Cost-utility analysis of provision of e-cigarette starter kits for smoking cessation in emergency departments: an economic evaluation of a randomised controlled trial

Cost-effectiveness of COSTED

Jinshuo Li[1], Qi Wu[1], Steve Parrott[1], Ian Pope[2], Lucy V Clark[3], Allan Clark[3], Emma Ward[4], Pippa Belderson[4], Susan Stirling[3], Timothy J Coats[5], Linda Bauld[6], Richard Holland[7], Sarah Gentry[4], Sanjay Agrawal[8], Benjamin M Bloom[9], Adrian Boyle[10], Alasdair Gray[11], M Geraint Morris[12], Jonathan Livingstone-Banks[13], Caitlin Notley[4]

[1] Department of Health Sciences, University of York, York, UK

[2] Norfolk and Norwich University Hospital, Norwich, UK

[3] Norwich Clinical Trials Unit, Norwich Medical School, University of East Anglia, Norwich, UK

[4] Norwich Medical School, University of East Anglia, Norwich, UK

[5] Department of Cardiovascular Sciences, University of Leicester, Leicester, UK

[6] Usher Institute and SPECTRUM Consortium, College of Medicine, University of Edinburgh, UK

[7] Medical School, University of Leicester, Leicester, UK

[8] University Hospitals of Leicester NHS Trust, Leicester, UK

[9] Royal London Hospital, Barts NHS Trust, London, UK

[10] Addenbrookes Hospital, Cambridge University Hospitals Foundation Trust, Cambridge, UK

[11] Royal Infirmary Edinburgh, NHS Lothian, Edinburgh, UK

[12] Homerton University Hospital NHS Trust, London, UK (MG Morris MBBS)

[13] Nuffield Department of Primary Care Health Sciences, Oxford, UK (J Livingstone-Banks PhD)

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ABSTRACTS

Aims

To assess the cost-effectiveness of the Cessation of Smoking Trial in Emergency Department (COSTED) intervention compared with signposting to local stop smoking service (SSS) from the National Health Service (NHS) and personal social services (PSS) perspective.

Design

A two-group, multi-centre, pragmatic, individually randomised controlled trial.

Setting

Six Emergency Departments (EDs) in urban and rural areas in the UK.

Participants

Adult (≥18 years) daily smokers (≥1 cigarette or equivalent per day) but not daily e-cigarette users, with carbon monoxide reading ≥8ppm, attending the ED (n=972).

Intervention and comparator

The intervention consisted of provision of an e-cigarette starter kit plus brief smoking cessation advice, and referral to a local SSS. Control was an information card on how to access local SSS.

Measurements

Intervention costs included costs of training and delivery. Control costs included costs of printing information cards. Costs of smoking cessation and healthcare services were estimated based on quantities reported by participants and unit costs extracted from secondary sources. The effects were measured by quality-adjusted life years (QALYs) derived from EQ-5D-5L. Other outcomes were smoking cessation measures. The primary outcome was incremental cost-effectiveness ratio (ICER), which was calculated by dividing the difference in costs by the difference in QALYs between groups.

Findings

The mean intervention costs were £48 (standard error [SE] £0) per participant and the mean control costs were £0.2 (SE £0) per participant. Using regression estimates, total costs were £31 (95% confidence interval [CI] -£341 to £283) higher and 6-month QALYs were 0.004 (95% CI -0.004 to 0.014) higher in the intervention group than in the control group. The ICER was calculated at £7,750 (probability of cost-effective at range £20,000 - £30,000: 72.2% - 76.5%).

Conclusions

The UK Cessation of Smoking Trial in Emergency Department (COSTED) intervention (provision of an e-cigarette starter kit plus brief smoking cessation advice) was cost-effective compared with signposting to local stop smoking services under the current recommendations of the maximum acceptable thresholds.

Keywords: Smoking cessation, emergency department, e-cigarette, cost-effectiveness, economic evaluation, randomised controlled trial, brief intervention, lifetime modelling, Markov model

INTRODUCTION

The government set an objective for England in 2019 that the smoking prevalence is to be reduced to 5% or lower by 2030 (1). In 2022, 12.7% of adult population in England smoked cigarettes, which was the lowest figure since 2011 but still would miss the target for 2030 without further actions (2, 3). In the meantime, smoking continues to cost the NHS England £3 billion a year (4).

In April 2023, a national 'Swap to Stop' scheme was announced, offering a free vaping starter kit to a million smokers across England in partnership with Stop Smoking Service (SSS) (4). However, the number of people accessing SSS has seen a huge decline since 2012 (4). Emergency departments (EDs) routinely see large volume of patients (5) and these patients are more likely to be smoking (6). Previously, brief advice and nicotine replacement therapy (NRT) have been identified as efficacious in the ED settings (7), but the same could not be said for vaping.

To determine clinical and cost-effectiveness, the Cessation of Smoking Trial in the Emergency Department (COSTED) was conducted to compare the provision of an e-cigarette starter kit plus brief smoking cessation advice and referral to local SSS (intervention group) with signposting to local SSS (control group) in EDs (8). The 6-month biochemically-verified abstinence rate was 7.2% in the intervention group and 4.1% in the control group (relative risk 1.76 [95% CI 1.03 to 3.01], p=0.038) (9). This article presents the economic evaluation conducted alongside the trial to determine the cost-effectiveness from the UK National Health Service (NHS) and personal social service (PSS) perspective.

