after the primary analysis was completed.

## Data collection

### Costs

All costs and expenses are presented in 2015/16 Sterling Pounds (£). Table S1 shows all the unit costs used in the analysis.

#### Treatment cost

Treatment costs consisted of training and delivery costs. Training for SSS advisors on EC use was a one-hour session delivered once at each site by two members of the research team. A total of 30 advisors attended the training. Each advisor was equipped with one demonstration ‘One Kit’ at a cost of £19.35 per kit including liquid and accessories. The advisors were costed at mid-point of NHS pay band 5 and 6. The two trainers were costed at NHS pay band 6. Including salary oncosts, overheads and capital, the cost was estimated at £37 per hour for advisors and £42 per hour for trainers [7]. We assumed that all advisors had received routine training in behavioural support and NRT use on the job so these costs only applied to the EC arm and the NRT arm did not require extra training.

For treatment delivery, attendance of weekly support sessions and the provision of NRT, LORs or EC was recorded at each session. We assumed that all LORs issued would be redeemed therefore the cost of prescribed NRT products incurred. NRTs were costed at their weighted average net ingredient cost (NIC) per prescription item by form and dosage plus dispense fee [8, 9]. The cost of EC and e-liquid provided by the study, and the printing cost of EC leaflets and pharmacy lists were recorded by the research team. Only the sessions attended and EC or NRT issued on record were costed.

#### Smoking cessation help costs and health care services costs outside of the trial

Smoking cessation and other health care services utilisation and quantities outside of the trial was collected through self-reported questionnaire at baseline, six- and 12-month follow-up for the previous six-month period. Quantities were then multiplied by the unit costs of the services or weighted average NIC plus dispensing fee of prescribed items using secondary data sources [7-13].

#### Participants’ expenses on smoking cessation

EC purchasing expenses (including refills), NRT over-the-counter, and prescription charges were estimated in both arms based on self-reported data collected at baseline, six- and 12-month follow-ups. NRT over-the-counter expenses were estimated using the quantities of the products multiplied by the NIC plus dispensing fee [8, 9]. EC expenses were reported in monetary terms. The prescription charges were costed at £8.2 per item where applicable [14].

### Quality-adjusted life years (QALYs)

The 5-level EuroQol 5-dimension (EQ-5D-5L) questionnaire was used to measure health-related quality of life at baseline, six and 12 months [15]. It consists of five domains (mobility, self-care, usual activities, pain/discomfort, anxiety/depression), each with five levels of severity ranging from no problem to severe problem, and a Visual Analogue Scale (EQ VAS) ranging from 0-100 with a higher score reflecting better health on the day. Following the NICE statement on valuation set at the time of the analysis, the recommended mapping function was used to calculate utility values [16, 17]. QALYs were then derived by calculating the area under the curve from baseline to six months and six to 12 months [18].

## Missing data

Missing data at baseline and follow-ups were handled by multiple imputation following Rubin’s rules, assuming missing at random [19]. The imputation was performed by treatment arms. The imputation model included variables: training cost, intervention delivery costs, smoking cessation help costs, pharmacotherapy costs, health care services use costs and EQ-5D (VAS and utility values) at baseline, six- and 12-month follow-ups, age, gender, ethnicity, study site, Fagerström Test of Cigarette Dependence (FTCD) at baseline, entitlement of free prescriptions, expenses on NRT over-the-counter, EC purchase, and prescription charges. A chained equation model was developed and predictive mean matching was used as the imputation method, using the 10 nearest neighbours to the prediction as a set to draw from. As a rule of thumb, the number of imputations was set to approximately the highest percentage of missing data in all variables [20]. Costs and QALYs of those who died were replaced with zero after the date of death.

Since smoking cessation outcomes were not revealed to health economists before the completion of the primary analysis, the cessation rate at 12 months after quit date was not imputed with other variables. Those who were lost to follow-up or had no CO reading were classified as smoking and those who died were excluded in the calculation.

