National Institute for Health and Care Excellence

Draft for Consultation

Tobacco: preventing uptake, promoting quitting and treating dependence: update

[O] Evidence review for tailored interventions for those with mental health conditions

NICE guideline <number>

Evidence reviews underpinning research recommendations in the NICE guideline

June 2021

Draft for Consultation

These evidence reviews were developed by PH-IGD

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Tailored interventions in those with mental health conditions

Review questions

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?

Introduction

Smoking prevalence is higher in those with mental health conditions and the decline of smoking in this group is at a much slower rate than in the general population. This is a group who are historically less likely to succeed in any quit attempt. Smoking cessation and harm reduction in this population is a key priority.

This review aims to identify which tailored behavioural and pharmacotherapy interventions are most effective and cost effective, when compared with no intervention or usual care, at helping those with mental health conditions quit smoking or reduce their smoking.

PICO table

The following table summarises the protocol for this review.

Table 1: PICO information for tailored mental health interventions review

Domain	Detail
Population	**Included:** 8.1a Anyone aged 18 and over with a mental health condition who smokes and wants to stop smoking. 8.1b Anyone aged 18 and over who smokes, with a mental health condition and wants to reduce their harm from smoking without stopping completely **Excluded**: • People who do not smoke, or only use smokeless tobacco • Pregnant and breastfeeding women • People aged 17 and under • Those who have recently quit smoking
Intervention	**Included**: Smoking cessation or harm reduction interventions that include both: • A behavioural intervention (brief advice, counselling, telephone support or other) • Pharmacotherapy and/or nicotine-containing e-cigarettes. The intervention must describe that it is clearly tailored for people with mental health conditions **Excluded**: • Interventions that do not include tailoring of the smoking cessation or harm reduction intervention. • Therapies not licensed in the UK.

Domain	Detail
	• Alternative and complementary therapies.
Comparator	• No intervention • Usual care • Non-tailored smoking cessation or harm reduction programmes
Outcome	**Critical outcomes 8.1a** Cessation: Smoking status at a minimum of 6 months, longer follow-up will be included where available. Measured as abstinence from smoking (relative risk) Where continued abstinence is presented, this is preferred over point-prevalence abstinence. Point prevalence measures will only be used where no continuous measure is reported **Critical outcomes 8.1b** Quit status (defined as for 8.1a) Harm reduction status at a minimum of 6 months, longer follow-up will be included where available. Measured as: Reduction in validated biochemical measures: • Carbon monoxide in expired air or blood sample • Urinary cotinine • Anabasine and anatabine in urine. **8.1a and 8.1b Important outcomes** Adverse or unintended (positive or negative) effects, this may include any impact on mental health outcomes if reported. Health-related quality of life (using validated patient-report measures, for example EQ-5D or validated measures of mental health or wellbeing). **8.1b Important outcomes** Reduction in smoking-related symptoms: • Cough • Phlegm • Shortness of breath • Wheezing
Study designs	Systematic reviews of RCTs RCTs (including clusters RCTs)

RCT – Randomised controlled trial

Methods and process

This evidence review was developed using the methods and process described in Developing NICE guidelines: the manual (2018). Methods specific to this review question are described in the review protocol in Appendix D.

Declarations of interest were recorded according to NICE's 2018 conflicts of interest policy.

See the methods chapter for additional information on methods for the Tobacco guideline.

Identification of public health evidence

Included studies

The search identified 5363 papers to be screened for this review, of these 32 papers with potential to answer the review questions were ordered for full-text review. Of these, 3 studies (1 effectiveness pilot RCT of 68 participants, 1 follow up effectiveness RCT with 510 participants in those with severe mental health conditions and 1 effectiveness RCT in those with posttraumatic stress disorder (PTSD) were included in the review. The studies were relevant to review question 8.1a only. No studies were identified for question 8.1b on harm reduction.

The 3 included effectiveness studies were judged to have a 'high' risk of bias or 'some concerns' due to missing outcome data and risk of bias in measurement of the outcome.

Excluded studies

28 full text documents were excluded for this question. The documents and the reasons for their exclusion are listed in Appendix K – Excluded studies

Summary of public health studies included in the evidence review

Table 2: Summary of studies

Study	Population	Intervention	Comparison	Outcome(s)	Risk of bias
McFall 2010 USA	Smokers with military related PTSD N=943	Smoking cessation treatment integrated within mental health care for PTSD delivered by mental health clinicians: (integrated care [IC])	Referral to Veterans Affairs smoking cessation clinics: (SCC).	Smoking status (12-month prolonged abstinence verified with carbon monoxide of ≤8 ppm and urine cotinine of <100 ng/ mL cotinine)	Some concerns
Gilbody 2015 UK	Smokers with severe mental health conditions N=68	Structured smoking cessation intervention (behavioural and pharmacological support) delivered with adaptations for those with severe mental illness.	Usual care participants were offered access to local smoking cessation services not specifically designed for people with severe mental illnesses	Smoking status (7-day point prevalence abstinence at 12 months verified with carbon monoxide <10 ppm). Mental health outcomes (depression, anxiety & mental health component scores)	High
Gilbody 2019 UK	Smokers with severe mental health conditions N=442	Structured smoking cessation intervention (behavioural and pharmacological support) delivered	Usual care participants were offered access to local smoking	Smoking status (7-day point prevalence abstinence at 6 and 12 months verified with carbon	Some concerns

Study	Population	Intervention	Comparison	Outcome(s)	Risk of bias
		with adaptations for those with severe mental illness.	cessation services not specifically designed for people with severe mental illnesses	monoxide <10 ppm). Mental health outcomes (depression, anxiety & mental health component scores)	

Synthesis and appraisal of public health studies included in the evidence review

Evidence appraisal

- This review addresses an intervention question. Randomised controlled trial (RCT) evidence was therefore assessed using Cochrane's *Risk of Bias* tool.
- All GRADE ratings start at 'high' and are downgraded as appropriate.

See Appendix F for full GRADE tables.

See Methods document for details of rationale for GRADE judgements.

Table 3: Minimal Important Differences (MIDs) agreed

Outcome	Importance	MID
Abstinence from smoking	Critical	Statistical significance
Mental health outcomes	Important	Published MID (PHQ-9 5 score points; GAD-7 4 score points)
Health-related quality of life	Important	Published MID if one available (e.g. SF-12 has published MID of 6.8 points; SF-36 of 2-4 points) Otherwise default: Dichotomous outcomes: 25% increase or 20% decrease (RR 0.8 to 1.25) Continuous outcomes: 0.5*standard deviation

Data synthesis

Three quantitative studies were identified for inclusion in this review.

All studies measured change in abstinence from smoking after versus before implementation of a tailored behavioural and pharmacological intervention for those with severe mental health conditions or PTSD (see GRADE tables 1 and 2).

Two studies (Gilbody 2015 and Gilbody 2019) also reported on mental health outcomes measured by various questionnaires (see GRADE table 3). Gilbody 2019, measured severity of depression, severity of anxiety and quality of life (mental health component), Gilbody 2015 measured severity of depression and quality of life (mental health component).

Economic evidence

Included studies

1703 records were assessed against the eligibility criteria for review question (RQ) 8.1.

1679 records were excluded based on information in the title and abstract for RQ 8.1. Both reviewers assessed all of the records. The level of agreement between the two reviewers was 100%.

The full-text papers of 24 documents were retrieved and assessed. 4 studies were assessed as meeting the eligibility criteria for RQ 8.1. Both reviewers assessed all of the full texts. The level of agreement between the two reviewers was 100%.

The study selection process can be found in Appendix G and economic evidence tables can be found in Appendix H

Excluded studies

54 full text documents were excluded for this question. The documents and the reasons for their exclusion are listed in Appendix K – Excluded studies.

Summary of studies included in the economic evidence review

Table 4: Summary of the studies

Study	Limitations	Applicability	Other comments	Incremental			Uncertainty
				Costs	Effects	Cost-effectiveness	
Barnett (2016) Integrated Care (IC) for smoking cessation which includes 5 weekly sessions, pharmacotherapy, 3 booster sessions and a monthly follow-up session vs. referral to standard specialised outpatient smoking clinic (SCC) for veterans receiving treatment for post-traumatic stress disorder (PTSD)	Minor limitations [a]	Partly applicable [b]	The study conducted cost-effectiveness analysis alongside a randomised controlled trial (RCT) with an 18-month time horizon from a US payer perspective. A Markov model was used to estimate costs and benefits.	**Total incremental total costs per person; mean, $ (discounted):** IC vs. SCC 836	**Incremental QALYs per person (discounted):** IC vs. SCC 0.026	**ICER, $:** IC vs. SCC 32,257 per QALY gained	Findings from a probabilistic sensitivity analysis showed that, at a cost-effectiveness threshold of $100,000 per QALY gained, IC was 86.0% likely to be cost-effective.
Abbreviations: IC: integrated care; ICER: incremental cost-effectiveness ratio; PTSD: post-traumatic stress disorder; QALY: quality-adjusted life year; RCT: randomised controlled trial; SCC: smoking cessation clinic							
There are some concerns about the validity of the health-related quality of life data used in the model. The model relied on quality of life estimates developed in the UK as no US estimates were available.							
The intervention considered is relevant to the UK context, but caution is required when transferring the results of the study given the difference in prices and healthcare systems between the UK and the US.							

Study	Limitations	Applicability	Other comments	Incremental			Uncertainty
				Costs	Effects	Cost-effectiveness	
Li (2020) A specialist bespoke smoking cessation (BSC) [a] package compared with standard smoking cessation services (usual care) for people with severe mental illness in England	Minor limitations [b]	Directly applicable	The study conducted an economic evaluation alongside a RCT with a 12-month time horizon. The perspective of the analysis was UK NHS and PSS. *The report of the project has been published in full in a health technology assessment (Peckham, 2019).*	**Incremental cost per person; adjusted [c], £ (95% CI):** BSC vs. usual care -270 (-1690 to 1424)	**Incremental QALYs per person; adjusted [d] (95% CI):** BSC vs. usual care 0.013 (-0.008 to 0.045)	**ICER; £:** BSC dominates usual care (less costly and more effective)	The probability of BSC being cost-effective compared with usual care was 76% at £20,000 per QALY threshold and 80% at £30,000 per QALY threshold. Complete case analysis (CCA) suggested that BSC was costlier than usual care and more effective and the ICER indicated that BSC was not cost-effective compared with usual care at the £20,000 per QALY threshold.

Abbreviations: BSC: bespoke smoking cessation; ICER: incremental cost-effectiveness ratio; MH-SCP: mental health smoking cessation practitioner; NHS: National Health Service; PSS: Personal Social Services; QALY: quality-adjusted life year; RCT: randomised controlled trial; SMI: severe mental illness

a. Participants randomised to receive the bespoke package were offered up to 12 individual face-to face (approx. 30 minutes) sessions with a 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.

b. The evaluation was carried out to a high standard and well reported. However, the effectiveness of the programme does not appear to have been robustly established and there is high uncertainty around the magnitude of both costs and benefits.

c. Adjusted for health resource use in the 6 months before randomisation, age, gender, pre-existing medical conditions, duration since first diagnosis of SMI, with study centre as random effect.

d. Adjusted for the EQ-5D-5 L utility value at baseline, age, gender, pre-existing medical conditions, duration since first diagnosis of SMI, with study centre as random effect.

Study	Limitations	Applicability	Other comments	Incremental			Uncertainty
				Costs	Effects	Cost-effectiveness	
Peckham (2019) A specialist bespoke smoking cessation (BSC) [a] package compared with standard smoking cessation services (usual care) for people with severe mental illness in England	Minor limitations [b]	Directly applicable	The study conducted an economic evaluation alongside a RCT with a 12-month time horizon. The perspective of the analysis was UK NHS and PSS.	**Incremental cost per person; adjusted [c], £ (95% CI):** BSC vs. usual care -270 (-1817 to 1297)	**Incremental QALYs per person; adjusted [d] (95% CI):** BSC vs. usual care 0.026 (-0.008 to 0.045)	**ICER; £:** BSC dominates usual care (less costly and more effective)	The probability of BSC being cost-effective could range from 62% at a cost-effectiveness threshold of £0 to nearly 90% at a threshold of £100,000 per QALY gained. Results from the complete case analysis (CCA) showed that the probability of the intervention being cost-effective was 61-65% for WTP thresholds between £20,000 and £30,000 per QALY gained.

Abbreviations: BSC: bespoke smoking cessation; CCA: complete case analysis; ICER: incremental cost-effectiveness ratio; MH-SCP: mental health smoking cessation practitioner; NHS: National Health Service; PSS: Personal Social Services; QALY: quality-adjusted life year; RCT: randomised controlled trial; SMI: severe mental illness; WTP: willingness to pay

a. Participants randomised to receive the bespoke package were offered up to 12 individual face-to face (approx. 30 minutes) sessions with a 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.

b. The evaluation was carried out to a high standard and well reported. However, the effectiveness of programme does not appear to have been robustly established and there is high uncertainty around the magnitude of both costs and benefits.

c. Adjusted for health resource use in the 6 months before randomisation, age, gender, pre-existing medical conditions, duration since first diagnosis of SMI, with study centre as random effect.

d. Adjusted for EQ-5D-5L utility value at baseline, age, gender, pre-existing medical conditions, duration since first diagnosis of SMI, with study centre as random effect.

Study	Limitations	Applicability	Other comments	Incremental			Uncertainty
				Costs	Effects	Cost-effectiveness	
Peckham (2015) A bespoke smoking cessation (BSC) intervention delivered by mental health specialists trained to deliver evidence-supported smoking cessation interventions compared with usual GP care for people with SMI.	Minor limitations [a]	Directly applicable [b]	The study conducted an economic evaluation alongside a pilot pragmatic two-arm RCT with a 12-month time horizon. The perspective of the analysis was UK NHS and PSS.	**Incremental total cost £ (SD):** 221 (160) per participant **Total costs £ (SD):** BSC: 12,674 (16,596) UC: 6867 (6026)	**Incremental effects:** Proportions of group quitting: BSC: 36% UC: 23% **Mean QALY gain per person (95% CI):** BSC group: 0.65 (0.58 to 0.72) UC group: 0.69 (0.63 to 0.75	**ICER; £:** 58,197 per quitter	The ICER should be treated with caution because of the small sample size and large variance of total cost. This pilot trial was not powered to detect a significant difference from an economic perspective.

Abbreviations: ICER: incremental cost-effectiveness ratio; MH-SCP: mental health smoking cessation practitioner; NHS=National Health Service; PSS: Personal Social Services; QALY: quality-adjusted life year; RCT: randomised control trial; SMI: severe mental illness; UC: usual care

a. The evaluation was carried out to a high standard and well reported. However, the intervention did not deliver benefits in terms of QALY gains. Furthermore, there is high uncertainty around the magnitude of mean costs

b. The RCT was undertaken in mental health and primary care settings in England and perspective of the study was the NHS and PSS. The health-related quality of life data used in the analysis were collected using the EQ-5D questionnaire

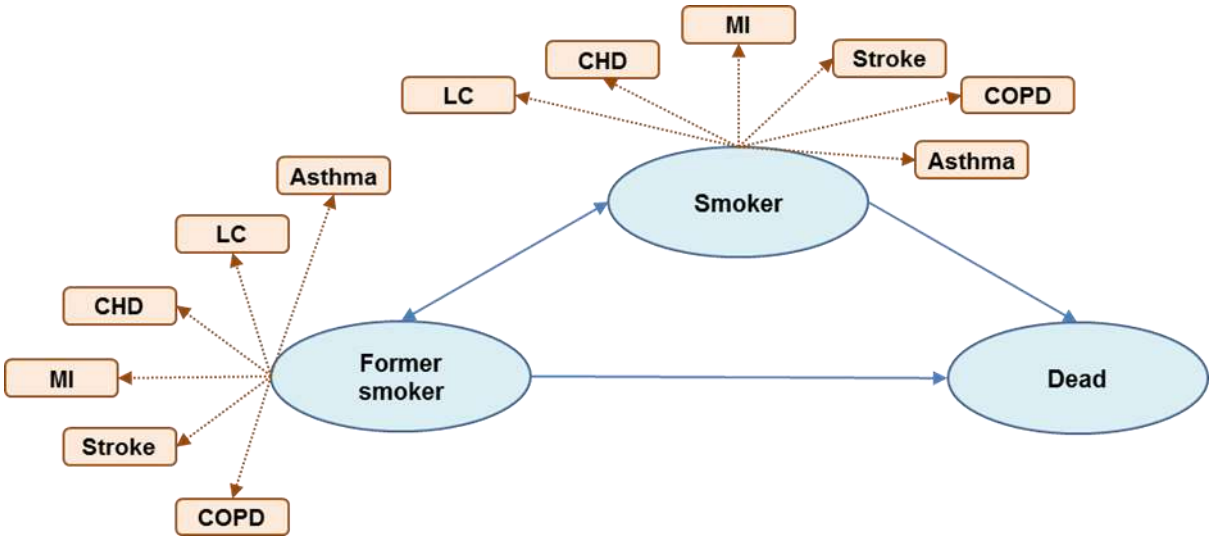
Economic model

This analysis updated an existing markov economic model which was previously used to inform NICE NG92 guidelines on smoking cessation. Updates to the NG92 model were limited to parameter values including intervention costs, resource usage, and effectiveness in terms of smoking abstinence. The cessation interventions for people with severe mental illness and PTSD included in this economic analysis were informed by effectiveness evidence in this review. Formal economic modelling was not possible for the research question related to smoking harm reduction as no relevant evidence was identified.

Model structure

The model estimates the costs and QALYs for the intervention and comparator from the perspective of the NHS and PSS over a lifetime horizon. It considers six smoking related diseases: COPD, stroke, myocardial infarction, coronary heart disease, lung cancer and asthma. It includes annual cycles where smokers have a probability of quitting (and becoming former smokers) and former smokers have a probability of relapsing. People from either the 'smoker' or 'former smoker' health state can move to the 'dead' health state. Each comorbidity has an associated cost and disutility associated with the disease occurring. These costs and utilities are applied during each annual cycle and summed to estimate lifetime costs and QALYs across all cycles.

Figure 1: Model structure



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 (Report Q). 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 Bespoke Smoking Cessation (BSC) intervention analysis which included a population with bipolar, schizophrenia and psychosis and for the Integrated Care (IC) intervention 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 (Report Q).

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 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.

The overall relative risk of mortality in mental health populations was identified in a meta-analysis by Walker et al. (2016)[1]. 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.

The odds of having a chronic physical disease for mental health populations vs. a general population was identified in a meta-analysis by Dare et al. (2019). The MA 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)[2], equal to 3.1, was converted to a relative risk for 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)[3]. 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

The effectiveness estimates for the two interventions modelled were obtained from the current review. The effectiveness of the BSC intervention was obtained from a meta-analysis

[1] Walker ER, McGee RE, Druss BG. Mortality in mental disorders and global disease burden implications: a systematic review and meta-analysis. JAMA psychiatry. 2015;72(4):334-341

[2] Daré LO, Bruand P-E, Gérard D, Marin B, Lameyre V, Boumédiène F, Preux P-M. Co-morbidities of mental disorders and chronic physical diseases in developing and emerging countries: a meta-analysis. BMC public health. 2019;19(1):304.

[3] Fernandez A, Saameno JAB, Pinto-Meza A, Luciano JV, Autonell J, Palao D, Salvador-Carulla L, Campayo JG, Haro JM, Serrano A. Burden of chronic physical conditions and mental disorders in primary care. *The British Journal of Psychiatry*. 2010;**196**(4):302-309.

conducted by NICE which pooled effectiveness estimates across two studies, these being the main SCIMITAR trial[4], and the pilot SCIMITAR study[5]. 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)[6]. 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)[6].

Table 5: 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 usage 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 usage, for example the IC intervention had healthcare resource usage with a mean equal to US$24,171 and a standard deviation equal to US $29,568[7]. The committee agreed that the 12-month service usage costs were very imprecise and likely to introduce uncertainty into the economic analysis. There was no significant difference between service usage for BSC

[4] Gilbody S, Peckham E, Bailey D, Arundel C, Heron P, Crosland S, Fairhurst C, Hewitt C, Li J, Parrott S. Smoking cessation for people with severe mental illness (SCIMITAR+): a pragmatic randomised controlled trial. The Lancet Psychiatry. 2019;6(5):379-390.

[5] Gilbody S, Peckham E, Man M-S, Mitchell N, Li J, Becque T, Hewitt C, Knowles S, Bradshaw T, Planner C. Bespoke smoking cessation for people with severe mental ill health (SCIMITAR): a pilot randomised controlled trial. *The Lancet Psychiatry*. 2015;**2**(5):395-402.

[6] McFall M, Saxon AJ, Malte CA, Chow B, Bailey S, Baker DG, Beckham JC, Boardman KD, Carmody TP, Joseph AM. Integrating tobacco cessation into mental health care for posttraumatic stress disorder: a randomized controlled trial. *Jama*. 2010;**304**(22):2485-2493.

[7] Barnett PG, Jeffers A, Smith MW, Chow BK, McFall M, Saxon AJ. Cost-effectiveness of integrating tobacco cessation into post-traumatic stress disorder treatment. *Nicotine & Tobacco Research*. 2015;**18**(3):267-274.

versus usual care and for IC versus SCC. The committee's preference was to exclude the 12-month healthcare service usage costs from the base case analysis. These costs were included in a scenario analysis.

Table 6: intervention costs, UK £2019 prices

	Costs (per person)	
Intervention	Intervention mean	Usual care mean
Bespoke smoking cessation total intervention costs only	£433	£0
Bespoke smoking cessation total intervention costs + usual care costs	£581	£96
Integrated Care intervention	£963	£412

Sensitivity and Scenario Analysis

Two scenario analyses were conducted for the 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.

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

Deterministic sensitivity analysis (DSA) was performed for key input parameters which included: effectiveness estimates, intervention costs, natural rate of smoking relapse per year, time horizon, discount rates; utility values and disutility and cost per smoking related comorbidities.