METHOD

Trial design

The COSTED trial was a two-group, multi-centre, pragmatic individually randomised controlled trial conducted in six UK EDs. Participants were eligible if they were adults (≥18 years), self-reporting daily smoking at least one cigarette verified by a Carbon Monoxide (CO) reading of ≥8ppm, and attending the ED for medical treatment or accompanying a patient attending the ED. Those who required immediate medical treatment, were in police custody, had a known history of allergy to nicotine, were currently using an e-cigarette daily, or did not have the capacity to consent, were excluded. If the patient and accompanying person were both eligible and consented to participate, the accompanying person was assigned to the same group that the patient was randomised. If only one of them was eligible and consented, the consented person was randomised (8). This procedure generated two samples: 1) the randomised participants; and 2) a broader sample including those non-randomised accompanying persons.

Participants in the intervention group were offered an e-cigarette starter kit plus brief smoking cessation advice and referral to local SSS. Participants in the control group were signposted to local SSS via a printed information card.

The randomisation was carried out on 1:1 ratio using a blocked design, stratified by site. The primary end point was 6 months post randomisation, with smoking status also collected at 1 and 3 months post randomisation.

Data collection

Costs

All monetary values are presented in 2021/22 pounds sterling.

Treatment costs. Intervention costs included staff training, CO-monitors, e-cigarette starter kits, and intervention delivery.

Training consisted of National Centre for Smoking Cessation and Training (NCSCT) e-learning (7.5 hours), one bespoke session for the intervention (3 hours), and one generic Smokefree Norfolk level 2 advisor training (2 hours). All training was delivered online. The bespoke session was delivered by two members of the research team. The Smokefree Norfolk training was delivered by two stop smoking advisors. The costs of staff time were valued using staff's respective salary plus salary on-costs. The hourly costs of the two research team members were £29.50 and £32.28 respectively. The hourly costs of stop smoking advisors was estimated as £18.01. Attendees were costed at band 4 hospital staff, whose hourly costs was £19.06 (10). The opportunity costs of time for training were calculated by multiplying staff hourly costs by the respective time spent.

Each site was equipped with one CO-monitor costing £150 and £30 worth of mouthpieces. Assuming a depreciation rate of 3.5% (11) over 5 years operating life with no resale value in the end and all mouthpieces consumed for the trial, the estimated costs of CO-monitors and accessories over the trial period were £276.30.

The e-cigarette starter kit (the DotPro by Liberty Flights) cost £7.71 for device and £15.44 for pods, including 5% bulk purchase discount and excluding 20% Value Added Tax (11). The opportunity costs of staff time for brief advice were calculated by multiplying the duration by band 4 hospital staff hourly costs. Participants were given a leaflet containing information on the intervention (£0.39) and a tote bag (£1.47).

The printing costs of the information card in the control group were £0.20 per card.

Smoking cessation support and healthcare services costs. The use of smoking cessation support and healthcare services were collected via a bespoke self-reported questionnaire as part of Case Report Form (CRF) at baseline and 6 months (Table 1) (10, 12-21).

Participants' spending on Nicotine Replacement Therapy (NRT) and e-cigarette. The quantities of NRT products participants bought and prices paid for e-cigarettes and accessories over the 6 months trial period were collected as part of CRF. The estimated prices of NRT products (Supplementary Information Table S1) were then applied to reported quantities.

Outcomes

Quality-adjusted life years (QALYs). EQ-5D-5L (22) was administered at baseline and 6 months. It consists of five domains that could be converted to a utility value and a Visual Analogue Scale (VAS) valuing the overall health on the day, ranging from 0 (worst imaginable) to 100 (best imaginable). QALYs were derived from the utility values at baseline and 6 months, following the area under the curve approach (23).

We originally planned to use the crosswalk mapping from EQ-5D-3L tariff to EQ-5D-5L responses (24), following the guidance from NICE on conversion of EQ-5D-5L utility values (25) at the time. However updated guidance has since been published recommending a new mapping approach (11) which we followed in our analysis (26).

Smoking cessation outcomes. CO-validated sustained abstinence (primary outcome of the trial) was defined as self-reported no more than 5 lapses at 6 months, biochemically validated by CO reading ≤7ppm (27). Self-reported sustained abstinence was defined as no more than 5 lapses reported by

participants at 6 months. Self-reported 7-day abstinence was defined as having smoked no cigarettes (not even a puff) in the past seven days, which was collected at 1, 3 and 6 months (8).

