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Smoking cessation for people with severe mental illness (SCIMITAR+): a pragmatic randomised controlled trial

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Summary

Background People with severe mental illnesses such as schizophrenia are three times more likely to smoke than the wider population, contributing to widening health inequalities. Smoking remains the largest modifiable risk factor for this health inequality, but people with severe mental illness have not historically engaged with smoking cessation services. We aimed to test the effectiveness of a combined behavioural and pharmacological smoking cessation intervention targeted specifically at people with severe mental illness.

Methods In the smoking cessation intervention for severe mental illness (SCIMITAR+) trial, a pragmatic, randomised controlled study, we recruited heavy smokers with bipolar disorder or schizophrenia from 16 primary care and 21 community-based mental health sites in the UK. Participants were eligible if they were aged 18 years or older, and smoked at least five cigarettes per day. Exclusion criteria included substantial comorbid drug or alcohol problems and people who lacked capacity to consent at the time of recruitment. Using computer-generated random numbers, participants were randomly assigned (1:1) to a bespoke smoking cessation intervention or to usual care. Participants, mental health specialists, and primary care physicians were unmasked to assignment. The bespoke smoking cessation intervention consisted of behavioural support from a mental health smoking cessation practitioner and pharmacological aids for smoking cessation, with adaptations for people with severe mental illness—such as, extended pre-quit sessions, cut down to quit, and home visits. Access to pharmacotherapy was via primary care after discussion with the smoking cessation specialist. Under usual care participants were offered access to local smoking cessation services not specifically designed for people with severe mental illnesses. The primary endpoint was smoking cessation at 12 months ascertained via carbon monoxide measurements below 10 parts per million and self-reported cessation for the past 7 days. Secondary endpoints were biologically verified smoking cessation at 6 months; number of cigarettes smoked per day, Fagerström Test for Nicotine Dependence (FTND) and Motivation to Quit (MTQ) questionnaire; general and mental health functioning determined via the Patient Health Questionnaire-9 (PHQ-9), the Generalised Anxiety Disorder-7 (GAD-7) questionnaire, and 12-Item Short Form Health Survey (SF-12); and body-mass index (BMI). This trial was registerd with the ISRCTN registry, number ISRCTN72955454, and is complete.

Findings Between Oct 7, 2015, and Dec 16, 2016, 526 eligible patients were randomly assigned to the bespoke smoking cessation intervention (n=265) or usual care (n=261). 309 (59%) participants were male, median age was 47·2 years (IQR 36·3–54·5), with high nicotine dependence (mean 24 cigarettes per day [SD 13·2]), and the most common severe mental disorders were schizophrenia or other psychotic illness (n=343 [65%]), bipolar disorder (n=115 [22%]), and schizoaffective disorder (n=66 [13%]). 234 (88%) of intervention participants engaged with the treatment programme and attended 6·4 (SD 3·5) quit smoking sessions, with an average duration of 39 min (SD 17; median 35 min, range 5–120). Verified quit data at 12 months were available for 219 (84%) of 261 usual care and 223 (84%) of 265 intervention participants. The proportion of participants who had quit at 12 months was higher in the intervention group than in the usual care group, but non-significantly (34 [15%] of 223 [13% of those assigned to group] *vs* 22 [10%] of 219 [8% of those assigned to group], risk difference 5·2%, 95% CI –1·0 to 11·4; odds ratio [OR] 1·6, 95% CI 0·9 to 2·9; p=0·10). The proportion of participants who quit at 6 months was significantly higher in the intervention group than in the usual care group (32 [14%] of 226 *vs* 14 [6%] of 217; risk difference 7·7%, 95% CI 2·1 to 13·3; OR 2·4, 95% CI 1·2 to 4·6; p=0·010). 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=0·079), and at 12 months was 1·00 (0·89 to 1·13; p=0·95). At both 6 months and 12 months, the intervention group was non-significantly favoured in the FTND (adjusted mean difference 6 months –0·18, 95% CI –0·53 to 0·17, p=0·32; and 12 months –0·01, –0·39 to 0·38, p=0·97) and MTQ questionnaire (adjusted mean difference 0·58, –0·01 to 1·17, p=0·056; and 12 months 0·64, 0·04 to 1·24, p=0·038). The PHQ-9 showed no difference between the groups (adjusted mean difference at 6 months 0·20, 95% CI –0·85 to 1·24 *vs* 12 months –0·12, –1·18 to 0·94). For the SF-12 survey, we saw evidence of improvement in physical health in the intervention group at 6 months (adjusted mean difference 1·75, 95% CI 0·21 to 3·28), but this difference was not evident at 12 months

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(0·59, –1·07 to 2·26); and we saw no difference in mental health between the groups at 6 or 12 months (adjusted mean difference at 6 months –0·73, 95% CI –2·82 to 1·36, and 12 months –0·41, –2·35 to 1·53). The GAD-7 questionnaire showed no difference between the groups (adjusted mean difference at 6 months –0·32 95% CI –1·26 to 0·62 *vs* 12 months –0·10, –1·05 to 0·86). No difference in BMI was seen between the groups (adjusted mean difference 6 months 0·16, 95% CI –0·54 to 0·85; 12 months 0·25, –0·62 to 1·13).

Interpretation This bespoke intervention is a candidate model of smoking cessation for clinicians and policy makers to address high prevalence of smoking. The incidence of quitting at 6 months shows that smoking cessation can be achieved, but the waning of this effect by 12 months means more effort is needed for sustained quitting.