Probabilistic sensitivity analysis (PSA) which considers the uncertainty in the value of multiple parameters in the model was conducted using 3,000 iterations. Input parameter distributions for the PSA followed recommendations in Briggs et al. (2006)[8].

A detailed description of the model with full results and sensitivity analyses is provided in a separate economic modelling report (evidence review S).

Economic results

Bespoke smoking cessation intervention

Base case analysis

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.

Table 7: Cost effectiveness results (per person): BSC intervention vs usual care

	BSC	**Usual care**	**Incremental**

[8] Briggs A, Sculpher M, Claxton K. *Decision modelling for health economic evaluation*: Oup Oxford; 2006.

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**

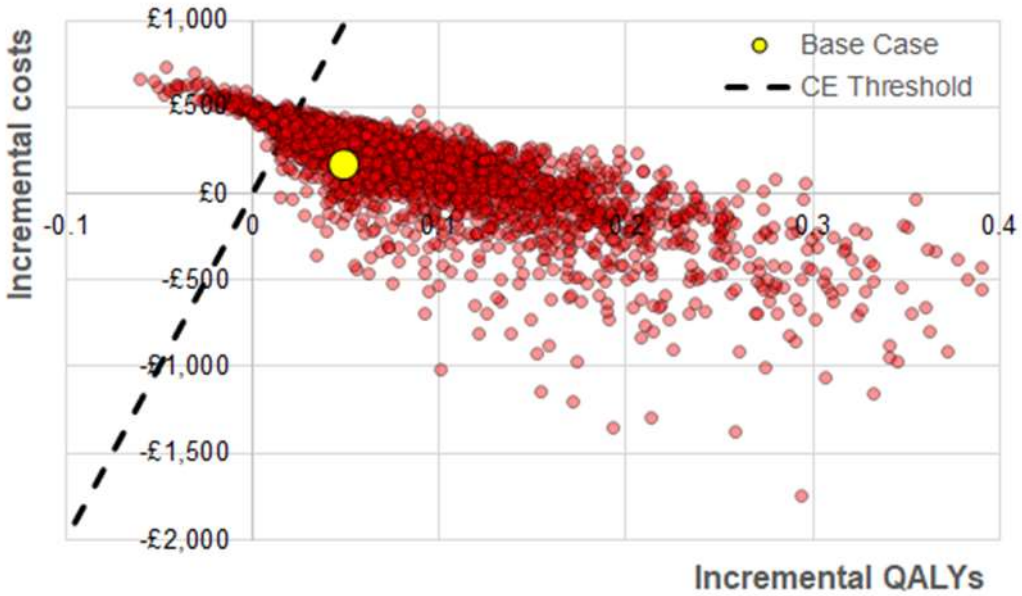
Deterministic sensitivity analysis

The results of the deterministic sensitivity analysis for the BSC indicated considerable uncertainty in the cost-effectiveness results when modifying the effectiveness estimates: Applying 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.

Probabilistic sensitivity analysis

The results of the PSA are presented in Figure 2 where incremental costs and incremental QALYs are plotted. As the figure shows most of the dots fall below the cost effectiveness threshold. At the threshold of £20,000 per QALY the probability of BSC being cost effective compared to current provision was estimated to be 89%.

Figure 2: PSA results for BSC versus usual care (base case)



Scenario analyses

The first scenario analysis used self-reported and biochemically validated quit rates. In this analysis the BSC intervention was cost-effective versus usual care, with an ICER equal to

£1,837. The PSA analysis showed the BSC intervention was cost-effective in 92% of PSA iterations when compared with usual care.

The second scenario analysis included healthcare service usage 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 (i.e. it was more effective and less costly than usual care). The PSA analysis showed the BSC intervention was cost-effective in 94% of PSA iterations when compared with usual care.

Integrated care intervention

Base case analysis

The IC intervention was cost-effective vs SCC with an ICER equal to £6,847 substantially below the £20,000 per QALY threshold (Table 8).

Table 8: Cost-effectiveness results (per person): IC 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**	**£291**
QALYs	**11.49**	**11.45**	**0.04**
ICER			**£6,847**

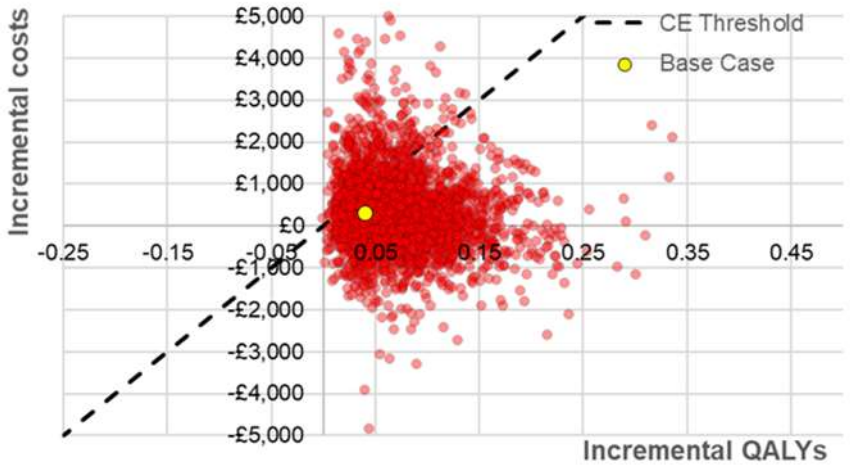
Deterministic sensitivity analysis

The results of the deterministic sensitivity analysis for the IC showed there was considerable uncertainty in the cost-effectiveness results when modifying the effectiveness estimates: Applying 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. Results across the other DSAs were robust with the IC intervention remaining cost-effective versus SCC with an ICER below the £20,000 threshold.

Probabilistic sensitivity analysis

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 3.

Figure 3: PSA results for Integrated care versus standard smoking cessation clinic



Scenario analyses

The first scenario analysis used self-reported quit rates. The IC intervention was cost-effective versus SCC, with an ICER equal to £1,565. The PSA analysis showed the IC intervention was cost-effective in 94% of PSA iterations when compared with usual care.

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. At a threshold of £20,000 per QALY, the IC intervention was cost-effective in 54% of PSA iterations when compared with SCC. The inclusion of healthcare resource usage costs resulted in a substantial increase in the variability of incremental costs which ranged from +/- £150,000 across all PSA iterations.

Summary of the evidence

This table is an overview of the results presented in the GRADE tables. The GRADE tables contain more information about confidence in the evidence and limitations (Appendix F).

Table 9: Evidence summary

Outcome	Population/Studies	Summary	Confidence	GRADE profile
Abstinence from smoking (pooled data)	Those with severe mental health conditions Gilbody 2015 & Gilbody 2019	• At 12 months a tailored behavioural/pharmacological intervention was associated with a significant increase in abstinence from smoking in two studies when both biochemically validated and self-reported outcome data were analysed. • Pooled RR for self-reported and biochemically validated outcome data: 1.54 (1.01 to 2.34) p=0.04 • At 12 months a tailored behavioural/pharmacological intervention was associated with no significant increase in abstinence from smoking	Very low to low	Profile 1

Outcome	Population/Studies	Summary	Confidence	GRADE profile
		in two studies when only biochemically validated outcome data was analysed. • Pooled RR for biochemically validated outcome data only: 1.46 (0.96 to 2.23) p=0.08		
Abstinence from smoking (individual data)	Those with severe mental health conditions Gilbody 2015	• At 12 months the intervention was associated with no significant increase in abstinence from smoking: • RR for self-reported and biochemically validated outcome data: 1.6 (0.7 to 3.4), • RR for biochemically validated outcome data only: 1.3 (0.6 to 2.9)	Low	Profile 2
Abstinence from smoking (individual data)	Those with severe mental health conditions Gilbody 2019	• At 6 months the intervention was associated with a significant increase in abstinence from smoking: • RR for biochemically validated outcome data: 2.2 (1.2 to 4.0) • At 12 months the intervention was associated with no significant increase in abstinence from smoking: • RR for biochemically validated outcome data: 1·5 (0·9 to 2·5)	Moderate	Profile 2
Abstinence from smoking (individual data)	Smokers with military related PTSD McFall 2010	• At 12 months follow up the intervention was associated with a significant increase in abstinence from smoking: • RR for self-report outcome data: 2.21 (1.49 to 3.26) • RR for biochemically validated outcome data: 2.00 (CI 1.20 to 3.32)	Moderate	Profile 2
Mental health outcomes	Those with severe mental health conditions Gilbody 2015	• At 6 months follow up there was no significant difference in severity of depression scores between the intervention and control group. MD 0.90 (-2.39 to 4.19) p=0.59. • At 12 months follow up the control group was associated with a significantly lower score in the severity of depression	Very low	Profile 3

Outcome	Population/Studies	Summary	Confidence	GRADE profile
		scores compared with the intervention group: MD 3.50 (0.08 to 6.92) p=0.05 • At 6 and 12 months follow up there was no significant difference in mental health component scores between the intervention and control group. MD -4.50 (-10.18 to 1.18) p=0.12, MD -2.70 (-7.98 to 2.58) p=0.32 respectively.		
Mental health outcomes	Those with severe mental health conditions Gilbody 2019	• At 6 and 12 months follow up there was no significant difference in severity of depression scores between the intervention and control group: MD 0·20 (–0·85 to 1·24) p=0.72, MD –0·12 (–1·18 to 0·94), p=0.82 respectively. • At 6 and 12 months follow up there was no significant difference in severity of anxiety scores between the intervention and control group: MD –0·32 (–1·26 to 0·62) p=0.50, MD –0·10 (–1·05 to 0·86), p=0.84 respectively. • At 6 and 12 months follow up there was no significant difference in mental health component scores between the intervention and control group: MD –0·73 (–2·82 to 1·36) p=0.49, MD –0·41 (–2·35 to 1·53), p=0.68 respectively.	Low	Profile 3

Health economics evidence statements

- Barnett (2016) found that the integrated care (IC) smoking cessation intervention dominates (i.e. is less costly and more effective than) usual care for smokers receiving treatment for PTSD. Results from a probabilistic sensitivity analysis (PSA) showed that the probability of IC being cost-effective compared with usual care was 86% at a cost-effectiveness threshold of $100,000. The reviewers highlight that the methods to estimate QALYs were unclear. The authors highlight that health care costs were not included in the analysis due to concerns about the reliability of the trial data. Further analysis of sensitivity of cost-effectiveness results to variations in HRQoL would have been useful. The analysis was assessed as partly applicable to the review question, with minor limitations.

- Li (2020) found that the bespoke smoking cessation (BSC) intervention dominates (less costly and more effective) usual care for people with severe mental illness (SMI), from an NHS and PSS perspective. Results from a probabilistic sensitivity analysis (PSA) showed that the probability of BSC being cost-effective compared with usual care was 76% at a cost-effectiveness threshold of £20,000 and 80% at a cost-effectiveness threshold of £30,000.

The reviewers highlight that wide standard error ranges show that incremental cost and QALY results are highly uncertain. Although the BSC intervention was more expensive than usual care (BSC: £190 per participant; usual care: £37 for months 1-6 and £26 for months 7-12 per participant), this did not lead to an increase in overall NHS/PSS costs in the short term. More research is needed to establish the long-term impact of smoking cessation among people with SMIs. It should be noted that Peckham (2019) published a full report of this project in a health technology assessment. The analysis was assessed as directly applicable to the review question, with minor limitations.

- Peckham (2019) found that, from an NHS and PSS perspective, the BSC intervention for people with SMI was likely (57%) to dominate (less costly and more effective) usual care and the probability of cost-effectiveness could reach 80% at a threshold of £30,000. However, this economic evaluation was undertaken alongside the SCIMITAR+ trial and results from the SCIMITAR+ trial showed that neither the difference in costs nor the difference in QALYs were statistically significant. The authors suggest that the impact of smoking cessation on health and wider health service use is unlikely to be observed over the 12-month trial period and that long-term follow-up is needed to assess the sustainability of quit and the associated impact of quitting on health. It should be noted that Li (2020) published a cost-effectiveness report of this project. The analysis was assessed as directly applicable to the review question, with minor limitations.

- Peckham (2015) found that the incremental cost effectiveness ratio (ICER) for the comparison of a bespoke smoking cessation (BSC) intervention versus usual care was £58,197 per quitter. The authors highlighted that this ICER should be treated with caution because of the small sample size and large variance of total cost. Sensitivity analyses were not carried out as this was the data underpinning the evaluation that were collected during a pilot study. Although results from the pilot trial show that there was a greater likelihood of smoking cessation in the BSC group than in the usual care group (odds ratio: 2.9 [95% confidence interval: 0.8 to 10.5]) this difference was not statistically significantly different. Furthermore, over the 12-month trial period, the mean quality adjusted life year gain per person was higher in the usual care group than in the BSC intervention group (0.69 versus 0.65). The authors highlight that the trial was not powered to show a statistically significant difference from an economics perspective and recommend that a definitive trial should be undertaken to establish the clinical and cost effectiveness of the BSC intervention versus usual care. The analysis was assessed as directly applicable to the review question, with minor limitations.

- One directly applicable cost utility analysis with minor limitations found that a bespoke smoking cessation intervention (BSC) for people with severe mental illness including bipolar, schizophrenia and psychosis and an integrated care (IC) intervention for people with PTSD were cost effective at the threshold of £20,000/QALY with ICERS of £3,145/QALY and £6,847/QALY respectively. Uncertainty in parameter values was explored using DSAs and PSAs. The results of the DSA indicated considerable uncertainty in the cost-effectiveness results for both BSC and IC 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 and IC from being highly cost effective to being not cost effective. In contrast when applying the upper 95% CI both interventions 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. In the PSA BSC and IC were identified as being cost effective versus usual care in 89% and 83% of PSA iterations.

The committee's discussion of the evidence

Interpreting the evidence

The outcomes that matter most

The committee agreed that cessation is the most important outcome. The committee also emphasised the importance of reporting mental health outcomes, as concerns over stopping smoking resulting in exacerbations of symptoms of mental health conditions may still be prevalent, despite evidence to the contrary. The committee therefore noted that, where no change in mental health symptoms following cessation is seen in relevant studies, this should be considered a positive outcome because it indicates the absence of adverse effects on mental health. Reviewing this outcome may strengthen confidence that the intervention does not exacerbate poor mental health.

Confidence in the evidence

The committee discussed the cessation outcomes at 6 and 12 months with the SCIMITAR intervention, both for those that were bioverified and those that were bioverified or self-reported. The SCIMITAR main study reported significant findings at 6 months for smoking cessation with the intervention, these were not significant at 12 months. There was moderate confidence in this outcome. Where both the bioverfied and self-report data was reported at 12months and pooled there was a significant increase in abstinence from smoking. For bioverified outcomes there was no difference found between the interventions. The committee discussed that though the results were similar, when considering the bioverified outcomes only the relative risk crossed the line of no effect. and had similar CI ranges. They discussed that the studies were underpowered, so the differences may be based on other factors. They noted the possible influence of this on the weight being given to this evidence.

The committee noted overall that the evidence was limited due to the small number of studies. The committee considered that the pilot and main SCIMITAR studies were relevant to UK practice.

They commented that there is evidence that smoking cessation interventions are effective and as discussed in review [K] those with mental health conditions should be treated equally when discussing cessation interventions. However, due to the persistently higher smoking prevalence in those with mental health conditions this group need additional consideration. At present there is limited evidence on specifically tailored mental health interventions. The committee discussed that those that have been considered have tended to focus on aspects of intervention delivery and intensity, not on novel, mental health-specific content. They discussed the impact of this on the developing of recommendations. They suggested the evidence should be taken as an indication of what is effective in this population but not the only interventions that may be used.

The committee agreed that further research was needed in this area. As SCIMITAR is only one intervention with a different delivery mode rather than a comprehensive body of evidence, they felt it should be considered the starting point for understanding what could be done better. Further research is needed on moderate to severe mental health conditions and with consideration of delivery of services included. They agreed the importance of strengthening the evidence for populations with mental health conditions.

Benefits and harms

The committee agreed the importance of smoking cessation support being available for everyone, and that having a mental health condition must not continue to constitute a barrier to being offered and accessing this support.

The reasons for reviewing smoking cessation evidence specific to populations with mental health conditions were discussed: there may historically have been misconceptions about whether this population should receive smoking cessation interventions, but this is not the case for other health conditions. This was supported by expert testimony 4 relating to inequalities for people with mental illness that was presented to the committee which had discussed the barriers that may exist throughout the system that can make it more difficult for those with mental health conditions to engage with smoking cessation services (expert testimony proformas can be found in Appendix K of Review K).

Some members were concerned that if the guideline implies that people with mental health conditions need to be treated differently to achieve smoking cessation, then they may miss out on standard treatment. It was concluded that there is little evidence that standard interventions don't work for mental health populations, but that specifically tailored interventions may be particularly beneficial; the guideline should reflect both of these points and also highlight the importance of further research in this important area to address persistent tobacco-related inequalities.

Cost effectiveness and resource use

The committee considered 4 published economic evaluations: 3 studies assessed a bespoke smoking cessation package (SCIMITAR,) for people with severe mental illness in England (Li 2020, Peckham 2015, 2019). The bespoke package comprised behavioural support from a mental health smoking cessation practitioner and pharmacotherapies for smoking cessation with adaptations for people with severe mental illness such as extended pre-quit sessions, cut down to quit and home visits. The comparator was access to local smoking cessation services not specifically designed for people with severe mental illness. The 4th study assessed an integrated care package for smoking cessation for veterans receiving treatment for post-traumatic stress disorder (Barnett 2016). It included 5 weekly sessions, pharmacotherapy, 3 booster sessions and a monthly follow-up session. The comparator was access to a standard outpatient smoking clinic.

Peckham (2015) conducted an evaluation alongside a pilot RCT (SCIMITAR) using a markov model, with a UK NHS and PSS perspective and 12 month time horizon. The main outcome was smoking cessation. The incremental cost per quitter was £58,197 but as noted by the authors the pilot trial was not powered to detect a significant difference from an economic perspective.

The evaluations by Peckham (2019) and Li (2020) both use data from the main RCT of SCIMITAR. They adopted an UK NHS and PSS perspective and 12 month time horizon and (not surprisingly) report the same results. The main basecase analyses show the intervention dominates usual care (i.e. is less costly and more effective). The PSA showed the intervention had a 76% probability of being cost effective at the £20,000 per QALY threshold, and 80% at £30,000 per QALY. Using a complete case analysis Li (2020) reports the intervention was more costly than usual care and more effective but not cost effective compared with usual care at the £20,000 per QALY threshold. Using the same data, Peckham (2019) showed the that the probability of the intervention being cost-effective was 61-65% for WTP thresholds between £20,000 and £30,000 per QALY gained.

Whilst the findings from the pilot study were of interest, the committee placed greater importance on the findings of the main RCT. Taking into account the uncertainty of the model inputs, the analyses showed the intervention is likely to be cost effective. The committee agreed with the limitations noted by the authors which included the lack of blinding, the short time horizon, missing data at baseline (around 20%), loss to follow up at 12 months (around 23%) and validity of EQ-5D in people with severe mental illness.

Barnett (2016) conducted the evaluation alongside an RCT using a markov model with a US health care perspective and lifetime horizon. The results showed a greater likelihood of smoking cessation for the integrated care package but the difference was not significantly

different. The cost per QALY gained was $32,257 and the PSA showed that at a threshold of $100,000 per QALY gain the intervention was 86% likely to be cost effective. The committee thought the evaluation may have underestimated the benefits of the intervention as it omitted specific smoking related disease. In addition, as noted by the authors, they were mindful the health care cost data does not account for confounding between illness and quitting. They considered the intervention relevant to the UK context but were mindful of transferring the results given differences between the UK and US in the costs and health care systems.

Overall, despite the limitations, the committee thought the findings were consistent in showing that intensive, tailored support for smoking cessation in people with severe mental illness and PTSD is likely to be cost effective. However, given the short time horizons, the committee agreed it would be useful to assess the interventions using a lifetime horizon.

The committee considered the evidence from the denovo model adapted for people with mental health problems. It adopted a NHS and PSS perspective and lifetime horizon. They noted that both interventions were highly cost effective. The bespoke smoking cessation intervention delivered by mental health specialists (SCIMITAR) had a cost per QALY of £3,145 and an 89% probability of being cost effective at a threshold of £20,000 per QALY. This analysis included only intervention costs for the main SCIMITAR study (no healthcare resource utilization costs or pilot study costs) and used the pooled effectiveness rates for biochemically validated quits across the pilot and main study. The integrated care intervention for people with PTSD had a cost per QALY of £6,847 and 83% probability of being cost effective.

Several other analyses requested by the committee were presented and discussed. Two analyses assessed the impact of including self-reported quit rates in the analysis. The committee thought this would be useful as it would increase the number of data points available for analysis. They observed that combining self-reported and biochemically validated quit rates for the BSC intervention resulted in an even lower ICER (£1,837/QALY) and increased the probability of cost effectiveness to 92%. They noted similar positive changes for the IC intervention when self-reported quit rates were used in the analysis (£691/QALY,94% probability of cost effectiveness).

Two further analyses assessed the impact of altering intervention costs. For the BSC intervention, the committee observed that including the 12-month healthcare service utilisation costs and anti-psychotic prescription costs changed the intervention from being cost effective to dominant. They noted this occurred because the intervention costs for BSC were less than for usual care due to savings in 12-month healthcare resource utilization. They also observed an increase in the probability (94%) of BSC being cost-effective at the threshold of £20,000 per QALY. Similarly, the IC intervention changed from being cost effective to dominant (i.e. more effective and less costly) when the costs of healthcare services were included. However, the committee noted an increase in the uncertainty (only 54% probability) of this intervention being cost effective. They noted this a result of a substantial increase in the variability of incremental costs which ranged from +/- £150,000 across all PSA iterations.

