National Institute for Health and Care Excellence

Draft for consultation

# Tobacco: preventing uptake, promoting quitting and treating dependence

## [S] Economic Modelling Report: Tailored interventions for mental health populations

*NICE guideline NGxx*

*Model*

*October 2020*

*Draft for Consultation*

*These evidence reviews were developed by the NICE Economic and Methodological Unit*

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ISBN:

**Contents**

# Acknowledgements

The authors would like to thank the Public Health Advisory Committee (PHAC) for their comments and suggestions.

# List of abbreviations

| | |
|---|---|
| BNF | British National Formulary |
| HSCIC | The Health and Social Care Information Centre |
| ICER | Incremental cost-effectiveness ratio |
| LSSS | Local stop smoking services |
| NHS | National Health Service |
| NHSCII | NHS Cost Inflation Index |
| NICE | National Institute for Health and Care Excellence |
| NRT | Nicotine replacement therapies |
| OTC | Over the counter |
| PHAC | Public Health Advisory Committee |
| PSSRU | Personal Social Services Research Unit |
| RCT | Randomised controlled trial |
| RR | Relative risk |
| SCIMITAR | Smoking Cessation Interventions for Severe Mental Illness |
| BSC | Bespoke Smoking Cessation Package |
| IC | Integrated Care |
| PTSD | Post-Traumatic Stress Disorder |
| SCC | Smoking Cessation Clinic |

# Plain Language Summary

Tobacco smoking can have a harmful impact on people's health. People who smoke are more likely to suffer from long-term health conditions including lung cancer, coronary heart disease (CHD), myocardial infarction (MI), stroke, chronic obstructive pulmonary disease (COPD) and asthma. Interventions which promote quitting are usually beneficial to the National Health Service (NHS) as they can decrease the occurrence of smoking related diseases, thereby improving health and reducing the associated NHS treatment costs.

Smoking is a particular public health concern for populations with mental health conditions. Populations with mental health conditions have a high prevalence of smoking and consume more cigarettes per day than the general population. In addition, mental health populations have a high dependence on nicotine and are less likely to engage with local stop smoking services. Consequently, typical interventions for smoking cessation that work in the wider population may be less effective in mental health populations.

Recently, tailored interventions specific for mental health populations have been implemented in clinical studies. These interventions are specifically designed to increase the uptake of smoking cessation services and provide appropriate support to people with mental health conditions. Tailored interventions which promote smoking cessation in mental health populations may be beneficial to the NHS as they could reduce smoking and consequently reduce the prevalence of smoking related diseases. There are currently no specific tailored interventions recommended by NICE for use in mental health populations in the NHS, or in local authority funded local stop smoking services (LSSS).

We conducted cost-effectiveness modelling to help the Public Health Advisory Committee (PHAC) develop recommendations on tailored smoking cessation interventions for mental health populations. The analysis adapted an economic model used for the current tobacco guidelines on smoking. The adapted economic model uses the best-available information in order to understand how different tailored interventions might reduce smoking in mental health populations, and the impact this might have on their health and the costs to the NHS.

The analysis evaluated the cost-effectiveness of two tailored interventions: A bespoke smoking cessation intervention (BSC) from the SCIMITAR trial, for people with serious mental illness including bipolar, schizophrenia and psychosis which was compared to usual care. An integrated care intervention that was compared with standard referral to smoking cessation clinics and was delivered to a population of US military veterans with post-traumatic stress disorder (PTSD).

We used evidence from NICE reviews, based on clinical trials, to calculate how effective the interventions were at promoting smoking cessation. Specifically, we used the evidence to calculate the total number people who had quit smoking at 12-months when receiving the interventions.

Once we had calculated the number of smokers/ non-smokers at 12-months, the economic model estimated the likelihood that people who did / did not smoke would die or develop a range of health complications, including lung cancer, CHD, COPD, MI, stroke and asthma. Because we also know the NHS treatment costs associated with each of these complications, it was possible to calculate the costs per smoker and non-smoker over their remaining lifetime. The model also measures health benefits for people who quit smoking by combining the increase in life expectancy with increases in quality of life that would be achieved by avoiding the previously listed health complications. This allowed us to calculate a measure known as the quality-adjusted life year (QALY) gain for each person who quit smoking.

The wider population model was adapted by including parameters that were specific to mental health populations. When compared to the original model for the wider population, the adapted mental health model had an increased the risk of mortality and smoking related comorbidities, and a decreased utility for smokers and ex-smokers.

For each intervention, the overall health benefits in terms of QALYs and NHS treatment costs avoided, were calculated. These lifetime health benefits and NHS treatment cost avoided were compared to the upfront costs of the intervention. Interventions were considered cost-effective if their incremental cost-effectiveness ratio (ICER) (the ratio of NHS treatment saving plus upfront intervention costs to QALYs gained) was less than £20,000, the predefined cost-effectiveness threshold used by NICE.

The results indicated that the bespoke smoking cessation (BSC) intervention was cost-effective when compared with usual care in a population with serious mental health conditions. The BSC intervention cost the NHS £165 per person, but achieved 0.05 QALYs per person, and was cost-effective as the resultant ICER was equal to £3,145 which is less than the £20,000 threshold.

The integrated care (IC) intervention was also cost-effective when compared to standard referral to a stop smoking clinic for populations with PTSD. The IC intervention cost the NHS £291 per person, but achieved 0.04 QALYs per person, and was cost-effective as the resultant ICER was equal to £6,847.

For each intervention, we also conducted comprehensive sensitivity and scenario analyses where we changed some of the models' key input parameter values and checked whether the results remained the same. The most important parameter in the economic model was the intervention effectiveness. We changed the effectiveness parameters from the average (mean) values reported in the NICE review, to the value of the lower 95% confidence interval. When we used the lower effectiveness value both BSC and IC interventions were no longer cost-effective.

We also conducted an analysis called probabilistic sensitivity analysis (PSA) where we estimate the probability of each intervention being cost-effective given the evidence that was available to inform the model. We found that the probability of BSC being cost-effective was very high, equal to 89%. Similarly, the IC intervention had a high probability of being cost-effective equal to 83%.

The results of our analysis show that the two tailored smoking cessation interventions for people with mental health conditions were highly likely to be cost-effective. As with any cost-effectiveness analysis, there were some factors that could be challenged, or alternative approaches that could have been taken. However, most areas that we left out of our analysis (for example due to being unable to find suitable evidence) are not likely to have influenced the results. For example, the model included some parameters for non-specific mental health conditions which included anxiety and depression whilst several parameters remained consistent with the economic model for the wider population. Had all of the model parameters been specific for populations with serious mental illness or PTSD then the benefits attached to quitting smoking would have likely been increased further. This would have only reinforced our findings that the tailored mental health interventions were highly likely to be cost-effective.

# Introduction

## Background

As stated in the NICE final scope, smoking is the main cause of preventable illness and premature death in England. The benefits of quitting smoking, for both society and the smoker themselves, are clear. Smoking kills over half of its users as well as causing significant long-term damage and distress due to poor quality of life. The Health and Social Care Information Centre (HSCIC, 2014) has published data which show that 17% of all deaths in adults aged 35 and over were caused by smoking (1). Treating smoking-related illness is estimated to cost the National Health Service (NHS) at least £2 billion per year (2).

A wide range of interventions that can help smokers make a successful quit attempt are available through local stop smoking services (LSSS). Intervention typically involves teaching people to anticipate and cope and usually requires behavioural, cognitive and pharmacological components (3). Several interventions including behavioural support, nicotine replacement therapy (NRT), bupropion and varenicline have been identified as cost-effective and are recommended to be made available for all adults who smoke in NICE guidelines (4).

Tobacco smoking is a particular public health concern in populations with mental health conditions. The rate of smoking in populations with severe mental health problems far exceeds than that in the general population. For example, people with schizophrenia may be up to three times more likely to smoke than the wider population (5). In addition, there is evidence that current smokers with mental health problems may inhale more nicotine per cigarette (6) and consume a greater quantity of cigarettes per day (7) than smokers without mental health problems. Consequently, mental health populations may be very dependent on tobacco smoking and have substantial difficulty quitting. Smokers in mental health populations also appear to be less likely to access the support available through local stop smoking services (8).

Recently, tailored interventions have been trialled in people with severe mental health problems (5). Such interventions offer bespoke cessation services that combine behavioural and pharmacological components, and are delivered by practitioners who are trained to provide stop smoking support specifically for people with mental health conditions. Tailored cessation interventions could provide much needed additional support for people with mental health problems who are highly dependent on tobacco smoking.

This is the first NICE guideline to include a full review question on the effectiveness and cost-effectiveness of tailored smoking cessation and harm reduction interventions in people with mental health conditions.

## Objectives

The key research questions from the NICE scope that were prioritised for economic modelling are listed below.

- In those with mental health conditions, what is the effectiveness and cost effectiveness of tailored smoking cessation interventions?
- In those with mental health conditions, what is the effectiveness and cost effectiveness of tailored smoking harm reduction interventions?

# Methods

## Overview

The following section summarises methods applied during the analysis of review questions related to tailored smoking cessation and harm reduction interventions for people with mental health conditions.

The new tobacco guidelines update brings together NICE's existing guidelines on tobacco. The guidelines contain new review areas, including tailored interventions for mental health populations. Further economic analysis was conducted for this review area as: there was no relevant economic modelling conducted in previous guidelines; and new effectiveness evidence had been generated from the NICE evidence reviews. The cost-effectiveness reviews identified three UK based studies for tailored smoking cessation interventions which assessed cost-effectiveness over a 12-month trial period (9-11); and one US based study assessing the cost-effectiveness of a tailored smoking cessation intervention across the lifetime for people with military related PTSD (12). Therefore, further economic modelling was required to establish the lifetime cost-effectiveness of tailored smoking cessation interventions for people with mental conditions in a UK setting.

