Statistical Analysis Plan

Helping people cope with temptations to smoke to reduce relapse: A factorial randomised controlled trial, V2.0

Person(s) contributing to the analysis plan	
Name(s) and position(s)	Hayden McRobbie (Co-Investigator) Peter Hajek (UK Chief Investigator) Anna Phillips-Waller (UK Study Manager) Francesca Pesola (Study Statistician) Sarah Lewis (Senior Study Statistician) James Balmford (Co-Investigator) Ron Borland (Australia Chief Investigator) Lin Li (Australia Study Manager) Stuart Ferguson (Co-investigator/EMA lead) Ann McNeill (Co-investigator/Qualitative lead) Catherine El Zerbi (Qualitative Researcher) Ryan Courtney (Co-investigator)
Authorisation	
Position	**Chief or principal investigator**
Name	**Peter Hajek**
Signature	
Date	25.09.2019
Position	**Trial statistician**
Name	**Francesca Pesola**
Signature	F. Pesola
Date	2.10.2019
Position	**Senior statistician**
Name	**Sarah Lewis**
Signature	S. Lewis
Date	1.10.2019

Background

Around 70% of smokers who quit in the short-term return to smoking within a year. The UK Government invests some £84.3 million annually to fund Stop Smoking Services (SSS), not including the cost of smoking cessation medicines, and there are other investments in encouraging smokers to stop smoking via media and primary care. The initial 4-week quit rates in smokers who engage in treatment are around 50%, but in the longer term, the ubiquitous relapse substantially reduces the impact of these initiatives [1]. As the health benefits of stopping smoking are primarily realised with long-term abstinence, relapse reduces the public health benefit of investment in smoking cessation interventions and remains the main unresolved issue of smoking cessation efforts.

Clinical data

A comprehensive research programme into the real-life causes and time-course of relapse by means of Ecological Momentary Assessment (EMA) has concluded that relapse situations are triggered by a host of different mechanisms and are difficult to predict and counteract [2].

Another important finding was that 90% of single lapses (i.e. smoking one cigarette or just taking a single puff) lead to full blown relapse [3]. It appears that even after a lengthy period of abstinence, a lapse generates a priming effect on the dopamine reward pathways [4] which leads to further smoking.

There are three main trajectories to long-term abstinence that interventions can influence. First they can focus on preventing a lapse from occurring. Secondly they can act to prevent a lapse progressing to relapse, and thirdly they can focus on people who relapse encouraging them to reengage with treatment again, within days of relapse [5].

Up to now, only two behavioural relapse prevention (RP) strategies have been formally evaluated: a 'skills-based' approach which focuses on teaching clients to identify relapse situations and put in place coping strategies [6]; and extending the initial treatment with maintenance sessions to provide ongoing support.

A systematic review of this literature for the Cochrane Collaboration [7] identified 54 studies relevant to relapse prevention. Disappointingly, despite good intuitive validity of these interventions, no single study or a combination of studies showed a significant benefit. Other systematic reviews have arrived at the same conclusions [8]. Clients may not learn the cognitive-behavioural skills or may not practice them, or the skills may not be helpful [9].

The Cochrane Review also identified eight studies that examined the extended use of stop smoking pharmacotherapy [7]. Extended use of varenicline (6 months versus the standard 3 months; 1 study) was

associated with a small increase in 1-year abstinence rates (RR = 1.18; 95% CI: 1.03-1.36), but no benefit was found for extended use of either bupropion or nicotine replacement therapy (NRT). Most successful quitters see little reason to continue using currently licensed smoking cessation medicines, resulting in low uptake [10, 11] and long-term use of these medicines also has serious financial implications. Our strategy overcomes these problems as it is testing a behavioural programme that will have no long-term costs, and the smoking replacement (SR) intervention is based on participants being prepared to continue use at their own cost, something we believe is viable.

New vaporised nicotine (VN) products, such as e-cigarettes (EC), have become popular among smokers [12, 13] and preliminary data suggest that they may be helpful for smoking cessation. EC may be more effective than current smoking cessation medicines for preventing relapse for several reasons including: (i) they are more psychologically attractive to smokers [14, 15] and therefore more likely to be used more often and for longer; and (ii) they replace more of the desired effects of smoking. VN, and EC in particular, are cheaper (from the NHS perspective) than standard medicines (e.g. NRT, varenicline) as they are likely to be purchased by the user. There are few other smoking cessation treatment improvements on the horizon and VN are the most promising current development awaiting objective scrutiny. SSS and policy makers are asking for data that will guide their decision making [16] and although the tobacco control community is divided on their opinions of EC, there is agreement that more data are urgently needed on the role these and other alternative nicotine devices may have to play.

Regarding behavioural support, there is evidence that extended support during the initial treatment period improves smoking cessation outcomes and several trials have looked at using this approach for preventing relapse [7]. However, the support relied on smokers taking the initiative to telephone the service when they felt in danger of lapsing or following a lapse. Not surprisingly, very few clients used the offer. Successful quitters do not see the necessity to have regular contact when they are not smoking, and once lapsed to smoking believe that there is no benefit in making contact. The intervention we will be using shows promise of sustaining its effects beyond the period of active training and support.

