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IntEgrating smoking cessation treAtment into usual online psychological care for people with common mEntal illness: Protocol for an online randomised feasibility and pilot study (ESCAPE digital)

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ABSTRACT

Background: In the UK, smoking prevalence in people with depression (34%) and anxiety (29%) is more than double that of the general population (13%). People who stop smoking improve their mental health with comparable effect sizes found for antidepressants. In England, online psychological therapy is a standard treatment for depression and anxiety. Online therapy is an acceptable setting for smoking cessation support; however, integrated smoking and mental health support is not available. This novel study aims to assess the acceptability and feasibility of an online smoking cessation intervention, and trial procedures, offered alongside online mental health treatment as it offers increased reach to people with common mental health difficulties who smoke.

Methods: A two-armed; Intervention (Integrated SilverCloud smoking cessation support) and control group (SilverCloud usual care), pragmatic, randomised controlled feasibility trial. We aim to recruit 500 adult smokers eligible for online mental health treatment. Follow-up will be conducted at 3-months and 6-months. We will assess the acceptability and feasibility of the trial procedures (i.e., recruitment, data completeness, self-reported acceptability and satisfaction) and the intervention (i.e., self-reported quit attempt, engagement with the smoking cessation and mental health programs, smoking cessation medicine and e-cigarette use, self-reported acceptability and satisfaction) and pilot clinical outcomes (i.e., biologically validated smoking abstinence, anxiety, depression, quality of health).

Conclusion: If the Trial is successful, a randomised controlled effectiveness trial will follow to examine whether integrated smoking cessation and mental health treatment increases smoking abstinence and improves depression and anxiety compared to usual care.

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1. Introduction

Smoking is the leading cause of preventable disease and death worldwide [1,2]. Smoking prevalence has decreased from 29% during the 1990s to 13% of UK adults in 2021 [3]. However, smoking is more than twice as prevalent in people with depression (34%) and anxiety (29%) compared to the general population [4]. Increased prevalence of smoking probably contributes to the reduced life expectancy of people with common mental health difficulties compared to the general population (mortality RR:1.92 [95%CI: 1.91 to 1.94]) [5]. This population is 19% less likely to successfully quit smoking [6], but is as motivated [7] as those without mental health difficulties.

There is growing evidence that smoking may worsen mental health [8], and that stopping smoking may improve mental health. A recent Cochrane review of 102 studies (>169,500 participants) [9] found that stopping smoking is associated with reduced anxiety, depression or mixed anxiety and depression scores (SMD −0.28 [95%CI: −0.43 to −0.13], −0.3 [95%CI: −0.39 to −0.21], −0.31 [95%CI: −0.40 to −0.22], respectively), similar to the effects of anti-depressant treatment [9,10]. A Cochrane review of smoking cessation interventions for people with depression found that adding psychosocial mood management to usual treatment increased cessation rates compared to usual treatment alone (RR:1.47[95%CI: 1.13 to 1.92]) [11]. Therefore, integrating smoking cessation support within mental health treatment could improve outcomes.

In England, people with common mental health difficulties can access psychological therapies through the National Health Service Improving Access to Psychological Therapies (NHS IAPT) services. A feasibility trial of smoking cessation integration within face-to-face IAPT treatment [12] found that patients and practitioners felt that IAPT was a suitable and acceptable setting for integrating smoking cessation treatment. A common treatment offered in IAPT is cognitive behavioural therapy (CBT) [13], offered face-to-face or online (iCBT), according to practitioner assessment, patient choice and availability. iCBT offers an opportunity to reach a larger number of patients more quickly. A 2018 systematic review and meta-analysis of 1418 participants suggests that face-to-face and guided iCBT can produce equivalent overall effects, with no evidence of a difference in dropout rates [14]. An example of a commercially available and evidence-based [15–17] iCBT platform is SilverCloud Health by Amwell (https://www.silvercloudhealth.com/).

A Cochrane review of internet interventions for smoking cessation showed that iCBT could help people to quit smoking (RR:1.15 [95%CI: 1.01 to 1.30]) [18]. Given that half of smokers are interested in using online support to quit [19], and the potential reach of online interventions, this modest effect may offer significant health benefits and financial savings for the NHS. However, no internet interventions for smoking cessation are tailored to people with common mental health difficulties [18,20]. Since the COVID-19 pandemic, the government has announced a new strategic focus on digital public health, and the NHS is urgently looking for novel and remote ways to deliver services to their patients [21].

The absence of research evidence about the effectiveness of an online integrated smoking cessation intervention, means a gap currently exists in our knowledge about the benefits of combined mental health and internet smoking cessation interventions. Because of this an opportunity is being missed to reach a large number of people who have a high prevalence of smoking, help them stop, which in turn could improve their mental health.

In this trial, we aim to assess: 1) the acceptability and feasibility to patients and IAPT staff of a tailored and integrated smoking cessation intervention delivered as part of usual online treatment via SilverCloud; and 2) the acceptability and feasibility of trial procedures in terms of recruitment, randomisation, retention, and data collection.

2. Methods

2.1. Design

A parallel two-arm, pragmatic, online randomised controlled, feasibility and pilot trial with nested qualitative research. Recruitment, eligibility, randomisation, and intervention delivery will be conducted online. This trial was prospectively registered on the ISRCTN registry on 02/02/2023 (ID: ISRCTN10612149, https://doi.org/10.1186/ISRCTN10612149).

2.2. Setting

NHS IAPT services in England, which provide evidence-based treatments for people with depression and anxiety disorders. Services are delivered using a stepped-care model in which people are offered the least intrusive intervention (e.g., guided iCBT) first.

2.3. Project timeline

The trial will take place over 20 months, including a 14-month recruitment period for sites and 3-month and 6-month follow-up with participants. See Fig. 1 and Table 1 for the study flow chart and 'Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT)' schedule of enrollment, interventions and assessments.