**Review question:**

- In those with mental health conditions, what is the effectiveness and cost effectiveness of tailored smoking cessation interventions?

The NICE evidence review (13) identified two specific tailored smoking cessation interventions for populations with mental health problems. The first intervention was a bespoke smoking cessation (BSC) package delivered to populations with severe mental illness including bipolar, schizophrenia and psychosis. The intervention was compared with standard smoking cessation services (i.e. usual care) including behavioural support and pharmacological therapy offered by LSSS. The BSC intervention was part of the smoking cessation for people with severe mental illness (SCIMITAR) trials, which included a pilot study (14) and a main RCT (5). The BSC intervention included up to 12 individual face-to face (approx. 30 minutes) sessions with a mental health smoking cessation practitioner (MH-SCP) in their home or NHS premises. The MH-SCPs provided advice on pharmacological smoking cessation aids and liaised with the participants' primary care physicians who would make decisions on prescribing pharmacotherapies chosen by participants.

The second intervention was integrated care (IC) for smoking cessation for US veterans with military related post-traumatic stress disorder (PTSD). Smokers receiving treatment for PTSD received smoking cessation services integrated with their mental health treatment. The IC intervention included 5 weekly support sessions on tobacco use education, behavioural skills and setting a quit date, and relapse prevention. Support sessions were delivered alongside, pharmacotherapy for those attempting to quit. The IC intervention also included 3 booster sessions, and monthly follow-up sessions. The services were delivered by the providers of each patient's PTSD therapy. The IC intervention was assessed in an RCT by Mc Fall (2010) (15) and a cost-effectiveness study by Barnett (2015) (12). IC was compared to standard referral to a smoking cessation clinic (SCC) which provided treatment within 6-weeks of referral and prescribed cessation medications directly through patient's primary care clinicians following smoking cessation practice guidelines.

**Review question:**

- In those with mental health conditions, what is the effectiveness and cost effectiveness of tailored smoking harm reduction interventions?

The NICE evidence review did not identify any studies which included tailored smoking harm reduction interventions for people with mental health conditions. Consequently, it was not possible to conduct further economic modelling for this review question.

# Modelling Approach

This analysis used an economic model to establish the cost-effectiveness of the tailored smoking cessation interventions. The economic model was an adapted version of the model previously used to inform NICE guidelines on smoking cessation [NG92] (4). The NG92 economic model has since been updated to inform separate questions in the current NICE scope for the new tobacco guideline, specifically on smoking cessation in the general population (16). The updates included a version of the economic model that specifically assessed the cost-effectiveness of smoking cessation interventions for a mental health sub-group. This analysis used the mental health sub-group version of the updated NG92 economic model.

# Model Structure

The economic model was described in detail in the economic modelling report for smoking cessation in the general population which including a full description of the model structure and epidemiological inputs (16). A brief summary of is provided below.

The model is a Markov model with 12-month annual cycles and including three health states, these being “former smoker”, “current smoker” and “dead” (Figure 1). The population enter the model in the “current smoker” health state. Intervention effectiveness is established by determining the probability of people entering the “former-smoker” health state after the first 12-month cycle. This probability was informed by effectiveness evidence obtained in the NICE evidence review (13).

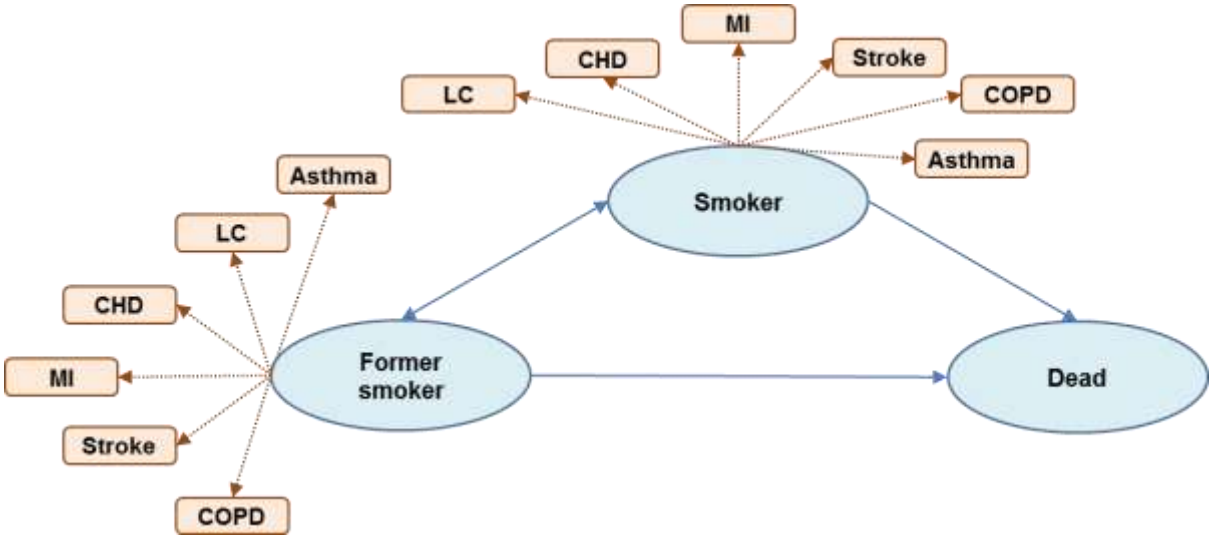
After the first 12-months, populations transition between each health state in annual cycles across a lifetime (100-year) time horizon. The transitions between health states are determined by the natural rate of cessation and relapse in the population each year. The model includes the following six smoking related comorbidities: lung cancer (LC), coronary heart disease (CHD), myocardial infarction (MI), stroke, chronic obstructive pulmonary disease (COPD), and asthma. The model uses published literature sources to establish the prevalence of LC, CHD, MI, stroke and COPD, and incidence of asthma, for smokers and non-smokers by age and gender. Each comorbidity has an associated NHS treatment cost and disutility. These costs and disutilities are applied based on prevalence and incidence rates for each cycle and summed to estimate lifetime costs and QALYs across all cycles. The model also calculates the lost productivity due to work absenteeism for each comorbidity using a human capital approach. This multiplies the percentage of days absent from work due to smoking related morbidities by mean ONS (2019) wage estimates per age and gender (17). A similar model structure has been used in past cost-effectiveness models for smoking interventions (PHG10, PHG45, Taylor *et al.* 2011 (18)).

The model calculates the average lifetime costs, lifetime QALYs, and subsequent cost-effectiveness across all adult populations. Average outcomes are calculated across all populations between the ages of 12 and 100. This age range was selected as it represented the youngest and oldest ages where we could identify smoking related prevalence rates. For people aged 12 to 15 smoking was defined as smoking at least one cigarette per week

based on the Action on Smoking and Health (ASH) fact sheet on young people and smoking (19). For people aged 16 to 100 smoking was defined by self-reported status as a current, ex or non-smoker in the Health Survey for England (2019) report (20).

Average outcomes across the population are calculated by obtaining results for each specific age and applying a weighted average based on the number of people of that age in the UK population as reported by the ONS (2019) (21). For example, the model obtains results for populations specifically aged 12, then aged 13, then aged 14, 15, 16 and so on until the final age of 100. Results for people aged 12, 13, 14, …, 100 are then multiplied by the percentage of people aged 12, 13, 14 , …, 100 and summed across all ages.

**Figure 1: Model structure**




* LC = lung cancer, CHD = coronary heart disease, MI = myocardial infarction, COPD = chronic obstructive pulmonary disease, asthma = asthma exacerbation.

# Model Parameters

All model parameter values are consistent with the mental health version of the updated NG92 model, as reported in the economic modelling report for smoking cessation in the general population (16). This excluded intervention effectiveness i.e. the probability of smoking cessation at 12-months, and intervention costs, both of which were obtained specifically for the tailored smoking cessation interventions. The model parameters for the mental health subgroup are not specific by mental health condition. Therefore, the same parameters are used for the BSC analysis which included a population with bipolar, schizophrenia and psychosis and for the IC analysis which included a population with PTSD. A summary of the model parameters for the mental health subgroup is provided below. Full detail of the model parameters in the updated NG92 model are provided in the economic modelling report for smoking cessation in the general population (RQ6) (16).

Due to resource constraints, it was not possible to conduct full literature searches to identify specific model parameters for the subgroup analysis. However, pragmatic literature searches were conducted by YHEC for several key parameters which involved searching for key terms across databases including Google Scholar, the CEA Registry and the burden of illness database HEORO.

The pragmatic searches conducted by YHEC attempted to identify relevant inputs to populate the model for the mental health sub-group including for mortality, utilities, risk of comorbidities, and costs per comorbidities. The searches did not identify any studies which reported the relevant parameters for mental health populations separately across health states included in the model (i.e. never, current and former smokers). Therefore, it was assumed that health risks by smoking status in the base case were applicable to the mental health subgroup. For example, mortality rates in the base case for non-, former and current smokers at age 75-84 were 67.4, 77.3 and 106.0 per 1000. To estimate mortality rates in the mental health subgroup, each of these rates was multiplied by the same relative risk of mortality for people with mental health problems, rather than a specific relative risk by each health state.

The overall relative risk of mortality in mental health populations was identified in a meta-analysis by Walker et al. (2016) (22). The meta-analysis identified the relative risk of mortality (equal to 2.22) for populations with any type of mental health conditions vs. the general population. The relative risk was multiplied by existing mortality rates for current, former and non-smokers in the base case model to establish overall mortality for the mental health subgroup, Table 1.