The committee discussed whether the cost estimates for the BSC pilot study (Gilbody, 2015) reflect the typical costs for the intervention or whether the initial costs of developing the intervention altered these. Some members questioned whether it is appropriate to use this data and agreed they should not be included. The committee also discussed the challenges in costing both the bespoke intervention and standard service delivery. Some members did not feel this was possible because of the wide variety of services provided across different healthcare settings. They agreed that the intervention used in the SCIMITAR study was not what people would get in standard services though. They considered that if the comparison of SCIMITAR was made with specialist mental health services that had implemented recommendations of previous NICE guidelines (PH48), the costs for the latter would be higher than standard care and so cost effectiveness of SCIMITAR would be better.

The committee then discussed the healthcare resource utilisation data. They did not consider it appropriate or meaningful to include these in the basecase analysis. They had concerns about the reliability of self-reporting due to the possibility of cognitive or memory problems for participants being treated with antipsychotic medications. They noted these costs occurred after delivery of the intervention so would not normally be included. Nevertheless, they considered it potentially useful to explore whether healthcare resource utilisation changes as a result of smoking cessation. They observed there was little difference in resource use between the intervention and comparator post intervention. They found these data difficult to interpret because it was not known whether the use was positive or negative or related to smoking cessation. They commented that a model of the long-term costs of smoking cessation should look at the epidemiology of smoking-related diseases and at the costs of continuing smoking. They questioned the appropriateness of factoring in these exploratory data given the close and careful attention paid to identifying the costs and benefits of smoking cessation. It was not clear how to use this information and some members would prefer not to use it.

The committee discussed the sub-population model. This population was not restricted to people with severe mental health conditions, it included a wider population. Based on this, they questioned how the findings would relate to a more restricted population; What would happen to benefits and costs in a group with more severe mental health problems? They would expect a higher prevalence of comorbidities in people with severe mental health problems. Whilst the committee noted the sub-population used in the model is comparable to the SCIMITAR population, they considered the model is likely to underestimate the cost effectiveness of interventions for this group due to the lower severity of mental health conditions and lower risk of co-morbidities of the population in the main model.

Other factors the committee took into account

The committee were keen to be able to recommend an intervention that is effective for mental health populations as it would be equitable for this disadvantaged group. They discussed that the intervention used in the SCIMITAR trial did make a positive impact. Though the committee further discussed that it is not clear if the impact was greater than could possibly be achieved with the implementation of the recommendations in previous NICE guidance. They discussed the importance of considering how similar the intervention is to what is currently offered to people in the UK. The committee discussed that the key differences were the delivery mode and the intensity of support. The committee noted that the trial in those with military PTSD also identified that an individually tailored intervention that was effective for smoking cessation. Though they also agreed that as this is a very specific population this study is less directly relevant to those in the UK with mental health conditions.

In the SCIMITAR trial, the intervention was delivered by mental health clinicians. The committee discussed that people with mental health conditions are less likely to access standard smoking cessation services. There was also more flexible individualised support given over a longer duration than would normally be offered. The individual tailored discussions participants had about smoking and their mental health would be used in standard smoking cessation programmes. The committee considered that the evidence presented, the expert testimony 4 relating to inequalities for people with mental illness, and their expertise broadly support the recommendations previously included in the NICE guideline PH48 (Smoking: acute, maternity and mental health services) (expert testimony proformas can be found in Appendix K of Review K). The recommendations in that guideline have been carried forwards into this guideline. They agreed that the SCIMITAR intervention included more intensive support and that mental health professionals were more involved with delivery, but overall, the intervention was not substantially different in terms of content. The issue of implementation was raised. There was agreement that the standard interventions should continue to be offered to those with mental health conditions. The committee discussed that groups with mental health conditions have been identified as a

priority population, where cessation rates are lower and that they may not be currently benefiting from the majority of smoking cessation interventions.

The committee discussed the differences between settings because they felt that the evidence indicated that the setting is an important part of the intervention. Some members of the committee discussed that there has been progress in implementation in mental health inpatient settings, but it is less clear that there has been implementation of the recommendations in PH48 in community settings. They discussed the importance of the continuity of care when people moved between settings; treatment that is started in an acute setting needs to be able to be continued in the community in the long term. The evidence from SCIMITAR indicated that having trained mental health professionals delivering tailored, intensive smoking cessation interventions in these settings could improve this. The committee discussed the importance of identifying where the additional aspects in the SCIMITAR study such as the availability of more flexible individualised smoking cessation support may add to the usual stop smoking support. The committee agreed that further research in those with mental health conditions who are trying to stop smoking is needed and that this should include both individual and system level considerations.

The committee further discussed that the recommendations that they have developed may be challenging to implement and that the provision of this kind of support may be variable. Nonetheless they agreed that due to the importance of providing stop smoking support for those with mental health conditions should include the option of the additional support for those who may find this beneficial.

Recommendations supported by this evidence review

This evidence review supports the research recommendation on support for people with mental health conditions to stop smoking. Other evidence supporting this recommendation can be found in the evidence reviews cessation and harm reduction treatments (review K).

Included study list

Gilbody S, Peckham E, Man M-S, et al. Bespoke smoking cessation for people with severe mental ill health (SCIMITAR): a pilot randomised controlled trial. The Lancet. 2015;2:395-402

Gilbody S, Peckham E, Bailey D, et al. Smoking cessation for people with severe mental illness (SCIMITAR+): a pragmatic randomised controlled trial. Lancet Psychiatry. 2019;6:379-390

McFall M, Saxon AJ, Malte CA, et al. Integrating tobacco cessation into menlla health care for posttraumatic stress disorder: a randomised controlled trial. JAMA. 2010;304:2485-2493

Health economics included studies

Barnett PG, Jeffers A, Smith MW, et al. Cost-Effectiveness of Integrating Tobacco Cessation Into Post-Traumatic Stress Disorder Treatment. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2016;18(3):267-74.

Li J, Fairhurst C, Peckham E, et al. Cost-effectiveness of a specialist smoking cessation package compared with standard smoking cessation services for people with severe mental illness in England: a trial-based economic evaluation from the SCIMITAR+ study. Addiction (Abingdon, England). 2020

Peckham E, Arundel C, Bailey D, et al. A bespoke smoking cessation service compared with treatment as usual for people with severe mental ill health: the SCIMITAR+ RCT. Health technology assessment (Winchester, England). 2019;23(50):1-116.

1 Peckham E, Man M-S, Mitchell N, et al. Smoking Cessation Intervention for severe Mental Ill
2 Health Trial (SCIMITAR): a pilot randomised control trial of the clinical effectiveness and
3 cost-effectiveness of a bespoke smoking cessation service. Health technology assessment
4 (Winchester, England). 2015;19(25):1-vi.

1 Appendices

2 Appendix A – Review protocols

3 Review protocol for tailored interventions in those with mental health conditions

4

ID	Field (based on PRISMA-P	Content
I	Review question	8.1a In those with mental health conditions, what is the effectiveness and cost effectiveness of tailored smoking cessation interventions? 8.1b In those with mental health conditions, what is the effectiveness and cost effectiveness of tailored smoking harm reduction interventions?
II	Type of review question	Intervention
III	Objective of the review	Smoking prevalence is higher in those with mental health conditions and the decline of smoking in this group is at a much slower rate than in the general population. This is a group who are historically less likely to succeed in any quit attempt. Smoking cessation and harm reduction in this population is a key priority.
IV	Eligibility criteria – population/disease/condition/issue/domain	**Included**: 8.1a Anyone aged 18 and over with a mental health condition who smokes and wants to stop smoking. 8.1b Anyone aged 18 and over who smokes and wants to reduce their harm from smoking without stopping completely **Excluded**: People who do not smoke, or only use smokeless tobacco Pregnant and breastfeeding women People aged 17 and under Those who have recently quit smoking. **Setting** All settings included
V	Eligibility criteria – intervention(s)/ exposure(s)/prognostic factor(s)	**Included**: Smoking cessation or harm reduction interventions that include both: • A behavioural intervention (brief advice, counselling, telephone support or other) • Pharmacotherapy and/or nicotine-containing e-cigarettes.

		The intervention must be clearly tailored for people with mental health conditions. **Excluded**: Interventions that do not include tailoring of the smoking cessation or harm reduction intervention, interventions. Therapies not licensed in the UK. Alternative and complementary therapies.
VI	Eligibility criteria – comparator(s)/ control or reference (gold) standard	**Included**: No intervention Usual care Non tailored smoking cessation or harm reduction programmes
VII	Outcomes and prioritisation	<u>8.1a Critical outcomes</u> Cessation: Smoking status at a minimum of 6 months, longer follow-up will be included where available. Measured as abstinence from smoking (relative risk) Where continued abstinence is presented, this is preferred over point-prevalence abstinence. Point prevalence measures will only be used where no continuous measure is reported. <u>8.1b Critical outcomes</u> Quit status (defined as for 8.1a) Harm reduction status at a minimum of 6 months, longer follow-up will be included where available. Measured as: Reduction in validated biochemical measures: • Carbon monoxide in expired air or blood sample • Urinary cotinine • Anabasine and anatabine in urine. Where biochemically validated measures are available (i.e. saliva cotinine / carbon monoxide validation), these will be preferred to self-reported measures. Self-reported measures will only be used where no validated measure is reported. <u>8.1a and 8.1b Important outcomes</u>

		Adverse or unintended (positive or negative) effects, this may include any impact on mental health outcomes if reported Health-related quality of life (using validated patient-report measures, for example EQ-5D or validated measures of mental health or wellbeing). 8.1b Important outcomes Reduction in smoking-related symptoms: • Cough • Phlegm • Shortness of breath • Wheezing **Cost/resource use associated with the intervention** The following outcomes will be extracted in reviews of the health economic evidence, where available: • cost per quality-adjusted life year • cost per unit of effect • net benefit • net present value • cost/resource impact or use associated with the intervention or its components • cost/resource impact or use associated with the comparator or its components
VIII	Eligibility criteria – study design	**Included study designs**: • Systematic reviews of RCTs • RCTs (including cluster RCTs) <u>Economic studies</u>: • Cost-utility (cost per QALY) • Cost benefit (i.e. net benefit) • Cost-effectiveness (Cost per unit of effect) • Cost minimization • Cost-consequence **Excluded study designs**: • Cohort studies • Cross-sectional surveys (except for qualitative data) • Correlation studies • Case control studies • Qualitative studies
IX	Other inclusion exclusion criteria	**Exclusion criteria** Only studies carried out in OECD countries will be included Only full published studies (not protocols or summaries even where they include some data) will be included. **Systematic Review**

		Relevant systematic reviews (SRs) identified from database searches will be citation searched. Highly relevant systematic reviews may be included as a primary source of data. These SRs will be assessed against the inclusion criteria for this protocol, and their quality will be assessed using the ROBIS tool. Where the SR is highly relevant and of high quality, details or data from the systematic review may be used. In addition to any SRs meeting the above criteria, other primary studies will be included if they were published after the publication date of the SR and meet the protocol inclusion criteria. Full economic analyses and costing studies identified from searches will be included. Costing data will not be used for the purpose of the effectiveness review. Health economics reviews and modelling will be conducted by the York Health Economics Consortium (YHEC).Only papers published in the English language will be included.
X	Possible sensitivity/sub-group analysis	The following factors will be of interest for possible subgroup analysis: • Those with severe mental health conditions, defined as so in the included RCT • Interventions in in-patient mental health settings • Interventions in community settings
XI	Selection process – duplicate screening/selection/analysis	It is not anticipated that the search results will be large, so priority screening will not be used. Double screening will be carried out for 10% of titles and abstracts by a second reviewer. Disagreements will be resolved by discussion. Inter-rater reliability will be assessed and reported. If below 90%, a second round of 10% double screening will be considered. The study inclusion and exclusion lists will be checked with members of the PHAC to ensure no studies are excluded inappropriately.
XII	Data management (software)	EPPI Reviewer will be used: • to store lists of citations • to sift studies based on title and abstract • to record decisions about full text papers • to order freely available papers via retrieval function • to request papers via NICE Information Services • to store extracted data Cochrane Review Manager 5 will be used to perform meta-analyses.
XIII	Information sources –	The following methods will be used to identify the evidence: • the databases listed below will be searched with an appropriate strategy.

	databases and dates	• the websites listed below will be searched or browsed with an appropriate strategy. • selected studies that are potentially relevant to the current review will be identified from the bibliography of any systematic reviews identified during the search process that are not being included in their own right. **Database strategies** The principal search strategy will be developed in MEDLINE (Ovid interface) and then adapted, as appropriate, for use in the other sources listed, taking into account their size, search functionality and subject coverage. The databases will be: • Applied Social Science Index and Abstracts (ASSIA) via ProQuest • British Nursing Index (BNI) via ProQuest • Cochrane Central Register of Controlled Trials (CENTRAL) via Wiley • Cochrane Database of Systematic Reviews (CDSR) via Wiley • Cumulative Index to Nursing and Allied Literature (CINAHL) via EBSCOhost • Embase via Ovid • Emcare via Ovid • Health Management Information Consortium (HMIC) via Ovid • MEDLINE ALL via Ovid • PsycINFO via Ovid • Social Policy and Practice (SPP) via Ovid **Database search limits** Database functionality will be used, where available, to exclude: • non-English language papers • animal studies • editorials, letters and commentaries • conference abstracts and posters • registry entries for ongoing or unpublished clinical trials • duplicates. Sources will be searched from 1998 to current. The database search strategies follow standard NICE practice and use the McMaster Therapy RCT filter and the Health-evidence.ca systematic review search filter. The principal search strategy is detailed in Appendix A. The outline of the search structure is: (Smoking cessation OR Smoking reduction) AND (Mental Health Services OR Mental Illness OR Named Mental Disorders) AND (RCTs OR SRs) AND Limits **Cost effectiveness evidence**

		A separate search will be done for cost effectiveness evidence. The standard NICE cost effectiveness search filter listed in Appendix A will be applied. The following databases will be searched again: • Embase via Ovid • MEDLINE ALL via Ovid In addition, the following sources will be searched without study-type filters: • Campbell Collaboration via https://campbellcollaboration.org/library.html • EconLit via Ovid • International HTA database via INAHTA https://database.inahta.org/ • NHS EED via CRD https://www.crd.york.ac.uk/CRDWeb The main website results will be rescanned to check if there are any results potentially relevant to cost effectiveness. **Web of Science** Forward citation searching and reference harvesting will be conducted using Web of Science (WOS) Core Collection. Only those references which NICE can access through its WOS subscription will be added to the search results. Only papers published in 1998-Current and in the English language will be included in the search results. Duplicates will be removed in WOS before downloading. **Websites** The following websites will be searched with an appropriate strategy: • Health Services/Technology Assessment Texts (HSTAT) https://www.ncbi.nlm.nih.gov/books/NBK16710 • NICE Evidence Search https://www.evidence.nhs.uk • Tobacco Control Database for the WHO European Region http://data.euro.who.int/tobacco The websites of relevant organisations, including the ones below, will be browsed: • Action on Smoking and Health (ASH) http://ash.org.uk/home • Centre for Mental Health https://www.centreformentalhealth.org.uk/ • Local Government Association https://www.local.gov.uk • Mind https://www.mind.org.uk/ • National Centre for Smoking Cessation and Training http://www.ncsct.co.uk • Northern Ireland Assembly http://www.niassembly.gov.uk/

		• Public Health England https://www.gov.uk/government/organisations/public-health-england • Royal College of Psychiatrists https://www.rcpsych.ac.uk/ • Royal College of Physicians https://www.rcplondon.ac.uk • Scottish Government https://www.gov.scot • Smokefree NHS https://www.nhs.uk/smokefree • Smoking Toolkit Study http://www.smokinginengland.info • Treat Tobacco http://www.treatobacco.net/en/index.php • UK Centre for Tobacco and Alcohol Studies http://ukctas.net/index.html • University of Bath Tobacco Control Research Group https://researchportal.bath.ac.uk/en/organisations/uk-centre-for-tobacco-control-studies • University of Stirling Centre for Tobacco Control Research https://www.stir.ac.uk/about/faculties-and-services/health-sciences-sport/research/research-groups/centre-for-tobacco-control-research/publications • Welsh Government https://gov.wales/?lang=en The website results will be reviewed on screen and documents in English and published from 1998-Current that are potentially relevant will be added to the EPPI-Reviewer 5 file. **Quality assurance** The Information Services team at NICE will quality assure the principal search strategy and peer review the strategies for the other databases according to the standard NICE checklist that was adapted from the 2015 Peer review of electronic search strategies (PRESS) checklist. Any revisions or additional steps will be agreed by the review team before being implemented. Any deviations and a rationale for them will be recorded in the search history document. **Search results** The database search results will be downloaded to EPPI-Reviewer 5 before duplicates are removed using a two-step process. First, automated deduplication using a high-value algorithm and second manual deduplication to assess 'low-probability' matches. All decisions are retained in the deduplication history.
XIV	Identify if an update	This question is a new question for the Tobacco update.
XV	Author contacts	Please see the guideline development page
XVI	Highlight if amendment to previous protocol	For details please see section 4.5 of Developing NICE guidelines: the manual

XVII	Search strategy – for one database	For details please see appendix B.
XVIII	Data collection process – forms/duplicate	A standardised evidence table format will be used and published as appendix D (effectiveness evidence tables) or H (economic evidence tables).
XIX	Data items – define all variables to be collected	For details please see evidence tables in appendix D (effectiveness evidence tables) or H (economic evidence tables).
XX	Methods for assessing bias at outcome/study level	Risk of bias for individual studies or systematic reviews will be assessed using the preferred study checklists. For details please see Appendix H of Developing NICE guidelines: the manual The risk of bias across all available evidence will be evaluated for each outcome using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group http://www.gradeworkinggroup.org/ GRADE will be used to assess confidence in the findings from quantitative evidence synthesis.
XXI	Criteria for quantitative synthesis (where suitable)	For details please see section 6.4 of Developing NICE guidelines: the manual
XXII	Methods for analysis – combining studies and exploring (in)consistency	**Heterogeneity** Data from different studies will be pooled in a meta-analysis where they are investigating the same outcome and where the resulting meta-analysis may be useful for decision-making. Cluster and individual randomised controlled trials will be pooled. It is anticipated that studies included in the review will be heterogeneous with respect to participants, interventions, comparators, setting and study design. Where significant between study heterogeneity in methodology, population, intervention or comparator is identified by the reviewer in advance of data analysis, random effects models will be used. If methodological heterogeneity is not identified in advance but the I2 value is ≥50%, random effects models will also be used. If the I^2 value is above 50%, heterogeneity will be judged to be serious and so will be downgraded by one level in GRADE. If the I^2 value is above 75%, heterogeneity will be judged to be very serious and will be downgraded by two levels in GRADE.

		If the studies are found to be too heterogeneous to be pooled statistically, a narrative synthesis will be conducted. **Imprecision** No minimally important difference (MID) thresholds relevant to this guideline were identified from the COMET database or other published source. MIDs were agreed by committee. Uncertainty is introduced where confidence intervals cross the MID threshold. If the confidence interval crosses one lower MID threshold, this indicates 'serious' risk of imprecision. Crossing both MID thresholds indicates 'very serious' risk of imprecision in the effect estimate. Where the MID is 'any significant change' there is effectively only one threshold (the line of no effect), and so only one opportunity for downgrading. In this instance, outcomes will be downgraded again if they are based on small samples (<300 people). MIDs for outcomes will be included in the methods section of the individual reviews.
XXIII	Meta-bias assessment – publication bias, selective reporting bias	For details please see Appendix H of Developing NICE guidelines: the manual.
XXIV	Assessment of confidence in cumulative evidence	For details please see sections 6.4 and 9.1 of Developing NICE guidelines: the manual.
XXV	Rationale/context – Current management	For details please see the introduction to the evidence review.
XXVI	Describe contributions of authors and guarantor	A multidisciplinary committee will develop the guideline. The committee will be convened by Public Health Internal Guidelines Development (PH-IGD) team and chaired by Sharon Hopkins in line with section 3 of Developing NICE guidelines: the manual. Staff from Public Health Internal Guidelines Development team will undertake systematic literature searches, appraise the evidence, conduct meta-analysis where appropriate and draft the guideline in collaboration with the committee. Cost-effectiveness analysis will be conducted by YHEC where appropriate. For details please see Developing NICE guidelines: the manual.
XXVII	Sources of funding/support	PH-IGD is funded and hosted by NICE
XXVIII	Name of sponsor	PH-IGD is funded and hosted by NICE
XXIX	Roles of sponsor	NICE funds PH-IGD to develop guidelines for those working in the NHS, public health and social care in England.

XXX	PROSPERO registration number	

1

2

3

Appendix B – Literature search strategies

Search approach

The principal search strategy was developed in MEDLINE (Ovid interface) and adapted, as appropriate, for use in the other sources listed in the protocol, taking into account their size, search functionality and subject coverage. The MEDLINE strategy below was quality assured (QA) by trained member of the IS team. All translated search strategies were peer reviewed to ensure their accuracy. Both procedures were adapted from the 2016 PRESS Checklist. The database searches were run on 7 August 2020 (see the table of sources searched below).

Additional search results were obtained from the scoping searches and from forwards citation searching and reference checking using Web of Science Core Collection.

The websites listed in the protocol were checked for additional publications.

The search results were managed in EPPI-Reviewer v5. Duplicates were removed in EPPI-R5 using a two-step process. First, automated deduplication is performed using a high-value algorithm. Second, manual deduplication is used to assess 'low-probability' matches. All decisions made for the review can be accessed via the deduplication history.

Full details of all the search strategies are available in a separate document from the NICE Information Services team.