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Introduction

People with severe mental illnesses, such as schizophrenia and bipolar disorder, are more likely to smoke and to smoke more heavily than the general population.[1,2] People with severe mental illness usually begin smoking at an earlier age and they usually smoke more cigarettes a day than smokers without severe mental illness.[3,4] Smokers with severe mental illness smoke each cigarette more intensely, extracting more nicotine per cigarette,[5] are more nicotine dependent, more likely to develop smoking-related illnesses, and less likely to receive help to quit than the general population of smokers.[6]

Smoking is part of the culture of mental health services, both among staff and patients.[7] This culture might be part of why mental health services have not historically increased efforts to develop and deliver improved smoking cessation treatments for this group of patients. Many believe smoking relieves depression and anxiety,[8] but the opposite is true;[9] smoking contributes to the general poor physical health of those

Research in context

Evidence before this study

When first designing this study, we did a systematic review of key databases (MEDLINE, Embase, CINAHL, PsycINFO, HMIC, the Cochrane Controlled Register of Trials, and The Database of Abstracts of Reviews of Effects) from database inception to Jan 5, 2008, for publications in English of smoking cessation studies and independently extracted data. We included randomised controlled trials done in any country or care setting with adult smokers with severe mental illness. We identified ten small-scale trials that highlighted the potential effectiveness of nicotine replacement, bupropion, and techniques to change behaviour to enable people with severe mental illness to quit smoking. Effect sizes were broadly in line with estimates of effect for non-severe mental illness populations in the ability of smoking cessation interventions to help people quit. We also found that smoking cessation is unlikely to cause deterioration in the mental health of people with severe mental illness. We repeated our review, from database inception to Sept 1, 2016, combining search terms for severe mental ill health, smoking cessation, and randomised controlled trials, adapted from terms developed by the Cochrane groups for schizophrenia and tobacco addiction (exact terms are listed in the appendix). We found few trials of behavioural interventions, no placebo-controlled trials of nicotine replacement therapy alone, and an absence of research showing how smoking cessation services should be organised and delivered within existing mental health services. Furthermore, although some trials tested the effectiveness of pharmacological treatments, they did not test the effectiveness of behavioural interventions based on evidence-supported techniques to change behaviour.

Added value of this study

This trial shows that delivery of a bespoke smoking cessation intervention to people with severe mental illness is feasible, with good levels of engagement with services compared with usual care. The use of smoking cessation interventions was much higher for people who received the bespoke cessation programme than among those who had usual care. We biochemically verified that over twice as many patients who received the bespoke cessation intervention had quit smoking at 6 months than those who received usual care. At 12 months, more patients in the intervention group had quit than those in the control group had, but the difference was not significant. We also noted some short-term improvements in self-reported physical health and no deterioration in mental health.

Implications of all the available evidence

Based on the results of our systematic reviews and this trial, clinicians should always ask people with severe mental illness about their desire to quit and ensure onward referral to the most suitable local smoking cessation service. Our research supports the provision of smoking cessation services specially designed for people with mental illnesses to address the high levels of smoking and the levels of unmet need for people with severe mental illness.

with severe mental illnesses. Cohort studies[10] have shown that people with severe mental illnesses, such as schizophrenia, on average die 20–25 years earlier than those without severe mental illnesses, and that smoking is the most important modifiable risk factor for this health inequality.

Public health guidance issued by the UK National Institute for Health and Care Excellence (NICE) in 2013[11] highlights the need for innovative approaches for this population to decrease this inequality. Guidance stresses that mental health services should become completely smoke free, and that all people who use mental health services should be given full access to smoking cessation interventions. However, little specific guidance exists on how smoking cessation services should be provided and in what way smoking cessation interventions might need to be adapted for those with severe mental illness. Trial-based evidence suggests that people with severe mental illness are able to give up smoking and that behavioural and pharmacological interventions to aid quitting might be as effective for people with severe mental illness as for the general population.[12] However, people with severe mental illness do not generally access generic smoking cessation services when they have been offered in the UK National Health Service (NHS).[13] In the general population, the prevalence of smoking is decreasing, but little shift has been seen in the past decade in the prevalence among people with severe mental illnesses.[14]

To address this widening health inequality, we designed a smoking cessation intervention specifically for people with severe mental illnesses, incorporating evidence-supported techniques to change behaviour and pharmacotherapy.[15,16] We have previously reported the results of the Smoking Cessation Intervention for Severe Mental Illness (SCIMITAR) pilot trial,[17] with acceptable levels of engagement and preliminary evidence of effectiveness. We now report the results of the full trial (SCIMITAR+) to examine the clinical effectiveness of a combined behavioural and pharmacological smoking cessation intervention for people with severe mental illnesses.

Methods

Study design and participants

In this randomised, controlled trial, which used a pragmatic design,[18] we recruited patients from 16 primary care and 21 community-based mental health sites in the UK (full list of mental health trusts is in appendix). Participants were made aware of the trial by members of the clinical team at each study site, either face to face or by personalised letter of invitation. The SCIMITAR+ study protocol has previously been published elsewhere.[19] Ethical approval was granted by the National Research Ethics Service Committee, Yorkshire and the Humber–Leeds East Research Ethics Committee (reference 15/YH/0051).

Patients were eligible if they were aged 18 years or older, had severe mental illness, smoked at least five cigarettes per day, and expressed an interest in cutting down or quitting smoking. No agreed definition of severe mental illness exists, so we adopted a pragmatic definition used in UK primary care[20]—ie, a documented diagnosis of schizophrenia, delusional or psychotic illness (corresponding with categories F20.0–20.9 and F22.0–22.9 from the 10th revision of the International Classification of Diseases [ICD-10]), or bipolar disorder (ICD-10 F31.0–31.9). This diagnosis needed to have been made by a specialist in mental health services and documented in either primary care records or psychiatric notes before recruitment. Exclusion criteria were pregnancy and breastfeeding, substantial comorbid drug or alcohol problems (as ascertained by the primary care physician or mental health worker), non-English speakers, currently receiving advice from a stop smoking advisor, and lack of capacity to consent.

Randomisation and masking

Participants were randomly assigned to either the bespoke smoking cessation service (intervention) or usual care (control). We used a secure telephone randomisation service run by the York Trials Unit (University of York, York, UK). Simple randomisation was used with a computer-generated random number sequence. Researchers (PH, SC, TM, TS, EB, PB, SB, DBr, TC, AC, CC, DC, ED, KE, HH, WK, LN, EN, HO, JRea, C-BR-H, KS, AS, and CV) phoned the service once the participant had consented and completed baseline assessments. Once given the details of the participant's allocation, the researcher immediately informed them of their allocation. A letter was sent to the participant's primary care physician and mental health specialist detailing their allocation and subsequent smoking cessation management. Due to the nature of the intervention, participants, mental health staff, primary care physicians and researchers (PH, SC, TM, TS, EB, PB, SB, DBr, TC, AC, CC, DC, ED, KE, HH, WK, LN, EN, HO, JRea, C-BR-H, KS, AS, and CV) were not masked to treatment allocation. Statistical analyses were blinded to treatment allocation.