**Table 1: Mortality by smoking status, base case versus mental health subgroup**

| Age | Mortality per 1000 men | | | | | |
|---|---|---|---|---|---|---|
| | Never smoker | | Former smoker | | Current smoker | |
| | Base case | MH subgroup | Base case | MH subgroup | Base case | MH subgroup |
| 12 to 15 | 0.1 | 0.31 | 0.2* | 0.45 | 0.3* | 0.77 |
| 16 to 24 | 0.2 | 0.57 | 0.3* | 0.80 | 0.6* | 1.35 |
| 25 to 34 | 0.6 | 1.37 | 0.8* | 1.88 | 1.3* | 3.06 |
| 35 to 44 | 1.6 | 3.55 | 2.0 | 4.44 | 2.8 | 6.22 |
| 45 to 54 | 4.0 | 8.88 | 4.9 | 10.88 | 8.1 | 17.98 |
| 55 to 64 | 9.5 | 21.09 | 13.4 | 29.75 | 20.3 | 45.07 |
| 65 to 74 | 23.7 | 52.61 | 31.6 | 70.15 | 47.0 | 104.34 |
| 75 to 84 | 67.4 | 149.63 | 77.3 | 171.61 | 106.0 | 235.32 |
| 85+ | 168.6 | 374.29 | 179.7 | 398.93 | 218.7 | 485.51 |

Values obtained for the mental health (MH) subgroup by multiplying mortality rates in the general population by a RR=2.22 of mortality in mental health populations from Walker et al (2016) (22).

The pragmatic searches also identified a meta-analysis by Dare et al. (2019) (23) which established the odds of having a chronic physical disease for mental health populations vs. general a general population. Dare et al. (2019) (23) included diabetes, obesity, cancer, COPD and coronary heart disease as physical diseases, and defined mental health populations as anxiety, depression, schizophrenia, and bipolar disorder. The odds ratio from Dare et al. (2019), equal to 3.1, was converted to a relative risk for each morbidity using the formula RR=OR/(1-p+(p*OR)), where p is the underlying probability of each morbidity. Each RR was then multiplied by the existing probabilities per morbidity for current, former and never-smokers in the base case model to establish overall occurrence of morbidities for the mental health subgroup.

Equivalent costs per morbidity were applied for the mental health subgroup and the base case analysis. Whilst it is possible that treatment costs per morbidity may be increased in

mental health populations when compared with the general population, this is unlikely to influence the cost-effectiveness results. Adding extra costs per morbidity to the model would result in cost-effective strategies appearing more favourable.

The overall disutility for mental health populations vs. general populations was identified from a study by Fernandez et al. (2010) (24). This study used regression models to estimate the mean reduction in SF-6D scores over 12-months for people with mood disorders (-0.196), anxiety disorders (-0.043) and substance misuse disorders (-0.278). A mean utility reduction across all mental health populations was calculated using the utility reductions reported by Fernandez, and weighting by the number of people with each condition in the study population (mood disorder = 38.8%, anxiety disorder = 51.6%, substance misuse disorder = 9.6%). The weighted disutility (-0.125) was applied to each baseline utility value in the base case model and applied equally across each smoking related health state.

## Effectiveness

Effectiveness estimates were entered into the model as probability of abstinence at 12-months. The probability of abstinence for each intervention and comparator are reported in Table 2. All effectiveness estimates were obtained from the NICE evidence review (13).

The effectiveness estimates for the BSC intervention was a pooled estimate from a meta-analysis that was conducted by NICE (13). The meta-analysis pooled effectiveness estimates across two studies, these being the main SCIMITAR trial (5), and the pilot SCIMITAR study (14). For the base case analysis, effectiveness was measured as biochemically validated quit only, with outcomes measured at 12-months. The rate of abstinence for usual care was calculated as the pooled number of events divided by the pooled number of participants in the meta-analysis arm for usual care. Abstinence rates for the BSC intervention were calculated by multiplying the relative risk (RR) of abstinence as reported in the NICE meta-analysis by the rate of abstinence for usual care. We also included a scenario analysis where abstinence was confirmed using both biochemically validated and self-report measures.

The effectiveness estimates for the IC intervention were only available from a single study and were therefore obtained directly from the outcomes of the study reported by McFall (2010) (15). The base case analysis used smoking abstinence at 12-months based on biochemically validated quit. We also conducted a scenario analysis based on self-reported quit rates in the study by McFall (2010) (15).

**Table 2: Intervention effectiveness**

| | **RR of abstinence vs. control** *Mean (95% CI)* | **P(abstinence) at 12-months** *Mean (95% CI)* |
|---|---|---|
| **Base case analyses: Biochemically validated quit** | | |
| BSC intervention | 1.46 (0.96, 2.23) | 17.38% (11.43% to 26.55%) |
| Usual care | N/A | 11.90% |
| | | |
| IC intervention | N/A | 8.9% |
| SCC | N/A | 4.5% |

### Intervention Costs

Interventions costs were obtained directly from the cost-effectiveness studies that were identified in the NICE evidence reviews. The cost-effectiveness studies for both interventions included intervention costs and all prescribed pharmacotherapies for smoking cessation. In

addition, the studies collected the costs of 12-month healthcare service utilisation which was not specific to mental health costs and included self-reported emergency, hospital inpatient and community care. There were very high levels of variation in 12-month healthcare service utilisation, for example the IC intervention had healthcare resource utilisation with a mean equal to US$24,171 and a standard deviation equal to US $29,568 (12). The committee agreed that the 12-month service utilisation costs were very imprecise and likely to introduce uncertainty into the economic analysis. There was no significant difference between service utilisation for BSC versus usual care and for IC versus SCC. The committee's preference was to exclude the 12-month healthcare service utilisation costs from the base case analysis. These costs were included in a scenario analysis.

**BSC Costs**

For the BSC intervention, intervention costs were reported for the 12-month time horizon in both the main SCIMITAR trial (10) and for the pilot SCIMITAR study (9). The 12-month costs for both studies were presented to the PHAC committee. The committee had concerns with using costs from a pilot study. The committee suggested that costs from the main study were likely to be more reliable due to better reporting methods. The committee's preference was for the base case analysis to only include intervention costs from the main SCIMITAR study.

The costs for the main SCIMITAR study were obtained from the cost-effectiveness analysis in the HTA report by Peckham (2019) (10). Intervention costs were split into training costs, supervision costs and intervention delivery costs. Training costs included costs for eight 2-day sessions delivered by the NCST, time required for 56 mental health smoking cessation practitioners, and material printing costs. Supervision costs consisted of one 30-minute session and included CO monitoring. Intervention delivery costs consisted of staff time required for the intervention, based on a mean number of sessions equal to 5.6 per participant. The total cost for the BSC intervention reported by Peckham (2019) was £418 per person over the 12-month trial period.

The HTA report by Peckham (2019) also included cost components for usual GP care, consisting of smoking cessation GP/telephone/pharmacist consultations, and all prescribed smoking cessation pharmacotherapies. The costs of usual GP care and prescribed cessation pharmacotherapies were calculated for both the BSC intervention and usual care arms of the SCIMITAR trial totalling £143 (BSC) and £94 (usual care) respectively.

The costs from were inflated from Peckham (2019) were inflated from 2016 prices to 2019 prices using the NHSCII pay and prices indexes reported by PSSRU 2019 (25). The inflated cost of the BSC intervention was equal to £581 and the cost of usual care was equal to £96. A full breakdown of intervention costs is provided in Table 3.

**Table 3: Intervention Costs BSC, UK £2019 prices**

| Cost category | Description | Costs (per person) | |
|---|---|---|---|
| | | BCS Mean | Usual care Mean |
| **Intervention costs** | | | |
| BSC Costs | MH SCP Training costs [a] | £165 | £0 |
| | Supervision costs [b] | £33 | £0 |

| | | | |
|---|---|---|---|
| | Intervention delivery (BSC session) [c] | £243 | £0 |
| Usual GP care | Includes cessation consultation with GP/pharmacist, smoking cessation services, NHS helpline | £53 | £67 |
| Pharmacotherapies | Drug therapies for smoking cessation (prescribed only). [d] | £94 | £30 |
| *Total intervention costs only* | | *£433* | *£0* |
| *Total intervention + usual care costs* [e] | | *£581* | *£96* |

All costs reported by Peckham (2019) have been inflated from 2016 to 2019 prices.
a: Training costs: eight 2-day sessions delivered by NCST (total £10,681); time costs for 56 mental health smoking cessation practitioners (MHSCP) (£24,340); printing costs (£109). Total training costs were £43,313 or £165 per BSC study member.
b: Supervision costs: Supervision sessions were 30-minutes per participant equal to £23 plus CO monitoring costs of £10 per participant. Total = £33 per person.
c: Staff time for intervention delivery. Mean sessions = 5.6 per person; mean total delivery time was 492 minutes per person, total cost = £243 per person.
d: obtained via contact with participants practices to extract prescription information.
e: total costs within table are not exact sum of individual components due to rounding

**IC costs**

Costs for the integrated care intervention were obtained from the cost-effectiveness study by Barnett (2015) (12). The intervention costs were the costs of smoking cessation services utilised by participants with PTSD in the IC and SCC trial arms. As stated by Barnett (2015), utilization of smoking cessation services was recorded on a case-report form. Study participants were asked to report services and medications received outside the study. The cost of counselling services was estimated based on the time required for employing a provider of PTSD services. Smoking cessation pharmacotherapy costs were obtained from a database that recorded activity-based costs for all study participants, including the initial prescribing visit and costs for the medication itself. (12)

The total costs for utilisation of smoking cessation services in the integrated care arm were equal to US$ 1286 and for standard referral smoking cessation clinic (SCC) was US$ 551. Costs were converted from US$ to UK £ Sterling using the average ONS (26) exchange rate for 2011 (the cost year for the study). Costs were then inflated from 2011 to 2019 prices using the NHSCII pay and prices indexes reported by PSSRU 2019 (25).

