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[1]Department of Health Sciences, University of York, York, UK
[2]Centre for Primary Care, University of Manchester, Manchester, UK
[3]Research and Development, Sheffield Health and Social Care NHS Foundation Trust, Sheffield, UK
[4]School of Healthcare, University of Leeds, Leeds, UK
[5]Research and Development, Leeds and York Partnership NHS Foundation Trust, Leeds, UK
[6]North East York Community Mental Health Team, Tees, Esk and Wear Valleys NHS Foundation Trust, York, UK
[7]Division of Psychiatry, University College London, London, UK
[8]Research and Development, Rotherham Doncaster and South Humber NHS Foundation Trust, Doncaster, UK
[9]Research and Development, Lancashire Care NHS Foundation Trust, Preston, UK
[10]Research and Development, Tees, Esk and Wear Valleys NHS Foundation Trust, Stockton on Tees, UK

[11]Research and Development, Lincolnshire Partnership NHS Foundation Trust, Sleaford, UK
[12]Research and Development, Solent NHS Trust, Portsmouth, UK
[13]Research and Development, Sussex Partnership NHS Foundation Trust, Hove, UK
[14]Research and Development, Berkshire Healthcare NHS Foundation Trust, Reading, UK
[15]Research and Development, Bradford District Care NHS Foundation Trust, Bradford, UK
[16]Research and Development, Kent and Medway NHS and Social Care Partnership Trust, Maidstone, UK
[17]Research and Development, South West Yorkshire Partnership NHS Foundation Trust, Wakefield, UK
[18]Research and Development, Southern Health NHS Foundation Trust, Southampton, UK
[19]Research and Development, Northumberland, Tyne and Wear NHS Foundation Trust, Newcastle upon Tyne, UK
[20]Research and Development, Cambridgeshire and Peterborough NHS Foundation Trust, Cambridge, UK
[21]Research and Development, Somerset Partnership NHS Foundation Trust, South Petherton, UK

*Corresponding author

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Abstract

A bespoke smoking cessation service compared with treatment as usual for people with severe mental ill health: the SCIMITAR+ RCT

Emily Peckham,[1]* Catherine Arundel,[1] Della Bailey,[1] Suzanne Crosland,[1] Caroline Fairhurst,[1] Paul Heron,[1] Catherine Hewitt,[1] Jinshuo Li,[1] Steve Parrott,[1] Tim Bradshaw,[2] Michelle Horspool,[3] Elizabeth Hughes,[4] Tom Hughes,[5] Suzy Ker,[6] Moira Leahy,[3] Tayla McCloud,[7] David Osborn,[7] Joseph Reilly,[6] Thomas Steare,[7] Emma Ballantyne,[8] Polly Bidwell,[9] Susan Bonner,[10] Diane Brennan,[11] Tracy Callen,[12] Alex Carey,[3] Charlotte Colbeck,[3] Debbie Coton,[13] Emma Donaldson,[14] Kimberley Evans,[15] Hannah Herlihy,[16] Wajid Khan,[17] Lizwi Nyathi,[11] Elizabeth Nyamadzawo,[15] Helen Oldknow,[8] Peter Phiri,[18] Shanaya Rathod,[18] Jamie Rea,[19] Crystal-Bella Romain-Hooper,[5] Kaye Smith,[12] Alison Stribling,[20] Carinna Vickers[21] and Simon Gilbody[1]

[1]Department of Health Sciences, University of York, York, UK
[2]Centre for Primary Care, University of Manchester, Manchester, UK
[3]Research and Development, Sheffield Health and Social Care NHS Foundation Trust, Sheffield, UK
[4]School of Healthcare, University of Leeds, Leeds, UK
[5]Research and Development, Leeds and York Partnership NHS Foundation Trust, Leeds, UK
[6]North East York Community Mental Health Team, Tees, Esk and Wear Valleys NHS Foundation Trust, York, UK
[7]Division of Psychiatry, University College London, London, UK
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[19]Research and Development, Northumberland, Tyne and Wear NHS Foundation Trust, Newcastle upon Tyne, UK

[20]Research and Development, Cambridgeshire and Peterborough NHS Foundation Trust, Cambridge, UK
[21]Research and Development, Somerset Partnership NHS Foundation Trust, South Petherton, UK

*Corresponding author emily.peckham@york.ac.uk

Background: There is a high prevalence of smoking among people with severe mental ill health (SMI). Helping people with SMI to quit smoking could improve their health and longevity, and reduce health inequalities. However, those with SMI are less likely to access and engage with routine smoking cessation services than the general population.

Objectives: To compare the clinical effectiveness and cost-effectiveness of a bespoke smoking cessation (BSC) intervention with usual stop smoking services for people with SMI.

Design: A pragmatic, two-arm, individually randomised controlled trial.

Setting: Primary care and secondary care mental health services in England.

Participants: Smokers aged ≥ 18 years with SMI who would like to cut down on or quit smoking.

Interventions: A BSC intervention delivered by mental health specialists trained to deliver evidence-supported smoking cessation interventions compared with usual care.

Main outcome measures: The primary outcome was self-reported, CO-verified smoking cessation at 12 months. Smoking-related secondary outcomes were self-reported smoking cessation, the number of cigarettes smoked per day, the Fagerström Test for Nicotine Dependence and the Motivation to Quit questionnaire. Other secondary outcomes were Patient Health Questionnaire-9 items, Generalised Anxiety Disorder Assessment-7 items and 12-Item Short-Form Health Survey, to assess mental health and body mass index measured at 6 and 12 months post randomisation.

Results: The trial randomised 526 people (265 to the intervention group, 261 to the usual-care group) aged 19 to 72 years (mean 46 years). About 60% of participants were male. Participants smoked between 3 and 100 cigarettes per day (mean 25 cigarettes per day) at baseline. The intervention group had a higher rate of exhaled CO-verified smoking cessation at 6 and 12 months than the usual-care group [adjusted odds ratio (OR) 12 months: 1.6, 95% confidence interval (CI) 0.9 to 2.8; adjusted OR 6 months: 2.4, 95% CI 1.2 to 4.7]. This was not statistically significant at 12 months ($p = 0.12$) but was statistically significant at 6 months ($p = 0.01$). In total, 111 serious adverse events were reported (69 in the BSC group and 42 in the usual-care group); the majority were unplanned hospitalisations due to a deterioration in mental health ($n = 98$). The intervention is likely (57%) to be less costly but more effective than usual care; however, this result was not necessarily associated with participants' smoking status.

Limitations: Follow-up was not blind to treatment allocation. However, the primary outcome included a biochemically verified end point, less susceptible to observer biases. Some participants experienced difficulties in accessing nicotine replacement therapy because of changes in service provision. Efforts were made to help participants access nicotine replacement therapy, but this may have affected participants' quit attempt.

Conclusions: People with SMI who received the intervention were more likely to have stopped smoking at 6 months. Although more people who received the intervention had stopped smoking at 12 months, this was not statistically significant.

Future work: Further research is needed to establish how quitting can be sustained among people with SMI.

Trial registration: Current Controlled Trials ISRCTN72955454.

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Contents

List of tables

List of figures

List of abbreviations

AIC	Akaike information criterion
BMI	body mass index
BSC	bespoke smoking cessation
CACE	complier-average causal effect
CI	confidence interval
CMHT	community mental health team
CONSORT	Consolidated Standards of Reporting Trials
CPA	care programme approach
CPN	community psychiatric nurse
DNA	did not attend
DSM	*Diagnostic and Statistical Manual of Mental Disorders*
EQ-5D-5L	EuroQol-5 Dimensions, five-level version
FTND	Fagerström Test for Nicotine Dependence
GAD-7	Generalised Anxiety Disorder Assessment-7 items
GEE	generalised estimating equation
GMS	General Medical Services
GP	general practitioner
ICD-10	*International Classification of Diseases*, Tenth Edition
ICER	incremental cost-effectiveness ratio
MH-SCP	mental health smoking cessation practitioner
MTQ	Motivation to Quit questionnaire
NCSCT	National Centre for Smoking Cessation and Training
NIC	net ingredient cost
NICE	National Institute for Health and Care Excellence
NRT	nicotine replacement therapy
OR	odds ratio
PHQ-9	Patient Health Questionnaire-9 items
QALY	quality-adjusted life-year
QOF	Quality and Outcomes Framework
RCT	randomised controlled trial
SAE	serious adverse event
SCIMITAR	smoking cessation intervention for severe mental ill health
SD	standard deviation
SE	standard error
SF-12	Short Form questionnaire-12 items
SMI	severe mental ill health
SSS	stop smoking service
TSC	Trial Steering Committee
VAS	visual analogue scale
WTP	willingness to pay

Plain English summary

Smoking is an important health issue, especially among people who have experienced mental ill health such as schizophrenia or bipolar disorder. This is because people with severe mental ill health (SMI) are more likely to smoke than the general population. Despite this, they are less likely to get help to stop smoking, and it may be that people with mental ill health problems need greater support to help them stop smoking.

To address this problem, we developed and tested a 'bespoke smoking cessation' (BSC) service tailored to people with SMI. People aged ≥ 18 years who said that they would like to stop smoking were randomly allocated to either a BSC service or the usual stop smoking services. Those in the BSC service were allocated a mental health professional who had been trained to deliver smoking cessation interventions. The mental health professional worked with the participant and their care team to advise on stop smoking medication and provide information, support and motivation. Usual-care participants were signposted to local smoking services, but their subsequent care was not directly provided or supervised by trial smoking cessation advisors.

Between October 2015 and December 2016, 526 people with SMI were recruited into the study: 265 of these people were randomly assigned to the BSC service and 261 were randomly assigned to usual care. At 6 and 12 months after randomisation, participants completed questionnaires that asked about their smoking status and health. Participants had their smoking status tested by measuring the amount of carbon monoxide in their breath.

After 6 months, more people who received the BSC intervention had stopped smoking than those who had received usual care. At 12 months, the results were less clear in terms of the difference in the number of people who had stopped smoking.

The BSC service cost less than or similar to usual care, when considering the overall health-care services. The improvement in health of people who received the BSC service remains uncertain. In addition, we do not know whether or not this was related to people stopping smoking.

Scientific summary

Background

Smoking is highly prevalent among patients who have experienced severe mental ill health (SMI). This is despite the fact that smoking is a known health hazard, a cause of cancer and associated with numerous diseases such as heart disease. People with SMIs such as bipolar disorder and schizophrenia smoke more heavily and are more likely to be nicotine dependent than the general population. Despite the 'culture' of smoking in mental health services, over half of people with SMI who are smokers express a desire to quit smoking. However, the services currently available to aid quitting may not be suitably responsive to or effective for patients with SMI. A bespoke smoking cessation (BSC) intervention tailored to the needs of people with SMI was developed and its acceptability to people with SMI was tested in a pilot randomised controlled trial (RCT) – the SCIMITAR (smoking cessation intervention for severe mental ill health) trial. The intervention was found to be acceptable to people with SMI and, therefore, the role of this study was to test the SCIMITAR intervention in a full-scale RCT.

Objectives

The specific objectives of the SCMITAR+ trial were to establish:

- the clinical effectiveness of a BSC intervention compared with usual care for people with SMI
- the cost-effectiveness of a BSC intervention for people with SMI.

Methods

Design

A pragmatic, two-arm, parallel-group, individually randomised controlled trial.

Interventions

Participants were randomised to receive either a BSC service or usual care. The BSC service was delivered by a mental health professional [mental health smoking cessation practitioner (MH-SCP)] trained to deliver smoking cessation interventions. The MH-SCP provided an individually tailored smoking cessation service, based on current guidelines for smoking cessation services, but with enhanced levels of contact and support. Participants randomised to usual care were advised to see their general practitioner (GP) or to consult with usual NHS quit smoking services with no specific adaptation or enhancement in relation to SMI.

Participants

Potential participants were identified by (1) GP database screening, (2) direct GP referral or primary care referral following an annual health check, (3) direct referral via community mental health teams and psychiatrists, (4) recruitment from service user groups and (5) recruitment via an ongoing interventional cohort study [the Lifestyle Health and Wellbeing Cohort; see www.york.ac.uk/healthsciences/closing-the-gap/cohort/ (accessed 25 April 2019)].

To be eligible, potential participants needed to be aged ≥ 18 years, have experienced severe mental ill health (e.g. bipolar disorder, schizophrenia or a related psychotic illness), smoke and have expressed a desire to either give up smoking or cut down to quit smoking.

Outcomes

The primary outcome was exhaled CO-verified smoking cessation at 12 months. Secondary smoking-related outcomes were CO-verified smoking cessation at 6 months, reduction in the number of cigarettes smoked, the Fagerström Test for Nicotine Dependence and the Motivation to Quit questionnaire. Other secondary outcomes were measures of depression and anxiety (Patient Health Questionnaire-9 items and Generalised Anxiety Disorder Assessment-7 items) and health status (Short Form questionnaire-12 items) to measure general physical and mental health, and a measure of health utility (EuroQol-5 Dimensions, five-level version) and the Health Economics/Service Utilisation Questionnaire as measures of cost-effectiveness. Secondary outcomes were each measured at 6 and 12 months. Body mass index was measured at both follow-ups to explore whether or not smoking cessation was associated with weight gain.

Results

Between October 2015 and December 2016, 526 participants were recruited into the SCIMITAR+ RCT. The most common severe mental health problems were schizophrenia or other psychotic illness ($n = 342$, 65.0%), bipolar disorder ($n = 115$, 21.9%) and schizoaffective disorder ($n = 66$, 12.5%). Two hundred and sixty-five participants were randomised to a BSC service and 261 were randomised to usual care. Participants were aged between 19 and 72 years (mean 46 years), and there were more male ($n = 309$) participants than female ($n = 216$) participants, with one participant identifying as transgender. At baseline, participants reported smoking an average of 25 cigarettes per day and had long smoking histories (mean 30 years).

Out of 265 participants allocated to the BSC intervention, 232 (88%) attended at least one session (average number of sessions attended was 6.4, range 1–14). The intervention group had a higher rate of CO-verified smoking cessation at 6 and 12 months than the usual-care group [adjusted odds ratio (OR) 12 months: 1.6, 95% confidence interval (CI) 0.9 to 2.8; OR 6 months: 2.4, 95% CI 1.2 to 4.7]. This was not statistically significant at 12 months ($p = 0.12$) but was statistically significant at 6 months ($p = 0.01$). Participant follow-up exceeded 85% at 12 months. In total, 111 serious adverse events (SAEs) were reported (69 in the BSC group and 42 in usual care); the majority were unplanned hospitalisations due to unrelated deterioration in mental health condition ($n = 98$). The remaining SAEs were unplanned hospitalisations associated with pre-existing health problems ($n = 6$) or death ($n = 7$). One event was deemed to be possibly related to the trial procedures (inpatient hospitalisation due to infective chronic obstructive pulmonary disease).

The mainstay of pharmacological treatment was nicotine replacement therapy. People in receipt of usual care rarely accessed any form of smoking cessation treatment, but often purchased over-the-counter nicotine replacement products.

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-adjusted life-year (QALY) gained. Although the difference in neither costs nor QALYs was statistically significant in itself, there was an indication that the intervention costs might be offset by the reduction in wider health-care services costs. However, this result was not necessarily associated with participants' smoking status.

Conclusions

In the SCIMITAR+ trial, we have shown that people with SMI are more ready to engage with a bespoke intervention that results in increased 6-month quit rates.

Implications for health care

Clinicians are sometimes reluctant to offer smoking cessation advice to patients under their care, and this is in part due to concerns that treatment is ineffective or that quitting might cause a deterioration in mental health. The results of the SCIMITAR+ trial will be helpful in informing clinical practice, as we have shown that quitting can be achieved for people who use mental health services just as much as it can be for all smokers. Clinicians should therefore ask all of their patients about their smoking status and offer referrals to effective smoking cessation services such as those described in the SCIMITAR+ trial. Clinicians can also be confident, on the basis of the results of this trial and systematic review evidence, that smoking cessation is likely to either be beneficial to mental health or not harm mental health.

The results of the SCIMITAR+ trial will be helpful for service commissioners who seek to implement guidance for smoking cessation among hard-to-reach groups, such as people with SMI.

Recommendations for future research

Research is needed to establish how quitting can be sustained among people with SMI who engage with an evidence-supported quit smoking intervention. The role of e-cigarettes in helping people with SMI to cut down on or quit smoking also needs to be explored.

In addition, research is needed to complement the findings of the SCIMITAR+ trial, to establish the clinical effectiveness and cost-effectiveness of very brief opportunistic interventions among people with SMI.

Trial registration

This trial is registered as ISRCTN72955454.

Funding

Funding for this study was provided by the Health Technology Assessment programme of the National Institute for Health Research.

Chapter 1 Background

Some of the information in this chapter is reported in Peckham *et al.*[1] This contains information licensed under the Non-Commercial Government Licence v2.0.

Smoking and severe mental ill health

People with severe mental ill health (SMI), such as schizophrenia and bipolar disorder, are more likely to smoke and to smoke more heavily than those without SMI.[2,3] Estimates of the percentage of people with SMI who smoke vary depending on the setting, with up to 70% of inpatients smoking.[4] The presence of mental ill health is associated with an elevated risk of smoking by a factor of odds ratio (OR) 2.2 [95% confidence interval (CI) 1.7 to 2.8].[2] Smokers with SMI are more nicotine dependent, more likely to become medically ill with smoking-related diseases and less likely to access help in quitting than the general population.[5] People with SMI tend to:

- begin smoking at a higher rate before diagnosis or treatment for SMI than smokers without SMI[6,7]
- smoke each cigarette more intensely, extracting more nicotine per cigarette.[8]

People with SMI are also more likely to be unemployed than the general population. Smoking is known to be part of the 'culture' of mental health services, among both staff and patients. In addition, people with SMI often lack self-esteem and see the future as 'bleak'; as a consequence, they may not be motivated to look after their physical health.[9] Many people with SMI are also misinformed about the risks and benefits of smoking versus nicotine dependence treatment.[10] They often fear and overestimate the medical risks of nicotine replacement therapy (NRT).[11] Many believe that smoking relieves depression and anxiety[12] (nicotine increases anxiety[13]).

Smoking contributes to the poor physical health of those with SMI. In the UK, the standardised mortality rate for all causes of death for people with schizophrenia was 289 (95% CI 247 to 337), amounting to a threefold increase in mortality compared with the population of England and Wales.[14] Although people with SMI are more likely to smoke than the general population, there is evidence that general practitioners (GPs) are less likely to intervene with smokers who have a mental disorder than those who do not have a mental disorder.[5] Although the number of people in the general population who smoke has declined over the last 20 years, the number of people with SMI who smoke has not seen a similar decline.[3] The smoking rate among people with SMI in England is 40.5%,[15] which is more than double that of the general population.[16] Smoking rates in people with SMI vary across settings, with up to 70% of people in psychiatric units smoking.[4]

It is within this context that a number of policy initiatives have emerged that emphasise improving the physical care of those with SMI, including taking initiatives to facilitate smoking cessation and the promotion of smoke-free environments in secondary care services.[2,17,18]

Existing knowledge

Smokers most commonly cite 'stress relief and enjoyment' as their main 'reason' for smoking,[19] although the major cause is nicotine dependence. Nicotine acts in the midbrain, creating impulses to smoke in the face of stimuli associated with smoking[20] and producing what may be thought of as a kind of 'nicotine hunger' (a feeling of needing to smoke) when blood nicotine concentrations are depleted. Smokers also experience nicotine withdrawal symptoms, such as unpleasant mood swings and physical symptoms, that occur on abstinence and are relieved by smoking.[21] Nicotine dependence is the main reason that most unassisted quit attempts fail within a week.[22] Cochrane systematic reviews[23–30] and guidance from the

National Institute for Health and Care Excellence (NICE)[31] highlight the following smoking cessation interventions (including medications used as smoking cessation aids) that help smokers reduce their tobacco intake and quit smoking.

Nicotine replacement therapy

At the time of the trial, there were seven different available forms of administering NRT for use as smoking cessation aids. These were the nicotine patch, gum, lozenge, inhaler, spray (oral or nasal) and sublingual tablet (microtab). These provide a 'clean' alternative source of nicotine without the other 4000 toxic chemicals found in cigarette smoke. All deliver a lower dose of nicotine than the dose that would be received through smoking, with the only difference being the differing absorption rates owing to different methods of delivery. Nicotine replacement products can be used singly or in combination, for example a patch combined with a product that delivers nicotine faster, such as the nasal spray. A meta-analysis of > 100 randomised controlled trials (RCTs) shows that any form of NRT is effective in terms of smoking cessation (risk ratio 1.55, 95% CI 1.49 to 1.61).[32] For those who are not ready to stop smoking but are interested in cutting down, NRT prescription has been shown to reduce smoking and to facilitate quit rates later on (reduce to stop, or cut down to quit).[33]

Antidepressants and nicotine receptor agonists

Two non-nicotine pharmacotherapies have been licensed as smoking cessation aids. These are varenicline [Chantix® (USA) and Champix® (the European Union and other countries); Pfizer Inc., New York, NY, USA], a nicotinic acetylcholine receptor partial agonist, and bupropion (Zyban®; GlaxoSmithKline plc, Brentford UK), a noradenaline and dopamine reuptake inhibitor, which was first introduced as an atypical antidepressant. Varenicline is almost certainly the most effective treatment to date (OR for 12-month continuous abstinence for varenicline vs. placebo 3.22, 95% CI 2.43 to 4.27). It is more efficacious than bupropion (OR for varenicline vs. bupropion 1.66, 95% CI 1.28 to 2.16).[29] However, its use in people with SMI may be limited by case reports of depression or mental health worsening in populations with a previous history of mental health difficulties. Yet, a recent systematic review found there to be no increase in adverse effects in people with SMI taking varenicline compared with those without SMI,[34] and a recent trial among people with a range of mental health problems showed varenicline as being effective and having a good safety profile.[35] Therefore, these fears appear to be unfounded.

Behavioural support

Advice, discussion and encouragement can be delivered via a range of means: individually or in a group, in an open (rolling) or closed group, face to face or over the telephone or internet. Meta-analyses of trials of multisession 'intensive behavioural support versus brief advice' found ORs of 1.56 (95% CI 1.32 to 1.84) for individual support and 2.04 (95% CI 1.60 to 2.60) for group support.[25,26] Regular support over the telephone is also effective. A meta-analysis of 10 trials of telephone support for people stopping smoking gave an OR of 1.64 (95% CI 1.41 to 1.92).[28] There is some evidence to suggest that group support may be more effective in general than one-to-one support[36] and that it should involve multiple sessions.[36]

The accumulated evidence for the use of current smoking cessation interventions has been distilled into clear recommendations for health professionals[31] and a manual for those designing and delivering smoking cessation services.[37] In addition, guidance has been issued by NICE to guide the use of smoking cessation interventions for those with SMI.[38]

Evidence on the effectiveness of smoking cessation strategies in SMI comes from a systematic review of randomised trials by Banham and Gilbody,[39] which was updated in 2017.[40] These reviews draw on the results of 26 RCTs of smoking cessation interventions among those with SMI and show that combinations of behavioural support and pharmacotherapy (NRT and bupropion) are effective in facilitating smoking cessation. The evidence is strongest from varenicline, through the use of which the odds of quitting were improved fourfold (five trials; risk ratio 4.13, 95% CI 1.36 to 12.53).

Rationale for the SCIMITAR+ trial

Despite the higher prevalence of smoking, a substantial proportion of people with SMI express a desire to quit, but they expect to find it harder than those in the general population.[41] The introduction in 2004 of a new General Medical Services (GMS) contract[42] created a policy impetus to improve the quality of primary care in priority areas. In terms of mental health, the new GMS contract specified that primary care is responsible for the provision of physical health care. Importantly, for smoking cessation initiatives, it 'incentivised' GPs to (1) produce a register of people with severe long-term mental health [Quality and Outcomes Framework (QOF) indicator MH8 – the SMI register] and (2) ensure that at least 90% of SMI patients have had a review that includes smoking status recorded within the previous 15 months (QOF indicator MH9 – SMI health check). This check included patients seen in primary care, secondary care and under shared care arrangements. Though this GMS target has now been withdrawn, this was an incentive at the time of conception of the SCIMITAR+ (smoking cessation intervention for severe mental ill health) trial.

In addition, for those who are admitted to hospital (including inpatient psychiatric units), the introduction of smoke-free policies provides an opportunity to address smoking (Public Health Guidance 48[17]). The admission of an individual to hospital, while being stressful and occurring at a time of personal crisis, also provides a unique opportunity to provide general health advice and to engage individuals in interventions targeted at smoking reduction and cessation.

Recent guidance issued by NICE[17] offers clear statements of purpose to make secondary care services (including mental health services) entirely smoke free and to promote a smoke-free culture among staff and users of the services. Mental health services are highlighted as an area of priority and an unmet need in relation to smoking cessation, and there is clear guidance that services should be developed and implemented as a matter of some priority.

In 2009, the SCIMITAR pilot trial was devised to test whether or not a bespoke smoking cessation (BSC) intervention tailored to the needs of people with SMI would be acceptable to people with SMI.[43] In addition, it tested whether or not it was feasible to recruit and retain participants in a RCT to test this intervention. Recruitment to the pilot trial took place between May 2011 and May 2012. Results from the SCIMITAR pilot trial indicated that the intervention was acceptable to participants and that it was possible to recruit and retain participants in such a trial.[43] Although the trial was not powered to detect a difference between the bespoke intervention and usual care, the results indicated that there was a potential but non-statistically significant benefit of the bespoke intervention over usual care in terms of the proportion of self-reported quitters [12/33 (36%) vs. 8/35 (23%) adjusted OR 2.9, 95% CI 0.8 to 10.5]. Following this, the National Institute for Health Research Health Technology Assessment programme commissioned a fully powered RCT (SCIMITAR+) to explore the clinical effectiveness and cost-effectiveness of the SCIMITAR BSC intervention.

Research objectives[44]

- To establish the clinical effectiveness of a BSC intervention compared with usual care for people with SMI.
- To establish the cost-effectiveness of a BSC intervention for people with SMI.

Chapter 2 Methods

Some of the information in this chapter is reported in Peckham *et al.*[1] This contains information licensed under the Non-Commercial Government Licence v2.0.

Study design

This study was a pragmatic, two-arm, parallel-group RCT. The setting was in primary care and specialist mental health services within secondary care. Given that patients with SMI are a 'hard-to-reach population', a range of complementary strategies were used to try to identify and recruit eligible participants. A two-stage recruitment process was employed to check for eligibility, to check understanding of the study and to obtain consent. Participants were individually randomised to receive usual care or usual care plus a BSC service. Participants were followed up over the course of 12 months, with data collected at 6 and 12 months post randomisation.[44]

Approvals obtained

Ethics approval was sought and granted on 15 March 2015 by Leeds East Research Ethic Committee (reference number 15/YH/0051). Approval was also obtained from the relevant research and development departments (see *Appendix 1*).

Trial sites

The study was conducted in 22 sites in England. Sites recruited throughout the duration of the study.

Participant eligibility

Inclusion criteria

To be eligible for inclusion in this study, participants needed to meet the following inclusion criteria:

- aged ≥ 18 years
- have SMI
- be a smoker who expresses an interest in wanting to cut down on smoking (though not necessarily quitting)
- smoke at least five cigarettes per day.

There is no agreed definition of SMI, so we adopted a pragmatic definition, that is, a documented diagnosis of schizophrenia or delusional/psychotic illness [*International Classification of Diseases*, Tenth Edition (ICD-10),[45] F20.X and F22.X or *Diagnostic and Statistical Manual of Mental Disorders* (DSM)[46] equivalent] or bipolar disorder (ICD F31.X or DSM equivalent). This SMI-inclusive diagnosis needed to have been made by specialist psychiatric services and to have been documented in either GP notes or psychiatric notes.

Exclusion criteria

People were ineligible if they met the following criteria:

- currently pregnant or breastfeeding
- with comorbid drug or alcohol problems (as ascertained by the GP or mental health worker)
- non-English speakers

- lacking capacity to participate in the trial (guided by the 2005 Mental Capacity Act 71[47])
- currently receiving advice from a smoking cessation advisor.

People with SMI who smoke while concurrently abusing substances may require additional medication or specialist advice, which was beyond the brief of the mental health smoking cessation practitioner (MH-SCP) and this trial. Similarly, smoking cessation in pregnancy also requires specialist knowledge. It was planned that any participant who became pregnant during the course of the trial would be fully withdrawn from the study and referred to local smoking cessation services specific to pregnancy.

Identifying participants

We used five methods to recruit participants.

Direct general practitioner referral or referral following database screening

General practitioners are encouraged to offer opportunistic advice and information about smoking cessation services to all people who smoke whenever they consult in primary care. GPs taking part in this study were provided with patient study information packs to give to people with SMI who were receptive to participating in the trial. GPs then completed and faxed a referral form and the person's 'consent to be contacted' form to the SCIMITAR+ researchers who approached the person for recruitment.

The GP practices were also asked to consult their patient databases and SMI register, if available, to screen for potentially eligible participants. Information packs were sent from the GP practice, inviting people willing to take part in the study to return a completed 'consent to be contacted' form to the SCIMITAR+ researchers, who then approached them to ascertain eligibility and recruitment.

Primary care referral following annual health check

At the time of the trial, the annual primary care health check for people with SMI (MH9) represented an opportunity to address smoking behaviour and to offer enhanced smoking cessation services within the context of a trial. Health checks are generally conducted by practice nurses, and we encouraged all primary care staff to make SMI smokers aware of the trial when they received their annual primary care health check. Information packs were given to interested and potentially eligible people during their health check. Similar to GP referrals, practice nurses were instructed to complete referral forms and to fax the persons' completed 'consent to be contacted' form to the SCIMITAR+ researchers, who then approached them for eligibility and recruitment.

Community mental health teams

Study researchers worked with care co-ordinators and members of the community mental health team (CMHT) to screen their caseloads for potentially eligible participants who matched the inclusion criteria. People identified as potentially suitable for the SCIMITAR+ trial were either provided with a copy of the information pack by their care co-ordinator or other mental health professional or sent an information pack in the post. The information pack contained a 'consent to be contacted' form for potential participants to return to the SCIMITAR+ researchers, giving permission for the researcher to contact them by telephone or letter or in person to discuss the trial further.

Service user groups[44]

Service user groups were provided with information about the study along with copies of a SCIMITAR+ flyer. Interested service users could then contact the mental health professional named on the flyer or their care co-ordinator. Alternatively, the staff member at the service user group could contact the service user's care co-ordinator on their behalf.

Lifestyle Health and Wellbeing Survey

The Lifestyle Health and Wellbeing Cohort is a prospective study that forms a platform for interventional studies ('Trials within cohorts'), co-ordinated by the University of York, recruiting adults with SMI aged ≥ 18 years from primary and secondary care. Participants in the Lifestyle Health and Wellbeing Survey complete a series of questions about their health and well-being, including questions about their smoking status. Cohort participants who reported smoking and were potentially interested in cutting down on or quitting smoking were invited to take part in the SCIMITAR+ trial.

Screening for eligibility

After receiving an information pack and once a person gave consent to be contacted (either verbally to the recruiting clinician or in writing to the SCIMTAR+ researchers), a SCIMITAR+ researcher approached them by telephone, face to face or by e-mail, depending on the person's preference. After briefly explaining the trial, the researcher checked the person's eligibility by asking about their smoking habits, specifically (1) whether or not they smoke; (2) if so, how much they smoke (they needed to smoke at least five cigarettes per day to be eligible); (3) if they would consider quitting or cutting down, with a view to quitting within the next 6 months; and (4) whether or not they were currently receiving advice from a smoking cessation advisor. These questions ensured that the person currently smoked but was contemplating quitting. The researcher also asked screening questions about pregnancy and breastfeeding, and drug and alcohol usage, which led to exclusion if present. The researcher then arranged a meeting at a mutually convenient time and venue.

Consenting participants

When a potential participant met with the SCIMITAR+ researcher, they were given the opportunity to clarify any points they did not understand and to ask any questions. A full explanation of the trial was given by the SCIMITAR+ researcher. It was emphasised that they may withdraw their consent to participate at any time without loss of treatment options that would otherwise be available to them. They were also informed that, by consenting, they agreed to their GP being informed of their participation in the trial. Written informed consent was then obtained, with both the participant and the researcher signing and dating the consent forms prior to collecting baseline data (see *Appendix 2* for participant information sheets and consent forms).

Baseline assessment

Once a participant had consented to take part in the trial, they completed the baseline questionnaires. Height and weight measurements were completed to calculate the participant's body mass index (BMI) and an exhaled breath carbon monoxide (CO) reading was taken. These made up the baseline data set. The participant was randomised on completion of this data set.

Randomisation

Eligible, consenting individuals were randomised 1 : 1 to either the BSC service or usual care. The researcher contacted a secure telephone randomisation service run by the York Trials Unit. Simple randomisation was used, following a computer-generated number sequence devised by an independent data manager otherwise not involved in the conduct of the trial. Once given the details of the participant's allocation, the researcher immediately informed the participant of their allocation and what would happen next. If allocated to the BSC arm, researchers at the University of York then contacted the MH-SCP in the participant's area and organised for them to contact the participant to arrange a mutually convenient time

to meet. A letter was sent to the GP and mental health specialist for the participant's records and to advise them on subsequent smoking cessation management. Owing to the nature of the intervention, it was not possible to blind participants, GPs, researchers or the MH-SCPs to the treatment allocation.

Ineligible and non-consenting individuals

All ineligible and non-consenting persons were referred back to their GP/mental health service.

Sample size

Results from the SCIMITAR pilot trial were used to inform the sample size calculation for this trial. In the pilot trial, a quit rate of 23% was observed at 12 months in the usual-care arm and a quit rate of 36% was observed in the BSC arm.[43] The SCIMITAR+ trial was powered at 80% to detect a relative risk increase in quitting of 1.7, assuming a control quit rate of 20% (an increase to a quit rate of 34% in the intervention group), equal randomisation and a two-sided alpha of 0.05. Allowing for a 20% loss to follow-up at 12 months required a total sample size of at least 393 to be recruited and randomised. We therefore proposed to recruit 400 participants in total to ensure sufficient power according to the preceding statistical assumptions.

Description of interventions

Trial intervention

Participants in the intervention group were allocated to receive a BSC intervention designed specifically to help people with SMI stop smoking. This intervention was delivered by a mental health professional (care co-ordinator, support worker, mental health nurse) trained in smoking cessation interventions. The training took place over 2 days and was provided by trained smoking cessation advisors. The BSC intervention consisted of up to 12 one-to-one face-to-face meetings between the participant and the MH-SCP, who worked in conjunction with the participant and their GP or mental health specialist to ensure that the participant received smoking cessation medication and medication monitoring. The initial meeting generally took 1 hour, with subsequent meetings lasting 30 minutes. Meetings were initially weekly; however, towards the end of the programme the participant had the choice of meeting fortnightly if preferred. Pharmacotherapies were provided for as long as was deemed necessary, in line with NICE guidance,[17] and were determined by the GP without the influence of the SCIMITAR+ trial team. In line with NICE recommendations, MH-SCPs offered advice on the range of treatment options available to people in the NHS (including medication, behavioural support and follow-up).[31] It was not the remit of the trial to assess specific smoking cessation pharmacotherapies or treatments per se, although data on frequency of their use were collected. The intervention was based on that used by the National Centre for Smoking Cessation and Training (NCSCT), but the following specific modifications were applied to tailor the intervention to people with SMI: (1) recognising the need for several assessment sessions 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) recognising 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) arranging meetings so that they take place in a mutually agreeable location, often in the participant's home rather than in the GP surgery or on NHS trust premises; (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 so that they can review antipsychotic medication doses in line with changes in metabolism. Participants were encouraged to (1) reduce smoking to quit, (2) set their own quit dates and (3) make several attempts to quit if their initial attempt failed. All participants remained under the care of their GP and continued to receive their usual NHS treatment.