2.4. Participants and recruitment

Adults (≥18 years) who have been referred for supported online psychological therapy via SilverCloud (i.e., self-guided iCBT with practitioner-led reviews) will be screened for smoking status when they first log-in (See Fig. 1 for flow chart). Patients who self-report smoking cigarettes regularly will be eligible and invited to take part. People will not be excluded according to any physical or mental health comorbidities and will not be required to be considering stopping smoking.

2.4.1. Sample size

We aim to recruit 500 participants. This will be sufficient to enable us to assess feasibility of adequate recruitment and retention of participants and completeness of data collection. We will aim to calculate estimates of key mediators of clinical effectiveness. This sample size is achievable as recruitment procedures will be automated online, and approximately 29–34% of online IAPT service users are smokers [4].

2.4.2. Participant reimbursement

Participants will be given a £5 shopping voucher for completing follow-ups (3-month and 6-months), i.e., up to £10. In addition, a £10 voucher will accompany the saliva testing kit to encourage the participants to send their samples to the laboratory for testing. A £15 voucher will be offered to Intervention participants at the end of the 6 month follow up survey, in return for taking part in a one-to-one interview at the end of the Trial.

2.5. Randomisation

The randomisation sequence will be generated via an algorithm within the Qualtrics online platform (https://www.qualtrics.com/uk/), using the Mersenne Twister, a standard general-purpose pseudorandom number generator used by software. Qualtrics will be nested into SilverCloud as part of the automated recruitment process. Allocation to the intervention or control arms by Qualtrics will ensure an equal number of participants are in both arms and will ensure allocation concealment, as neither trial staff nor clinicians will have any way to predict the next allocation.

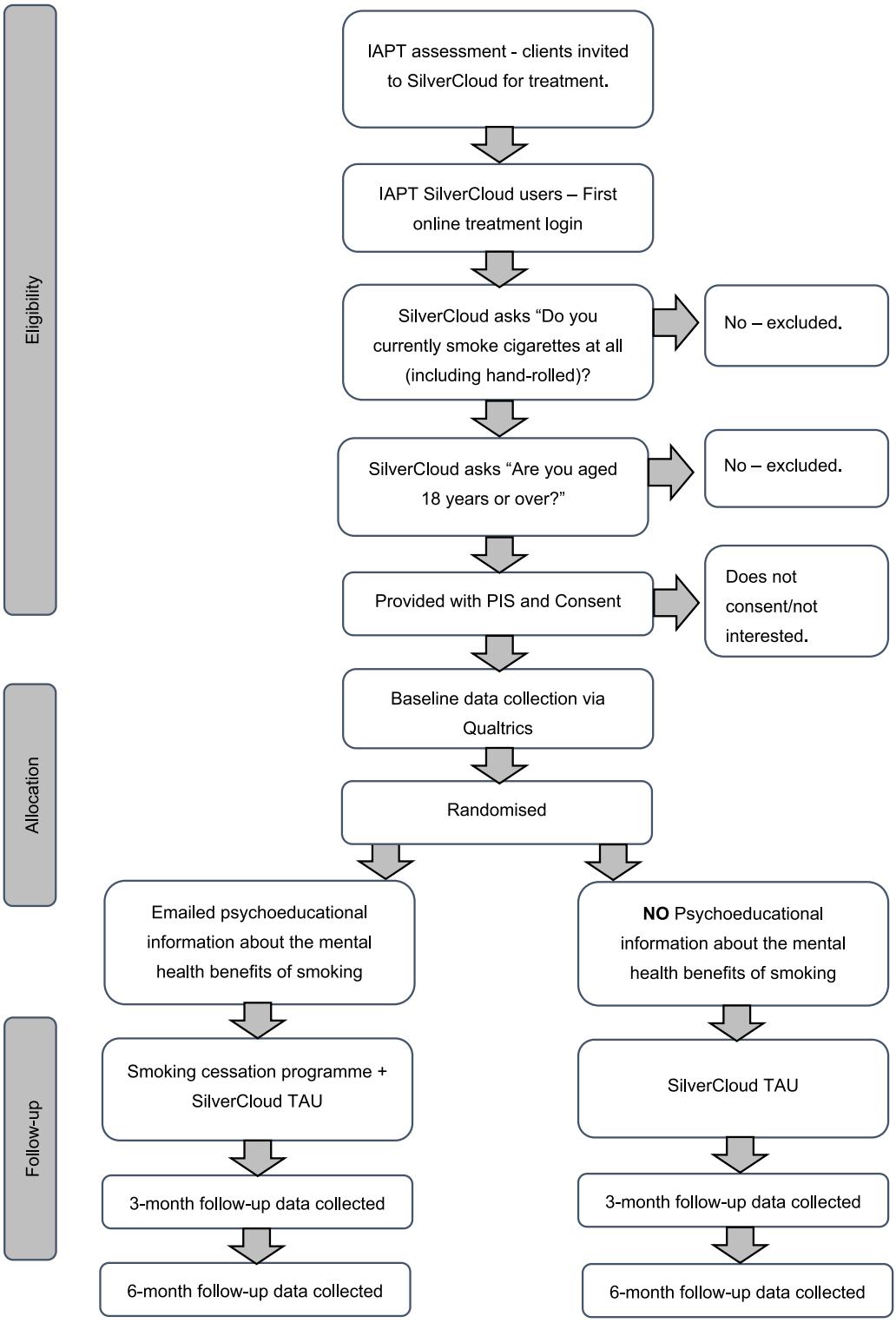

Fig. 1. ESCAPE trial flow chart.