Procedures

Once participants had consented to take part in the trial, they were asked to complete baseline questionnaires that comprised questions on general health; demographics; smoking status and smoking history; use of e-cigarettes; and health service use questions;. Patients also answered questions from the Fagerström Test of Nicotine Dependence (FTND),[21] Motivation to Quit (MTQ)[22] questionnaire, Patient Health Questionnaire-9 (PHQ-9),[23] Generalised Anxiety Disorder-7 (GAD-7) questionanire,[24] EuroQol five-dimensional five-level (EQ-5D-5L)[25] questionnaire, and 12-Item Short-Form Health Survey (SF-12).[26] Additionally, height and weight measurements were taken to calculate participants' body-mass index (BMI) and a carbon

monoxide reading of their exhaled breath was obtained by use of a carbon monoxide monitor (piCO smokerlyzer, Bedfont Scientific, Maidstone, UK). These baseline measurements were done at NHS sites or in the participant's home by the study research staff (PH, SC, TM, TS, EB, PB, SB, DBr, TC, AC, CC, DC, ED, KE, HH, WK, LN, EN, HO, JRea, C-BR-H, KS, AS, and CV).

All participants in the trial received usual care and had access to the full range of smoking cessation treatments that were offered by their local NHS trust. Under usual care, people with severe mental illness were able to access smoking cessation services provided by their primary care physician or in a locally-provided service not specifically designed for people with severe mental illness, at no direct cost. They were also able to access a free telephone helpline (the Smokefree National Helpline) that offers smoking cessation advice. All participants remained under the care of their primary care physician and continued to receive their usual service from the mental health team throughout the trial.

For the **NHS Smokefree website** see https://www.nhs.uk/smokefree/help-and-advice/support

Participants allocated to the bespoke smoking cessation group were offered a structured smoking cessation intervention delivered by a trained mental health smoking cessation practitioner. The smoking cessation practitioners were generally experienced mental health nurses who worked in conjunction with the participant and the participant's primary care physician or mental health specialist to provide an individually tailored smoking cessation service. The intervention was delivered according to the Manual of Smoking Cessation (developed by the National Centre for Smoking Cessation Training [NCSCT], UK)[27] with several adaptations to cater for people with severe mental illness. These adaptations included making several assessments before setting a quit date, offering nicotine replacement before setting a quit date (ie, cut down to quit),[15,28] recognising the purpose of smoking in the context of a person's mental illness, providing home visits, providing additional face-to-face support after an unsuccessful quit attempt or relapse, and informing the primary care physician and psychiatrist of a successful quit attempt, such that they can review doses of antipsychotic medication if their metabolism changes. The smoking cessation practitioners were drawn from local NHS staff and attended one of a number of 2-day training events run by study staff at the University of York (York, UK), University of Manchester (Manchester, UK), and University College London (London, UK) based on the NCSCT's practitioner training with some additional training on specific adaptations for people with severe mental illness. The smoking cessation practitioner advised the patients on a range of pharmacological aids for smoking cessation (eg, nicotine replacement, varenicline) and liaised with their primary care physician to ensure that these options were offered in line with patient choice. The full range of nicotine replacement and smoking cessation products from the British National Formulary were made available to participants.[29] However, the final prescription of treatments was left to the discretion of the primary care physician. Participants were offered up to 12 individual face-to-face sessions in their home or NHS premises lasting approximately 30 min. The intervention had been developed and tested in the context of a pilot randomised controlled trial and the full details have been published elsewhere.[16,17] Participants were contacted and the treatment programme initiated within 7 days of assignment.

SCIMITAR+ was a pragmatic trial,[18] and the comparator was the care that patients with severe mental illness would access under usual circumstances (ie, usual care). In the UK, all patients (including people with severe mental illness) have access to statutory smoking cessation services at no direct personal cost, which would include access to a smoking cessation counsellor who would administer evidence-supported treatments, including behavioural support and access to pharmacotherapy. Research has shown that the uptake of such services is quite low for patients with severe mental illness[13] and we anticipated from the outset that treatment accessed under usual care would fall short of evidence-supported guidelines.[11] Participants allocated to the usual care group were advised to quit, see their primary care physician, and contact local NHS stop smoking services. Thereafter, no additional treatment was offered in the context of the SCIMITAR+ trial. We measured the degree of engagement with statutory smoking cessation services to see if control participants sought help to quit after they received this advice.

12 months after treatment allocation, we contacted the primary care physician of each participant to obtain primary care records, which were screened for details of any nicotine replacement treatment or other smoking cessation products that had been prescribed to participants in the study. Participants were also asked about their purchase of over-the-counter products during follow-up, as part of the health-service use questionnaire, and we recorded nicotine therapy use via self-report.

Participants were followed up at 6 and 12 months after treatment allocation. At the two follow-up timepoints, participants completed the same series of questionnaires as at baseline apart from the demographics questionnaire. Additionally, participants were asked to provide a carbon monoxide breath measure and have their height and weight measured. When possible, participants were followed up face to face, but if not possible they were followed up by phone or by postal questionnaire.

The FTND[21] is a six-item questionnaire measuring nicotine dependence. Item scores are summed to give a total score between 1 and 10, where a score of 1–2 indicates low dependence, 3–4 indicates low-to-moderate dependence, 5–7 indicates moderate dependence, and 8–10 indicates high dependence. The MTQ questionnaire[22] is a four-item questionnaire measuring an individual's motivation to quit smoking. Scores are from 4 to 19 by

summing the responses to each item, where a higher score indicates greater motivation to quit. The PHQ-9[23] instrument measures severity of depression. This nine-item questionnaire is scored from 0 to 27, and a higher scores indicates more severe depressive symptoms. The GAD-7 questionnaire[24] is a seven-item instrument designed to measure severity of anxiety, scored from 0 to 21, with a higher score indicating more severe anxiety. The SF-12[26] consists of two subscales: a physical component and a mental component, both scored from 0 to 100, with 0 indicating the lowest level of health and 100 the highest level of health measured by the scale.

Adverse events were recorded at 6 months and 12 months. As part of the follow-up questionnaires participants were asked about their health service use, and if a participant reported having a suspected serious adverse event, an independent reviewer was contacted to provide a review of the events and determine whether the event was likely to have been related to the trial and whether or not it was expected. An event was classed as serious if it met any of the following criteria: life threatening (ie, event in which patient is at risk of death at the time of the event occurring); fatal; requiring unplanned admission to hospital resulting in an inpatient stay or extension of hospital stay beyond what was expected (ie, patient operated on as an outpatient but remains in hospital overnight); resulting in persistent or substantial disability or incapacity; resulting in a congenital abnormality or birth defect; or any other medical condition not listed here that might require medical or surgical intervention to prevent the above criteria occurring.