## Primary analysis

The analysis was undertaken according to a pre-specified analysis plan [21]. The primary analysis was an incremental cost-effectiveness analysis on an intention-to-treat basis from a NHS and PSS perspective in the 12-month trial period [22]. The total costs consisted of treatment cost and the costs to the SSS and NHS (smoking cessation services cost outside of the trial and health care services use costs) during the 12-month period. The difference in costs between arms was estimated by a generalised linear regression model controlling for the costs to the SSS and NHS at baseline, age, gender, study site, entitlement of free prescriptions, and FTCD at baseline. The effectiveness was presented in terms of QALYs, the difference in which was estimated by a generalised linear regression model controlling for utility value at baseline, age, gender, study site, entitlement of free prescriptions, and FTCD at baseline. By dividing the difference in total costs by the difference in QALYs, an incremental cost-effectiveness ratio (ICER) was calculated to measure the additional cost per QALY gained by EC, compared with NRT. It was then measured against the NICE recommended willingness-to-pay (WTP) threshold of £20,000 and £30,000 per QALY gained [22]. Neither costs nor QALYs were discounted as they were collected within one year.

The uncertainty surrounding the ICER was assessed through a non-parametric bootstrap re-sampling technique [23]. Bootstrap randomly drew individuals from the original sample by arm to construct a slightly different replicate sample with the same sample size. Each bootstrap iteration then estimated the incremental costs and QALYs based on the replicate sample of that iteration. A cost-effectiveness plane (CEP) and cost-effectiveness acceptability curves (CEACs) was plotted with 5,000 bootstrapped estimates [24].

## Secondary analyses

To assess the impact of imputation, a complete case analysis (CCA) was undertaken using the same regression method in the primary analysis. Only the participants who had complete data on all variables in the regression model were included.

Presently, participants bore the whole financial burden of EC after the initial pack, while NRT could be acquired on prescription for a longer period. To assess if provision of a free starter kit for smoking cessation shifts the later cost burden to smokers, participants’ expenses on smoking cessation aids were estimated and compared descriptively between arms.

A Markov model used in a previous trial was updated and used to project long-term costs and effectiveness [11]. Figure 1 illustrates the three-state model structure: smoker, ex-smoker and death. The arrows between states indicate the possible pathways of transition and their direction. The model simulated a cohort of 1,000 smokers who were assigned to the states proportionally according to the one-year quit rate from trial results at the end of the first cycle of the model. An annual relapse rate of 10% was applied for the following 10 years and abstinence was assumed to be permanent after that [25-27].

Death occurred during the trial were used to estimate the mortality rate of the first cycle. The long-term mortality rates were obtained from the Deaths registered in England and Wales in 2016 by the Office for National Statistics, adjusted for the increased risk for smokers and ex-smokers based on the Doll’s British doctors’ study [28, 29]. The model then ran on one-year cycles until the survivors reached their 90th year, which could be considered a lifetime horizon. It was assumed that no attempt to quit was made in the modelling period.

The total costs and QALYs estimated from the trial were taken as costs and effectiveness input for the first cycle of the model. Table 1 shows the model inputs after the first cycle estimated from various literature [25, 29-32]. The model took into account the lifetime incidence of smoking-related diseases and the costs of secondary care for treating smoking-related diseases. Patients’ utilisation of hospital inpatient care were derived from Hospital Episode Statistics [33] and combined with the NHS reference costs [12] to calculate the annual costs of secondary care for smoking-related diseases by age and gender. Using the methods introduced by the World Health Organisation Economics of Tobacco Toolkit [34], the costs attributable to smoking for smokers and ex-smokers were estimated by multiplying the calculated annual costs for smoking-related diseases by their respective smoking-attributable proportion (Equation 1). These attributable costs formed the long-term cost inputs after the first cycle of the model.

(Equation 1)

where

pcur/ pex =smoking prevalence / proportion of ex-smokers

rcur / rex =increased risk for having smoking-related diseases for current /ex-smokers compared to people who never smoked

The annual QALYs were derived from the EQ-5D utility values based on a study of Health Survey for England data with a sample size of 13,241 [30]. Both costs and QALYs were discounted at a yearly 3.5% rate beyond 12 months after randomisation [22].