2.5.1. Blinding

This is a behavioural intervention; therefore, it will not be possible to blind participants to treatment allocation as they will know whether they have access to the stop smoking programme. Similarly, IAPT staff will know whether their clients have access through their SilverCloud account. Outcome assessment will be self-report and collected remotely by participants via online Qualtrics surveys.

2.6. Patient and public involvement (PPI)

Recruitment of PPI members took place via the University of Bath Addiction and Mental Health Group (AIM) research database, and existing PPI groups, databases and/or social media accounts of participating IAPT services. The PPI members co-designed the intervention using a person-based approach [22], with five people with lived experience of smoking and mental health difficulties and five IAPT staff with

Table 1
SPIRIT Schedule of enrollment, interventions, and assessments.

	Pre-allocation	Allocation	Post-allocation[b]					Follow up		Trial end
	t0		t1	t2	t3	t4	t5	3-m	6-m	
Enrollment										
Eligibility screen	x									
Informed consent	x									
Allocation		x								
Intervention										
Treatment			x	x	x	x	x			
Control			x	x	x	x	x			
Assessments										
Age	x									
Gender	x									
Ethnicity	x									
Education	x									
Heaviness of Smoking Index (HSI)	x									
Previous quit attempts	x									
Primary mental health condition	x									
Physical and mental health comorbidities	x									
(Previous and) current use of smoking cessation medicine/e-cigarette use	x		x	x	x	x	x	x	x	
Patient Health Questionnaire (PHQ-9)[a]	x		x	x	x	x	x	x	x	
General Anxiety Disorder Questionnaire (GAD-7)[a]	x		x	x	x	x	x	x	x	
EQ visual analogue scale (EQ VAS)	x							x	x	
Self-reported smoking cessation (prolonged 12-week, and 4-weeks abstinent)								x	x	
Saliva sample (for those reporting cessation)								x	x	
Self-reported quit attempt			x	x	x	x	x	x		
Engagement with SilverCloud programme(s): Mental health treatment (treatment as usual) and smoking cessation (intervention arm only), e.g., frequency, duration, logins, logoffs, time spent, pages viewed			x	x	x	x	x			
Completion of SilverCloud programme(s)			x	x	x	x	x	x	x	
Stop Smoking Service Patient Satisfaction Survey (intervention arm only)								x		
Qualitative interviews with participants **(intervention arm only)**									x	x
Qualitative interviews with IAPT staff								x	x	x
Number of attended IAPT appointments (SilverCloud reviews and any other clinical contact)			x	x	x	x	x	x	x	
Number of missed IAPT appointments (DNAs) (SilverCloud reviews and any other clinical contact)			x	x	x	x	x	x	x	
Discharge/completion of IAPT treatment status			x	x	x	x	x	x	x	
Trial satisfaction questionnaire									x	

[a] PHQ-9 and GAD-7 assessments will be collected via SilverCloud for pre- and post-allocation time points, and directly from participants (online/by telephone) for 3- and 6-month follow ups.
[b] Five post-allocation time-points will be scheduled at fortnightly intervals after randomisation. These may differ from the timing of review sessions with the mental health service (which vary from approximately weekly over six weeks to fortnightly over 12 weeks).

experience delivering SilverCloud. The details of PPI involvement in the trial design are outlined in Step 1 to Step 3 in the next section.

2.7. Patient and public involvement in intervention development

2.7.1. Step 1: Review of existing published research and guidelines

Researchers reviewed the guidance and steps contained in the National Centre for Smoking Cessation and Training (NCSCT) standard treatment programme [23,24], the StopAdvisor programme [25,26], and a previous trial conducted in face-to-face IAPT treatment [27]. Alongside this happening, the Bath researchers reviewed templates for creating a Silvercloud intervention programme, and examples of online intervention development and content map. PPI contributors were involved in reviewing the research aims and design, during the period of conceptualisation.

2.7.2. Step 2: Workshop 1: Co-design with PPI members and Silvercloud team

The workshop output provided suggestions for the programme content; changes to the language used; setting patient expectations for combined support; and ensuring the content was aligned with IAPT messages. The think-aloud interviews enabled attendees to provide feedback on an earlier version of the smoking cessation programme, including suggested changes to the structure and text. Additional suggestions by PPI members (that were implemented) include coping strategies for dealing with withdrawal; second-hand second smoke effects; the impact of smoking on physical health; tips to help normalise and cope with unintended consequences of successfully quitting, such as weight gain. Also, suggestions were provided to use more day-to-day language to describe quitting or cessation of smoking and anecdotes to help create personal stories. The detailed feedback was documented in a spreadsheet and informed the final version of the smoking cessation intervention.

2.7.3. Step 3: Co-design workshop with IAPT staff

An interactive two-hour workshop took place and attendees included staff involved in the delivery of SilverCloud, and the ESCAPE digital research team. The recording of the workshop was transcribed and used to inform the final version of the smoking cessation intervention. Implemented staff suggestions included, adding explanatory text to the study's introduction at the start of baseline survey and also the Patient Information Sheet (PIS). The added information is intended to allay patient suspicions about being taken out of Silvercloud, and into the Qualtrics survey platform to complete the questionnaires.

2.7.4. Step 4: Trial steering committee

A Trial Steering Committee will be established to include independent smoking cessation academic experts and PPI members. The Term of Reference includes the role of having oversight of the overall Trial; ensuring the rights, safety and wellbeing of the participants are the most

important consideration in all deliberations; and ensuring adherence to the protocol (i.e., conducting the trial as planned) and approving any changes thereof.