Modern information technology, in particular web-based resources and text messaging, offers a new and more convenient way of maintaining contact with clients to provide ongoing support. Recent data show that an online Structured Planning and Prompting Protocol (S3P) reduced relapse rates between 1-24 weeks from 71% to 61% [17]. The S3P is designed to focus planning on strategies to deal with temptations to smoke. The core element is using a method of “If in a particular situation, then do some specific set of actions to prevent relapse”. This form of self-statement has been shown in experimental work to improve the cuing of the desired action in the context of the situation occurring where it is likely to be needed [18]. This approach can be delivered online and can be enhanced by mobile phone text messages. Digital technology promises a new approach to extending supportive contact. Texting interventions are inexpensive and can be easily

disseminated on a large scale. We have piloted the use of ongoing text-based contact to prevent relapse in 202 SSS clients, who were abstinent 4-weeks after their quit date [11]. Clients received 17 personalised messages, 9 that were interactive, which were sent weekly for 12 weeks and fortnightly for 6 months. Unlike invitations to attend sessions or call their advisors, the texting intervention was well received by recent ex-smokers (70% gave an overall score for helpfulness of the messages of 4 or 5 on a 5-point scale) and the retention rates were much better than with face-to-face or reactive telephone-based approaches.

The proposed trial would be the first randomised study of these interventions for relapse prevention, and thus will generate new knowledge. The intervention itself would build directly on previous UK and Australian work while the trial would use methods validated extensively in previous research.

Early termination and curtailed trial

Due to slow and low recruitment and following discussions with the NIHR HTA in December 2018, it was decided to terminate the study after 6 month follow-up data collection without reaching the planned recruitment target. Findings based on baseline data and 6-month follow-up will still be relevant for meta-analysis in this research area and to guide wider research in the field with regard to feasibility, study design, implementation and challenges faced in relapse prevention trials. In addition, data from the qualitative and EMA sub studies will lead to enhanced knowledge surrounding relapse prevention and strategies used. Data collection for 6-month follow-up is expected to be complete by June/July 2019. The first draft of the statistical analysis plan (SAP) was drafted in January 2019.

This SAP was written once the decision to shut down the study (December 2018) was made as original endpoints and analyses planned in the study protocol, no longer apply. Indeed, no 12-month follow-up data will be collected. The present SAP is a revised plan for the curtailed trial based on the information in the study protocol V4.1 which was finalised on 8 August 2018. The trial statistician has not seen any trial data apart from recruitment updates and has remained blinded throughout the SAP revision.

Amendments to the objectives, aims and analyses are also necessary as the trial did not reach its expected target sample size (N = 1400), in which the trial was powered for. In total, 235 participants were randomised (105 in the UK and 130 in Australia).

Primary Objective

Original

To determine if providing additional strategies designed to help people cope with temptations to smoke (online Structured Planning and Prompting Protocol [S3P] and/or access to smoking replacement [SR] products) when provided following the successful completion of a smoking cessation programme (i.e. at around 4 weeks post quit), reduce relapse rates at 12 months post quit date.

Curtailed Trial

To determine if providing additional strategies (the number of interventions: 0 (UC) vs. 1 (SR or S3P) vs 2 (SR+S3P)) designed to help people cope with temptations to smoke when provided following the successful completion of a smoking cessation programme, reduce relapse rates at 6 months post quit date. See page 13 for full details.

Secondary Objectives

Original

1. Are the outcomes of the trial affected by alternative definitions of successful quitting and/or assumptions made about the status of missing cases?
2. If the strategies work, is this by reducing slip-ups and/or by enhancing recovery from slips, including short term relapse, or by some combination of the two? (EMA/qualitative sub studies complementing reports at follow-ups)
3. What, if any, sustained reductions in cigarette consumption occur (particularly reductions to non-daily use), among treatment failures and does this relate to any coping strategy?
4. What is the cost-effectiveness of any effective strategies, and does this differ between countries?
5. Do the strategies have different effects on people from different socioeconomic and ethnic groups, of different gender, with different prior smoking habits, and those who stopped smoking using different forms of medication?
6. How feasible and acceptable are the strategies to participants, and what are the barriers and facilitators to sustained cessation during the trial period? How are the relapse prevention strategies used, and are patterns of use related to cessation outcomes?
7. What are the rates of negative aspects (adverse events) reported in people who use a smoking replacement product compared to those who do not and does this vary by type of product used?

Curtailed Trial

Due to the small sample size and, hence, limited power, it will only be possible to assess the following objectives.

1. Are the outcomes of the trial affected by alternative definitions of successful quitting and/or assumptions made about the status of missing cases?
2. Do the strategies reduce slip-ups and/or enhance recovery from slips, including short term relapse, or by some combination of the two? (Explorative analyses of EMA/qualitative sub study data complementing lapse/relapse reports at follow-ups; e.g. EMA data will be used to calculate the frequency of self-reported slips by treatment group. Furthermore, multilevel models will be use to compare daily level of craving and withdrawal across groups overtime).