Sources searched to identify the evidence

Database name	Date searched	Database Platform	Database segment or version	No. of records
Applied Social Science Index and Abstracts (ASSIA)	07/08/20	ProQuest	1987 - current	383
British Nursing Index (BNI)	07/08/20	ProQuest	1994 - current	140
Cochrane Central Register of Controlled Trials (CENTRAL)	07/08/20	Wiley	Cochrane Central Register of Controlled Trials Issue 8 of 12, August 2020	1198
Cochrane Database of Systematic Reviews (CDSR)	07/08/20	Wiley	Cochrane Database of Systematic Reviews Issue 8 of 12, August 2020	35
Cumulative Index to Nursing and Allied Literature (CINAHL)	07/08/20	EBSCOhost	1981-current	1246
Embase	07/08/20	Ovid	Embase 1974 to 2020 August 06	2296
Emcare	07/08/20	Ovid	Ovid Emcare 1995 to 2020 Week 31	1372
Health Management Information Consortium (HMIC)	07/08/20	Ovid	HMIC Health Management Information Consortium 1979 to May 2020	285
MEDLINE ALL	07/08/20	Ovid	Ovid MEDLINE(R) ALL 1946 to August 06, 2020	1540
PsycINFO	07/08/20	Ovid	APA PsycInfo 1806 to July Week 4 2020	2079
Social Policy and Practice (SPP)	07/08/20	Ovid	Social Policy and Practice 202004	163

Reference harvesting	07/08/20	Web of Science	Web of Science Core Collection (1990-present) • Science Citation Index Expanded (1990-present) • Social Sciences Citation Index (1990-present) • Arts & Humanities Citation Index (1990-present) • Emerging Sources Citation Index (2015-present)	455
Scoping searches	07/08/20	N/A	N/A	30
Forward citation searching	07/08/20	Web of Science	Web of Science Core Collection (1990-present) • Science Citation Index Expanded (1990-present) • Social Sciences Citation Index (1990-present) • Arts & Humanities Citation Index (1990-present) • Emerging Sources Citation Index (2015-present)	334
Websites	11/08/20	N/A	As listed in the protocol	28
Added after main search	25/08/20	N/A	New publication identified as screening being conducted from a table of contents alert.	1

Database strategy– main search as run in MEDLINE and adapted for other sources

Database(s): **Ovid MEDLINE(R) ALL** 1946 to August 06, 2020
Search Strategy:

#	Searches	Results
1	"tobacco use cessation"/	1167
2	"smoking cessation"/	28604
3	Smoking cessation agents/	158
4	exp "tobacco use cessation devices"/	1818
5	smoking reduction/	52
6	Smokers/	1874
7	Ex-smokers/	73
8	Electronic Nicotine Delivery Systems/	3449
9	vaping/	1035
10	((quit or quits or quitting* or stop or stops* or stopping* or stopped* or stoppage* or cease or ceases* or ceasing* or cessation* or cut or cuts or cutting or abstain* or abstinen* or "giv* up" or discontinu*) adj3 (nicotin* or smok* or tobacco* or cigar* or cigs or bidi or bidis or beedi or beedis or kretek* or "hand roll*" or handroll* or rollies or "roll up*" or rollup* or waterpipe* or "water pipe*" or dokha* or hooka* or shisha* or sheesha* or sheeka*)).ti,ab.	39173
11	((prequit* or "pre quit*" or "cut* down*" or stopstart* or "stop start*" or "cold turkey*" or reduc* or declin* or limit* or decreas* or minimal* or minimis* or minimiz* or gradual* or withdraw* or substitut* or fading* or taper* or swap* or swop* or switch* or replace* or replacing*) adj3 (nicotin* or smok* or tobacco* or cigar* or cigs or bidi or bidis or	31185

	beedi or beedis or kretek* or "hand roll*" or handroll* or rollies or "roll up*" or rollup* or waterpipe* or "water pipe*" or dokha* or hooka* or shisha* or sheesha* or sheeka*)).ti,ab.	
12	((harm* or risk*) adj1 (cut or cuts* or cutting* or reduc* or declin* or limit* or decreas* or minimal* or minimis* or minimiz* or less* or lower* or small*) adj3 (nicotin* or smok* or tobacco* or cigar* or cigs or bidi or bidis or beedi or beedis or kretek* or "hand roll*" or handroll* or rollies or "roll up*" or rollup* or waterpipe* or "water pipe*" or dokha* or hooka* or shisha* or sheesha* or sheeka*)).ti,ab.	1537
13	(antismok* or "anti smok*" or exsmoker* or "ex smoker*" or "controlled smoking*").ti,ab.	6492
14	(ecig* or e-cig* or e-voke* or juul* or vape* or vaping* or ENNDS).ti,ab.	5139
15	(electronic* adj3 (tobacco* or nicotin* or cigar* or cigs or vapor* or vapour*)).ti,ab.	3458
16	((tobacco* or nicotin* or cigar* or cigs) adj3 (vapor* or vapour* or device* or inhalator* or inhaler*)).ti,ab.	1007
17	(nicotin* and (ENDS or ANDS)).ti,ab.	496
18	(nicotin* adj3 deliver* system*).ti,ab.	609
19	((tobacco* or nicotin* or cigar* or cigs) adj3 (dual* or multiple* or multi) adj3 ("use" or uses or user* or usage* or using*)).ti,ab.	554
20	(polytobacco* or "poly tobacco*" or multitobacco* or "multi tobacco*").ti,ab.	137
21	(nrt or nicorette* or niquitin* or nicotinell* or nicassist*).ti,ab.	2174
22	(nicotin* adj3 (replacement* or substitut* or gum* or inhaled* or inhaler* or inhalant* or inhalator* or spray* or lozenge* or tablet* or transdermal* or patch* or vaccin* or device* or gel* or pastil* or deliver* or sublingual* or therap* or treatment* or nasal* or microtab* or polacrilex* or product or products)).ti,ab.	11304
23	or/1-22	80905
24	Varenicline/	1295
25	Bupropion/	3034
26	24 or 25	3969
27	"tobacco use disorder"/	11217
28	exp Tobacco Smoking/	3037
29	27 or 28	14033
30	26 and 29	641
31	((bupropion* or zyban* or amfebutamone* or quomen* or wellbutrin* or zyntabac* or varenicline* or champix* or chantix*) adj3 (smok* or tobacco* or cigar* or cigs or bidi or bidis or beedi or beedis or kretek* or "hand roll*" or handroll* or rollies or "roll up*" or rollup* or waterpipe* or "water pipe*" or dokha* or hooka* or shisha* or sheesha* or sheeka*)).ti,ab.	871
32	23 or 30 or 31	80939
33	Mental Health Services/	33884
34	Community Mental Health Services/	18536
35	Community Mental Health Centers/	2952
36	Emergency Services, Psychiatric/	2441
37	Social Work, Psychiatric/	2683
38	Psychiatric Department, Hospital/	6755
39	Hospitals, Psychiatric/	25213
40	Psychiatric Nursing/	17464
41	Mental Health/	38521
42	mental health recovery/	137
43	Mentally Ill Persons/	6160
44	Mental Disorders/	162600
45	exp Anxiety Disorders/	79359
46	exp "Bipolar and Related Disorders"/	40316
47	exp Dissociative Disorders/	4281
48	exp "Feeding and Eating Disorders"/	30651

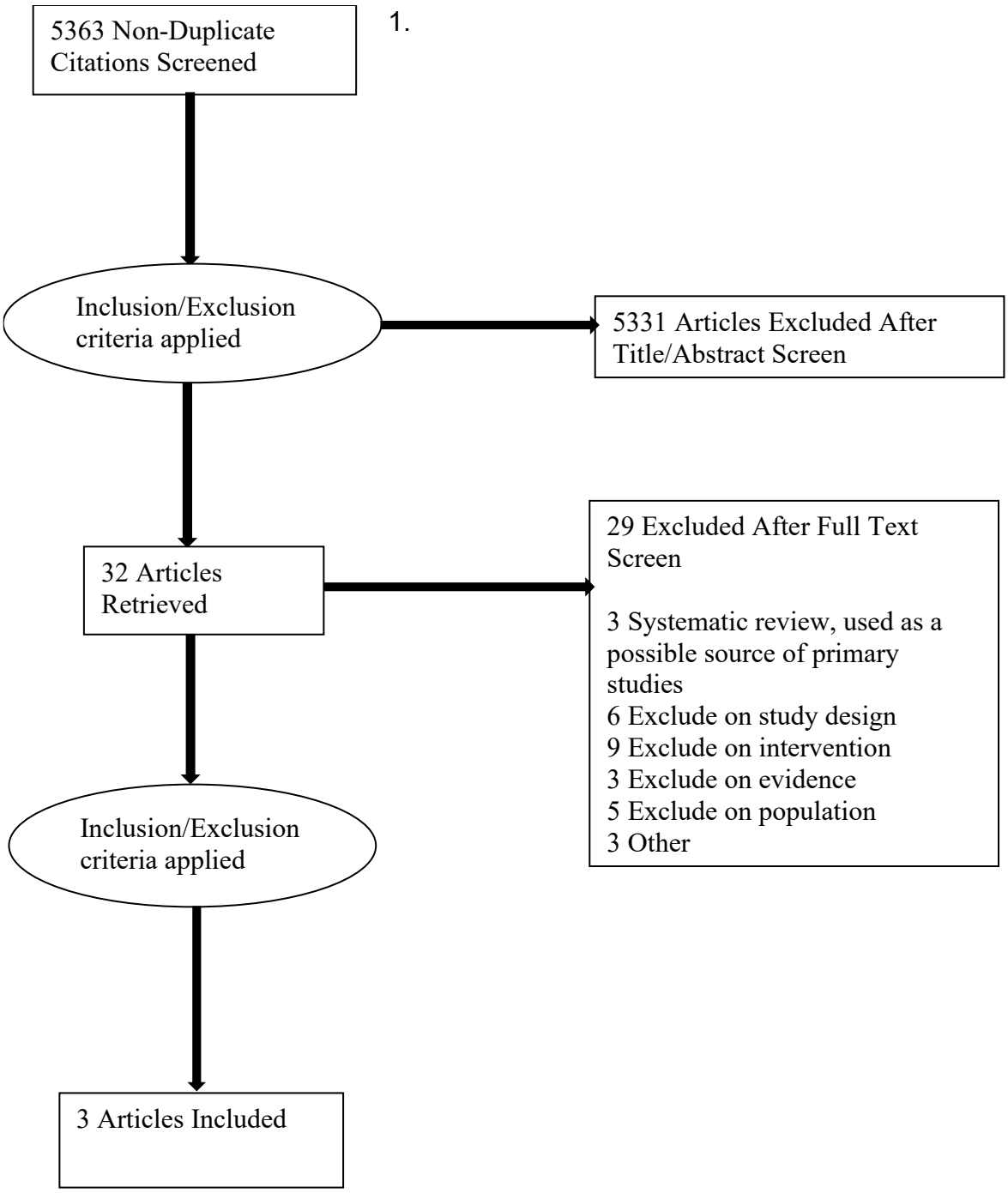
49	exp Mood Disorders/	122096
50	exp Neurotic Disorders/	17977
51	exp Personality Disorders/	41314
52	exp Neurocognitive Disorders/	254287
53	exp "Schizophrenia Spectrum and Other Psychotic Disorders"/	147744
54	Schizophrenic Psychology/	33378
55	exp Somatoform Disorders/	19024
56	exp "Trauma and Stressor Related Disorders"/	40630
57	exp "Attention Deficit and Disruptive Behavior Disorders"/	32750
58	Neurodevelopmental Disorders/	2224
59	Motor Skills Disorders/	2890
60	exp Autism Spectrum Disorder/	30120
61	exp Stress, Psychological/	131360
62	Depression/	119264
63	exp Self-Injurious Behavior/	70830
64	"Disruptive, Impulse Control, and Conduct Disorders"/	2501
65	Trichotillomania/	973
66	Catatonia/	2483
67	exp Memory Disorders/	29538
68	exp Confusion/	14031
69	Affective Symptoms/	12975
70	exp Dyslexia, Acquired/	963
71	exp Psychomotor Disorders/	13522
72	((mental* or psychological*) adj2 (disturb* or distress* or stress* or disorder* or syndrome* or ill* or health or healthcare* or "health care*" or emergency* or inpatient* or "in patient*" or nursing* or hospital* or "secure unit*" or service* or intervention* or patient* or condition* or specialist* or department* or "social work*" or "social care*" or service* or organisation* or organization* or disease* or recover*)).ti,ab.	263867
73	((mental* or psychological* or emotional* or affective*) adj2 (unstable* or instabilit* or labil* or symptom*)).ti,ab.	21638
74	((anxiety* or bipolar* or dissociat* or feeding* or eating* or mood* or neurotic* or personality* or neurocognitive* or psychotic* or somatoform* or somatisat* or somatizat* or neurodevelopmental* or "neuro developmental*" or trauma* or stress* or panic* or phobic* or phobia* or identity* or "binge eat*" or binging* or "food addiction*" or rumination* or appetite* or depressive* or affective* or cyclothymic* or dysthymic* or cognition* or cognitive* or huntington* or consciousness* or "attention deficit*" or hyperactiv* or overactive* or "over active*" or hyperkinetic* or conduct* or paranoid* or dysmorphi* or conversion* or behavior* or behaviour* or "post traumatic*" or posttraumatic* or rett* or delusion* or trance* or possessi* or obsessi* or compulsion* or compulsive* or adjustment* or "pervasive development*" or depersonali* or dereali* or disintegrativ* or hallucinati* or "motor skill*" or factitious* or munchausen* or "passive aggressive*" or impulse* or impulsive* or disrupt* or distress* or Diogenes* or psychomotor* or memory* or confusion*) adj3 (disorder* or syndrome*)).ti,ab.	326517
75	(amnesi* or psychosis* or psychotic* or schizo* or agoraphobi* or anorexi* or bulimia* or bulimic* or pica or depress* or delirium* or dementia* or Alzheimer* or adhd or addh or ocd or paranoia* or autis* or asperger* or astheni* or neurastheni* or neurosis* or sociopath* or psychopath* or psychoses* or cyclothymi* or dysthymi* or "severe stress*" or "acute stress*" or PTSD* or suicidal* or suicide* or parasuicid* or hypomani* or hysteria* or hallucinosis* or postencephaliti* or "post encephaliti*" or postconcussion* or "post concussion*" or "folie a deux*" or anankasti* or catatoni* or fugue* or oligophreni* or dyslexi* or hypochondriasis* or psychiatr* or trichotillomani* or psychastheni* or mania* or alexia* or automutilat* or alexithymi* or psychotrauma* or "psycho trauma*" or apraxi* or dyspraxi*).ti,ab.	1207543
76	(self* adj2 (harm* or injur* or mutilat*)).ti,ab.	13099
77	or/33-76	1831136

78	32 and 77	7814
79	Animals/ not (Animals/ and Humans/)	4690558
80	78 not 79	7223
81	limit 80 to (letter or historical article or comment or editorial or news or case reports)	514
82	80 not 81	6709
83	limit 82 to english language	6378
84	limit 83 to yr="1998 -Current"	5872
85	randomized controlled trial.pt.	510873
86	randomi?ed.mp.	889148
87	placebo.mp.	216829
88	or/85-87	948401
89	84 and 88	1260
90	(MEDLINE or pubmed).tw.	209385
91	systematic review.tw.	160063
92	systematic review.pt.	132436
93	meta-analysis.pt.	118058
94	intervention*.ti.	150338
95	or/90-94	467414
96	84 and 95	541
97	89 or 96	1540

Key to search operators

/	Medical Subject Heading (MeSH) term
Exp	Explodes the MeSH terms to retrieve narrower terms in the hierarchy
.ti	Searches the title field
.ab	Searches the abstract field
*	Truncation symbol (searches all word endings after the stem)
adj*n*	Adjacency operator to retrieve records containing the terms within a specified number (*n*) of words of each other

Appendix C – Public health evidence study selection



Appendix D – Public health evidence tables

McFall 2010

<table>
<tr><td>Bibliographic reference/s</td><td colspan="3">McFall, M; Saxon, A.J; Malte, C.A et al; Integrating Tobacco Cessation Into Mental Health Care for Posttraumatic Stress Disorder: A randomized controlled trial. JAMA. 8: 2485-2493</td></tr>
<tr><td>Study name</td><td colspan="3">Integrated smoking cessation with mental health care for PTSD</td></tr>
<tr><td>Registration</td><td colspan="3">Clinicaltrials.gov Identifier NCT00118534</td></tr>
<tr><td>Study type</td><td colspan="3">RCT</td></tr>
<tr><td>Study dates</td><td colspan="3">November 2004 to December 2007</td></tr>
<tr><td>Objective</td><td colspan="3">To determine whether integrating smoking cessation treatment into mental health care for PTSD improves abstinence</td></tr>
<tr><td>Country/ Setting</td><td colspan="3">USA, PTSD clinics at 10 VA medical centres</td></tr>
<tr><td>Number of participants / clusters</td><td colspan="3">943</td></tr>
<tr><td>Attrition</td><td colspan="3">Intervention group, N=387/472 (82%) completed final visit (46 lost to follow up, 23 withdrew, 16 died)
Control group, N=373/471 (79%) completed final visit (50 lost to follow up, 27 withdrew, 21 died)</td></tr>
<tr><td>Participant /community characteristics.</td><td colspan="3">
<table>
<tr><td></td><td>Intervention group n=472</td><td>Control group n=471</td></tr>
<tr><td>Male</td><td>444 (94.1%)</td><td>439 (93.2%)</td></tr>
<tr><td>Female</td><td>14 (30%)</td><td>25 (49%)</td></tr>
<tr><td>Mean age</td><td>54.4</td><td>54.7</td></tr>
<tr><td colspan="3">Cigarettes usually smoked (per day)</td></tr>
<tr><td>Mean</td><td>26.5</td><td>23.3</td></tr>
<tr><td colspan="3">Regular smoking cigarettes, years</td></tr>
<tr><td>Mean (95% CI)</td><td>34.5 (33.5 to 35.5)</td><td>35.1 (34.1 to 36.1)</td></tr>
<tr><td>Average cig/day last 30days, mean (95% CI)</td><td>21.9 (21.0 to 22.9)</td><td>21.4 (20.4 to 22.3)</td></tr>
<tr><td>Quit attempt in the last year</td><td>202 (42.9%)</td><td>192 (40.8%)</td></tr>
</table>
</td></tr>
<tr><td>Method of allocation</td><td colspan="3">Randomised in a 1:1 ratio, stratified by sex, current alcohol abuse or dependence in partial remission, current major depressive disorder, prior smoking abstinence, heavy smoking (>25cig/day)
Telephone randomisation system.
Neither site investigators nor patients were blinded to treatment assignment.</td></tr>
<tr><td>Inclusion criteria</td><td colspan="3">Engaged in outpatient PTSD care
PTSD related to military service
Smoked at least 10 cigarettes on at least 15 of 30 days before screening</td></tr>
<tr><td>Exclusion criteria</td><td colspan="3">Use of non-cigarette tobacco
Current psychotic, bipolar, or substance dependence disorder other than nicotine
Severe psychiatric symptoms, psychosocial instability, or cognitive impairment assessed by medical record review and discussion with patients' mental health clinicians</td></tr>
<tr><td>Intervention</td><td>TIDieR Checklist criteria</td><td colspan="2">Details</td></tr>
<tr><td></td><td>Brief Name</td><td colspan="2">Integrated care</td></tr>
</table>

Bibliographic reference/s	**McFall, M; Saxon, A.J; Malte, C.A et al; Integrating Tobacco Cessation Into Mental Health Care for Posttraumatic Stress Disorder: A randomized controlled trial. JAMA. 8: 2485-2493**	
Study name	Integrated smoking cessation with mental health care for PTSD	
	Rationale/theory/Goal	Evidence-based practices and recommended interventions addressing specific PTSD symptoms dynamically related to smoking relapse
	Materials used	See below
	Procedures used	Individual sessions; 5 weekly core tobacco cessations sessions focusing on tobacco use education, behavioural skills for quitting smoking, setting a quit date and relapse prevention Cessation medication, if desired by the patient – prescribers followed an algorithm of prescribing practices for NRT, bupropion and varenicline Sessions typically were incorporated into regularly scheduled PTSD visits bit could be scheduled separately if necessary
	Provider	PTSD clinic
	Method of delivery	Via PTSD clinicians, mostly psychologists and social workers
	Location	As above
	Duration	As above
	Intensity	N/A
	Tailoring/adaptation	N/A
	Planned treatment fidelity	N/A
	Actual treatment fidelity	N/A
	Other details	None
Comparison	**TIDieR Checklist criteria**	**Details**
	Brief Name	Specialised cessation clinic
	Rationale/theory/Goal	Usual standard of care within the VA
	Materials used	See below
	Procedures used	Followed smoking cessation practice guidelines, provided within 6 weeks of referral, prescribed cessation medications directly or through patients' primary care clinicians Typical treatment course to 4 to 16 treatment sessions (median, 7)
	Provider	Specialised cessation clinics
	Method of delivery	Via clinic directors and patient care staff
	Location	Specialised cessation clinics
	Duration	
	Intensity	
	Tailoring/adaptation	N/A
	Modifications	N/A
	Planned treatment fidelity	N/A