Final agreed silvercloud smoking cessation programme design

The programme will comprise the following components:

- *Behavioural smoking cessation support:* comprising of five modules see **Appendix I**). Practitioners will have access to the programme product descriptor, the NCSCT stop smoking aids quick reference sheet [28], and a FAQs document; no smoking cessation training will be provided as they will not be delivering smoking cessation advice.
- *Stop smoking aids:* The programme will provide information about smoking cessation medicines like bupropion or nicotine replacement therapy (NRT), e.g., NRT patches or gum, and e-cigarettes [23,24]. NRT is first-line treatment for smoking cessation, usually offered as combination NRT (i.e., taking two types of NRT together). *E*-cigarettes (vapes, e-cigs) are less harmful than smoking tobacco and more effective for smoking cessation than NRT [29]. Some risks to vulnerable groups, as well as the benefits of these medications, are emerging [30]. The section of the Smoking Module about Stop Smoking Aids, advises anyone thinking of using e-cigarettes etc. to speak to their doctor initially so they can decide what is suitable for them. Access to stop smoking aids will be via signposting to e-cigarette vendors, pharmacies and GP surgeries. Participants will be able to download a template letter requesting a prescription for NRT from their GP.

2.8. Procedure

At the first login, SilverCloud users will complete the standard assessments (e.g., PHQ-9, GAD-7) followed by the study screeners. Those eligible to participate will be provided with the trial participant information sheet PIS. The PIS has been developed in consultation with the PPI members and approved by Research Governance bodies and NHS Research Ethics Committee. The PIS explains purpose of study; the reason they are seeing an invite; a description of study and what their participation involves. The participants read the PIS in Silvercloud, and before consenting, they will be informed that they can take their time to consider whether they would like to take part, contact the research team with any questions, and return later to the same page to decide. Evidence of consent will be collected via Qualtrics. Participants who consent to take part will answer demographic questions and baseline assessments via Qualtrics and then be randomised (see **Randomisation**).

Information about all participants' engagement with, and completion of the SilverCloud programme(s) and PHQ-9, GAD-7 assessments (before 3- and 6-month follow-up) will be collected as part of usual care and recorded by SilverCloud. Also, a Qualtrics with 2 questions will collect information about their use of smoking cessation medication and e-cigarettes and quit attempts. Participants will be sent follow-up surveys (3 months and 6-months after randomisation) to collect information about their use of smoking cessation medication and e-cigarettes, quit attempts (3-months only), smoking cessation (prolonged 4-week and 12-week abstinence, respectively), intervention acceptability (intervention arm at 3-months only), trial acceptability (6-months only), and to complete PHQ-9, GAD-7 and EQ VAS assessments. Intervention participants will be asked at the 6-month follow-up stage if they are interested in taking part in a one-to-one interview and if they do, they will receive a £15 voucher. If participants do not respond to the 3-month or 6-month follow-up survey, they will be contacted by a member of the research team (via telephone or email) and prompted to complete them online. Shopping vouchers for £5 will be sent to participants for completing follow-ups (see **Participant reimbursement**).

Primary mental health condition and physical and mental health comorbidities, the number of attended or missed appointments (including SilverCloud reviews or any other clinical contacts) and the discharge or completion status will be provided to Bath researchers by the SilverCloud therapists, as it is collected as part of usual care and recorded in patient management software. Data will be extracted by a member of staff at participating NHS sites and shared securely with the research team. Data for trial participants about engagement with the Smoking Modules will be requested from SilverCloud by NHS sites and shared securely with the research team.

Anyone reporting smoking abstinence will be posted a saliva sample pack, including instructions for completion, a £10 voucher, and a pre-paid envelope to post the sample to the laboratory (ACM Bioanalytical Services) for biological verification. The research team will contact participants if they do not return their samples. The laboratory will only receive participant saliva samples with the participant ID number and will not hold personal or sensitive information. Participants' genetic data will not be extracted or stored in this study. The saliva samples will be destroyed within 60 days of analysis.

2.8.1. Control arm: SilverCloud usual care

Participants in the control arm will receive SilverCloud usual care. Participants will be signposted to NHS stop smoking information and support via Qualtrics after completing their 6-month follow up (or via email if they do not complete follow-up).

2.8.2. Intervention arm: Integrated SilverCloud smoking cessation support

In addition to SilverCloud usual care, participants in the intervention arm after randomisation, will be automatically emailed written psychoeducational information about smoking and mental health, including the role of nicotine withdrawal (which leads to feelings of irritability, low mood and anxiousness) in reinforcing the misperception that smoking can improve mental health (when smoking relieves withdrawal symptoms); the mental health benefits of quitting smoking; the value of stop smoking aids; and where to find more information from SilverCloud [10,31]. Participants can access the smoking cessation program alongside their usual mental health treatment, from their SilverCloud account.

2.8.3. Trial and intervention outcome measures

See Table 1 for the full list of variables, outcome measures and Table 2 for progression criteria. The feasibility and acceptability outcome measures were derived from previous epidemiological studies which indicated that approximately 25% of people referred for online CBT for common mental health problems should meet eligibility criteria (smoker, aged 18+) [4,19]. Data suggested the proportion making a quit attempt would lie between 7% and 25% [4,19]. The measures are also based on a pilot study of the integration of Smoking Cessation into Silvercloud [12] and the ESCAPE (intEgrating Smoking Cessation treatment as part of usual Psychological care for dEpression and anxiety) trial conducted in face-to-face IAPT treatment [27]. Also, the outcomes criteria for smoking cessation trials [31]. New feasibility measures agreed during the conceptualisation co-design workshops, by research team are being piloted in this feasibility study.

Table 2
Progression criteria to determine whether it is feasible to progress to an effectiveness trial.

Criteria	Red	Amber	Green
Proportion of eligible SilverCloud clients (i.e., adult smokers) who enroll in trial [4,19].	<15%	15–19%	≥20%
Recruitment compared with target.	<60%	60–79%	≥80%
Data completeness of future trial outcomes (i.e., self-reported abstinence status, depression, and anxiety scores).	<50%	50–69%	≥70%
Behavioural marker of engagement with smoking cessation program: self-reported quit attempt(s) in intervention group [4,19].	<5%	5–7%	≥8%

2.8.4. Trial procedures feasibility and acceptability outcomes

- Participants recruited relative to target and recruitment rate/month.