A detailed description of the development and content of the smoking cessation intervention is given in the report of the SCIMITAR pilot trial.[1]

Control intervention

This was a 'usual-care' control group, whereby participants were encouraged to consult with their GP or local NHS quit smoking services. GPs were given advice to follow current NICE guidelines for smoking cessation, without the additional support of a bespoke MH-SCP. Usual care could include pharmacotherapies to aid smoking cessation (NRTs, bupropion or varenicline either separately or in combination), access to self-help materials and referral to local NHS stop smoking clinics (which would not be specifically tailored to the needs of those with SMI). Participants were encouraged to reduce smoking to quit and set their own quit dates; however, they were managed solely by their own GP or mental health specialist and, crucially, did not receive regular visits from a MH-SCP. Details of NRT that control participants received were gathered by accessing participants' GP notes, and details of any smoking cessation management were requested from participants in the follow-up questionnaires.

Smoking cessation medication provision

Clear guidance on the prescription of anti-smoking medications in the presence of SMI (including safety considerations) has been published and was made available to all GPs to help inform their prescribing decisions (for both control and intervention participants).[48] A key feature of the SCIMITAR+ trial was to ensure that GPs manage anti-smoking medications within this framework and in accordance with their prior knowledge of the patient and their concomitant use of medication. This was carried out with the aim of replicating 'real-life practice' of the use of anti-smoking medications in primary care. The medication profile of the individual participants was reviewed by their GP or mental health specialist to assess any potential safety issues (in line with the latest practice guidance on the provision of smoking cessation interventions in the NHS[2]). An important aspect of the design of this study was that the SCIMITAR+ team had no direct influence over prescribing decisions by GPs, as this was not a drug trial or an investigation of a medicinal product(s).

Follow-up

Participants were followed up 6 months and 12 months after randomisation.

All assessments were carried out face to face where possible and, where not possible, a systematic approach was used to explore other avenues to collect self-report data; the participant was offered the option of completing the questionnaires over the telephone or having the questionnaires sent by post for them to complete and return. If it was not possible to make contact with the participant, a family member or friend, designated by the participant at their baseline interview, was contacted to verify the participant's current smoking status.

Outcomes

Primary outcomes

The primary outcome was self-reported abstinence from smoking at 12 months post randomisation, defined as answering 'not even a puff' to the question 'have you smoked in the last week?', validated by CO breath measure, with abstinence defined as a CO measurement of < 10 parts per million (p.p.m.).

Secondary outcomes

- Self-reported smoking cessation.
- Number of cigarettes smoked per day (self-report).
- Fagerström Test for Nicotine Dependence (FTND).[49]

- Motivation to Quit questionnaire (MTQ).[50]
- Patient Health Questionnaire-9 items (PHQ-9).[51]
- Generalised Anxiety Disorder-7 items (GAD-7).[52]
- Health-related quality of life [Short Form questionnaire-12 items (SF-12) version 1 was used, as this was used in the pilot trial].[53]
- EuroQol-5 Dimensions, five-level version (EQ-5D-5L).[54]
- BMI.
- Health service use collected via a bespoke questionnaire.

Table 1 gives details of the measures collected and the time points at which they were collected.

Withdrawal

A study participant could be withdrawn from the trial by their GP, mental health specialist or smoking cessation practitioner, or may choose to do so themselves, at any time. If the withdrawal was due to an adverse event, procedures followed a trial-specific standard operating procedure (SOP) for adverse events (see *Appendix 3*).

Where possible, data were collected on the nature of the withdrawal. Reasons for a practitioner to withdraw a participant included pregnancy, admission to hospital for reasons unrelated to the trial and, inability to attend treatment or assessment sessions. Relapse to resuming smoking was not a reason to withdraw a participant, as they could resume treatment and make several attempts to quit smoking.

Participants were given a choice of (1) withdrawal from treatment only (participants were still followed up at 6 and 12 months), (2) withdrawal from follow-up or (3) complete withdrawal from the study, including follow-up and medication data collection. Withdrawal from the study did not affect the participants' treatment or access to NHS services.

Any data collected from the participant prior to withdrawal were still included in the final analysis of the data.

Participant concordance

Mental health smoking cessation practitioners were asked to complete a treatment log that recorded all participants' contacts (face-to-face meetings, telephone calls and joint appointments with MH-SCPs and GPs) to judge the degree to which the intervention, as designed on a session-by-session basis, was actually delivered in practice by MH-SCPs.

At each meeting, MH-SCPs would take a CO measurement from the participant. Measurements of $\geq$ 10 p.p.m. indicated that the participant had not ceased smoking. If the participant claimed to have stopped but their CO readings were $\geq$ 10 p.p.m., they were probed about when they last smoked and whether or not they had had any minor relapses during their quit attempt.

Statistical analysis

All analyses were conducted following the principles of intention to treat, including all randomised participants in the groups to which they were randomised, where data were available. Analyses were conducted in Stata® version 15 (StataCorp LP, College Station, TX, USA). All statistical tests were two-sided at the 5% significance level.

TABLE 1 Assessments and the time points at which they were carried out

Assessment	Time point		
	Baseline	6 months post randomisation	12 months post randomisation
Eligibility and consent			
Eligibility	✗		
Consent	✗		
Background and follow-up			
Personal details, general health	✗		
BMI	✗	✗	✗
Mental health details			
Mental health history	✗		
Current mental health status	✗	✗	✗
Current medications	✗	✗	✗
Referrals to mental health services		✗	✗
Admissions to hospital related to mental health		✗	✗
Smoking details			
Smoking history	✗		
Current smoking status	✗	✗	✗
Use of electronic cigarettes	✗	✗	✗
Use of smoking cessation services	✗	✗	✗
CO measurement	✗	✗	✗
Adverse event reporting	Ongoing collection		
Questionnaires			
FTND	✗	✗	✗
MTQ	✗	✗	✗
PHQ-9	✗	✗	✗
GAD-7	✗	✗	✗
Health-related quality of life (SF-12)	✗	✗	✗
Health-state utility (EQ-5D-5L)	✗	✗	✗
Health economics/service utilisation questionnaire	✗	✗	✗

Recruitment and retention

The flow of participants through the trial is described in Consolidated Standards of Reporting Trials (CONSORT) flow diagrams (see *Figures 3–5*), two of which describe recruitment up to randomisation (one for primary care and one for secondary care) and one of which presents the flow of participants from randomisation to analysis. The response rates, time to return and mode of completion of the 6- and 12-month participant questionnaires are summarised by treatment group.

Baseline data

Baseline data are summarised by treatment group, using mean standard deviation (SD), median and range for continuous data, and count and percentage for categorical variables. No formal statistical comparisons between the two groups were undertaken on baseline data.

Data manipulations and questionnaire scoring

Number of cigarettes smoked

Participants were asked how many cigarettes they normally smoked per day and how much tobacco they used per day. It was assumed that 0.5 g of tobacco equates to one cigarette.[55]

Fagerström Test for Nicotine Dependence

The FTND is a 6-item questionnaire.[49] Item scores are added together to give a total score between 1 and 10: 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.

Motivation to Quit questionnaire

The MTQ is a 4-item questionnaire scored from 4 to 19, by adding together the responses to each item, with higher scores indicating a greater motivation to stop smoking.[50]

Patient Health Questionnaire-9 items

The PHQ-9 is a 9-item instrument. It asks the subject to indicate how often in the last 2 weeks they have been bothered by nine problems, which are each scored on the scale of 0 = not at all, 1 = several days, 2 = more than half the days, and 3 = nearly every day.[51] A total score is obtained from adding together the nine item scores. Scores can be categorised as follows: 0–4 indicates minimal depression, 5–9 indicates mild depression, 10–14 indicates moderate depression, 15–19 indicates moderately severe depression and 20–27 indicates severe depression. If one or two values are missing from the score, then they can be substituted with the average score of the non-missing items (scored pro rata and total score rounded to nearest integer). Questionnaires with more than two missing values are disregarded.

Generalised Anxiety Disorder Assessment-7 items

The GAD-7 is a 7-item instrument.[52] For each item, scores of 0, 1, 2 and 3 are given to the possible responses of 'not at all', 'several days', 'more than half the days' and 'nearly every day', respectively. The GAD-7 total score ranges from 0 to 21. Scores of 5, 10 and 15 represent cut-off points for mild, moderate and severe anxiety, respectively. If one or two values are missing from the score, then they can be substituted with the average score of the non-missing items (scored pro rata and total score rounded to nearest integer). Questionnaires with more than two missing values are disregarded.

Short Form questionnaire-12 items (version 1)

The SF-12 consists of two subscales – a physical component and a mental component – both of which are scored within the range of 0–100, with 0 indicating the lowest level of health and 100 indicating the highest level of health measured by the scale. Scoring was conducted in accordance with the SF-12 scoring manual.[53]

Body mass index

A participant's weight was measured in kilograms at each follow-up visit and their height was measured in metres at the baseline visit. BMI was calculated by dividing weight by height squared and is expressed in the units kg/m^2.

Primary analysis

The primary outcome of CO-verified smoking cessation at 12 months was intended to be analysed via a mixed-effect logistic regression model to compare the BSC service intervention with usual care. The model was to include CO-verified smoking status at 6 and 12 months (repeated measures within participants)

and be adjusted for baseline smoking severity (self-reported number of cigarettes smoked per day), time, treatment group and a treatment group-by-time interaction, with site as a random effect. Participants nested within site were also to be treated as a random effect to account for the repeated measures within the subjects. However, this model failed to converge. Therefore, separate multilevel logistic regression models were run to compare the outcomes at 6 and 12 months, that is, two models, instead of one model that incorporates the repeated measurements. The two models were each adjusted for baseline smoking severity, with site as a random effect. The OR, corresponding two-sided 95% CI and *p*-value for the treatment effect at 6 and 12 months are presented. The treatment effect at 12 months serves as the primary end point, and the effect at 6 months serves as a secondary end point. Participants were analysed according to their original random group allocation and were included in the models if they provided a CO reading and a response to the self-reported question relating to amount smoked in the previous week at that particular time point.

Sensitivity analyses

Unadjusted odds ratio

The unadjusted, marginal OR for smoking status at 6 and 12 months is presented for comparability.

Post hoc generalised estimating equations analysis

Given that the prespecified repeated measures mixed logistic regression model did not converge, post hoc sensitivity analyses were conducted using generalised estimating equation (GEE) techniques. This allowed for the repeated measures within participants to be accounted for, but the multilevel nature of the data (i.e. participants within site) cannot be controlled in the same way that including a random effect for site in the mixed logistic regression can be. Two GEE models were run: (1) one controlling for baseline smoking severity, and including an interaction between allocation and time, and (2) one controlling for both baseline smoking severity and site as covariates, and including an interaction between allocation and time. Both specified a binomial family and logit link, with an exchangeable correlation structure.

Accounting for missing carbon monoxide-verified smoking status

Self-reported smoking status was considered when CO-verified smoking status was missing. Further sensitivity analyses were conducted treating participants who still had missing outcome data in the following two ways: one treated participants with missing data as smokers under a worst case scenario, and the other used multiple imputation techniques. Twenty imputations were generated by multiple imputation using chained equations with a burn-in of 10. To avoid bias, the imputation model used all variables that were included in the analysis models (baseline smoking severity, CO-verified smoking status at 6 and 12 months, site and allocation).[56]

Secondary analyses

All data collected at 6 and 12 months are summarised descriptively by treatment group, including an investigation into the number of missing data.

Self-reported smoking cessation

The primary analysis was repeated using self-reported smoking status at 6 and 12 months as the outcome (cessation defined as answering 'not even a puff' to the question 'have you smoked in the last week?').

Number of cigarettes smoked per day

The number of cigarettes smoked per day, as reported as part of the FTND, at 6 and 12 months was compared between the two groups using a mixed-effect negative binomial regression model, adjusting for the same covariates as the primary analysis and the repeated measures within participants. Incidence rate ratios and their associated 95% CIs and *p*-values are provided.

Continuous secondary outcomes: Fagerström Test for Nicotine Dependence, Motivation to Quit questionnaire, Patient Health Questionnaire-9 items, Generalised Anxiety Disorder Assessment-7 items, Short Form questionnaire-12 items and body mass index

The FTND, MTQ, PHQ-9, GAD-7, SF-12 physical component and SF-12 mental component scores and BMI were all analysed in the same way. Scores were compared between treatment groups using a covariance pattern linear mixed model. The outcome modelled was the total score at 6 and 12 months. Each model included baseline score, baseline smoking severity, treatment group, time and a treatment group-by-time interaction term as fixed effects, and site as a random effect.

Different covariance structures for the repeated measurements that are available as part of Stata were explored and the most appropriate pattern was used for the final model, based on the one that produced the smallest Akaike information criterion (AIC). Model assumptions were checked via a Q–Q plot to assess the normality of the standardised residuals and a scatterplot of the residuals against fitted values.

Predicted means for each group and the adjusted mean difference (with 95% CI and *p*-value) between treatment groups at 6 and 12 months are given.

Other outcomes

Self-reported number of attempts to quit, periods of cessation and e-cigarette use will be summarised descriptively by treatment group and time point.

Compliance with the intervention

Treatment session data are summarised for participants in the intervention group, including the number of sessions attended, and the duration and location (e.g. participant's home) of the sessions. A complier-average causal effect (CACE) analysis for the primary outcome (CO-verified smoking status at 12 months post randomisation) was conducted to obtain an unbiased estimate of the intervention effectiveness in the presence of full compliance. A two-stage least squares instrumental variable approach, with randomised group as the instrumental variable, was used. We defined compliance with the intervention for those allocated to BSC as the number of sessions attended.

Health economic analysis

The health economic analysis for the SCIMITAR+ trial assessed the cost-effectiveness of supplementing usual care with BSC, compared with usual care alone, within the trial. Although the impact of smoking cessation is likely to be observed in the long term, the within-trial evaluation could provide a relatively realistic estimate of intervention costs, necessary parameter inputs for model projection and potentially some insights into the difference in change, in the case of lacking in capacity of a long-term follow-up. The economic evaluation took the form of an incremental cost-effectiveness analysis from a NHS and Personal Social Services perspective, as recommended by NICE guidance.[57]

The costs of BSC and usual care were identified, measured and valued. Costs and outcomes were collected at participant level and based on the trial population. Health outcomes were measured using quality-adjusted life-years (QALYs), as per NICE guidance.[57] QALYs were constructed from the EQ-5D-5L,[54] which was collected at baseline and during follow-up.

Costs

The total costs encompassed intervention costs and health-care and social services use costs. A wider range of societal costs were collected but analysed separately.

Intervention costs

The intervention costs were identified by two stages corresponding to the timeline of the trial, which were the pre-intervention stage and the intervention stage.

Training and supervision

The pre-intervention stage is the training period for MH-SCPs. To deliver the intervention, four members of the SCIMITAR+ team attended a 2-day training session delivered by the NCSCT, and then acted as trainers for all MH-SCPs. The MH-SCPs received a 2-day training session, in line with that provided by the NCSCT, with specific adaptations for people with SMI. This was delivered by the four trained members of the SCIMITAR+ team, two at a time. The cost of the initial training from the NCSCT was estimated using the invoice. The opportunity cost of time spent on the initial training by our research team and the cost of delivering the training for MH-SCPs were costed at NHS band 6 instead of researchers' wages to reflect the costs to the NHS. The opportunity costs of time spent on these training sessions by the MH-SCPs were also estimated for 2 working days for NHS band 4 staff. A full day was considered 7.5 working hours. The staff cost included salary oncosts, overheads and capital.

Each practitioner was given a 43-page SCIMITAR+ Standard Treatment Protocol and a 51-page NCSCT Standard Treatment Programme. These were printed in-house at £0.02 per page.

After training, all MH-SCPs received regular supervision, which was delivered by the trainer of the additional training. Supervision time was recorded by the supervisor and allocated to each participant in the BSC group.

Intervention delivery

The intervention stage is the period during which the intervention/control treatment was delivered. Costs were estimated for both the BSC group and the usual-care group accordingly.

For the intervention group, costs included costs of BSC and usual GP care. BSC was costed based on the working time and caseload of MH-SCPs, including travel time to the prearranged location for the appointment. These sessions were recorded in treatment logs by MH-SCPs. Each practitioner was equipped with a CO monitor, which cost £120 and had a life span of 5 years. The depreciation value of the CO monitor in the first year was calculated using double-declining balance to estimate the cost of the CO monitor during the trial period.

Usual GP care included participants' contact with usual-care practitioners [e.g. GPs, pharmacists, stop smoking services (SSSs), etc.] for smoking cessation and prescriptions of pharmacotherapies for smoking cessation. Usual-care contact was collected through self-reported questionnaires, and prescriptions were extracted from their medical records. The overall cost of contact with practitioners was then calculated by multiplying the number of contact sessions by their national average unit costs (see *Table 2*). The prescriptions were matched by their generic names, dosage and form to the *Prescription Cost Analysis – England*,[58] and their costs were calculated by multiplying the weighted average net ingredient cost (NIC) per unit by the recorded quantities used within the trial period. In the case of missing values on dosage or form, a weighted average matching available information was used for estimation. Some medications were recorded by prescription instead of quantity; these were consequently estimated based on the weighted average NIC per prescription item.

Health-care and social services costs

Health-care and social service resources utilised by participants outside the trial were measured by an adapted Health Economic/Service Utilisation Questionnaire. These included mainly secondary care and community-based services.

This questionnaire was part of the questionnaire for baseline, 6- and 12-month follow-up and collected the quantity of resources utilised by participants, covering the usage in the 6 months before each time point. After the physical unit of resources was identified by the questionnaire, their quantities were multiplied by their national average unit costs extracted from *Unit Costs of Health and Social Care 2017*,[59] *NHS Reference Costs 2016–17*[60] or inflated from *Unit Costs of Health and Social Care 2015*[61] if recent data were unavailable (*Table 2*).

TABLE 2 Unit costs of smoking cessation services, health care and social services, and market prices of selected NRT products (2016/17 values)

Service items/products	Unit cost (2016/17)	Sources
Usual GP care for smoking cessation		
Cessation consultation with GP	£40/session	61
Cessation consultation with pharmacist	£7/session	61
SSS	£19/session	61,62
SSS helpline	£7/call	61,63
Health care and social services		
A&E department	£175/attendance	60
Hospital admission	£604/night; £1938/FCE	60
Hospital outpatient appointment	£138/attendance	60
Day case/procedure	£736/episode	60
Emergency ambulance	£99/use	60
GP home visit	£56/9.22-minute consultation plus 12 minutes of travel	59,61
GP surgery	£31/9.22-minute consultation	59
GP telephone	£15/call	59
Practice nurse	£9/15.5-minute consultation	59,61
District nurse	£36/contact	60
Community psychiatric nurse	£61/contact	60
Health visitor	£64/contact	60
Clinical psychologist	£40/45-minute session	59
NHS counsellor	£39/55-minute session	59
NHS dentist	£138/contact	60
Podiatrist	£44/contact	60
Occupational therapist	£77/contact	60
Physiotherapist	£53/contact	60
CBT	£100/session	59
MBCT	£15/session	59
Crisis team	£192/team contact	59
CMHT	£197/contact	59
Day care service	£92/patient day	60
Social worker	£30/30-minute visit	59
Family support worker	£27/30-minute visit	59
Drug/alcohol support worker	£118/contact	60
NRT products		
Nasal spray	£23/bottle	Estimated market price
Microtab	£16/pack	Estimated market price
Patch	£13/7-piece pack	Estimated market price
Gum	£13/96-piece pack	Estimated market price

TABLE 2 Unit costs of smoking cessation services, health care and social services, and market prices of selected NRT products (2016/17 values) (*continued*)

Service items/products	Unit cost (2016/17)	Sources
Lozenge	£13/96-piece pack	Estimated market price
Mouth spray	£19/bottle	Estimated market price
Inhalator	£21/20 cartridges	Estimated market price

A&E, accident and emergency; CBT, cognitive–behavioural therapy; FCE, finished consultant episode; MBCT, mindfulness-based cognitive therapy.

All costs were presented in 2016/17 Great British pounds. Discounting was not required in this study, as the evaluation was conducted within a 12-month time frame.

The use of antipsychotics was extracted from participants' medical notes. As with prescription of pharmacotherapies, they were matched by their generic names, dosage and form to the *Prescription Cost Analysis – England*.[58]

The costs of health-care and social services use in the 6 months before baseline were used as one of the baseline covariates for costs.

Wider societal costs

Costs incurred outside the NHS perspective were collected in the questionnaire by self-report and added to the base-case analysis to present a separate analysis from a societal perspective. These included out-of-pocket purchases of NRT products and e-cigarettes, and travel costs for the participants to attend the smoking cessation appointments. As the market pricing of NRT products is highly complicated because of deals, bundles or packaging, a set of estimated market prices was summarised, based on prices from big supermarkets and pharmacies, such as Sainsbury's (www.sainsburys.co.uk), Morrison's (www.groceries.morrisons.com), Boots (www.boots.com) and Lloyds Pharmacy (www.lloydspharmacy.com). It was further simplified by using only one package size for patch, gum, lozenge and inhalator, as they were available in various package sizes (see *Table 2*).

Health-related quality of life

The EQ-5D-5L was used to measure health-related quality of life in both the BSC group and the usual-care group. The instrument was used at baseline and at 6- and 12-month follow-up. An index score was calculated using the mapping function developed by van Hout *et al.*[64] The index score ranges from –0.594 to 1, with higher scores indicating better health-related quality of life. QALYs were then derived from EQ-5D-5L index score at three time points by calculating the area under the curve.[65] The accompanied visual analogue scale (VAS) was also reported, ranging from 0 to 100, with higher numbers indicating better health-related quality of life.

After the original plan was finalised, a EQ-5D-5L value set for England was released by the Office of Health Economics.[66] Following that development, NICE released a position statement in August 2017 stating that, for the data gathered using EQ-5D-5L, the mapping function approach is still the preferred method for reference case analysis and the five-level version valuation set is not recommended for use at this time.[67] The updated statement in November 2018 retained this position.[68] Therefore, we maintained the original plan and disregarded the available five-level version valuation set for England.

Missing data

For the baseline covariates, little to no missing data were expected. These missing values were imputed by the mean of the parameter in the whole sample because these were information collected before the intervention began and the randomisation functioned to balance the parameters between two arms.

Methods for dealing with missing data on the primary outcome (CO-verified smoking cessation) followed the approach used in the previous statistical analysis. The missing data on costs and quality-of-life elements at follow-ups were imputed using multiple imputation. A chained equation model was developed, and predictive mean matching was used as the main imputation method for continuous variables, using 10 nearest neighbours to the prediction as a set from which to draw. All missing data were imputed separately by trial group. The imputation was performed on the aggregated level estimate, that is, EQ-5D-5L utility value converted from data provided by participants. As a rule of thumb, the number of imputations was set to the highest percentage of all missing values.[69]

Analysis

Primary analysis

The primary health economic analysis was conducted on an intention-to-treat basis, including all randomised participants in the groups to which they were randomised. The CO-verified smoking cessation rate at 12 months was calculated for both groups in the statistical analysis. Intervention cost per CO-verified quitter at 12 months and incremental intervention cost per additional quitter was reported to provide a comparison with the SSS statistics.

Intervention costs and wider health-care and social services costs were used to calculate total cost per participant. The EQ-5D-5L was used to calculate QALYs per participant. An incremental cost-effectiveness ratio (ICER) was calculated and compared with the willingness-to-pay (WTP) threshold recommended by NICE (£20,000–30,000).[57]

Sensitivity analysis

Uncertainty around the ICER was quantified using a non-parametric bootstrap technique whereby 5000 samples were generated by resampling. Confidence intervals around the ICER were estimated and plotted on a cost-effectiveness plane to illustrate the overall uncertainty of both costs and QALYs. Cost-effectiveness acceptability curves were constructed from the bootstrapped samples by converting ICER to net monetary benefit.[70]

A complete-case analysis was also carried out to assess the uncertainty due to missing data.

Secondary analysis

Several exploratory analyses were also conducted in addition to the reference case analysis recommended by the NICE guidance.[57]

Wider societal costs were summarised and presented as a separate analysis to provide an estimate of costs outside the NHS. Using the information on the number of cigarettes smoked per day, an estimate of money spent on cigarettes was calculated to demonstrate the monetary impact on the financial condition of the participants. Previous evidence suggested that smokers with SMI might require a lower dosage of antipsychotics to achieve the same effect if they stop smoking.[2] Therefore, a comparison of the costs of antipsychotics between two halves of the trial period by participants' smoking status among this sample was conducted.

Adverse events

A trial-specific procedure for detecting and reporting adverse events was implemented.

An adverse event was defined as any unexpected effect or untoward clinical event affecting the participant. Standard criteria for serious adverse events (SAEs) were used.

The participant's MH-SCP, GP or mental health specialist was requested to inform the research team of any SAEs or non-SAEs. In addition, when participants indicated hospital attendance or use of emergency services either during a visit or in questionnaire responses, this was followed up by the research team as required.

All adverse events and SAEs were independently reviewed by a clinician and were routinely reported to the Data Monitoring and Ethics Committee and the Independent Trial Steering Committee (TSC).

Adverse event data are summarised descriptively by treatment group.

Suicide and self-harm risk protocol

A protocol for identifying and reporting potential suicide risk was implemented (see *Appendix 3* for protocol). Item 9 on the PHQ-9, which asks if the participant has had 'thoughts that you would be better off dead or of hurting yourself in some way', was used to identify any suicide risk.

If the participant indicated a response of 3 (i.e. nearly every day) for this item at baseline or at any of the follow-up interviews, then the suicide protocol was implemented and the participant was asked if they had talked to their GP, psychiatrist or care co-ordinator/community psychiatric nurse (CPN) about these feelings. If they had not, consent was sought to contact the participant's GP to inform them of the situation. If the participant refused, the relevant designated psychiatrist/health professional was contacted. If the health professional agreed, the participant's GP or psychiatrist was contacted immediately. A Suicidal Intent Form was completed and, when applicable, a Suicidal Intent Form: Psychiatrist/Health Professional was also completed. These forms were stored with the participant's trial records.

Patient and public involvement in research

The SCIMITAR+ trial benefited from the involvement of users of mental health services and carers of people with SMI throughout the research period. Our TSC included representation from carers and service users. Our protocol and study materials were scrutinised and supported by users and carers in the north-west of England.

We invited service users from a patient and public involvement (PPI) group based in the north-west to be involved in the study. One of the collaborators works at the University of Manchester, the institution that organised the PPI group. From this group, service users provided input on the recruitment materials. Service users from this group were also invited to sit on the TSC; we had two service users sit on the TSC and provide input into the running of the trial. We also had the benefit of a carer who sat on the TSC in the pilot trial and continued to sit on the TSC in the main trial.

A service user and carer were invited to attend one of our yearly SCIMITAR+ meetings, which we held for all the organisations taking part in the study. They gave a presentation on smoking and giving up smoking and provided useful input into the study. They continue to remain involved and provide advice on our work. We are seeking advice from service users regarding the dissemination of the SCIMITAR+ trial and have recently formed a PPI group at the University of York for service users with SMI. We will be asking this group to provide input into our dissemination plan.

Chapter 3 Changes to the protocol

The current version of the protocol is version 2.5.

Recruitment from service user groups

After the trial had been recruiting for 3 months, recruitment from service user groups was added as an additional recruitment method. This involved providing service user groups with information about the SCIMITAR+ trial, along with copies of the flyer. Interested service users could then contact the mental health professional named on the flyer or their care co-ordinator, or, if the service user preferred, the staff member at the service user group could contact the service users' care co-ordinator on their behalf.

This recruitment method was added to broaden the range of recruitment methods and therefore broaden the range of participants invited to take part in the SCIMITAR+ trial. This method also had the potential to offer service users who may not routinely be attending a clinic, and therefore not approached by a clinician, the opportunity to take part in the study.

Recruitment from the Lifestyle Health and Wellbeing Survey

Using the Lifestyle Health and Wellbeing Survey to recruit was added as a recruitment option after the trial had been recruiting for 8 months. The survey is a questionnaire-based prospective study involving adults aged $\geq$ 18 years with SMI. Participants in the survey complete a series of questions about their health and well-being, including questions about their smoking. Participants in the survey who consented to being contacted by the research team and who smoked and were potentially interested in cutting down on or quitting smoking were invited to take part in the SCIMITAR+ trial.

The use of the Lifestyle Health and Wellbeing Survey was included to broaden the range of recruitment options and to offer people who may not have been invited by their mental health team or GP to take part in the SCIMITAR+ trial the opportunity to do so. During the course of the SCIMITAR+ trial, we noticed that some clinicians were gatekeeping: instead of checking whether or not a person wanted to do something about their smoking, they were stating that the person did not want to stop smoking. In the survey, each person was asked whether or not they wanted to do something about their smoking, thus removing the possibility of an incorrect assumption being made.

Chapter 4 Results

Recruitment

Recruitment started in October 2015 and ended in December 2016. Over the course of the trial, 40 GP surgeries mailed out recruitment packs, and 21 mental health trusts were enlisted to recruit participants.

A total of 526 participants were recruited to the trial. The target and actual rates of recruitment are shown in *Figure 1*, and monthly recruitment figures are shown in *Figure 2*. Recruitment took place at 21 mental health trusts and 16 GP surgery sites (one GP site was a standalone site and the other GP sites were acting as participant identification centres for the mental health trusts), although eligible and randomised participants were primarily identified from mental health trusts. *Table 3* shows the recruitment broken down by method. Mental health trusts recruited between four and 52 participants per trust, and GP surgeries recruited between one and five participants. Participant flow through the trial is shown in CONSORT flow diagrams in *Figures 3–5*. Of the 526 participants, 265 were randomised to the BSC group and 261 were randomised to the usual-care group.

Primary care

A total of 1162 participants were identified as potentially eligible from GP practice lists and were sent a recruitment pack, of which 48 (4.1%) returned a 'consent to contact' form. Twenty-six of these were ineligible and the remaining 22 were randomised, 11 to each trial arm. The randomisation rate for the GP mailout was 1.9%.

Secondary care

The number of direct referrals received was 1558. Two-thirds of these were ineligible, non-consenting and/or could not be contacted ($n = 1054$, 67.7%) and the remaining 504 were randomised, 254 to the BSC group and 250 to the usual-care group. The randomisation rate for direct referrals was 32.3%.

Taking part in another study was not one of the exclusion criteria for the SCIMITAR+ trial; however, some people were taking part in a study that precluded participants from taking part in other research studies.

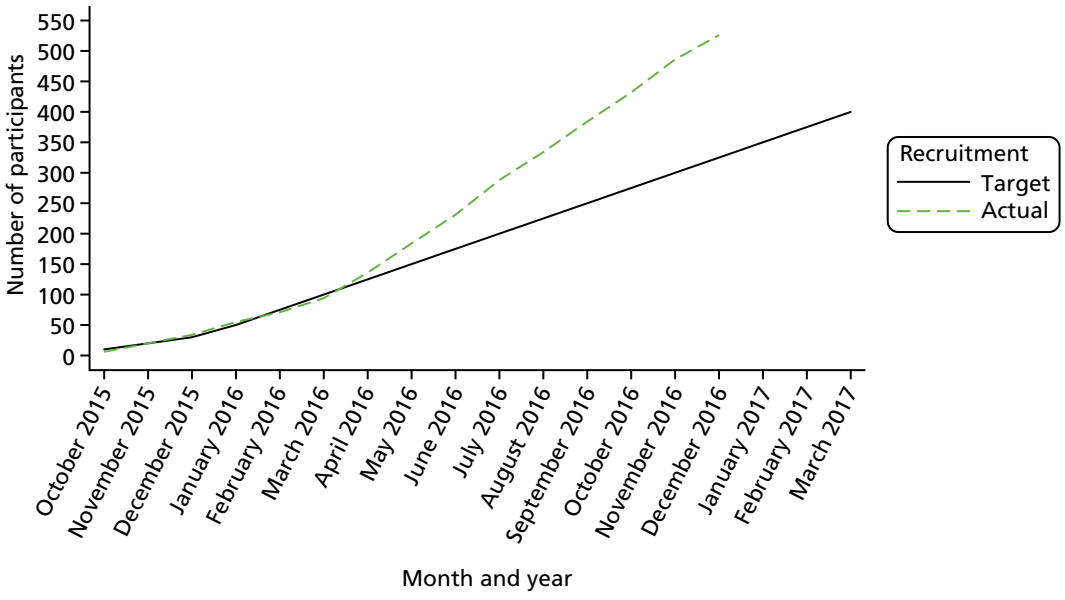

FIGURE 1 The SCIMITAR+ target and actual recruitment rates.

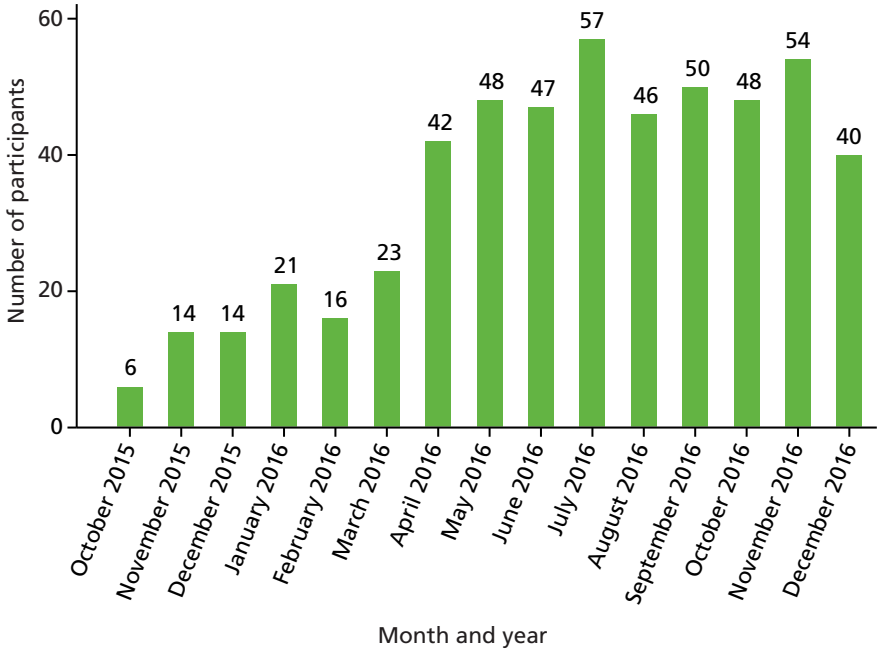

FIGURE 2 Monthly recruitment into the SCIMITAR+ trial.

TABLE 3 Recruitment by method

Recruitment method	Number recruited ($N = 526$), *n* (%)
CMHT direct referral	377 (72)
Psychiatrist direct referral	40 (8)
CMHT database screen	37 (7)
CMHT/psychiatrist unknown	28 (5)
GP database screen	22 (4)
Recruitment from Lifestyle Health and Wellbeing Survey	13 (2)
GP direct referral	1 (0.2)
GP unknown	1 (0.2)
Service user group	1 (0.2)
Unknown	6 (1)

Baseline data

The baseline characteristics of participants are summarised in the following tables, and the treatment groups appear well balanced across baseline data. *Table 4* summarises the sociodemographic and employment data for the participants. Overall, 58.7% of the participants were male, 41.1% were female and one participant identified as transgender (0.2%). The mean age of participants was 46 years, with a range from 19 to 72 years. The vast majority of participants were white (89.7%). Over two-thirds of the participants were unemployed but not seeking work owing to ill health (67.7%).

Table 5 presents data on the general health of the participants at baseline. Most participants reported at least moderate health in the last year (65.4%), despite most participants reporting that they experienced at least one of the listed medical conditions (85.6%). The majority of participants (83.5%) felt that smoking had negatively affected their health, and 70.9% reported that they had been advised to stop smoking by their GP. The mean BMI of participants was 29.9 kg/m^2 (range 16.6–59.8 kg/m^2), which falls in the overweight range.