The final intervention costs were equal to £963 for IC and £412 for SCC.

# Economic Evaluation

## Decision Rule

Cost-effectiveness models are used to assess the relative benefits of a given treatment using patient outcomes and the costs incurred in achieving those outcomes. Economic evaluations use decision rules to identify the cost-effective intervention. This was an incremental analysis involving pairwise comparisons for each intervention vs. a relevant comparator. The key outcome for this analysis was the incremental cost-effectiveness ratio (ICER) which is calculated by dividing incremental costs by incremental effects as shown in the formula below.

$$ICER = \frac{Cost_{\text{int ervention}} - Cost_{Comparator}}{Effect_{\text{int ervention}} - Effect_{Comparator}}$$

All health benefits in the economic modelling were measured as QALYs. In line with the NICE methods manual (27), a cost-effectiveness threshold equal to £20,000 per QALY was adopted. This meant that any intervention with an ICER less than £20,000 was considered cost-effective vs the comparator.

## Discounting

Future costs and outcomes were discounted in the model at a rate of 3.5% per year, in line with the values suggested in the NICE methods manual (27).

## Time horizon

In the base case, the time horizon was equal to 100 years, covering the remaining lifetime of the hypothetical study population.

## Perspective

The economic modelling was conducted from a healthcare perspective, including health outcomes measured as QALYs and healthcare costs incurred by the NHS and PSS. At the time of publication, smoking cessation interventions are provided by LSSS and funded by local authorities.

# Sensitivity and Scenario Analyses

## Scenario Analyses

### Effectiveness

Two scenario analyses were conducted for both BSC and IC interventions. The first scenario altered the probabilities of abstinence at 12-months. For the base case analysis, the probability of abstinence at 12-months was determined by biochemically validated quit rates. For the scenario analysis, probabilities were informed by self-reported and/or validated quit. All quit rates for the scenario analyses were obtained directly from the NICE evidence review and are reported in

Table **4**

**Table 4: Intervention effectiveness: Self-report and/or biochemically validated quit**

| | **RR of abstinence vs. control** *Mean (95% CI)* | **P(abstinence) at 12-months** *Mean (95% CI)* |
|---|---|---|
| **Scenario analysis: Self report and/or biochemically validated quit** | | |
| BSC intervention | 1.54 (1.01 to 2.34) | 18.19% (11.93% to 27.91%) |
| Placebo | N/A | 11.81% |
| | | |
| IC intervention | N/A | 15.5% |
| SCC | N/A | 7% |

**Intervention Costs**

The second scenario altered the intervention costs. Following the PHAC committee's preference, the base case analysis excluded 12-month healthcare service utilization costs. These costs were included in the scenario analysis.

For the BSC intervention, Peckham (2019) collected service utilisation costs for emergency, hospital and community care and all prescribed antipsychotics. Participants indicated use of services during visits or via questionnaires including. All A&E, emergency ambulance and hospital admissions for outpatient and day case procedures were recorded. Community services included GP home/surgery and telephone appointments, appointments with practice, district and psychiatric nurses; healthcare visitor; clinical psychologist; NHS counsellor, NHS dentist; podiatrist; occupational therapist; physiotherapist; CBT sessions; mindfulness based cognitive therapy sessions; crisis team; community mental health team; day care services; social worker; family support worker; drug and alcohol support workers.

Peckham (2019) (10) calculated a total incremental cost for BSC versus usual including all intervention, prescription and healthcare service utilization costs. The total incremental costs were adjusted for baseline characteristics using regression analysis, with covariates for age, gender, pre-existing medical conditions, duration since diagnosis of serious mental illness and healthcare costs incurred during 6-months prior to randomization. The total adjusted incremental costs for BSC versus usual care were -£270 with a 95% CI equal to (-£1,817 to £1,297). The costs were inflated from 2016 prices to 2019 prices using the NHSCII pay and prices indexes reported by PSSRU 2019 (25) and were equal to -£279 (95% CI -£1,881 to £1,342). The incremental costs were entered into the model by first applying mean total costs to usual care as reported in Peckham (2019), which after inflation were equal to £8,763. The intervention costs for BSC were entered by adding the incremental total costs to the cost in usual care (i.e. £8,763 + (- £279)). The total costs for BSC were £8,483 and for usual care were £8,763.

For the IC intervention, Barnett (2015) collected service utilisation costs including mental health treatment for PTSD and all cause hospital inpatient stay and outpatient visits and pharmacy costs. The total costs for service utilisation during the first 12-months were equal to US$24,171 for IC and US$25,305 for SCC. The aggregated costs, which included intervention and service utilisation costs were equal to US$25,457 for IC and $25,857 for SCC. The costs were converted to pounds sterling (GDP) using ONS exchange rates (26) and inflated from 2011 to 2019 prices using the NHSCII pay and prices indexes reported by PSSRU 2019 (25). The final costs applied in the scenario analysis for IC were equal to £19,054 (SD = £22,265) and for SCC were equal to £19,353 (SD= £22,655).

## Deterministic Sensitivity Analysis

Deterministic sensitivity analysis (DSA) was performed by manually changing the value of individual input parameters and re-estimating the model results. The DSA was performed for key input parameters which included: effectiveness estimates where the RR was varied to equal the value of the 95% upper and lower confidence intervals; intervention costs which were varied to equal the value of the 95% upper and lower confidence intervals; and the natural rate of smoking relapse per year which was changed from 0% in the base case to 5%. DSA were also conducted for the time horizon which was reduced to 5-years, for increased (5% costs, 5% QALYs) and decreased (1.5% costs, 1.5% QALYs) discount rates; utility values which were set equal for smokers and non-smoker; and disutility and cost per smoking related comorbidities which were increased and decreased by 25%.

## Probabilistic Sensitivity Analysis

Probabilistic sensitivity analysis is a technique used in economic modelling that allows the modeler to quantify the level of confidence in the output of the analysis, in relation to uncertainty in the model inputs. There is usually uncertainty associated with input parameter values of an economic model, which may have been derived from clinical trials, observational studies or in some cases expert opinion. In the base case analysis, the point estimate of each input parameter value is used. In the probabilistic analysis, these parameters are represented as distributions around the point estimate, which can be summarised using a few parameters (such as mean and standard deviation for a normal distribution).

In a PSA, a set of input parameter values is drawn by random sampling from each distribution, and the model is 'run' to generate outputs (cost and health outcome), which are stored and repeated many times. The key output of PSA is the proportion of times an intervention is identified as cost-effective vs. the comparator across all random samples. It is important to note that PSA does not, usually, quantify uncertainty associated with the model's structure or design – only its quantitative inputs.

The PSA for the economic model required an added layer of complexity as the base case ICERs were not a single model output but were calculated using weighted averages of incremental costs and QALYs for populations aged between 12 and 100. That is, the base case model was run and obtained incremental costs and QALYs for a population aged 12, then run again to obtain incremental costs and QALYs for populations aged 13, and so on for ages 14, 15, 16, … , 100. Incremental costs and QALYs across all population ages were calculated as a weighting mean across all individual ages with weighting based on the proportion of the UK population at each age.

For each PSA iteration, results were obtained similarly as for the base case model, i.e. by obtaining a weighted average of incremental costs and QALYs across different age ranges. However, to reduce the computational burden, the PSA age categories were condensed from yearly increments i.e. age 12, 13, 14, 15, … , 100, to two-yearly increments. This meant the PSA calculated outcomes for populations aged 13, 15, 17, 19, 21, …, 99. The PSA then calculated a weighted average across the results for populations aged 13, 15, 17, 19, 21, …, 99 to obtain the final model result. The weightings were based on the total number of people aged 13, 15, 17, 19, 21, …, 99 in the population based on ONS UK population estimates (21). In total the PSA was run for 3,000 iterations, with weighted averages calculated within each iteration.

Input parameter distributions for the PSA followed recommendations in Briggs et al. (2006) (28): beta distributions were applied to probabilities, prevalence rates and utilities; inverse normal distributions were applied to RR parameters; and gamma distributions were applied to costs. In addition, a (beta) dirichlet distribution was applied to the age-related probabilities of being a current smoker, former smoker, and non-smoker to ensure the PSA values across these three parameters summed to one. The PSA distributions were fit using standard errors and 95% confidence intervals, or alpha (event rates) and beta (non-event rates) values, if these were available in the published literature i.e. reported alongside the mean estimates used to populate the base case model. If these were not available, then we applied an assumption that the value of the standard error was equal to 15% of the mean (base case) parameter value. The parameters and distributions used in the PSA are summarised in

Table 5.

The PSA analysis was conducted using 3,000 iterations to reduce the computational burden. The iteration number was selected by conducting a PSA with 10,000 iterations. We then

plotted a graph with the number of PSA iterations against the associated probabilistic ICER, for iterations 1, 1& 2, 1 & 2 & 3, …, 1 & 2 & 3 … & 10,000. The probabilistic ICER had stabilized at 3,000 iterations, being largely equivalent to the probabilistic ICER obtained at 10,000 iterations.