Bibliographic reference/s	**McFall, M; Saxon, A.J; Malte, C.A et al; Integrating Tobacco Cessation Into Mental Health Care for Posttraumatic Stress Disorder: A randomized controlled trial. JAMA. 8: 2485-2493**	
Study name	Integrated smoking cessation with mental health care for PTSD	
	Actual treatment fidelity	N/A
	Other details	None
Follow up	6- 18months	
Data collection	Outcomes assessed at 3-month intervals through month 18. At each assessment, daily use of cigarettes, other tobacco products, and cessation medications were determined using the timeline follow-back method, which uses a calendar with specific anchor dates to help patients identify the quantity and frequency of tobacco use. Exhaled CO obtained at every in-person assessment. Urine cotinine levels were measured using Accutest NicAlert test strips when patients self-reported no use of tobacco or nicotine replacement therapy in the prior 7 days. Laboratory assays of urine cotinine were obtained when self-reported abstinence disagreed with test strip results. Patients missing 1 or more assessments were retained in the study and encouraged to return for future assessments *Primary outcome:* Prolonged abstinence at 12 months defined non-abstinence as (1) smoking for 7 consecutive days or at least once a week for 2 consecutive weeks or (2) using noncigarette tobacco for 7 consecutive days or at least once a week for 2 consecutive weeks. Verified by exhaled carbon monoxide of 8 ppm or less and urine cotinine of less than 100 ng/ mL cotinine equivalents at the 9- through 18-month visits. If carbon monoxide or cotinine was missing (eg, due to current nicotine replacement therapy use or telephone assessment), a single measure was used for verification. If both carbon monoxide and cotinine were missing at any visit between 9 and 15 months, patients reporting prolonged abstinence were considered abstinent if all other available bioverification data confirmed abstinence. Patients who lacked carbon monoxide and cotinine readings at 18 months or failed to attend the 18- month visit were considered non-abstinent *Secondary outcome:* 7- and 30-day point prevalence abstinence at each assessment, where abstinence was defined as no tobacco use in the prior 7 or 30 days, respectively. Self-reported point prevalence abstinence was determined for all patients, with patients not completing a visit presumed to be non- abstinent. Patients with missing data were presumed to be non-abstinent.	
Critical outcomes measures and effect size. (time points)	**<u>Primary outcome: 12 months prolonged abstinence*:</u>** *****defined non-abstinence as (1) smoking for 7 consecutive days or at least once a week for 2 consecutive weeks or (2) using noncigarette tobacco for 7 consecutive days or at least once a week for 2 consecutive weeks **Self-reported abstinence:** 73/472 (15.5%) in the IC group and 33/471 patients (7.0%) in the SCC group self-reported prolonged abstinence at 12 months (unadjusted odds ratio [OR], 2.43; 95% confidence interval [CI], 1.58-3.74; P < .001). **Unadjusted RR (CI) calculated by NICE: 2.21 (1.49 to 3.26) p<0.0001** **Bioverified abstinence:** 42 patients/472 (8.9%) in IC and 21/471 patients (4.5%) in SCC achieved bioverified prolonged abstinence (unadjusted OR, 2.09; 95% CI, 1.22-3.59; P=.007; and adjusted OR, 2.26; 95% CI, 1.30-3.91; P = .004). **Unadjusted RR calculated by NICE: 2.00 (CI 1.20 to 3.32) p=0.008**	

Bibliographic reference/s	**McFall, M; Saxon, A.J; Malte, C.A et al; Integrating Tobacco Cessation Into Mental Health Care for Posttraumatic Stress Disorder: A randomized controlled trial. JAMA. 8: 2485-2493**
Study name	Integrated smoking cessation with mental health care for PTSD
	Secondary outcomes: 7 and 30 day point prevalence assessed at 6 and 18 months*: *Data not used in analysis as per the protocol continued abstinence is the preferred outcome, only included here for added information. bioverified 7 day point prevalence at 6 months: 78/472 [16.5%] for IC vs 34/471 [7.2%] for SCC, **RR calculated by NICE: 2.29 (CI 1.56 to 3.35) p<0.001** 30-day point prevalence at 6 months: 65/472 [13.8%] for IC vs 28/ 471 [5.9%] for SCC, **RR calculated by NICE 2.32 (CI 1.52 to 3.54) p<0.001** bioverified 7 day point prevalence at 18 months 86/472 [18.2%] for IC vs 51/471 [10.8%] for SCC, **RR calculated by NICE 1.68 (CI 1.22 to 2.32) to P =0.002** 30-day point prevalence at 18 months 80/472 [16.9%] for IC vs 44/471 [9.3%] for SCC, **RR calculated by NICE 1.57 (CI 1.13 to 2.17) p=0.007**
Important outcomes measures and effect size. (time points)	**Mental health outcomes:** Over 18 months, no significant differences were observed between the IC and SCC groups on PTSD Checklist or PHQ-9 scores. Nonquitters worsened slightly on the PHQ-9 relative to quitters (differences ranged between 0.4 and 2.1, P =.03), whose PHQ-9 scores did not change over time.

	Integrated care (N=472)	Smoking cessation clinic (N=471)	
	Mean change from baseline (95%CI)	Mean change from baseline (95%CI)	Difference in mean change (95%CI)
Clinician administered PTSD scale (18mths)	-7.2 (-9.1 to -5.2)	-7.0 (-9.0 to -5.0)	-0.2 (-3.0 to 2.6)
PTSD checklist (12mths)	-1.6 (-2.7 to -0.5)	-1.4 (-2.5 to -0.3)	-0.2 (-1.7 to 1.4)
PTSD checklist (18mths)	-3.2 (-4.3 to -2.1)	-2.4 (-3.5 to -1.2)	-0.8 (-2.4 to 0.8)
PHQ-9 (12mths)	1.6 (1.0 to 1.2)	1.2 (0.6 to 1.8)	0.4 (-0.4 to 1.2)
PHQ-9 (18mths)	-0.2 (-0.7 to 0.4)	-0.3 (-0.8 to 0.3)	0.1 (-0.7 to 0.9)

Adverse events: The number of patients who experienced serious adverse events during the study did not differ significantly by treatment (218/472 [46%] for IC vs 220/471 [47%] for SCC, P =.87) or by prolonged abstinence (26/63 [41%] for abstinent vs 412/880 [47%] for non-abstinent, P= .39). The number with serious adverse events possibly related to the study was small (11/472 [2%] for IC vs 8/471 [2%] for SCC, P =.49); psychiatric hospitalisations, psychiatric conditions that did not result in hospitalisation, medical hospital admissions (2 cardiac, 1 GI), conditions that did not result in hospitalisation (1 cardiac, 2 GI, 1 nervous system related)

Bibliographic reference/s	**McFall, M; Saxon, A.J; Malte, C.A et al; Integrating Tobacco Cessation Into Mental Health Care for Posttraumatic Stress Disorder: A randomized controlled trial. JAMA. 8: 2485-2493**		
Study name	Integrated smoking cessation with mental health care for PTSD		
Statistical Analysis	ITT analysis Target sample size (n=1400) designed to have a 90% power to detect the difference of between 6% (SCC) and 11% (IC) prolonged abstinence rates, using a 20sided 0.05 level Final enrolment of 943 was because of power than expected recruitment rate – recruitment was not extended as the achieved sample size provided 78% power to detect the hypothesized prolonged abstinence rates There were differences in those completing (N=851) and not completing (N=92) the 18 month visit Age, mean (95%CI); completed 54.9 (54.4 to 55.5), not completed 51.0 (48.7 to 53.4), p<0.001 Years smoking regularly, mean (95%CI); completed 35.2 (34.5 to 35.9), not completed 30.9 (28.2 to 33.6), p<0.001 Clinician administered PTSD scale total score, mean (95%CI); completed 74.8 (73.6 to 76.1), not completed 78.8 (75.2 to 82.4), p=0.05		
Risk of bias (ROB) **Overall ROB**	**Outcome name**		
	Outcome	**Judgement (Low / High / some concerns)**	**Comments**
	Risk of bias arising from the randomisation process	Low	Randomisation was done by a telephone system. Groups were well balanced in terms of prognostic and socio demographic characteristics.
	Risk of bias due to deviations from intended interventions (assignment) OR Risk of bias due to deviations from intended interventions (adherence)	Some concerns	Neither site investigators nor patients were blinded to treatment assignment groups. Although the majority of IC clinicians delivered the treatment as designed, a small minority failed to do so, which may have produced less favourable IC outcomes
	Missing outcome data	Some concerns	82% completed final visit at 18 months in in the intervention group. 79% completed final visit at 18 months in the control group. Some differences in those who completed and those who did not
	Risk of bias in measurement of the outcome	Low	Staff obtaining outcome data were not blinded with respect to treatment condition; however, the use of objective outcome measures such as bioverified abstinence lessens the likelihood that outcomes were biased
	Risk of bias in selection of the reported result	Low	Trial analysed in accordance with pre-specified plan. Result not likely to have been selected based on results

Bibliographic reference/s	**McFall, M; Saxon, A.J; Malte, C.A et al; Integrating Tobacco Cessation Into Mental Health Care for Posttraumatic Stress Disorder: A randomized controlled trial. JAMA. 8: 2485-2493**		
Study name	Integrated smoking cessation with mental health care for PTSD		
			either from multiple outcome measurements or multiple analyses of data.
	Other sources of bias	None	
	Overall Risk of Bias	Some concerns	
	Other outcome details	N/A	
Source of funding	US Department of Veterans Affairs Cooperative Studies Program (CSP 519)		
Comments	None		
Additional references	N/A		

Gilbody 2015

Bibliographic reference/s	**Gilbody, S; Peckham, E; Man, M et al; (2015) Bespoke smoking cessation for people with severe mental ill health (SCIMITAR): a pilot randomised controlled trial. Lancet Psychiatry. 2: 395–402.**
Study name	Bespoke smoking cessation for people with severe mental ill health (SCIMITAR): a pilot randomised controlled trial
Registration	The trial is registered at ISRCTN.com, number ISRCTN79497236.
Study type	RCT pilot study
Study dates	Between May 2011, and May 2012 participants were recruited
Objective	To pilot an intervention targeted at smokers with severe mental ill health and to test methods of recruitment, randomisation, and follow up before implementing a full trial, (see Gilbody 2019)
Country/ Setting	Adults (aged 18 years or older) with bipolar disorder or schizophrenia, who were current smokers, were recruited from NHS primary care and mental health settings in the UK (York, Scarborough, Hull, and Manchester).
Number of participants / clusters	97 participants were recruited to the trial 51 were allocated to usual care (control group) and 46 were assigned to usual care plus the bespoke smoking cessation
Attrition	Study aimed to recruit 100 participants to the pilot trial. Assuming loss to follow-up of 30% of participants, with a sample size of 100 the 95% CI for this level of attrition would be between 21% and 39%. Hence, an external pilot trial of 100 participants should ensure robust estimates of recruitment and follow-up in this population.

Participant /community characteristics.

Presented as mean values	Intervention group n=51	Control group n=46	Overall n=97
Male	32 (70%)	26 (51%)	58 (60%)
Female	14 (30%)	25 (49%)	39 (40%)
Mean age	47.3	46.4	47.2
Cigarettes usually smoked (per day)			
Mean	26.5	23.3	24.8
Smoking duration, years			
Mean	28.5	25.8	27.1

Bibliographic reference/s	**Gilbody, S; Peckham, E; Man, M et al; (2015) Bespoke smoking cessation for people with severe mental ill health (SCIMITAR): a pilot randomised controlled trial. Lancet Psychiatry. 2: 395–402.**	
Study name	Bespoke smoking cessation for people with severe mental ill health (SCIMITAR): a pilot randomised controlled trial	
Method of allocation	Eligible participants were randomly allocated to either usual care (control group) or usual care plus the bespoke smoking cessation strategy (intervention group). Randomisation was done via a central telephone system, with computer-generated random numbers. Due to the nature of the intervention, participants, mental health staff, primary care physicians and researchers were not masked to treatment allocation. Statistical analyses were blinded to treatment allocation.	
Inclusion criteria	Participants had to be 18 years or older, had a severe mental health disorder, currently smoked and had expressed an interest in cutting down smoking (although not necessarily quitting). No definition of severe mental ill health has been agreed, so we adopted a pragmatic definition and included people with a documented diagnosis of either schizophrenia or a delusional or psychotic illness (corresponding with categories F20·X and F22·X in the 10th revision of the International Classification of Diseases [ICD 10]) or bipolar disorder (F31·X in ICD 10).	
Exclusion criteria	people who were pregnant or breastfeeding, had comorbid drug or alcohol problems (as ascertained by the family doctor or mental health worker), were non- English speakers, or did not have capacity to consent	
Intervention	**TIDieR Checklist criteria**	**Details**
	Brief Name	Usual care in the UK for those with severe mental illness
	Rationale/theory/Goal	To test the effectiveness of a combined behavioural and pharmacological smoking cessation intervention targeted specifically at people with severe mental illness
	Materials used	Under usual care participants were offered access to local smoking cessation services not specifically designed for people with severe mental illnesses.
	Procedures used	Usual care group – all participants in the trial received usual care for people with severe mental illness. I.e. they were able to access smoking cessation services provided by their primary care physician or in a locally provided service not specifically designed for people with severe mental illness, at no direct cost. They were also able to access a free telephone helpline (the Smokefree National Helpline) that offers smoking cessation advice. All participants remained under the care of their primary care physician and continued to receive their usual service from the mental health team throughout the trial.
	Provider	As above
	Method of delivery	As above
	Location	As above
	Duration	As above
	Intensity	N/A
	Tailoring/adaptation	N/A
	Planned treatment fidelity	N/A

Bibliographic reference/s	**Gilbody, S; Peckham, E; Man, M et al; (2015) Bespoke smoking cessation for people with severe mental ill health (SCIMITAR): a pilot randomised controlled trial. Lancet Psychiatry. 2: 395–402.**	
Study name	Bespoke smoking cessation for people with severe mental ill health (SCIMITAR): a pilot randomised controlled trial	
	Actual treatment fidelity	N/A
	Other details	None
Comparison	**TIDieR Checklist criteria**	**Details**
	Brief Name	SCIMITAR+ trial
	Rationale/theory/Goal	To test the effectiveness of a combined behavioural and pharmacological smoking cessation intervention targeted specifically at people with severe mental illness
	Materials used	The bespoke smoking cessation intervention consisted of behavioural support from a mental health smoking cessation practitioner and pharmacological aids for smoking cessation, with adaptations for people with severe mental illness—such as, extended pre-quit sessions, cut down to quit, and home visits. Access to pharmacotherapy was via primary care after discussion with the smoking cessation specialist
	Procedures used	*Intervention group*- offered a structured smoking cessation intervention delivered by a trained mental health smoking cessation practitioner. The smoking cessation practitioners were generally experienced mental health nurses who worked in conjunction with the participant and the participant's primary care physician or mental health specialist to provide an individually tailored smoking cessation service. The intervention was delivered according to the Manual of Smoking Cessation (developed by the National Centre for Smoking Cessation Training [NCSCT], UK) with several adaptations to cater for people with severe mental illness.
	Provider	Trained mental health smoking practitioner
	Method of delivery	As above
	Location	Participants were offered up to 12 individual face-to-face sessions in their home or NHS premises lasting approximately 30 min.
	Duration	
	Intensity	
	Tailoring/adaptation	Adaptations included making several assessments before setting a quit date, recognising the reasons for smoking in the context of an individual's mental illness, providing home visits, giving additional face-to-face support after an unsuccessful quit attempt or relapse, and informing the participant's family doctor and psychiatrist of a successful quit attempt so the clinician could review antipsychotic drug doses in case their metabolism changed.
	Modifications	12 months after treatment allocation, researchers contacted the primary care physician of each participant to obtain primary care records, which were screened for details of any nicotine replacement treatment or other smoking cessation

Bibliographic reference/s	**Gilbody, S; Peckham, E; Man, M et al; (2015) Bespoke smoking cessation for people with severe mental ill health (SCIMITAR): a pilot randomised controlled trial. Lancet Psychiatry. 2: 395–402.**	
Study name	Bespoke smoking cessation for people with severe mental ill health (SCIMITAR): a pilot randomised controlled trial	
		products that had been prescribed to participants in the study. Participants were also asked about their purchase of over-the-counter products during follow-up, as part of the health-service use questionnaire, and we recorded nicotine therapy use via self-report.
	Planned treatment fidelity	N/A
	Actual treatment fidelity	N/A
	Other details	None
Follow up	6 and 12 months	
Data collection	Once participants had consented to take part in the trial, they were asked to complete baseline questionnaires that comprised questions on general health; demographics; smoking status and smoking history; use of e-cigarettes; and health service use questions. Patients also answered questions from the FagerstrÖm Test of Nicotine Dependence (FTND),21 Motivation to Quit (MTQ)22 questionnaire, Patient Health Questionnaire-9 (PHQ-9),23 Generalised Anxiety Disorder-7 (GAD-7) questionanire,24 EuroQol five dimensional five-level (EQ-5D-5L)25 questionnaire, and 12-Item Short-Form Health Survey (SF-12).26 Additionally, height and weight measurements were taken to calculate participants' body-mass index (BMI) and a carbon monoxide reading of their exhaled breath was obtained by use of a carbon monoxide monitor (piCO smokerlyzer, Bedfont Scientific, Maidstone, UK). The FTND21 is a six-item questionnaire measuring nicotine dependence. Item scores are summed to give a total score between 1 and 10, where a score of 1–2 indicates low dependence, 3–4 indicates low-to-moderate dependence, 5–7 indicates moderate dependence, and 8–10 indicates high dependence. At the two follow-up timepoints, participants completed the same series of questionnaires as at baseline apart from the demographics questionnaire. Additionally, participants were asked to provide a carbon monoxide breath measure and have their height and weight measured. When possible, participants were followed up face to face, but if not possible they were followed up by phone or by postal questionnaire. Primary outcome was smoking cessation at 12 months after randomisation. A successful quitter was defined as someone with a carbon monoxide measurement below 10 parts per million (ppm),30 indicating no smoking in the past 12 h, and who reported that they had not smoked (responding "not even a puff" to the question "Have you smoked in the past week?") in the past week (ie, 7-day point prevalence abstinence at 12 months with carbon monoxide <10 ppm).	
Critical outcomes measures and effect size. (time points)	**Primary outcome: smoking cessation at 12 months. Validated by exhaled CO with a CO monitor. Smoking cessation defined as CO reading less than 10 ppm. If CO measurement could not be obtained the participant's self-report of abstinence was excepted.** **<u>Relative risk calculated by NICE</u>** At 12 months, 64 participants had a CO measurement available and 4 people self-reported their smoking status (two in each group). 8/35 (23%) of individuals allocated to the control group had stopped smoking compared with 12/33 (36%) assigned to the intervention group. **Unadjusted RR was 2·2 (95% CI 1·2 to 4·0)*** *Calculated by NICE review team	

<table>
<tr><td>Bibliographic reference/s</td><td>Gilbody, S; Peckham, E; Man, M et al; (2015) Bespoke smoking cessation for people with severe mental ill health (SCIMITAR): a pilot randomised controlled trial. Lancet Psychiatry. 2: 395–402.</td></tr>
<tr><td>Study name</td><td>Bespoke smoking cessation for people with severe mental ill health (SCIMITAR): a pilot randomised controlled trial</td></tr>
<tr><td></td><td><u>Odds ratios reported by study</u>
By logistic regression, adjusted for sex, age, baseline number of cigarettes smoked, and baseline alcohol consumption, the likelihood of stopping smoking in the intervention group was three times higher than in the control group (odds ratio 2·9, 95% CI 0·8–10·5). Assuming that missing information meant the individual was still smoking, eight (16%) of 51 participants had stopped smoking in the control group compared with 12 (26%) of 46 people assigned to the intervention group (odds ratio 2·5, 95% CI 0·8–7·7).

Adverse events
21 adverse events in 17 participants
12 classed as serious – all unlikely to be related to the study
6 judged as definitely or probably related to the intervention:
- 4 were effects from NRT use (burning mouth, feeling sleepy, headaches)
- 2 were minor known effects of smoking cessation (headaches, nightmares)</td></tr>
<tr><td>Important outcomes measures and effect size. (time points)</td><td>Impact on mental health outcomes:
Patients also answered questions from the Patient Health Questionnaire-9 (PHQ-9 measuring severity of depression), Generalised Anxiety Disorder-7 (GAD-7) questionnaire, EuroQol five dimensional five-level (EQ-5D-5L) questionnaire, and 12-Item Short-Form Health Survey (SF-12)

Presented as mean (CI):
*Calculated by NICE review team
<table>
<tr><th></th><th>Intervention</th><th>Control</th><th>Mean Difference*</th><th>P value</th></tr>
<tr><td>Patient Health Questionnaire-9</td><td></td><td></td><td></td><td></td></tr>
<tr><td>6 months</td><td>9·6 (7.30 to 11.90)</td><td>8·7 (6.18 to 11.2)</td><td>0.90 (-2.39 to 4.19)</td><td>p=0.59</td></tr>
<tr><td>12 months</td><td>11·2 (8.72 to 13.68)</td><td>7·7 (5.15 to 10.25)</td><td>3.50 (0.08 to 6.92)</td><td>p=0.05</td></tr>
<tr><td>12-Item Short Form Health Survey (mental component)</td><td></td><td></td><td></td><td></td></tr>
<tr><td>6 months</td><td>37·1 (32.67 to 41.53)</td><td>41·6 (37.87 to 45.33)</td><td>-4.50 (-10.18 to 1.18)</td><td>p=0.12</td></tr>
<tr><td>12 months</td><td>39·1 (35.13 to 43.07)</td><td>41·8 (37.83 to 45.77)</td><td>-2.70 (-7.98 to 2.58)</td><td>p=0.32</td></tr>
</table></td></tr>
<tr><td>Statistical Analysis</td><td>Study was an external pilot trial of a complex intervention with the primary aim to test the feasibility of the intervention and methods of recruitment,
randomisation, and follow-up in a population with severe mental ill health ahead of a full trial. Two treatment groups were compared by logistic regression, with adjustment for the prognostic variables sex, age, number of cigarettes smoked at baseline, and alcohol consumption. Odds ratios and corresponding 95% CIs were reported from this model.</td></tr>
</table>

Bibliographic reference/s	**Gilbody, S; Peckham, E; Man, M et al; (2015) Bespoke smoking cessation for people with severe mental ill health (SCIMITAR): a pilot randomised controlled trial. Lancet Psychiatry. 2: 395–402.**		
Study name	Bespoke smoking cessation for people with severe mental ill health (SCIMITAR): a pilot randomised controlled trial		
Risk of bias (ROB) **Overall ROB**	**Outcome name**		
	Outcome	**Judgement (Low / High / some concerns)**	**Comments**
	Risk of bias arising from the randomisation process	Low	Participants were randomly assigned to either the bespoke smoking cessation service (intervention) or usual care (control) using computer generated randomisation. Groups were well balanced in terms of prognostic and socio demographic characteristics.
	Risk of bias due to deviations from intended interventions (assignment) OR Risk of bias due to deviations from intended interventions (adherence)	Low	Due to the nature of the intervention participants and people delivering the intervention were aware of their assigned intervention during the trial, however no apparent deviations from intended interventions.
	Missing outcome data	High	30% of participants were lost to follow-up or had missing data for the primary outcome at 12 months. Pilot study
	Risk of bias in measurement of the outcome	Some concerns	Not all outcome data was confirmed with biochemical testing. 4 out of 68 subjects gave self-report smoking status at follow up. Biochemical testing was only done at 12 months follow up and not 6 also. Outcome assessors were not reported as being blinded.
	Risk of bias in selection of the reported result	Low	Trial analysed in accordance with pre-specified plan. Result not likely to have been selected based on results either from multiple outcome measurements or multiple analyses of data.
	Other sources of bias	None	
	Overall Risk of Bias	High	
	Other outcome details None		
Source of funding	National Institute for Health Research Health Technology Assessment Programme		
Comments	None		
Additional references	N/A		

Gilbody 2019

<table>
<tr><td>Bibliographic reference/s</td><td>Gilbody, S; Peckham, E; Bailey, D; et al; (2019) Smoking cessation for people with severe mental illness (SCIMITAR+): a pragmatic randomised controlled trial. Lancet Psychiatry. 6: 379–90</td></tr>
<tr><td>Study name</td><td>Smoking cessation for people with severe mental illness (SCIMITAR+): a pragmatic randomised controlled trial</td></tr>
<tr><td>Registration</td><td>This trial was registered with the ISRCTN registry, number ISRCTN72955454, and is complete</td></tr>
<tr><td>Study type</td><td>RCT</td></tr>
<tr><td>Study dates</td><td>Between Oct 7, 2015, and Dec 16, 2016</td></tr>
<tr><td>Objective</td><td>To test the effectiveness of a combined behavioural and pharmacological smoking cessation intervention targeted specifically at people with severe mental illness (predominantly bipolar disorder or schizophrenia)</td></tr>
<tr><td>Country/ Setting</td><td>16 primary care and 21 community-based mental health sites in the UK.</td></tr>
<tr><td>Number of participants / clusters</td><td>526 participants enrolled – 265 assigned to bespoke smoking intervention, 261 assigned to usual care.