- Data completeness: proportion of people from whom data is obtained at 3-months and 6-months.
- Proportion of saliva sample packs sent to people reporting abstinence that yield a measure of cotinine or anabasine.
- Data completeness for depression scoring (PHQ-9) and anxiety scoring (GAD-7) at 3- and 6-months.
- Participants' views of the study procedures assessed by questionnaire and by interview.
- Mental health practitioners' views of the study procedures assessed by interview.

2.8.5. Intervention feasibility and acceptability outcomes

A key early indicator of effectiveness is the proportion of people who report making a quit attempt, which can be measured in each arm of the trial. The outcome here is defined as a quit attempt lasting at least 24 h. The outcome is recorded as the primary outcome measure on the ISRCTN Registry and is a key measure of intervention feasibility.

- Self-reported quit attempt (up to 3-month follow-up)
  - 'Have you made a serious attempt to stop smoking (lasting at least 24 hours) in the last two weeks/three months [post-allocation t1-t5/3-month follow up survey]?'
- Engagement with the SilverCloud program(s): smoking cessation (intervention arm only) and usual mental health treatment (all participants), e.g., length of support, frequency (number of logins) and duration (time spent) of program use, the proportion of program completion and completion of the quit date module [32]
- Self-reported smoking cessation medicine use
- Self-reported e-cigarette use
- Proportion of people completing their mental health treatment
- Number of attended online IAPT appointments.
- Self-report questionnaires: Modified version of the Stop Smoking Service Patient Satisfaction Survey [33] (intervention arm participants only)
- Qualitative interviews will be offered in the online survey to all intervention arm participants (as above) who have reached the 6 month follow up stage. No >15 participants will be interviewed, and they will be recruited at different stages of the Trial. The questions will explore; why they signed up for trial; their use of smoking program; their experience of the trial procedures and data collection through questionnaires. They will also be asked if they have made any quit attempts and how they feel about having smoking cessation support included as part of their usual mental health program.
- Qualitative interviews with IAPT staff to explore their perceptions of; the acceptability of the smoking cessation treatment, acceptability of data collection procedures, positive and negative impacts of smoking cessation treatment on IAPT usual care and mental health recovery.

2.8.6. Pilot clinical outcomes

This feasibility study will assess indicative measures of smoking cessation and mental health, which would be the primary outcomes of an effectiveness trial:

- Smoking cessation
  - Abstinence at 3 and 6 months (4-week abstinence at 3 months, biochemically validated; 12-week prolonged abstinence between 3 and 6 months, biochemically validated)
  - Self-reported abstinence is defined as not smoking >5 cigarettes during the abstinence period [31]
  - ACM Bioanalytical Services (https://www.acmgloballab.com/bioanalytical-services) will analyse saliva samples for biochemical validation to detect cotinine (cut-off: 15 ng/ml [31,34], which is present in nicotine, or anabasine (cut-off: <1 ng/ml), which is present in tobacco, if participants report using nicotine products
- Depression and anxiety
  - Patient Health Questionnaire (PHQ-9) [35] (which includes item on anhedonia)
  - General Anxiety Disorder Questionnaire (GAD-7) [36]
- Quality of life
  - EQ visual analogue scale (EQ VAS) from the EuroQuol three-dimensional questionnaire (EQ. 5D 3 L) [37]

2.8.7. Baseline demographic measures

- Age (years).
- Gender ('man', 'woman', 'non-binary', 'I identify as [free text]').
- Ethnicity ('Asian or Asian British', 'Black, Black British, Caribbean or African', 'Mixed or multiple ethnic groups', 'White', 'Other ethnic group').
- Highest level of education ('Higher Education or professional / vocational equivalents (e.g., post-school diploma, university degree)', 'A levels or vocational level 3 or equivalents (e.g., school exams age 18)', 'GCSE / O Level grade A*-C or vocational level 2 or equivalents (e.g., school exams age 16)', 'Qualifications at level 1 and below (e.g., essential work-based skills)', 'Other qualifications: level unknown', or 'No qualifications')
- Heaviness of smoking index (HSI) [38]
- Previous quit attempts ('Have you quit smoking for at least 24 hours in the last 12 months?')
- The primary mental health reason for treatment (e.g., depression) and any recorded physical / mental health comorbidities will be collected from the IAPT patient management system.

2.9. Program adverse events

Any serious adverse events (SAEs) will be recorded and assessed to determine whether they are related unexpected serious adverse events (RUSAEs) and kept in the study file with a note that will identify when the event occurred, the details of the event, any potential study relation, action taken and resolution/closure of the event. The independent Trial Steering Committee chair will review adverse events. An assessment of seriousness will be made and reported to a research governance officer at the University of Bath.

3. Data analysis plan

Statistical analyses will be performed on an intention-to-treat (ITT) basis, with participants being analysed in the study arms they were allocated to, regardless of actual intervention received or levels of adherence to the intervention. We will report data missingness for all variables.

3.1. Analysis of baseline data

For each trial arm, we will report means, proportions and a relevant measure of variance for each baseline variable.

3.2. Feasibility and acceptability outcomes

The number and proportion of participants recruited into the trial will be reported, relative to the target, for each trial arm; we will report the number of participants who were screened, randomised, treated, and followed-up in a CONSORT flow chart. We will report percentages and/or the median for categorical variables, and the mean and standard deviation for continuous variables.