3. What, if any, sustained reductions in cigarette consumption occur (particularly reductions to non-daily use), among treatment failures and does this relate to any coping strategy? (Explorative analyses of EMA/qualitative sub study data complementing reduction reports at follow-ups; quantitative analysis will not be possible in the curtailed trial.)
4. How feasible and acceptable are the strategies to participants, and what are the barriers and facilitators to sustained cessation during the trial period? How are the relapse prevention strategies used, and are patterns of use related to cessation outcomes? (Explorative analyses of EMA/qualitative sub study data complementing cessation reports at follow-ups; quantitative analysis will not be possible in the curtailed trial.)
5. What are the rates of negative aspects (adverse events) reported in people who use a smoking replacement product compared to those who do not and does this vary by type of product used?

Primary Outcome

Original

Sustained abstinence between 1 and 12 months post quit date, with no reported relapse (7 or more days of continuous smoking) and no smoking at all in the last month, biochemically verified.

Curtailed Trial

Sustained abstinence (i.e. no relapse) between 1 and 6 months post quit date. Relapse is defined as 7 or more days of continuous smoking reported at any follow up or any cigarettes smoked (even just a puff) in the last month at 6 months. Abstinence will be based on self-report as no biochemical validation was planned at 3- or 6-month follow-up.

Original Secondary Outcome

1a. Sustained abstinence using different criteria for the primary outcome (e.g. 6 months sustained abstinence according to Russel Standard definition) and different assumptions about missing cases.

1b. Point prevalence abstinence at 3 and 6 months and shorter-term period prevalence outcomes

1c. Sustained reduction in cigarette consumption of at least 50% from baseline in those who do not achieve abstinence at 6 months.

2. Evaluations of likely mechanisms of effect in particular focusing on these strategies that were encouraged and participant perceptions of effect (e.g. participant ratings), including use of EMA/qualitative sub studies

3. Dose response effects - is the dose of the interventions, or extent of compliance, associated with relapse

4. Effects of intervention components (e.g. on relapse rates, participant ratings etc.) by country and on people from different socioeconomic and ethnic groups, of different gender, with different prior smoking habits, and those who stopped smoking using different forms of medication

5. Cost-effectiveness of the different strategies

Curtailed Trial Secondary Outcome

1a. Sensitivity analyses using different criteria to define abstinence, e.g. Russel Standard, defined as not smoking more than 5 cigarettes since 2-weeks post quit date. Sensitivity analyses using different approaches to imputed missing smoking status at 6 months; specifically, multiple imputation by chained equation and complete case analysis

1b: Point prevalence abstinence at 3- and 6-months, defined as no smoking (not even a puff) in the past seven days.

1c. Sustained reduction in cigarette consumption, defined as at least 50% reduction in cigarettes smoked per day (or week if originally non-daily smoker) from baseline in those who do not achieve abstinence at 6 months.

2. Evaluations of likely mechanisms of effect in particular focusing on these strategies that were encouraged and participant perceptions of effect (e.g. participant ratings), including use of explorative EMA/qualitative sub studies, e.g. using the EMA data, we will compare the characteristics of lapses across the four groups. Using multilevel models, characteristics of smoking lapses (triggers, levels of craving and withdrawal etc.) will be compared across the four treatment groups.

3. Rates of adverse events/serious adverse events (using MedDRA terminology) reported in people who use a smoking replacement product compared to those who do not and by type of product used.

Qualitative sub study

Original trial

At 3, 6- and 12-months post QD a sub sample of participants who had relapsed, lapsed, or remained abstinent will be invited to take part in a qualitative interview (N=160 in total, split equally between the 2 countries and 4 arms).

Curtailed trial

The qualitative study will provide data on the likely mechanisms of effect from ~100 participants who have and have not relapsed, and including lapsers, in the control and intervention arms from both countries, at 3 and 6 months. The following concepts will be looked at:

1. Feasibility, acceptability, use and perceived impact of study processes and interventions
2. How do lapses influence relapse?
3. Barriers and facilitators to maintaining abstinence
4. Cross-cultural perspectives, between UK and Australia, on cessation and relapse prevention support

All interviews will be audio recorded and transcribed verbatim. After familiarisation with the transcripts, the data will be indexed and imported into Nvivo 9 to facilitate systematic analysis. The initial coding frame will be based on the interview topic guides and new codes will be added as they emerge from the data during the coding process.

Coded data will then be analysed using the 'Framework' method, successfully used by the applicants in previous research. This involves examining key themes from the interviews organised through 'charting' which will allow us to investigate relationships between treatment arms and successes and failures and interviewees' views and how the facilitators and barriers to the relapse prevention interventions varied by treatment group.

More than one researcher will be involved in all data analysis to enhance the validity of findings.

Ecological Momentary Assessment (EMA) sub study

Original trial

At 4-12 weeks post quit date (QD) a subset of 50 participants from each arm will be recruited to take part in three weeks of EMA monitoring, which includes detailed monitoring of the use and relationship to cravings and slips of the two interventions using a handheld electronic diary [19].