Outcomes

The primary outcome was smoking cessation at 12 months after randomisation. A successful quitter was defined as someone with a carbon monoxide measurement below 10 parts per million (ppm),[30] indicating no smoking in the past 12 h, and who reported that they had not smoked (responding "not even a puff" to the question "Have you smoked in the past week?") in the past week (ie, 7-day point prevalence abstinence at 12 months with carbon monoxide <10 ppm).

Secondary outcomes were biologically verified smoking cessation at 6 months; and number of cigarettes smoked per day using the FTND[21] and MTQ questionnaire;[22] general and mental health functioning determined via the PHQ-9,[23] the GAD-7 questionnnaire,[24] and SF-12;[26] and BMI, all measured at 6 and 12 months. Additional outcomes of interest were health service use for both treatment groups and adherence to smoking cessation advice for the intervention group only. Another secondary outcome was health state utilities measured by use of the EQ-5D-5L questionnaire[25] to undertake a cost–utility analysis, and these results will be presented elsewhere as part of the health economic evaluation.

We also compared the prescribed nicotine replacement treatment or other smoking cessation products between participants in the intervention and usual care groups, which will be presented as part of the health economic analysis.

Safety was assessed in all participants who were allocated to treatment, with assessment of adverse events and ascertaining their association with the intervention. BMI, health service use, and anxiety measured by use of the GAD-7 questionnaire were included in the protocol from the beginning of the study but omitted from the original ISRCTN registration in error.

Statistical analysis

We used descriptive statistics to show the baseline demographic data and smoking status of the participants who were enrolled, by treatment group. All statistical tests were two-sided at the 5% significance level. We made no adjustment for multiplicity because a clear primary outcome was defined and all other outcomes served as secondary investigations.

We used results from the SCIMITAR pilot trial[17] and earlier systematic reviews[12] to inform the sample size calculation. This study was powered at 80% to detect a relative 1·7 times increase in quitting, assuming a 20% incidence of quitting among control participants, equal randomisation, and a two-sided α level of 0·05. Allowing for 20% loss to follow-up at 12 months, we calculated that 393 participants needed to be recruited and randomised. We therefore proposed to conservatively recruit 400 participants overall.

We present the proportion of participants who were verified as quitters by use of carbon monoxide measurements at 6 months and 12 months with an unadjusted absolute risk difference and 95% CI, and we analysed these outcomes on an intention-to-treat basis via separate mixed-effect logistic regression models (for each timepoint), adjusted for baseline smoking severity (self-reported number of cigarettes smoked per day), with site as a random effect. We present the adjusted odds ratio (OR), and corresponding two-sided 95% CI and p value for the treatment effect at months 6 and 12. As sensitivity analyses, we also did multiple imputation to account for missing data,[31] imputed self-reported quitting when biochemically verified quitting data were not available, and assumed that people with missing data were still smoking. A full description of the planned and completed statistical analysis are in the appendix.

See Online for appendix

We compared the number of cigarettes smoked per day (reported as part of the FTND) at 6 and 12 months between the two groups using a mixed-effect negative binomial regression model using the log link function, adjusted for baseline smoking severity, treatment group, assessment timepoint (6 or 12 months), and a treatment group-by-time interaction term, and site as a random effect. We provide incidence rate ratios (IRRs) and their associated 95% CIs and p values for this measure. We compared scores for FTND, MTQ, PHQ-9, GAD-7, SF-12 physical component, SF-12 mental