**Table 5: Summary of PSA distributions**

| Parameter | PSA Distribution | Source |
|---|---|---|
| Intervention effectiveness (RR) | Log-normal | (29) |
| Probability of abstinence (control arms) | Beta [0,1] | (29) |
| Smoking status (by age & gender) | | |
| Former smoker | Beta [0,1] (Dirichlet) | (20) |
| Current smoker | Beta [0,1] (Dirichlet) | |
| Non-smoker | Beta [0,1] (Dirichlet) | |
| Mortality per 1000 (by age & smoking status) | Beta [0,1000] | (30) |
| Comorbidities RR parameters | | |
| Stroke | Log-normal | (31) |
| Lung cancer | Log-normal | (32) |
| MI | Log-normal | (33) |
| CHD | Log-normal | (34) |
| COPD | Log-normal | (35) |
| Comorbidities prevalence & incidence rates | Beta [0,1] | Assumption |
| Utilities | | |
| Smoker/ former smoker/ non-smoker | Beta [0,1] | (36) |
| CHD | Beta [0,1] | (37) |
| All other comorbidities (excluding CHD) | Beta [0,1] | Assumption |
| Intervention costs | Gamma | Assumption |
| Comorbidity costs | Gamma | Assumption |

Beta [a, b] = beta distribution with lower and upper bounds equal to a and b.

All assumptions applied a standard error equal to 15% of the mean.

# Results

## Bespoke Smoking Cessation Intervention

### Base case analysis

Based on the SCIMITAR pilot and main trials, the NICE evidence review (13) found that a BSC intervention was more effective than usual care in promoting smoking cessation in a population with severe mental illness including bipolar, schizophrenia and psychosis, RR= 1.46 (95% CI = 0.96, 2.23). Consequently, in a hypothetical population of 1,000 current smokers, the model estimated that BSC would produce 55 additional quitters at 12-months than usual care.

The BSC intervention was cost-effective vs usual care with an ICER equal to £3,145 substantially below the threshold of £20,000 per QALY. The incremental lifetime healthcare costs of the BSC intervention were equal to £165, meanwhile incremental lifetime QALYs were equal to 0.05. Cost-effectiveness results were driven by effectiveness rates: The BSC intervention increased the number of people who quit smoking after 12-months. This led to a decrease in the prevalence of smoking related comorbidities across the lifetime which positively affected health and reduced treatment costs. The total reduction in costs associated with treating each comorbidity was equal to -£320 per person, which almost compensated for the incremental intervention costs which were equal to £484 per person. A full breakdown of the base case results is provided in Table 6.

**Table 6: Cost-effectiveness results (per person): BSC intervention vs. usual care**

| | BSC | Usual care | Incremental |
|---|---|---|---|
| *Healthcare perspective* | | | |
| Intervention costs | £581 | £96 | £484 |
| Comorbidity costs | | | |
| Stroke | £9,054 | £9,165 | -£111 |
| Lung cancer | £2,133 | £2,195 | -£63 |
| MI | £2,249 | £2,294 | -£45 |
| CHD | £3,775 | £3,795 | -£20 |
| COPD | £2,546 | £2,627 | -£81 |
| Asthma | £13 | £13 | -£0 |
| **Total costs** | **£20,351** | **£20,187** | **£165** |
| **QALYs** | **11.57** | **11.52** | **0.05** |
| **ICER** | | | **£3,145** |

The results of the deterministic sensitivity analysis for the BSC are provided in Table 7. There was considerable uncertainty in the cost-effectiveness results when modifying the effectiveness estimates: The DSA that applied the lower 95% CI changed BSC from being highly cost-effective to being dominated (i.e. costlier and less effective) versus usual care. In contrast when applying the upper 95% CI BSC became dominant (i.e. less costly and more effective).

Results across the other DSAs were robust with the BSC intervention remaining cost-effective versus usual care with a dominant ICER or an ICER below the £20,000 threshold. BSC was cost-effective: when restricting populations to people aged 20 and 60; after increasing the annual smoking cessation rate or relapse rate to 5%; when increasing

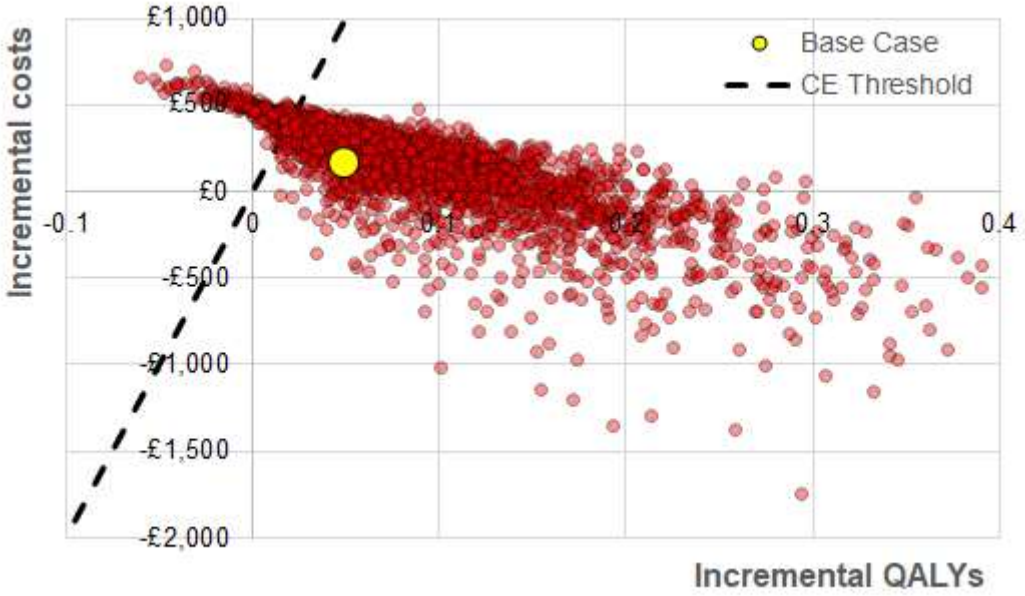
intervention costs by 25%; and when increasing discount rates equal to 5% for costs and QALYs. The BSC intervention was also cost-effective when increasing the natural relapse rate to not cost-effective when reducing the time horizon to 5-years only.

**Table 7: Deterministic sensitivity analysis: BSC intervention versus usual care**

| DSA Scenario | DSA Parameter Value | Absolute (BSC) | | Incremental (BSC vs. usual care) | | |
|---|---|---|---|---|---|---|
| | | Costs | QALYs | Costs | QALYs | ICER |
| Base Case | N/a | £20,351 | 11.57 | £165 | 0.05 | £3,145 |
| Effectiveness | Lower 95% CI RR (0.96) | £20,699 | 11.52 | £512 | -0.00 | Dominated |
| | Upper 95% CI RR (2.23) | £19,816 | 11.66 | -£371 | 0.14 | Dominant |
| Intervention costs | Increase by 25% | £20,496 | 11.57 | £310 | 0.05 | £5,918 |
| | Decrease by 25% | £20,206 | 11.57 | £19 | 0.05 | £372 |
| Time horizon | 5 years | £5,407 | 3.09 | £389 | 0.01 | £54,618 |
| Cessation rate | Increase to 5% per year | £18,915 | 11.80 | £260 | 0.04 | £6,939 |
| Relapse rate | Increase to 5% per year | £21,671 | 11.38 | £306 | 0.03 | £10,100 |
| Discount rate | Costs 5%, QALYs 5% | £16,465 | 9.62 | £212 | 0.04 | £5,201 |
| | Costs 1.5%, QALYs 1.5% | £29,231 | 15.67 | £70 | 0.08 | £899 |
| Utility | Same QoL for smokers and non-smokers | £20,351 | 11.95 | £165 | 0.04 | £3,759 |
| Disease costs | Decrease by 25% | £15,409 | 11.57 | £245 | 0.05 | £4,672 |
| | Increase by 25% | £25,294 | 11.57 | £85 | 0.05 | £1,618 |
| Disease disutility | Decrease by 25% | £20,351 | 11.85 | £165 | 0.05 | £3,470 |
| | Increase by 25% | £20,351 | 9.78 | £165 | 0.09 | £1,886 |
| Age of population | Age = 20 | £9,967 | 17.35 | £358 | 0.04 | £9,569 |
| | Age = 60 | £29,734 | 7.98 | -£22 | 0.07 | Dominant |

The PSA identified BSC as being the cost-effective strategy in 89% of the 3,000 iterations, with usual care being cost-effective in the remaining 11%. The results of the PSA are illustrated in Figure 2. The figure plots PSA results on a cost-effectiveness plane, each point (in red) represents one PSA iteration. Interventions are cost-effective if their incremental costs and QALYs fall to the south-east of the cost-effectiveness threshold, equal to £20,000 per QALY.

**Figure 2: PSA results, BSC vs. usual care (base case)**



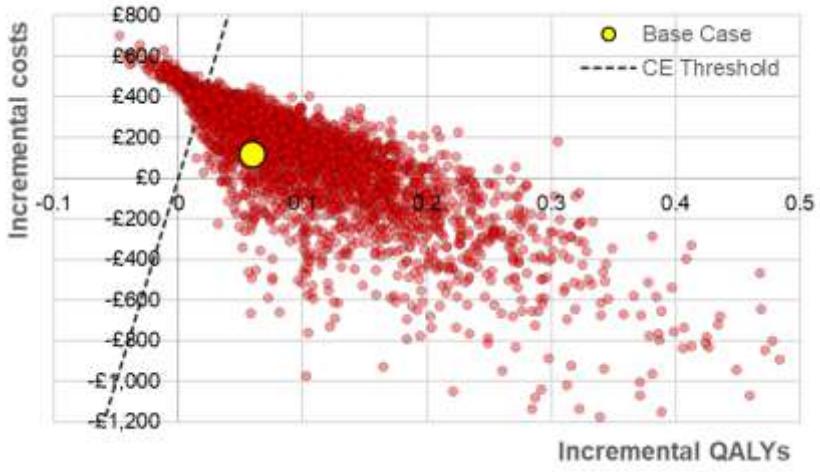
## Scenario Analyses

The first scenario analysis used self-reported and biochemically validated quit rates. The BSC intervention was more effective than usual care in promoting smoking cessation RR=1.54 (95% CI = 1.01 to 2.34). Consequently, in a hypothetical population of 1,000 current smokers, the model estimated that BSC would produce 64 additional quitters at 12-months than usual care. In the effectiveness scenario analysis, the BSC intervention was cost-effective versus usual care, with an ICER equal to £1,837. The incremental lifetime healthcare costs were equal to £112 and incremental lifetime QALYs were equal to 0.06. A full breakdown of the deterministic cost-effectiveness results is show in **Error! Reference source not found.**. For the effectiveness scenario analysis, the BSC intervention was cost-effective in 92% of PSA iterations when compared with 8% for usual care Figure 3.