Curtailed trial

The EMA sub study will provide data on the use of interventions and relationship to cravings and slips for ~85 participants in the control and intervention arms for both countries at around 8-12 weeks quit.

The following concepts will be looked at:

1. Barriers and facilitators to maintaining abstinence
2. Cross-cultural perspectives, between UK and Australia, on cessation and relapse prevention support

Data collected during lapse assessments themselves will also be compared to parallel data collected during random prompt assessments to examine whether the context in which participants lapse differs by groups [20]. Additionally, we will explore group differences in the number of, and responses to, temptation episodes.

EMA data will predominately be analysed using repeated measures mixed models.

METHODOLOGY

Inclusion Criteria

- Users of the SSS in the UK and the Quitline in Australia who are abstinent in the last 2 weeks of treatment (treatment period is typically 4 weeks post QD) and are still abstinent at point of recruitment. Additionally, in Australia, ethics permission was secured to recruit those quit between 7 and 100 days, and recruit from two additional sources: social media (via Facebook advertising) and St Vincent's Hospital, Melbourne.
- Willing to use a smoking replacement product or online behavioural support tool if allocated to use
- Aged 18 years and older
- Own a mobile phone
- Has Internet access
- Able to read/write/understand English

Exclusion Criteria

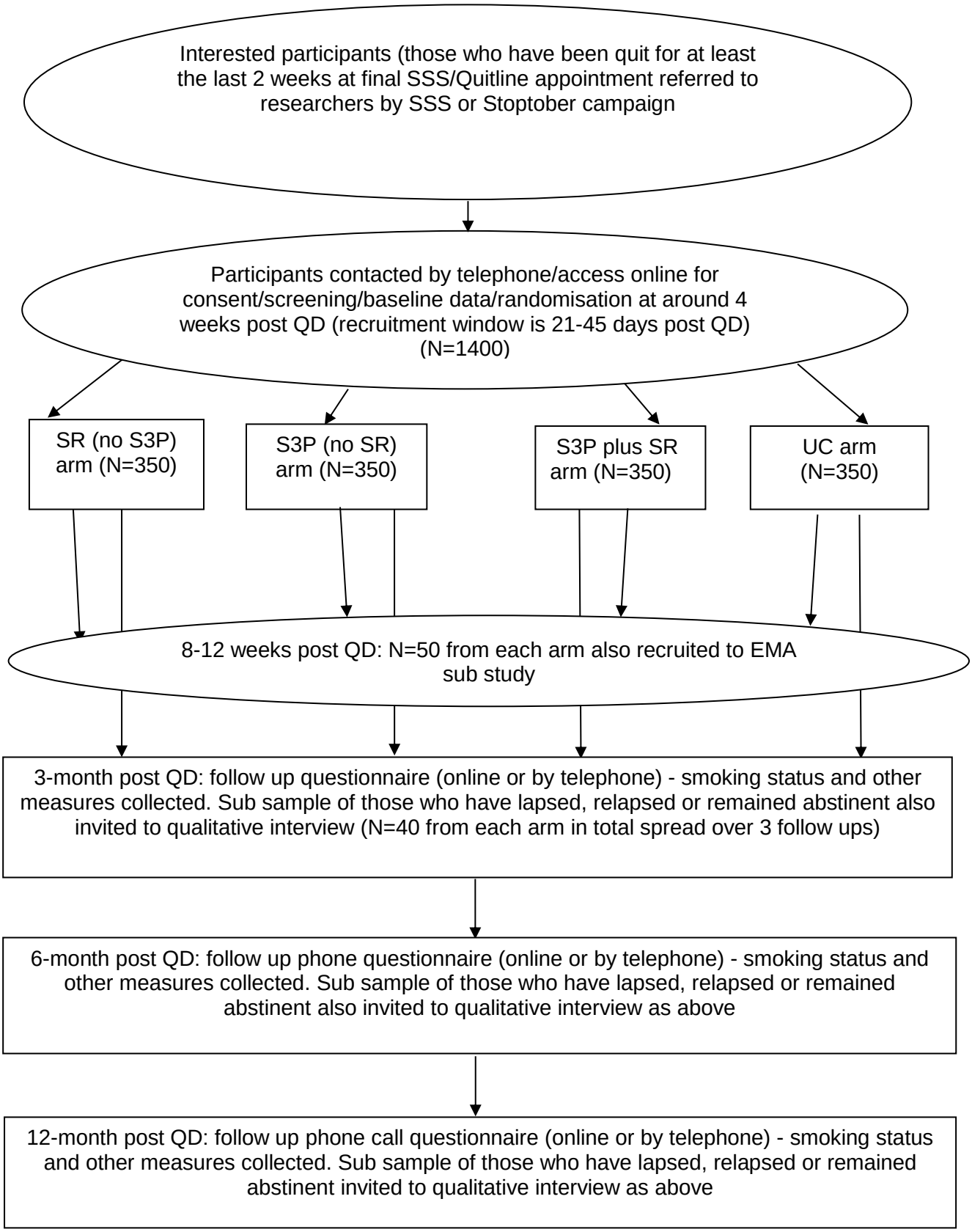
- Enrolled in other smoking cessation/relapse prevention research
- Currently using EC/oral NRT and planning to use for longer than 3 months