Analyses

Missing data

Missing values on all smoking cessation outcomes were considered as not abstinent (27). Missing data on other variables were handled following the methods proposed by Faria et al (28). Missing values in baseline covariates were imputed using the mean value of the variable of the full sample, as these were assumed unrelated to the treatments. Missing values in follow-up variables were dealt with using multiple imputation chained equation method, following Rubin's rule and assuming missing at random (MAR) (29). The imputation model included all variables necessary to the analysis or associated with missingness which were identified by univariate logistic regression or χ^2 test. Outcome variables were imputed using predictive mean matching, with the 10 closest neighbouring values to draw from (30). The imputation was performed separately by randomised groups and stratified by sites, augmented for perfect prediction. The number of imputations was set as approximately the highest percentage figure of missing data (30). Unless otherwise specified, all analyses were performed on the multiple imputed dataset.

Primary analysis

Using costs of treatments and smoking cessation support over the 6 months and CO-validated 6-month sustained abstinence, cessation costs per abstainer were calculated for both groups, along with incremental costs per additional abstainer. Total costs included costs of treatments, smoking cessation support and healthcare services. An incremental cost-utility analysis (CUA) was conducted using total costs and QALYs over the 6-month period. No discount was applied. Incremental costs and QALYs were estimated using generalised linear regression models, adjusting for demographic covariates, costs of smoking cessation and healthcare services before baseline and EQ-5D-5L utility at baseline respectively, and ED site. Incremental costs were divided by incremental QALYs to generate an incremental cost-effectiveness ratio (ICER) when the intervention group resulted in both higher costs and higher QALYs than the control group. The ICER was compared with the maximum acceptable thresholds of £20,000 to £30,000 per QALY gain (11).

Uncertainty was assessed using a non-parametric bootstrap re-sampling technique (31). The bootstrap and multiple imputation generated 5,000 pairs of estimates of incremental costs and effects to construct the 95% confidence intervals (CIs) for incremental costs and effects. A cost-effectiveness plane (CEP) was plotted to demonstrate the uncertainty of the ICER. Cost-effectiveness acceptability curves (CEACs) (9) were plotted to show the probability that the intervention is cost-effective at different thresholds.

Sensitivity analyses. Self-reported sustained smoking abstinence at 6 months was adopted to examine the impact of missing CO readings. Self-reported 7-day point prevalence abstinence at follow-ups was adopted to estimate costs per quitter at different timepoints and provide wider comparability with existing literatures.

To assess the impact of imputing missing data, a complete case analysis was conducted among the participants who had complete costs and QALYs at baseline and 6-month follow-up, and smoking status at 6 months, following the same method of the primary analysis. Sensitivity analyses using pattern mixture modelling were conducted to examine the MAR assumption for multiple imputation methods (28). Under the missing not at random (MNAR) assumption, it was assumed that those who

had missing outcome measures at 6 months were either in higher need of healthcare services or experiencing worse health, or both at the same time. To examine how MNAR assumptions would affect the results, the incremental estimates were re-estimated based on: 1) imputed costs increased by 10%, 20%, and 30%; 2) imputed utility at 6 months reduced by 10%, 20%, and 30%; 3) the combination of 1) and 2).

Secondary analyses

Participants' spending on NRT and e-cigarette. Difference in spending was estimated using generalised linear regression model, adjusting for demographic covariates, spending on e-cigarette at baseline and ED site. The uncertainty was presented using bootstrapped 95% CI.

Analysis on the broader sample. An incremental CUA was conducted following the same approach as the primary analysis, but on the broader sample including the non-randomised accompanying persons.

Long-term cost-effectiveness projection. As improved health and healthcare cost saving resulting from reduced risks of developing smoking related diseases (SRDs) due to quitting are likely to be reflected in the long run (32), time horizon of 6 months may fail to capture the full benefit of the intervention (33). A Markov model (34) was adapted to project lifetime impacts of the intervention compared to control. The model runs on 1-year cycle transitioning between smokers, ex-smokers and deaths, until a cohort of 1,000 smokers reach 90 years or death. The transition probabilities were estimated based on mortalities (35), relative risk (RRs) of death among smokers (32), natural quit rate and relapse rates (36, 37). Smoking-attributable costs (SACs) were estimated following smoking attributable proportion approach (38), based on RRs of SRDs (39), hospital admission episodes of SRDs (40) and matching inpatient costs by Hospital Resources Grouper (41), inflated to the analysis year (10). QALYs were estimated based on age, gender and smoking status (42). A discount rate of 3.5% per annum was applied to all costs and QALYs (11). A probabilistic sensitivity analysis was conducted using Monte Carlo simulation. Detailed description of the model and parameters are presented in Supplementary Information Long-term model description.

All analyses were undertaken following the pre-registered analysis plan (https://osf.io/gevch). All analyses adopted the NHS and PSS perspective, as per NICE guidance (11), except for participants' spending on smoking cessation aids. Participants were analysed in their allocated groups, following the intention-to-treat principle. The long-term model projection was performed in Microsoft Excel. Other analyses were performed in StataMP 18.0.

RESULTS

From January to August 2022, 972 participants were randomised to control group (n=488) or intervention group (n=484). The mean age was 40.5 (SD 13.7) years old in the control group, with 38.3% (187/488) female and 40.5 (SD 13.6) years old in the intervention group, with 37.6% (182/484) female (Supplementary Information Sample characteristics).