[Insert Figure 1 here]

[Insert Table 1 here]

The model reported a lifetime ICER of a one-off use of EC, compared with NRT, as smoking cessation aid in English SSS setting from the NHS and PSS perspective. For a probabilistic sensitivity analysis, beta distribution was assigned to parameters for probabilities and gamma distribution to those for costs and QALYs. Monte Carlo simulation was used to randomly draw values for the parameters from their assigned distribution and the expected values of costs and QALYs were calculated. The process was repeated 10,000 times and the results were presented by CEP and CEACs.

All analyses were undertaken using STATA SE 15.0, except that the Markov model was programmed in Microsoft Excel 2016.

# Results

## Treatment cost

The training cost amounted to £4.40 per participant for the EC arm and zero cost for the NRT arm.

Session 1 and 2 lasted for 30 minutes each and the following sessions were estimated at 20 minutes. The cost of behavioural support sessions was £80 (SD £12) per participant in the EC arm (mean number of sessions: 5.5, SD 1.0) and £77 (SD £15) per participant in the NRT arm (mean number of sessions: 5.2, SD 1.2). Information sheets for the use of EC costed £0.09 per participant and pharmacy lists for redeeming NRT costed £0.05 per participant. LOR was £0.01 each and issued in total 732 times. Forty-two participants in the EC arm were given One Kit 2016, at £30.54 per kit. One participant did not accept the kit. Thirty participants requested an extra bottle of e-liquid costed at £1.34 each. The mean cost of products was £20 (SD £4) per participant in the EC arm, and £124 (SD £67) per participant in the NRT arm. The delivery cost was therefore £100 (SD £13) per participant in the EC arm and £201 (SD £77) per participant in the NRT arm.

## Missing data

In the NRT arm, 59% (265/447) participants completed health service use section of six-month follow-up questionnaire, and in the EC arm, 69% (304/439) participants did so (Pearson’s chi-squared test P=0.002). This rate at 12-month follow-up was 62% (277/447) in the NRT arm and 71% (312/439) in the EC arm (Pearson’s chi-squared test P=0.004). The missing data pattern showed that most missed the entire section rather than single items (Table S2 & S3). The cost, expenses and EQ-5D-5L variables at six- and 12-month follow-ups all required imputation. The highest level of the missing data was 35% at six months (Table S4). The number of imputation was therefore set to 35. Unless otherwise specified, analyses were performed on the 35 imputed datasets.

## Primary analysis

Table 2 (left) summarises the results of the primary analysis. The mean cost of treatment was £201 (SE £4) per participant in the NRT arm and £105 (SE £1) in the EC arm. The mean total costs were £1,116 (SE £163) in the NRT arm and £1,174 (SE £147) in the EC arm during the 12-month trial period. After adjustment, the mean total costs in the EC arm was £11 (95% CI -£104 to £147) higher than in the NRT arm. The mean QALYs in the NRT arm was 0.882 (SE 0.009) and 0.886 (SE 0.008) in the EC arm. After adjustment, the mean QALYs in the EC arm was 0.010 (95% CI -0.003 to 0.023) higher than in the NRT arm. The ICER was calculated at £1,100 per QALY gained, indicating that compared with the NRT arm, EC arm spent an extra £1,100 to yield an additional QALY per person. If the decision maker is willing to pay £1,100 and above for an additional QALY per person, the EC treatment would be considered as the cost-effective option.

[Insert Table 2 here]

Figure 2 (upper) shows the CEP and CEACs constructed with bootstrapped replicates. The overall majority (93%) of them fell on the right of the Y-axis on the CEP, indicating a highly likely effective intervention while the existence of difference in costs was less certain. However, most of the replicates fell below the WTP thresholds, suggesting the EC was likely to be more cost-effective than the NRT. The CEACs further illustrated this point by estimating the probability of EC being cost-effective in comparison with NRT to be 87% at £20,000/QALY and 90% at £30,000/QALY.