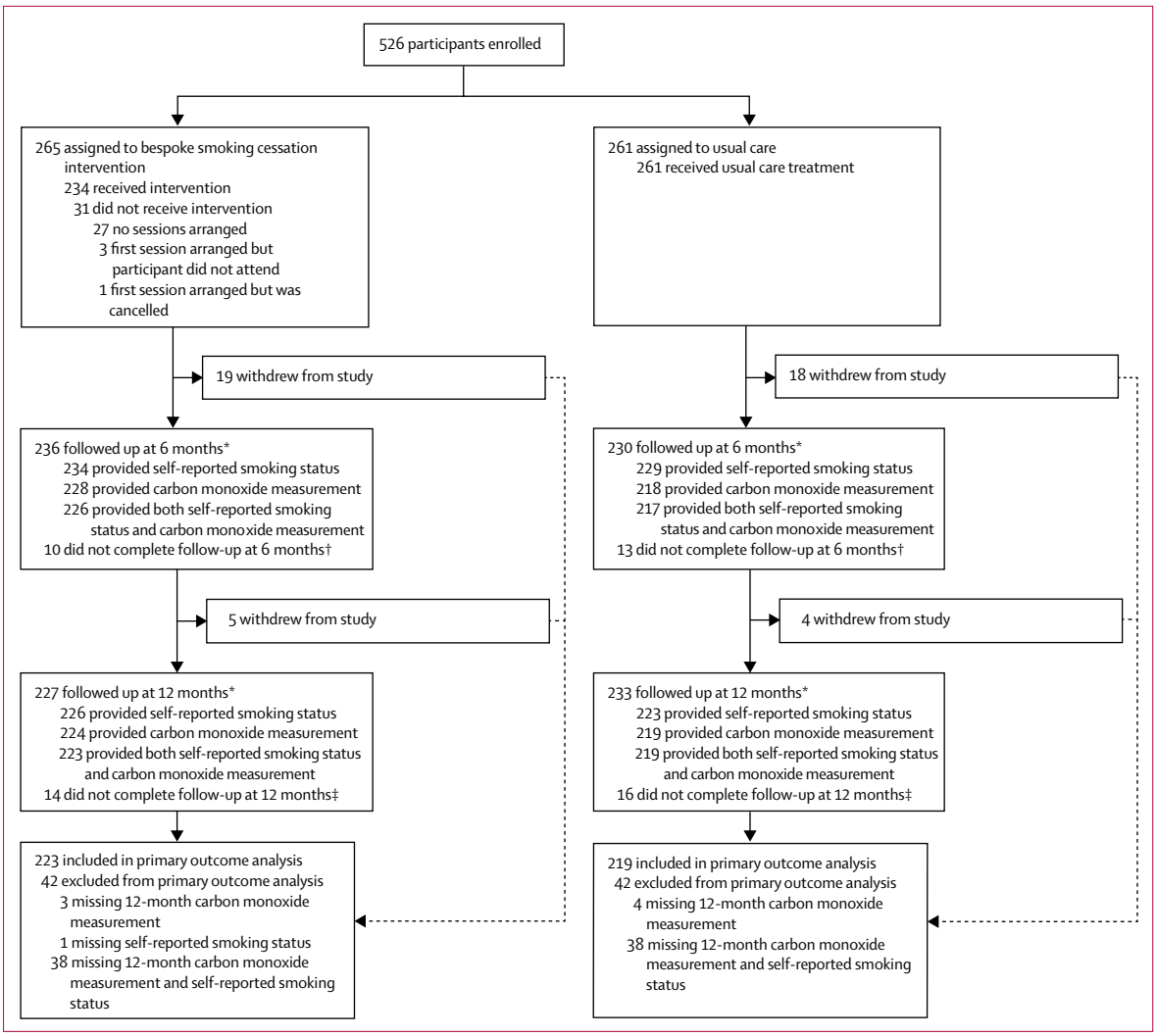

Figure: **Trial profile**
*Defined as providing some follow-up outcome data at this timepoint. †These participants were contacted for follow-up at 6 months because they had not formally withdrawn before this timepoint. They were not considered lost to follow-up beyond this point and were contacted again for follow-up at 12 months unless they had subsequently withdrawn. ‡These participants were contacted for follow-up at 12 months because they had not formally withdrawn before this timepoint, but did not provide any outcome data.

component, and BMI between treatment groups using a covariance pattern linear-mixed model. The outcome modelled was total score at 6 and 12 months. Each model included the following as fixed effects: baseline score, baseline smoking severity, treatment group, assessment timepoint, and a treatment group-by-time interaction term, and site as a random effect. We report predicted means for each group and the adjusted mean difference (with 95% CI and p value) between treatment groups at 6 and 12 months. We did a post-hoc, non-randomised comparison of BMI between quitters and non-quitters at 6 and 12 months using a mixed-effect linear model adjusting for baseline BMI, baseline smoking severity, and treatment group, with site as a random effect. For participants in the intervention group, we summarised treatment session data including the number of sessions attended, the mode of those sessions (eg, face to face, phone visits) and the duration and location (eg, participant's home) of the sessions.

We did all analyses using Stata version 15. This trial was prospectively registered with the ISRCTN registry (ISRCTN72955454).

Role of the funding source

The funder of this study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

Between Oct 7, 2015, and Dec 16, 2016, 526 eligible participants were randomly assigned to the intervention group (n=265) or usual care group (n=261; figure). 504 (96%) participants were recruited via direct referrals via an NHS mental health trust, and 22 (4%) via mailouts to potentially eligible participants at primary care sites. We did not record the number of invitations that were sent out in all settings. The most common severe mental disorders were schizophrenia or other psychotic illness (n=343 [65%]), bipolar disorder (n=115 [22%]), and schizoaffective disorder (n=66 [13%]). 309 (59%) participants were male, the median age was 47·2 years (IQR 36·3–54·5), and most participants were overweight (median BMI 29·3 [IQR 25·0–33·7]), with long smoking histories (mean duration of smoking 29·9 years [SD 12·9]), and high nicotine dependence (mean 24·0 cigarettes per day [SD 13·2]). Most participants (439 [83%]) felt that smoking had negatively affected their health, and 373 (71%) reported that they had been advised to stop smoking by their general practitioner; baseline demographic characteristics are shown in table 1.

At 12 months, 84 (16%) participants did not attend follow-up or had missing data, and 442 (84%) provided sustained quit data (self-reported smoking status and carbon monoxide reading), of whom 223 (50%) were in the intervention group and 219 (50%) were in the usual care group. 34 (15%) of 223 participants (13% of 265 assigned to group) in the intervention group, and 22 (10%) of 219 (8% of 261 assigned to group) in the usual care group had quit smoking (risk difference 5·2%, 95% CI –1·0 to 11·4). The unadjusted OR was 1·6 (95% CI 0·9 to 2·9; p=0·10), and the adjusted OR was 1·6 (0·9 to 2·8, p=0·12).

At 6 months, 443 (84%) of 526 participants provided sustained quit data (n=226 intervention group, n=217 usual care group). 32 (14%) of 226 participants (11% of 265 assigned to group) in the intervention group, and 14 (6%) of 217 (5% of 261 assigned to group) in the usual care group had quit (risk difference 7·7%, 95% CI 2·1% to 13·3%). The unadjusted OR was 2·4 (95% CI 1·2 to 4·6; p=0·010) and the adjusted OR was 2·4 (95% CI 1·2 to 4·7; p=0·010).

At 6 months, only three participants (all in the usual care group) reported they were abstinent but were above the 10 ppm threshold. At 12 months, 57 reported "not smoking a puff" in the past week (n=35 in intervention group, n=22 in usual care group), of whom one in the intervention group did not provide a carbon monoxide measurement and the other 56 were all below the 10 ppm threshold.

Secondary outcomes were summarised by group and the results are shown in tables 2 and 3. The IRR for number of cigarettes smoked per day at 6 months was 0·90 (95% CI 0·80 to 1·01; p=0·079), and at 12 months was 1·00 (0·89 to 1·13; p=0·95). Results of the FTND and MTQ showed a trend towards the intervention group at both 6 months and 12 months, but it was not significant. When measuring