3.3. Piloting main trial clinical outcomes

The outcome measures that we intend to assess in an effectiveness trial (biochemically validated smoking abstinence, depression and anxiety scores, quality of life scores) will be piloted in this feasibility study. We will compare continuous outcome values between trial arms using linear regression modelling and compare categorical outcome values between trial arms using logistic regression modelling. We will report odds ratios, coefficients and 95% confidence intervals from regression models.

3.4. Analysis of qualitative data

Interview data will be transcribed by a university-approved and GDPR-compliant transcription service. To ensure the quality of data transcription a researcher will do a 50% check of audio data against the transcripts. The audio recordings will then be deleted. The data will be analysed using thematic analysis, applying a framework method: transcription, familiarisation, coding, development and application of an analytical framework, creation of a matrix and interpretation of data [39].

4. Discussion

This feasibility and pilot trial will test if it is possible to offer online smoking cessation intervention offered alongside usual online mental health treatment (via SilverCloud), Self-reported quit attempts and a biochemically validated measure of smoking cessation will be used to assess the effectiveness of the intervention in a larger trial.

4.1. Strengths and limitations

The SilverCloud smoking cessation program used has been developed to combine best practices from evidence-based and cost-effective interventions, and learning from a previous feasibility trial and the present co-design process to be used within the IAPT setting [12,29]. The automated processes also mean the burden on participants taking part is minimal, particularly as this population is already engaging with an online SilverCloud intervention at the point of screening and recruitment. However, it is possible that the lack of face-to-face communication could affect interest in enrollment and retention in the intervention and follow-up data collection. In addition, the lack of contact with a trained smoking cessation advisor could impact engagement with the intervention and the lack of access to direct, cost-free stop smoking aids could impede their use.

5. Conclusion

Integrating smoking cessation treatment into online intervention for mental health difficulties may offer a promising vehicle to reach a large number of people who have a high smoking prevalence. If the intervention and trial procedures are found to be acceptable and feasible, we can conduct a future effectiveness randomised controlled trial.

Ethics approval and consent to participate

This trial received NHS Research Ethics Committee (Wales Research Ethics Committee 6 Swansea) and HRA and Health and Care Research Wales (HCRW) approval on 23/03/2022 (IRAS ID: 304857; REC reference: 22/WA/0051). Subsequent amendments were approved on 08/06/2022, 01/09/2022, 11/01/2023, 03/08/2023. Current protocol version 4.0 (22/11/2022). Any further protocol amendments will be communicated to the sponsor, REC, HRA and participating sites. All participants will give written informed consent.

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Authors' contributions

G.T., K.S., B.A., D.H., J.B., M.R.M., and P.A. conceived the study. A.K.M.B., S.D., DR., P.A., and P.J. are responsible for the conduct of all stages of this trial. A.K.M.B., S.D., D.D., G.H., K.S., B.A., D.R., D.H., S.P., J.B., M.R.M., P.J., P.A., and G.T. contributed to the design of the study and the study protocol. All authors contributed to writing and editing the manuscript. All authors read and approved the final manuscript.

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Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

DD, GH, DR, and DH are employees of Amwell, a telehealth company that owns the Silvercloud product.

Data availability

At the end of the study, we will archive anonymised research data. Data will be uploaded to the University of Bath's Research Data Archive (https://researchdata.bath.ac.uk/). All data and data access will be

restricted due to the sensitive nature of the data being collected (https://researchdata.bath.ac.uk/policies/). Data will be made available to approved bona-fide researchers, after they have signed a data access agreement, the person will be granted access to the University of Bath's Research Data Archive by the Research Data Services (https://data.blogs.ilrt.org/). Participants will consent to this process at the start of the study. Data stored in the Archive will have a Data Object identifier (DOI).

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Appendix I: SilverCloud smoking cessation programme overview

Table A1
Summary of the goals and activities in each of the five SilverCloud smoking cessation programme modules.

Module	Goals	Topics/Content	Activities/Tools
1: Smoking and You	• Address beliefs about smoking and mental health • Inform about smoking cessation program. • Assess current smoking. • Assess nicotine dependence. • Explain tobacco withdrawal cycle. • Explain importance of abrupt cessation and 'not a puff' rule. • Explain benefits of quitting smoking • Introduce visualisation and relaxation practice. • Summarise learning	• Introduction • Myths and facts about smoking quiz • Smoking habits • The Tobacco Withdrawal Cycle • Not a puff • Benefits of not smoking • Making a change • Visualise life as a non-smoker. • Staying in the present • Personal stories • Summing up	• Myths and facts about smoking quiz • Tobacco Withdrawal Cycle animation • Heaviness of Smoking Index • Journal • Breathing space relaxation exercise • Summary sheet • Key messages record • Daily practice
2: Becoming a non-smoker	• Identify motivations for quitting. • Reflect on current smoking habits. • Identify smoking cues and high-risk situations. • Identify risk reduction strategies. • Inform about withdrawal symptoms and cravings. • Identify how to use and access stop smoking medications and e-cigarettes. • Set a quit date. • Address smoking contacts and how to get support during quit attempt. • Confirm importance of abrupt cessation and prompt commitment • Summarise learning	• Introduction • Smoking effects and risks quiz • My reasons to stop smoking. • My smoking diary • Situations and smoking cues • My risk reduction strategies • Stop smoking medication and NRTs. • Quit date. • Personal stories • Staying in the present • Summing up	• Smoking effects and risks quiz • Money saving calculator • My reasons for quitting list • Smoking diary • Smoking cues list • Coping strategies planner • GP prescription request letter • Journal • Quit date commitment. • Sounds listening exercise. • Summary sheet • Key messages record • Daily practice
3: Your Quit Date	• Log in on Quit Date • Review commitment to quit. • Normalise difficulties. • Confirm importance of 'not a puff' rule and prompt commitment • Reminder of stop smoking medication • Review quit date checklist (e.g., supply of medication, removed tobacco products, informed social network)	• Introduction • Today is your quit date. • Mood monitor • My smoking diary • Personal stories • My commitment • Staying in the present • Summing up	• Quit date checklist. • Mood monitor • Smoking diary • Progressive muscle relaxation exercise • Summary sheet • Key message record
4: Making Progress	• Review progress • Normalise difficulties and reflect on lapses or relapses. • Review cravings and difficult situations, experience dealing with them and how to manage going forward. • Review quit date checklist. • Review use of stop smoking medication and ensure sufficient supply. • Confirm importance of 'not a puff' rule and prompt commitment • Summarise learning.	• Introduction • Triggers and risky situations quiz • Lapses and relapses • Progress since your quit date • Difficult situations and how to cope. • Using your stop smoking medications • Personal stories • My commitment • Staying in the present • Summing up	• Triggers and risky situations quiz • Quit date checklist. • Belly breathing exercise. • Summary sheet • Key messages record
5: Moving Forward	• Prepare user for continuing as a non-smoker. • Review progress • Review original goals and plans for future. • Identify useful stop smoking resources. • Summarise learning.	• Introduction • Your progress • Future goals • Helpful resources • My moving forward checklist • Personal stories • My commitment • Staying in the present • Summing up	• Set reminders. • Mood monitor • Smoking diary • Resources • Moving forward checklist • Progressive muscle relaxation exercise • Summary sheet • Key messages record