Treatment costs

Intervention costs

The training costs for the COSTED intervention were estimated at £6,690, equalling £14 per participant. One participant in the intervention group did not receive the e-cigarette. Five participants were not referred to local SSSs. The mean duration of intervention delivery was 25.7 minutes (SD 7.3 minutes). The mean intervention costs were £48 (SD £3) per participant (Table 2).

Control costs

All 488 participants in the control group were given the information card, making the mean control costs £0.20 (SD £0) per participant.

Missing data

The follow-up rate at 6 months was 65.0% (317/488) in the control group and 72.5% (351/484) in the intervention group (χ^2=6.4642, p=0.011). Most missing values were due to lost-to-follow up rather than individual items missing, leading to a higher level of missing values in the control group than in the intervention group (Supplementary Information Table S4). After examining the missing data (Supplementary Information Table S5 – S7), the multiple imputation model included the baseline covariates (age, gender, Fagerstrom Test of Cigarette Dependence (FTCD), other smokers in the household, reason for ED attendance, and ED site), outcome measures at baseline and 6 months (costs of smoking cessation advice, spending on e-cigarette, EQ-5D-5L utility and VAS), costs of healthcare services at baseline, and outcome measures at 6 months (CO-validated abstinence, costs of pharmacotherapies (NRT, varenicline and bupropion), costs of primary care services, costs of secondary care services, and spending on NRT). The number of multiple imputations was set as 45. For detailed information please see Supplementary Information Missing data.

Primary analysis

The CO-validated 6-month sustained abstinence rate was 4.1% (20/488, SE 0.9%) in the control group and 7.2% (35/484, SE 1.2%) in the intervention group. The mean costs of control were £0.2 (SE £0) and that of intervention was £48 (SE £0). The mean control and intervention costs per CO-validated sustained abstainer were estimated at £5 (SE £1) and £657 (SE £107), respectively. In addition, costs of smoking cessation help that was not provided by our study were £24 (SE £4) per participant in the control group and £16 (SE £4) per participant in the intervention group over the 6 months follow-up. Including these costs, the mean costs per CO-validated sustained abstainer increased to £597 (SE £164) in the control group and £876 (SE £151) in the intervention group. The incremental costs per additional abstainer for the intervention compared to control were £1,255 (95% CI £550 to £6,090).

The mean total costs per participant over the 6 months period were £1,651 (SE £276) in the control group and £1,408 (SE £171) in the intervention group (Table 3). The mean QALYs per participant over the 6 months period were 0.290 (SE 0.007) in the control group and 0.303 (SE 0.006) in the intervention group.

After adjusting for baseline covariates (age, gender, reason for ED attendance, FTCD, if other smoker(s) in household, and healthcare costs in the previous 3 months as fixed effects, and ED site as random effect), the mean total costs in the intervention group were £31 (95% CI -£341 to £283) higher than in the control group. After adjusting for baseline covariates (age, reason for ED attendance, FTCD, if other smoker(s) in household, and EQ-5D-5L utility at baseline as fixed effects, and ED site as random effect), the mean QALYs in the intervention group were 0.004 (95% CI -0.004 to 0.014) higher than in the control group. The intervention was more costly and more effective than control, with an ICER calculated at £7,750 per QALY gained. Most of the dots (representing bootstrapped ICERs) in Figure 1 (left) fell below the ICER threshold lines, indicating cost-effective. This is further demonstrated by Figure 1 (right), where the probability of the intervention being cost-effective between £20,000/QALY gain and £30,000/QALY gain was from 72.2% to 76.5%.

Sensitivity analyses

Other smoking cessation outcomes. Using self-reported outcomes, the sustained abstinence at 6 months was 13.1% (64/488, SE 1.5%) in the control group and 25.2% (122/484, SE 2.0%) in the intervention group, with the mean costs of control and intervention at £2 (SE £0) and £189 (SE £15) per abstainer respectively. Figure 2 illustrates the 7-day quit rate at 1, 3, and 6 months and the respective control/intervention costs per quit.

Complete case analysis. In total, 285 participants in the control group and 296 participants in the intervention group were included in the complete case analysis (Supplementary Information Table S8). Compared to the primary analysis, complete cases in both groups appeared healthier and incurred lower costs (Table 3). The adjusted incremental analysis showed the intervention was less costly but more effective than control, with higher uncertainty surrounding both estimates (Table 4). Supplementary Information Figure S2 illustrates this increased uncertainty, but the intervention remained likely to be cost-effective.

Analysis under MNAR assumptions. Scenario 1) and 2) showed that adjusted incremental costs decreased with the increase of imputed costs and adjusted incremental QALYs increased with the decrease of imputed utilities (Supplementary Information Table S9). Scenario 3) reported highest ICER at £5,217/QALY gain when both changed by 10% and lowest ICER at £1,765/QALY gain when both changed by 30% (Supplementary Information Figure S3).

Secondary analyses

Participants' spending on NRT and e-cigarettes

After adjusting for baseline covariates (age, gender, reason for ED attendance, deprivation index, FTCD, spending on e-cigarettes in the 3 months before baseline, and ED site), the mean spending on smoking cessation aids in the intervention group was £45 (95% CI £32 to £63) higher than in the control group (Supplementary Information Table S10).