**Table 8: Cost-effectiveness results (per person): BSC intervention vs. usual care (self-report + biochemically validated quit)**

| | BSC | Usual care | Incremental |
|---|---|---|---|
| *Healthcare perspective* | | | |
| Intervention costs | £581 | £96 | £484 |
| Comorbidity costs | | | |
| Stroke | £9,037 | £9,167 | -£130 |
| Lung cancer | £2,123 | £2,196 | -£73 |
| MI | £2,242 | £2,295 | -£53 |
| CHD | £3,772 | £3,795 | -£23 |
| COPD | £2,535 | £2,629 | -£94 |
| Asthma | 14 | £14 | -£0 |
| **Total costs** | **£20,304** | **£20,192** | **£112** |
| **QALYs** | **11.58** | **11.52** | **0.06** |
| **ICER** | | | **£1,837** |

**Figure 3: PSA results, BSC vs. usual care (self-report + biochemically validated quit)**




The second scenario analysis included healthcare service utilization and antipsychotic prescription costs as part of the total intervention costs for BSC and usual care. For the cost

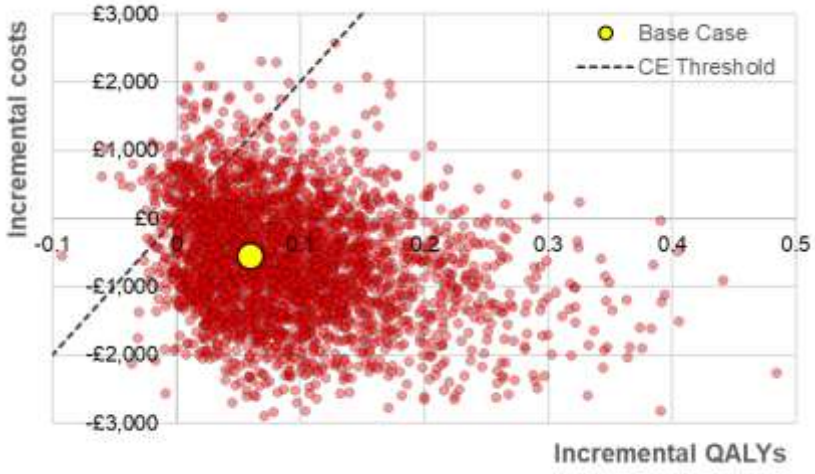
scenario, BSC was cost-effective with a dominant ICER. This occurred as the intervention costs for BSC were less than for usual care due to savings in 12-month healthcare resource utilization. The full results for the cost scenario are displayed in Table 9.

**Table 9: Cost-effectiveness results (per person): BSC intervention vs. usual care (cost scenario, including 12-month healthcare resource utilisation)**

| | BSC | Usual care | Incremental |
|---|---|---|---|
| *Healthcare perspective* | | | |
| Intervention costs | £8,484 | £8,763 | -£279 |
| Comorbidity costs | | | |
| Stroke | £9,054 | £9,165 | -£111 |
| Lung cancer | £2,133 | £2,195 | -£63 |
| MI | £2,249 | £2,294 | -£45 |
| CHD | £3,775 | £3,795 | -£20 |
| COPD | £2,546 | £2,627 | -£81 |
| Asthma | £13 | £13 | -£0 |
| **Total costs** | **£28,254** | **£28,853** | **-£599** |
| **QALYs** | **11.57** | **11.52** | **0.05** |
| **ICER** | | | **Dominant** |

For the cost scenario analysis, the BSC intervention was cost-effective in 94% of PSA iterations when compared with 6% for usual care. The inclusion of healthcare resource utilisation costs resulted in much larger variability in the incremental costs which ranged from +/- £3,000 across all PSA iterations. The results of the PSA are displayed in Figure 4.

**Figure 4: PSA results, BSC vs. usual care (healthcare service utilisation cost scenario)**




## Integrated Care Intervention

### Base Case

The NICE evidence review (13) found that IC was more effective than SCC where the probabilities of smoking abstinence at 12-months were equal to 8.9% and 4.5% respectively.

Consequently, in the economic model, IC resulted in 44 additional quitters per 1,000 versus SCC at 12-months.

The IC intervention was cost-effective vs SCC with an ICER equal to £6,847 substantially below the £20,000 per QALY threshold. The incremental lifetime healthcare costs of the IC intervention were equal to £291, meanwhile incremental lifetime QALYs were equal to 0.04. Cost-effectiveness results were driven by effectiveness rates: The IC intervention increased the number of people who quit smoking after 12-months. This led to a decrease in the prevalence of smoking related comorbidities across the lifetime which positively affected health and reduced treatment costs. The total reduction in costs associated with treating each comorbidity was equal to -£260 per person, which almost compensated for the incremental intervention costs which were equal to £551 per person. A full breakdown of the base case results is provided in Table 10.

**Table 10: Cost-effectiveness results (per person): BSC intervention vs. usual care (self-report + biochemically validated quit)**

| | IC | SCC | Incremental |
|---|---|---|---|
| *Healthcare perspective* | | | |
| Intervention costs | £963 | £412 | £551 |
| Comorbidity costs | | | |
| Stroke | £9,226 | £9,317 | -£90 |
| Lung cancer | £2,229 | £2,280 | -£51 |
| MI | £2,319 | £2,356 | -£37 |
| CHD | £3,806 | £3,822 | -£16 |
| COPD | £2,672 | £2,737 | -£66 |
| Asthma | 14 | £14 | -£0 |
| **Total costs** | **£21,229** | **£20,192** | **£292** |
| **QALYs** | **11.49** | **11.45** | **0.04** |
| **ICER** | | | **£6,875** |

The results of the deterministic sensitivity analysis for the IC are provided in Table 11. There was considerable uncertainty in the cost-effectiveness results when modifying the effectiveness estimates: The DSA that applied the lower 95% CI for the probability of cessation at 12-month changed IC from to being not cost-effective versus IC with an ICER equal to £58,670. In contrast when applying the upper 95% CI the IC intervention became dominant (i.e. less costly and more effective).

Results across the other DSAs were robust with the IC intervention remaining cost-effective versus SCC with an ICER below the £20,000 threshold. IC was cost-effective: when restricting populations to people aged 20 or 60; after increasing the annual smoking cessation rate or relapse rate to 5%; when increasing intervention costs by 25%; and when increasing discount rates equal to 5% for costs and QALYs. The IC intervention was not cost-effective when reducing the time horizon to 5-years only.

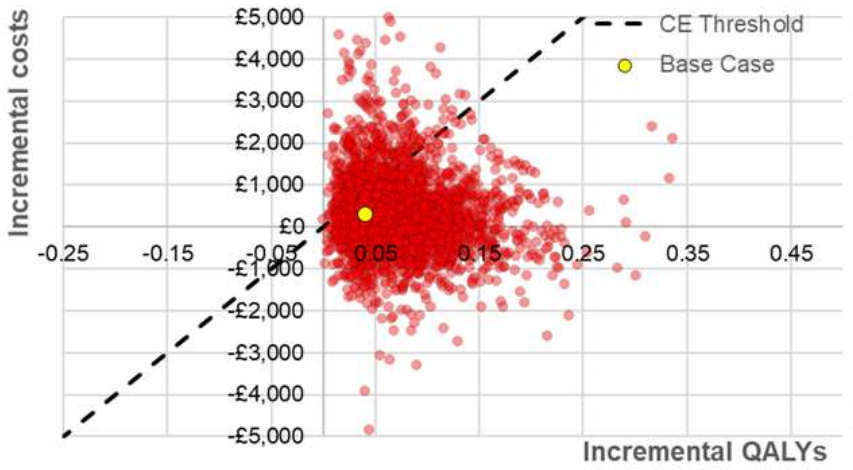
**Table 11: Deterministic sensitivity analysis: IC intervention versus SCC**

| DSA Scenario | DSA Parameter Value | Absolute (IC) | | Incremental (IC vs. SCC) | | |
|---|---|---|---|---|---|---|
| | | Costs | QALYs | Costs | QALYs | ICER |
| Base Case | N/a | £21,229 | 11.49 | £292 | 0.04 | £6,875 |
| Effectiveness | Lower 95% CI Prob (5.3%) | £21,437 | 11.46 | £499 | 0.01 | £58,670 |
| | Upper 95% CI Prob (14.8%) | £20,886 | 11.55 | -£52 | 0.10 | Dominant |

| | | | | | | |
|---|---|---|---|---|---|---|
| Intervention costs | Increase by 25% | £21,470 | 11.49 | £532 | 0.04 | £12,508 |
| | Decrease by 25% | £20,940 | 11.49 | £2 | 0.04 | £55 |
| Time horizon | 5 years | £5,938 | 3.08 | £473 | 0.01 | £81,849 |
| Cessation rate | Increase to 5% per year | £19,645 | 11.74 | £369 | 0.03 | £12,115 |
| Relapse rate | Increase to 5% per year | £22,328 | 11.33 | £406 | 0.02 | £16,444 |
| Discount rate | Costs 5%, QALYs 5% | £17,269 | 9.56 | £330 | 0.03 | £9,947 |
| | Costs 1.5%, QALYs 1.5% | £30,255 | 15.55 | £215 | 0.06 | £3,381 |
| Utility | Same QoL for smokers and non-smokers | £21,229 | 11.89 | £292 | 0.04 | £8,185 |
| Disease costs | Decrease by 25% | £16,162 | 11.49 | £356 | 0.04 | £8,374 |
| | Increase by 25% | £26,295 | 11.49 | £226 | 0.04 | £5,320 |
| Disease disutility | Decrease by 25% | £21,229 | 11.77 | £292 | 0.04 | £7,556 |
| | Increase by 25% | £21,229 | 9.65 | £292 | 0.07 | £4,107 |
| Age of population | Age = 20 | £10,544 | 17.29 | £449 | 0.03 | £14,744 |
| | Age = 60 | £30,901 | 7.87 | £139 | 0.06 | £2,467 |

The probabilistic sensitivity analysis identified IC as being the cost-effective strategy in 83% of the 3,000 iterations, with usual care being cost-effective in the remaining 17%, when applying a cost-effectiveness threshold of £20,000 per QALY. The results of the PSA are illustrated in Figure 5.