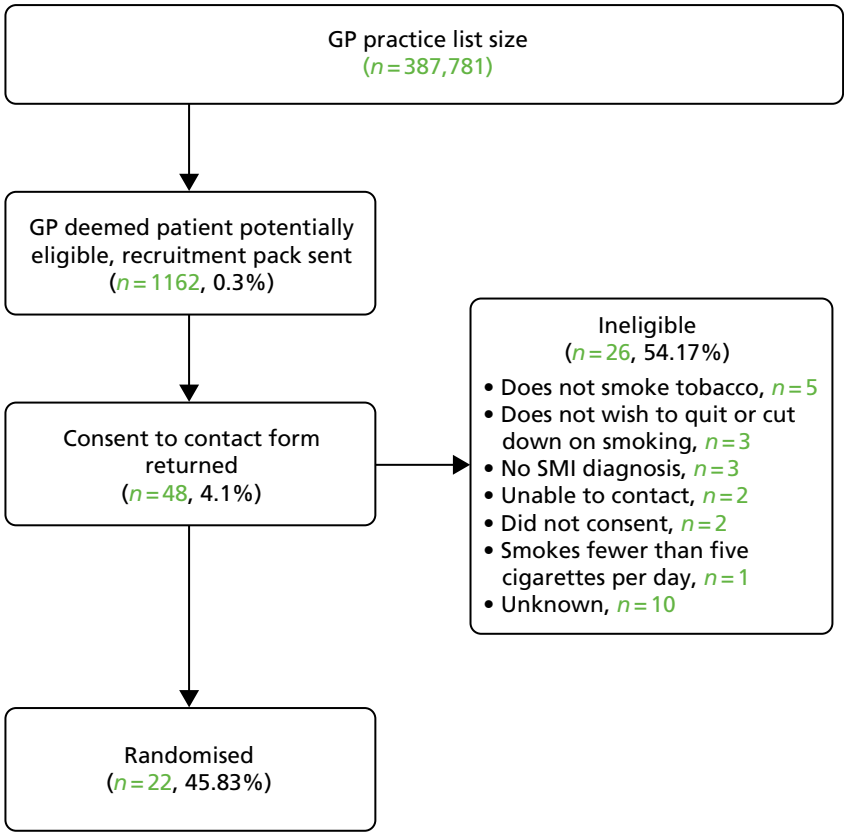

FIGURE 3 Primary care CONSORT flow diagram up to randomisation.

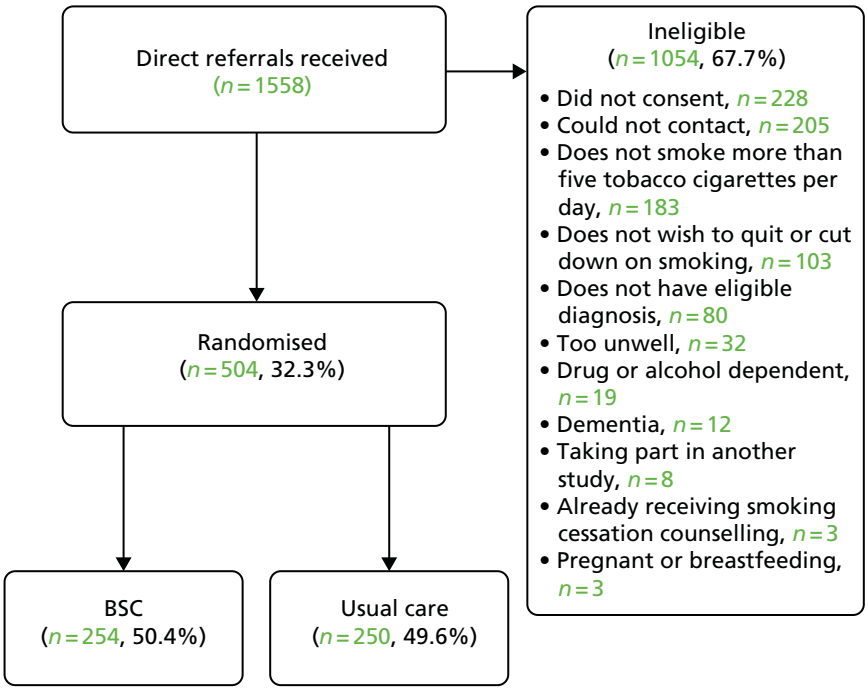

FIGURE 4 Secondary care CONSORT flow diagram up to randomisation.

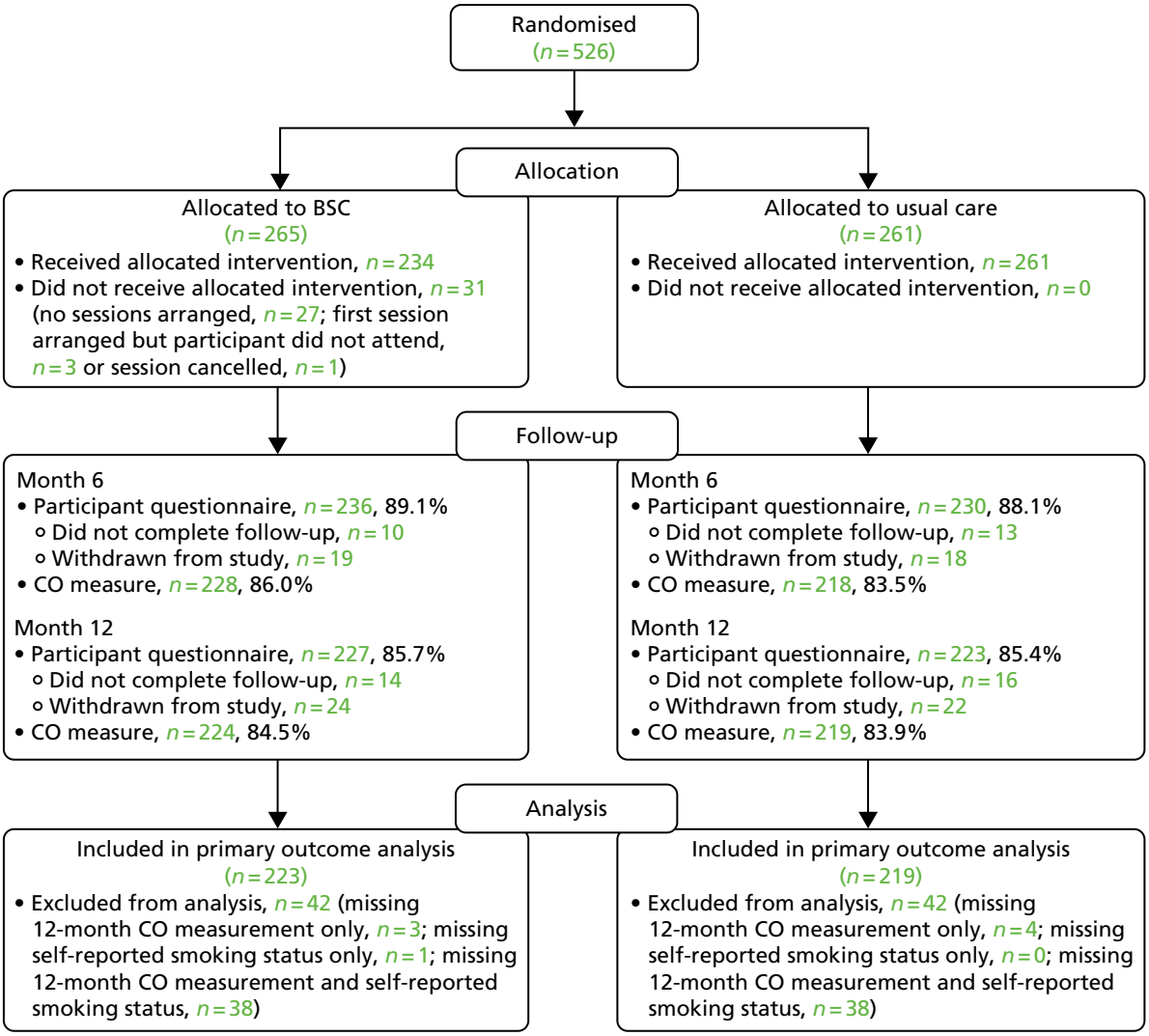

FIGURE 5 The CONSORT flow diagram showing participant flow through the trial, from randomisation.

TABLE 4 Baseline participant characteristics, sociodemographic data and employment status

Characteristic	BSC (*N* = 265)	Usual care (*N* = 261)	Overall (*N* = 526)
Sex/gender*, n *(%)			
Male	159 (60.0)	150 (57.5)	309 (58.7)
Female	105 (39.6)	111 (42.5)	216 (41.1)
Transgender	1 (0.4)	0 (0.0)	1 (0.2)
Age (years)			
Mean (SD)	46.5 (12.5)	45.5 (11.7)	46.0 (12.1)
Median (min., max.)	47 (19, 72)	46 (19, 71)	47 (19, 72)
Missing, *n* (%)	0 (0.0)	0 (0.0)	0 (0.0)
Ethnicity*, n *(%)			
White	241 (90.9)	231 (88.5)	472 (89.7)
Mixed	9 (3.4)	10 (3.8)	19 (3.6)
Asian	5 (1.9)	11 (4.2)	16 (3.0)

TABLE 4 Baseline participant characteristics, sociodemographic data and employment status (*continued*)

Characteristic	BSC (*N* = 265)	Usual care (*N* = 261)	Overall (*N* = 526)
Black	9 (3.4)	7 (2.7)	16 (3.0)
Chinese	1 (0.4)	1 (0.4)	2 (0.4)
Missing	0 (0.0)	1 (0.4)	1 (0.2)
Highest educational qualification,* n *(%)			
None	42 (15.8)	41 (15.7)	83 (15.8)
GCSE/O level	74 (27.9)	91 (34.9)	165 (31.4)
GCE A/AS level or Scottish Higher	20 (7.5)	23 (8.8)	43 (8.2)
NVQ/SVQ levels 1–3	39 (14.7)	21 (8.0)	60 (11.4)
GNVQ (Advanced)	2 (0.8)	7 (2.7)	9 (1.7)
BTEC certificate	4 (1.5)	2 (0.8)	6 (1.1)
BTEC diploma	7 (2.6)	11 (4.2)	18 (3.4)
National Certificate or Diploma	7 (2.6)	5 (1.9)	12 (2.3)
Qualified teacher status	0 (0.0)	1 (0.4)	1 (0.2)
Higher education diploma	5 (1.9)	7 (2.7)	12 (2.3)
Degree (first degree/ordinary degree)	24 (9.1)	13 (5.0)	37 (7.0)
Postgraduate certificate	2 (0.8)	2 (0.8)	4 (0.8)
Postgraduate diploma	2 (0.8)	1 (0.4)	3 (0.6)
Master's degree	4 (1.5)	6 (2.3)	10 (1.9)
PhD	1 (0.4)	0 (0.0)	1 (0.2)
Other	30 (11.3)	25 (9.6)	55 (10.5)
Missing	2 (0.8)	5 (1.9)	7 (1.3)
Employment,* n *(%)			
Employed full time	3 (1.1)	16 (6.1)	19 (3.6)
Employed part time	9 (3.4)	11 (4.2)	20 (3.8)
Self-employed	2 (0.8)	2 (0.8)	4 (0.8)
Retired	19 (7.2)	16 (6.1)	35 (6.7)
Looking after family or home	4 (1.5)	3 (1.1)	7 (1.3)
Student	5 (1.9)	5 (1.9)	10 (1.9)
Voluntary worker	11 (4.2)	18 (6.9)	29 (5.5)
Not employed but seeking work	16 (6.0)	15 (5.7)	31 (5.9)
Not employed but not seeking work because of ill health	185 (69.8)	171 (65.5)	356 (67.7)
Not employed but not seeking work for some other reason	8 (3.0)	4 (1.5)	12 (2.3)
Other	3 (1.1)	0 (0.0)	3 (0.6)
Marital status,* n *(%)			
Single	177 (66.8)	171 (65.5)	348 (66.2)
Married	32 (12.1)	26 (10.0)	58 (11.0)
Living with a partner/co-habiting	13 (4.9)	16 (6.1)	29 (5.5)
Divorced/separated	33 (12.5)	46 (17.6)	79 (15.0)
Widowed	10 (3.8)	2 (0.8)	12 (2.3)

continued

TABLE 4 Baseline participant characteristics, sociodemographic data and employment status (*continued*)

Characteristic	BSC (*N* = 265)	Usual care (*N* = 261)	Overall (*N* = 526)
Accommodation,* n *(%)			
Detached house	10 (3.8)	18 (6.9)	28 (5.3)
Semidetached house	40 (15.1)	48 (18.4)	88 (16.7)
Terraced house	45 (17.0)	32 (12.3)	77 (14.6)
Flat	123 (46.4)	113 (43.3)	236 (44.9)
Bedsit/studio	6 (2.3)	11 (4.2)	17 (3.2)
Communal establishment	36 (13.6)	35 (13.4)	71 (13.5)
Caravan/other mobile shelter	1 (0.4)	0 (0.0)	1 (0.2)
No fixed abode	2 (0.8)	2 (0.8)	4 (0.8)
Missing	2 (0.8)	2 (0.8)	4 (0.8)

A/AS level, Advanced/Advanced Subsidiary level; BTEC, Business and Technology Education Council; GCE, General Certificate of Education; GCSE, General Certificate of Secondary Education; GNVQ, General National Vocational Qualification; max., maximum; min., minimum; NVQ, National Vocational Qualification; O level, Ordinary level; PhD, Doctor of Philosophy; SVQ, Scottish Vocational Qualification.

TABLE 5 Baseline participant general health data

Characteristic	BSC (*N* = 265)	Usual care (*N* = 261)	Overall (*N* = 526)
Health over the past year,* n *(%)			
Excellent	14 (5.3)	1 (0.4)	15 (2.9)
Good	50 (18.9)	62 (23.8)	112 (21.3)
Moderate	101 (38.1)	116 (44.4)	217 (41.3)
Poor	77 (29.1)	62 (23.8)	139 (26.4)
Very poor	23 (8.7)	18 (6.9)	41 (7.8)
Missing	0 (0.0)	2 (0.8)	2 (0.4)
Feel smoking has negatively affected health,* n *(%)			
Yes	220 (83.0)	219 (83.9)	439 (83.5)
No	45 (17.0)	42 (16.1)	87 (16.5)
GP or doctor gave advice on quitting smoking,* n *(%)			
Yes	192 (72.5)	181 (69.3)	373 (70.9)
No	73 (27.5)	80 (30.7)	153 (29.1)
Health problems,* n *(%)			
Asthma	89 (33.6)	82 (31.4)	171 (32.5)
Chronic bronchitis	29 (10.9)	34 (13.0)	63 (12.0)
Other chest trouble	83 (31.3)	106 (40.6)	189 (35.9)
Diabetes	39 (14.7)	38 (14.6)	77 (14.6)
Stomach/digestive disorder	67 (25.3)	87 (33.3)	154 (29.3)
Haemorrhoids (piles)	44 (16.6)	48 (18.4)	92 (17.5)
Liver trouble	19 (7.2)	19 (7.3)	38 (7.2)
Rheumatic disorder or arthritis	43 (16.2)	56 (21.5)	99 (18.8)
Lung cancer	0 (0.0)	1 (0.4)	1 (0.2)

TABLE 5 Baseline participant general health data (*continued*)

Characteristic	BSC (*N* = 265)	Usual care (*N* = 261)	Overall (*N* = 526)
Other cancer	9 (3.4)	9 (3.4)	18 (3.4)
Varicose veins	26 (9.8)	25 (9.6)	51 (9.7)
Stroke	12 (4.5)	11 (4.2)	23 (4.4)
Migraine	79 (29.8)	71 (27.2)	150 (28.5)
Back trouble	116 (43.8)	122 (46.7)	238 (45.2)
Epilepsy	17 (6.4)	11 (4.2)	28 (5.3)
ME or chronic fatigue	18 (6.8)	26 (10.0)	44 (8.4)
High blood pressure	56 (21.1)	62 (23.8)	118 (22.4)
Healthy life,* n *(%)			
A very healthy life	17 (6.4)	11 (4.2)	28 (5.3)
A fairly healthy life	118 (44.5)	114 (43.7)	232 (44.1)
A not very healthy life	94 (35.5)	101 (38.7)	195 (37.1)
An unhealthy life	36 (13.6)	32 (12.3)	68 (12.9)
Missing	0 (0.0)	3 (1.1)	3 (0.6)
BMI (kg/m²)			
Mean (SD)	30.2 (7.1)	29.7 (6.3)	29.9 (6.7)
Median (min., max.)	29.0 (16.6, 59.8)	29.4 (16.9, 48.4)	29.3 (16.6, 59.8)
Missing, *n* (%)	2 (0.8)	3 (1.1)	5 (1.0)
Eat five portions of fruit and vegetables a day,* n *(%)			
Yes	113 (42.6)	106 (40.6)	219 (41.6)
No	152 (57.4)	152 (58.2)	304 (57.8)
Missing	0 (0.0)	3 (1.1)	3 (0.6)
Exercise for 20 minutes or more,* n *(%)			
Daily	92 (34.7)	89 (34.1)	181 (34.4)
Weekly	72 (27.2)	68 (26.1)	140 (26.6)
Monthly	9 (3.4)	7 (2.7)	16 (3.0)
Seldom	33 (12.5)	43 (16.5)	76 (14.4)
Never	59 (22.3)	51 (19.5)	110 (20.9)
Missing	0 (0.0)	3 (1.1)	3 (0.6)
Drink alcohol,* n *(%)			
Yes	141 (53.2)	140 (53.6)	281 (53.4)
No	122 (46.0)	121 (46.4)	243 (46.2)
Missing	2 (0.8)	0 (0.0)	2 (0.4)
If yes, units in last week	n = *141*	n = *140*	n = *281*
Mean (SD)	10.1 (15.8)	8.8 (16.0)	9.5 (15.9)
Median (min., max.)	4 (0, 84)	4 (0, 140)	4 (0, 140)
Missing, *n* (%)	0 (0.0)	0 (0.0)	0 (0.0)

ME, myalgic encephalomyelitis; max., maximum; min., minimum.

Table 6 summarises baseline mental health status. The most common severe mental health problems were schizophrenia or other psychotic illness (*n* = 342, 65.0%), bipolar disorder (*n* = 115, 21.9%) and schizoaffective disorder (*n* = 66, 12.5%). Nearly two-thirds of the participants had a care programme approach (CPA) co-ordinator (64.4%) and/or a CPN (64.6%), and 83.3% were under the care of a CMHT. On average, participants were aged 26 years when they were first diagnosed with their mental health problem and had required psychiatric treatment in hospital an average of 2.8 times (range 0–100 times) in the last 10 years. Most (64.3%) participants described their condition as 'stable', but 13.7% described their condition as 'unstable' (although each participant had been judged to be stable from the point of view of their condition by either their GP or a responsible mental health professional), and 22.0% either were unsure or did not respond to this question.

TABLE 6 Baseline participant mental health status

Characteristic	BSC (*N* = 265)	Usual care (*N* = 261)	Overall (*N* = 526)
Age at first diagnosis (years)			
Mean (SD)	26.1 (10.3)	26.4 (10.5)	26.3 (10.4)
Median (min., max.)	24 (2, 60)	25 (0, 59)	24 (2, 60)
Missing, *n* (%)	4 (1.5)	7 (2.7)	11 (2.1)
Most recent diagnosis,* n *(%)			
Bipolar disorder	59 (22.3)	56 (21.5)	115 (21.9)
Schizoaffective disorder	25 (9.4)	41 (15.7)	66 (12.5)
Schizophrenia	138 (52.1)	125 (47.9)	263 (50.0)
Other psychotic disorder	41 (15.5)	39 (14.9)	80 (15.2)
Missing	2 (0.8)	0 (0.0)	2 (0.4)
Type of professional seen by participant,* n *(%)			
CPA co-ordinator	166 (62.6)	173 (66.3)	339 (64.4)
CPN	171 (64.5)	169 (64.8)	340 (64.6)
CMHT	217 (81.9)	221 (84.7)	438 (83.3)
Time since last health check (months)			
Mean (SD)	5.4 (11.9)	4.4 (6.7)	4.9 (9.6)
Median (min., max.)	1.9 (0.1, 116.5)	2.1 (0.1, 63.0)	2.0 (0.1, 116.5)
Missing, *n* (%)	102 (38.5)	94 (36.0)	196 (37.3)
Number of times needed psychiatric treatment in hospital in last 10 years			
Mean (SD)	2.9 (6.9)	2.7 (4.7)	2.8 (5.9)
Median (min., max.)	1 (0, 100)	1 (0, 50)	1 (0, 100)
Missing, *n* (%)	4 (1.5)	6 (2.3)	10 (1.9)
Would you describe your condition as . . . ,* n *(%)			
Stable	172 (64.9)	166 (63.6)	338 (64.3)
Unstable	40 (15.1)	32 (12.3)	72 (13.7)
Unsure	53 (20.0)	62 (23.8)	115 (21.9)
Missing	0 (0.0)	1 (0.4)	1 (0.2)

Max., maximum; min., minimum.

Participants reported that they started smoking, on average, at the age of 16 years (range 5–50 years) and had been smoking for a mean of 29.9 (SD 12.9) years (*Table 7*). The most common form of tobacco used was factory-made cigarettes, reportedly used by 63.3% of participants, followed by hand-rolled cigarettes (58.7%). The mean number of cigarettes smoked per day was 24.9 (range 3–100 cigarettes) (although all participants reported smoking at least five cigarettes per day when the eligibility check was carried out, one participant stated that they smoked three cigarettes per day in the self-complete smoking questionnaire). The median number of attempts to quit ever was 3, with a range of 0–200. The median duration of longest quit attempt reported was 40 days, with a range of 0 days to 188 months. The most common self-reported previous strategies used to stop smoking were 'cold turkey' (55.3%) followed by NRTs (20.3%).

The reasons for smoking and their importance are summarised in *Table 8*. The reasons most commonly reported as very important for smoking were helping to cope with stress (61.2%) and to give them something to do (39.7%).

TABLE 7 Baseline participant smoking history

Characteristic	BSC (*N* = 265)	Usual care (*N* = 261)	Overall (*N* = 526)
Age started smoking (years)			
Mean (SD)	15.7 (5.3)	16.5 (6.0)	16.1 (5.7)
Median (min., max.)	15 (5, 47)	15 (7, 50)	15 (5, 50)
Missing, *n* (%)	0 (0.0)	1 (0.4)	1 (0.2)
Length of time smoking (years)			
Mean (SD)	30.7 (13.2)	29.0 (12.5)	29.9 (12.9)
Median (min., max.)	31.9 (0.1, 61.1)	29.3 (2.1, 56.2)	30.6 (0.1, 61.1)
Missing, *n* (%)	1 (0.4)	1 (0.4)	2 (0.4)
Type of tobacco used,* n *(%)			
Factory-made cigarettes	173 (65.3)	160 (61.3)	333 (63.3)
Hand-rolled cigarettes	150 (56.6)	159 (60.9)	309 (58.7)
Cigars	17 (6.4)	10 (3.8)	27 (5.1)
Pipe	4 (1.5)	2 (0.8)	6 (1.1)
Chewing tobacco	0 (0.0)	0 (0.0)	0 (0.0)
Water pipe/hookah/shisha pipe	3 (1.1)	2 (0.8)	5 (1.0)
Number of cigarettes per day			
Mean (SD)	24.7 (13.5)	23.2 (12.8)	24.0 (13.2)
Median (min., max.)	20 (3, 100)	20 (0, 80)	20 (0, 100)
Missing, *n* (%)	0 (0.0)	0 (0.0)	0 (0.0)
If using roll-ups or pipe, amount of tobacco used per day (g)	**n = *151***	**n = *159***	**n = *310***
Mean (SD)	12.4 (10.7)	12.8 (10.1)	12.6 (10.4)
Median (min., max.)	10 (0.25, 75)	12 (0.5, 80)	10 (0.25, 80)
Missing, *n* (%)	18 (11.9)	13 (8.2)	31 (10.0)
Number of quit attempts in the past 6 months			
Mean (SD)	1.4 (5.4)	1.5 (3.4)	1.5 (4.5)
Median (min., max.)	0 (0, 80)	0 (0, 30)	0 (0, 80)
Missing, *n* (%)	0 (0.0)	1 (0.4)	1 (0.2)

continued

TABLE 7 Baseline participant smoking history (*continued*)

Characteristic	BSC (*N* = 265)	Usual care (*N* = 261)	Overall (*N* = 526)
Total number of quit attempts			
Mean (SD)	6.6 (13.2)	8.2 (19.0)	7.4 (16.3)
Median (min., max.)	3 (0, 100)	4 (0, 200)	3 (0, 200)
Missing, *n* (%)	4 (1.5)	8 (3.1)	12 (2.3)
Length of most recent quit attempt (months)			
Mean (SD)	1.9 (9.4)	2.8 (14.5)	2.4 (12.2)
Median (min., max.)	0.1 (0.0, 105.7)	0.1 (0.0, 187.9)	0.1 (0.0, 187.9)
Missing, *n* (%)	13 (4.9)	12 (4.6)	25 (4.8)
Longest quit attempt (months)			
Mean (SD)	8.8 (22.9)	9.3 (23.8)	9.0 (23.3)
Median (min., max.)	0.9 (0.0, 152.6)	1.5 (0.0, 187.9)	1.3 (0.0, 187.9)
Missing, *n* (%)	19 (7.2)	7 (2.7)	26 (4.9)
Previous methods used to stop smoking,* n *(%)			
Cold turkey	139 (52.5)	152 (58.2)	291 (55.3)
NRT	51 (19.2)	56 (21.5)	107 (20.3)
Champix (varenicline)	18 (6.8)	34 (13.0)	52 (9.9)
Hypnosis	22 (8.3)	18 (6.9)	40 (7.6)
E-cigarettes	15 (5.7)	14 (5.4)	29 (5.5)
Acupuncture	15 (5.7)	12 (4.6)	27 (5.1)
Zyban (bupropion)	12 (4.5)	12 (4.6)	24 (4.6)
Other	2 (0.8)	9 (3.4)	11 (2.1)

Max., maximum; min., minimum.

TABLE 8 Baseline reasons for smoking and their importance

Characteristic, *n* (%)	BSC (*N* = 265)	Usual care (*N* = 261)	Overall (*N* = 526)
I enjoy it			
Very important	103 (38.9)	90 (34.5)	193 (36.7)
Quite important	106 (40.0)	96 (36.8)	202 (38.4)
Not important	55 (20.8)	74 (28.4)	129 (24.5)
Missing	1 (0.4)	1 (0.4)	2 (0.4)
It keeps my weight down			
Very important	36 (13.6)	45 (17.2)	81 (15.4)
Quite important	64 (24.2)	48 (18.4)	112 (21.3)
Not important	163 (61.5)	166 (63.6)	329 (62.5)
Missing	2 (0.8)	2 (0.8)	4 (0.8)
It helps me to socialise			
Very important	43 (16.2)	32 (12.3)	75 (14.3)
Quite important	68 (25.7)	72 (27.6)	140 (26.6)
Not important	153 (57.7)	154 (59.0)	307 (58.4)
Missing	1 (0.4)	3 (1.1)	4 (0.8)

TABLE 8 Baseline reasons for smoking and their importance (*continued*)

Characteristic, *n* (%)	BSC (*N* = 265)	Usual care (*N* = 261)	Overall (*N* = 526)
It helps my concentration			
Very important	44 (16.6)	38 (14.6)	82 (15.6)
Quite important	81 (30.6)	64 (24.5)	145 (27.6)
Not important	138 (52.1)	157 (60.2)	295 (56.1)
Missing	2 (0.8)	2 (0.8)	4 (0.8)
It gives me something to do			
Very important	106 (40.0)	103 (39.5)	209 (39.7)
Quite important	106 (40.0)	109 (41.8)	215 (40.9)
Not important	53 (20.0)	48 (18.4)	101 (19.2)
Missing	0 (0.0)	1 (0.4)	1 (0.2)
It helps me to cope with stress			
Very important	162 (61.1)	160 (61.3)	322 (61.2)
Quite important	71 (26.8)	72 (27.6)	143 (27.2)
Not important	29 (10.9)	27 (10.3)	56 (10.6)
Missing	3 (1.1)	2 (0.8)	5 (1.0)
It helps combat pain			
Very important	32 (12.1)	15 (5.7)	47 (8.9)
Quite important	37 (14.0)	31 (11.9)	68 (12.9)
Not important	194 (73.2)	211 (80.8)	405 (77.0)
Missing	2 (0.8)	4 (1.5)	6 (1.1)
I feel bad when I try to stop			
Very important	93 (35.1)	85 (32.6)	178 (33.8)
Quite important	63 (23.8)	59 (22.6)	122 (23.2)
Not important	104 (39.2)	110 (42.1)	214 (40.7)
Missing	5 (1.9)	7 (2.7)	12 (2.3)
I like being a smoker			
Very important	41 (15.5)	27 (10.3)	68 (12.9)
Quite important	60 (22.6)	59 (22.6)	119 (22.6)
Not important	162 (61.1)	172 (65.9)	334 (63.5)
Missing	2 (0.8)	3 (1.1)	5 (1.0)
It gives me confidence			
Very important	38 (14.3)	22 (8.4)	60 (11.4)
Quite important	48 (18.1)	53 (20.3)	101 (19.2)
Not important	177 (66.8)	183 (70.1)	360 (68.4)
Missing	2 (0.8)	3 (1.1)	5 (1.0)

Table 9 summarises the reasons for wanting to try to give up smoking; the reasons most commonly reported as very important were that it is bad for health (87.5%) and that it is expensive (71.9%).

Participant use of e-cigarettes is summarised in *Table 10*. Over two-thirds (70.3%) of the participants reported having ever tried an e-cigarette, of whom 77 (22.0%) had used e-cigarettes at least once per week in the

TABLE 9 Baseline reasons for trying to give up smoking

Characteristic, *n* (%)	BSC (*N* = 265)	Usual care (*N* = 261)	Overall (*N* = 526)
It is expensive			
Very important	193 (72.8)	185 (70.9)	378 (71.9)
Quite important	49 (18.5)	49 (18.8)	98 (18.6)
Not important	23 (8.7)	26 (10.0)	49 (9.3)
Missing	0 (0.0)	1 (0.4)	1 (0.2)
It is bad for my health			
Very important	236 (89.1)	224 (85.8)	460 (87.5)
Quite important	20 (7.5)	31 (11.9)	51 (9.7)
Not important	9 (3.4)	5 (1.9)	14 (2.7)
Missing	0 (0.0)	1 (0.4)	1 (0.2)
I do not like feeling dependent on cigarettes			
Very important	1. 170 (64.2)	1. 167 (64.0)	1. 337 (64.1)
Quite important	1. 59 (22.3)	1. 67 (25.7)	1. 126 (24.0)
Not important	1. 35 (13.2)	1. 25 (9.6)	1. 60 (11.4)
Missing	1. 1 (0.4)	1. 2 (0.8)	1. 3 (0.6)
It makes my clothes and breath smell			
Very important	151 (57.0)	155 (59.4)	306 (58.2)
Quite important	74 (27.9)	64 (24.5)	138 (26.2)
Not important	40 (15.1)	40 (15.3)	80 (15.2)
Missing	0 (0.0)	2 (0.8)	2 (0.4)
It is a bad example for children			
Very important	156 (58.9)	163 (62.5)	319 (60.6)
Quite important	53 (20.0)	45 (17.2)	98 (18.6)
Not important	54 (20.4)	50 (19.2)	104 (19.8)
Missing	2 (0.8)	3 (1.1)	5 (1.0)
It is unpleasant for people near me			
Very important	140 (52.8)	139 (53.3)	279 (53.0)
Quite important	80 (30.2)	80 (30.7)	160 (30.4)
Not important	45 (17.0)	40 (15.3)	85 (16.2)
Missing	0 (0.0)	2 (0.8)	2 (0.4)
It makes me less fit			
Very important	186 (70.2)	184 (70.5)	370 (70.3)
Quite important	60 (22.6)	55 (21.1)	115 (21.9)
Not important	19 (7.2)	21 (8.0)	40 (7.6)
Missing	0 (0.0)	1 (0.4)	1 (0.2)
People around me disapprove of my smoking			
Very important	107 (40.4)	101 (38.7)	208 (39.5)
Quite important	78 (29.4)	68 (26.1)	146 (27.8)
Not important	80 (30.2)	89 (34.1)	169 (32.1)
Missing	0 (0.0)	3 (1.1)	3 (0.6)

TABLE 9 Baseline reasons for trying to give up smoking (*continued*)

Characteristic, *n* (%)	BSC (*N* = 265)	Usual care (*N* = 261)	Overall (*N* = 526)
It is bad for the health of people near me			
Very important	147 (55.5)	136 (52.1)	283 (53.8)
Quite important	72 (27.2)	72 (27.6)	144 (27.4)
Not important	45 (17.0)	51 (19.5)	96 (18.3)
Missing	1 (0.4)	2 (0.8)	3 (0.6)

TABLE 10 Participant use of e-cigarettes at baseline

Characteristic, *n* (%)	BSC (*N* = 265)	Usual care (*N* = 261)	Overall (*N* = 526)
Ever tried an e-cigarette			
Yes	186 (70.2)	184 (70.5)	370 (70.3)
No	79 (29.8)	77 (29.5)	156 (29.7)
Missing	0 (0.0)	0 (0.0)	0 (0.0)
If yes:	n = *186*	n = *184*	n = *370*
Use of e-cigarette in last 30 days			
Never	128 (68.8)	124 (67.4)	252 (68.1)
Less than once per week	21 (11.3)	18 (9.8)	39 (10.5)
Less than daily but at least once per week	22 (11.8)	20 (10.9)	42 (11.4)
Every day	14 (7.5)	21 (11.4)	35 (9.5)
Missing	1 (0.5)	1 (0.5)	2 (0.5)
Length of use of e-cigarettes			
< 1 month	58 (31.2)	76 (41.3)	134 (36.2)
1–6 months	44 (23.7)	38 (20.7)	82 (22.2)
6–12 months	28 (15.1)	21 (11.4)	49 (13.2)
> 1 year	38 (20.4)	31 (16.8)	69 (18.6)
Missing	18 (9.7)	18 (9.8)	36 (9.7)
Nicotine levels in cartridges used in e-cigarette			
None (0 mg)	10 (5.4)	10 (5.4)	20 (5.4)
Low (< 8 mg)	24 (12.9)	26 (14.1)	50 (13.5)
Medium (8–16 mg)	56 (30.1)	60 (32.6)	116 (31.4)
High (> 16 mg)	51 (27.4)	44 (23.9)	95 (25.7)
Missing	45 (24.2)	44 (23.9)	89 (24.1)
Use of tobacco changed since using e-cigarettes			
Yes, I smoke less tobacco	62 (33.3)	64 (34.8)	126 (34.1)
Yes, I smoke more tobacco	11 (5.9)	5 (2.7)	16 (4.3)
No, it has not changed	97 (52.2)	101 (54.9)	198 (53.5)
Missing	16 (8.6)	14 (7.6)	30 (8.1)

continued

TABLE 10 Participant use of e-cigarettes at baseline (*continued*)

Characteristic, *n* (%)	BSC (*N* = 265)	Usual care (*N* = 261)	Overall (*N* = 526)
Reason started using e-cigarettes			
To quit smoking tobacco	92 (49.5)	97 (52.7)	189 (51.1)
To try a safer alternative to tobacco	25 (13.4)	23 (12.5)	48 (13.0)
To try something new	14 (7.5)	13 (7.1)	27 (7.3)
To smoke less tobacco	29 (15.6)	19 (10.3)	48 (13.0)
Other	14 (7.5)	20 (10.9)	34 (9.2)
Missing	12 (6.5)	12 (6.5)	24 (6.5)

past month. Of the participants who reported ever having tried an e-cigarette, over half stated that their use of tobacco had not changed since they started using e-cigarettes (53.5%), with only 34.1% saying that they now smoke less tobacco. The most commonly cited reason for using e-cigarettes was to try to quit smoking tobacco (51.1%).

Participant questionnaire return rates

Response rates to the participant questionnaires at 6 and 12 months are presented in *Table 11*. Over 95% of the forms given to participants at 6 months were returned (466/489, 95.3%; 88.6% of 526 randomised participants). The median number of days between the form being due and being returned was 6 (replacing those that were completed early with 0 days), and the majority were completed face to face (95.9%). At the primary time point of 12 months, 450 (93.8%) of the 480 forms sent out were returned (85.6% of 526 randomised participants). The median time to return was 4 days, and only eight (1.8%) were not completed face to face (six over the telephone and two on paper via post).

Primary analysis

The CO breath measurement readings are summarised by treatment group at baseline, 6 and 12 months in *Table 12*. The mean reading at baseline was 24.6 (SD 15.2) p.p.m. and was similar between the two groups. Seventy (13.3%) participants had a reading of < 10 p.p.m. at baseline. In both groups, the mean reading decreased from baseline to 6 months and then increased slightly at 12 months.