[Insert Figure 2 here]

## Secondary analyses

### Complete case analysis

Table 2 (right) summarises the results of the CCA which was undertaken on 254/439 (58%) participants in the EC arm and 204/447 (46%) in the NRT arm. The treatment cost was £216 (SD £73) per participant in the NRT arm and £108 (SD £10) in the EC arm. After similar adjustment as the primary analysis, the incremental costs became negative, suggesting a cost saving in the EC arm. The adjusted mean difference in QALYs was 0.003 (95% CI -0.018 to 0.023), with the EC arm slightly higher. The mean ICER indicated a dominance situation where the EC arm was less costly but more effective. Figure 2 (lower) shows that the difference in QALYs became more uncertain while the overall majority (86%) fell below zero for the difference in costs. The probability of cost-effective was 75% at £20,000/QALY and 70% at £30,000/QALY. Table 3 compares the estimated mean costs to the SSS and NHS and mean EQ-5D-5L utility in the CCA with the primary analysis. Both arms indicated slightly higher mean costs to the SSS and NHS but the difference in the NRT arm was more prominent. Mean utility in the CCA appeared consistently higher than in the primary analysis in the NRT arm.

[Insert Table 3 here]

### Comparison of Participants’ Expenses on smoking cessation between arms

The mean expenses on smoking cessation aids were £158 (SE £27) per participant in the NRT arm in the 12 months post-TQD, including £89 (SE £26) for NRT, £49 (SE £6) for EC, and £20 (SE £2) for prescription charge. During the same period, the mean expenses were £168 (SE £11) in the EC arm, including £12 (SE £5) for NRT, £152 (SE £10) for EC, and £4 (SE £2) for prescription charge.

### Long-term model

The cohort of 1,000 people entered the model at the age of 41. The mean lifetime smoking-attributable costs were estimated at £3,175 (SE £161) per smoker who used NRT as cessation aid and £3,184 (SE £169) per smoker who used EC. The mean QALYs were estimated at 24.14 (SE 0.31) per person who used NRT and 24.28 (SE 0.31) per person who used EC. The ICER was calculated at £65 per QALY gained by using EC as smoking cessation aid, in comparison with NRT. Figure 3 shows the life-time CEP and CEACs constructed from the probabilistic sensitivity analysis. It indicated that the lifetime costs were likely to be similar between using EC and NRT but the EC intervention resulted in a positive QALY gain with high certainty. The probability of EC being more cost-effective than NRT remains at 85% at £20,000 and £30,000 per QALY WTP threshold.

[Insert Figure 3 here]

# Discussion

The mean treatment cost was £201 (SE £4) per participant in the NRT arm and £105 (SE £1) in the EC arm. The 12-month ICER in the primary analysis was £1,100 per QALY gained from a NHS and PSS perspective, with the probability of cost-effective being 87% at £20,000 and 90% at £30,000 WTP thresholds. The CCA suggested the effect of missing data was more prominent in the NRT arm, possibly due to the lower completion rate, which renders the estimates of the NRT arm in the primary analysis less certain. The long-term modelling estimated a lifetime ICER at £65 per QALY gained, with a probability of 85% that EC is more cost-effective at both £20,000 and £30,000 per QALY gained. This indicated EC as a highly cost-effective cessation aid, compared with NRT, as part of the English SSS, from the NHS and PSS perspective. The comparison between participants’ expenses on smoking cessation between arms showed no apparent difference, while the costs of smoking cessation borne by the SSS and NHS were lower in the EC arm. This suggested that the EC intervention could potentially reduce the costs to the SSS and NHS without increasing the financial burden on smokers’ part.

The sample size of 886 reduced the possibility of random individuals with particularly high health care use being allocated to one arm. However, 79% one-year follow-up rate, adding on the incomplete rate of health economic section, contributed to a 35% missing data level at the highest. Although multiple imputation and complete case analyses showed consistent conclusion, the high level of missing data makes it less certain as to how cost-effective the intervention really is and represents one of the limitations of the study. In addition, the six-month recall period for self-reported healthcare services use and comprehensive but long questionnaire could potentially cause recall bias.

We used the long-term model to evaluate the EC use in an appropriate time horizon for smoking cessation. It showed a favourable result of EC use mainly due to the significantly higher abstinence rate at 12 months post-TQD in the EC arm. However, the model did not take into account repeated attempts to quit nor the possible long-term effects of using EC on health and personal finance. There is a lack of evidence on user behaviour regarding EC and the impact of continuous use of EC on health in the long term. Whilst the costs of smoking-related diseases were better identified and estimated, the QALYs were derived from population tariff based on smoking status and were not disease-specific.