Analysis of the broader sample

Thirty-five accompanying persons were allocated alongside randomised participants, with 14 (9 female) to control group and 21 (13 female) to intervention group. Table 3 shows slightly lower costs and higher QALYs in the broader sample. The adjusted incremental values were similar to those of primary analysis (Table 4). Supplementary Information Figure S4 illustrates the reduced probability of the intervention being cost-effective with these non-randomised participants included (£20,000-£30,000: 61.0%-64.8%).

Long-term projection

Supplementary Information Table S11 presents the input parameters estimated from the trial results. The estimated mean lifetime SACs and QALY gains of control and intervention were similar (Table 5). Compared to control, the intervention was £32 more costly per person but 0.029 QALYs more effective. The lifetime ICER was estimated at £1,131 per QALY gained. Increasing the threshold from £20,000 to £30,000 per QALY gain made little change of the probability of the intervention being cost-effective in the long-term (Figure 3).

DISCUSSION

While the control only comprised one information card, the COSTED intervention comprised multiple components, which led to an increased cost at £48 per participant compared to £0.2 in the control

group. This added complexity and cost were associated with more benefits, as the intervention resulted in a higher 6-month CO-validated sustained abstinence rate of 7.2%, compared to the 4.1% achieved with control. Consequently, the average costs per CO-validated sustained abstainer at the 6-month were £5 for control and £657 for the COSTED intervention. The intervention was more costly and more effective than control, with the ICER over the 6 months calculated at £7,750 per QALY (probability of cost-effectiveness between £20,000 and £30,000: 72.2% to 76.5%). The lifetime ICER was projected at £1,131 per QALY (probability of cost-effectiveness increased negligibly from 54.06% to 54.12% between £20,000 and £30,000).

From April to December 2022, the SSS statistics in England reported on average a cost of £797 per self-report quitter, ranging from £24 to £6,806, where data were available (43). The definition of quit adopted by the SSS is having not smoked at all in the last 2 weeks at 4 weeks after quit date, to which the closest measure for our intervention group is 7-day quit at 1 month. The estimated £245 per self-reported 7-day quitter only included the intervention costs because we did not collect smoking cessation costs outside of our study at 1 month. But considering the mean costs of smoking cessation outside of our study over 6 months were £16 (SE £4), our costs would appear comparable with the SSS.

Miller et al. (44) estimated the costs of interventions for quitting smoking set in ED in two studies in the USA. The brief negotiated interviewing + NRT was the most similar intervention to COSTED, both in participant contact time (31.9 minutes) and the format (brief interview and cessation aid). After inflating the costs from 2018 to December 2022 and converting to Pound Sterling (0.85 GBP = 1 USD) (45, 46), costs per quit of brief negotiated interviewing + NRT beyond usual care were approximately £1,846. The definition of the quit in the studies was CO-validated abstinence in the past 7 days at 3 months. The costs per 7-day abstinence at 3 months of our intervention beyond our control were very similar at £1,771, though this was based on self-reported outcome.

The probability of lifetime cost-effectiveness appears plateaued soon after willingness-to-pay increased from £0 per QALY. This was because in the long-term, the difference in SACs and QALYs between groups was estimated to be smaller, making the distribution of simulated pairs of incremental costs and QALYs almost symmetric surrounding the origin point, as shown on the CEPs. As willingness-to-pay increases, the simulated ICERs fluctuate above and below the thresholds in similar amount. The slight spread towards positive incremental QALYs resulted in probability appearing plateaued above 50%.

Participants' spending on e-cigarettes in the intervention group double the spending in the control group. This was expected and even encouraged - as the intervention only provided a starter kit of e-cigarette and information on where to purchase further supplies. To a population with a relatively deprived socio-economic status, decision to encourage people who smoke to adopt e-cigarette to quit should not be made lightly under current policies, whereby NRT offers alternative free of charge way of acquiring but e-cigarette does not. While suggestions could be made that switching from cigarettes to e-cigarettes could save money from buying fewer cigarettes (47), this would only be true if they manage to at least cut down smoking.

The biggest strength of our study was the large sample size with broad inclusion criteria and sites in several locations across UK with diverse population, enabling wider generalisability and avoiding differences between groups appearing by chance, especially in terms of costs. It also shows that EDs can provide a feasible setting for opportunistic smoking cessation interventions. To our knowledge this is the first large trial to test e-cigarettes for smoking cessation among ED attendees.

The most concerning issue was the imbalance of follow-up between groups, which led to higher uncertainty in estimates of the control group and in turn the ICER. Our analysis assumed intervention delivery by existing ED staff within their working schedule. However, in a busy ED environment staff might not have the capacity. As shown by Miller et al (44), there was considerable difference between using existing staff delivering the intervention among their multitude of other tasks, and hiring extra staff dedicated to the delivery of this intervention. Deploying staff from an in-hospital smoking cessation department or local SSS might be potential solutions, but these rely on the availability of those services. The results estimated in this article should not be taken for reference if extra or external staff are to be employed. In addition, our analysis did not consider the overheads, capital and other administrative costs. Inclusion of these could potentially double the intervention costs. Moreover, the long-term effects of continued use of e-cigarette remains unknown at the time of the analysis and were not considered.