Self-reported smoking status and quit attempt data reported on the participant questionnaires at 6 and 12 months are presented in *Table 13*. At 6 months, 463 participants (88.0%) provided a valid response to the self-reported smoking status question, and 51 of these (11.0%) reported that they had not smoked even a puff in the last week [34 (14.5%) in the BSC group and 17 (7.4%) in the usual-care group]. At the primary time point of 12 months, 449 participants (85.4%) provided a valid response to the self-reported smoking status question, and 57 of these (12.7%) reported that they had not smoked even a puff in the last week [35 (15.5%) in the BSC group and 22 (9.9%) in the usual-care group). For those who said that they did still smoke, the most common hour of the day to have the first puff of a cigarette is between 08.00 and 09.00 (20% at both time points). At 12 months, of the participants with valid data for this question, 16.1% of BSC participants and 10.6% of usual-care participants reported that they had stopped smoking completely, and participants reported a median of one quit attempt in the previous 6 months, with the most recent quit attempt lasting an average of 3.5 weeks before the participant returned to smoking. Responses to the items in *Table 13* relating to smoking status and smoking in the last week did not always agree, as might be expected. For example, replying 'not a puff' in relation to the amount smoked in the last week did not always imply that participants reported that

TABLE 11 Return of participant questionnaires at 6 and 12 months

Time point	BSC (*N* = 265)	Usual care (*N* = 261)	Overall (*N* = 526)
6 months			
Sent,[a] *n* (%)	246 (92.8)	243 (93.1)	489 (93.0)
Completed,[b] *n* (%)	236 (95.9)	230 (94.7)	466 (95.3)
Days to complete, median (IQR)	7 (0–20)	5 (0–20)	6 (0–20)
Mode of completion,[c] n *(%)*			
Face to face	228 (96.6)	219 (95.2)	447 (95.9)
Telephone	4 (1.7)	10 (4.4)	14 (3.0)
Paper	4 (1.7)	1 (0.4)	5 (1.1)
12 months			
Sent,[a] *n* (%)	241 (90.0)	239 (91.6)	480 (91.3)
Completed,[b] *n* (%)	227 (94.2)	223 (93.3)	450 (93.8)
Days to complete, median (IQR)	3 (0–15)	4 (0–16)	4 (0–15)
Mode of completion,[c] n *(%)*			
Face to face	223 (98.2)	219 (98.2)	442 (98.2)
Telephone	3 (1.3)	3 (1.4)	6 (1.3)
Paper	1 (0.4)	1 (0.4)	2 (0.4)

IQR, interquartile range.
a Percentage of sent.
b Percentage of completed.
c Percentage of randomised participants.

TABLE 12 CO reading by treatment group and time point

Time point	CO measurement	BSC (*N* = 265)	Usual care (*N* = 261)	Overall (*N* = 526)
Baseline	Mean (SD)	24.9 (15.4)	24.3 (15.1)	24.6 (15.2)
	Median (min., max.)	22.0 (1.0, 95.0)	21.0 (2.0, 100.0)	21.0 (1.0, 100.0)
	Missing, *n* (%)	1 (0.4)	3 (1.1)	4 (0.8)
6 months	Mean (SD)	18.0 (14.1)	19.4 (12.9)	18.7 (13.5)
	Median (min., max.)	16.5 (0.0, 89.0)	17.5 (0.0, 71.0)	17.0 (0.0, 89.0)
	Missing, *n* (%)	37 (14.0)	43 (16.5)	80 (15.2)
12 months	Mean (SD)	18.1 (13.6)	20.2 (13.7)	19.2 (13.7)
	Median (min., max.)	16.0 (0.0, 71.0)	20.0 (0.0, 77.0)	18.0 (0.0, 77.0)
	Missing, *n* (%)	41 (15.5)	42 (16.1)	83 (15.8)

Max., maximum; min., minimum.
Note
CO measurements are in p.p.m.

they had 'stopped smoking completely', and vice versa. For instance, one participant who reported that they had not smoked a puff in the past week at 12 months in the usual-care group reported that they 'smoke cigarettes (including hand-rolled) but not every day', and this could be because they still smoke occasionally but just had not smoked in the previous week.

TABLE 13 Self-reported smoking status and quit attempts at 6 and 12 months by randomised group

Time point	Outcome	BSC (*N* = 265)	Usual care (*N* = 261)	Overall (*N* = 526)
Smoked in last week*, n *(%)				
6 months	Not even a puff	34 (12.8)	17 (6.5)	51 (9.7)
	Just a few puffs	5 (1.9)	0 (0.0)	5 (1.0)
	Between one and five cigarettes	12 (4.5)	1 (0.4)	13 (2.5)
	More than five cigarettes	183 (69.1)	211 (80.8)	394 (74.9)
	Missing	31 (11.7)	32 (12.3)	63 (12.0)
12 months	Not even a puff	35 (13.2)	22 (8.4)	57 (10.8)
	Just a few puffs	2 (0.8)	3 (1.1)	5 (1.0)
	Between one and five cigarettes	11 (4.2)	10 (3.8)	21 (4.0)
	More than five cigarettes	178 (67.2)	188 (72.0)	366 (69.6)
	Missing	39 (14.7)	38 (14.6)	77 (14.6)
Self-reported smoking status*, n *(%)				
6 months	Smoke the same amount of cigarettes (including hand-rolled) every day	77 (29.1)	106 (40.6)	183 (34.8)
	Cut down on the number of cigarettes (including hand-rolled) I smoke	100 (37.7)	96 (36.8)	196 (37.3)
	Smoke cigarettes (including hand-rolled) but not every day	19 (7.2)	5 (1.9)	24 (4.6)
	Stopped smoking completely	37 (14.0)	18 (6.9)	55 (10.5)
	Missing	32 (12.1)	36 (13.8)	68 (12.9)
At 12 months	Smoke the same amount of cigarettes (including hand-rolled) every day	91 (34.3)	101 (38.7)	192 (36.5)
	Cut down on the number of cigarettes (including hand-rolled) I smoke	86 (32.5)	83 (31.8)	169 (32.1)
	Smoke cigarettes (including hand-rolled) but not every day	11 (4.2)	10 (3.8)	21 (4.0)
	Stopped smoking completely	36 (13.6)	23 (8.8)	59 (11.2)
	Missing	41 (15.5)	44 (16.9)	85 (16.2)
Quit attempts in last 6 months				
At 6 months	Mean (SD)	2.0 (3.7)	1.6 (2.3)	1.8 (3.1)
	Median (min., max.)	1 (0, 50)	1 (0, 20)	1 (0, 50)
	Missing, *n* (%)	39 (14.7)	40 (15.3)	79 (15.0)
At 12 months	Mean (SD)	1.8 (4.0)	1.3 (1.7)	1.6 (3.1)
	Median (min., max.)	1 (0, 35)	1 (0, 12)	1 (0, 35)
	Missing, *n* (%)	49 (18.5)	44 (16.9)	93 (17.7)
Length of cessation (weeks)				
At 6 months	Mean (SD)	5.7 (37.2)	2.8 (5.6)	4.3 (26.6)
	Median (min., max.)	0.6 (0, 520)	0.4 (0, 26)	0.4 (0, 26)
	Missing, *n* (%)	67 (25.3)	65 (24.9)	132 (25.1)
At 12 months	Mean (SD)	4.0 (10.4)	3.0 (7.1)	3.5 (8.9)
	Median (min., max.)	0.3 (0, 52)	0.3 (0, 52)	0.3 (0, 52)
	Missing, *n* (%)	87 (32.8)	71 (27.2)	158 (30.0)

Max., maximum; min., minimum.

Smoking cessation at 6 and 12 months was defined as a CO measure of < 10 p.p.m. (indicating no smoking in the last 12 hours) and self-reported cessation (indicating no smoking in the last week). At 6 months, 446 participants (84.8%) provided a CO reading, 463 (88.0%) had valid data for self-reported smoking status and 443 (84.2%) had both (*Table 14*); 32 out of 226 (14.2%; 10.6% of 265 randomised participants) fulfilled the definition for smoking cessation in the BSC group and 14 out of 217 (6.5%; 5.4% of 261 randomised participants) fulfilled the definition in the usual-care group. At 12 months, 443 (84.2%) provided a CO reading, 449 (85.4%) had valid data for self-reported smoking status and 442 (84.0%) had both; 34 out of 223 (15.2%; 12.8% of 265 randomised participants) fulfilled the definition for smoking cessation in the BSC group and 22 out of 219 (10.0%; 8.4% of 261 randomised participants) fulfilled the definition in the usual-care group.

The OR for the difference between the two groups from the model adjusting for baseline number of cigarettes smoked, and site as a random effect, at 12 months was 1.6 (95% CI 0.9 to 2.8; $p = 0.12$). The OR at 6 months was 2.4 (95% CI 1.2 to 4.7; $p = 0.01$).

Sensitivity analysis

Unadjusted odds ratio

The unadjusted, marginal ORs for CO-verified smoking cessation at 6 and 12 months are 2.4 (95% CI 1.2 to 4.6; $p = 0.01$) and 1.6 (95% CI 0.9 to 2.9; $p = 0.10$), respectively.

Post hoc generalised estimating equations analysis

Using GEE to account for the repeated measures, the OR adjusting for baseline number of cigarettes smoked is 2.3 (95% CI 1.2 to 4.5; $p = 0.01$) at 6 months and 1.6 (95% CI 0.9 to 2.8; $p = 0.12$) at 12 months. When the GEE model was additionally adjusted for site, the treatment effects were estimated at an OR of 2.5 (95% CI 1.3 to 4.8; $p = 0.01$) at 6 months and 1.6 (95% CI 0.9 to 2.9; $p = 0.12$) at 12 months.

TABLE 14 Smoking status measures at 6 and 12 months

Time point	Outcome, *n* (%)	BSC (*N* = 265)	Usual care (*N* = 261)	Overall (*N* = 526)
6 months	Number with CO measurement[a]	228 (86.0)	218 (83.5)	446 (84.8)
	Number with CO < 10 p.p.m.[b]	69 (30.3)	50 (22.9)	119 (26.7)
	Number with self-report[a]	234 (88.3)	229 (87.7)	463 (88.0)
	Number self-reporting as quitter[b]	34 (14.5)	17 (7.4)	51 (11.0)
	Total number with CO and self-reported measure[a]	226 (85.3)	217 (83.1)	443 (84.2)
	Total number quit[b]	32 (14.2)	14 (6.5)	46 (10.4)
	Total number quit[a]	32 (12.1)	14 (5.4)	46 (8.7)
12 months	Number with CO measurement[a]	224 (84.5)	219 (83.9)	443 (84.2)
	Number with CO < 10 p.p.m.[b]	73 (32.6)	62 (28.3)	135 (30.5)
	Number with self-report[a]	226 (85.3)	223 (85.4)	449 (85.4)
	Number self-reporting as quitter[b]	35 (15.5)	22 (9.9)	57 (12.7)
	Total number with CO and self-reported measure[a]	223 (84.2)	219 (83.9)	442 (84.0)
	Total number quit[b]	34 (15.2)	22 (10.0)	56 (12.7)
	Total number quit[a]	34 (12.8)	22 (8.4)	56 (10.6)

a Percentage of total randomised.
b Percentage of those with non-missing data for both CO measure and self-reported smoking status.

Accounting for missing CO-verified smoking status

When imputing self-reported smoking status when CO measures were missing in separate logistic regressions at 6 and 12 months and adjusting for number of cigarettes smoked as a fixed effect and site as a random effect, the following treatment effects were obtained: 6 months, OR 2.6, 95% CI 1.3 to 5.0 ($p = 0.005$); 12 months, OR 1.7, 95% CI 0.9 to 3.0 ($p = 0.08$).

Then, assuming that anyone else with missing smoking status data is a smoker yielded the following results: 6 months, OR 2.6, 95% CI 1.4 to 5.0 ($p = 0.004$); 12 months, OR 1.7, 95% CI 0.9 to 2.9 ($p = 0.08$).

When multiple imputation was used to impute missing primary outcome data, the treatment effect at 6 months was observed to be an OR of 2.4 (95% CI 1.3 to 4.4; $p = 0.007$), and at 12 months it was observed to be an OR of 1.7 (95% CI 0.9 to 3.0; $p = 0.08$).

Secondary analysis

Self-reported smoking cessation

Among those with a valid response to the self-reported smoking status question at 6 months, 34 out of 234 (14.5%) in the BSC group and 17 out of 229 (7.4%) in the usual-care group reported that they had not smoked even a puff in the last week (*Table 15*) (adjusted OR 2.1, 95% CI 1.1 to 3.9; $p = 0.02$). At 12 months, 35 out of 226 (15.5%) in the BSC group and 22 out of 223 (9.9%) in the usual-care group reported that they had not smoked even a puff in the last week (see *Table 15*) (adjusted OR 1.7, 95% CI 0.9 to 3.0; $p = 0.08$).

Number of cigarettes smoked per day

The incidence rate ratio for number of cigarettes smoked per day at 6 months was 0.90 (95% CI 0.80 to 1.01; $p = 0.08$), marginally favouring the BSC group, and at 12 months it was 1.00 (95% CI 0.89 to 1.13; $p = 0.95$). Neither of these differences is statistically significant.

Fagerström Test for Nicotine Dependence

The FTND score is summarised by randomised group and time point in *Table 15*. Adjusted FTND means and group differences are presented in *Table 21* and displayed in *Figure 6*. The adjusted mean difference at 6 months was –0.18 (95% CI –0.53 to 0.17) and at 12 months it was –0.01 (95% CI –0.39 to 0.38), both marginally favouring the BSC group but not statistically significantly ($p = 0.32$ and 0.97, respectively).

TABLE 15 The FIND scores by treatment group and time point

Time point	FTND questionnaire	BSC ($N = 265$)	Usual care ($N = 261$)	Overall ($N = 526$)
Baseline	Mean (SD)	6.5 (2.0)	6.4 (1.9)	6.4 (2.0)
	Median (min., max.)	7.0 (1.0, 10.0)	6.0 (1.0, 10.0)	7.0 (1.0, 10.0)
	Missing, *n* (%)	7 (2.6)	7 (2.7)	14 (2.7)
Month 6	Mean (SD)	5.3 (2.1)	5.4 (2.0)	5.3 (2.1)
	Median (min., max.)	5.0 (1.0, 10.0)	6.0 (1.0, 10.0)	5.5 (1.0, 10.0)
	Missing, *n* (%)	80 (30.2)	66 (25.3)	146 (27.8)
Month 12	Mean (SD)	5.6 (2.0)	5.3 (2.3)	5.5 (2.2)
	Median (min., max.)	6.0 (1.0, 10.0)	6.0 (1.0, 10.0)	6.0 (1.0, 10.0)
	Missing, *n* (%)	96 (36.2)	75 (28.7)	171 (32.5)

Max., maximum; min., minimum.

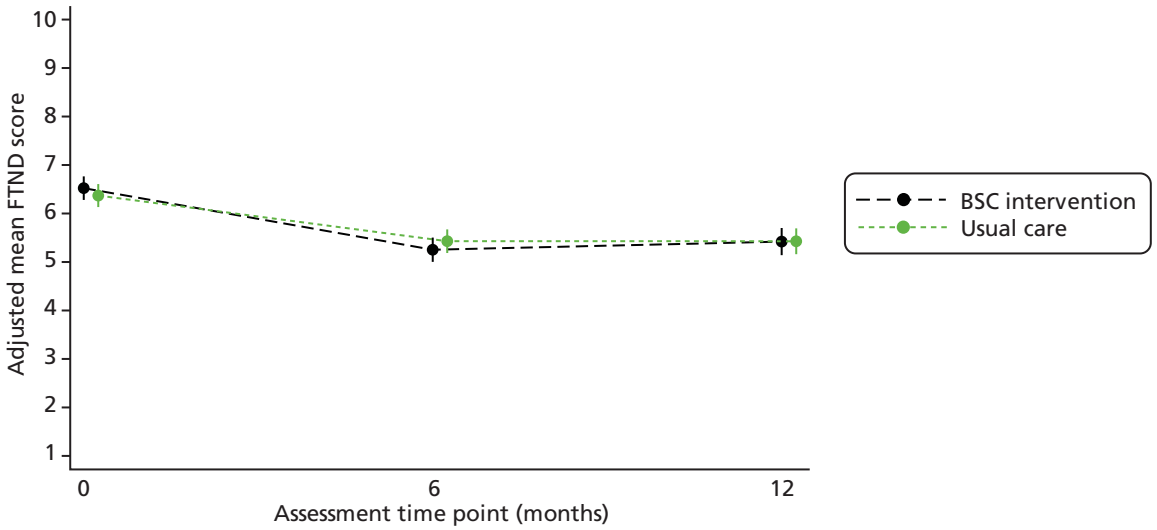

FIGURE 6 Adjusted means for the FTND by treatment group and time point.

These results were extracted from a mixed-effects model in which a participant was treated as a random effect and observations over time (6 and 12 months) were nested within participant. The effect of randomised treatment group was assessed while adjusting for time, group-by-time interaction, baseline FTND score and baseline smoking severity (fixed effects), and site as a random effect. Different covariance structures were applied to the model. An unstructured pattern that models all variances and covariances separately resulted in the lowest AIC and so was used in the final model. Diagnostics of model fit revealed that the standardised residuals were normally distributed and were uniform against fitted values; therefore, data transformation was not required.

Motivation to Quit questionnaire

The MTQ score is summarised by randomised group and time point in *Table 16*. Adjusted MTQ means and group differences are presented in *Table 21* and displayed in *Figure 7*. The adjusted mean difference at 6 months was 0.58 (95% CI –0.01 to 1.17) and at 12 months was 0.64 (95% CI 0.04 to 1.24), both marginally favouring the BSC group. The difference is almost statistically significant at the 5% level at 6 months ($p = 0.06$) and is below this level at 12 months ($p = 0.04$).

TABLE 16 The MTQ scores by treatment group and time point

Time point	MTQ	BSC ($N = 265$)	Usual care ($N = 261$)	Overall ($N = 526$)
Baseline	Mean (SD)	13.9 (2.7)	13.7 (2.6)	13.8 (2.7)
	Median (min., max.)	14.0 (6.0, 19.0)	14.0 (5.0, 19.0)	14.0 (5.0, 19.0)
	Missing, *n* (%)	5 (1.9)	2 (0.8)	7 (1.3)
Month 6	Mean (SD)	13.2 (3.4)	12.4 (3.1)	12.8 (3.3)
	Median (min., max.)	14.0 (4.0, 19.0)	12.0 (4.0, 19.0)	13.0 (4.0, 19.0)
	Missing, *n* (%)	48 (18.1)	60 (23.0)	108 (20.5)
Month 12	Mean (SD)	13.0 (3.3)	12.3 (3.4)	12.6 (3.4)
	Median (min., max.)	13.0 (5.0, 19.0)	13.0 (4.0, 19.0)	13.0 (4.0, 19.0)
	Missing, *n* (%)	65 (24.5)	61 (23.4)	126 (24.0)

Max., maximum; min., minimum.

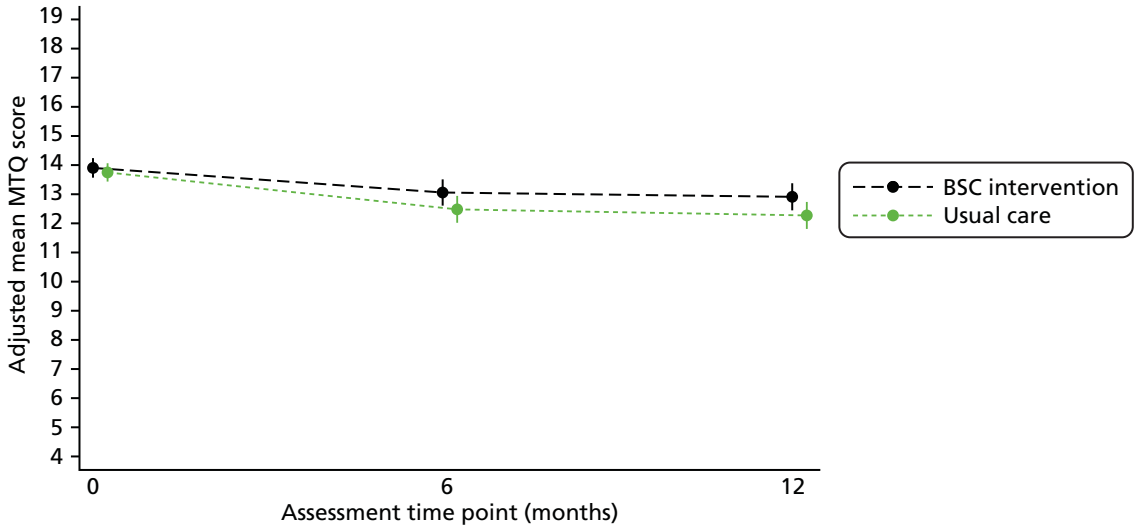

FIGURE 7 Adjusted means for the MTQ by treatment group and time point.

These results were extracted from a mixed-effects model in which participant was treated as a random effect and observations over time (6 and 12 months) were nested within participant. The effect of randomised treatment group was assessed while adjusting for time, group-by-time interaction, baseline MTQ score and baseline smoking severity (fixed effects), and site as a random effect. Different covariance structures were applied to the model. A compound symmetric (or exchangeable) pattern that assumes equal correlation of errors between each pair of time points within participants resulted in the lowest AIC and so was used in the final model. Diagnostics of model fit revealed that the standardised residuals were normally distributed, and were uniform against fitted values; therefore, data transformation was not required.

Patient Health Questionnaire-9 items

The PHQ-9 score is summarised by randomised group and time point in *Table 17*. Adjusted PHQ-9 means and group differences are presented in *Table 21* and displayed in *Figure 8*. The adjusted mean difference at 6 months was 0.20 (95% CI –0.85 to 1.24), marginally favouring usual care, and at 12 months was –0.12 (95% CI –1.18 to 0.94), marginally favouring BSC, but neither statistically significantly ($p = 0.72$ and 0.82, respectively).

TABLE 17 The PHQ-9 scores by treatment group and time point

Time point	PHQ-9	BSC ($N = 265$)	Usual care ($N = 261$)	Overall ($N = 526$)
Baseline				
Score				
	Mean (SD)	10.3 (6.7)	10.8 (6.6)	10.5 (6.6)
	Median (min., max.)	10.0 (0.0, 27.0)	10.0 (0.0, 27.0)	10.0 (0.0, 27.0)
	Missing, *n* (%)	1 (0.4)	1 (0.4)	2 (0.4)
How difficult,[a] *n* (%)		*n* = 255	*n* = 254	*n* = 509
	Not at all	65 (25.5)	64 (25.2)	129 (25.3)
	Somewhat	106 (41.6)	111 (43.7)	217 (42.6)
	Very	42 (16.5)	45 (17.7)	87 (17.1)
	Extremely	42 (16.5)	34 (13.4)	76 (14.9)

TABLE 17 The PHQ-9 scores by treatment group and time point (*continued*)

Time point	PHQ-9	BSC (*N* = 265)	Usual care (*N* = 261)	Overall (*N* = 526)
Month 6				
Score				
	Mean (SD)	9.3 (6.7)	9.4 (6.4)	9.3 (6.6)
	Median (min., max.)	8.0 (0.0, 27.0)	8.0 (0.0, 27.0)	8.0 (0.0, 27.0)
	Missing, *n* (%)	42 (15.8)	47 (18.0)	89 (16.9)
How difficult,[a] *n* (%)		*n* = 216	*n* = 210	*n* = 426
	Not at all	67 (31)	56 (26.7)	123 (28.9)
	Somewhat	89 (41.2)	98 (46.7)	187 (43.9)
	Very	33 (15.3)	36 (17.1)	69 (16.2)
	Extremely	27 (12.5)	20 (9.5)	47 (11)
Month 12				
Score				
	Mean (SD)	9.0 (6.7)	9.7 (6.7)	9.3 (6.7)
	Median (min., max.)	8.0 (0.0, 27.0)	9.0 (0.0, 27.0)	8.0 (0.0, 27.0)
	Missing, *n* (%)	52 (19.6)	50 (19.2)	102 (19.4)
How difficult,[a] *n* (%)		*n* = 206	*n* = 206	*n* = 412
	Not at all	70 (34)	42 (20.4)	112 (27.2)
	Somewhat	70 (34)	93 (45.1)	163 (39.6)
	Very	47 (22.8)	47 (22.8)	94 (22.8)
	Extremely	19 (9.2)	24 (11.7)	43 (10.4)

Max., maximum; min., minimum.
a If you checked off problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

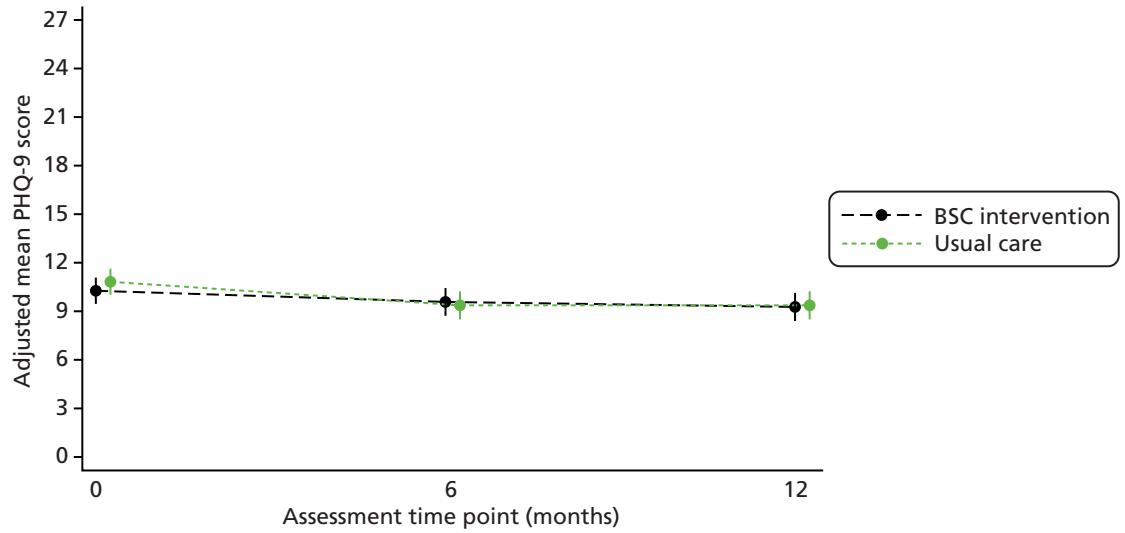

FIGURE 8 Adjusted means for the PHQ-9 by treatment group and time point.

These results were extracted from a mixed-effects model in which participant was treated as a random effect and observations over time (6 and 12 months) were nested within participant. The effect of randomised treatment group was assessed while adjusting for time, group-by-time interaction, baseline PHQ-9 score and baseline smoking severity as fixed effects, and site as a random effect. Different covariance structures were applied to the model. A compound symmetric (or exchangeable) pattern that assumes equal correlation of errors between each pair of time points within participants resulted in the lowest AIC and so was used in the final model. Diagnostics of model fit revealed that the standardised residuals were normally distributed, and were uniform against fitted values; therefore, data transformation was not required.

Generalised Anxiety Disorder Assessment-7 items

The GAD-7 score is summarised by randomised group and time point in *Table 18*. Adjusted GAD-7 means and group differences are presented in *Table 21*, and displayed in *Figure 9*. The adjusted mean difference at 6 months was –0.32 (95% CI –1.26 to 0.62) and at 12 months was –0.10 (95% CI –1.05 to 0.86), both marginally favouring BSC, but neither statistically significantly ($p = 0.50$ and 0.84, respectively).

These results were extracted from a mixed-effects model in which participant was treated as a random effect and observations over time (6 and 12 months) were nested within participant. The effect of randomised treatment group was assessed while adjusting for time, group-by-time interaction, baseline GAD-7 score and baseline smoking severity as fixed effects, and site as a random effect. Different covariance structures were applied to the model. A compound symmetric (or exchangeable) pattern that assumes equal

TABLE 18 The GAD-7 scores by treatment group and time point

Time point	GAD-7 questionnaire	BSC (*N* = 265)	Usual care (*N* = 261)	Overall (*N* = 526)
Baseline				
Score				
	Mean (SD)	8.4 (6.2)	8.4 (6.1)	8.4 (6.1)
	Median (min., max.)	7.0 (0.0, 21.0)	8.0 (0.0, 21.0)	8.0 (0.0, 21.0)
	Missing, *n* (%)	1 (0.4)	1 (0.4)	2 (0.4)
How difficult,[a] *n* (%)		*n* = 249	*n* = 249	*n* = 498
	Not at all	72 (28.9)	63 (25.3)	135 (27.1)
	Somewhat	93 (37.3)	113 (45.4)	206 (41.4)
	Very	53 (21.3)	41 (16.5)	94 (18.9)
	Extremely	31 (12.4)	32 (12.9)	63 (12.7)
Month 6				
Score				
	Mean (SD)	7.0 (5.9)	7.3 (5.8)	7.1 (5.9)
	Median (min., max.)	6.0 (0.0, 21.0)	7.0 (0.0, 21.0)	6.0 (0.0, 21.0)
	Missing, *n* (%)	41 (15.5)	44 (16.9)	85 (16.2)
How difficult,[a] *n* (%)		*n* = 202	*n* = 197	*n* = 399
	Not at all	70 (34.7)	52 (26.4)	122 (30.6)
	Somewhat	73 (36.1)	86 (43.7)	159 (39.8)
	Very	35 (17.3)	45 (22.8)	80 (20.1)
	Extremely	24 (11.9)	14 (7.1)	38 (9.5)

TABLE 18 The GAD-7 scores by treatment group and time point (*continued*)

Time point	GAD-7 questionnaire	BSC (*N* = 265)	Usual care (*N* = 261)	Overall (*N* = 526)
Month 12				
Score				
	Mean (SD)	7.0 (6.3)	7.4 (6.0)	7.2 (6.2)
	Median (min., max.)	5.0 (0.0, 21.0)	7.0 (0.0, 21.0)	6.0 (0.0, 21.0)
	Missing, *n* (%)	51 (19.2)	49 (18.8)	100 (19.0)
How difficult,[a] *n* (%)		*n* = 196	*n* = 202	*n* = 398
	Not at all	62 (31.6)	51 (25.2)	113 (28.4)
	Somewhat	74 (37.8)	88 (43.6)	162 (40.7)
	Very	38 (19.4)	41 (20.3)	79 (19.8)
	Extremely	22 (11.2)	22 (10.9)	44 (11.1)

Max., maximum; min., minimum.
a If you checked off problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

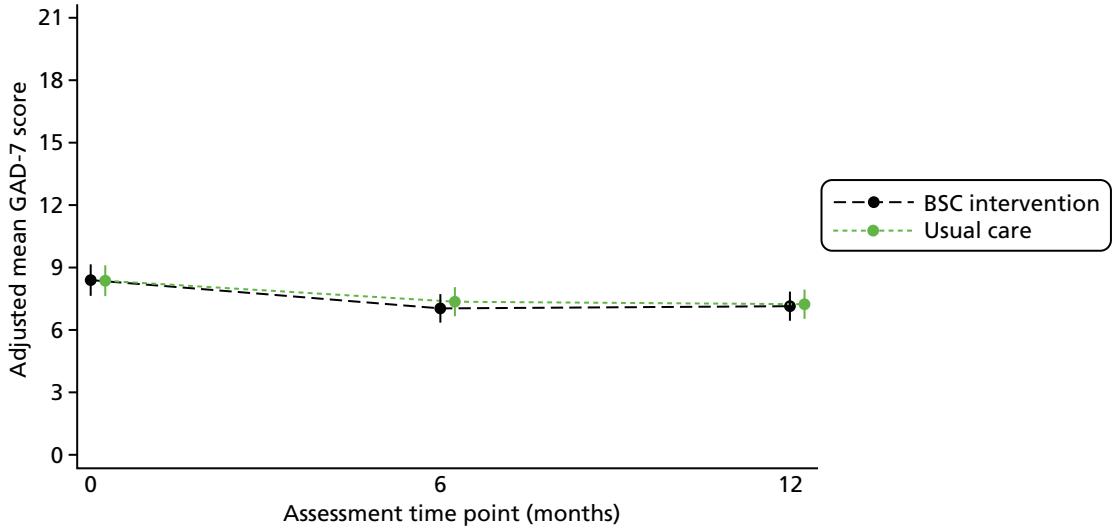

FIGURE 9 Adjusted means for the GAD-7 by treatment group and time point.

correlation of errors between each pair of time points within participants resulted in the lowest AIC and so was used in the final model. Diagnostics of model fit revealed that the standardised residuals were normally distributed, and were uniform against fitted values; therefore, data transformation was not required.

Short Form questionnaire-12 items

The SF-12 mental and physical health component subscale scores are summarised by randomised group and time point in *Table 19*. Adjusted SF-12 means and group differences are presented in *Table 21* and displayed in *Figure 10*. The adjusted mean difference for the mental component score at 6 months was –0.73 (95% CI –2.82 to 1.36) and at 12 months was –0.41 (95% CI –2.35 to 1.53), both marginally favouring usual care, but neither statistically significantly ($p = 0.49$ and 0.68, respectively). The adjusted mean difference for the physical component score at 6 months was 1.75 (95% CI 0.21 to 3.28), indicating a statistically significant benefit of BSC ($p = 0.03$); however, this difference reduced at 12 months to 0.59 (95% CI –1.07 to 2.26) and was not statistically significant ($p = 0.48$).

TABLE 19 The SF-12 mental and physical health component scores by treatment group and time point

Time point	SF-12	BSC (*N* = 265)	Usual care (*N* = 261)	Overall (*N* = 526)
Mental component score				
Baseline	Mean (SD)	38.6 (12.6)	37.9 (11.7)	38.2 (12.2)
	Median (min., max.)	37.2 (14.8, 63.5)	37.4 (14.4, 62.6)	37.4 (14.4, 63.5)
	Missing, *n* (%)	8 (3.0)	5 (1.9)	13 (2.5)
Month 6	Mean (SD)	38.4 (13.1)	38.9 (12.2)	38.6 (12.6)
	Median (min., max.)	37.1 (9.3, 64.4)	38.3 (14.3, 65.1)	37.9 (9.3, 65.1)
	Missing, *n* (%)	51 (19.2)	53 (20.3)	104 (19.8)
Month 12	Mean (SD)	39.3 (11.9)	38.9 (11.9)	39.1 (11.9)
	Median (min., max.)	38.7 (12.2, 65.6)	38.1 (12.4, 63.9)	38.3 (12.2, 65.6)
	Missing, *n* (%)	53 (20.0)	54 (20.7)	107 (20.3)
Physical component score				
Baseline	Mean (SD)	43.7 (10.4)	42.2 (11.0)	43.0 (10.7)
	Median (min., max.)	45.0 (17.0, 64.1)	42.0 (19.4, 62.1)	43.9 (17.0, 64.1)
	Missing, *n* (%)	8 (3.0)	5 (1.9)	13 (2.5)
Month 6	Mean (SD)	45.6 (9.8)	42.9 (11.0)	44.3 (10.5)
	Median (min., max.)	47.0 (22.7, 61.7)	43.4 (17.4, 63.8)	45.5 (17.4, 63.8)
	Missing, *n* (%)	51 (19.2)	53 (20.3)	104 (19.8)
Month 12	Mean (SD)	44.3 (10.1)	42.4 (11.4)	43.3 (10.8)
	Median (min., max.)	45.6 (20.2, 63.7)	44.1 (16.3, 61.3)	45.3 (16.3, 63.7)
	Missing, *n* (%)	53 (20.0)	54 (20.7)	107 (20.3)

Max., maximum; min., minimum.