This study was powered at 80% to detect a relative 1·7 times increase in quitting, assuming a 20% incidence of quitting among control participants, equal randomisation, and a two-sided α level of 0·05. Allowing for 20% loss to follow-up at 12 months, we calculated that 393 participants needed to be recruited and randomised. Authors therefore proposed to conservatively recruit 400 participants overall.</td></tr>
<tr><td>Attrition</td><td>223 intervention participants and 223 usual care participants included in primary outcome analysis.

At 12 months, 84 (16%) participants did not attend follow-up or had missing data, and 442 (84%) provided sustained quit data (self-reported smoking status and carbon monoxide reading), of whom 223 (50%) were in the intervention group and 219 (50%) were in the usual care group.</td></tr>
<tr><td>Participant /community characteristics.</td><td>
<table>
<tr><td></td><td>Intervention group n=265</td><td>Control group n=261</td><td>Total n=526</td></tr>
<tr><td>Male</td><td>159 (60%)</td><td>150 (57%)</td><td>309 (59%)</td></tr>
<tr><td>Female</td><td>105 (40%)</td><td>111 (43%)</td><td>216 (41%)</td></tr>
<tr><td>Transgender</td><td>1 (-1%)</td><td>0</td><td>1 (-1%)</td></tr>
<tr><td>Mean age</td><td>46.5</td><td>45.5</td><td>46.0</td></tr>
<tr><td>Bipolar disorder</td><td>59 (22%)</td><td>56 (21%)</td><td>115 (22%)</td></tr>
<tr><td>Schizoaffective disorder</td><td>25 (10%)</td><td>41 (16%)</td><td>66 (13%)</td></tr>
<tr><td>Schizophrenia</td><td>138 (52%)</td><td>125 (48%)</td><td>263 (50%)</td></tr>
<tr><td>Other psychotic disorder</td><td>41 (16%)</td><td>39 (15%)</td><td>80 (15%)</td></tr>
<tr><td colspan="4">Cigarettes usually smoked (per day)</td></tr>
<tr><td>Mean</td><td>24.7 (13.5)</td><td>23.2 (12.8)</td><td>29.9 (13.2)</td></tr>
<tr><td colspan="4">Smoking duration, years</td></tr>
<tr><td>Mean</td><td>30.7 (13.2)</td><td>29.0 (12.5)</td><td>29.9 (12.9)</td></tr>
<tr><td></td><td></td><td></td><td></td></tr>
</table>
</td></tr>
<tr><td>Method of allocation</td><td>Using computer-generated random numbers,</td></tr>
</table>

Bibliographic reference/s	**Gilbody, S; Peckham, E; Bailey, D; et al; (2019) Smoking cessation for people with severe mental illness (SCIMITAR+): a pragmatic randomised controlled trial. Lancet Psychiatry. 6: 379–90**	
Study name	Smoking cessation for people with severe mental illness (SCIMITAR+): a pragmatic randomised controlled trial	
	participants were randomly assigned (1:1) to a bespoke smoking cessation intervention or to usual care, via computer-generated random number sequence. Participants, mental health specialists, and primary care physicians were unmasked to assignment. Due to the nature of the intervention, participants, mental health staff, primary care physicians and researchers were not masked to treatment allocation. Statistical analyses were blinded to treatment allocation.	
Inclusion criteria	Participants were eligible if they were aged 18 years or older, and smoked at least five cigarettes per day and expressed interest in cutting down or quitting. No agreed definition of severe mental illness, used a pragmatic definition used in UK primary care (documented diagnosis, by a specialist in mental health services, of schizophrenia, delusional or psychotic illness or bipolar disorder).	
Exclusion criteria	Exclusion criteria included substantial comorbid drug or alcohol problems and people who lacked capacity to consent at the time of recruitment. Currently receiving advice from a stop smoking advisor.	
Intervention	**TIDieR Checklist criteria**	**Details**
	Brief Name	Usual care in the UK for those with severe mental illness
	Rationale/theory/Goal	To test the effectiveness of a combined behavioural and pharmacological smoking cessation intervention targeted specifically at people with severe mental illness
	Materials used	Under usual care participants were offered access to local smoking cessation services not specifically designed for people with severe mental illnesses.
	Procedures used	Usual care group - people with severe mental illness were able to access smoking cessation services provided by their primary care physician or in a locally-provided service not specifically designed for people with severe mental illness, at no direct cost. They were also able to access a free telephone helpline (the Smokefree National Helpline) that offers smoking cessation advice. All participants remained under the care of their primary care physician and continued to receive their usual service from the mental health team throughout the trial.
	Provider	As above
	Method of delivery	As above
	Location	As above
	Duration	As above
	Intensity	N/A
	Tailoring/adaptation	N/A
	Planned treatment fidelity	N/A
	Actual treatment fidelity	N/A
	Other details	None

Bibliographic reference/s	**Gilbody, S; Peckham, E; Bailey, D; et al; (2019) Smoking cessation for people with severe mental illness (SCIMITAR+): a pragmatic randomised controlled trial. Lancet Psychiatry. 6: 379–90**	
Study name	Smoking cessation for people with severe mental illness (SCIMITAR+): a pragmatic randomised controlled trial	
Comparison	**TIDieR Checklist criteria**	**Details**
	Brief Name	SCIMITAR+ trial
	Rationale/theory/Goal	To test the effectiveness of a combined behavioural and pharmacological smoking cessation intervention targeted specifically at people with severe mental illness
	Materials used	The bespoke smoking cessation intervention consisted of behavioural support from a mental health smoking cessation practitioner and pharmacological aids for smoking cessation, with adaptations for people with severe mental illness—such as, extended pre-quit sessions, cut down to quit, and home visits. Access to pharmacotherapy was via primary care after discussion with the smoking cessation specialist
	Procedures used	*Intervention group*- offered a structured smoking cessation intervention delivered by a trained mental health smoking cessation practitioner. The smoking cessation practitioners were generally experienced mental health nurses who worked in conjunction with the participant and the participant's primary care physician or mental health specialist to provide an individually tailored smoking cessation service. The intervention was delivered according to the Manual of Smoking Cessation (developed by the National Centre for Smoking Cessation Training [NCSCT], UK) with several adaptations to cater for people with severe mental illness.
	Provider	Trained mental health smoking practitioner
	Method of delivery	As above
	Location	Participants were offered up to 12 individual face-to-face sessions in their home or NHS premises lasting approximately 30 min.
	Duration	
	Intensity	
	Tailoring/adaptation	Adaptations of the intervention for people with severe mental illness included making several assessments before setting a quit date, offering nicotine replacement before setting a quit date (ie, cut down to quit), recognising the purpose of smoking in the context of a person's mental illness, providing home visits, providing additional face-to-face support after an unsuccessful quit attempt or relapse, and informing the primary care physician and psychiatrist of a successful quit attempt, such that they can review doses of antipsychotic medication if their metabolism changes
	Modifications	12 months after treatment allocation, researchers contacted the primary care physician of each participant to obtain primary care records, which were screened for details of any nicotine replacement treatment or other smoking cessation products that had been prescribed to participants in the study. Participants were also asked about their purchase of

Bibliographic reference/s	**Gilbody, S; Peckham, E; Bailey, D; et al; (2019) Smoking cessation for people with severe mental illness (SCIMITAR+): a pragmatic randomised controlled trial. Lancet Psychiatry. 6: 379–90**	
Study name	Smoking cessation for people with severe mental illness (SCIMITAR+): a pragmatic randomised controlled trial	
		over-the-counter products during follow-up, as part of the health-service use questionnaire, and we recorded nicotine therapy use via self-report.
	Planned treatment fidelity	
	Actual treatment fidelity	
	Other details	None
Follow up	6 and 12 months	
Data collection	Once participants had consented to take part in the trial, they were asked to complete baseline questionnaires that comprised questions on general health; demographics; smoking status and smoking history; use of e-cigarettes; and health service use questions. Patients also answered questions from the FagerstrÖm Test of Nicotine Dependence (FTND) Motivation to Quit (MTQ) questionnaire, Patient Health Questionnaire-9 (PHQ-9), Generalised Anxiety Disorder-7 (GAD-7) questionanire, EuroQol five dimensional five-level (EQ-5D-5L) questionnaire, and 12-Item Short-Form Health Survey (SF-12). Additionally, height and weight measurements were taken to calculate participants' body-mass index (BMI) and a carbon monoxide reading of their exhaled breath was obtained by use of a carbon monoxide monitor (piCO smokerlyzer, Bedfont Scientific, Maidstone, UK). The FTND21 is a six-item questionnaire measuring nicotine dependence. Item scores are summed to give a total score between 1 and 10, where a score of 1–2 indicates low dependence, 3–4 indicates low-to-moderate dependence, 5–7 indicates moderate dependence, and 8–10 indicates high dependence. At the two follow-up timepoints, participants completed the same series of questionnaires as at baseline apart from the demographics questionnaire. Additionally, participants were asked to provide a carbon monoxide breath measure and have their height and weight measured. When possible, participants were followed up face to face, but if not possible they were followed up by phone or by postal questionnaire. Primary outcome was smoking cessation at 12 months after randomisation. A successful quitter was defined as someone with a carbon monoxide measurement below 10 parts per million (ppm),30 indicating no smoking in the past 12 h, and who reported that they had not smoked (responding "not even a puff" to the question "Have you smoked in the past week?") in the past week (ie, 7-day point prevalence abstinence at 12 months with carbon monoxide <10 ppm). The PHQ-923 instrument measures severity of depression. This nine item questionnaire is scored from 0 to 27, and a higher scores indicates more severe depressive symptoms. The GAD-7 questionnaire is a seven-item instrument designed to measure severity of anxiety, scored from 0 to 21, with a higher score indicating more severe anxiety. The SF-12 consists of two subscales: a physical component and a mental component, both scored from 0 to 100, with 0 indicating the lowest level of health and 100 the highest level of health measured by the scale.	
Critical outcomes measures and effect size. (time points)	**Primary outcomes** – At 12 months 442 (84%) provided sustained quit data (self-reported smoking status and carbon monoxide reading), of whom 223 (50%) were in the intervention group and 219 (50%) were in the usual care group. 34 (15%) of 223 participants (13% of 265	

<table>
<tr><td>Bibliographic reference/s</td><td>Gilbody, S; Peckham, E; Bailey, D; et al; (2019) Smoking cessation for people with severe mental illness (SCIMITAR+): a pragmatic randomised controlled trial. Lancet Psychiatry. 6: 379–90</td></tr>
<tr><td>Study name</td><td>Smoking cessation for people with severe mental illness (SCIMITAR+): a pragmatic randomised controlled trial</td></tr>
<tr><td></td><td>assigned to group) in the intervention group, and 22 (10%) of 219 (8% of 261 assigned to group) in the usual care group had quit smoking (risk difference 5·2%, 95% CI–1·0 to 11·4).
Unadjusted RR was 1·5 (95% CI 0·9 to 2·5)*
*Calculated by NICE review team

At 6 months, 443 (84%) of 526 participants provided sustained quit data (n=226 intervention group, n=217 usual care group). 32 (14%) of 226 participants (11% of 265 assigned to group) in the intervention group, and 14 (6%) of 217 (5% of 261 assigned to group) in the usual care group had quit (risk difference 7·7%, 95% CI 2·1% to 13·3%). The unadjusted RR was 2·2 (95% CI 1·2 to 4·0)*
*Calculated by NICE review team</td></tr>
<tr><td>Important outcomes measures and effect size. (time points)</td><td>Impact on mental health outcomes:
Patients also answered questions from the Patient Health Questionnaire-9 (PHQ-9 measuring severity of depression), Generalised Anxiety Disorder-7 (GAD-7) questionnaire, EuroQol five dimensional five-level (EQ-5D-5L) questionnaire, and 12-Item Short-Form Health Survey (SF-12)

Presented as mean (CI):
<table>
<tr><th></th><th>Intervention</th><th>Control</th><th>Mean Difference</th><th>P value</th></tr>
<tr><td>Patient Health Questionnaire-9</td><td></td><td></td><td></td><td></td></tr>
<tr><td>6 months</td><td>9·6 (8·7 to 10·4)</td><td>9·4 (8·5 to 10·2)</td><td>0·20 (–0·85 to 1·24)</td><td>0.72</td></tr>
<tr><td>12 months</td><td>9·3 (8·4 to 10·1)</td><td>9·4 (8·5 to 10·2)</td><td>–0·12 (–1·18 to 0·94)</td><td>0.82</td></tr>
<tr><td>Generalised Anxiety Disorder-7 questionnaire</td><td></td><td></td><td></td><td></td></tr>
<tr><td>6 months</td><td>7·0 (6·3 to 7·7</td><td>7·4 (6·7 to 8·1)</td><td>–0·32 (–1·26 to 0·62)</td><td>0.50</td></tr>
<tr><td>12 months</td><td>7·1 (6·4 to 7·8)</td><td>7·2 (6·5 to 7·9)</td><td>–0·10 (–1·05 to 0·86)</td><td>0.84</td></tr>
<tr><td>12-Item Short Form Health Survey (mental component)</td><td></td><td></td><td></td><td></td></tr>
<tr><td>6 months</td><td>37·9 (36·2 to 39·5)</td><td>38·6 (36·9 to 40·3)</td><td>–0·73 (–2·82 to 1·36)</td><td>0.49</td></tr>
<tr><td>12 months</td><td>38·6 (37·0 to 40·1)</td><td>39·0 (37·4 to 40·5)</td><td>–0·41 (–2·35 to 1·53)</td><td>0.68</td></tr>
</table></td></tr>
</table>

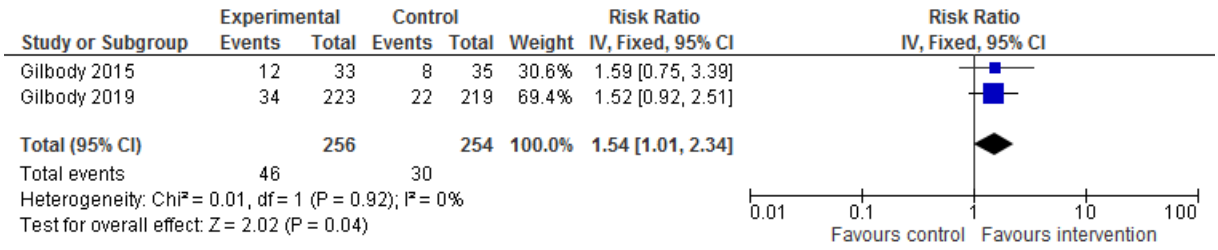
Bibliographic reference/s	**Gilbody, S; Peckham, E; Bailey, D; et al; (2019) Smoking cessation for people with severe mental illness (SCIMITAR+): a pragmatic randomised controlled trial. Lancet Psychiatry. 6: 379–90**		
Study name	Smoking cessation for people with severe mental illness (SCIMITAR+): a pragmatic randomised controlled trial		
Statistical Analysis			
Risk of bias (ROB) **Overall ROB**	**Outcome name**		
	Outcome	**Judgement (Low / High / some concerns)**	**Comments**
	Risk of bias arising from the randomisation process	Low	Participants were randomly assigned to either the bespoke smoking cessation service (intervention) or usual care (control) using computer generated randomisation. Participants, mental health specialists, and primary care physicians were unmasked to assignment due to the nature of intervention. No baseline difference to suggest a problem with the randomisation process.
	Risk of bias due to deviations from intended interventions (assignment) OR Risk of bias due to deviations from intended interventions (adherence)	Low	Participants and people delivering the intervention were aware of their assigned intervention during the trial (as above), however no apparent deviations from intended interventions.
	Missing outcome data	Some concerns	16% of participants were lost to follow-up or had missing data for the primary outcome at 12 months; however, the loss to follow up was non-differential. The trial was also underpowered to detect a difference in the proportion of patients who quit from 10% to 15%.
	Risk of bias in measurement of the outcome	Low	Statistical analyses were blinded to treatment allocation
	Risk of bias in selection of the reported result	Low	Trial analysed in accordance with pre-specified plan. Result not likely to have been selected based on results either from multiple outcome measurements or multiple analyses of data.
	Other sources of bias	None	
	Overall Risk of Bias	Some concerns	
	Other outcome details	None	
Source of funding	National Institute for Health Research Health Technology Assessment Programme		

Bibliographic reference/s	**Gilbody, S; Peckham, E; Bailey, D; et al; (2019) Smoking cessation for people with severe mental illness (SCIMITAR+): a pragmatic randomised controlled trial. Lancet Psychiatry. 6: 379–90**
Study name	Smoking cessation for people with severe mental illness (SCIMITAR+): a pragmatic randomised controlled trial
Comments	None
Additional references	None

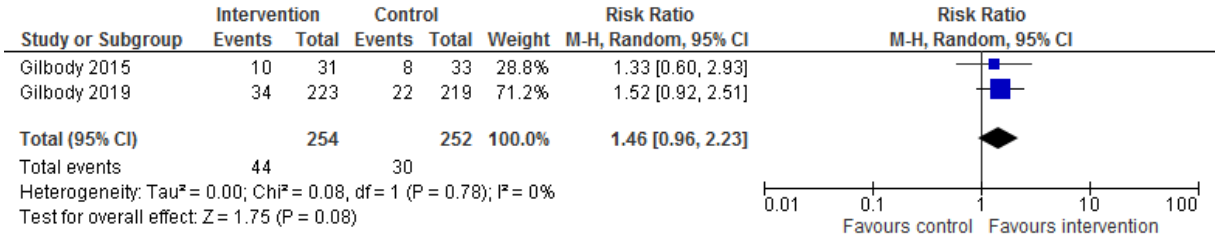
Appendix E – Forest plots

Tailored behavioural/pharmacological intervention compared with usual care for those with severe mental health conditions

Abstinence from smoking at 12 months (biochemically validated and self-reported data)



Abstinence from smoking at 12 months (biochemically validated data only)



Appendix F – GRADE tables

Profile 1: Abstinence from smoking (results presented from pooled studies)

Quality assessment							No of patients		Effect		Confidence
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Intervention	Control	Relative (95% CI)	Absolute	
Combined behavioural and pharma intervention, not smoking at follow-up (12 months; biochemically validated and self-report)											
2[a]	RCT	Very serious[1]	No serious	No serious	No serious	None	46/256 (18%)	30/254 (12%)	1.54 (1.01 to 2.34) p=0.04	64 more per 1000 (from 1 more to 158 more)	⊕⊕OO Low
Combined behavioural and pharma intervention, not smoking at follow-up (12 months; biochemically validated only)											
2[a]	RCT	Very serious[1]	No serious	No serious	Serious[2]	None	44/254 (17%)	30/252 (12%)	1.46 (0.96 to 2.23) p=0.08	55 more per 1000 (from 5 fewer to 146 more)	⊕OOO Very Low

a) Gilbody 2015 and Gilbody 2019

[1]One study judged to be at an overall risk of bias as 'some concerns' one study judged to be an overall risk of bias as 'high'
[1]Gilody 2015 judged to have a 'high' ROB, Gilbody 2019 judged to have 'some concerns'
[2]Confidence interval crosses one line of the MID threshold

Profile 2: Abstinence from smoking (results presented from individual studies)