Our study provided the initial EC products at no costs to the participants, which is not common practice within SSS at present time. While the relevant policy change remains uncertain, people who want to quit might ask for advice on the use of EC. This requires staff in the SSS and NHS to be equipped with correct and sufficient information about the potential role of EC in aiding smoking cessation. Decision makers should also be aware that the implementation costs of EC treatment was not in the scope of our analysis but might add an influence if free provision of EC starter pack is incorporated in standard SSS.

Existing evidence suggests varenicline, as a smoking cessation aid, to be more cost-effective or even cost-saving comparing with bupropion and NRT [35-37]. While counselling is a cost-effective treatment for smoking cessation, it has been suggested that counselling plus NRT might be more cost-effective [38]. There are few published RCTs studying EC as a smoking cessation or reduction aid. Hartmann-Boyce and colleagues identified four [39, 40], none of which compared EC with NRT in the standard SSS settings. As far as we know, this is the first cost-effectiveness study comparing EC and NRT as alternative cessation aids as part of the SSS. The relative cost-effectiveness of varenicline and EC remains unstudied.

The provision of an EC starter pack, compared with using NRT, in a standard SSS for smoking cessation is cost-effective. There was no evidence in the trial to suggest the participants’ expenses on smoking cessation aids increased due to the initiation of EC. The long-term impact on cost-effectiveness requires further research on the possible health side-effects of EC.

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# Tables and Figures with legends

Table 1 Model inputs from the literature

|  |  |  |  |
| --- | --- | --- | --- |
| Parameters | Value (SE) | | Source |
| Annual probability of relapse | | | |
| In the 10 years after first cycle | 10.00% (3.06%) | | [25-27] |
| After 10 years after first cycle | 0% | | [25-27] |
| Mortality | | | |
| Male – age group | Continuing smokers | Ex-smokers |  |
| 35 - 44 | 0.24% (0.40%) | 0.18% (0.35%) | [28, 29] |
| 45 - 54 | 0.80% (0.40%) | 0.51% (0.73%) | [28, 29] |
| 55 - 64 | 1.94% (0.52%) | 1.24% (0.58%) | [28, 29] |
| 65 - 74 | 5.15% (0.82%) | 3.08% (0.59%) | [28, 29] |
| 75+ | 25.36% (2.04%) | 15.12% (1.14%) | [28, 29] |
| Female – age group | Continuing smokers | Ex-smokers |  |
| 35 - 44 | 0.14% (0.31%) | 0.11% (0.27%) | [28, 29] |
| 45 - 54 | 0.53% (0.33%) | 0.34% (0.59%) | [28, 29] |
| 55 - 64 | 1.30% (0.43%) | 0.83% (0.48%) | [28, 29] |
| 65 - 74 | 3.45% (0.68%) | 2.06% (0.49%) | [28, 29] |
| 75+ | 20.79% (1.90%) | 12.40% (1.05%) | [28, 29] |
| Annual smoking-related healthcare costs after the first year | | | |
| Male – age group | Continuing smokers | Ex-smokers |  |
| 35 - 44 | £54.48 (£0) | £16.57 (£0) | [12, 32, 33] |
| 45 - 54 | £54.48 (£0) | £16.57 (£0) | [12, 32, 33] |
| 55 - 64 | £181.97 (£0) | £64.99 (£0) | [12, 32, 33] |
| 65 - 74 | £315.75 (£0) | £83.82 (£0) | [12, 32, 33] |
| 75+ | £535.22 (£0) | £105.36 (£0) | [12, 32, 33] |
| Female – age group | Continuing smokers | Ex-smokers |  |
| 35 - 44 | £41.31 (£0) | £10.72 (£0) | [12, 32, 33] |
| 45 - 54 | £41.31 (£0) | £10.72 (£0) | [12, 32, 33] |
| 55 - 64 | £119.83 (£0) | £40.95 (£0) | [12, 32, 33] |
| 65 - 74 | £249.03 (£0) | £71.25 (£0) | [12, 32, 33] |
| 75+ | £470.69 (£0) | £103.18 (£0) | [12, 32, 33] |
| Annual QALY gain after the first year | | | |
| Male – age group | Continuing smokers | Ex-smokers |  |
| 35 - 44 | 0.889 (0.007) | 0.908 (0.005) | [30] |
| 45 - 54 | 0.841 (0.007) | 0.861 (0.005) | [30] |
| 55 - 64 | 0.780 (0.008) | 0.803 (0.005) | [30] |
| 65 - 74 | 0.756 (0.008) | 0.781 (0.006) | [30] |
| 75+ | 0.710 (0.009) | 0.737 (0.006) | [30] |
| Female – age group | Continuing smokers | Ex-smokers |  |
| 35 - 44 | 0.870 (0.007) | 0.889 (0.004) | [30] |
| 45 - 54 | 0.830 (0.007) | 0.850 (0.005) | [30] |
| 55 - 64 | 0.763 (0.008) | 0.784 (0.005) | [30] |
| 65 - 74 | 0.751 (0.008) | 0.773 (0.006) | [30] |
| 75+ | 0.676 (0.009) | 0.700 (0.007) | [30] |