Study Design

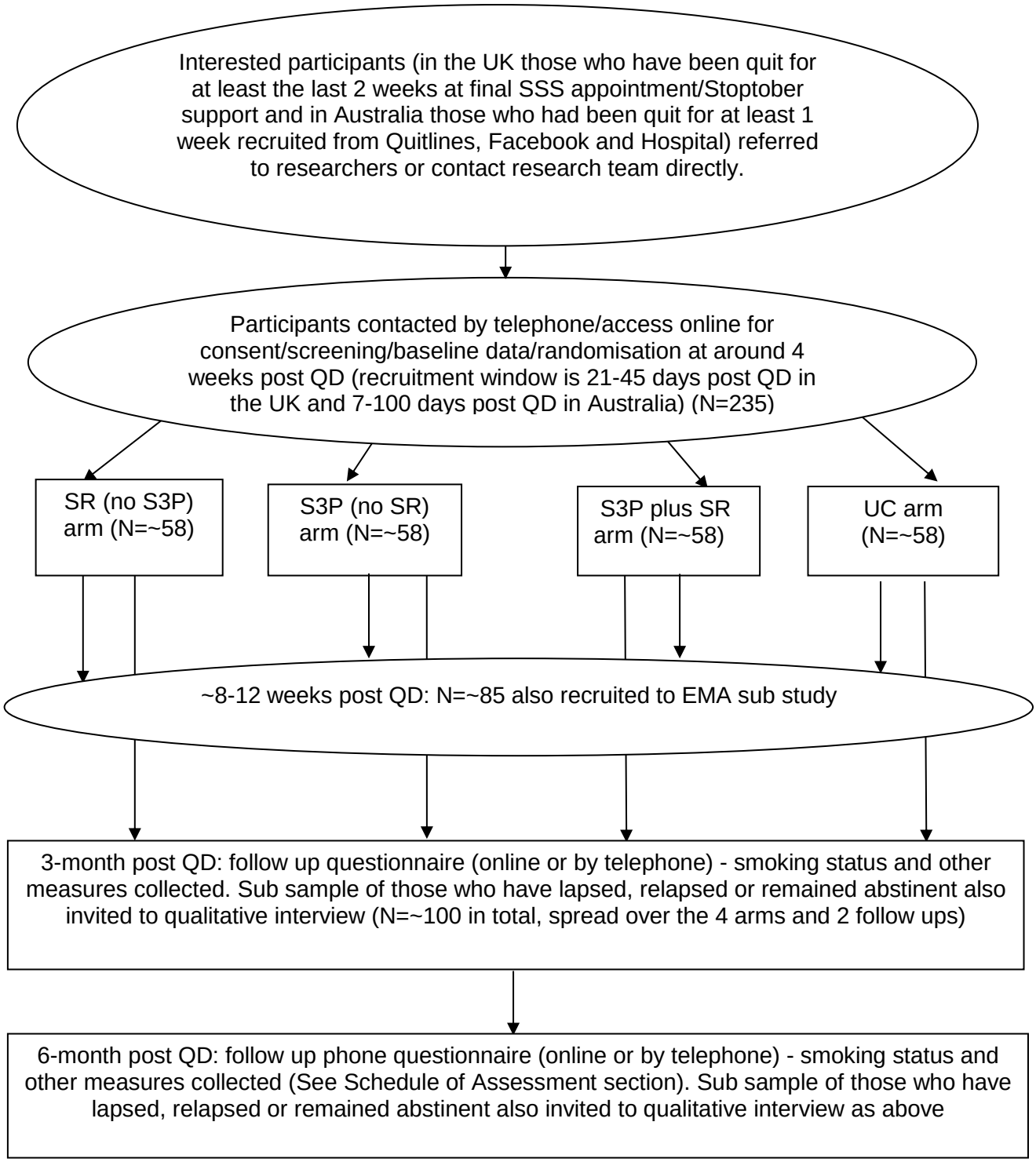
This is a factorial randomised controlled trial with two comparisons added to usual care (UC; UC is generally 8-12 weeks of pharmacotherapy (e.g. varenicline or NRT), plus standard counselling provided from the commencement of the quit attempt), augmented by a series of text messages available in all conditions. Participants will be individually randomised to one of four arms: UC (Usual Care), SR (Smoking Replacement), S3P (Structured Planning and Prompting Protocol), or SR plus S3P.

Study Scheme Diagram

The study scheme below outlines the flow of participants through the trial and key time points for the original trial and curtailed trial.