Quality assessment							No of patients		Effect		Confidence
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Intervention	Control	Relative (95% CI)	Absolute	
Combined behavioural and pharma intervention, not smoking at follow-up (12 months; biochemically validated & self-report)											
1[a]	RCT pilot	Very serious[3]	N/A	No serious	Serious[2]	None	12/33 (36%)	8/35 (23%)	1.6 (0.7 to 3.4)	137 more per 1000 (from 69 fewer to 549 more)	⊕⊕OO Very Low
Combined behavioural and pharma intervention, not smoking at follow-up (12 months; biochemically validated only)											
1[a]	RCT pilot	Very serious[3]	N/A	No serious	Serious[2]	None	10/31 (32%)	8/33 (24%)	1.3 (0.6 to 2.9)	73 more per 1000 (from 97 fewer to 461 more)	⊕⊕OO Very Low
Combined behavioural and pharma intervention, not smoking at follow-up (6 months; biochemically validated)											
1[b]	RCT	Serious[1]	N/A	No serious	No Serious	None	32/226 (14%)	14/217 (6%)	2.2 (1.2 to 4.0)	77 more per 1000 (from 13 more to 194 more)	⊕⊕⊕O Moderate
Combined behavioural and pharma intervention, not smoking at follow-up (12 months; biochemically validated											
1[b]	RCT	Serious[1]	N/A	No serious	Serious[2]	None	34/223 (13%)	22/219 (10%)	1·5 (0·9 to 2·5)	50 more per 1000 (from 10 fewer to 151 more)	⊕⊕OO Low
Combined behavioural and pharma intervention in veterans, not smoking at follow-up (12 months; self-report)											
1[c]	RCT	Serious[1]	N/A	Serious[4]	No serious	None	73/472 (15.5%)	33/471 7.0%)	2.21 (1.49 to 3.26)	85 more per 1000 (from 34 more to 158 more)	⊕⊕OO Low
Combined behavioural and pharma intervention in veterans, not smoking at follow-up (12 months; biochemically validated only)											
1[c]	RCT	Serious[1]	N/A	Serious[4]	No serious	None	42/472 (8.9%)	21/471 (4.5%)	2.00 (CI 1.20 to 3.32)	45 more per 1000 (from 9 more to 103 more)	⊕⊕OO Low

a) Gilbody 2015
b) Gilbody 2019
c) McFall 2010

[1]Study judged to be at an overall risk of bias as having 'some concerns'
[2]Confidence interval crosses one line of the MID threshold
[3] Study judged to be at an overall risk of bias as 'high'
[4]Miltary related PTSD

Profile 3: Mental health outcomes

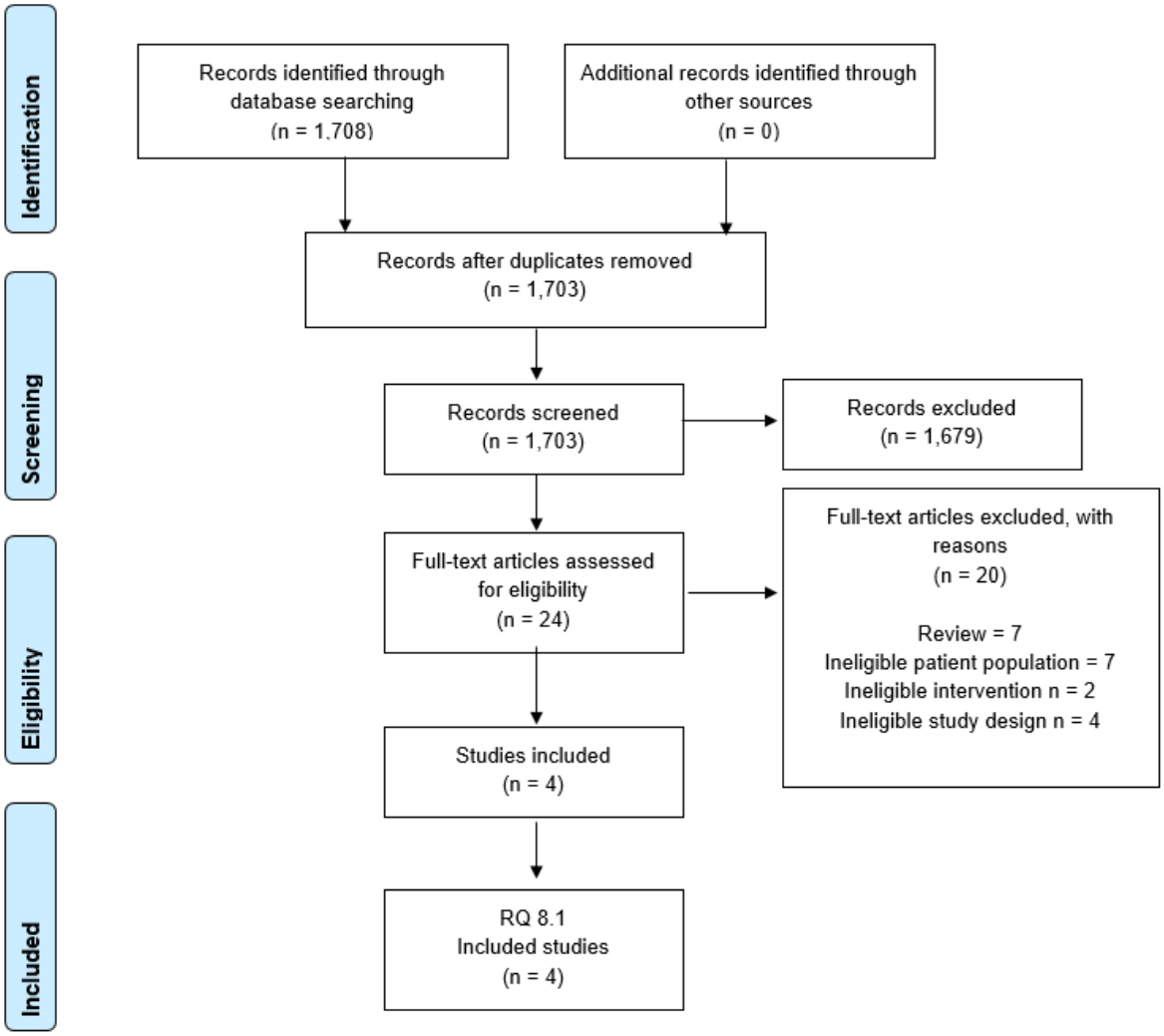
Quality assessment							Mean (CI)		Effect	Confidence
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Intervention	Control	MD (95% CI)	
Combined behavioural and pharma intervention, severity of depression (6 months, PHQ-9 questionnaire)										

1[a]	RCT	Serious[1]	N/A	No serious	No serious	None	9·6 (8·7 to 10·4)	9·4 (8·5 to 10·2)	0·20 (–0·85 to 1·24) p=0.72	⊕⊕⊕O Moderate
1[b]	RCT	Very Serious[2]	N/A	No serious	Serious[3]	None	9·6 (7.30 to 11.90	8·7 (6.18 to 11.2)	0.90 (-2.39 to 4.19) p=0.59	⊕OOO Very Low
Combined behavioural and pharma intervention, severity of depression (12 months, PHQ-9 questionnaire)										
1[a]	RCT	Serious[1]	N/A	No serious	No serious	None	9·3 (8·4 to 10·1)	9·4 (8·5 to 10·2)	–0·12 (–1·18 to 0·94), p=0.82	⊕⊕⊕O Moderate
1[b]	RCT	Very Serious[2]	N/A	No serious	Serious[3]	None	11·2 (8.72 to 13.68)	7·7 (5.15 to 10.25)	3.50 (0.08 to 6.92) p=0.05	⊕OOO Very Low
Combined behavioural and pharma intervention, severity of anxiety (6 months, GAD-7 questionnaire)										
1[a]	RCT	Serious[1]	N/A	No serious	No serious	None	7·0 (6·3 to 7·7	7·4 (6·7 to 8·1)	–0·32 (–1·26 to 0·62) p=0.5	⊕⊕⊕O Moderate
Combined behavioural and pharma intervention, severity of anxiety (12 months, GAD-7 questionnaire)										
1[a]	RCT	Serious[1]	N/A	No serious	No serious	None	7·1 (6·4 to 7·8)	7·2 (6·5 to 7·9)	–0·10 (–1·05 to 0·86), p=0.84	⊕⊕⊕O Moderate
Combined behavioural and pharma intervention, mental health component (6 months, SF-12 questionnaire)										
1[a]	RCT	Serious[1]	N/A	No serious	No Serious	None	37·9 (36·2 to 39·5)	38·6 (36·9 to 40·3)	–0·73 (–2·82 to 1·36) p=0.49	⊕⊕⊕O Moderate
1[b]	RCT	Very Serious[2]	N/A	No serious	Serious[3]	None	37·1 (32.67 to 41.53)	41·6 (37.87 to 45.33)	-4.50 (-10.18 to 1.18) p=0.12	⊕OOO Very Low
Combined behavioural and pharma intervention, mental health component (12 months, SF-12 questionnaire)										
1[a]	RCT	Serious[1]	N/A	No serious	No Serious	None	38·6 (37·0 to 40·1)	39·0 (37·4 to 40·5)	–0·41 (–2·35 to 1·53), p=0.68	⊕⊕⊕O Moderate
1[b]	RCT	Very Serious[2]	N/A	No serious	Serious[3]	None	39·1 (35.13 to 43.07)	41·8 (37.83 to 45.77)	-2.70 (-7.98 to 2.58) p=0.32	⊕OOO Very Low
Combined behavioural and pharma intervention in veterans, PTSD scale (18 months, clinician administered)										
1[c]	RCT	Very Serious[2]	N/A	Serious[4]	Serious[3]	None	-7.2 (-9.1 to -5.2)	-7.0 (-9.0 to -5.0)	-0.2 (-3.0 to 2.6)	⊕⊕OO Low
Combined behavioural and pharma intervention in veterans, PTSD checklist (12 months)										
1[c]	RCT	Very Serious[2]	N/A	Serious[4]	Serious[3]	None	-1.6 (-2.7 to -0.5)	-1.4 (-2.5 to -0.3)	-0.2 (-1.7 to 1.4)	⊕⊕OO Low
Combined behavioural and pharma intervention in veterans, PHQ-9 (12 months)										
1[c]	RCT	Serious[1]	N/A	Serious[4]	No Serious	None	1.6 (1.0 to 1.2)	1.2 (306 to 1.8)	0.4 (-0.4 to 1.2)	⊕⊕OO Low

a) Gilbody 2019
b) Gilbody 2015
c) McFall 2010

[1]Study judged to be at an overall risk of bias as having 'some concerns'
[2]Study judged to be at an overall risk of bias as 'high'
[3] CI crosses one line of the MID threshold
[4]Miltary related PTSD

Appendix G – Economic evidence study selection



Appendix H – Economic evidence tables

Barnett (2016)						
Study	**Method of Analysis**	**Costs**	**Outcomes**	**Results**	**Limitations**	**Comments**
Study type: Economic evaluation alongside a randomised controlled trial (RCT) and a Markov model **Country:** USA **Population:** Smokers receiving treatment for PTSD at VA medical centres [a] **Population size:** RCT: 943 Veterans Model: hypothetical **Intervention:** Smoking cessation services integrated with their mental health treatment (IC) including 5 weekly sessions, pharmacotherapy for those attempting to quit, 3 booster sessions, and monthly follow-up sessions. These services were delivered by the provider of their PTSD therapy. **Comparator:**	**Perspective:** Health care payer **Time horizon:** RCT: 18 months Model: Lifetime **Discounting:** 3.0% costs 3.0% effects **Data sources** **Costs:** RCT and literature **Utilities:** RCT and literature	**Total lifetime cost per person; mean, $:** IC 145,359 SCC 145,809 **Total cost per person; mean, $:** **RCT Costs** IC 24,171 SCC 25,305 **Total cost of smoking cessation services only per person, $:** **RCT Costs** IC 1286 SCC 551	**Total lifetime QALYs per person:** IC 7.054 SCC 7.028	**ICER, $:** 32,257 per QALY gained **Uncertainty:** The one-way sensitivity analyses carried out from the company generated results that ranged from IC being dominant (cost less and higher QALYs) when health cost accrued during the trial were included to $64,015 per QALY when the assumption that former smokers incur health care costs that are higher than current smokers (published finding) was modelled. Findings from a probabilistic sensitivity analysis showed that, at a cost-effectiveness threshold of $100,000 per QALY gained, IC	**Author identified:** • Development of specific smoking-related diseases was not considered. • Relapse rates and future quitting were adjusted to reflect the smoking behaviour of people with PTSD. • Health care cost data does not account for confounding between illness and quitting • Model relied on UK quality of life estimates. **Reviewer identified:** None	**Source of funding:** Cooperative Studies Program and National Institute on Drug Abuse **Further research:** Not reported

Barnett (2016)						
Study	**Method of Analysis**	**Costs**	**Outcomes**	**Results**	**Limitations**	**Comments**
Referral to a specialised outpatient smoking clinic (SCC)		**Currency & cost year:** US ($); 2010		was 86.0% likely to be cost-effective.		
Overall applicability: Partly applicable		**Overall quality: Minor limitations**				
Abbreviations: IC: integrated care; ICER: incremental cost-effectiveness ratio; PTSD: post-traumatic stress disorder; QALY: quality-adjusted life year; RCT: randomised controlled trial; SCC: smoking cessation clinic; VA: Veterans Affairs						
Li (2020)						
Study	**Method of Analysis**	**Costs**	**Outcomes**	**Results**	**Limitations**	**Comments**
Study type: Economic evaluation alongside an RCT **Country:** UK **Population:** People aged ≥18 years with serve mental illness (SMI) [a] who smoked ≥5 cigarettes per day and expressed an interest in cutting down or quitting smoking [b] **Population size:** 526 adult smokers (16 primary care and 21 secondary care mental health sites in England) **Intervention:** Smoking cessation packaged delivered by trained mental health smoking cessation practitioners (MH-SCP) who	**Perspective:** UK NHS and PSS **Time horizon:** 12-months **Discounting:** Not applicable **Data sources Costs:** SCIMITAR+ trial **Effects:** SCIMITAR+ trial **Utilities:** SCIMITAR+ trial	**Total cost per person; mean, £ (SE):** BSC 8447 (596) Usual care 8489 (775) **Treatment cost per person; mean, £ (SE) [d]:** BSC 561 (19) Usual care 93 (9) **Currency & cost year:** GBP (£); 2016/2017	**Total QALYs per person; mean (SE):** BSC 0.664 (0.015) Usual care 0.647 (0.017)	**ICER:** BSC dominates usual care (less costly and more effective) **Uncertainty:** The probability of BSC being cost-effective compared with usual care was 76% at £20,000 per QALY threshold and 80% at £30,000 per QALY threshold. Complete case analysis (CCA) suggested that BSC was costlier than usual care and more effective, but the ICER indicated that BSC was not cost-effective compared	**Author identified:** • Blinding was not possible • Short time horizon and limited number of quitters • Baseline questionnaire long and complex which might explain missing baseline data • Reliance on primary care practices to extract data from participants' medical records. However, the withdrawal and closure of practices caused a considerable level of missing data • EQ-5D-5L data were cross walked to 3L – there is considerable uncertainty in relation to this mapping function	**Source of funding:** NIHR Health Technology Assessment Programme (project number or ref. 11/136/52) NIHR Collaboration for Leadership in Applied Health Re- search and Care Yorkshire and Humber (NIHR CLAHRC YH) **Further research:** To explore the integration of smoking cessation interventions with routine mental health services so as to maximize the benefits of intensive sessions.

Barnett (2016)						
Study	**Method of Analysis**	**Costs**	**Outcomes**	**Results**	**Limitations**	**Comments**
were experienced mental health clinicians. Individuals were offered up to 12 individual face-to-face support sessions with a MH-SCP (approx. 30-minute duration) in their homes or NHS premises. MH-SCPs advised participants on available pharmacological smoking cessation aids and liaised with the participants' primary care physicians who would make decisions on prescribing pharmacotherapies chosen by participants [c] **Comparator(s):** Participants were advised to seek help from their primary care physician and local Stop Smoking Service (SSS)				with usual care at the £20,000 per QALY threshold.	• The validity and responsiveness of the EQ-5D-5L tool in people with SMI has been called into question **Reviewer identified:** • Differences in costs and QALYs between the intervention and comparator. groups were low • High level of uncertainty around mean incremental costs and incremental QALYs	The long-term impact of smoking cessation among people with SMIs should also be studied, especially in relation to the use of antipsychotics, and the mechanism behind the lowered hospitalisation for those who receive smoking cessation intervention.
Overall applicability: Directly applicable **Overall quality: Minor limitations**						

Abbreviations: BSC: bespoke smoking cessation; CLAHRC YH: Collaboration for Leadership in Applied Health Research and care Yorkshire and Humber; MH-SCP: mental health-smoking cessation practitioners; NHS: National Health Service; NIHR: National Institute for Health Research; PSS: Personal Social Services; QALY: quality-adjusted life year; RCT: randomised controlled trial; SE: standard error; SMI: severe mental illness; UC: usual care;

a. SMI was defined pragmatically as schizophrenia or delusional/psychotic illness (ICD-10: F20X and F22 X) or bipolar disorder (ICD-10: F31 X) diagnosed by specialist mental health services and documented in either primary care records of psychiatric notes.

b. Excluded population: people who were pregnant or breast feeding, had significant comorbid drug or alcohol problems, lacked capacity or were non-English speakers.

c. All participants had access to the full range of smoking cessation treatments offered by local authorities and the NHS. However, participants in the BSC group were asked not to take other treatments before the intervention ended. No additional treatment was offered in the context of the SCIMITAR+ trial.

d. Total treatment cost consisted of the intervention cost (BSC group only), cost of usual care and cost of pharmacotherapy prescriptions.

Barnett (2016)						
Study	**Method of Analysis**	**Costs**	**Outcomes**	**Results**	**Limitations**	**Comments**
a. Study inclusion criteria included a diagnosis of PTSD resulting from military-related trauma, verified according to the Diagnostic and Statistical Manual of Disorders (fourth edition), regular cigarette use (≥10 per day for at least half of the days in the past month without use of other tobacco products), motivation to quit smoking, completion of at least 1 month at a specialised VA outpatient treatment programme for PTSD. Exclusion criteria included diagnosis of any psychotic disorder, bipolar disorder, substance dependence not in remission, imminent risk of suicide or violence, or gross impairment from an organic condition						

Peckham (2019)						
Study	**Method of Analysis**	**Costs**	**Outcomes**	**Results**	**Limitations**	**Comments**
Study type: Economic evaluation alongside a RCT **Country:** UK **Population:** People aged ≥18 years with serve mental illness (SMI) [a] who smoked ≥5 cigarettes per day and expressed an interest in cutting down or quitting smoking [b] **Sample size:** 442 participants (219 in the usual care group and 223 in the BSC group) who had CO-verified smoking status at 12-month follow-up **Intervention:** Smoking cessation packaged delivered by trained mental	**Perspective:** UK NHS and PSS **Time horizon:** 12-months **Discounting:** Not applicable **Data sources** **Costs:** SCIMITAR+ trial **Effects:** SCIMITAR+ trial **Utilities:** SCIMITAR+ trial EQ-5D-5L	**Total cost per person; mean, £ (SE):** BSC 8446 (596) Usual care 8489 (775) **Smoking cessation; mean, £ (SE) [d]:** BSC 561 (19) Usual care 93 (9) **Health resource use; mean, £ (SE)** BSC 7886 (594) Usual care 8396 (774)	**Total QALYs per person; mean (SE):** BSC 0.664 (0.015) Usual care 0.647 (0.017)	**ICER:** BSC dominates usual care (less costly and more effective) **Uncertainty:** The BSC intervention for people with SMI is likely (57%) to be less costly but more effective than usual care, from a NHS and Personal Social Services perspective. Depending on the threshold considered, the probability of BSC being cost-effective could range from 62% at a willingness to pay threshold of £0 to nearly 90% at £100,000 per quality-	**Author identified:** • Blinding was not possible. • Short time horizon and limited number of quitters • Baseline questionnaire long and complex which might explain missing baseline data • Reliance on primary care practices to extract data from participants' medical records. However, the withdrawal and closure of practices caused a considerable level of missing data • EQ-5D-5L data were cross walked to 3L – there is considerable	**Source of funding:** NIHR Health Technology Assessment Programme (project number or ref. 11/136/52) NIHR Collaboration for Leadership in Applied Health Re- search and Care Yorkshire and Humber (NIHR CLAHRC YH) **Further research:** • Needed to establish how quitting can be sustained among people with SMI. • Evaluate the role of e-cigarettes in helping people with SMI to cut down or quit smoking. • To establish the clinical effectiveness

Peckham (2019)						
Study	**Method of Analysis**	**Costs**	**Outcomes**	**Results**	**Limitations**	**Comments**
health smoking cessation practitioners (MH-SCP) who were experienced mental health clinicians. Individuals were offered up to 12 individual face-to-face support sessions with a MH-SCP (approx. 30-minute duration) in their homes or NHS premises. MH-SCPs advised participants on available pharmacological smoking cessation aids and liaised with the participants' primary care physicians who would make decisions on prescribing pharmacotherapies chosen by participants [c] **Comparator(s):** Participants were advised to seek help from their primary care physician and local Stop Smoking Service (SSS)		**Currency & cost year:** GBP (£); 2016/2017		adjusted life-year (QALY) gained. Results from the complete case analysis (CCA) – carried out to assess the uncertainty due to missing data – showed that the probability of the intervention being cost-effective was 61-65% for WTP thresholds between £20,000 and £30,000 per QALY gained	uncertainty in relation to this mapping function • The validity and responsiveness of the EQ-5D-5L tool in people with SMI has been called into question **Reviewer identified:** • Differences in costs and QALYs between the intervention and comparator groups were low • High level of uncertainty around mean incremental costs and incremental QALYs	and cost effectiveness of very brief opportunistic interventions for smoking cessation. • Explore NRT update and the barriers to this for people with SMI. • In future trials, analyse aspects of the interventions that did not work, for which groups, and in which contexts. • Explore other factors that affect the health of people with SMI that can be influenced by the BSC intervention. • Long-term follow-up is needed to establish cost-effectiveness.
Overall applicability: Directly applicable		**Overall quality: Minor limitations**				

Peckham (2015)						
Study	**Method of Analysis**	**Costs**	**Outcomes**	**Results**	**Limitations**	**Comments**
Study type: Economic evaluation alongside a pilot RCT	**Perspective:** UK NHS and PSS **Time horizon:**	**Total cost per participant; mean, £ (SD) [range]:**	**Effectiveness; %:** At 12 months, 36% participants had stopped smoking in	**ICER:** £58,197 per quitter **Uncertainty:**	**Author identified:** The ICER should be treated with caution because of the small	**Source of funding:** NIHR Health Technology Assessment

Peckham (2019)						
Study	**Method of Analysis**	**Costs**	**Outcomes**	**Results**	**Limitations**	**Comments**
Country: UK **Population:** People aged ≥18 years with SMI [a] who smoked and expressed an interest in wanting to cut down smoking (though not necessarily quitting) [b] **Sample size:** BSC: n=46 UC: n=51 **Intervention** Mental health professional trained in smoking cessation interventions (MHSCP) worked in conjunction with the patient and the patient's GP or mental health specialist to provide a smoking cessation service individually tailored to each patient. The service included support sessions specifically adapted for patients with SMI [c] run by their MHSCP and GP-prescribed pharmacotherapies to aid smoking cessation, in addition to regular follow-ups by the MHSCP. **Comparator:** In the usual care control group participants were encouraged	12-months **Discounting:** Not applicable **Data sources** **Costs:** SCIMITAR pilot trial **Effects:** SCIMITAR pilot trial **Utilities:** SCIMITAR pilot trial	BSC 12,674 (16,595) [716 to 97,232] UC 6,867 (6,026) [343 to 33,217] **Intervention cost per participant (12 months); £ (SD) [range]:** BSC 221 (160) [37 to 824] UC 0 (0) [-] **Antipsychotic medicine prescription cost per participant (12 months); £ (SD) [range]:** BSC 474 (913) [0 to 3,712] UC 428 (782) [0 to 3,247] **Pharmacy for stop smoking prescription cost**	the BSC group compared with 23% in the usual care group. The adjusted OR was 2.9 (95% CI: 0.8 to 10.5) indicating a greater likelihood of smoking cessation in the BSC group, but the difference was not statistically significant **Mean QALY gain per person (95% CI):** BSC 0.65 (0.58 to 0.72) UC 0.69 (0.63 to 0.75)	Not reported	sample size and large variance of total cost. This pilot trial was not powered to detect a significant difference from an economic perspective. **Reviewer identified:** None	Programme (project number or ref. 07/41/05) **Further research:** A definitive trial to establish the clinical and cost-effectiveness of BSC services for people with SMI (based on the SCMITAR template).