Table 2 Incremental cost-effectiveness analysis for the primary analysis (left) and the complete case analysis (right)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Primary analysis | | Complete case analysis | |
|  | NRT (n=447) | EC (n=439) | NRT (N=204) | EC (N=254) |
| Costs during the trial period | Mean (SE) | | Mean (SD) | |
| Treatment cost | £201 (£4) | £105 (£1) | £216 (£73) | £108 (£10) |
| Smoking cessation costs | £77 (£13) | £48 (£11) | £71 (£165) | £46 (£190) |
| Health care costs | £839 (£162) | £1,022 (£147) | £1,051 (£4,611) | £1,110 (£3,018) |
| Total costs during the trial period | £1,116 (£163) | £1,174 (£147) | £1,339 (£4,616) | £1,264 (£3,031) |
| Incremental costs, mean (95% CI) | | | | |
| Adjusted difference in total costs during the trial period | £11 (-£104 to £147) | | -£96 (-£304 to £81) | |
| Quality of life during the trial period | Mean (SE) | | Mean (SD) | |
| QALYs | 0.882 (0.009) | 0.886 (0.008) | 0.893 (0.162) | 0.883 (0.170) |
| Incremental QALYs, mean (95% CI) | | | | |
| Adjusted difference in QALYs | 0.010 (-0.003 to 0.023) | | 0.003 (-0.018 to 0.023) | |
| Incremental cost-effectiveness ratio (ICER), mean (Uncertainty) | | | | |
| ICER at 12 months post quit date | £1,100 per QALY gained (Figure 2 upper left Cost-effectiveness plane) | | EC dominant (less costly, more effective) (Figure 2 lower left Cost-effectiveness plane) | |

Table 3 Comaprison of costs to the NHS and EQ-5D-5L utility values between the imputed data and the complete case

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Analysis | | | NRT | | EC | |
|  | | | n | Mean | n | Mean |
| Costs to the SSS and NHS | | | | | | |
|  | In the 6 months before trial | | | | | |
|  | | Imputed (SE) | 447 | £645 (£109) | 439 | £539 (£62) |
|  | | Complete case (SD) | 204 | £688 (£2,811) | 254 | £593 (£1,490) |
|  | In the 12 months trial period | | | | | |
|  | | Imputed (SE) | 447 | £915 (£163) | 439 | £1,069 (£147) |
|  | | Complete case (SD) | 204 | £1,123 (£4,621) | 254 | £1,156 (£3,032) |
| EQ-5D-5L utility | | | | | | |
|  | Baseline | | | | | |
|  | | Imputed (SE) | 447 | 0.878 (0.008) | 439 | 0.868 (0.009) |
|  | | Complete case (SD) | 204 | 0.885 (0.162) | 254 | 0.868 (0.193) |
|  | Six months | | | | | |
|  | | Imputed (SE) | 447 | 0.882 (0.011) | 439 | 0.888 (0.010) |
|  | | Complete case (SD) | 204 | 0.897 (0.198) | 254 | 0.882 (0.199) |
|  | Twelve months | | | | | |
|  | | Imputed (SE) | 447 | 0.887 (0.011) | 439 | 0.898 (0.011) |
|  | | Complete case (SD) | 204 | 0.893 (0.205) | 254 | 0.900 (0.202) |