Interested participants (those who have been quit for at least the last 2 weeks at final SSS/Quitline appointment referred to researchers by SSS or Stoptober campaign
Participants contacted by telephone/access online for consent/screening/baseline data/randomisation at around 4 weeks post QD (recruitment window is 21-45 days post QD) (N=1400)
SR (no S3P) arm (N=350)
S3P (no SR) arm (N=350)
S3P plus SR arm (N=350)
UC arm (N=350)
8-12 weeks post QD: N=50 from each arm also recruited to EMA sub study
3-month post QD: follow up questionnaire (online or by telephone) - smoking status and other measures collected. Sub sample of those who have lapsed, relapsed or remained abstinent also invited to qualitative interview (N=40 from each arm in total spread over 3 follow ups)
6-month post QD: follow up phone questionnaire (online or by telephone) - smoking status and other measures collected. Sub sample of those who have lapsed, relapsed or remained abstinent also invited to qualitative interview as above
12-month post QD: follow up phone call questionnaire (online or by telephone) - smoking status and other measures collected. Sub sample of those who have lapsed, relapsed or remained abstinent invited to qualitative interview as above

Curtailed trial



Randomisation Procedures

Participants were randomised (stratified by country in permuted blocks of random size) to one of four study arms described in the Schedule of Intervention below. The randomisation ratio was 1:1:1:1 across the 4 study arms. Randomisation was done automatically via Stata code with the results imported into the web based program (Quest Engage) that directed the baseline study questionnaire, and occurred after all key baseline information was collected. The 4 arms are described as follows:

1. **UC arm (control group, receives neither intervention):** If used as part of UC, this group will be encouraged to continue use of base medication (e.g. varenicline or patch) until the end of the recommended period of use.

   They will be offered a version of the text messaging program without the specific strategies focused on in the S3P intervention. They will not be provided with any SR products (although they may be using them as part of their continued UC at the SSS).

2. **Only SR:** This group will be offered a SR product. Participants will choose one SR product from up to three NRT and EC options (two fast acting NRT and one EC) to use as a coping strategy if at risk of relapse.

3. **S3P / No SR arm:** After answering some additional questions participants will receive an initial personalised, tailored plan, focusing on S3P (Structured Planning and Prompting Protocol) strategies, and access to a tool designed to help them form implementation intentions for situational temptations to smoke (Problem Planner). These will be reinforced with additional text messages that will remind them to rehearse these self-statements, replacing and extending the more general messages used in the UC condition. These resources will be available to them on the internet for future use, with prompts to use when recommended (around the time of stopping base medication or when having additional problems).

4. **S3P plus SR arm:** Participants will receive both interventions, with S3P modified to include integrated references to SR as a relapse prevention strategy.

Curtailed Trial Follow-up (no 12-month follow-up)

Participants will complete online questionnaires at 3 and 6 months post-QD (approximately 2- and 5-month post-recruitment) for smoking status and other measures. Participants will be contacted by telephone to complete the questionnaires if they prefer, or if they do not respond to the email prompts to complete them. Participants will receive £10 (UK)/$20 (Australia) for completing the questionnaires at 3 and 6 months.

Although the research team had telephone contact with some participants at 3 and 6 months to assess outcomes no counselling was provided at these follow-up calls.

NB. Participants who did not want to use a nicotine based product were not randomised into the study, but were offered access to the S3P program, and were followed up passively only (i.e. they received email reminders to complete the follow up questionnaires online, but were not actively followed up by the study team). The analysis of this subsidiary study is not included in this SAP.

Curtailed Measures

Baseline:

- Demographic details, smoking measures (e.g. heaviness of smoking index referenced to when they were smoking [21] information regarding previous quit attempts) and medical history (e.g. screening for depression, measures of perceived stress and affect)
- Information regarding the current quit attempt (including type of support/medicines used), frequency and strength of cravings, extent of slipups if any, plans on how long to continue use of base medication, self-efficacy for maintenance, perceived challenges, number of smokers in social network

All follow ups:

- Self-reported smoking status and cigarette consumption
- Detailed lapse/relapse report for those relapsing (e.g. no. of lapses, when, where, reasons, how many cigarettes at first lapse, how soon after first cigarette was full relapse)
- Strategies used to prevent relapse
- Cravings to smoke
- Participants who stop using SR/S3P/UC will be asked their reasons for doing so (if using at previous survey).
- Use of any, including non-allocated, smoking cessation/relapse prevention treatments
- Detailed use of SR/S3P/UC and ratings of the interventions, including helpfulness (3 month only) and adverse events.

12-month follow up additions – not available in the curtailed trial:

Saliva sample collection for those abstinent at 12 months. Cut off for abstinence is cotinine < 15 ng/ml [22] for those not reporting using any nicotine product and anabasine < 1 ng/ml [23] for those reporting other forms of nicotine use

- European Quality of Life-5 Dimensions (EQ5D) questionnaire
- Health Service Use Questionnaire
- Consumption of alcohol (binge drinking), including changes in consumption [24]).

Routinely collected data:

Use of the S3P will be collected by capturing data on the number of log-ins, number of assessments completed and number of text messages received.

Original Sample Size

We expect 70% of participants to relapse between 1-12 months in UC [25], and that each RP intervention will reduce the rate to 58%, and to 48% in those receiving both. Under these assumptions and comparing those who receive (2 arms) and do not receive (2 arms) each intervention individually, 257 participants are needed

per arm to detect a difference with 90% power (alpha=0.025). We planned to recruit 350 in each arm, for the primary analysis, maximizing power, but retaining sufficient power if there is evidence that participation in the EMA study may have affected outcomes and these participants need to be excluded.