**Figure 5: PSA results, IC vs. SCC (base case)**



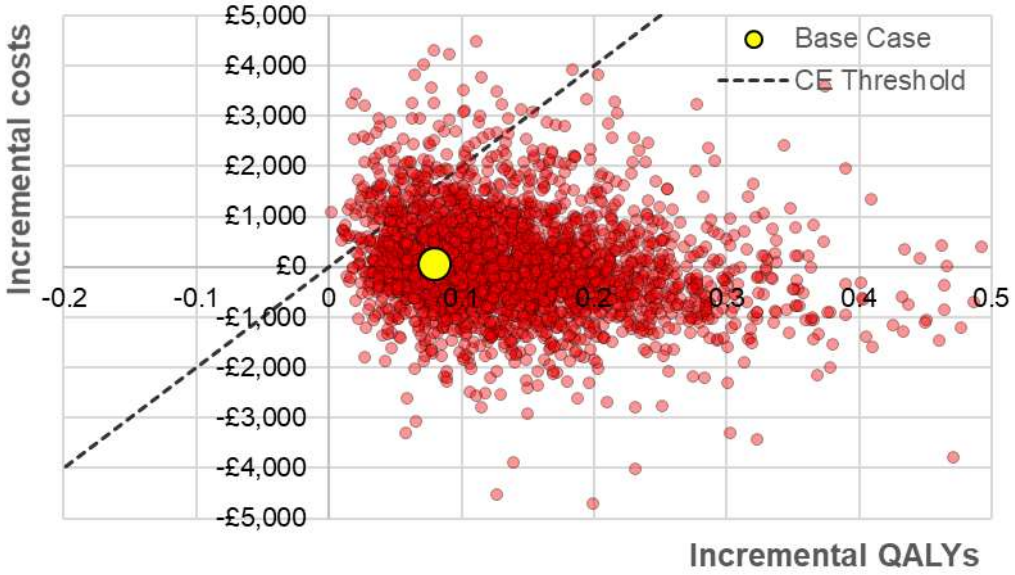

## Scenario Analyses

The first scenario analysis used self-reported quit rates. The IC intervention was more effective than SCC in promoting smoking cessation with the probability of abstinence at 12-months equal to 7.00% and 15.48% respectively. Consequently, in a hypothetical population of 1,000 current smokers, the model estimated that IC would produce 85 additional quitters at 12-months than SCC. In the effectiveness scenario analysis, the IC intervention was cost-effective versus SCC, with an ICER equal to £1,565. The incremental lifetime healthcare costs were equal to £56 and incremental lifetime QALYs were equal to 0.08. A full breakdown of the deterministic cost-effectiveness results is show in Table 12. For the effectiveness scenario analysis, the IC intervention was cost-effective in 94% of PSA iterations when compared with 6% for SCC Figure 6.

**Table 12: Cost-effectiveness results (per person): IC vs. SCC (self-reported quit)**

| | IC | SCC | Incremental |
|---|---|---|---|
| *Healthcare perspective* | | | |
| Intervention costs | £963 | £412 | £551 |
| Comorbidity costs | | | |
| Stroke | £9,092 | £9,265 | -£170 |
| Lung cancer | £2,154 | £2,251 | -£97 |
| MI | £2,265 | £2,335 | -£70 |
| CHD | £3,782 | £3,813 | -£30 |
| COPD | £2,574 | £2,699 | -£125 |
| Asthma | 14 | £14 | -£0 |
| **Total costs** | **£20,844** | **£20,788** | **£56** |
| **QALYs** | **11.55** | **11.47** | **0.08** |
| **ICER** | | | **£691** |

**Figure 6: PSA results, IC vs. SCC (self-reported quit)**




The second scenario analysis included healthcare service as part of the total intervention costs for IC and SCC. For the cost scenario, IC was cost-effective with a dominant ICER. This occurred as the intervention costs for IC were less than for SCC due to savings in 12-month healthcare resource utilization. The full results for the cost scenario are displayed in Table 13.

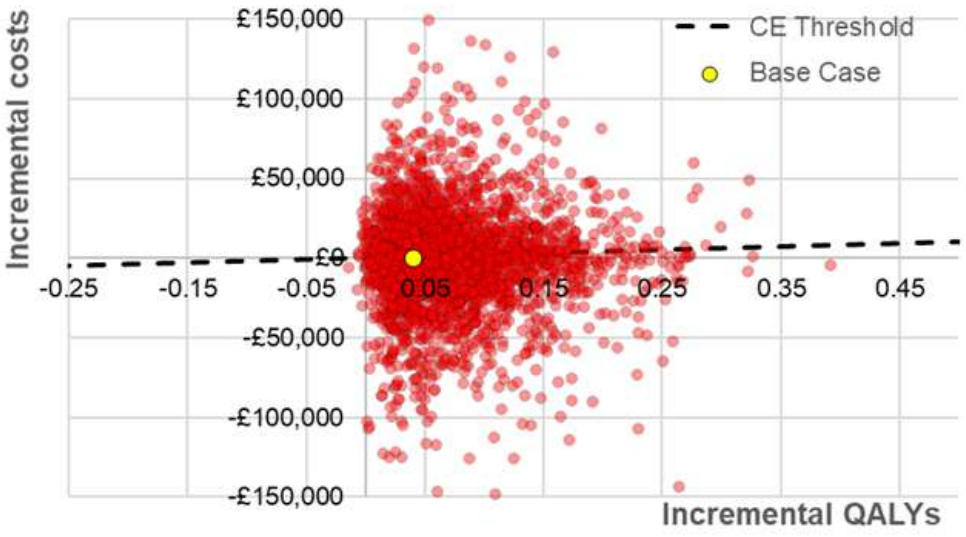
**Table 13: Cost-effectiveness results (per person): BSC intervention vs. usual care (cost scenario, including 12-month healthcare resource utilisation)**

| | IC | SCC | Incremental |
|---|---|---|---|
| *Healthcare perspective* | | | |
| Intervention costs | £19,054 | £19,353 | -£299 |
| Comorbidity costs | | | |

| | | | |
|---|---|---|---|
| Stroke | £9,226 | £9,316 | -£91 |
| Lung cancer | £2,229 | £2,280 | -£51 |
| MI | £2,319 | £2,356 | -£37 |
| CHD | £3,806 | £3,822 | -£16 |
| COPD | £2,671 | £2,737 | -£66 |
| Asthma | £14 | £14 | -£0 |
| **Total costs** | **£39,319** | **£39,878** | **-£559** |
| **QALYs** | **11.49** | **11.45** | **0.04** |
| **ICER** | | | **Dominant** |

For the cost scenario analysis, at a threshold of £20,000 per QALY, the IC intervention was cost-effective in 54% of PSA iterations when compared with 46% for SCC. The inclusion of healthcare resource utilisation costs resulted in a substantial increase in the variability of incremental costs which ranged from +/- £150,000 across all PSA iterations. The results of the PSA are displayed in Figure 7.

**Figure 7: PSA results, IC vs. SCC (healthcare service utilisation cost scenario)**



# Discussion

## Key findings

This economic evaluation demonstrated that two tailored smoking cessation interventions for mental health populations were cost-effective. The bespoke smoking cessation intervention, that was delivered in the SCIMITAR studies to populations with severe mental illness including bipolar, schizophrenia and psychosis, was cost-effective versus usual care. The integrated care intervention, that was delivered in a population of military veterans with PTSD in the RCT by McFall (2011), was cost-effective versus standard referral to a smoking cessation clinic.

The results of the cost-effectiveness model were driven by intervention effectiveness which determined the number of smokers and non-smokers and consequently the lifetime health and economic burden of smoking. In the model, populations who quit tobacco smoking have a decreased risk of stroke, myocardial infarction, lung cancer, coronary heart disease, COPD and asthma throughout the remainder of their lifetime. Consequently, the tailored smoking cessation intervention resulted in QALYs gained, and NHS treatment costs avoided due to reductions in the smoking related diseases. Whilst the upfront intervention costs were relatively substantial (equal to £484 for BSC vs usual care and £581 for IC vs SCC per person), these were outweighed by the lifetime cost savings and QALYs gained due to reductions in mortality and the prevalence of smoking related diseases.