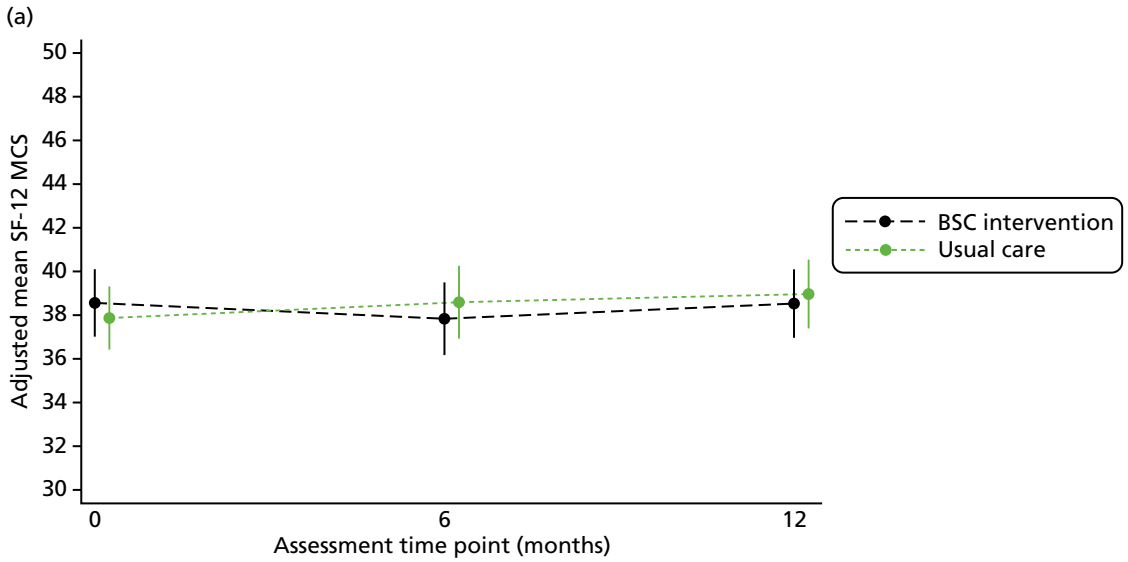

FIGURE 10 Adjusted means for the SF-12 mental and physical health components by treatment group and time point. (a) Mental; and (b) physical. MCS, mental component score; PCS, physical component score. (*continued*)

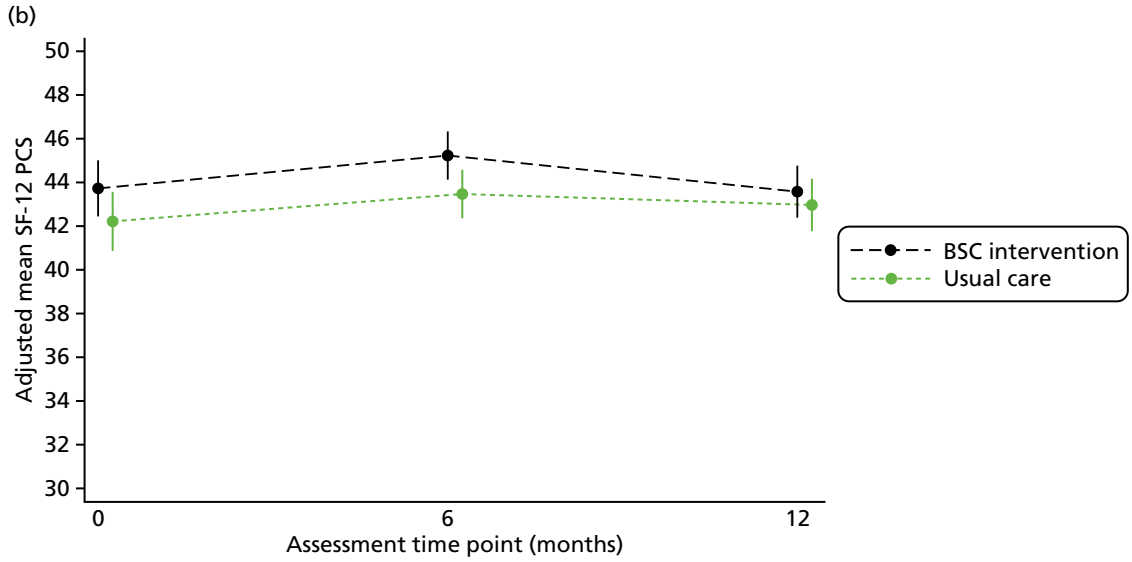

FIGURE 10 Adjusted means for the SF-12 mental and physical health components by treatment group and time point. (a) Mental; and (b) physical. MCS, mental component score; PCS, physical component score.

These results were extracted from mixed-effects models in which participant was treated as a random effect and observations over time (6 and 12 months) were nested within participant. The effect of randomised treatment group was assessed while adjusting for time, group-by-time interaction, baseline SF-12 mental/physical component score and baseline smoking severity as fixed effects, and site as a random effect. Different covariance structures were applied to the model. An unstructured pattern that models all variances and covariances separately resulted in the lowest AIC for both models and so was used. Diagnostics of model fit revealed that the standardised residuals were normally distributed, and were uniform against fitted values; therefore, data transformation was not required.

Body mass index

Body mass index is summarised by randomised group and time point in *Table 20*. Adjusted BMI means and group differences are presented in *Table 21* and displayed in *Figure 11*. The adjusted mean difference at 6 months was 0.16 (95% CI –0.54 to 0.85) and at 12 months was 0.25 (95% CI –0.62 to 1.13), both marginally favouring usual care, but neither statistically significantly ($p = 0.65$ and 0.57, respectively).

TABLE 20 Body mass index by treatment group and time point

Time point	BMI	BSC ($N = 265$)	Usual care ($N = 261$)	Overall ($N = 526$)
Baseline	Mean (SD)	30.2 (7.1)	29.7 (6.3)	29.9 (6.7)
	Median (min., max.)	29.0 (16.6, 59.8)	29.4 (16.9, 48.4)	29.3 (16.6, 59.8)
	Missing, *n* (%)	2 (0.8)	3 (1.1)	5 (1.0)
Month 6	Mean (SD)	30.5 (7.0)	29.9 (6.0)	30.2 (6.5)
	Median (min., max.)	30.0 (14.8, 60.7)	29.1 (16.6, 48.5)	29.4 (14.8, 60.7)
	Missing, *n* (%)	49 (18.5)	56 (21.5)	105 (20.0)
Month 12	Mean (SD)	30.4 (7.2)	29.7 (6.7)	30.0 (6.9)
	Median (min., max.)	29.7 (0.0, 61.9)	29.3 (0.0, 45.8)	29.4 (0.0, 61.9)
	Missing, *n* (%)	57 (21.5)	60 (23.0)	117 (22.2)

Max., maximum; min., minimum.

TABLE 21 Adjusted means and group differences for continuous secondary outcomes

Time point	BSC, mean (95% CI)	Usual care, mean (95% CI)	Difference (95% CI), SE	*p*-value
FTND				
Month 6	5.25 (5.00 to 5.50)	5.43 (5.19 to 5.67)	–0.18 (–0.53 to 0.17), 0.18	0.32
Month 12	5.42 (5.14 to 5.70)	5.43 (5.16 to 5.69)	–0.01 (–0.39 to 0.38), 0.20	0.97
MTQ				
Month 6	13.1 (12.6 to 13.5)	12.5 (12.0 to 12.9)	0.58 (–0.01 to 1.17), 0.30	0.06
Month 12	12.9 (12.4 to 13.4)	12.3 (11.8 to 12.7)	0.64 (0.04 to 1.24), 0.31	0.04
PHQ-9				
Month 6	9.6 (8.7 to 10.4)	9.4 (8.5 to 10.2)	0.20 (–0.85 to 1.24), 0.53	0.72
Month 12	9.3 (8.4 to 10.1)	9.4 (8.5 to 10.2)	–0.12 (–1.18 to 0.94), 0.54	0.82
GAD-7				
Month 6	7.0 (6.3 to 7.7)	7.4 (6.7 to 8.1)	–0.32 (–1.26 to 0.62), 0.48	0.50
Month 12	7.1 (6.4 to 7.8)	7.2 (6.5 to 7.9)	–0.10 (–1.05 to 0.86), 0.49	0.84
SF-12 MCS				
Month 6	37.9 (36.2 to 39.5)	38.6 (36.9 to 40.3)	–0.73 (–2.82 to 1.36), 1.07	0.49
Month 12	38.6 (37.0 to 40.1)	39.0 (37.4 to 40.5)	–0.41 (–2.35 to 1.53), 0.99	0.68
SF-12 PCS				
Month 6	45.2 (44.1 to 46.3)	43.5 (42.4 to 44.6)	1.75 (0.21 to 3.28), 0.78	0.03
Month 12	43.6 (42.4 to 44.8)	43.0 (41.8 to 44.2)	0.59 (–1.07 to 2.26), 0.85	0.48
BMI				
Month 6	30.3 (29.8 to 30.8)	30.1 (29.6 to 30.6)	0.16 (–0.54 to 0.85), 0.35	0.65
Month 12	30.2 (29.5 to 30.8)	29.9 (29.3 to 30.5)	0.25 (–0.62 to 1.13), 0.45	0.57

MCS, mental component score; PCS, physical component score; SE, standard error.

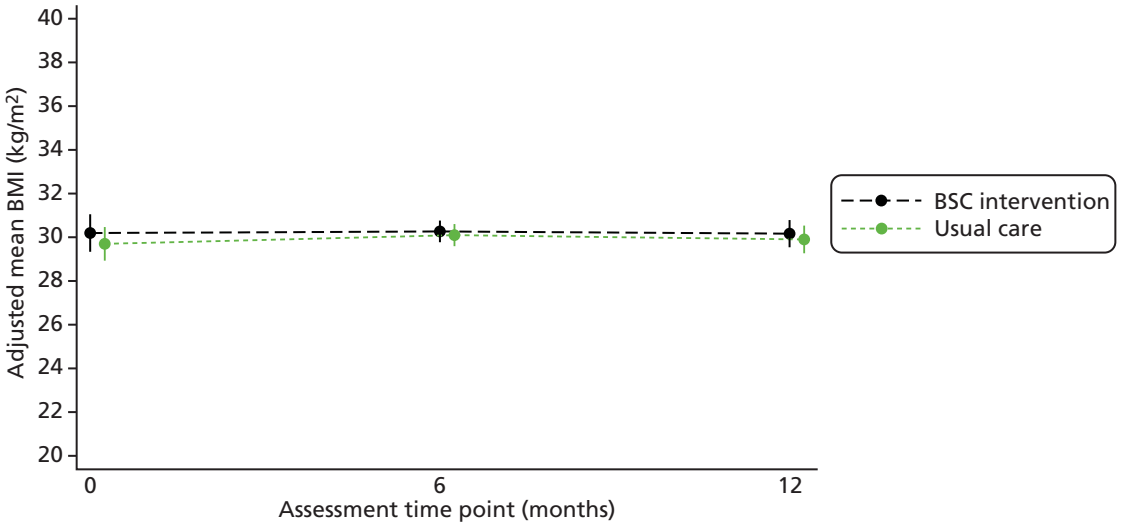

FIGURE 11 Adjusted means for BMI by treatment group and time point.

These results were extracted from a mixed-effects model in which the participant was treated as a random effect and observations over time (6 and 12 months) were nested within participant. The effect of randomised treatment group was assessed while adjusting for time, group-by-time interaction, baseline BMI and baseline smoking severity as fixed effects, and site as a random effect. Different covariance structures were applied to the model. An unstructured pattern that models all variances and covariances separately resulted in the lowest AIC and so was used in the final model. Diagnostics of model fit revealed a minor violation: the 'body' (centre) of the distribution of the standardised residuals was normal, but the distribution was short-tailed; however, the residuals were uniform against fitted values. Data transformations of the outcome (log, square root and square) did not substantially improve the model fit and so analyses were conducted on untransformed data.

Summary of results for secondary outcomes

Use of e-cigarettes and lifestyle data at 6 and 12 months

Participant-reported use of e-cigarettes and lifestyle data collected at 6 and 12 months are summarised in *Tables 22* and *23*. Fifty-four per cent of randomised participants reported having ever tried an e-cigarette at the 12-month time point (66.7% of those with valid response to this question). Of these, however, most (64.7%) reported that they had not used an e-cigarette in the past month. Approximately half said that their use of tobacco had not changed since they started to use e-cigarettes. Of those with valid data, 59.0% of the BSC group and 56.6% of the usual-care group reported leading a fairly or very healthy life at 6 months. Of those with valid data, 57.1% of the BSC group and 56.8% of the usual-care group reported leading a fairly or very healthy life at 12 months. At month 12, a similar proportion of participants in each group reported that they drank alcohol (48.4% in the BSC group and 47.7% in the usual-care group), with the BSC group consuming an average of 8.7 units in the last week (11.9 units in the usual-care group).

TABLE 22 Use of e-cigarettes at 6 and 12 months by randomised group

Characteristic, *n* (%)	Month 6			Month 12		
	BSC (*N* = 265)	Usual care (*N* = 261)	Overall (*N* = 526)	BSC (*N* = 265)	Usual care (*N* = 261)	Overall (*N* = 526)
Ever tried an e-cigarette						
Yes	157 (59.3)	155 (59.4)	312 (59.3)	135 (50.9)	151 (57.9)	286 (54.4)
No	69 (26.0)	59 (22.6)	128 (24.3)	79 (29.8)	64 (24.5)	143 (27.2)
Missing	39 (14.7)	47 (18.0)	86 (16.4)	51 (19.3)	46 (17.6)	97 (18.4)
If yes:	n = *157*	n = *155*	n = *312*	n = *135*	n = *151*	n = *286*
Use of e-cigarette in last 30 days						
Never	86 (54.8)	98 (63.2)	184 (59.0)	89 (65.9)	96 (63.6)	185 (64.7)
Less than once per week	14 (8.9)	12 (7.7)	26 (8.3)	6 (4.4)	11 (7.3)	17 (5.9)
Less than daily but at least once per week	21 (13.4)	13 (8.4)	34 (10.9)	11 (8.1)	17 (11.3)	28 (9.8)
Every day	36 (22.9)	32 (20.6)	68 (21.8)	28 (20.7)	27 (17.9)	55 (19.2)
Missing	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.7)	0 (0.0)	1 (0.3)
Length of use of e-cigarettes						
< 1 month	48 (30.6)	56 (36.1)	104 (33.3)	36 (26.7)	39 (25.8)	75 (26.2)
1–6 months	30 (19.1)	30 (19.4)	60 (19.2)	25 (18.5)	36 (23.8)	61 (21.3)
6–12 months	21 (13.4)	16 (10.3)	37 (11.9)	23 (17.0)	22 (14.6)	45 (15.7)
> 1 year	40 (25.5)	40 (25.8)	80 (25.6)	37 (27.4)	36 (23.8)	73 (25.5)
Missing	18 (11.5)	13 (8.4)	31 (9.9)	14 (10.4)	18 (11.9)	32 (11.2)

continued

TABLE 22 Use of e-cigarettes at 6 and 12 months by randomised group (*continued*)

Characteristic, *n* (%)	Month 6			Month 12		
	BSC (*N* = 265)	Usual care (*N* = 261)	Overall (*N* = 526)	BSC (*N* = 265)	Usual care (*N* = 261)	Overall (*N* = 526)
Nicotine levels in cartridges used in e-cigarette						
None (0 mg)	6 (3.8)	10 (6.5)	16 (5.1)	4 (3.0)	6 (4.0)	10 (3.5)
Low (< 8 mg)	22 (14)	25 (16.1)	47 (15.1)	28 (20.7)	39 (25.8)	67 (23.4)
Medium (8–16 mg)	39 (24.8)	41 (26.5)	80 (25.6)	39 (28.9)	32 (21.2)	71 (24.8)
High (> 16 mg)	34 (21.7)	37 (23.9)	71 (22.8)	28 (20.7)	40 (26.5)	68 (23.8)
Missing	56 (35.7)	42 (27.1)	98 (31.4)	36 (26.7)	34 (22.5)	70 (24.5)
Use of tobacco changed since using e-cigarettes						
Yes, I smoke less tobacco	70 (44.6)	61 (39.4)	131 (42.0)	63 (46.7)	56 (37.1)	119 (41.6)
Yes, I smoke more tobacco	4 (2.5)	9 (5.8)	13 (4.2)	4 (3.0)	3 (2.0)	7 (2.4)
No, it has not changed	65 (41.4)	75 (48.4)	140 (44.9)	55 (40.7)	78 (51.7)	133 (46.5)
Missing	18 (11.5)	10 (6.5)	28 (9.0)	13 (9.6)	14 (9.3)	27 (9.4)
Reason started using e-cigarettes						
To quit smoking tobacco	67 (42.7)	71 (45.8)	138 (44.2)	74 (54.8)	84 (55.6)	158 (55.2)
To try a safer alternative to tobacco	28 (17.8)	18 (11.6)	46 (14.7)	16 (11.9)	12 (7.9)	28 (9.8)
To try something new	18 (11.5)	9 (5.8)	27 (8.7)	7 (5.2)	18 (11.9)	25 (8.7)
To smoke less tobacco	23 (14.6)	33 (21.3)	56 (17.9)	21 (15.6)	20 (13.2)	41 (14.3)
Other	11 (7.0)	14 (9.0)	25 (8.0)	10 (7.4)	9 (6.0)	19 (6.6)
Missing	10 (6.4)	10 (6.5)	20 (6.4)	7 (5.2)	8 (5.3)	15 (5.2)

TABLE 23 Lifestyle data at 6 and 12 months by randomised group

Characteristic	Month 6			Month 12		
	BSC (*N* = 265)	Usual care (*N* = 261)	Overall (*N* = 526)	BSC (*N* = 265)	Usual care (*N* = 261)	Overall (*N* = 526)
Healthy life,* n *(%)						
A very healthy life	18 (6.8)	7 (2.7)	25 (4.8)	12 (4.5)	12 (4.6)	24 (4.6)
A fairly healthy life	116 (43.8)	117 (44.8)	233 (44.3)	113 (42.6)	109 (41.8)	222 (42.2)
A not very healthy life	72 (27.2)	72 (27.6)	144 (27.4)	70 (26.4)	71 (27.2)	141 (26.8)
An unhealthy life	21 (7.9)	23 (8.8)	44 (8.4)	24 (9.1)	21 (8.0)	45 (8.6)
Missing	38 (14.3)	42 (16.1)	80 (15.2)	46 (17.4)	48 (18.4)	94 (17.9)
Eat five portions of fruit and vegetables a day,* n *(%)						
Yes	107 (40.4)	104 (39.8)	211 (40.1)	109 (41.1)	100 (38.3)	209 (39.7)
No	121 (45.7)	114 (43.7)	235 (44.7)	110 (41.5)	115 (44.1)	225 (42.8)
Missing	37 (14.0)	43 (16.5)	80 (15.2)	46 (17.4)	46 (17.6)	92 (17.5)
Exercise for ≥ 20 minutes,* n *(%)						
Daily	94 (35.5)	94 (36.0)	188 (35.7)	98 (37.0)	77 (29.5)	175 (33.3)
Weekly	61 (23.0)	42 (16.1)	103 (19.6)	61 (23.0)	60 (23.0)	121 (23.0)
Monthly	3 (1.1)	6 (2.3)	9 (1.7)	4 (1.5)	6 (2.3)	10 (1.9)

TABLE 23 Lifestyle data at 6 and 12 months by randomised group (*continued*)

Characteristic	Month 6			Month 12		
	BSC (*N* = 265)	Usual care (*N* = 261)	Overall (*N* = 526)	BSC (*N* = 265)	Usual care (*N* = 261)	Overall (*N* = 526)
Seldom	30 (11.3)	25 (9.6)	55 (10.5)	21 (7.9)	36 (13.8)	57 (10.8)
Never	40 (15.1)	51 (19.5)	91 (17.3)	35 (13.2)	35 (13.4)	70 (13.3)
Missing	37 (14.0)	43 (16.5)	80 (15.2)	46 (17.4)	47 (18.0)	93 (17.7)
Drink alcohol,* n *(%)						
Yes	119 (44.9)	106 (40.6)	225 (42.8)	106 (40.0)	103 (39.5)	209 (39.7)
No	110 (41.5)	113 (43.3)	223 (42.4)	113 (42.6)	113 (43.3)	226 (43.0)
Missing	36 (13.6)	42 (16.1)	78 (14.8)	46 (17.4)	45 (17.2)	91 (17.3)
If yes, units in last week						
Mean (SD)	10.2 (18.5)	9.9 (18.3)	10.0 (18.4)	8.7 (11.5)	11.9 (27.2)	10.3 (20.8)
Median (min., max.)	5 (0, 164)	4 (0, 126)	4 (0, 164)	4 (0, 58)	4 (0, 220)	4 (0, 220)
Missing, *n* (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Max., maximum; min., minimum.

Compliance with intervention

Intervention session attendance

A total of 1654 treatment sessions were arranged for 238 of the 265 intervention participants between November 2015 and December 2017, of which 1483 (89.7%) were attended. A total of 48 sessions were cancelled and in 123 cases the participant did not attend the session (*Table 24*). Overall, 234 out of the 265 intervention participants (88.3%) attended at least one treatment session (the remaining 27 did not partake in any intervention sessions as they withdrew from the trial or were unwell). For these 234 participants, the mean number of sessions attended was 6.4 (SD 3.5, median 6, range 1–14). Sessions lasted an average of 39.4 minutes (SD 17.2 minutes, median 35, range 5–120 minutes). Most (85.0%) sessions took place face to face, 4.1% took place over the telephone and 10.9% took place via another mode. The majority (81.1%) took place at the participant's home.

Complier-average causal effect analysis

The CACE estimate of attending one additional intervention session was a small, non-statistically significant, increase in the likelihood of being a CO-verified quitter at 12 months (OR 1.07, 95% CI 0.97 to 1.18; $p = 0.20$).

Use of usual-care stop smoking services

The most used usual-care smoking cessation services were consultations with the GP, the pharmacist and the SSS. In the first 6 months of the trial, 100 out of the 212 responders (47.2%) in the usual-care group reported not using any of them, while 144 out of the 218 responders (66.1%) in the intervention group reported having used them. Among those who reported any use, the mean number of consultations was 2.8 (SD 3.5, median 2, range 1–31) in the usual-care group and 3.3 (SD 2.8, median 2, range 1–13) in the intervention group. In the second half of the trial, 142 out of 213 responders (66.7%) in the usual-care group reported not using any of the three services, while 141 out of 213 responders (66.2%) in the intervention group reported so. Among those who reported any use, the mean number of consultations was 3.3 (SD 3.4, median 2, range 1–18) in the usual-care group and 2.7 (SD 3.2, median 2, range 1–24) in the intervention group. Participants also reported consulting with other health-care professionals, such as practice nurse and health-care assistant, but these were rare cases.

TABLE 24 Intervention details for the BSC group

Intervention details	BSC (*N* = 265)
Number of sessions attended, n (%)	
0	31 (11.7)
1	19 (7.2)
2	23 (8.7)
3	23 (8.7)
4	22 (8.3)
5	16 (6.0)
6	15 (5.7)
7	16 (6.0)
8	25 (9.4)
9	24 (9.1)
10	22 (8.3)
11	12 (4.5)
12	12 (4.5)
13	3 (1.1)
14	2 (0.8)
Attended at least one session	234 (88.3)
Number of sessions attended	
Mean (SD)	6.3 (3.5)
Median (min., max.)	6 (1, 14)
Total number of sessions attended	1483
Length of sessions (minutes)	
Mean (SD)	39.6 (17.2)
Median (min., max.)	35 (5, 120)
Mode,* n *(%)	
Face to face	1260 (85.0)
Telephone	61 (4.1)
Other	156 (10.5)
Missing	6 (0.4)
Location,* n *(%)	
Home	1202 (81.1)
Other	276 (18.6)
Missing	5 (0.3)

Max., maximum; min., minimum.

Withdrawals

Some of the information reported in this section is given in Peckham *et al.*[1] This contains information licensed under the Non-Commercial Government Licence v2.0.

There were four categories of participant withdrawal:

1. Full withdrawal – participant withdrawn from the trial with regard to completion of both postal questionnaires and collection of GP data.
2. Withdrawal from follow-up – participant withdrawn from the completion of postal questionnaires but agreed to the continuing collection of GP data.
3. Withdrawal from treatment – participant withdrawn from trial intervention treatment, but agreed to continuing completion of postal questionnaires and collection of GP data.
4. Too unwell to continue – participant was deemed too unwell by medical staff to complete any questionnaires. This generally occurred only when a participant has been hospitalised.

Overall, there were 93 (17.7%) participant withdrawals (all types) during the trial: 23 participants (8.8%) from the usual-care group and 70 participants (26.4%) from the BSC group.

A total of 47 participants (8.9%) withdrew fully from the trial, two participants (0.4%) withdrew from follow-up, two (0.4%) were too unwell to continue and 42 (15.8%) withdrew from the intervention (*Table 25*).

Adverse events

There were 365 adverse events among 174 participants during the course of the trial. Of these, 111 were classed as serious. More participants in the BSC group (42.1%) experienced one or more adverse events than those in the usual-care group (24.5%). All adverse events ($n = 58$) that were deemed to be definitely or probably related to the intervention or trial participation were all non-serious adverse events (*Table 26*). This includes three events, related to NRT side effects, which were experienced by usual-care participants as part of a routine care quit attempt.

Of the 111 serious adverse events reported, the majority were related to unplanned hospital admission due to a deterioration in the participant's mental health condition ($n = 98$). The remaining serious adverse events were associated with unplanned hospital admissions associated with comorbidities ($n = 6$) or death ($n = 7$). The one event deemed to be possibly related was an inpatient hospitalisation due to infective chronic obstructive pulmonary disease.

TABLE 25 Withdrawals by type

Withdrawals type	Usual care	BSC	Total
Full withdrawal	21	26	47[a]
Withdrawal from follow-up	1	1	2
Withdrawal from treatment	0	42	42
Too unwell to continue	1	1	2
Total	23	70	93

a Includes five participants who initially withdrew from treatment and subsequently withdrew in full.

TABLE 26 Relationship of adverse events to trial procedures

Adverse event	Relationship	BSC	Usual care	Total
Serious adverse event	Definitely related	0	0	0
	Probably related	0	0	0
	Possibly related	1	0	1
	Unlikely to be related	36	18	54
	Unrelated	31	24	55
	Unclassified[a]	1	0	1
Non-serious adverse event	Definitely related	2	0	2
	Probably related	53	3[b]	56
	Possibly related	28	3	31
	Unlikely to be related	52	33	85
	Unrelated	56	24	80
Total		260	105	365

a One serious adverse event unclassified (participant deceased, no cause of death available).
b Side effects related to use of NRT as part of usual-care quit attempt.

Of the 254 non-serious adverse events reported, the majority of events were associated with participant comorbidities ($n = 124$). Sixty-six events were associated with NRT side effects and 57 with the participant's mental ill health. Of the remaining events, five were associated with accident and emergency or emergency ambulance use, but no information was available with regard to the reasons for this and two were unable to be classified (smoking teabags, $n = 1$; media coverage of family member, $n = 1$). Of the 56 events deemed to be probably related, the majority were associated with NRT side effects ($n = 50$) and of those possibly related, the majority were associated with participant comorbidities ($n = 14$). The two events deemed to be definitely related were both associated with NRT side effects (nausea following Champix use, $n = 1$; itching and redness caused by NRT patch, $n = 1$).

Summary of findings

Attempts were made to contact a total of 1606 people for eligibility and consent to partake in the trial, of which 526 were randomised (a rate of 33%). A primary reason for ineligibility, besides being unable to contact the person and non-consent, was that the person did not smoke or did not smoke at least five tobacco cigarettes a day. Over two-thirds of the participants were recruited from CMHT direct referral (72%). Between October 2015 and December 2016, 265 participants were randomised to BSC and 261 participants were randomised to usual care. This was over our original sample size target of 400 participants. Almost 60% of the participants were male and the average age was 46 years (range 19–72 years). The most common mental health diagnosis was schizophrenia or other psychotic illness (65%), followed by bipolar disorder (22%) and schizoaffective disorder (12%). The mean number of cigarettes smoked per day at baseline was 25, and the most commonly reported reasons for wanting to quit smoking were that it is bad for your health (88%) and is expensive (72%).

Retention rates in the trial were high. At the primary time point of 12 months, 450 (94%) of the 480 participant questionnaires intended to be completed were returned (86% of 526 randomised participants), with most (98%) being completed face to face with the MH-SCP. In total, 442 participants were included in the primary analysis (i.e. provided a CO breath measurement and completed the self-reported smoking

status question on the 12-month participant questionnaire). A total of 34 out of 223 participants (15%; 13% of 265 randomised participants) fulfilled the definition for CO-verified smoking cessation in the BSC group, and 22 out of 219 participants (10%; 8% of 261 randomised participants) in the usual-care group. Therefore, participants in the BSC group were more likely to be a CO-verified 1-week quitter at 12 months post randomisation than participants in the usual-care group, but this difference was not statistically significant (OR 1.6, 95% CI 0.9 to 2.8; $p = 0.12$). A larger difference was, however, observed at the 6-month time point and this was statistically significant (OR 2.4, 95% CI 1.2 to 4.7; $p = 0.01$), perhaps suggesting an early benefit of the intervention, which waned over time.

The trial was originally powered at 80% to detect a relative increase of 1.7 in quitting from 20% in the usual-care group to 34% in the BSC group, allowing for a 20% loss to follow-up at 12 months. Ultimately, 526 participants were randomised and 442 (84%) were included in the primary analysis, so the loss to follow-up rate was lower than 20%. However, the quit rate was half that expected in the usual-care group (10% as opposed to 20%); therefore, the power needed to detect a relative increase in quit rate of 1.7 (to 17% in the BSC group) was ultimately 58%. Although this was not statistically significant at 12 months, the difference (10% vs. 15%) may still be clinically meaningful.

The primary result was robust to sensitivity checks, both the pre-planned and post hoc analyses, and similar results were seen when considering only self-reported smoking cessation. There was no evidence of a difference between the two groups in secondary outcomes at any time point except for the MTQ, which statistically significantly favoured the BSC group at 12 months, with a borderline *p*-value of 0.06 at 6 months. The physical component of the SF-12 also statistically significantly favoured the BSC group at 6 months (but not at 12 months).

The proportion of participants reporting that they had ever used e-cigarettes remained reasonably stable throughout the trial, as did the proportion reporting use in the previous month, suggesting that e-cigarettes were not frequently used as a NRT for those attempting to quit in the trial.

The uptake of the BSC intervention was reasonable, with 88% of participants randomised to the BSC group attending at least one session (median 6, range 1–14 sessions). The majority of sessions took place in the participants' homes.

A total of 111 serious adverse events were reported in the trial and more participants in the BSC group (42%) reported one or more adverse events than in the usual-care group (25%); however, none of the SAEs was deemed to be related to trial participation.

Chapter 5 Health economic analysis

Costs

Intervention costs

Training and supervision

The initial training session delivered by the NCSCT was invoiced at a total of £5325. The opportunity cost for time attended by team members was estimated at £43 per hour[59] for 15 hours, costing £2589. The 2-day training sessions for the MH-SCPs were delivered by two trainers at £43 per hour,[59] costing £1290. In total, eight 2-day training sessions were held, amounting to £10,320. The time costs spent by the practitioners were costed at £28 per hour,[59] resulting in £23,520 for 56 people for 2 days in total. The total printing cost was recorded as £105. Therefore, the total training costs were £41,850. The training costs were then allocated evenly to the participants in the BSC group. Training costs per participant were therefore estimated at £158.

Supervisors recorded the supervision sessions and estimated approximately 30 minutes of supervision per participant. The cost of supervision was estimated at £22 per participant. The first-year depreciation value of 56 CO monitors was £6720. It gave a cost of £10 per participant. In total, training, supervision and material cost per participant was £190 in the BSC group.

The control treatment was usual care that required no special training. The costs of training and supervision were considered zero for the usual-care group.

Intervention delivery

There were two parts of intervention delivery: (1) the BSC session in the BSC group and (2) usual care in both groups.

Bespoke smoking cessation delivery in the bespoke smoking cessation group

Attendance of bespoke smoking cessation sessions For the BSC support sessions, among the 265 participants randomised to the BSC group, two participants attended one session but the session records were missing. There were 27 participants who had withdrawn or been otherwise uncontactable before the treatment began, and four participants who had been contacted but failed to attend the first support session.

Among the 231 participants who had at least one support session, 28% attended one to three support sessions, 22% attended four to six support sessions, 28% attended seven to nine support sessions, and 22% attended $\geq$ 10 sessions. There were 1481 sessions delivered in total. The duration of the sessions varied hugely, ranging from 5 minutes to 120 minutes. There were 695 (47%) sessions that lasted 5–30 minutes and 715 (48%) sessions that lasted 35–60 minutes. There were 65 (4%) sessions that lasted 65–90 minutes and only six sessions (< 1%) that were > 90 minutes.

For each attended session, an estimated 10 minutes of administration time was added to account for the necessary paperwork for the session. There were 1370 appointments that entailed travel by the practitioners, including some of the did not attend (DNA) or late cancellation. Owing to the difficulty in collecting travel time for all individual appointments, an estimated 40 minutes of travel time for a return journey was added to the appointments that required travelling.

There were 149 participants who recorded no DNA or cancellation during the trial period and 89 participants who recorded 171 occasions of DNA/cancellation, the majority of whom recorded only once (47/89). Once a DNA or cancellation occurred, attempts were often made to re-establish contact or reschedule appointments. The time spent on these attempts ranged from 5 to 30 minutes per DNAs/cancellations but it should be noted that not all DNAs/cancellations entailed this staff time. The majority (87%) of these attempts were within 10 minutes.

Mean cessation session time and cost in the bespoke smoking cessation group In total, among the 263 participants whose session data were not missing, the mean number of attended sessions was 5.6 (SD 3.8) per participant and the duration of total session time per participant was 222 minutes (SD 166 minutes, range 0–775 minutes). The total time on rearrangement in the case of DNA/cancellation was 5 minutes (SD 10 minutes, range 0–65 minutes) per participant, while the mean number of DNAs/cancellations was 1 (SD 1). The total travel time per participant was 208 minutes (SD 155 minutes, range 0–560 minutes). The total administration time per participant was 56 minutes (SD 38 minutes, range 0–140 minutes). Excluding the two participants whose session data were missing, the mean total BSC delivery time was 492 minutes (SD 339 minutes, range 0–1425 minutes) per participant in the BSC group. Applying an hourly cost of £28, the mean cost of BSC delivery was estimated at £229 (SD £158).

Usual-care delivery in both groups

Mean use and cost of usual-care services for smoking cessation based on structured questions For usual GP care, both groups reported asking for help/advice for smoking cessation from GPs, pharmacists, SSSs and stop smoking helplines. The mean usage was low in both groups, with large standard deviation, indicating a wide variance on a participant level (*Table 27*). The usage of individual services did not appear to differ between groups, except for SSS. The mean usage of SSSs in the usual-care group was twice as high as that in the BSC group in months 1–6 post randomisation. In months 7–12 post randomisation, the mean usage of SSSs was still higher in the usual-care group than in the BSC group, but not as considerable.

TABLE 27 Mean usage and mean cost of usual GP care services based on structured questions, by group

		BSC		UC	
Usual GP care services	Unit cost	Mean usage (SD)	Mean cost (SD)	Mean usage (SD)	Mean cost (SD)
Months 1–6		**n = *218***		**n = *212***	
Cessation consultation with GP	£40/session	0.50 (1.38)	£20 (£55)	0.62 (1.65)	£22 (£46)
Cessation consultation with pharmacist	£7/session	0.35 (1.00)	£2 (£7)	0.33 (1.78)	£2 (£12)
Smoking cessation service	£19/session	0.27 (1.07)	£5 (£20)	0.62 (1.65)	£12 (£31)
NHS stop smoking helpline	£7/call	0.07 (0.54)	£1 (£4)[a]	0.08 (0.38)	£1 (£3)
Total		–	£28 (£62)[a]	–	£37 (£60)
Months 7–12		**n = *213***		**n = *213***	
Cessation consultation with GP	£40/session	0.35 (1.09)	£14 (£43)	0.36 (0.96)	£14 (£38)
Cessation consultation with pharmacist	£7/session	0.22 (0.75)	£2 (£5)	0.28 (0.88)	£2 (£6)
Smoking cessation service	£19/session	0.35 (1.81)	£7 (£34)	0.45 (1.60)	£8 (£30)
NHS stop smoking helpline	£7/call	0.02 (0.14)[b]	£0 (£1)[b]	0.08 (0.47)[b]	£1 (£3)[b]
Total		–	£22 (£56)[c]	–	£25 (£59)

a $n = 217$.
b $n = 214$.
c $n = 212$.