References

[1] World Health Organisation, World Health Organisation [cited 2020 Jan 1]. WHO report on the global tobacco epidemic, 2011: Warning about the dangers of tobacco. Available from: https://apps.who.int/iris/handle/10665/44616, 2011.

[2] Cancer Research UK, Cancer Research UK, Cancer Risk Statistics, 2023 Feb 20. Available from: https://www.cancerresearchuk.org/health-professional/cancer-statistics/risk#heading-Two.

[3] ONS, Office for National Statistics (ONS) Statistical Bulletin [cited 2023 Mar 27]. Adult smoking habits in the UK: 2021. Available from, https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/healthandlifeexpectancies/bulletins/adultsmokinghabitsingreatbritain/2021, 2022.

[4] G.M.J. Taylor, T. Itani, K.H. Thomas, D. Rai, T. Jones, F. Windmeijer, et al., Prescribing prevalence, effectiveness, and mental health safety of smoking cessation medicines in patients with mental disorders, Nicotine Tob. Res. 22 (1) (2020) 48–57.

[5] O. Plana-Ripoll, C.B. Pedersen, E. Agerbo, Y. Holtz, A. Erlangsen, V. Canudas-Romo, et al., A comprehensive analysis of mortality-related health metrics associated with mental disorders: a nationwide, register-based cohort study, Lancet 394 (10211) (2019 Nov) 1827–1835.

[6] B. Hitsman, G. Papandonatos, D. McChargue, A. DeMott, M. Herrera, B. Spring, et al., Past major depression and smoking cessation outcome: a systematic review and meta-analysis update, Addiction 108 (2) (2013) 294–306.

[7] R. Siru, G.K.K. Hulse, R.J.J. Tait, Assessing motivation to quit smoking in people with mental illness: a review, Addiction 104 (5) (2009) 719–733.

[8] G.M.J. Taylor, M.R. Munafò, Does smoking cause poor mental health? Lancet Psychiatry 6 (1) (2019) 2–3.

[9] G.M. Taylor, N. Lindson, A. Farley, A. Leinberger-Jabari, K. Sawyer, Naudé R. te Water, et al., Smoking cessation for improving mental health, Cochrane Database Syst. Rev. 3 (2021 Mar 9).

[10] G.M.J. Taylor, A. McNeill, A. Girling, A. Farley, N. Lindson, P. Aveyard, Change in mental health after smoking cessation: systematic review and meta-analysis, BMJ 348 (g1151) (2014).

[11] R. van der Meer, M. Willemsen, F. Smit, P. Cuijpers, Smoking cessation interventions for smokers with current or past depression, Cochrane Database System. Rev. [Internet] 8 (2013), https://doi.org/10.1002/14651858.CD006102.pub2. Available from:.

[12] K. Sawyer, K. Fredman Stein, P. Jacobsen, T.P. Freeman, A.K.M. Blackwell, C. Metcalfe, et al., Acceptability of integrating smoking cessation treatment into routine care for people with mental illness: A qualitative study. Health Expectations [Internet], 2022 Oct 12, https://doi.org/10.1111/hex.13580 [cited 2023 Jan 17];n/a(n/a).

[13] NHS Digital, Psychological Therapies, Annual report on the use of IAPT services, 2021–22: Additional analysis of therapy-based outcomes in IAPT services [Internet] [cited 2023 Feb 16]. Available from: https://digital.nhs.uk/data-and-information/publications/statistical/psychological-therapies-annual-reports-on-the-use-of-iapt-services/annual-report-2021-22/therapy-based-outcomes, 2022.

[14] P. Carlbring, G. Andersson, P. Cuijpers, H. Riper, E. Hedman-Lagerlöf, Internet-based vs. face-to-face cognitive behavior therapy for psychiatric and somatic disorders: an updated systematic review and meta-analysis, Cogn. Behav. Ther. 47 (1) (2018 Jan 2) 1–18.

[15] D. Richards, A. Enrique, N. Eilert, M. Franklin, J. Palacios, D. Duffy, et al., A pragmatic randomized waitlist-controlled effectiveness and cost-effectiveness trial of digital interventions for depression and anxiety, NPJ Digit. Med. 3 (1) (2020 Jun 15) 85.

[16] J. Palacios, A. Adegoke, R. Wogan, D. Duffy, C. Earley, N. Eilert, et al., Comparison of outcomes across low-intensity psychological interventions for depression and anxiety within a stepped-care setting: A naturalistic cohort study using propensity score modelling, Br. J. Psychol. [Internet] (2022 Nov 24), https://doi.org/10.1111/bjop.12614 [cited 2023 Mar 9];n/a(n/a).