	Intervention group (n=265)	Control group (n=261)	Total (n=526)
Sex			
Male	159 (60%)	150 (57%)	309 (59%)
Female	105 (40%)	111 (43%)	216 (41%)
Transgender	1 (<1%)	0	1 (<1%)
Age, years			
Mean	46·5 (12·5)	45·5 (11·7)	46·0 (12·1)
Median	47·6 (35·6–55·2)	46·6 (36·5–53·8	47·2 (36·3–54·5)
Body-mass index,* kg/m²			
Mean	30·2 (7·1)	29·7 (6·3)	29·9 (6·7)
Median	29·0 (25·1–34·0)	29·4 (24·9–33·3)	29·3 (25·0–33·7)
Most recent diagnosis			
Bipolar disorder	59 (22%)	56 (21%)	115 (22%)
Schizoaffective disorder	25 (10%)	41 (16%)	66 (13%)
Schizophrenia	138 (52%)	125 (48%)	263 (50%)
Other psychotic disorder	41 (16%)	39 (15%)	80 (15%)
Cigarettes usually smoked (per day)			
Mean	24·7 (13·5)	23·2 (12·8)	24·0 (13·2)
Median	20 (16–30)	20 (15–30)	20 (15–30)
Smoking duration,† years			
Mean	30·7 (13·2)	29·0 (12·5)	29·9 (12·9)
Median	31·9 (20·6–40·6)	29·3 (20·4–39·1)	30·6 (20·5–39·7)
Exhaled carbon monoxide,‡ ppm			
Mean	24·9 (15·4)	24·3 (15·1)	24·6 (15·2)
Median	22 (14–33)	21 (14–31)	21 (14–32)
Alcohol consumption§			
Yes	141 (53%)	140 (53·6%)	281 (53%)
No	122 (46%)	121 (46·4%)	243 (46%)
Do you feel that smoking has affected the state of your health?			
Yes	220 (83%)	219 (84%)	439 (83%)
No	45 (17%)	42 (16%)	87 (17%)
Advised to quit smoking by doctor			
Yes	192 (72%)	181 (69%)	373 (71%)
No	73 (28%)	80 (31%)	153 (29%)
Recreational drug use¶			
Yes	20 (8%)	25 (10%)	45 (9%)
No	244 (92%)	234 (90%)	478 (91%)

Data are n (%), mean (SD), and median (IQR). ppm=parts per million. *Data are missing for three participants in the control group and two in the intervention group. †Data are missing for one participant in the control group. ‡Data are missing for three participants in the control group and one in the intervention group. §Data are missing for two participants in the intervention group. ¶Data are missing for one participant in the control group and one in the intervention group.

Table 1: **Baseline characteristics and smoking history**

	Intervention group			Control group		
	Baseline (n=265)	6 months (n=236)	12 months (n=227)	Baseline (n=261)	6 months (n=230)	12 months (n=223)
Number of cigarettes						
n	265 (100%)	188 (80%)	176 (76%)	261 (100%)	198 (86%)	191 (86%)
Mean	24·7 (13·5)	17·8 (12·7)	20·2 (12·3)	23·2 (12·8)	18·3 (10·0)	18·7 (12·1)
Fagerström Test for Nicotine Dependence						
n	258 (97%)	185 (78%)	169 (74%)	254 (97%)	195 (85%)	186 (83%)
Mean	6·5 (2·0)	5·3 (2·1)	5·6 (2·0)	6·4 (1·9)	5·4 (2·0)	5·3 (2·3)
Motivation to Quit questionnaire						
n	260 (98%)	217 (92%)	200 (88%)	259 (99%)	201 (87%)	200 (90%)
Mean	13·9 (2·7)	13·2 (3·4)	13·0 (3·3)	13·7 (2·6)	12·4 (3·1)	12·3 (3·4)
Patient Health Questionnaire-9						
n	264 (>99%)	223 (94%)	213 (94%)	260 (>99%)	214 (93%)	211 (95%)
Mean	10·3 (6·7)	9·3 (6·7)	9·0 (6·7)	10·8 (6·6)	9·4 (6·4)	9·7 (6·7)
Generalised Anxiety Disorder-7 questionnaire						
n	264 (>99%)	224 (95%)	214 (94%)	260 (>99%)	217 (94%)	212 (95%)
Mean	8·4 (6·2)	7·0 (5·9)	7·0 (6·3)	8·4 (6·1)	7·3 (5·8)	7·4 (6·0)
12-Item Short Form Health Survey						
n	257 (97%)	214 (91%)	212 (93%)	256 (98%)	208 (90%)	207 (93%)
Physical component, mean	43·7 (10·4)	45·6 (9·8)	44·3 (10·1)	42·2 (11·0)	42·9 (11·0)	42·4 (11·4)
Mental component, mean	38·6 (12·6)	38·4 (13·1)	39·3 (11·9)	37·9 (11·7	38·9 (12·2)	38·9 (11·9)
Body-mass index, kg/m²						
n	263 (99%)	216 (92%)	208 (92%)	258 (99%)	205 (89%)	201 (90%)
Mean	30·2 (7·1)	30·5 (7·0)	30·4 (7·2)	29·7 (6·3)	29·9 (6·0)	29·7 (6·7)
Recreational drug use						
n	264 (>99%)	221 (94%)	214 (94%)	259 (99%)	212 (92%)	213 (96%)
Yes	20 (8%)	14 (6%)	14 (7%)	25 (10%)	22 (10%)	19 (9%)
No	244 (92%)	207 (94%)	200 (93%)	234 (90%)	190 (90%)	194 (91%)

Data are n (%) or mean (SD).

Table 2: **Summary of secondary outcomes**

depression with the PHQ-9, we saw no between-group difference. Measuring anxiety with the GAD-7 questionnaire we found no difference between the groups.

The SF-12 measured both physical and mental health using the physical component subscale and mental component subscale. We saw evidence of improvement in physical health in the intervention group at 6 months, but this difference was not evident at 12 months (table 3). For mental health, we saw no difference between the groups at 6 or 12 months.

No differences in BMI between the groups was seen at either timepoint (table 3). At 6 months, in a post-hoc non-randomised comparison between quitters verified by carbon monoxide measurements (n=43) and those still smoking (n=376), quitters had a slightly higher mean BMI (mean 31·4 [SD 6·0]) than smokers did (mean 30·1 [SD 6·6]). The mean difference adjusting for baseline BMI, treatment allocation, and number of cigarettes smoked at baseline, with site as a random effect, was 1·3 (95% CI 0·2 to 2·5; p=0·0026). The difference at 12 months was in the same direction but was smaller and non-significant (quitters [n=52] mean BMI 30·6 [SD 7·1] *vs* smokers [n=357] mean BMI 29·9 [SD 6·9]; adjusted mean difference 0·2, 95% CI –1·1 to 1·5; p=0·77).

234 (88%) of 265 intervention participants attended at least one treatment session. 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 min (SD 17·2; median 35 min, range 5–120). Most (85% [1260 of 1483]) took place face to face, 4% (61) over the phone and 11% (162) via another mode (eg, web teleconference, email). 1202 (81%) sessions occurred at the participant's home.