The PSA identified low levels of uncertainty in the cost-effectiveness results for the base case analyses where 89% and 83% of PSA iterations were cost-effective versus the comparator for the BSC and IC interventions respectively. There was minor uncertainty identified in the deterministic sensitivity analyses. The BSC and IC interventions were not cost-effective when the effectiveness estimate was set equal to lower 95% confidence interval. However, both interventions were dominant when setting the effectiveness parameter to the upper 95% confidence interval. The range in the cost-effectiveness results for the lower and upper 95% confidence intervals reflects the imprecision in the effectiveness estimates which came from only two studies for the BSC intervention, and one study for IC intervention.

Both the BSC and IC interventions remained cost-effective for all other DSA’s, excluding when reducing the lifetime time horizon to 5-years. In addition, cost-effectiveness was increased (i.e. ICERs reduced) for both interventions for the scenario which used an effectiveness estimate based on self-reported quit. Self-reported quit rates are generally higher than biochemically validated quit rates, and therefore interventions often appear more effective, and consequently more cost-effective when using these outcome measures.

Taken together, the results from the base case, probabilistic and deterministic sensitivity analyses suggested that the tailored mental health interventions are likely to be cost-effective if they are effective in promoting smoking cessation.

## Inclusion of healthcare resource utilization costs

The cost-effectiveness studies for the BSC intervention by Peckham (2019), and the IC intervention by Barnett (2015) calculated total intervention costs, and also costs associated with healthcare resource utilisation during the 12-month trial period. The tailored mental health interventions for smoking cessation were designed to increase contact between participants and healthcare staff and service providers. Whilst the increased contact was

specific to smoking cessation services, it was possible the interventions could lead to general increases in uptake of healthcare services. Therefore, the likely rationale for collecting 12-month healthcare resource utilisation data was to determine whether the interventions resulted in an increase in costs for the intervention versus the comparator.

The cost-effectiveness studies by Peckham (2019) and Barnett (2015) found that there was no significant difference in 12-month healthcare resource utilisation between the tailored cessation interventions and the comparators. In fact, the BSC intervention had reduced resource usage versus usual care. Similarly, IC had reduced resource usage versus SCC. Therefore, when including the 12-month healthcare resource usage costs in the scenario analysis, both interventions were highly cost-effective with a dominant ICER i.e. being less costly and more effective than the comparator.

The inclusion of 12-month healthcare resource utilisation costs reduced the probability of cost-effectiveness for the IC intervention from 83% to 54%. The reason for the substantial reduction was due to the added uncertainty associated with these costs. For example, Barnett (2015) report that the standard deviation around intervention costs for IC only was equal to US$1046 but the standard deviation around the 12-month healthcare resource utilisation costs was equal to US$29,568.

The PHAC agreed that 12-month healthcare resource usage costs should not be included in the base case analysis as: (i) they were very imprecise; and (ii) there was no significant difference between healthcare resource utilisation for IC vs. SCC in the study by Barnett (2015) or for BSC vs usual care in either the main and pilot SCIMITAR studies. The results of the scenario analysis indicate that the tailored mental health interventions are cost-effective even when these costs are included.

## Relevance of model population

A key concern raised by the PHAC was the relevance of the model population, which was parameterized for a non-specific mental health subgroup, when compared to the populations for which the tailored interventions were designed. The BSC intervention was delivered in the SCIMITAR study to a population with severe mental illness, including bipolar, schizophrenia and psychosis (5). The integrated care intervention was delivered specifically for a population with military related post-traumatic stress disorder (15).

The mental health version of the economic model included three key parameter changes when compared to the economic model for the general population. Firstly, the underlying risk of mortality was increased in the mental health model by a relative risk of 2.22 which was applied to both smokers and ex-smokers. This value was obtained from a meta-analysis by Walker (2016) (22), where the inclusion criteria included any mental health diagnosis. Secondly the underlying risk of the smoking related morbidities was increased in the mental health model using an odds ratio of 3.1 which was applied to both smokers and ex-smokers. This value was obtained from a meta-analysis by Dare (2019) (23), where the inclusion criteria included people with anxiety, depression, schizophrenia and bipolar disorder. Thirdly, the model applied a disutility (equal to -0.125) to both smokers and ex-smokers. The disutility was obtained from a regression-based analysis by Fernandez (2010) (24) and was a weighted average for populations with mood, anxiety and substance misuse disorders.

The combined impact of the three parameters was to increase lifetime healthcare costs and decrease lifetime QALYs. In addition, the benefits of stopping smoking were more pronounced in the mental health subgroup when compared to the general population version of the economic model. The parameters in the economic model included populations with

less severe mental health conditions, e.g. general mood and anxiety disorders. If the population had been specific for people with serious mental health conditions/PTSD then the benefits of stopping smoking would likely have increased further.

It is not possible to state exactly how the cost-effectiveness results would change if the model was populated with specific parameters for the BSC (i.e. serious mental health conditions) and IC (military related PTSD) interventions. If these populations are associated with an increased risk of mortality, smoking related comorbidities, or disutility than the current model parameters then the ICER is likely to be an over estimate. The tailored mental health interventions may be more cost-effective than identified in this analysis as we are potentially missing some of the benefits associated with stopping smoking for populations with severe mental health conditions.

## Comparison with other models

The NICE cost-effectiveness evidence review identified the study by Barnett (2015) (12), which established the cost-effectiveness of IC versus SCC across the lifetime in a population of veterans with PTSD. When converted from US dollars to pounds sterling, the ICER for IC versus SCC in Barnett (2015) (12) was between £20,000 and £30,000. The ICER for IC versus SCC in this analysis was substantially lower, equal to £6,847. The value of the ICER was higher in the study by Barnett (2015) (12) as the cost-effectiveness model only included effects on smoking related mortality. The ICER in Barnett (2015) (12) would have been decreased if the study had included utility decrements and treatment costs for smoking related morbidities, as were included in the economic model for this analysis.

Results from this economic modelling report were comparable to results from other economic modelling reports in the NICE tobacco guideline update for smoking cessation (16) and relapse prevention (38) in the general population. A theme across all of the economic modelling is that effective interventions are cost-effective. People who quit smoking are less likely to suffer from smoking related diseases later in life. Interventions which promote smoking cessation are associated with substantial health benefits and cost savings across the lifetime, even after discounting. As demonstrated in this analysis, the health benefits and treatment savings even outweigh the relatively large upfront costs of tailored mental health interventions.

The economic modelling report in the NICE guideline update for smoking cessation in the general population (16) included a mental health subgroup analysis which assessed the cost-effectiveness of pharmacotherapies versus placebo. The cost-effectiveness results (i.e. total costs and QALYs) from this study should not be directly compared with results from the mental health subgroup. This is because the effectiveness estimates for the subgroup were obtained from a network meta-analysis which included mental health conditions such as generalised depression and anxiety. In general, the rate of smoking cessation is likely to be substantially lower for more severe mental health populations, for example the population in the SCIMITAR study.

The evidence from this analysis does indicate that tailored interventions for smoking cessation are likely to be cost-effective above the current usual care that is provided by LSSS. Usual care for mental health populations typically includes some form of pharmacotherapy such as NRT, bupropion and varenicline and these interventions were included in the economic modelling for smoking cessation in the general population (16). However, the most cost-effective treatment for the mental health subgroup was bupropion plus combination therapy with NRT long and short acting products. Combination strategies are not likely to represent the typical usual care provided to mental health populations.

Additional research is required to determine whether tailored interventions for mental health populations are effective and cost-effective versus the most cost-effective pharmacotherapies.

# Limitations

As with any economic evaluation, there are a number of limitations inherent within the analysis. Due to resource constraints, and a lack of relevant evidence in the published literature, it was not possible to fully parameterise the model for specific mental health populations. Therefore, several parameters are assumed to be consistent with the economic model for a general population without mental health conditions. Had we identified parameters specific for mental health populations then the cost-effectiveness of the tailored interventions may have been further increased. For example, due to a lack of evidence equivalent costs and disutilities were applied to each smoking related morbidity for the mental health and general population economic models. It is potentially more likely that comorbidity costs and disutilities would be increased rather than decreased for people with mental health conditions. Increased costs and disutilities per comorbidity would increase the benefits attached to quitting smoking, and would have decreased the ICERs for the tailored cessation interventions.

In addition, all of the limitations associated with the economic model for the general population are relevant to the mental health model adaptation. The model structure, resource constraints and a lack of data made it impossible to categorize former smokers as achieving either ‘recent’ or ‘long-term’ abstinence and the impact of this on our findings is unclear. If, at some point after permanently stopping smoking, the probability of developing some or all of the model co-morbidities returns to that of non-smokers, the model will have overestimated the numbers of people with co-morbidities and, hence, co-morbidity costs, resulting in an underestimation of each interventions’ cost effectiveness. For the same reasons the model was not adjusted to model sub-groups with different risk profiles for example, patients with severe mental illness or with underlying cardiovascular conditions.

The model does not explicitly include multiple quit attempts beyond the initial intervention in the first year. However, the incorporation of a background ‘net’ quit rate into the model addresses this limitation. Sensitivity analysis showed that this input has some impact on the results but would need to change significantly in order for the direction of results to change.

Finally, it should be noted that the following potential benefits associated with smoking cessation were not included in the analysis:

- Reduction in other smoking-related diseases (apart from the five long-term comorbidities and asthma exacerbations)
- Improved recovery from other healthcare interventions such as surgery
- Impact on other people’s smoking behaviour
- Second-hand smoke
- Level of tobacco consumption

The exclusion of these factors (due to a lack of reliable data and resource limitations) suggests that the current analysis may be underestimating the real benefits of preventing a smoking relapse. Given that the conclusion of this report is that the tailored mental health interventions were cost-effective, including these additional benefits would only make the interventions appear more cost effective. This would not alter any of the conclusions presented.

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