In conclusion, our study found that the COSTED intervention is likely to be cost-effective compared to simple signposting. Provision of brief smoking cessation in ED should be considered with further exploration into the financial impact of different implementation approaches.

REFERENCES

1. Department of Health & Social Care. Advancing our health: prevention in the 2020s - consultation document; 2019.
2. Office for National Statistics (ONS). Adult smoking habits in the UK: 2022, ONS website, p. statistical bulletin.
3. Khan J. The Khan review: Making smoking obsolete; 2022.
4. Department of Health & Social Care. Stopping the start: our new plan to create a smokefree generation; 2023.
5. NHS Digital. Hospital Accident & Emergency Activity, 2022-23. Hospital Accident & Emergency Activity; 2023.
6. Tolmie A. D., Erker R., Oyedokun T., Sullivan E., Graham T., Stempien J. Prevalence of Cigarette Smoking Among Adult Emergency Department Patients in Canada, West J Emerg Med 2020: 21: 190-197.
7. Bernstein S. L., Dziura J., Weiss J., Brooks A. H., Miller T., Vickerman K. A. et al. Successful Optimization of Tobacco Dependence Treatment in the Emergency Department: A Randomized Controlled Trial Using the Multiphase Optimization Strategy, Ann Emerg Med 2023: 81: 209-221.
8. Notley C., Clark L., Belderson P., Ward E., Clark A. B., Parrott S. et al. Cessation of smoking trial in the emergency department (CoSTED): protocol for a multicentre randomised controlled trial, BMJ open 2023: 13: e064585.
9. Pope I., Clark L. V., Clark A., Ward E., Belderson P., Stirling S. et al. Cessation of Smoking Trial in the Emergency Department (COSTED): a multicentre randomised controlled trial, Emerg Med J 2024.
10. Jones K., H. W., Birch S., Castelli A., Chalkley M., Dargan A. et al. Unit Costs of Health and Social Care 2022; 2022.
11. National Institute for Health and Care Excellence. NICE health technology evaluations: the manual (PMG36). In: Process and Methods, editor: National Institute for Health and Care Excellence; 2022, p. 196.
12. Wu Q., Parrott S., Godfrey C., Gilbert H., Nazareth I., Leurent B. et al. Cost-effectiveness of computer-tailored smoking cessation advice in primary care: a randomized trial (ESCAPE), Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco 2014: 16: 270-278.
13. Curtis L., Burns A. Unit Costs of Health & Social Care 2016, Canterbury: Personal Social Services Research Unit, University of Kent; 2016.
14. Curtis L. A., Burns A. Unit Costs of Health & Social Care 2020: PSSRU, University of Kent; 2020.
15. Glassdoor I. Stop Smoking Advisor Salaries in United Kingdom; 2022.
16. NHS Business Services Authority. Prescription Cost Analysis - England 2021/22. Prescription Cost Analysis - England; 2022.
17. National Institute for Health and Care Excellence (NICE). British National Formula: BMJ Group and Pharmaceutical Press; 2023.
18. NHS Business Services Authority. PD1 reports. In: NHS Business Services Authority, editor; 2023.
19. Curtis L., Burns A. Unit Costs of Health and Social Care 2015, Kent: Personal Social Services Research Unit, The University of Kent; 2015.
20. NHS England, NHS Improvement. National Cost Collection 2021/22. National Cost Collection for the NHS; 2023.
21. National institute for Health and Care Excellence (NICE). Resource impact report: Tobacco: preventing uptake, promoting quitting, and treating dependence (NG209); 2021.
22. The EuroQol Group. EQ-5D-5L User Guide: Basic information on how to use the EQ-5D-5L instrument (version 2.1); 2015.