Prescription information was obtained from primary care sites for 160 (61%) participants in the control group and 156 (59%) in the intervention group. 147 (55%) participants in the intervention group and 97 (37%) in the control group recorded pharmacotherapy use via self-report. By smoking cessation product, missing data ranged from 14% to 41% of participants per group, with

the most missing data being for the prescription of varenicline (table 4). Among nicotine replacements therapies, nicotine patches were the most used medication in both groups. E-cigarettes were used by participants in both groups as a smoking cessation aid, with slightly more participants in the control group reporting use of e-cigarettes than those in the intervention group did. Varenicline was rarely prescribed; at the commencement of the SCIMITAR+ trial it was contraindicated for people with severe mental illness.

In our sensitivity analyses, in which we imputed self-reported smoking status when carbon monoxide measurements were missing, the treatment effects were not substantially altered (6-month adjusted OR 2·6, 95% CI 1·3–5·0, p=0·0046; 12-month adjusted OR 1·7, 0·9–3·0, p=0·079). When assuming anyone else with missing smoking status data was a smoker, the 6-month adjusted OR was 2·6 (95% CI 1·4–5·0; p=0·004) and the 12-month adjusted OR was 1·7 (0·9–2·9; p=0·081). Multiple chained imputation of missing data also gave similar results at both timepoints (6 months adjusted OR 2·4, 1·3–4·4, p=0·0067; 12 months adjusted OR 1·7, 0·9–3·0, p=0·083).

Discussion

The main outcome of interest was whether smoking cessation could be achieved using a biochemical measure, and the SCIMITAR+ trial used long-term quitting as measured at 12 months after randomisation as its primary endpoint. The difference in the proportion of participants who quit was not significant at 1 year. This finding is in line with research in the general population that shows that long-term cessation of smoking is difficult to achieve and remains a challenge in treatment for nicotine dependence in any population.[32]

The influence of the bespoke smoking cessation intervention was seen in the secondary outcomes. We found that smoking cessation can be achieved among people with severe mental illnesses. Compared with usual care, the provision of a bespoke smoking cessation intervention increased engagement and the chances of successful quitting as estimated by a biochemically verified outcome measure. The chances of successful quitting at 6 months after randomisation among those who received the bespoke smoking cessation intervention were more than twice those who received usual care. We also found an improvement in short-term physical health (measured by use of the SF-12) and trend towards decreased numbers of cigarettes smoked per day at 6 months and increased motivation to quit at 12 months. We also found no differences between the groups on measures of mental health, which included depression and anxiety. These findings provide supportive evidence that offering a smoking cessation intervention is not detrimental to mental health

SCIMITAR+ was a pragmatic trial[18] and our comparator was therefore usual care. As such, the treatment that

	Intervention group	Control group	Difference	p value
Number of cigarettes per day				
Month 6	17·7 (15·8 to 19·5)	18·0 (16·5 to 19·4)	IRR 0·90 (0·80 to 1·01)	0·079
Month 12	19·7 (17·8 to 21·7)	18·7 (16·9 to 20·4)	IRR 1·00 (0·89 to 1·13)	0·95
Fagerström Test for Nicotine Dependence				
Month 6	5·25 (5·00 to 5·50)	5·43 (5·19 to 5·67)	−0·18 (−0·53 to 0·17)	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)	0·97
Motivation to Quit questionnaire				
Month 6	13·1 (12·6 to 13·5)	12·5 (12·0 to 12·9)	0·58 (−0·01 to 1·17)	0·056
Month 12	12·9 (12·4 to 13·4)	12·3 (11·8 to 12·7)	0·64 (0·04 to 1·24)	0·038
Patient Health Questionnaire-9				
Month 6	9·6 (8·7 to 10·4)	9·4 (8·5 to 10·2)	0·20 (−0·85 to 1·24)	0·72
Month 12	9·3 (8·4 to 10·1)	9·4 (8·5 to 10·2)	−0·12 (−1·18 to 0·94)	0·82
Generalised Anxiety Disorder-7 questionnaire				
Month 6	7·0 (6·3 to 7·7)	7·4 (6·7 to 8·1)	−0·32 (−1·26 to 0·62)	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)	0·84
12-Item Short Form Health Survey				
Mental component				
Month 6	37·9 (36·2 to 39·5)	38·6 (36·9 to 40·3)	−0·73 (−2·82 to 1·36)	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)	0·68
Physical component				
Month 6	45·2 (44·1 to 46·3)	43·5 (42·4 to 44·6)	1·75 (0·21 to 3·28)	0·026
Month 12	43·6 (42·4 to 44·8)	43·0 (41·8 to 44·2)	0·59 (−1·07 to 2·26)	0·48
Body-mass index				
Month 6	30·3 (29·8 to 30·8)	30·1 (29·6 to 30·6)	0·16 (−0·54 to 0·85)	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)	0·57

Data are mean and adjusted mean difference, unless otherwise stated, with 95% CIs in parentheses. IRR=incidence rate ratio.

Table 3: **Adjusted means and group differences for secondary outcomes**

	Intervention group (n=265)			Control group (n=261)		
	Used medication	Did not use medication	Missing data	Used medication	Did not use medication	Missing data
Patch	90 (34%)	128 (48%)	47 (18%)	52 (20%)	171 (66%)	38 (15%)
Gum	28 (11%)	190 (72%)	47 (18%)	16 (6%)	207 (79%)	38 (15%)
Lozenge	29 (11%)	190 (72%)	46 (17%)	15 (6%)	209 (80%)	37 (14%)
Microtab	2 (1%)	215 (81%)	48 (18%)	0	223 (85%)	38 (15%)
Inhalator	34 (13%)	183 (69%)	48 (18%)	13 (5%)	211 (81%)	37 (14%)
Nasal spray	11 (4%)	206 (78%)	48 (18%)	2 (1%)	221 (85%)	38 (15%)
Mouth spray	37 (14%)	180 (68%)	48 (18%)	18 (7%)	205 (79%)	38 (15%)
Varenicline*	7 (3%)	149 (56%)	109 (41%)	7 (3%)	153 (59%)	101 (39%)
E-cigarette	95 (36%)	116 (44%)	54 (20%)	102 (39%)	101 (39%)	58 (22%)

Data are n (%). The proportions do not add up to 100% because some participants used multiple aids. Use of smoking cessation aids is a combination of self-report and prescription data. *Higher rates of missing data for varenicline, because this medication was not recorded by self-report and medical records were the only source for this information.