The mean cost of these services for smoking cessation was £37 (SD £60) per participant among the 212 responders in the usual-care group and £28 (SD £62) per participant among the 217 responders in the BSC group in months 1–6 post randomisation. In months 7–12 post randomisation, the mean cost of these services for smoking cessation was £25 (SD £59) per participant among the 213 responders in the usual-care group, and £22 (SD £56) per participant among the 212 responders in the BSC group.

Mean use and cost of usual-care services for smoking cessation based on open questions In addition to responses to the structured questions, there were individual participants who reported asking for help/advice from community psychiatric nurses, practice nurses, support workers, family therapists, hospital nurses, psychiatrists and dentists. The report of these service uses was rare, with only one or two participants in one group.

Costing was undertaken for a 10-minute brief advice session for stop smoking as equivalent to the length of opportunistic brief advice session by GPs and practice nurses;[59] the unit costs of these SSSs are shown in *Table 30*. Applying the unit, an estimated cost was calculated and added to the costs estimated from the structured questions.

Mean total cost of usual-care services for smoking cessation in both groups Accounting for both structured and open questions, the mean cost of usual care for SSSs was £37 (SD £60) per participant among the 212 responders in the usual-care group and £28 (SD £62) per participant among the 217 responders in the BSC group, during months 1–6 post randomisation. The mean cost of usual care for SSSs was £26 (SD £59) per participant among the 213 responders in the usual-care group and £23 (SD £56) per participant among the 212 responders in the BSC group, during months 7–12 post randomisation.

Participants' prescription of pharmacotherapies for smoking cessation Practices were contacted to extract participants' prescription information on pharmacotherapies for smoking cessation. The prescription information for 160 (61%) participants was returned in the usual-care group and the prescription information for 156 (59%) participants was returned in the BSC group. Of the participants with returned data collection, 45 participants in the usual-care group and 100 participants in the BSC group recorded being prescribed pharmacotherapies at some point during the trial period. There were four participants in the usual-care group and 17 participants in the BSC group who had prescription data insufficient for cost estimation.

Therefore, the mean NIC of pharmacotherapy prescription was £26 (SD £73) per participant among the 156 respondents in the usual-care group and £92 (SD £198) per participant among the 139 respondents in the BSC group.

Health-care and social services costs

Mean use of emergency and hospital services *Table 28* presents the number of participants who responded to the questions regarding emergency and hospital services, and their mean use of each service. More than 80% of the participants in either group responded to the questions at either follow-up. In months 1–6 post randomisation, the usual-care group reported nearly twice as many hospital admissions as the BSC group among the responders, both in number of times (0.14 vs. 0.08) and number of nights (1.59 vs. 0.88), while the BSC group reported nearly twice as many use of emergency ambulance as the usual-care group (0.28 vs. 0.15). In months 7–12 post randomisation, the usual-care group reported many more hospital admissions than the BSC group (0.80 vs. 0.13). However, the relatively large SD (8.68) of the mean number of admissions in the usual-care group indicated that there was a small group of responders being admitted frequently.

TABLE 28 Number of responders and their mean use (SD) of emergency services and hospital services, by group

	BSC				Usual care			
	Months 1–6		Months 7–12		Months 1–6		Months 7–12	
Services	*n*	Mean (SD)	*n*	Mean (SD)	*n*	Mean (SD)	*n*	Mean (SD)
A&E department	218	0.39 (0.81)	211	0.34 (0.80)	212	0.37 (0.95)	209	0.43 (0.96)
Hospital admission								
Times	221	0.08 (0.29)	211	0.13 (0.51)	214	0.14 (0.58)	209	0.80 (6.24)
Nights	219	0.88 (6.77)	212	1.00 (4.68)	210	1.59 (10.61)	208	1.58 (8.68)
Hospital outpatient appointment	217	1.40 (2.79)	212	1.43 (3.15)	213	1.72 (4.04)	208	1.66 (3.49)
Day case/procedure	219	0.13 (0.57)	211	0.18 (0.70)	213	0.14 (0.43)	209	0.12 (0.42)
Emergency ambulance	219	0.28 (0.73)	213	0.22 (0.67)	215	0.15 (0.43)	210	0.25 (1.32)

A&E, accident and emergency.

Mean use of primary and community services

Over 80% of the participants in either group responded to the questions regarding the primary and community services at follow-ups. The mean use of the services was generally lower than once per responder in both groups with a few exceptions (*Table 29*). The highest mean usage was reported for community psychiatric nurse, with over five times in the usual-care group in both follow-up periods and over six times in the BSC group. This was followed by CMHT visits. The mean number of visits by CMHT was close to five per responder in the usual-care group throughout the trial period. In the BSC group, the mean number of visits was over five per responder in months 1–6 and over four per responder in months 7–12. The third highest used service was day care. Both groups reported a mean number of use over three times during a 6-month period. Both groups reported over two visits to a GP in surgery during a 6-month period and over one visit to a practice nurse. The large SDs indicated a skewed distribution of service use.

TABLE 29 Mean use (SD) of primary and community services in months 1–6 and months 7–12, respectively, by group

	BSC		Usual care	
Services	Months 1–6 ($n = 220$)	Months 7–12 ($n = 214$)	Months 1–6 ($n = 214$)	Months 7–12 ($n = 213$)
GP home visit	0.21 (1.14)	0.20 (0.87)	0.26 (1.43)	0.29 (1.39)
GP surgery	2.34 (2.97)	2.37 (3.46)	2.63 (3.69)	2.69 (3.69)
GP telephone	0.51 (1.39)	0.61 (1.70)	0.73 (2.21)	0.56 (1.26)
Practice nurse	1.16 (2.38)	1.06 (2.19)	1.42 (2.93)	1.15 (2.28)
District nurse	0.20 (1.36)	0.07 (0.60)	0.17 (1.07)	0.20 (1.53)
Community psychiatric nurse	6.25 (10.58)	6.33 (10.55)	5.24 (7.13)	5.48 (10.80)
Health visitor	0.17 (1.79)	0.15 (1.76)	0.19 (1.30)	0.89 (12.33)
Clinical psychologist	1.05 (3.77)	0.65 (2.97)	0.81 (3.47)	0.58 (1.99)
NHS counsellor	0.29 (2.21)	0.12 (1.64)	0.18 (1.24)	0.05 (0.44)
NHS dentist	0.63 (1.20)	0.78 (1.33)	0.74 (1.54)	0.79 (1.42)
Podiatrist	0.26 (0.81)	0.20 (0.71)	0.22 (0.76)	0.15 (0.61)
Occupational therapist	0.64 (3.53)	0.72 (5.33)	0.32 (1.48)	0.49 (2.60)

TABLE 29 Mean use (SD) of primary and community services in months 1–6 and months 7–12, respectively, by group (*continued*)

Services	BSC		Usual care	
	Months 1–6 ($n = 220$)	Months 7–12 ($n = 214$)	Months 1–6 ($n = 214$)	Months 7–12 ($n = 213$)
Physiotherapist	0.22 (1.83)	0.20 (1.23)	0.19 (1.00)	0.23 (1.27)
CBT	0.19 (1.26)	0.38 (2.27)	0.50 (3.11)	0.18 (1.85)
MBCT	0.24 (1.51)	0.69 (8.26)	0.19 (1.75)	0.13 (0.82)
Crisis team	0.47 (2.41)	1.10 (5.02)	0.59 (2.09)	0.62 (2.04)
CMHT	5.67 (10.54)	4.74 (10.77)	4.91 (8.17)	4.98 (8.31)
Day care service	3.72 (19.56)	4.14 (23.97)	3.64 (19.46)	3.54 (20.89)
Social worker	1.66 (12.68)	0.68 (2.56)	1.23 (5.96)	0.73 (2.62)
Family support worker	0.12 (1.02)	0.76 (7.92)	1.48 (13.17)	1.20 (10.44)
Drug/alcohol support worker	0.73 (8.15)	0.23 (1.68)	0.37 (2.59)	0.46 (2.52)

CBT, cognitive–behavioural therapy; MBCT, mindfulness-based cognitive therapy.

Other services reported by open question In addition to the structured service questions, there were a few participants who reported other services used. These included support worker, psychotherapist, specialist nurse, art therapist, forensic community team, health-care assistant, rehabilitation facility, outreach team, phlebotomist and midwife. The most reported service was support worker. There were 11 participants who reported 578 visits in months 1–6 in the usual-care group and 12 participants who reported 1498 visits in the BSC group. In months 7–12, there were nine participants who reported 611 visits in the usual-care group and nine participants in the BSC group reported 994 visits. Some of these participants reported daily visits by a support worker during the entire period. There was one participant in the usual-care group who stayed in a rehabilitation facility for 171 days and another reported 24 visits to a psychotherapist. The other services were reported by only one or two participants for no more than 10 visits.

According to the additional services reported by the participants, the corresponding unit costs were estimated from published resources (*Table 30*).

Summary of costs of health-care and social services use Applying the unit costs to the quantities reported, the estimated costs of emergency and hospital services were £1443 (SD £6470) per responder in the usual-care group and £932 (SD £4228) per responder in the BSC group in months 1–6 post randomisation (*Table 31*). The estimated costs of primary and community care were £2367 (SD £2893) per responder in the usual-care group and £2529 (SD £3178) per responder in the BSC group in months 1–6 post randomisation. In months 7–12 post randomisation, the estimated costs of emergency and hospital services were £1317 (SD £5330) per responder in the usual-care group and £953 (SD £3027) per responder in the BSC group. During the same period, the estimated costs of primary and community care were £2303 (SD £3234) per responder in the usual-care group and £2429 (SD £3458) per responder in the BSC group.

Participants' prescription of antipsychotics Practices were contacted to extract participants' prescription information on antipsychotic medication. There were 223 (85%) participants for whom prescription information was returned in the usual-care group and 229 (86%) participants for whom prescription information was returned in the BSC group. Of the participants with returned data collection, 207 participants in the usual-care group and 219 participants in the BSC group recorded being prescribed antipsychotics at some point during the trial period. There were 28 participants in the usual-care group and 25 participants in the BSC group who had prescription data that were insufficient for cost estimation. Therefore, the mean NIC of antipsychotic prescription was £736 (SD £1081) per participant among the 195 respondents in the usual-care group and

TABLE 30 Unit cost of other health-care personnel for stop smoking advice, and other health care and social services reported by the participants

Services	Unit cost (2016/17)	Sources
Other health-care personnel for stop smoking advice		
Community psychiatric nurse	£6/10-minute brief advice for smoking	59
Practice nurse	£6/10-minute brief advice for smoking	59
Support worker	£4/10-minute brief advice for smoking	59
Nurse at hospital	£15/10-minute brief advice for smoking	59
Psychiatrist	£18/10-minute brief advice for smoking	59
Family therapist	£6/10-minute brief advice for smoking	59
Other health care and social services		
Dentist	£21	59
Support worker	£13/30-minute visit	61
Early intervention team	£184/contact	61
Psychotherapist	£194/contact	60
Specialist nurse	£64/contact	60
Outreach team	£132/contact	61
Pharmacist	£7/contact	61
Speech and language therapist	£96/one-to-one contact	60
Arts therapist	£40/40-minute contact	61
Forensic community team	£238/contact	60
Health-care assistant	£12/30-minute contact	61
Phlebotomist	£3/contact	60
Midwife	£62/contact	60

TABLE 31 Estimated costs of emergency and hospital services and primary and community care in months 1–6 and months 7–12, by group

	BSC		Usual care	
Services	*n*	Mean cost (SD)	*n*	Mean cost (SD)
Months 1–6				
Emergency and hospital services	211	£932 (£4228)	208	£1443 (£6470)
Primary and community care	220	£2529 (£3178)	214	£2367 (£2893)
Months 7–12				
Emergency and hospital services	203	£953 (£3027)	202	£1317 (£5330)
Primary and community care	214	£2429 (£3458)	213	£2303 (£3234)

£820 (SD £1296) per participant among the 204 respondents in the BSC group, including those reported for whom no antipsychotics were prescribed.

Wider societal costs

Other sources of smoking cessation advice

In addition to the smoking cessation services provided by the NHS and Personal Social Services, the participants reported their use of other sources of help. These included a smoking cessation helpline run by non-NHS

organisations, the internet and books. These were reported by only a small group of participants. The most often used source of advice was the internet. In the 6 months post randomisation, 18 participants reported, in total, 82 times of internet use for advice on smoking cessation in the BSC group, and 22 participants reported a total of 61 times of use in the usual-care group. From 6 months to 12 months post randomisation, 21 participants in the usual-care group reported a total of 86 times of internet use and 16 participants in the BSC group reported 64 times of use. Among them, the highest number of uses appeared in the usual-care group where one participant reported 28 times of use in the 7–12 months post randomisation. It was followed by two participants who reported 25 times of use and 26 times of use in the BSC group in the 6 months post randomisation. The costs of internet use were not estimated because of the lack of details. In the 1–6 months post randomisation, books were used by 18 participants in the BSC group and 10 participants in the usual-care group. In the 7–12 months post randomisation, 10 participants in the BSC group and nine participants in the usual-care group used books. Only two participants in the BSC group and five in the usual-care group called another smoking cessation helpline during the 12-month period.

Participants' out-of-pocket expenses in relation to smoking cessation

Participants were asked about their expenses for the purchase of NRT products, the purchase of e-cigarettes and travel to GP/SSS at the follow-ups.

There were 157 participants (81% of 195 responders) in the BSC group who reported not purchasing any NRT products and 152 participants (77% of 197 responders) in the usual-care group in the 12 months post randomisation. Among the 38 participants who reported any purchase in the BSC group, 27 purchased a single form of NRT product, eight purchased two forms of NRT products and three purchased three forms of NRT products. Among the 45 participants who reported any purchase in the usual-care group, 27 purchased a single form of NRT product, 13 purchased two forms of NRT products and three purchased three forms of NRT products.

Among all the NRT products asked about the most purchased one was the nicotine patch. There were 27 participants who reported purchasing patches in the usual-care group, compared with 14 in the BSC group (*Figure 12*). The next most purchased were the lozenge and mouth spray. There were 12 participants who reported purchase of a lozenge in either group and the purchase of mouth spray was almost the same (11 in the usual-care group and 12 in the BSC group). These were followed by nicotine gum, which was reported by nine participants in the usual-care group and 11 participants in the BSC group. There were five participants who reported purchasing an inhalator in the usual-care group and two in the BSC group. Only one participant reported purchasing nasal spray (in the BSC group). None of the participants reported purchasing microtabs.

Comparing the sources of NRT products in those who had both self-report response and prescription records (132 in the usual-care group and 129 in the BSC group), the majority of the NRT products in the BSC group were acquired on prescription, whereas the usual-care group acquired their NRT products, if any, over the counter. A small number of participants in both groups acquired their products via both prescription and purchase.

Given that the majority of the responders reported no purchase at all during the 12 months post randomisation, the mean amount of purchase of individual forms of NRT products was low and the SD was comparatively large, indicating a skewed distribution of purchase (*Table 32*).

Applying *Table 2* to the quantities in *Table 32*, the mean expense of NRT products was £8 (SD £30) among 209 responders in the usual-care group and £13 (SD £83) among 206 responders in the BSC group in months 1–6 post randomisation. In months 7–12, the mean expense for NRT products was £5 (SD £22) among 209 responders in the usual-care group and £17 (SD £97) among the 214 responders in the BSC group.

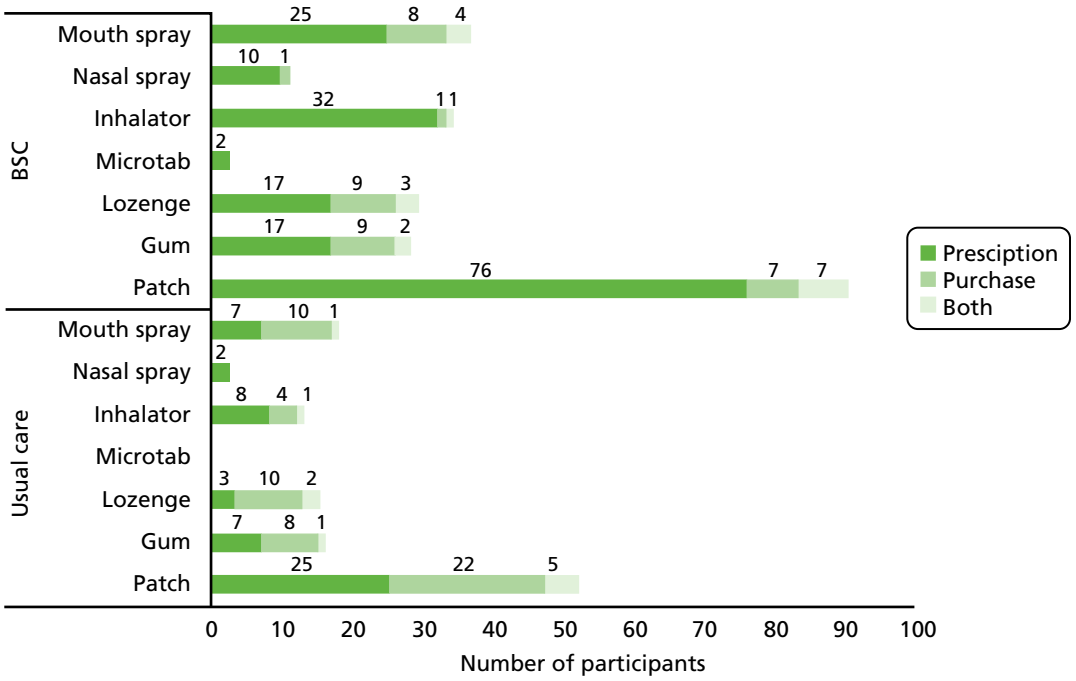

FIGURE 12 Number of participants who acquire NRT products on prescription, purchase or both, by group.

TABLE 32 The mean amount of purchase of NRT products (SD) in months 1–6 and months 7–12, by group

NRT products	BSC, mean (SD)	Usual care, mean (SD)
Months 1–6	**n = *206***	**n = *209***
Patches (pack)	0.02 (0.14)	0.20 (0.90)
Gum (pack)	0.20 (1.79)	0.09 (0.91)
Lozenges (pack)	0.64 (5.97)	0.11 (0.80)
Microtabs (pack)	–	–
Inhaler (bottle)	–	0.08 (0.75)
Nasal spray (bottle)	0.01 (0.21)	–
Mouth spray (bottle)	0.07 (0.57)	0.05 (0.33)
Months 7–12	**n = *214***	**n = *209***
Patches (pack)	0.11 (0.58)	0.19 (1.01)
Gum (pack)	0.02 (0.17)	0.03 (0.22)
Lozenges (pack)	0.62 (5.28)	0.13 (1.16)
Microtabs (pack)	–	–
Inhaler (bottle)	0.01 (0.15)	0.00 (0.07)
Nasal spray (bottle)	–	–
Mouth spray (bottle)	0.35 (3.40)	0.03 (0.21)

There were 136 participants who reported no purchase of e-cigarettes in the usual-care group and 152 participants in the BSC group in months 1–6 post randomisation. In months 7–12, there were 143 participants in the usual-care group and 148 participants in the BSC group who reported no purchase of e-cigarettes. The mean expense of e-cigarettes was £21 (SD £47) among 208 responders in months 1–6 and £21 (SD £59) among 205 responders in months 7–12 in the usual-care group. In the BSC group, the

mean expense on e-cigarettes was £17 (SD £64) among 219 responders in months 1–6 and £19 (SD £68) among 210 responders in months 7–12.

The majority of the responders reported walking as their way of travelling to see their GP or SSS, followed by driving, taking a bus or taking a taxi. Fewer than five responders reported taking trains to see their GP or SSS. In the usual-care group, 173 responders in months 1–6 and 171 in months 7–12 reported no expense on travel. In the BSC group, 187 in months 1–6 and 176 in months 7–12 reported no expense on travel. The mean expense on travel to GP/SSS was £6 (SD £30) among 203 responders in months 1–6 and £3 (SD £11) among 199 responders in months 7–12, in the usual-care group. In the BSC group, it was £3 (SD £12) among 213 responders in months 1–6 and £2 (SD £9) among 205 responders in months 7–12. However, this expense might have been underestimated because some of the participants did not take into account when they used cars and others did.

Health-related quality of life

The EQ-5D-5L was returned by 260 participants in the usual-care group at baseline and 265 participants in the BSC group. The mean VAS score was 54.2 (SD 20.5) in the usual-care group and 54.8 (SD 22.9) in the BSC group. Two participants in the usual-care group had missing items on the descriptive system of EQ-5D-5L and, therefore, utility could not be calculated. Among the rest of the participants, the mean utility was 0.640 (SD 0.304) in the usual-care group and 0.638 (SD 0.280) in the BSC group. At 6 months, 217 participants in the usual-care group and 224 participants in the BSC group returned the questionnaire. The mean VAS score was 55.6 (SD 21.2) in the usual-care group and 58.3 (SD 21.8) in the BSC group. The mean utility was 0.659 (SD 0.307) in the usual-care group and 0.682 (SD 0.269) in the BSC group. At 12 months, 213 participants in the usual-care group and 216 participants in the BSC group returned information. The mean VAS score was 55.9 (SD 20.9) in the usual-care group and 55.8 (SD 23.9) in the BSC group. Three participants in the usual-care group and two in the BSC group had missing items on the descriptive system of EQ-5D-5L. Among the remaining participants, the mean utility was 0.662 (SD 0.306) in the usual-care group and 0.688 (SD 0.275) in the BSC group.

Missing data

The percentage of missing data varies from variable to variable (*Table 33*). As expected, the lowest missing percentage occurs among the variables at baseline. Missing data level ranges between 20% and 30% on participants' self-reported items at follow-ups, which is consistent with the overall follow-up rate of the trial. The highest percentage of missing values is that of the costs of pharmacotherapy prescriptions in the trial period, which was collected from practices directly. This percentage of missing values is 44%; the number of multiple imputations was therefore set to 45. The missing values in the continuous variables were imputed using the predictive mean matching method, with 10 nearest neighbours to draw from. Binary variables were imputed using the logit method.

There were five participants who died before the 6-month follow-up and another two died before the 12-month follow-up. All of them were unable to be followed up at both follow-up points. For those who died before the 6-month follow-up, the costs and expenses in the first 6 months of the trial were to be imputed as others, while the costs and expenses in months 7–12 were set to zero. For the two who died after the 6-month follow-up but before the 12-month follow-up, their costs and expenses were to be imputed as others. The utility and VAS from EQ-5D-5L were set to zero at 6 months and 12 months for those died before the 6-month follow-up, and those who died after 6 months were to have 6-month values imputed but 12-month values set to zero. Other measures including cigarettes per day, alcohol drinking and FTND score were to be imputed conditioned on the death status at that time point.

TABLE 33 Number and percentage of missing data in the variables included in the imputation model

Variables	Number of missing values	Percentage of missing values
Characteristics		
Age	1	0
Gender	0	0
Study centre	0	0
Pre-existing medical condition	4	1
Duration since first diagnosis of SMI	10	2
Duration since start of smoking	2	0
Costs		
Cost of BSC training and supervision	0	0
Cost of BSC delivery	2	0
Cost of usual smoking cessation in 6 months before baseline	9	2
Cost of usual smoking cessation in months 1–6	97	18
Cost of usual smoking cessation in months 7–12	101	19
Costs of pharmacotherapy prescriptions in months 1–12	231	44
Cost of emergency and hospital services in 6 months before baseline	14	3
Cost of emergency and hospital services in months 1–6	107	20
Cost of emergency and hospital services in months 7–12	121	23
Cost of primary and community services in 6 months before baseline	2	0
Cost of primary and community services in months 1–6	92	17
Cost of primary and community services in months 7–12	99	19
Costs of antipsychotics in months 1–12	127	24
Other measures		
Cigarettes per day at baseline	0	0
Cigarettes per day at 6 months	140	27
Cigarettes per day at 12 months	159	30
FTND score at baseline	14	3
FTND score at 6 months	146	28
FTND score at 12 months	171	33
Outcomes		
VAS at baseline	1	0
VAS at 6 months	85	16
VAS at 12 months	97	18
EQ-5D-5L utility at baseline	3	1
EQ-5D-5L utility at 6 months	85	16
EQ-5D-5L utility at 12 months	102	19

TABLE 33 Number and percentage of missing data in the variables included in the imputation model (*continued*)

Variables	Number of missing values	Percentage of missing values
Out-of-pocket expenses		
Travel expenses to GP surgery/stop smoking clinic in 6 months before baseline	21	4
Travel expenses to GP surgery/stop smoking clinic in months 1–6	110	21
Travel expenses to GP surgery/stop smoking clinic in months 7–12	122	23
Purchase of e-cigarette in 6 months before baseline	10	2
Purchase of e-cigarette in months 1–6	99	19
Purchase of e-cigarette in months 7–12	111	21
Purchase of NRT products in 6 months before baseline	13	2
Purchase of NRT products in months 1–6	111	21
Purchase of NRT products in months 7–12	103	20

Analysis

The BSC intervention cost, consisted of a fixed training cost and delivery cost, was estimated at £418 [standard error (SE) £10] per participant. The cost of usual GP care during the trial period was £65 (SE £6) per participant in the usual-care group and £52 (SE £6) per participant in the BSC group. The BSC group received more pharmacotherapies for smoking cessation on prescription than the usual-care group. The mean cost of pharmacotherapies on prescription was £91 (SE £13) in the BSC group, three times the mean cost in the usual-care group [£29 (SE £6)]. The total smoking cessation costs during the trial period were therefore £93 (SE £9) per participant in the usual-care group and £561 (SE £19) per participant in the BSC group.

In the 6 months before randomisation, both groups had similar levels of cost of smoking cessation from usual GP care [£38 (SE £4) vs. £37 (SE £4)]. The mean costs of emergency and hospital services were higher in the BSC group [£2030 (SE £494), compared with £1507 (SE £406) per participant in the usual-care group]. The costs of primary and community services were the first cost drive in both groups, with £2614 (SE £260) per participant in the usual-care group and £2746 (SE £223) per participant in the BSC group. The total health resource use costs were estimated at £4160 (£512) per participant in the usual-care group and £4813 (£548) per participant in the BSC group in the 6 months before randomisation.

Throughout the trial period, primary and community services remained the first cost driver in both groups, with the mean costs never dropping below £2000 per participant, and the mean costs of emergency and hospital services in the same period never reaching this threshold. The mean costs of emergency and hospital services were £1513 (SE £492) per participant and costs of primary and community services were £2391 (SE £204) in the usual-care group in the first 6 months of the trial. In the same period, the mean costs of emergency and hospital services were £982 (SE £285) per participant and costs of primary and community services were £2597 (SE £218) in the BSC group. In the second 6-month period of the trial, the mean costs of emergency and hospital services were £1404 (SE £361) per participant in the usual-care group and costs of primary and community services were £2320 (SE £232). In the BSC group, the mean costs of the mean costs of emergency and hospital services were £1004 (SE £211) per participant and costs of primary and community services were £2504 (SE £245) in the second 6-month period of the trial. The mean cost of antipsychotics on prescription in the trial period was estimated at £768 (SE £81) per participant in the usual-care group and £799 (SE £84) in the BSC group. The total health resource use costs were therefore £8396 (£774) per participant in the usual-care group and £7886 (SE £594) in the BSC group.

In the usual-care group, the mean VAS score was 54.2 (SE 1.3) at baseline, 54.9 (SE 1.9) at 6 months and 55.3 (SE 1.4) at 12 months. In the BSC group, the mean VAS score was 54.8 (SE 1.4) at baseline, 57.3 (SE 1.5) at 6 months and 55.1 (SE 1.6) at 12 months. In the usual-care group, the mean utility value was 0.640 (SE 0.019) at baseline, 0.647 (SE 0.020) at 6 months and 0.654 (SE 0.020) at 12 months. In the BSC group, the mean utility value was 0.638 (SE 0.017) at baseline, 0.670 (SE 0.018) at 6 months and 0.678 (SE 0.019) at 12 months. The mean QALYs were estimated at 0.647 (SE 0.017) in the usual-care group and 0.664 (SE 0.015) in the BSC group.

Primary analysis

There were 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. Without imputing missing data on this outcome, the quit rate at 12 months was 10.0% (SE 2.0%) in the usual-care group and 15.3% (SE 2.4%) in the BSC group. The mean intervention cost among these participants was £93 (SE £9) per participant in the usual-care group and £584 (SE £21) in the BSC group. The mean intervention cost per quitter was £906 (95% CI £612 to £1456) in the usual-care group and £3828 (95% CI £2901 to £5409) in the BSC group. The incremental intervention cost per additional quitter was £9472 (95% CI –£44,016 to £73,503).

Combining costs of smoking cessation and health resource use during the trial period, the total costs were estimated at £8489 (SE £775) per participant in the usual-care group and £8446 (SE £596) per participant in the BSC group (*Table 34*). The mean total costs were similar between groups during the trial period. After adjusting for age, gender, pre-existing medical conditions, duration since first diagnosis of SMI and health resource use costs in the 6 months before randomisation, the adjusted difference in mean total costs was –£270 (95% CI –£1817 to £1297), with the BSC group lower than the usual-care group. Although the unadjusted difference in QALYs between groups was 0.017, after adjusting for the same set of baseline covariates with the exception of replacing health resource use costs with EQ-3D-5L utility value at baseline, the adjusted difference became 0.026 (95% CI –0.008 to 0.045).

With the incremental costs being negative (BSC was less costly) and the incremental QALYs being positive (BSC was more effective), the BSC group dominated the usual-care group and was cost-effective based on the point estimation. However, both incremental costs and incremental QALYs have wide 95% CIs including zero, indicating the presence of high uncertainty.

TABLE 34 Results of primary analysis

Results	BSC ($n = 265$)	Usual care ($n = 261$)
Costs		
Smoking cessation, mean (SE)	£561 (£19)	£93 (£9)
Health resource use, mean (SE)	£7886 (£594)	£8396 (£774)
Total, mean (SE)	£8446 (£596)	£8489 (£775)
Adjusted difference,[a] mean (95% CI)	–£270 (–£1817 to £1297)	
QALYs, mean (SE)	0.664 (0.015)	0.647 (0.017)
Adjusted difference,[b] mean (95% CI)	0.026 (–0.008 to 0.045)	
Incremental cost-effectiveness ratio		
ICER, mean	BSC dominates (uncertainty: *Figure 13*)	

a 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.
b 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.

Sensitivity analysis

Mapping incremental costs and incremental QALYs estimated from 5000 bootstrapped replicates onto the cost-effectiveness plane, *Figure 13a* shows the overall majority (92%) of dots that represented ICERs of the replicates, scattered on the right side of the *y*-axis (zero effect), indicating that the BSC is very likely to achieve higher QALYs. The distribution of these dots in relation to incremental costs is less clear, where 62% are scattered below zero and 38% above. This suggests that the BSC is likely to be cost-saving, but the uncertainty is higher. Taking into account the combination of both, 57% fall in the south-east quadrant, where the BSC group dominates the usual-care group (less costly but more effective). *Figure 13b* is the cost-effectiveness acceptability curve with WTP thresholds at £20,000/QALY and £30,000/QALY as reference line. For the probability of BSC being cost-effective, compared with usual care, although it starts high (> 60%) and rises with the increase of WTP, the increase in the probability shows a trend of becoming smaller. This leads to a gradual upwards curve and almost flat line close to 90%.

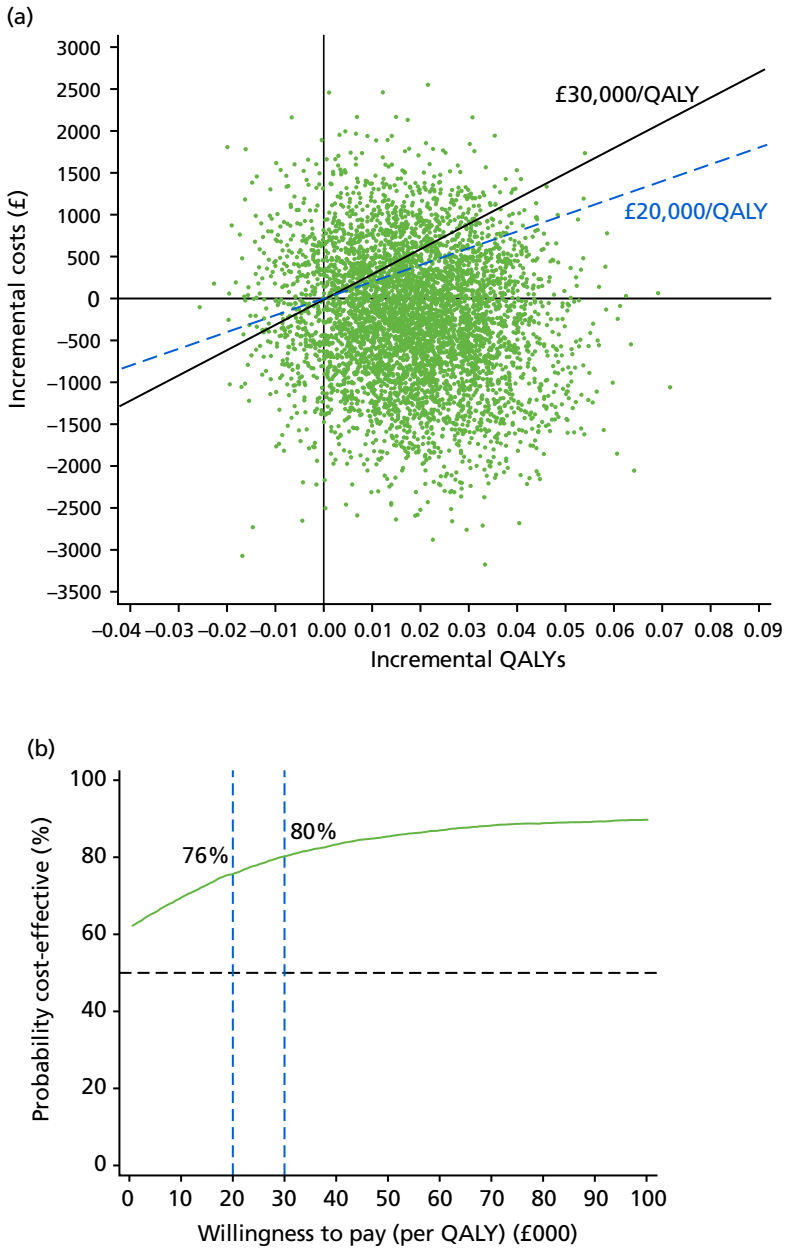

FIGURE 13 Cost-effectiveness plane and cost-effectiveness acceptability curve of primary analysis results. (a) Cost-effectiveness plane; and (b) cost-effectiveness acceptability curve.

Complete-case analysis

Taking into account the outcome measures and baseline variables for adjustment, there were 80 participants in the usual-care group and 88 participants in the BSC group included in the complete-case analysis. The intervention cost was similar in the usual-care group between primary analysis (£93, SE £9) and complete-case analysis (£92, SD £128) while in the BSC group it was slightly higher in complete-case analysis (£593, SD £338) than in primary analysis (£561, SE £19). In the usual-care group, the mean costs of health services were £4822 (SD £7881) in the 6 months before randomisation, £3440 (SD £3745) in months 1–6 of the trial and £4293 (SD £8490) in months 7–12 of the trial, in complete-case analysis. In the BSC group, the mean costs of health services were £4594 (SD £7449) in the 6 months before randomisation, £3599 (SD £4173) in months 1–6 of the trial and £3555 (SD £5078) in months 7–12 of the trial, in complete-case analysis. The difference between primary analysis and complete-case analysis was more prominent in the usual-care group than in the BSC group.

For the BSC group, the mean costs in complete-case analysis did not vary from those in primary analysis by much. For the usual-care group, however, the mean costs became higher than those in primary analysis in the 6 months before randomisation and months 7–12 of the trial, and were lower than in primary analysis in months 1–6 of the trial. This change led to a reverse of the relative position when comparing between groups and the reduction of the difference in the 6 months before randomisation and months 1–6 of the trial. In the second 6-month period of the trial, although the mean costs of health services were still higher in the usual-care group, the difference between the mean costs in the two groups was widened.

For EQ-5D-5L utility value, the pattern of change was more consistent. In complete-case analysis, the mean utility value was 0.595 (SD 0.319) at baseline, 0.612 (SD 0.336) at 6 months and 0.641 (SD 0.303) at 12 months in the usual-care group, while it was 0.661 (SD 0.257) at baseline, 0.686 (SD 0.254) at 6 months and 0.684 (SD 0.262) at 12 months in the BSC group. Although in the usual-care group the mean utility values were always lower in complete-case analysis than in primary analysis, the BSC group was the opposite.