23. Richardson G., Manca A. Calculation of quality adjusted life years in the published literature: a review of methodology and transparency, Health Econ 2004: 13: 1203-1210.
24. van Hout B., Janssen M. F., Feng Y. S., Kohlmann T., Busschbach J., Golicki D. et al. Interim scoring for the EQ-5D-5L: mapping the EQ-5D-5L to EQ-5D-3L value sets, Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research 2012: 15: 708-715.
25. National Institute for Health and Care Excellence (NICE). Position statement on use of the EQ-5D-5L value set for England (updated October 2019); 2019.
26. Hernandez Alava M., Pudney S., Wailoo A. Estimating the Relationship Between EQ-5D-5L and EQ-5D-3L: Results from a UK Population Study, PharmacoEconomics 2023: 41: 199-207.
27. West R. Assessing smoking cessation performance in NHS Stop Smoking Services: The Russell Standard (Clinical); 2005.
28. Faria R., Gomes M., Epstein D., White I. R. A guide to handling missing data in cost-effectiveness analysis conducted within randomised controlled trials, PharmacoEconomics 2014: 32: 1157-1170.
29. Rubin D. B. Statistical Matching Using File Concatenation with Adjusted Weights and Multiple Imputations, Journal of Business & Economic Statistics 1986: 4: 87-94.
30. White I. R., Royston P., Wood A. M. Multiple imputation using chained equations: Issues and guidance for practice, Statistics in medicine 2011: 30: 377-399.
31. Briggs A. H., Wonderling D. E., Mooney C. Z. Pulling cost-effectiveness analysis up by its bootstraps: a non-parametric approach to confidence interval estimation, Health Econ 1997: 6: 327-340.
32. Doll R., Peto R., Boreham J., Sutherland I. Mortality in relation to smoking: 50 years' observations on male British doctors, BMJ 2004: 328: 1519.
33. Drummond M. Methods for the economic evaluation of health care programmes Oxford, United Kingdom ; New York, NY, USA: Oxford University Press; 2015.
34. Wu Q., Gilbody S., Li J., Wang H. I., Parrott S. Long-Term Cost-Effectiveness of Smoking Cessation Interventions in People With Mental Disorders: A Dynamic Decision Analytical Model, Value in health : the journal of the International Society for Pharmacoeconomics and Outcomes Research 2021: 24: 1263-1272.
35. Office for National Statistics (ONS). Deaths registered in England and Wales: 2021edition; 2021.
36. Hughes J. R., Peters E. N., Naud S. Relapse to smoking after 1 year of abstinence: a meta-analysis, Addictive behaviors 2008: 33: 1516-1520.
37. Godfrey C., Ali S., Parrott S., Pickett K. Economic model of adult smoking related costs and consequences for England; 2011.
38. World Health Organization. Economics of tobacco toolkit: assessment of the economic costs of smoking, Geneva: World Health Organization; 2011.
39. Royal College of Physicians of London. Tobacco Advisory G., Royal College of Physicians of London. Tobacco Advisory G., Royal College of Physicians of L. Hiding in plain sight : Treating tobacco dependency in the NHS : a report London: Royal College of Physicians; 2018.
40. Hospital Episode Statistics Analysis, Health and Social Care Information Centre. Hospital Episode Statistics: Accident and Emergency Attendances in England 2014-15; 2016.
41. Department of Health. Reference costs 2015-16; 2016.
42. Vogl M., Wenig C. M., Leidl R., Pokhrel S. Smoking and health-related quality of life in English general population: implications for economic evaluations, BMC public health 2012: 12: 203.
43. Population Health, Clinical Audit and Specialist Care, NHS England. Statistics on NHS Stop Smoking Services - England, April 2022 to December 2022. Statistics on NHS Stop Smoking Services - England; 2023.

44. MILLER T. R., JOHNSON M. B., DZIURA J. D., WEISS J., CARPENTER K. M., GRAU L. E. et al. Cost-Effectiveness of Smoking Cessation Approaches in Emergency Departments, American journal of preventive medicine 2023: 65: 39-44.
45. U.S. BUREAU OF LABOR STATISTICS. CPI Inflation Calculator; 2023.
46. INTERNATIONAL MONETARY FUND. Exchange Rates selected indicators. International Financial Statistics: IMF; 2023.
47. JACKSON S. E., SHAHAB L., KOCK L., WEST R., BROWN J. Expenditure on smoking and alternative nicotine delivery products: a population survey in England, Addiction 2019: 114: 2026-2036.

TABLES

Table 1 Smoking cessation support and healthcare services collected and their respective unit costs (2021/2022)

	Unit costs (2021/22)	Sources
Pharmacotherapies		
Nicotine patches	£11/pack	(16, 17)
Nicotine gums	£11/pack	
Nicotine tablets (microtab)	£16/pack	
Nicotine inhalators	£1/cartridge	(16)
Nicotine lozenges	£14/pack	
Nicotine nasal spray	£17/bottle	(16, 17)
Nicotine mouth spray	£13/bottle	
Varenicline (Champix)		
0.5mg/1mg 2 week treatment initiation pack	£29/pack	(16)
0.5mg/1mg 4 week treatment initiation pack	£55/pack	
0.5mg tablet	£0.98/tablet	
1mg tablet	£0.98/tablet	
Bupropion (Zyban)		
150mg tablet	£0.70/tablet	(16)
	£41.76/pack	(17)
Smoking cessation advice		
Group session in SSS	£1/session	(15, 21)
Individual session in SSS	£9/session	
GP	£38/session	(10, 14)
Practice nurse	£8/session	
Pharmacist	£5/session	
NHS Smoking Helpline	£8/call	(10, 12, 13)
Health care services		
A&E attendance	£113/attendance	(20)
A&E admission	£303/admission	
Hospital outpatient	£165/appointment	
Hospital admission	£2,621/episode	
Day case	£1,038/case	
Ambulance convoy	£390/convoy	
GP	£38/consultation	(10)
Practice nurse	£13/consultation	(10, 19)
Prescription	£19/prescription	(18)

Only number of individual and group sessions in SSS, and number of GP visits and hospital stays in the previous 3 months was collected at baseline due to limited time in ED settings.