Peckham (2019)						
Study	**Method of Analysis**	**Costs**	**Outcomes**	**Results**	**Limitations**	**Comments**
to consult with the GP or local NHS quit smoking services. GPs were given advice to follow current NICE guidelines for smoking cessation. [d]		**per participant (12 months); £ (SD) [range]:** BSC 62 (132) [0 to 706] UC 17 (60) [0 to 300] **Health care resource/community services cost per participant (12 months); £ (SD) [range]:** BSC 11,917 (16,601) [352 to 96,896] UC 6,421 (6,089) [86 to 33,217] **Currency & cost year:** UK £ 2011/2012				
Overall applicability: Directly applicable **Overall quality: Minor limitations**						
Abbreviations: BSC: bespoke smoking cessation; CI: confidence interval; NIHR: National Institute for Health Research; NHS=National Health Service; MHSCP: mental health-smoking cessation practitioners; OR: odds ratio; PSS: Personal Social Services; SD: standard deviation; SMI: severe mental illness; QALY: quality-adjusted life year; UC: usual care						

Peckham (2019)						
Study	**Method of Analysis**	**Costs**	**Outcomes**	**Results**	**Limitations**	**Comments**
a. SMI was defined pragmatically as a documented diagnosis of schizophrenia or delusional/psychotic illness (International Classification of Disease [ICD] F20.X & F22.X or Diagnostic and Statistical Manual of Mental Disorders (DSM) equivalent) or bipolar disorder (ICD F31.X or DSM equivalent). This SMI-inclusive diagnosis needed to have been made by specialist psychiatric services and have been documented in either the GP or psychiatric notes.						
b. Excluded population: people who were pregnant or breast feeding, had comorbid drug or alcohol problems (as ascertained by the GP or mental health worker), were non-English speakers, or lacked capacity to participate (guided by the 2005 Mental Capacity Act).						
c. Examples of specific adaptations to the needs of those with SMI are (1) the need to make several assessments prior to setting a quit date; (2) recognising the purpose of smoking in the context of their mental illness, such as the use of smoking to relieve side effects from antipsychotic medication (and how this will be managed during a cessation attempt); (3) the need to involve other members of the multidisciplinary team in planning a successful quit attempt for those with complex care needs and multiagency programmes of care; (4) a greater need for home visits, rather than planned visits in GP surgeries; (5) providing additional face-to-face support following an unsuccessful quit attempt or relapse; and (6) informing the GP and psychiatrist of a successful quit attempt, such that they can review antipsychotic medication doses if metabolism changes.						
d. Usual care could include pharmacotherapies to aid smoking cessation, access to self-help materials and referral to local NHS stop smoking clinics. Patients were encouraged to reduce smoking to quit and set their own quit dates, but were managed solely by their GP.						
Abbreviations: BSC: bespoke smoking cessation; CLAHRC YH: Collaboration for Leadership in Applied Health Research and Care Yorkshire and Humber; MH-SCP: mental health-smoking cessation practitioners; NHS: National Health Service; NIHR: National Institute for Health Research; PSS: Personal Social Services; QALY: quality-adjusted life year; RCT: randomised controlled trial; SE: standard error; SMI: severe mental illness; UC: usual care; WTP: willingness to pay						
a. SMI was defined pragmatically as schizophrenia or delusional/psychotic illness (ICD-10: F20X and F22 X) or bipolar disorder (ICD-10: F31 X) diagnosed by specialist mental health services and documented in either primary care records of psychiatric notes.						
b. Excluded population: people who were pregnant or breast feeding, had significant comorbid drug or alcohol problems, lacked capacity or were non-English speakers.						
c. All participants had access to the full range of smoking cessation treatments offered by local authorities and the NHS. However, participants in the BSC group were asked not to take other treatments before the intervention ended. No additional treatment was offered in the context of the SCIMITAR+ trial.						
d. The authors highlighted that the difference in neither costs nor QALYs was statistically significant in itself, but that there was an indication that the intervention costs might be offset by the reduction in wider health-care services costs, although, this result was not necessarily associated with participants' smoking status.						

Appendix I – Health economic evidence profiles

See Appendix H

Appendix J – Health economic analysis

See evidence review S for full details

Appendix K – Excluded studies

Public health studies

Study	Code [Reason]
Brunette, M.F., Ferron, J.C., Geiger, P. et al. (2019) Pilot study of a mobile smoking cessation intervention for low-income smokers with serious mental illness. Journal of Smoking Cessation	- Not a relevant study design *Maximum 8 week follow up*
Byars, J.A., Frost-Pineda, K., Jacobs, W.S. et al. (2005) Naltrexone augments the effects of nicotine replacement therapy in female smokers. Journal of Addictive Diseases 24(2): 49-60	- Does not contain a population of people with mental health conditions
Curtis, Jackie, Zhang, Charry, McGuigan, Bernadette et al. (2018) y-QUIT: Smoking Prevalence, Engagement, and Effectiveness of an Individualized Smoking Cessation Intervention in Youth With Severe Mental Illness. Frontiers in psychiatry 9: 683	- Does not contain a population of people with mental health conditions *Wrong age group*
Evins, A. Eden, Cather, Corinne, Laffer, Alexandra et al. (2015) Treatment of tobacco use disorders in smokers with serious mental illness: Toward clinical best practices. Harvard Review of Psychiatry 23(2): 90-98	- Systematic review used as source of primary studies
Gonzalez, Adam, Friedberg, Fred, Li, Xiaotong et al. (2017) Trauma-Focused Smoking Cessation for Smokers Exposed to the World Trade Center Disaster: A Randomized Clinical Trial. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco 19(8): 968-975	- Extrapolation issue - population very specific
Hammett, Patrick J, Lando, Harry A, Erickson, Darin J et al. (2020) Proactive outreach tobacco treatment for socioeconomically disadvantaged smokers with serious mental illness. Journal of Behavioral Medicine 43(3): 493-502	- Not a relevant study design
Hebert, Emily T, Stevens, Elise M, Frank, Summer G et al. (2018) An ecological momentary intervention for smoking cessation: The associations of just-in-time, tailored messages with lapse risk factors. Addictive behaviors 78: 30-35	- Does not contain a population of people with mental health conditions
Japuntich, Sandra J, Hammett, Patrick J, Rogers, Erin S et al. (2020) Effectiveness of	- Study does not contain a relevant intervention

Study	Code [Reason]
proactive tobacco cessation outreach in smokers with serious mental illness. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco	*Intervention was to offer tailored counselling, not the counselling itself*
Lancaster, T Stead, LF (2005) Individual behavioural counselling for smoking cessation. COCHRANE DATABASE OF SYSTEMATIC REVIEWS	- Systematic review used as source of primary studies
Lappin, Julia M, Thomas, Dennis, Curtis, Jackie et al. (2020) Targeted Intervention to Reduce Smoking among People with Severe Mental Illness: Implementation of a Smoking Cessation Intervention in an Inpatient Mental Health Setting. Medicina (Kaunas, Lithuania) 56(4)	- Study does not contain a relevant intervention
Li, Jinshuo, Fairhurst, Caroline, Peckham, Emily et al. (2020) Cost-effectiveness of a specialist smoking cessation package compared with standard smoking cessation services for people with severe mental illness in England: a trial-based economic evaluation from the SCIMITAR+ study. Addiction (Abingdon, England)	- Duplicate reference
Li, JS Fairhurst, C Peckham, E Bailey, D Arundel, C Hewitt, C Heron, P Crosland, S Parrott, S Gilbody, S Cost-effectiveness of a specialist smoking cessation package compared with standard smoking cessation services for people with severe mental illness in England: a trial-based economic evaluation from the SCIMITAR plus study. ADDICTION	- Duplicate reference
Luo, Sean X, Covey, Lirio S, Hu, Mei-Chen et al. (2015) Toward personalized smoking-cessation treatment: Using a predictive modeling approach to guide decisions regarding stimulant medication treatment of attention-deficit/hyperactivity disorder (ADHD) in smokers. The American journal on addictions 24(4): 348-56	- Study does not contain a relevant intervention
McCarthy, D.E., Piasecki, T.M., Lawrence, D.L. et al. (2008) A randomized controlled clinical trial of bupropion SR and individual smoking cessation counseling. Nicotine and Tobacco Research 10(4): 717-729	- Review article but not a systematic review
Niaura, R Hays, JT Jorenby, DE Leone, FT Pappas, JE Reeves, KR Williams, KE Billing, CB (2008) The efficacy and safety of varenicline for	- Study does not contain a relevant intervention

Study	Code [Reason]
smoking cessation using strategy in adult a flexible dosing smokers: a randomized controlled trial. CURRENT MEDICAL RESEARCH AND OPINION 24(7): 1931 - 1941	
Parker, Camilla; McNeill, Ann; Ratschen, Elena (2012) Tailored tobacco dependence support for mental health patients: a model for inpatient and community services. Addiction (Abingdon, England) 107suppl2: 18-25	- Study does not contain a relevant intervention
Pearsall, Robert; Smith, Daniel J; Geddes, John R (2019) Pharmacological and behavioural interventions to promote smoking cessation in adults with schizophrenia and bipolar disorders: a systematic review and meta-analysis of randomised trials. BMJ open 9(11): e027389	- Systematic review used as source of primary studies
Peckham, E Arundel, C Bailey, D Crosland, S Fairhurst, C Heron, P Hewitt, C Li, JS Parrott, S Bradshaw, T Horspool, M Hughes, E Hughes, T Ker, S Leahy, M McCloud, T Osborn, D Reilly, J Steare, T Ballantyne, E Bidwell, P Bonner, S Brennan, D Callen, T Carey, A Colbeck, C Coton, D Donaldson, E Evans, K Herlihy, H Khan, W Nyathi, L Nyamadzawo, E Oldknow, H Phiri, P Rathod, S Rea, J Romain-Hooper, CB Smith, K Stribling, A Vickers, C Gilbody, S (2019) A bespoke smoking cessation service compared with treatment as usual for people with severe mental ill health: the SCIMITAR plus RCT. HEALTH TECHNOLOGY ASSESSMENT 23(50): 1 - +	- Secondary publication of an included study that does not provide any additional relevant information
Peckham, Emily, Arundel, Catherine, Bailey, Della et al. (2019) A bespoke smoking cessation service compared with treatment as usual for people with severe mental ill health: the SCIMITAR+ RCT. Health technology assessment (Winchester, England) 23(50): 1-116	- Duplicate reference
Peckham, Emily, Man, Mei-See, Mitchell, Natasha et al. (2015) Smoking Cessation Intervention for severe Mental Ill Health Trial (SCIMITAR): a pilot randomised control trial of the clinical effectiveness and cost-effectiveness of a bespoke smoking cessation service. Health technology assessment (Winchester, England) 19(25): 1-vi	- Secondary publication of an included study that does not provide any additional relevant information
Secades-Villa, Roberto, Gonzalez-Roz, Alba, Vallejo-Seco, Guillermo et al. (2019) Additive effectiveness of contingency management on	- Study does not contain a relevant intervention

Study	Code [Reason]
cognitive behavioural treatment for smokers with depression: Six-month abstinence and depression outcomes. Drug and alcohol dependence 204: 107495	
Segan, Catherine J. (2011) Helping smokers with depression to quit smoking: collaborative care with Quitline. Medical Journal of Australia 195	- Study does not contain a relevant intervention
Smith, Stevens S, Jorenby, Douglas E, Leischow, Scott J et al. (2003) Targeting smokers at increased risk for relapse: treating women and those with a history of depression. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco 5(1): 99-109	- Study does not contain a relevant intervention
Steinberg, Marc L, Williams, Jill M, Stahl, Naomi F et al. (2016) An Adaptation of Motivational Interviewing Increases Quit Attempts in Smokers With Serious Mental Illness. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco 18(3): 243-50	- Not a relevant study design *Follow up at 1 month*
Steinberg, Marc L, Ziedonis, Douglas M, Krejci, Jonathan A et al. (2004) Motivational interviewing with personalized feedback: a brief intervention for motivating smokers with schizophrenia to seek treatment for tobacco dependence. Journal of consulting and clinical psychology 72(4): 723-8	- Not a relevant study design *Brief intervention - short follow up times*
Swan, G.E., McAfee, T., Curry, S.J. et al. (2003) Effectiveness of Bupropion Sustained Release for Smoking Cessation in a Health Care Setting: A Randomized Trial. Archives of Internal Medicine 163(19): 2337-2344	- Not population of interest
Tomko, R.L.; Bountress, K.E.; Gray, K.M. (2016) Personalizing substance use treatment based on pre-treatment impulsivity and sensation seeking: A review. Drug and Alcohol Dependence 167: 1-7	- Review article but not a systematic review
Vander Weg, Mark W, Cozad, Ashley J, Howren, M Bryant et al. (2016) An individually-tailored smoking cessation intervention for rural Veterans: a pilot randomized trial. BMC public health 16(1): 811	- Does not contain a population of people with mental health conditions

Study	Code [Reason]
Vilardaga, Roger, Rizo, Javier, Palenski, Paige et al. (2019) Pilot Randomized Controlled Trial of a Novel Smoking Cessation App Designed for Individuals with Co-Occurring Tobacco Dependence and Serious Mental Illness. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco	- Study does not contain a relevant intervention

Economic studies

Reference	Reason for exclusion
Ashton M, Rigby A, Galletly C. Do population-wide tobacco control approaches help smokers with mental illness? Australian and New Zealand Journal of Psychiatry. 2014;48(2):121-23.	Wrong study design
Baker AL, Richmond R, Kay-Lambkin FJ, et al. Randomized Controlled Trial of a Healthy Lifestyle Intervention Among Smokers With Psychotic Disorders. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2015;17(8):946-54.	Wrong intervention
Barnett PG, Wong W, Hall S. The cost-effectiveness of a smoking cessation program for out-patients in treatment for depression. Addiction (Abingdon, England). 2008;103(5):834-40.	Wrong patient population
Barnett PG, Wong W, Jeffers A, et al. Cost-effectiveness of smoking cessation treatment initiated during psychiatric hospitalization: analysis from a randomized, controlled trial. The Journal of clinical psychiatry. 2015;76(10):e1285-91.	Wrong patient population
Campion J, Checinski K, Nurse J. Review of smoking cessation treatments for people with mental illness. Advances in Psychiatric Treatment. 2008;14(3):208-16.	Review
Earl-Slater A, Walley T. Smoking cessation and bupropion. British Journal of Clinical Governance. 2001;6(1):69-74.	Wrong study design
Faulkner MA. Smoking cessation: An economic analysis and review of varenicline. ClinicoEconomics and Outcomes Research. 2009;1(1):25-34.	Wrong patient population
Gonzalez-Roz A, Weidberg S, Garcia-Perez A, et al. One-year efficacy and incremental cost-effectiveness of contingency management for	Wrong intervention

Reference	Reason for exclusion
cigarette smokers with depression. Nicotine & tobacco research : official journal of the Society for Research on Nicotine and Tobacco. 2020	
Hall SM, Lightwood JM, Humfleet GL, et al. Cost-effectiveness of bupropion, nortriptyline, and psychological intervention in smoking cessation. The journal of behavioral health services & research. 2005;32(4):381-92.	Wrong patient population
Jaehne A, Loessl B, Frick K, et al. The efficacy of stepped care models involving psychosocial treatment of alcohol use disorders and nicotine dependence: A systematic review of the literature. Current Drug Abuse Reviews. 2012;5(1):41-51.	Review
Keating GM, Lyseng-Williamson KA. Varenicline: A pharmacoeconomic review of its use as an aid to smoking cessation. PharmacoEconomics. 2010;28(3):231-54.	Review
Keiding H. Cost-effectiveness of varenicline for smoking cessation. Expert Review of Pharmacoeconomics and Outcomes Research. 2009;9(3):215-21.	Wrong patient population
Liu F. Effect of Medicaid coverage of tobacco-dependence treatments on smoking cessation. International journal of environmental research and public health. 2009;6(12):3143-55.	Wrong patient population
Miller N, Frieden TR, Liu SY, et al. Effectiveness of a large-scale distribution programme of free nicotine patches: a prospective evaluation. Lancet (London, England). 2005;365(9474):1849-54.	Wrong patient population
Park AL, McDaid D, Weiser P, et al. Examining the cost effectiveness of interventions to promote the physical health of people with mental health problems: a systematic review. BMC public health. 2013;13:787.	Review
Peckham E, Brabyn S, Cook L, et al. Smoking cessation in severe mental ill health: what works? an updated systematic review and meta-analysis. BMC psychiatry. 2017;17(1):252.	Review
Rejas-Gutierrez J, Bruguera E, Cedillo S. Modelling a budgetary impact analysis for funding drug-based smoking cessation therapies for patients with major depressive disorder in Spain. European psychiatry : the journal of the Association of European Psychiatrists. 2017;45:41-49.	Wrong study design
Secades-Villa R, Vallejo-Seco G, Garcia-Rodriguez O, et al. Contingency management for cigarette smokers with depressive symptoms. Experimental and Clinical Psychopharmacology. 2015;23(5):351-60.	Wrong study design
Woolacott N F, Jones L, Forbes C A, et al. The clinical effectiveness and cost-effectiveness of bupropion and nicotine replacement therapy for smoking cessation: a systematic review and economic evaluation. England: 2002.	Review
Xiao D, Chu S, Wang C. Smoking cessation in Asians: Focus on varenicline. Patient Preference and Adherence. 2015;9:579-84.	Review

Appendix L – Research recommendations

Research recommendation 4

How can people with mental health conditions be supported effectively to stop smoking (at individual and system level)? What are the challenges and opportunities and how can they be addressed?

Why this is important

Smoking prevalence remains disproportionately high among people with mental health conditions compared to the general population, despite evidence that smoking cessation strategies that may be effective for the general population may also work for people with mental health conditions. Both evidence and expert testimony 4 relating to inequalities for people with mental illness highlighted that the development of further support strategies that target specific barriers to smoking cessation at an individual and at a system level need to be developed (expert testimony proformas can be found in Appendix K of Review K). This is an important gap in the evidence which needs to be addressed in order to reduce inequalities in this area.

Rationale for research recommendation

Importance to 'patients' or the population	Smoking prevalence is higher among people with mental health conditions, including those in mental health settings, than among the general population. However, evidence highlights that they are motivated to quit smoking.
Relevance to NICE guidance	There is a need for further evidence to inform the development of recommendations to support people with mental health conditions to quit smoking using tailored approaches.
Relevance to the NHS	There may be some inequalities in prescribing practices for some pharmacotherapies and variation in implementation of, and use of, stop smoking support.
National priorities	The NHS Long Term Plan outlines a universal smoking cessation offer as part of specialist mental health services for long term users of these services.
Current evidence base	Some evidence was identified relating to interventions to support smoking cessation in people with mental health conditions using specifically tailored approaches, but evidence on how to support people at an individual and system level so that they can benefit from those interventions is in general lacking.
Equality considerations	Smoking prevalence is high among people with mental health conditions. Despite being motivated to quit smoking, people with mental health conditions may face additional challenges to successfully quitting.

Modified PICO table

Population	People with mental health conditions, including those in mental health settings.
Intervention	Smoking cessation interventions (individual or system based)
Comparator	Other intervention No intervention
Outcome	Abstinence from smoking Uptake of stop smoking support in people with mental health conditions