The mean total cost was £911 (95% CI –£2769 to £2631) higher in the BSC group than in the usual-care group, after adjusting for costs of health resource use in the 6 months before randomisation, age, gender, pre-existing medical conditions and duration since first diagnosis of SMI (*Table 35*). The mean QALYs were 0.008 (95% CI –0.030 to 0.074) higher in the BSC group than in the usual-care group, after adjusting for utility value at baseline, age, gender, pre-existing medical conditions and duration since first diagnosis of SMI. The ICER ratio was therefore £113,875 (uncertainty: *Figure 14*) per QALY gained.

TABLE 35 Results of complete-case analysis

Results	BSC ($n = 88$)	Usual care ($n = 80$)
Costs		
Smoking cessation, mean (SD)	£593 (£338)	£92 (£128)
Health resource use, mean (SD)	£7741 (£8649)	£8437 (£11,386)
Total, mean (SD)	£8434 (£8642)	£8530 (£11,405)
Adjusted difference,[a] mean (95% CI)	£911 (–£2768 to £2631)	
Quality of life		
QALYs, mean (SD)	0.679 (0.219)	0.615 (0.283)
Adjusted difference,[b] mean (95% CI)	0.008 (–0.030 to 0.074)	
Incremental cost-effectiveness ratio		
ICER, mean	£113,875 (uncertainty: *Figure 14*)	

a 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.
b 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.

Compared with the primary analysis, *Figure 14a* shows the dots scattered more widely on the cost-effectiveness plane, indicating a higher level of uncertainty. The BSC is still likely to achieve higher QALYs as 79% of the dots fall to the right side of *y*-axis. The difference in costs, however, almost disappears as about half (49%) fall below zero. Only 39% of the dots fall in the south-east quadrant, suggesting a less costly but more effective intervention. The cost-effectiveness acceptability curve demonstrates that the probability of the intervention being cost-effective was 61–65% between £20,000 and £30,000 per QALY (see *Figure 14b*). Similar to the primary analysis, the increase of the probability becomes smaller the higher the WTP gets, and flattens close to 80%.

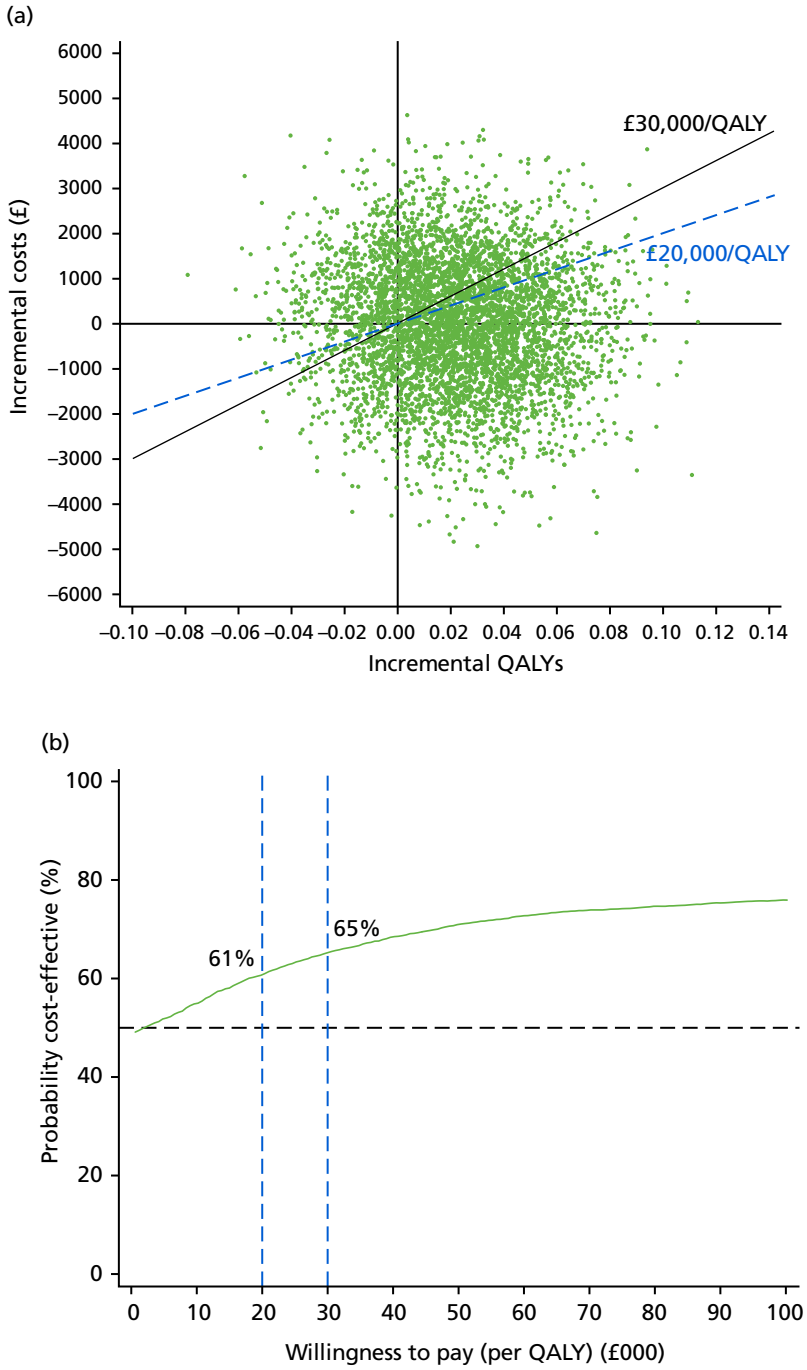

FIGURE 14 Cost-effectiveness plane and cost-effectiveness acceptability curve of complete-case analysis results. (a) Cost-effectiveness plane; and (b) cost-effectiveness acceptability curve.

Secondary analysis

Participants' expenses

In months 1–6 of the trial, the participants' expenses on travel were estimated at £5 (SE £2) per participant in the usual-care group and £3 (SE £1) in the BSC group. In months 7–12, it was £3 (SE £1) in the usual-care group and £2 (SE £1) in the BSC group. In months 1–6, the participants in the usual-care group spent on average £22 (SE £3) per person on e-cigarettes, while the participants in the BSC group spent on average £16 (SE £4) per person. In months 7–12, the expense on e-cigarette was £23 (SE £4) per participant in the usual-care group and £20 (SE £5) per participant in the BSC group. The expense on NRT over the counter was £8 (SE £2) per participant in the usual-care group and £12 (SE £5) per participant in the BSC group, in the first 6 months of the trial. In the second half of the trial, this expense was £6 (SE £2) per participant in the usual-care group and £16 (SE £6) per participant in the BSC group. The total expenses during the trial period were £67 (SE £8) per participant in the usual-care group and £70 (SE £11) per participant in the BSC group. In comparison with the huge health resource use costs, the participants' expenses were almost negligible.

Financial impact of smoking cigarettes

Excluding seven people who died during the trial period, there were 262 participants in the BSC group and 257 in the usual-care group as the basis for estimating the expenses on cigarettes. The average numbers of cigarettes per day were 17.6 (SE 0.9) in the 1–6 months post randomisation and 19.7 (SE 0.8) in the 7–12 months post randomisation in the BSC group. In the usual-care group, average cigarettes per day were 18.5 (SE 0.7) in the 1–6 months post randomisation and 18.5 (SE 0.8) in the 7–12 months post randomisation. Assuming the number of cigarettes smoked per day was the average over the recall period and did not vary day to day, an estimated price of £9.37 per 20 cigarettes was applied to estimate the expenses.[71] The estimated expenses on cigarettes over 6 months were over £1500 per participant in the usual-care group [£1590 (SE £69) and £1596 (SE £70)]. In the BSC group, the estimated expenses were £1516 (SE £76) per participant in the first half of the trial and £1691 (SE £72) per participant in the second. Overall, smoking would add £3186 (SE £111) per person per year to the participants' cost in the usual-care group and £3207 (SE £128) per person per year in the BSC group.

Antipsychotics among quitters and non-quitters

Without imputing missing smoking status, there were 344 participants in total who had complete data on CO-verified smoking status at both follow-ups and cost of antipsychotics in the trial period. Owing to the incompliance to normality, a Wilcoxon signed-rank test was used to access if the cost of antipsychotics differed from the first half of the trial to the second. *Table 36* presents the mean cost of antipsychotics according to participants' CO-verified quit status. There were 286 participants who did not quit at both follow-ups, 14 quit at 6 months but relapsed at 12 months, 23 did not quit at 6 months but quit at 12 months and 21 quit at both follow-ups. Except for the first category, there was no evidence of significant change between the first and the second half of the trial. However, this might be because limited numbers of participants fell into these categories. The participants who did not quit at any time showed an increased cost on antipsychotics ($p = 0.0018$).

TABLE 36 Cost of antipsychotics over 6-month periods, by CO-verified quit status

CO-verified quit status at 6- and 12-month follow-ups	Cost of antipsychotics [£, mean (SD)]		
	Months 1–6	Months 7–12	Wilcoxon signed-rank test
Not quit at both follow-ups ($n = 286$)	353 (509)	369 (511)	$z = 3.119$; $p = 0.0018$
Quit at 6 months but not at 12 months ($n = 14$)	246 (212)	243 (216)	$z = -0.372$; $p = 0.7100$
Not quit at 6 months but at 12 months ($n = 23$)	324 (409)	248 (418)	$z = 1.683$; $p = 0.0924$
Quit at both follow-ups ($n = 21$)	582 (929)	713 (1298)	$z = 0.245$; $p = 0.8061$

Discussion

This study collected extensive data to provide a comprehensive picture of costs to the NHS and Personal Social Services in this population. The mean intervention cost per quitter in the BSC group was around four times the mean intervention cost per quitter in the usual-care group (£3828 vs. £906). Although the cost per quitter of SSS in the general population was £690 per quitter for CO-validated 4-week quit in 2017/18 in England where data are available,[72] this could not be compared directly. Our study offered a more flexible timeline to suit the needs of people with SMI and, therefore, did not measure 4-week smoking status. The participants in the usual-care group showed a more active engagement with usual smoking cessation services, especially in months 1–6 of the trial. This is understandable as the participants in the BSC group would have mostly been engaging with the intervention during that period while the help-seeking behaviour in the usual-care group might have been triggered by participation in the trial. Both groups became less engaged with usual-care services in months 7–12.

The use of various health-care and social services was highly intensive. The costs of primary and community services were the largest component of the overall costs. These costs were relatively stable from before the trial to the end of the trial and did not change significantly during the trial, indicating this population's constant demand for community support. The lower total costs of the BSC group were mainly the results of the consistently lower costs of emergency and hospital services during the trial and higher costs in the 6 months before the trial, while the costs of emergency and hospital services remained on the same level in the usual-care group. This difference in costs of emergency and hospital services was probably related to the higher frequency and longer stay of hospital admission in the usual-care group than in the BSC group. However, it is unclear if this difference is related to the intervention or smoking status, or if it happened by chance. As the use of services was collected through self-report, the possibility of recall bias should be kept in mind when interpreting the results.

The data on prescriptions of antipsychotics and pharmacotherapies for smoking cessation were extracted from participants' medical records. The information collected through this approach was more reliable and accurate than participants' self-report, especially when there were multiple medicines involved. However, the information on prescriptions was completely missing for some participants because of the closure or lack of capacity of their general practices. Although attempts were made to ensure a uniform extraction of data, there were still discrepancies among data returns. As a result, clinic supervision and therefore staff cost necessitated by some antipsychotics [e.g. clozapine (Clozaril®, Sandoz Pharmaceuticals)] were not included in the analysis as individual visits to the clinic could not be identified for all participants. For the same reason, the prescription charge was also not included in the participants' expenses as individual prescription items were not always identifiable. The cost of pharmacotherapies for smoking cessation might be overestimated. As we extracted data from GPs' prescription records, it should be noted that not all people redeem their prescriptions.

With the development and increased accessibility of the internet, people become rapidly used to seeking information online. The level and costs of smoking cessation help available online vary. The publicly available information provided by the NHS or charities costs only individuals' internet charge, whereas the private organisations might offer more intensive online treatment for a fee. It is not clear if this particular population has a preference for internet use or not and to what extent they rely on the internet for smoking cessation help. A brief browse of free information might be negligible in terms of costs but more intensive help could add to participants' financial burden.

Both groups had an upwards trend of EQ-5D-5L scores, although the BSC group's increase was more drastic. This resulted in the positive QALY gains of the BSC intervention. This might be related to the lower frequency and shorter stay of hospital admission in the BSC group. Both appeared to reflect a better general health of the participants in this group. However, within such a short period, participants' smoking status, successfully quit or not, is unlikely to have contributed to their better general health.

A disadvantage of collecting comprehensive service use data is that data are more likely to be missing because of the length of the questionnaire. However, owing to a high follow-up rate, the missing data level was not unacceptably high. When comparing primary analysis (multiple imputation of missing data) and complete-case analysis (remove all incomplete observations), it appears that missing data on costs have a larger impact on costs in the usual-care group than in the BSC group. The impact of missing data on EQ-5D-5L is less straightforward. In the usual-care group, it appears that the participants who managed better dropped out, whereas in the BSC group the participants who did not do well were the source of missing data.

The biggest impact of smoking on the individual's private costs came from purchase of cigarettes itself. On average, the participants in the in the trial were estimated to spend > £3000 per year on cigarettes and there did not appear to be any difference between groups. Because the amount of money spent on cigarettes was estimated based on the data collected at three time points, the change in smoking patterns in between was not captured. The assumption of unchanging number of cigarettes per day throughout the estimated period might not hold. Another thing to keep in mind is that we estimated the expenses on smoking by converting all tobacco to cigarettes and costing it based on market price of manufactured cigarettes. This might lead to an overestimate as there are cheaper options available for purchasing tobacco. Although there were some participants purchasing e-cigarettes during the trial, the expenses did not appear significant in comparison to those of cigarettes. Previous evidence has recommended that people with SMI could reduce their antipsychotics intake if they stop smoking. Although the results showed that the participants who smoked throughout the trial had a significant increase in their costs of antipsychotics, the current study did not find evidence to support the reverse situation. One of the reasons might be that there were insufficient numbers of quitters in the trial to draw meaningful conclusions. Moreover, the quit status was measured by asking the question 'have you smoked in the last week', which is not a measure of abstinence. Clinical guidelines suggest that if a person makes a quit attempt their antipsychotic medication should be closely monitored as smoking affects the way these drugs are metabolised and the person may need to reduce their antipsychotic medication and if they subsequently relapse back to smoking their dose of antipsychotic medication may need to be increased. Finally, this comparison was undertaken based on the participants whose costs of antipsychotics and smoking status were both available. There is a possibility of selection bias.

The primary analysis showed a higher than 50% probability of the BSC intervention being cost-effective, compared with usual care, at a WTP threshold of £0 per QALY gained. This was largely attributable to the lower level of health-care services costs offsetting the intervention costs in the BSC group and a QALY gain with relatively high level of certainty. Although the likely cost-saving effect in the primary analysis disappeared in the complete-case analysis, the offset effect remained. This suggested that in the complete-case analysis, the mean health-care services costs in the BSC group remained lower than those in the usual-care group. Given that the primary outcome of CO-validated quit at 12 months post randomisation did not show a statistical significance, it could raise concerns over the more favourable results of the economic evaluation. As a perfect association between smoking status and health services and quality of life is not expected in 1 year, it is possible that the analysis shows a better outcome in terms of costs and QALYs. However, unless there were some unknown factors in participants' life affected by the intervention that could be identified later, the result of this study might be hard to generalise.

Conclusion

The BSC intervention for people with SMI is likely (57%) to dominate usual GP care, from a NHS and Personal Social Services perspective. Although neither the difference in costs nor in QALYs was statistically significant, the probability of cost-effectiveness could reach 80% at a threshold of £30,000 based on the primary analysis and 65% based on the complete-case analysis. However, it remains uncertain whether or not this was the result of smoking cessation, as the smoking status at 12 months did not show a significant difference between groups. Furthermore, the impact of smoking cessation on health and wider health services use is unlikely to be observed in a short period of 12 months. A longer-term follow-up would be ideal to observe the sustainability of quit and impact on health.

Chapter 6 Discussion

Some of the information in this section is reported in Peckham *et al.*[1] This contains information licensed under the Non-Commercial Government Licence v2.0.

This report presents the results of the first UK trial of a BSC intervention designed specifically for people with SMI. The SCIMITAR+ trial was commissioned by the National Institute for Health Research Health Technology Assessment programme in view of the clinical need of this population and the widening health inequalities that exist in relation to smoking and smoking-related illness. We have previously reported the results of the SCIMITAR pilot trial, which demonstrated acceptability but was not sufficiently powered to estimate clinical effectiveness and cost-effectiveness. The SCIMITAR programme has followed a developmental pathway to produce a feasible intervention to the point where we were able to judge the value of an evidence-informed smoking cessation intervention within the context of a definitive trial. We drew on existing evidence (taken from high-quality systematic reviews) of 'what works' in helping people to cut down or quit smoking.[23] In linked work, we have also conducted a systematic review of 'what works' in relation to people with SMI, and have shown that the same pharmacological and behavioural approaches to smoking cessation are effective among people with SMI as with the rest of the population.[39,40] Despite this evidence, it is clear that people with SMI do not access conventional NHS quit smoking services, and a coherent response is to design a service and intervention that ensures that evidence-supported pharmacotherapies and behaviour change techniques are applied with specific reference to the needs of people with SMI.

The BSC intervention at the centre of the SCIMITAR+ trial was designed to address the unmet needs of and barriers to accessing smoking cessation interventions for this population. We will now review the main findings and address the main objectives of the SCIMITAR+ trial in turn.

Main findings

The main finding of the SCIMITAR+ trial is that smoking cessation can be achieved among people with SMI, and that, in people who express a desire to quit smoking, the use of a BSC intervention increased the chances of sustained quitting as estimated by a gold-standard biologically verified outcome measure (exhaled CO).[73] The observed odds of successful quitting at 12 months was higher among those who received BSC but this was not statistically significant. However, the observed odds of successful quitting at 6 months were higher among those who received BSC and this was statistically significant. The SCIMITAR+ trial used quitting as measured at 12 months post randomisation as its primary end point, and although there was a trend in favour of the BSC intervention, the difference in quit rates was no longer statistically significant at 1 year. This finding is in line with research in the general population, which shows that long-term quit rates are difficult to achieve, and this remains a challenge for the wider evidential basis of treatment for nicotine dependence in any population.[74] The results of the effect of the BSC intervention were seen in secondary outcomes, and we found an improvement in short-term physical health (as measured by the SF-12) and some evidence of reduced numbers of cigarettes smoked per day and increased motivation to quit. We also found that there were no between-group differences on measures of mental health, including depression and anxiety, supporting the notion that offering a smoking cessation intervention is not detrimental to mental health.

To our knowledge, this is the first large-scale UK RCT of a bespoke intervention designed for people with SMI. Trials to date have been small scale and with short periods of follow-up, and have focused on pharmacological treatments, with limited consideration of behavioural approaches.[40] The SCIMITAR+ trial adapted and enhanced an evidence-supported smoking cessation strategy that has been developed and forms the mainstay of successful UK SSSs. This structured intervention was delivered by a mental health professional and a 'cut down to quit' approach was also offered. The results of the SCIMITAR+ trial,

alongside trials[35] and systematic review evidence[34,39,40] of the safety and effectiveness of pharmacological treatments for nicotine dependence in people with SMI, represents accumulating evidence of the effectiveness of smoking cessation interventions for people with severe mental ill health. Across both arms of the trial, people smoked a higher number of cigarettes per day and had a higher mean number of years of smoking history than those in the general population (25.5 per day compared with 11.3 per day in the general population).[75] This adds to the justification for the need to intervene and develop new and novel interventions for this population.

Is the treatment acceptable to participants?

The SCIMITAR+ trial found that participants generally engaged with BSC services. The levels of engagement were high, with 88% taking up treatment and with an average of six sessions attended. In an earlier qualitative evaluation conducted in the developmental phase of the SCIMITAR pilot trial, it was found that participants valued the fact that smoking cessation therapists were drawn from staff working within mental health services.[76] Smoking cessation practitioners therefore had a familiarity with SMI and the specific needs of that group, and this was seen as a positive aspect of the intervention by participants. By addressing these factors, the participants felt that their smoking was more readily addressed and they felt less stigmatised than might have been the case in conventional services. Participants were attracted to a service that offered the prospect of cutting down prior to quitting and they appreciated the opportunity to receive NRT prior to setting a quit date. In the control group, there was a lack of engagement with conventional NHS quit smoking services despite control participants being given smoking cessation literature and encouraged to visit their GP or NHS quit smoking service. The intervention was clearly more intensive than what would be offered in conventional NHS services, and the overall cost of BSC was higher than usual care.

Within the SCIMITAR+ trial, participants were encouraged to choose an appropriate form of smoking cessation medication in collaboration with their GP. The mainstay of treatment was NRT and only a small number of participants were prescribed varenicline. None was prescribed bupropion. There were, however, some difficulties observed within the trial with regard to access to NRT, partly because provision (e.g. via SSSs, local councils or GP practices) varied across the trial sites. In some settings, access to provision was restricted, either by a requirement to attend all elements of a SSS provision or by restricting access to specific groups (e.g. pregnant women, those with respiratory disorders). Where this occurred this was often driven by funding being linked with smoking cessation accruals, and through discussions with services it was possible to access NRT provision, without accessing behavioural intervention components provided by the service, once a mechanism was implemented to provide accruals data to the relevant organisation. In some locations it was, however, almost impossible for participants to receive NRT through local provision and in the limited number of cases where this could not be facilitated, NRT was prescribed by the secondary care provider as is recommended by the 2013 NICE guidance on smoking cessation provisions for people with mental ill health,[17] which recommends that mental health services make this provision for smokers who use their services. Where NRT was provided, in some instances only one product was prescribed, and in some cases the preferred product identified by the patient in discussion with the smoking cessation practitioner was not prescribed. In both instances this was often attributed to cost implications. There were also some delays in initial prescribing that resulted in participants having to delay their quit attempt. These delays or changes in prescribing had potential to demoralise patients and so reduce their interest in and willingness to make a quit attempt. It is important to note that this was not observed within the trial. NRT was also often not prescribed as a repeat medication or was prescribed only for a fixed duration, which had an impact on longer-term abstinence from smoking. Contact with GPs, councils or SSSs by members of the core SCIMITAR+ trial team helped to identify and to facilitate implementation of methods or routes to remove barriers and so to enable access to NRT provision. Previous qualitative interview data have shown that GPs can be reluctant to prescribe smoking cessation products other than NRT, and, as described, this was evident in the SCIMITAR+ trial. GPs therefore welcomed this direct contact as this enabled the team to provide assurance that GPs would retain oversight for their patient's care, and to directly tackle concerns or misconceptions with regard to prescribing of pharmacological treatments for patients with SMI.

The advice from the NCSCT regarding e-cigarettes when the SCIMITAR+ trial began in 2015 was that, if people wished to use e-cigarettes in their quit attempt specific advice on their use should not be given, but that behavioural support could still be provided (NCSCT, 2015, personal communication). This was the advice that was followed when the trial began. MH-SCPs in the trial neither encouraged nor discouraged the use of e-cigarettes. A subsequent briefing produced by the NCSCT, *Electronic cigarettes: A Briefing for Stop Smoking Services*,[77] led to a change in the advice MH-SCP gave and although they could not provide advice on which e-cigarette to use, they did give more information about e-cigarettes in line with NCSCT guidance. This updated advice was published towards the end of the recruitment period and, therefore, only the participants recruited towards the end of the trial were given the amended advice. This may have resulted in fewer participants using e-cigarettes than would be the case if the trial was conducted now.

Is bespoke smoking cessation cost-effective?

The results of the SCIMITAR+ trial provide preliminary evidence that a BSC intervention is likely to be cost-effective in terms of total health-care costs and quality of life. However, it is uncertain if this conclusion is the result of the intervention as an approach to nicotine dependence for people with SMI.

The BSC intervention for people with SMI probably dominates usual GP care, from a NHS and Personal Social Services perspective. Depending on the relevant WTP threshold, the probability of cost-effectiveness could be higher (80% at £30,000). Although neither difference in total costs nor difference in QALYs was significant, there is an indication that the reduction of health-care services costs might offset the intervention costs.

Limitations of the SCIMITAR+ trial

There were limitations to the SCIMITAR+ trial. First, we lost 16% of participants to follow-up, but note that this was better than we achieved in our pilot trial[43] and that there was non-differential loss to follow-up. Second, a lower 12-month cessation rate was observed in the usual-care group than was hypothesised in the sample size calculation (10% vs. 20%), and the actual percentage increase was lower (5 vs. 14 percentage points). Therefore, although the trial recruited more participants than originally planned and the loss to follow-up rate was lower (16% vs. 20% hypothesised), the trial was ultimately underpowered to detect a difference in quit rates from 10% to 15%. Third, we noted difficulties in ensuring that some participants received pharmacological treatment, as are detailed previously. Given that smoking is the single most modifiable risk factor for early mortality, we recommend that local services have in place robust mechanisms to remove barriers to the provision of medication both when implementing the results of the SCIMITAR+ trial and to support smoking cessation more generally. Last, we were not able to ensure that all follow-up was blind to treatment allocation. However, we also put in place a biochemically verified end point that is less susceptible to observer biases.

Given the trial could not conclude that the intervention is effective in terms of smoking cessation at 12 months, it is uncertain if the result of the economic evaluation was associated with cessation itself. It is possible that the intervention triggered some changes in aspects other than smoking behaviour, which had a positive impact on health, or the differences in health-care costs occurred by chance. In addition, we lacked the capacity to conduct a longer follow-up and a well-correlated relationship between smoking status and health is not expected in the short term.

Conclusions

In the face of significant health inequalities for people with SMI, smoking is the most important modifiable risk factor for poor health and reduced life expectancy.[78] At 12 months we did not find a statistically significant difference between the intervention and usual care; however, we did find that there was an increased quit rate in the intervention at 6 months. Quitting smoking did not appear to have had any

impact on mental health and there were no statistically significant differences between PHQ-9 scores in the intervention and control group at 6 or 12 months. Those in the intervention group had a slightly higher number of quit attempts than those in the usual-care arm.

In this trial, we have shown that people with SMI more readily engage with a bespoke intervention that results in increased 6-month quit rates; however, this difference was not sustained at 12 months. Further research is needed to establish how long-term quitting can be supported.

Implications for health care

Clinicians are sometimes reluctant to offer smoking cessation advice to patients under their care and this is in part because of concerns that treatment is ineffective, or that quitting might cause deterioration in mental health. The results of the SCIMITAR+ trial will be helpful in informing clinical practice, as we have shown that quitting can be achieved for people who use mental health services just as it can for all smokers. As per Public Health Guidance 48,[17] clinicians should ask all of their patients about smoking status and offer referral to effective smoking cessation services. The SCIMITAR+ intervention could provide a candidate model for such a service. The results of this trial will provide clinicians with increased confidence that smoking cessation is likely to be either beneficial or not harmful to mental health.

The SCIMITAR+ trial experienced a range of difficulties in procuring NRT provision for participants ahead of, or during, their quit attempt. Given that smoking is the single most modifiable risk factor for early mortality, both within the general and SMI populations, it is suggested that policy and practice should be reviewed and revised so as to facilitate ease of access to NRT for any person wishing to make a smoking cessation attempt. Ensuring adequate provision to support smoking cessation is likely to reduce NHS expenditure in the longer term, by virtue of limiting potential for comorbidities attributable to tobacco use. Furthermore, consideration should be given to ensuring sufficient provision to ensure that a quit attempt is sustained; this is particularly imperative for SMI patients where additional support may be required.

The results of the SCIMITAR+ trial will be helpful for service commissioners who seek to implement guidance for smoking cessation among hard-to-reach groups, such as people with SMI.[79]

Recommendations for future research

Following on from the SCIMITAR+ trial, further research is needed to establish how quitting can be sustained among people with SMI who engage with an evidence-supported quit smoking intervention.

In addition, although the SCIMITAR+ trial explored the use of e-cigarettes, we suggest that research is needed to evaluate the role of e-cigarettes in helping people with SMI to cut down or to quit smoking.

Additional research is also needed to complement the findings of the SCIMITAR+ trial, specifically to establish the clinical effectiveness and cost-effectiveness of very brief opportunistic interventions for smoking cessation among people with SMI, such as people with SMI being offered advice on giving up smoking in a routine appointment or other opportunistic encounter with a clinician.[80]

It may also be useful to explore NRT update and the barriers to this in this population through qualitative research.

In future trials, conducting a process evaluation to analyse aspects of the intervention that did not work, for which groups and in which contexts, may be helpful.

It may be helpful to explore if there are other factors that affect the health of people with SMI and that can be influenced by a BSC intervention.

Finally, in order to capture the whole impact of smoking cessation intervention in this population, a long-term follow-up is needed to establish the cost-effectiveness.

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Trial Steering Committee members

Professor Ann McNeil (Independent Chairperson), Professor of Tobacco Addiction, King's College London, London, UK.

Dr Andrew Elmslie, Consultant Psychiatrist, Tees, Esk and Wear Valleys NHS Foundation Trust, York, UK.

Dr David Shiers, Retired GP, North Staffordshire, UK.

Mr David Waldram (Service User Representative).

Data Monitoring and Ethics Committee members

Professor Mike Crawford (Chairperson), Professor of Mental Health Research, Imperial College London, London, UK.

Dr Elena Ratschen, Lecturer in Epidemiology/Tobacco Control, Faculty of Medicine and Health Sciences, University of Nottingham, Nottingham, UK.

Professor Richard Emsley, Professor of Medical Statistics and Trials Methodology, King's College London, London, UK.

Hazel Cheeseman, Director of Policy, Action on Smoking and Health, London, UK.

Contributions of authors

Emily Peckham and **Simon Gilbody** wrote the original protocol.

Catherine Arundel, **Della Bailey**, **Suzanne Crosland**, **Caroline Fairhurst**, **Paul Heron**, **Catherine Hewitt**, **Jinshuo Li**, **Steve Parrott**, **Tim Bradshaw**, **Michelle Horspool**, **Elizabeth Hughes**, **Tom Hughes**, **Suzy Ker**, **Moira Leahy**, **David Osborn**, **Joseph Reilly**, **Diane Brennan** and **Simon Gilbody** refined the protocol.

Catherine Arundel, **Suzanne Crosland**, **Tayla McCloud**, **Paul Heron** and **Thomas Steare** were trial co-ordinators for the study.

Tayla McCloud, **Thomas Steare**, **Emma Ballantyne**, **Polly Bidwell**, **Susan Bonner**, **Diane Brennan**, **Tracy Callen**, **Alex Carey**, **Charlotte Colbeck**, **Debbie Coton**, **Emma Donaldson**, **Kimberley Evans**, **Hannah Herlihy**, **Wajid Khan**, **Lizwi Nyathi**, **Elizabeth Nyamadzawo**, **Helen Oldknow**, **Jamie Rea**, **Crystal-Bella Romain-Hooper**, **Kaye Smith**, **Alison Stribling** and **Carinna Vickers** recruited participants to the study, provided feedback on the recruitment methods and helped refine the study procedures.

Peter Phiri and **Shanaya Rathod** helped refine the study procedures.

Emily Peckham, **Catherine Hewitt**, **Steve Parrott**, **Tim Bradshaw**, **Elizabeth Hughes**, **Tom Hughes**, **Suzy Ker**, **Moira Leahy**, **David Osborn**, **Joseph Reilly** and **Simon Gilbody** were co-applicants on the Health Technology Assessment application.

Emily Peckham was the trial manger.

Della Bailey supervised the delivery of the intervention.

Caroline Fairhurst conducted the clinical analysis.

Catherine Hewitt oversaw the conduct of the analysis.

Jinshuo Li designed and undertook the economic analysis in conjunction with **Steve Parrott**.

Simon Gilbody was the chief investigator and oversaw the study.

Emily Peckham, **Catherine Arundel**, **Della Bailey**, **Suzanne Crosland**, **Caroline Fairhurst**, **Paul Heron**, **Jinshuo Li** and **Simon Gilbody** were the writing team.

All authors read and reviewed the transcript.

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Data-sharing statement

All data requests should be submitted to the corresponding author for consideration. Access to available anonymised data may be granted following this.

Patient data

This work uses data provided by patients and collected by the NHS as part of their care and support. Using patient data is vital to improve health and care for everyone. There is huge potential to make better use of information from people's patient records, to understand more about disease, develop new treatments, monitor safety, and plan NHS services. Patient data should be kept safe and secure, to protect everyone's privacy, and it's important that there are safeguards to make sure that it is stored and used responsibly. Everyone should be able to find out about how patient data are used. #datasaveslives You can find out more about the background to this citation here: https://understandingpatientdata.org.uk/data-citation.

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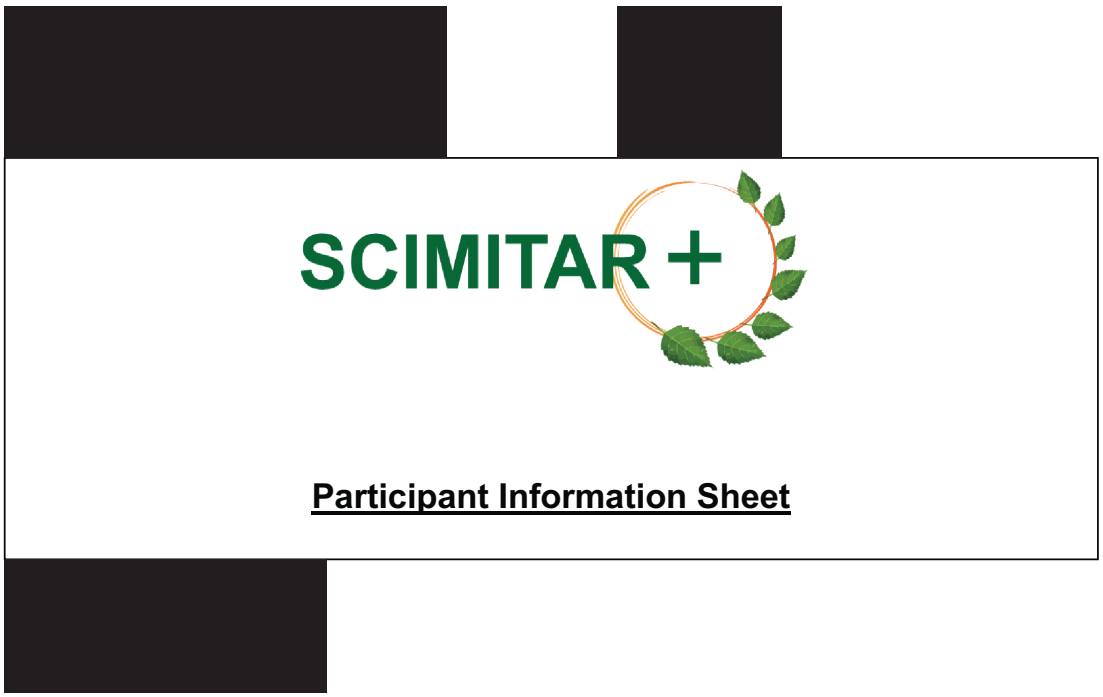
Appendix 1 Regulatory approvals

Trust	Date research and development approval granted
2gether NHS Foundation Trust	5 February 2016
Berkshire Healthcare NHS Foundation Trust	14 December 2015
Bradford District Care NHS Foundation Trust	18 February 2016
Cambridgeshire and Peterborough NHS Foundation Trust	27 April 2016
Camden and Islington NHS Foundation Trust	5 February 2016
Greater Manchester West Mental Health NHS Foundation Trust	25 November 2015
Kent and Medway NHS and Social Care Partnership Trust	1 October 2015
Lancashire Care NHS Foundation Trust	29 February 2016
Lincolnshire Partnership NHS Foundation Trust	28 September 2015
Leeds and York Partnership NHS Foundation Trust	5 January 2016
Northumberland, Tyne and Wear NHS Foundation Trust	27 June 2016
Oxford Health NHS Foundation Trust	30 March 2016
Rotherham, Doncaster and South Humber NHS Foundation Trust	22 October 2015
Sheffield Health and Social Care NHS Foundation Trust	12 October 2015
Solent NHS Trust	28 January 2016
Somerset Partnership NHS Foundation Trust	8 June 2016
South Essex Partnership University NHS Foundation Trust	29 March 2016
Southern Health NHS Foundation Trust	15 October 2015
South West Yorkshire NHS Foundation Trust	2 November 2015
Sussex Partnership NHS Foundation Trust	14 September 2015
Tees, Esk and Wear Valleys NHS Foundation Trust	9 November 2015
Vauxhall Health Centre (formerly Liverpool Primary Care Trust)	11 April 2016

Appendix 2 Patient information sheet and consent form



- We would like you to take part in a research study. Before you decide, you need to understand why this study is being done and what it will involve for you.
- Please take time to read the following information carefully.
- Talk to others about the study if you wish.
- Ask us if there is anything that is not clear or if you would like more information.
- Take time to decide whether or not you wish to take part.