Curtailed Trial Sample Size

The analysis plan is for the curtailed trial. The study was originally powered to be able to assess the effectiveness of the SR and S3P interventions (main effects); SR (2 arms) vs. no SR (2 arms) & S3P (2 arms) vs. no S3P with power = .90 and alpha = 0.025.

With a final sample size of 235 and using alpha 0.025, we have 30% power to detect a difference between arms (i.e. S3P vs no S3P or SR vs no SR), if one really exists. If we wanted to compare the 4 arms simultaneously in 1 model, the analysis would have 51% power with alpha 0.05 (one-sided).

An alternative approach is to consider the study arms as an ordinal measure where participants are allocated to 0 (UC), 1 (S3P or SR arm), or 2 interventions (S3P+SR). We can assess whether the number of interventions received affects continued abstinence. With a final sample size of 235 and alpha = 0.05 one-sided we have 78% power and this would also avoid multiple testing. We expect the intervention to be more effective at 12 months and, therefore, this is an optimistic power estimate but we can't estimate to what degree.

Overall, the latter approach offers us a viable option to explore differences in therapy on smoking relapse. The revised analyses for the curtailed trial will be useful for future meta- analysis looking at the impact of smoking replacement and/or Structured Planning and Prompting Protocol (S3P) on relapse.

ANALYSIS PLAN

Descriptive statistics

Participants' characteristics at baseline and follow-up will be presented broken down by all 4 arms using appropriate descriptive statistics; mean and standard deviation for continuous measures that are approximately symmetric; median and quartiles if they are skewed distributions. Discrete outcomes should be described using both the number and proportion (percentage). Similarly, summary measures of the primary (i.e. quit rates) and secondary outcomes by arms will also be presented.

Analysis of primary and secondary outcomes

Analyses for the primary and secondary outcomes will use the intention-to-treat (ITT) approach. All participants will be included in the analysis and will be analysed according to the treatment group to which they were randomised. All participants with missing outcomes at six months will be considered to be smoking (relapsed) as per Russell Standard, and to have not reduced their number of cigarettes smoked per day from baseline.

All analyses will be conducted using a logistic regression where relapse status is regressed onto an ordinal predictor which codes the number of active interventions assigned (0, 1, or 2) adjusted for the stratified (i.e. country). A likelihood ratio test will be conducted initially to assess whether the ordinal predictor should be modelled as continuous or categorical. If the treatment effect is positive, we will also explore the moderating role of country on the treatment effect by including an interaction term between 'treatment' and country. Estimates and 95% confidence intervals will be presented.

Sensitivity analyses of the primary outcome

To assess the robustness of the results, a series of sensitivity analyses will be conducted using different approaches to impute missing information; specifically, we will use multiple imputation by chained equation [26] and complete case analysis where we exclude cases with missing outcomes. To build the multiple imputation model, we will explore differences in baseline measures between participants with complete and missing outcome measures.

Sensitivity analyses will also explore alternative definition of sustained abstinence for the primary outcome, e.g. Russel standard defined as not smoking more than 5 cigarettes since 2-weeks post quit.

Lastly, per protocol analysis will also be conducted to exclude those participants who were not using their allocated product. This will allow us to assess the robustness of the results following departures from the randomised treatment.

No statistical testing (p-value) will be reported for the sensitivity analyses as we are mostly interested in assessing how robust the results are.

All analyses will be carried out in Stata.

Number needed to treat

The number needed to treat (95%CI) for one additional person not to relapse will also be estimated.

Adverse events

The number of adverse events and serious adverse events by study arm will be presented and specific events will be listed.

Tables to be included

- Descriptive statistics of baseline characteristics by study arm.
- Proportion of missing information on the primary and secondary outcomes by study arm.

- Differences in baseline characteristics between patients with complete vs. missing information on the primary outcome.

Figures to be included

- CONSORT diagram

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Appendix 1

Data source for each outcome

Primary outcome

Outcome and definition	**Data source**
Sustained abstinence (i.e. no relapse) between 1 and 6 months post quit date. Relapse is defined as 7 or more days of continuous smoking reported at any follow up or any cigarettes smoked (even just a puff) in the last month at 6 months.	**6 month survey:** Have you smoked at all since we last surveyed you on <inset date>? 1. No, not even a puff 2. Yes – just a few puffs 3. Yes – 1- 5 cigarettes in total 4. Yes – more than 5 cigarettes in total When did you last smoke a cigarette? 1. Today 2. Yesterday 3. 2-6 days ago 4. 1-2 weeks ago 5. More than 2 weeks to 30 days (1 month) ago 6. More than 1 month ago **3 and 6 month survey:** At any time since <last survey> did you smoke every day for a week or more? 1. Yes 2. No