[17] D. Duffy, A. Enrique, S. Connell, C. Connolly, D. Richards, Internet-delivered cognitive behavior therapy as a prequel to face-to-face therapy for depression and anxiety: a naturalistic observation, Front. Psychiatry [Internet]. (2020) 10. Available from: https://doi.org/10.3389/fpsyt.2019.00902.

[18] G.M.J. Taylor, M.N. Dalili, M. Semwal, M. Civljak, A. Sheikh, J. Car, Internet-based interventions for smoking cessation, Cochrane Database Syst. Rev. 2017 (9) (2017).

[19] J. Brown, S. Michie, T. Raupach, R. West, Prevalence and characteristics of smokers interested in internet-based smoking cessation interventions: cross-sectional findings from a national household survey, J. Med. Internet Res. 15 (3) (2013) e50.

[20] Medical Research Council, Developing and Evaluating Complex Interventions: New Guidance, 2006.

[21] New Office for Health Promotion to Drive Improvement of Nation's Health - GOV.UK [Internet], Available from: https://www.gov.uk/government/news/new-office-for-health-promotion-to-drive-improvement-of-nations-health, 2021 Sep 11.

[22] L. Yardley, B. Ainsworth, E. Arden-Close, I. Muller, The person-based approach to enhancing the acceptability and feasibility of interventions, Pilot Feasibil. Stud. 1 (1) (2015 Oct 26) 37.

[23] NCSCT, Standard Treatment Programme: A Guide to Behavioural Support for Smoking Cessation, London, UK, UK, 2019.

[24] National Institute for Health and Care Excellence (NICE), Tobacco: preventing uptake, promoting quitting and treating dependence. NICE guideline [NG209] [Internet] [cited 2023 Mar 27]. Available from: https://www.nice.org.uk/guidance/ng209, 2023.

[25] J. Brown, S. Michie, A.W.A. Geraghty, L. Yardley, B. Gardner, L. Shahab, et al., Internetbased intervention for smoking cessation (StopAdvisor) in people with low and high socioeconomic status: a randomised controlled trial, Lancet Respir. Med. 2 (12) (2014) 997–1006.

[26] S. Michie, J. Brown, A.W.A. Geraghty, S. Miller, L. Yardley, B. Gardner, et al., Development of StopAdvisor: a theory-based interactive internet-based smoking cessation intervention, Transl. Behav. Med. 2 (3) (2012) 263–275.

[27] G. Taylor, P. Aveyard, K. Bartlem, A. Shaw, J. Player, C. Metcalfe, et al., IntEgrating smoking cessation treatment as part of usual psychological care for dEpression and anxiety (ESCAPE): protocol for a randomised and controlled, multicentre, acceptability, feasibility and implementation trial, Pilot Feasibil. Stud. 5 (1) (2019 Dec) 16.

[28] NCSCT, Stop smoking aids quick reference sheet [Internet], 2023 [cited 2023 Mar 27]. Available from: https://www.ncsct.co.uk/publication_stop_smoking_medications_quick_reference.php.

[29] A. McNeill, L. Brose, R. Calder, L. Bauld, D. Robson, Evidence review of e-cigarettes and heated tobacco products 2018. A report commissioned by Public Health England, London, UK, 2018.

[30] S. Feeney, V. Rossetti, J. Terrien, E-cigarettes-a review of the evidence-harm versus harm reduction, Tob Use Insights. (15) (2022 Mar 29), https://doi.org/10.1177/1179173X221087524, 1179173X221087524. (PMID: 35370428; PMCID: PMC8968985).

[31] G.M.J. Taylor, A. McNeill, A. Farley, N. Lindson, P. Aveyard, Smoking cessation for improving mental health, Cochrane Database Syst. Rev. (2020) CD013522.

[32] O. Perski, A. Blandford, R. West, S. Michie, Conceptualising engagement with digital behaviour change interventions: a systematic review using principles from critical interpretive synthesis, in: Translational Behavioral Medicine 7, Springer New York LLC, 2017, pp. 254–267.

[33] The National Centre for Smoking Cessation and Training, Stop Smoking Service Client Satisfaction Questionnaire, 2017.

[34] N.L. Benowitz, J.T. Bernert, J. Foulds Phd, S.S. Hecht, P.J. Iii, M.J.J. Ba, et al., Biochemical verification of tobacco use and abstinence: 2019 update, Nicotine Tob. Res. 2020 (7) (2020 Jun 12) 1086–1097.

[35] K. Kroenke, R.L. Spitzer, J.B.W. Williams, The PHQ-9, J. Gen. Intern. Med. 16 (9) (2001 Sep 1) 606–613.

[36] R.L. Spitzer, K. Kroenke, J.B.W. Williams, B. Löwe, A brief measure for assessing generalized anxiety disorder: the GAD-7, Arch. Intern. Med. 166 (10) (2006 May 22) 1092–1097.

[37] R. Rabin, F. de Charro, EQ-SD: a measure of health status from the EuroQol group, Ann. Med. 33 (5) (2001 Jan 1) 337–343.

[38] T.F. Heatherton, L.T. Kozlowski, R.C. Frecker, W. Rickert, J. Robinson, Measuring the heaviness of smoking: using self-reported time to the first cigarette of the day and number of cigarettes smoked per day, Br. J. Addict. 84 (7) (1989 Jul 1) 791–800.

[39] N.K. Gale, G. Heath, E. Cameron, S. Rashid, S. Redwood, Using the framework method for the analysis of qualitative data in multi-disciplinary health research, BMC Med. Res. Methodol. 13 (1) (2013 Sep 18) 117.