Table 2 Breakdown of COSTED intervention costs (n=484)

Cost item	Unit cost (2022/23)	Description	Costs
Staff training			
Research team Band 8 Band 7	 £32.28/hour £29.50/hour	 Bespoke online training 3 hours * (£32.28 + £29.50)	 £185
Stop smoking advisor	£18.01/hour	Generic smokefree Norfolk level 2 training 2 hours * £18.01 *2 persons	£72
Trainees (Band 4 hospital staff)	£19.06/hour	(NCSCT e-learning 7.5 hours + bespoke online training 3 hours + generic smokefree Norfolk level 2 training 2 hours) * £19.06 * 27 persons	£6,433
Total training costs			**£6,690**
Average training costs per participant			**£14**
Intervention delivery			
CO-monitors	£150/device £30 worth of mouthpieces	£150 per device/site * 6 sites over 6 months, with 5 years operating life and 3.5% depreciation rate + £30/site * 6 sites = £276.30	£0.57 per participant
e-cigarette starter kits	£23.15/kit	£7.71 for device + £15.44 for pods One participant did not receive	£23.10 (SD £1.05) per participant
Information leaflets	£0.39/leaflet	Invoice payments £472 / 1,200 leaflets	£0.39 per participant
Tote bags	£1.47/bag	Invoice payments £953.40 / 650 bags	£1.47 per participant
Brief advice	£19.06/hour	Mean duration 25.7 minutes (SD 7.3) per participant * £19.06/hour (Band 4 hospital staff) / 60 minutes	£8.17 (SD £2.33) per participant
Average intervention delivery costs per participant			**£34 (SD £3)**
Mean intervention costs per participant			**£48 (SD £3)**

Table 3 Results of mean (SE) costs and QALYs of primary analysis, complete case analysis and analysis of broader sample

	Primary analysis based on imputed dataset		**Complete case analysis**		**Analysis of broader sample**	
	Control (n=488)	**Intervention (n=484)**	**Control (n=502)**	**Intervention (n=505)**	**Control (n=502)**	**Intervention (n=505)**
	Mean (SE)					
Baseline costs						
Costs of smoking cessation and healthcare services	£710 (96)	£631 (110)	£529 (99)	£333 (69)	£691 (94)	£613 (105)
Costs over 6 months period						
Costs of control/intervention	£0.2 (0)	£48 (0)	£0.2 (0)	£48 (0)	£0.2 (0)	£47 (0)

Costs of smoking cessation	£24 (4)	£16 (4)	£27 (5)	£17 (5)	£24 (4)	£15 (3)
Costs of primary care services	£133 (12)	£127 (12)	£132 (14)	£130 (14)	£132 (12)	£128 (11)
Costs of secondary care services	£1,494 (274)	£1,218 (169)	£1,403 (290)	£1,101 (170)	£1,427 (263)	£1,153 (147)
Total costs	**£1,651 (276)**	**£1,408 (171)**	**£1,561 (293)**	**£1,295 (174)**	**£1,584 (265)**	**£1,343 (149)**
EQ-5D-5L utility						
Baseline	0.527 (0.015)	0.550 (0.015)	0.564 (0.018)	0.552 (0.019)	0.534 (0.015)	0.560 (0.015)
6 months	0.634 (0.017)	0.660 (0.016)	0.654 (0.019)	0.662 (0.019)	0.639 (0.017)	0.660 (0.017)
QALYs	**0.290 (0.007)**	**0.303 (0.006)**	**0.305 (0.008)**	**0.304 (0.008)**	**0.293 (0.007)**	**0.305 (0.006)**

Table 4 Adjusted incremental costs and QALYs using generalised linear regression models

	Primary analysis based on imputed dataset	**Complete case analysis**	**Analysis of broader sample**
Adjusted incremental values (95% CI)			
Adjusted incremental costs	£31 (-£341, £283)	-£43 (-£559, £278)	£28 (-£322, £319)
Adjusted incremental QALYs	0.004 (-0.004, 0.014)	0.002 (-0.010, 0.013)	0.003 (-0.005, 0.013)
ICER			
	£7,750 per QALY gained (Uncertainty please see Figure 1)	Intervention was less costly but more effective (Uncertainty please see Supplementary Information Figure S2)	£9,333 per QALY gained (Uncertainty please see Supplementary Information Figure S4)

Table 5 Results of model-based incremental cost-effectiveness analysis

	Control Mean (SE)	**Intervention Mean (SE)**	**Incremental outcomes Mean (95% CI)**
Quit defined as CO-validated abstinence at 6 months			
Costs	£2,368 (£3)	£2,400 (£3)	£32 (-£163, £231)
QALYs	25.507 (0.037)	25.535 (0.037)	0.029 (-0.489, 0.847)
ICER	£1,131 per QALY gained (Uncertainty see Figure 3a)		
Quit defined as self-reported abstinence at 6 months			
Cost	£2,348 (£3)	£2,361 (£3)	£13 (-£186, £207)
QALYs	25.552 (0.037)	25.626 (0.037)	0.074 (-0.746, 0.898)
ICER	£174 per QALY gained (Uncertainty see Figure 3b)		

FIGURE LEGENDS

Figure 1 Cost-effectiveness plane and cost-effectiveness acceptability curve of primary analysis

Figure 2 7-day quit at 1, 3 and 6 months and their respective control/intervention costs per quit

Figure 3 Lifetime cost-effectiveness plane and cost-effectiveness acceptability curve estimated by model projection