Thank you for taking the time to read this.

What is the purpose of the research?

Smoking is a major cause of poor physical health, but stopping smoking is not easy. There are no quit smoking support services especially for people with mental health problems. So we have created a support service designed specifically for people who have had problems with their mental health. The aim of this service is to help people to cut down smoking until they are ready to quit. We need to know if this service is any better than current NHS services for smoking. We will also compare the costs of the support service with current NHS services for smoking to see if the support service represent a good investment.

Why have I been chosen?

You have been chosen because you are a smoker and you have received care from mental health services either recently or in the past.

Do I have to take part?

No, it is up to you whether or not you decide to take part. If you do decide to be included you will be asked to sign a consent form. If you decide to take part you are still free to withdraw at any time and without giving a reason. If you decide to withdraw you will not be followed up and you will have no further part in the study. A decision not to take part will not affect any of the care you receive now or in the future.

What will be involved if I decide to take part?

Once we receive your permission to contact form a study researcher will telephone you to tell you about the study and ask a few questions to see if you are eligible to participate. Unfortunately, we cannot include people who are or become pregnant or are breast-feeding because they would require some additional support which we cannot provide as part of this study. We also need to check that your GP is happy for you to take part in the study. If you are eligible to take part in the study we will invite you to meet with a researcher where you will have an opportunity to ask any questions about the study. This meeting will last about one hour.

At this meeting the researcher will ask you to complete some questionnaires about your smoking habits, your general health and ask to measure your height, weight and breath carbon monoxide levels (this is a commonly used method to find out how much you smoke).

You will be asked to attend to further meetings with the researcher 6 and 12 months after joining the study. At these meetings you will be asked to complete some questionnaires about your smoking habits, your general health and we will measure your height, weight and breath carbon monoxide levels. We will ask you to give us the names of up to three family members/friends/carers who we can contact to ask if you have given up smoking if we are unable to contact you for the 6 months and 12 months follow up meetings. At the 6 and 12 month meetings we will give you a £10 voucher as a gesture of thanks.

After your first meeting with the researcher you will be allocated to one of two groups, you will have an equal chance of being allocated to either:

Group 1 - Participants receive visits from a smoking cessation practitioner plus continue with usual GP care.

Group 2 - Participants continue to receive usual GP care.

We cannot say which of these treatments you will receive as this will be randomly selected and completely down to chance.

Group 1 - Smoking Cessation Practitioner group

If you are allocated to this group you will be assigned a smoking cessation practitioner who will advise on the best way to cut down or give up smoking. They will tailor the advice they give you to your individual needs. The smoking cessation practitioner is someone with a background in mental health care and is an accredited level 2 Quit smoking officer.

We will arrange your first appointment with your smoking cessation practitioner at your convenience either at your home, local GP clinic or hospital. The smoking cessation practitioner will try to arrange regular meetings with you and/or visits to the GP to see how things are working and whether you need to change your treatment as necessary. It is important that you tell the practitioner if you have any side effects from cutting down your smoking or if you change your medication. This will affect how your treatment is managed by your GP.

We may ask you for permission to record some of your sessions with the smoking cessation practitioner; you do not have to give permission for your sessions to be recorded. Any recordings made will only be used for analysis as part of the research. If you do not wish to be recorded you can still take part in the study and meet with the smoking cessation practitioner.

Group 2 - Usual GP care treatment group

If you are allocated to this group you will be provided with some advice produced by the NHS about what to do if you are interested in stopping smoking and encouraged to make an appointment with your GP. You will receive the care that is usually offered to all people in your practice or community.

What do I have to do now?

If you would like to take part in this study you need to complete and return the enclosed permission to contact form in the pre-paid envelope provided.

What are the possible benefits of taking part?

Stopping smoking is the single most helpful thing you can do to improve your own health. Smoking causes serious illnesses such as lung cancer and heart disease. Cutting down the total number of cigarettes you smoke is a step in the right direction. Giving up smoking completely will not only improve your own well being, it will help protect the health of your friends and family around you. Stopping smoking also has the added benefit of saving you a lot of money that you would have spent on cigarettes.

We cannot promise that the study will directly help you but the information we get from this study will help health professionals decide the best way to help people with mental health problems to quit smoking in the future.

What are the disadvantages of taking part?

When you stop smoking you may experience withdrawal symptoms. These symptoms may include feeling depressed, anxious or irritable, having difficulty concentrating or feeling restless. You may also feel hungry and put on weight. These are normal symptoms which may be particularly strong when you first quit but should lessen over time. The smoking cessation practitioner will help and support you so that when you are ready to quit smoking you will be motivated and able to cope.

There may be other risks from mixing smoking cessation drugs with medication used to manage your mental illness. The risk of side effects are low, but if you get headaches or worsening of your mental health symptoms, you should tell your GP or smoking cessation practitioner immediately.

What happens when the study ends?

The study will last for 12 months, once you have had your 12 month follow up the smoking cessation practitioner will no longer be funded to help manage your smoking. Your GP will continue managing any smoking cessation drugs you may be taking and you will still be able to access your local Quit smoking clinics and services. You will still be entitled to your usual GP care including prescription medication.

What will happen if I don't want to carry on with the study?

Your participation is voluntary and you are free to withdraw from the study at any time without giving any reason. If you withdraw from the study we will delete your contact details from our records but we will need to use the data collected up to your withdrawal. You may also choose to withdraw from treatment but continue being followed up. This will not affect your rights or your future care in any way.

Will my taking part in this study be kept confidential?

All information that you give us will be kept strictly confidential. Your name will not be mentioned in any reports. Only members of the research team and your GP will know that you have agreed to take part in the study. As we will be sending you further questionnaires we need your name and contact details. These personal details will be stored in locked filing cabinets and all electronic copies will be stored on a secure server accessed by password protected computers.

Some parts of your medical records may need to be looked at by authorised persons from the research team to check medication and medical history. Your information will not be disclosed to any unauthorised person. Your GP and mental health team will be informed of your participation in this study and they may be approached if circumstances occur where we may be concerned for your health and safety.

Results of the research study

The results of this research study will be available after we have analysed the data and we will send you a copy of the results if you would like us to.

What happens if something goes wrong?

This research only includes treatments that you would normally receive. The clinicians and health care professionals will take every opportunity to reduce risk. If something were to go wrong, they would offer you the best possible solution to resolve it. If you believe that you have been harmed by taking part in the study, you have the right to pursue a complaint through the usual NHS procedures.

Who reviewed the study

This study has been reviewed by Leeds East Research Ethics Committee.

Who is organising and funding this research?

This study is being funded by the Health Technology Assessment Programme. The trial is sponsored by the University of York and managed by researchers at the York Trials Unit, University of York.

Who can I contact for more information?

If you have any queries or wish to obtain further information about this study, please contact Emily Peckham, phone: [redacted], email: [redacted].

For independent information about participating in this study, contact your local <insert local Patient Advisory Liaison Service (PALS) details or equivalent (if not known locally as PALS) here>, <local contact details entered here>, <local contact detail entered here>.

If you are unhappy with any aspect of this study, you can speak with any study researcher (contact details above) or your care coordinator who can relay your dissatisfaction to the lead investigator, Prof Simon Gilbody. You can also file a formal complaint with the NHS complaints procedure (Tel: [redacted] or free phone: [redacted]). Taking part in this study in no way affects your right to complain about any aspect of the way in which you have been treated during the course of this study.

Thank you for taking this the time to read this information sheet.

Please keep this copy.

What to do now

If you **do not** want to take part – do nothing

If you **do** want to take part - complete:

- The permission to contact form

Then post it in the prepaid envelope provided.

Participant consent form

Patient Consent Form

☐☐☐☐

Participant Identification number:

Title of Study: The SCIMITAR trial - Smoking Cessation In Mental Ill health Trial.

Please read carefully. If you agree with each point please **initial each box** below:

1. I confirm that I have read the information sheet version <no> dated <date> for the above study and have had the opportunity to consider the information, to ask questions and to have these answered satisfactorily. ☐

2. I understand that my participation is entirely voluntary and that I am free to withdraw at any time without giving any reason, if I chose to withdraw I will not be followed up and will have no further part in the study, and that my medical care and legal rights will not be affected. ☐

3. I give permission to members of the research team, regulatory authorities and NHS trust where relevant to access my medical records and data collected from the study. Information held at the General Register Office may be used to keep in touch with me and follow up my health status for the duration of the study. ☐

4. I agree to complete the relevant questionnaires at the start, 6 and 12 months follow-up, and also have my weight, height and breath carbon monoxide measured during the study. ☐

5. I agree to my GP and mental health care professionals being informed of my participation in the study. They may also be approached during the study if information or advice is required for my health and safety. ☐

6. I agree to this consent form and other data collected as part of this study being kept by researchers at the University of <York/Manchester>. I understand that my participation in this study is confidential and that no materials which could identify me will be used in any reports of this study. ☐

7. I agree to up to three family members/friends/carers being contacted to ask whether I have quit smoking in the event that the researcher has been unable to contact me. ☐

8. I understand that I may be asked for permission to record treatment sessions and that I am free to refuse, and that I can still take part in the study if I refuse to be recorded and that any recordings made will only be used for analysis as part of the research. ☐

9. I agree to take part in the SCIMITAR study.

……. …/…/……

……

Name of participant (BLOCK CAPITALS) Date Signature

……. …/…/……

……

Name of researcher (BLOCK CAPITALS) Date Signature

Other research studies

Researchers from the SCIMITAR team would like to contact people who agree to take part in the main SCIMITAR study to see if they are interested in helping with other related studies – these are entirely optional. If you would like to be sent information related to other studies, please tick this box ☐

Appendix 3 Adverse events and risk protocol

Adverse event SOP

TITLE: Adverse Event Reporting	
VERSION: 1.2	
Prepared by: Catherine Arundel Date: 11.12.15	Approved by: Emily Peckham Date: 17.12.15
PURPOSE: To describe the process of adverse event reporting and follow up of adverse events for all staff involved in the SCIMITAR+ Study	

1) **PURPOSE**

To describe responsibilities and procedures for identifying, collecting, recording and reporting of Serious and Non Serious Adverse Events occurring in the SCIMITAR+ trial.

2) **DEFINITIONS**

The definitions listed comply with ICH GCP guidance (1996)

SERIOUS ADVERSE EVENT – Any untoward medical occurrence that results in one of the following criteria:

- Life threatening (i.e. event in which patient is at risk of death at the time of the event occurring).
- Is fatal (i.e. results in death).
- Requires unplanned or prolonged hospitalisation*.
- Results in persistent or significant disability or incapacity.
- Results in a congenital abnormality or birth defect.
- Any other medical condition not listed above, which may require medical or surgical intervention to prevent the above criteria occurring.

*Unplanned refers to emergency hospitalisations resulting in an inpatient stay. Prolonged hospitalisation is deemed to be where a patient's stay is longer than expected (e.g. patient is operated on as day case but remains in hospital overnight).

NON SERIOUS ADVERSE EVENT – This is any untoward medical occurrence in a participant to whom an intervention has been administered, including occurrences not necessarily caused by or related to that intervention.

EVENT OUTCOME - For any adverse event the outcome of the event must be detailed. Events may be:

- **RECOVERED:** e.g. Participant is no longer experiencing any unfavourable symptoms related to the event.

- **RECOVERED PARTIALLY:** Participant is still experiencing some unfavourable symptoms related to the event however the impact of these has improved since the event.

- **DEATH:** Participant is deceased as a result of the event.

- **ONGOING:** Participant continues to experience unfavourable symptoms which currently remain unresolved.

3) SCIMITAR+ REPORTING PROCEDURE

WHO

1) All trial staff that are in contact with patients are responsible for noting adverse events that are reported by the patient and making them known to York Trials Unit in a timely fashion. Patients entered into SCIMITAR+ must be encouraged from the outset to contact their researcher at the time of an event occurring.
2) The Trial Coordinator at York Trials Unit is responsible for the processing and reporting of serious and non-serious adverse events in line with procedure detailed below.
3) Clinical staff members at the University of York are responsible for the reviewing of Serious Adverse Events.
4) The Chief Investigator (Professor Simon Gilbody) is responsible signing off all Serious Adverse Events. Any events deemed to be related **and** unexpected will be reported to the REC and Sponsor by the Chief Investigator.

WHEN

- At each visit adverse events that might have occurred since the previous visit or assessment should be elicited from the patient. In many cases this will be captured at the point of data collection and further elaboration by the participant may be required to assist with recording.
- Adverse Events reported at any other time should also be reported to York Trials Unit within the time frames set out below.

- Adverse events which are **related to the research** and are **'On-going'**, when a participant completes their study involvement, should be followed up as required by the protocol and as clinically indicated.
- Adverse Events which are not related to the research and remain 'On-going' do not need to be followed up after study completion.

HOW

STUDY SITE

1) Document details of the event clearly, using the **SCIMITAR+ Adverse Events form**. Please ensure that the following are clearly documented;
- Date of Event. (*If the participant cannot remember please indicate as closely as possible*)
- Action taken including treatment and/or medication and dates that this commenced and/or stopped or was changed.
- Whether the event is deemed to be Serious or Non Serious (using the criteria as detailed in Section 4).
- The outcome of the event.

Please ensure that no patient identifiable detail is provided on the Adverse Event Form.

2) Events that are **serious** must be reported to York Trials Unit **within 24 hours** of study staff being made aware of the event.

   Events that are **non-serious** must be reported to York Trials Unit **within 5 days** of study staff being made aware of the event.

   Reporting of adverse events should be completed by sending the Adverse Event form to York Trials Unit by fax on [redacted] or via the University of York Drop Off. Events should be marked for the attention of/sent to Catherine Arundel [redacted] and Emily Peckham [redacted].

3) Study sites should respond promptly to any requests made for further information.

4) Copies of all correspondence and notes relating to an adverse event should be retained in the individual patient's research records or master site file. Reasons for late reporting must be documented on the SAE form and in the patient's research records or the master site file.

YORK TRIALS UNIT

Upon receipt of completed adverse event form(s), the form will be processed as described below.

1) The adverse event forms will be reviewed by trial staff at York Trials Unit. In the event that the event is deemed to be 'Serious' this will be provided to Professor Ian Watt for initial review.

2) All correspondence about the adverse event will be saved and held securely at York Trials Unit.

   Should a site provide patient identifiable details on any adverse event form (other than participant date of birth), this will be destroyed upon receipt at York Trials Unit. The site will be contacted to inform them of this breach of Data Protection and the need to destroy any copy that they have and to recomplete and resend the Adverse Event form removing any patient identifiable information.

3) The frequency of all adverse events will be reported internally to the DMEC and TSC at regular meetings. The DMEC will be responsible for completing immediate review of serious, unexpected **and** related events. They will then see unrelated SAE and NSAE at the next scheduled meeting. Details of serious and non-serious adverse events will also be reported externally to the HTA in regular progress reports.

4) YTU, in conjunction with the Chief Investigator, will complete an NRES SAE form for any related AND unexpected SAEs and will notify the REC, Sponsor and Funder **within 15 days.**

CHIEF INVESTIGATOR/DELEGATED CLINICIAN

1) The Chief Investigator will, upon receipt of a copy of a Serious Adverse Event form, review the event and complete a **CI Sign Off Form.**
2) A signed copy of the CI Sign Off Form should be returned to York Trials Unit.

DOI: 10.3310/hta23500

Appendix 1: SCIMITAR+ Adverse Event Reporting Guidelines

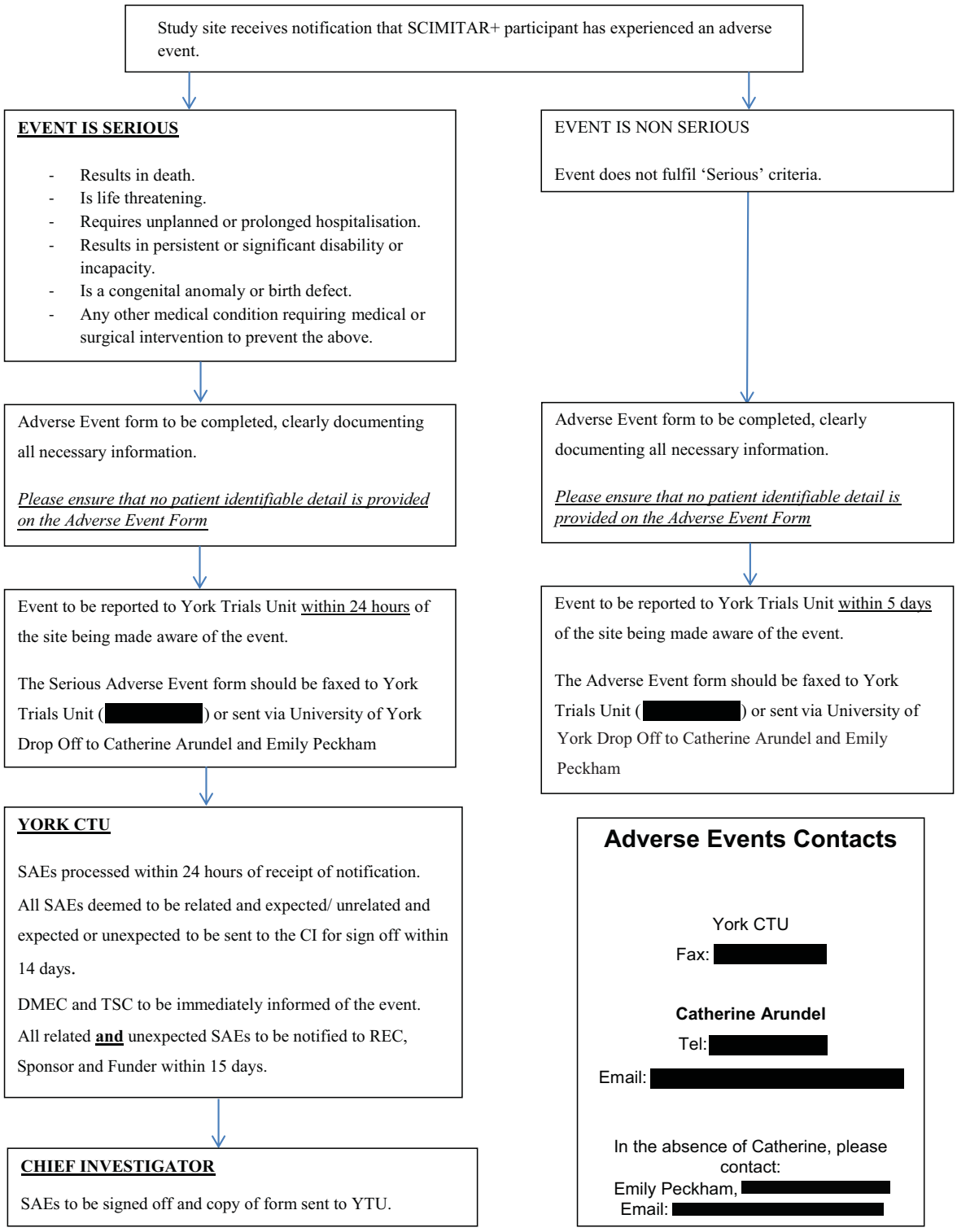
Is the event serious?

	SITE	CHIEF INVESTIGATOR	YTU	
	Site to report to YTU within*:	Chief Investigator to report to REC	YTU to report to DMEC /TSC	YTU to report to Funder
SERIOUS	24 hours of being made aware of the event.	Only if event is related AND unexpected. Within 15 days.	Event is related AND unexpected: To be reported and reviewed immediately. All other events to be reported at next scheduled meeting.	YTU to provide details for routine funder progress reports.

Is the event non serious?

	SITE	YTU		
	Site to report to YTU within:	Chief Investigator to report to REC	YTU to report to DMEC/TSC	YTU to report to Funder
NON SERIOUS	5 days of being made aware of the event.	Not required.	To be reported at next scheduled meeting.	YTU to provide details for routine funder progress reports.

Appendix 2: SCIMITAR+ – Site Adverse Event Reporting Flowchart



Appendix 4: How to use University of York Drop Off

1) To access the University of York Drop Off service go to: https://dropoff.york.ac.uk

2) To access the system, click on 'Drop Off'

3) Enter your name, your organisation and email address and enter the numbers/letters displayed

4) You will receive an email from University of York Drop Off. Click on the link which will take you to the following page

5) Enter Catherine and Emily's email addresses in the 'To' box

6) Select the files you need to upload using the 'Choose File' button. This will allow you to browse to access the relevant files. *NB: please ensure files are password protected/encrypted before uploading.*

Please note the system can only upload one file at a time.

7) Once all relevant files have been uploaded, click the 'Drop Off Files' button. This will send the files back to York Trials Unit.

Suicide Protocol

If at any time you believe that there is significant suicide risk with a patient who is participating in the study that has not been recently communicated to their GP, psychiatrist or care coordinator/CPN, you must contact the relevant designated centre psychiatrist or health professional or Prof Simon Gilbody (Consultant psychiatrist) if the relevant designated centre psychiatrist or health professional is unavailable.

Contact numbers can be found on the back page of this protocol.

The designated psychiatrist/ health professional or Prof Gilbody, will then assess the patient and if it believed necessary, and if there is a significant risk,

Suicide risk identified during face-to-face or telephone interview

The PHQ-9 questionnaire asks if the patient has had '**Thoughts that you would be better off dead or hurting yourself in some way**' **(Question 9).**

If the participant indicates a response of 3 for this item, then you should ask whether the patient has talked to their GP, psychiatrist or care coordinator/CPN about these feelings. **If the patient has spoken of these thoughts to their GP or psychiatrist, then no action is required.**

If not, you should ask the patient whether it is OK for you to contact their GP and inform them of the situation. If the patient refuses, contact the relevant designated psychiatrist/health professional. If the patient agrees, you should immediately get in touch with the patients GP or psychiatrist.

If unable to contact the patients GP or psychiatrist contact any of the designated centre psychiatrists/health professionals, if unable to contact any

of the designated centre psychiatrists/health professionals contact Prof Gilbody, if unable to contact Prof Gilbody, contact the Trial manager, Emily Peckham or the Trial Intervention Co-ordinator, Della Bailey. If unable to contact any of the above contact any other of the co-investigators who will advise further.

Please also complete the attached Suicidal Intent Form, if the patient agrees to you contacting their GP/psychiatrist and inform the Trial Manager. If relevant, Professor Gilbody or the relevant designated centre psychiatrist/health professional should also complete the Suicidal Intent Form: Psychiatrist/ Health Professional. These forms should be stored with the patient's trial records and a copy faxed to York Trials Unit on [redacted].

If any other responses during the face-to-face or telephone interview give you cause for concern, raise this with the relevant designated psychiatrist/health professional.

Suicide risk identified on a postal questionnaire

At 6 month and 12 month follow up points, some patients can choose to receive and return questionnaires by post. If you receive a PHQ-9 in which the patient has indicated a score of 3 for question 9, you will need to follow the suicide protocol.

Contact the patient by phone and say that you are concerned with their response to this question. Ask if they have discussed these feelings with their GP or psychiatrist. **If the patient has spoken of these thoughts to their GP or psychiatrist, then no action is required.**

If not, you should ask the patient whether it is OK for you to contact their GP and/or psychiatrist and inform them of the situation. If the patient refuses, contact the relevant designated psychiatrist/health professional or if unable to contact the relevant designated psychiatrist/health professional contact Prof Gilbody. If the patient agrees, you should immediately get in touch with the appropriate GP and/or health professional.

If unable to contact the patients GP or psychiatrist contact any of the designated centre psychiatrists/health professionals, if unable to contact any of the designated centre psychiatrists/health professionals contact Prof Gilbody, if unable to contact Prof Gilbody, contact the Trial manager, Emily Peckham or the Trial Intervention Co-ordinator, Della Bailey. If unable to contact any of the above contact any other of the co-investigators who will advise further.

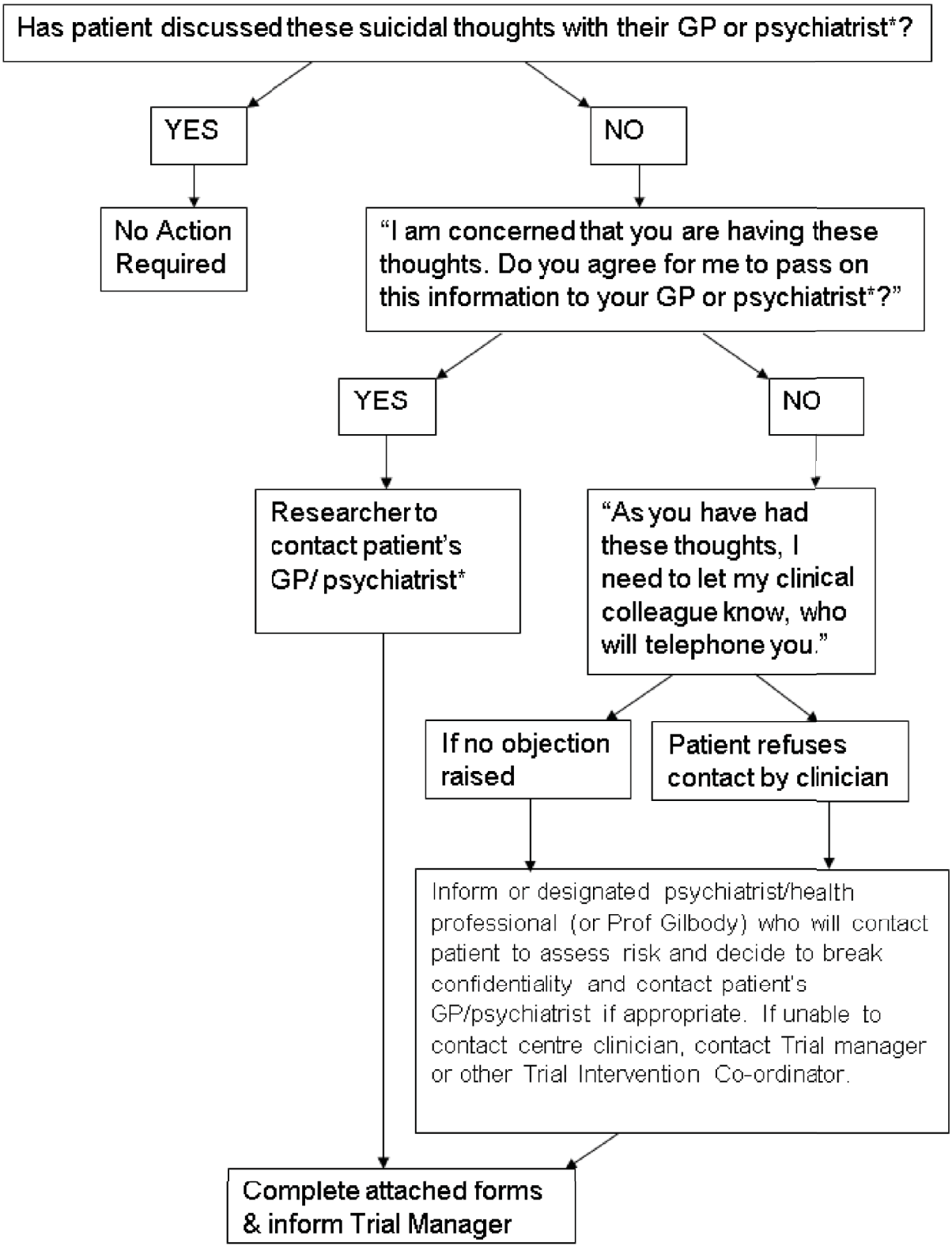
If any other written responses on the questionnaires give you cause for concern, raise this with the relevant designated psychiatrist/health professional.

If you are unable to contact the patient within 24 hours, contact the patient's GP or psychiatrist. Inform them of the patient's questionnaire response and that you have been unable to contact the patient to assess the situation further.

At this point also check the patient's contact telephone number is correct. It may be that the telephone number on the database is out of date. If an alternative number is provided and the GP/ health professional agrees, attempt to contact the patient again.

If still unable to contact the patient and if no alternative contact details are available, confirm with the GP/ health professional that they will follow up with the patient as they feel appropriate based on their clinical knowledge of the patient.

Inform the relevant designated psychiatrist/health professional or Prof Gilbody of the patient's questionnaire response and details of resultant contacts with the patients GP/psychiatrist.


Has patient discussed these suicidal thoughts with their GP or psychiatrist*?
YES
NO
No Action Required
"I am concerned that you are having these thoughts. Do you agree for me to pass on this information to your GP or psychiatrist*?"
YES
NO
Researcher to contact patient's GP/ psychiatrist*
"As you have had these thoughts, I need to let my clinical colleague know, who will telephone you."
If no objection raised
Patient refuses contact by clinician
Inform or designated psychiatrist/health professional (or Prof Gilbody) who will contact patient to assess risk and decide to break confidentiality and contact patient's GP/psychiatrist if appropriate. If unable to contact centre clinician, contact Trial manager or other Trial Intervention Co-ordinator.
Complete attached forms & inform Trial Manager

Non- Suicide risk

If any other areas of risk arise in the interviews that are not related to suicide or self-harm but that give cause for concern please complete the non-suicide risk form.

If a non-suicide risk is identified check whether the participants care coordinator/ GP/ psychiatrist is aware of the risk and document this on the non-suicide risk form. If the none of the above are aware contact the site PI for advice and complete the non-suicide risk form. Note the Site PI only needs to sign the non-suicide risk form if the researcher/ mental health smoking cessation practitioner has contacted the site PI.

If a participant has a very high CO reading (above 100ppm), they should be given advice about possible acute CO poisoning, and should be advised to attend their local Accident and Emergency department. A non-suicide risk form should be completed.

If a participant has a reading between 51ppm and 100ppm please recommend that they get their car and home appliances etc serviced in order to check they are not being exposed to CO via other means and advise them to speak to their GP.

Suicidal Intent Form

The patient below has shown thoughts of suicidal intent on the PHQ-9 Questionnaire and has agreed for their GP and/or psychiatrist to be contacted by the researcher.

Date of birth: _____/_____/_____

SCIMITAR Participant ID: __ __ __ __

Action taken

Name of GP/Psychiatrist contacted: _____

Date of contact: _____/_____/_____ Time: ___:___ am/pm

Outcome of contact/Action/Comments:

Suicidal Intent Form: Psychiatrist/Health Professional

Name of Participant: _____

Date of birth: _____/_____/_____

Name of Psychiatrist/trial health professional notified: _____

Date notified: _____/_____/_____

Action taken

Patient contacted: Yes ☐ No ☐

GP/Psychiatrist contacted Yes ☐ No ☐

If yes, GP/psychiatrist contacted with Patient's consent?

Yes ☐ No ☐

Name of GP contacted:_____

Date: __/__/___

Name of Psychiatrist contacted: _____

Date: __/__/___

Outcome of contact/Action/Comments:

Non-Suicide Risk Form

The participant below has been identified as being a risk other than self-harm/ suicide during a SCIMITAR+ follow up or meeting with a mental health smoking cessation practitioner (MH-SCP).

Participant ID Code:

Date of Assessment:

Assessment: Baseline / 6 month follow up / 12 month follow up / meeting with MH-SCP

Risk identified and how:

Summary of how risk protocol implemented:

(Which clinician gave advice, what advice was given, was risk judged as passive or active? If advised to contact GP/mental health professional – name of practice/team, name of GP/mental health professional spoken to, date of contact)

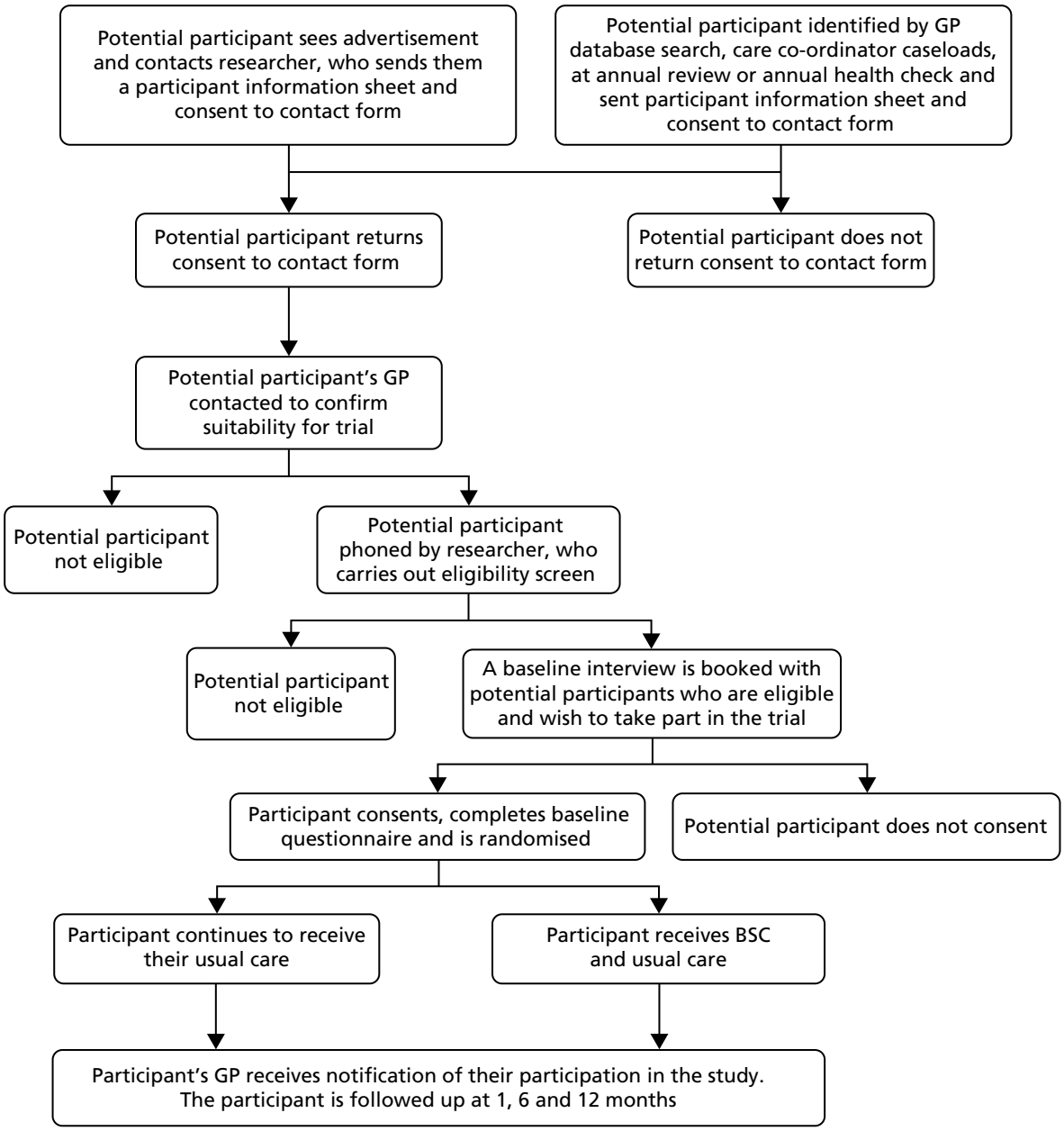
Researcher Name: ……..... Study Site: ☐ ..... ☐

Research Signature: ……. Date: ……...

Name of Clinical Contact: …….....

Clinical Contact Signature Date

Appendix 4 Flow chart for the SCIMITAR+ trial



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