Table 4: **Proportion of participants who used quit smoking aids during 12 months of follow-up**

is offered under conditions of usual care will vary by site, and will often fall short of the ideal or that recommended in evidence-supported guidelines.[11] Previous research has shown that the uptake of smoking cessation services by people with severe mental illnesses is lower than that of the general population,[13] and we also found this lower uptake under conditions of usual care in the SCIMITAR+ trial. An important finding was that the provision of a bespoke service had a direct effect on the proportion of participants who engaged with the intervention and received effective pharmacotherapy. Notably, few participants were prescribed the most effective form of pharmacotherapy, varenicline, despite this medication having now been shown to be safe and effective among people with severe mental illness.[33] This paucity of prescription might be because varenicline has been thought to be associated with suicidality or deterioration in mental health.[34]

To our knowledge, this is the first large-scale randomised controlled trial in the UK of a combined behavioural and pharmacological intervention designed for people with severe mental illnesses. Trials to date have been small scale, with short periods of follow-up, and focused on pharmacological treatments with little consideration of behavioural approaches.[35] We adapted and enhanced an evidence-supported smoking cessation strategy that was developed for and forms the mainstay of successful stop smoking services in the UK.[36] This structured intervention was delivered by a mental health professional and a so-called cut down to quit approach was also offered.[37] The results of the SCIMITAR+ trial, alongside other trials[38] and evidence from systematic reviews[12,33] of the safety and effectiveness of pharmacological treatments for nicotine dependence in people with mental illness, are accumulating evidence of the effectiveness of smoking cessation interventions for this disadvantaged group. Evidence is also emerging that smoking cessation can be delivered in inpatient settings,[39,40] although the SCIMITAR+ trial did not include such populations. Further research is needed to examine whether this intervention could be adapted to be delivered in inpatient environments where patients often abstain from smoking for the first time.

The results of the SCIMITAR+ trial will be helpful in informing clinical practice, since we have shown that quitting can be achieved for people who use mental health services just as it can for the general population of smokers. Clinicians should therefore ask all of their patients about smoking status and offer referrals to effective smoking cessation services, such as those described in this study. On the basis of the results of this trial and systematic review evidence,[9,35] smoking cessation is likely to be either beneficial or not harmful to mental health. Decision makers should consider commissioning and providing intensive smoking cessation services as a core feature of comprehensive mental health care to ensure the needs of people within mental health services are met. Evidence-supported guidance, such as that offered by NICE regarding tobacco policies and the provision of smoking cessation interventions in mental health services,[11] have not been widely implemented. The intervention described in this study (alongside other such models of care[41,42]) could form a template for mental health services and would ensure that they are compliant with NICE guidance. We would also suggest that clinical services should ensure longer-term follow-up to maintain the proportion of patients who quit smoking in the short term observed in this study, although more research is still needed in this area. A further issue for implementation is the use of e-cigarettes. The SCIMITAR+ trial coincided with a general increase in the use of e-cigarettes throughout the population. This topic is one of substantial debate[43] and consensus is emerging that e-cigarettes are safer than tobacco.[44]

This trial had several limitations. First, 16% of participants were lost to follow-up or had missing data for the primary outcome at 12 months; however, this loss was lower than in our pilot trial[17] and the loss to follow-up was non-differential. Second, more participants in the usual care group had quit smoking at 12 months than was hypothesised in the sample size calculation (10% *vs* 20%), and the actual percentage increase was lower (5% actual *vs* 14% predicted). Therefore, although the trial recruited more participants than originally planned and loss to follow-up was lower than anticipated (16% *vs* 20%), the trial was ultimately underpowered to detect a difference in the proportion of patients who quit from 10% to 15%. Third, difficulties in ensuring that some participants received pharmacological treatment because of changes in the way that smoking cessation services are commissioned and in some areas primary care physicians were unwilling to prescribe nicotine replacement therapy because of smoking cessation services being contracted out to third parties who were unwilling to prescribe for participants unless they entered their service. Such attitudes could lead to difficulties were in implementing the results of the SCIMITAR+ trial, and so we would recommend that local services put robust mechanisms in place to remove barriers to the provision of medication, including varenicline.

In the face of substantial health inequalities for people with severe mental illness, smoking is the most important modifiable risk factor for poor health and reduced life expectancy.[11,45] In this study, we have shown that people with severe mental illnesses more readily engage with a bespoke intervention than usual care, and that the intervention results in an increased proportion of patients who quit at 6 months. Health systems should provide smoking cessation interventions that are responsive to the needs of people who use mental health services. Further research is needed to establish how long-term quitting can be supported.

Contributors

SG and EP wrote the original protocol. TB, CH, EH, TH, SK, ML, DO, EP, SP, JRei, and SG, were co-applicants on the Health Technology Assessment application. CA, DBa, DBr, TB, SC, CF, CH, EH, MH, PH, TH, SK, JL, ML, DO, SP, JRei, and SG refined the protocol. SG was the chief investigator and oversaw the study. EP was the trial manger. CF did the clinical analysis and CH oversaw the analysis. JL designed and undertook the economic analysis in conjunction with SP. DBa supervised the delivery of the intervention and CA, SC, TM, PH, and TS were trial coordinators for the study. TM, TS, EB, PB, SB, DBr, TC, AC, CC, DC, ED, KE, HH, WK, LN, EN, HO, JRea, C-BR-H, KS, AS, and CV recruited participants to the study, provided feedback on the recruitment methods, and helped refine the study procedures. PP and SR helped refine the study procedures. The writing team consisted of EP, CA, DBa, SC, CF, PH, JL, and SG, who drafted the report. All authors were responsible for critical review of the manuscript for important intellectual content and all authors read and reviewed the transcript.

Declaration of interests

We declare no competing interests.

Data sharing

De-identified individual-participant data that underlie the results presented in this Article, the study protocol, statistical analysis plan, and analytical code will be available to investigators for individual participant data meta-analyses that have been approved by independent review committees. Data will be available from the publication date of this Article, with no end date. Proposals for use of data and requests for access should be directed to simon.gilbody@york.ac.uk. To gain access, data requestors will need to sign a data access agreement with the study sponsor (University of York, York, UK).

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