Secondary outcomes

Outcome and definition	**Data source**
Sensitivity analyses using different approaches to imputed missing smoking status at 6 months;	**6 month survey:** Have you smoked at all since we last surveyed you on <inset date>? 1. No, not even a puff 2. Yes – just a few puffs

specifically, multiple imputation by chained equation.	3. Yes – 1- 5 cigarettes in total 4. Yes – more than 5 cigarettes in total When did you last smoke a cigarette? 1. Today 2. Yesterday 3. 2-6 days ago 4. 1-2 weeks ago 5. More than 2 weeks to 30 days (1 month) ago 6. More than 1 month ago **3 and 6 month survey:** At any time since <last survey> did you smoke every day for a week or more? 1. Yes 2. No
Point prevalence abstinence at 3 months, defined as no smoking (not even a puff) in the past seven days	**3 month survey:** Have you smoked at all since we last surveyed you on <inset date>? 1. No, not even a puff 2. Yes – just a few puffs 3. Yes – 1- 5 cigarettes in total 4. Yes – more than 5 cigarettes in total **3 month survey:** When did you last smoke a cigarette? 1. Today 2. Yesterday 3. 2-6 days ago 4. 1-2 weeks ago 5. More than 2 weeks to 30 days (1 month) ago 6. More than 1 month ago

Point prevalence abstinence at 6 months, defined as no smoking (not even a puff) in the past seven days	**6 month survey:** Have you smoked at all since we last surveyed you on <inset date>? 1. No, not even a puff 2. Yes – just a few puffs 3. Yes – 1- 5 cigarettes in total 4. Yes – more than 5 cigarettes in total **6 month survey:** When did you last smoke a cigarette? 1. Today 2. Yesterday 3. 2-6 days ago 4. 1-2 weeks ago 5. More than 2 weeks to 30 days (1 month) ago 6. More than 1 month ago
Sustained reduction in cigarette smoking at 6 months in those who do not achieve abstinence. Defined as a 50% (or greater) reduction in cigarettes smoked (either per day or per week) at from baseline to 6 months post quit	**6 month survey:** How many cigarettes do you currently smoke per day (OR per week if nondaily smoker)
6 month sustained abstinence according to the Russel standard, defined as smoking no more than 5 cigarettes since 2 weeks post target quit date	**Baseline survey:** Have you smoked as much as a puff of a cigarette since you quit? 1. No, not even a puff 2. Yes – just a few puffs 3. Yes – 1- 5 cigarettes in total 4. Yes – more than 5 cigarettes in total When did you last smoke? 1. Earlier today 2. Yesterday 3. 2-3 days ago 4. 4-7 days ago 5. 8-14 days ago 6. More than 2 weeks ago **3 and 6 month survey:** Have you smoked at all since we last surveyed you on <inset date>? 1. No, not even a puff 2. Yes – just a few puffs

	3. Yes – 1- 5 cigarettes in total 4. Yes – more than 5 cigarettes in total

Evaluations of likely mechanisms of effect in particular focusing on these strategies that were encouraged and participant perceptions of effect (e.g. participant ratings), including use of EMA/qualitative sub studies.	**3 and 6 month survey:** Thinking about the period before you returned to smoking.] We are interested in the extent to which you may have done certain things to help you stay quit. When you [If M3_SMKSTAT=2: have been/ If M3_SMKSTAT=1: were] strongly tempted to have a cigarette, which of the following [If M3_SMKSTAT=2: have you done/ If M3_SMKSTAT=1: did you do] regularly? (YES/NO) (YES/NO) • Reminded myself of my reasons for quitting • Distracted myself by doing something else • Put in place a plan I had for resisting • Just tried to ignore it • Just waited until the craving went away • Told myself that I am beating my addiction • Some other strategy. If other, please specify the other strategy: **3 and 6 month survey:** Do/Did you make a list of your reasons for quitting? 1. Yes, and I remind myself whenever I feel the need 2. Yes, but I never look at it these days 3. No OR: Did you make a list of your reasons for quitting? 1. Yes, and I kept reminding myself of it up to the time I relapsed 2. Yes, but I wasn't using it at the time I relapsed 3. No **3 and 6 month survey:** Have/Had you been giving yourself rewards for achieving milestones? (e.g. spending some of the money you have saved on something nice) 1. Yes 2. No **3 and 6 month survey:** How useful do you think the QuitCoach has been [was] in helping you stay quit? 1. Very useful 2. Somewhat useful

	3. Neither 4. Somewhat useless 5. Very useless **3 month survey:** Do you plan to visit the QuitCoach again? 1. Yes 2. Not sure 3. No **3 and 6 month survey:** How useful do you think the text messages have been in helping you stay quit? 1. Very useful 2. Somewhat useful 3. Neither 4. Somewhat useless 5. Very useless

Adverse events/serious adverse events	**3 and 6 month survey:** Have you experienced any **<u>new</u>** health problems, or worsening of existing health problems since you joined this study? Yes/No Please list the new/worsened health problems you have experienced (list up to 3 problems): Problem 1:_____ Has the health problem stopped you from doing things you would normally do? 1) No 2) A little 3) A lot Are/were any of these health problems serious (e.g. life threatening, resulted in hospitalisation, resulted in ongoing or significant disability/incapacity, or otherwise considered significant)? 1. Yes 2. No