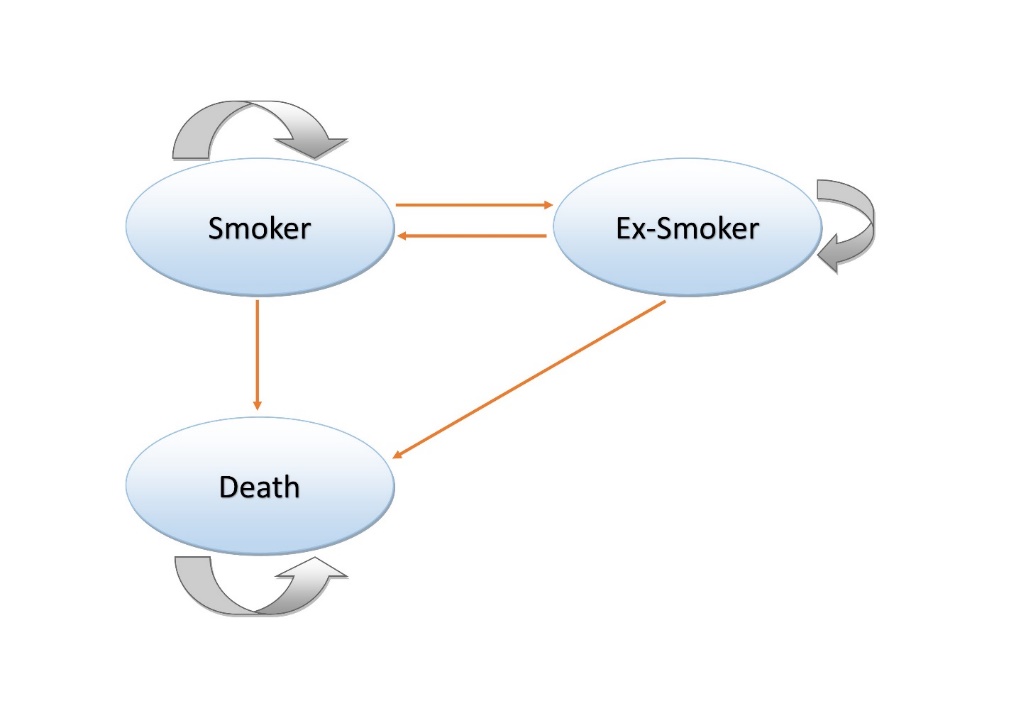


Figure 1 Schematic representation of Markov model



Figure 2 Cost-effectiveness plane and cost-effectiveness acceptability curve for the primary analysis (upper) and complete case analysis (lower)

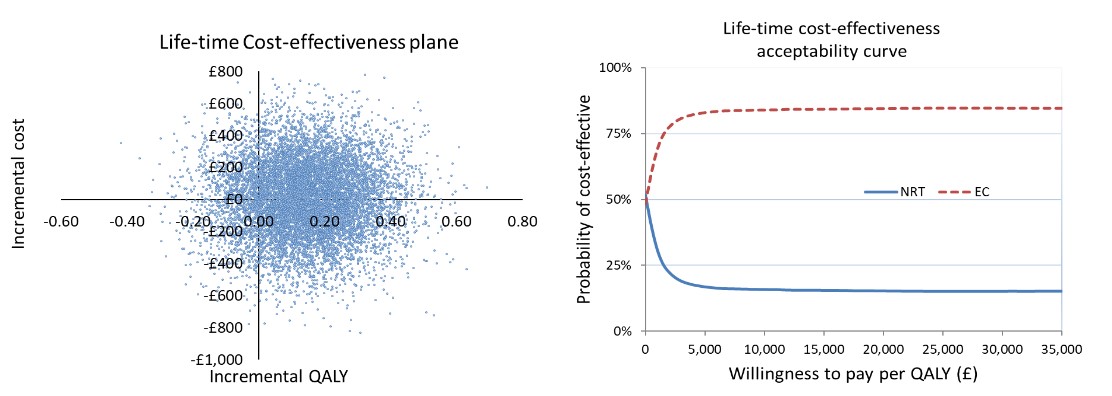


Figure 3 Life-time cost-effectiveness plane and cost-effectiveness acceptability curve