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A multi-component smoking cessation intervention for individuals living with diabetes: study protocol for an open-label pragmatic randomised controlled feasibility trial

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ABSTRACT

Introduction Smoking cessation is an essential, but often overlooked aspect of diabetes management. Despite the emphasised need for tailored smoking cessation support for individuals with diabetes, evidence of effective interventions for this cohort is limited. Additionally, individuals with diabetes do not easily adopt such interventions, resulting in low uptake and abstinence rates. This study aims to assess the feasibility and acceptability of a unique smoking cessation intervention, based on evidence, theory, and the needs of individuals with diabetes among patients and providers, the diabetes nurse educators. This study protocol reports the methods and analysis that will be undertaken.

Methods and analysis An open-label pragmatic randomised controlled trial. Eighty to 100 individuals with type 1 or type 2 diabetes who smoke will be recruited from the diabetes outpatients at the main acute public hospital in Malta, starting in August 2023. Participants will be randomly assigned (1:1 ratio) to the intervention or control arm for 12 weeks. The experimental intervention will consist of three to four smoking cessation behavioural support sessions based on the 5A's (Ask, Advise, Assess, Assist and Arrange) algorithm, and a six-week supply of Nicotine Replacement Therapy. The control intervention will consist of an active referral to the National Health Service's one-to-one smoking cessation support, which is based on motivational interviewing. The primary feasibility and acceptability outcomes include the recruitment and participation rates, resources utilised, and problems identified by the nurses, the nurses' perceived challenges and facilitators to implementation, and the nurses and patients' acceptability of the study intervention. Per feasibility study guidelines, data analyses will be descriptive and no statistical comparisons between the randomised groups will be conducted.

Ethics and dissemination Ethical clearance was obtained from the Faculty of Health Sciences Research Ethics Committee, University of Malta. The study results will be disseminated through conference presentations and a publication in a peer-reviewed journal.

Trial Registration Number ClinicalTrials.gov NCT05920096

Keywords Diabetes Mellitus; Tobacco Use Cessation; Clinical Trial; Healthcare Acceptability; Feasibility Studies; Information Motivation Behavioral Skills Model; Counselling; Smoking Cessation Agents; 5A's Framework

Strengths and limitations of this study

- This paper outlines the study protocol of a feasibility trial, an overlooked, but critical step in the development and evaluation of smoking cessation interventions among individuals with diabetes, in preparation for a future definitive evaluation.
- Since healthcare interventions are highly context-dependent, this study will adopt a pragmatic approach, assessing the feasibility of the intervention in the real-world context of diabetes ambulatory care, where formal diabetes education is locally provided.
- A unique multi-component smoking cessation intervention based on evidence, theory and the needs of individuals living with diabetes is sufficiently described to allow its replication.
- Blinding is not possible in this feasibility study; however, it is not strictly required as there is no formal hypothesis testing.
- This is a feasibility trial and is not powered to determine the effectiveness of the intervention.

INTRODUCTION

Diabetes mellitus (DM) is a major public health concern both worldwide and in the Maltese context. DM, characterised by chronically elevated blood glucose levels that lead to the development of various macro- and micro-vascular complications, thus increasing the risk of morbidity and even death, is estimated to affect approximately one out of every ten adults aged 20 to 79 worldwide.[1] While the European region has the second-lowest diabetes prevalence (at 9.2%; 95% Confidence Interval, CI: 7.1-10.4), Malta, a European country, has a high diabetes prevalence, estimated at 11.2% (95% CI: 8.7-13.8).[1]

Individuals living with DM require medical care, self-management education, and support that goes beyond glucose management.[2] Tobacco cessation is an essential, but often overlooked aspect of diabetes management.[3] In persons with DM, tobacco smoking appears to contribute to greater insulin resistance, worsened beta-cell function and impaired insulin secretion, glucolipotoxicity and dyslipidaemia.[4,5] This exacerbates both macro- and micro-vascular complications of DM. Both individuals with type 1 and type 2 DM who smoke are at approximately 50% higher risk of developing cardiovascular events, such as coronary heart disease and stroke, compared to non-smokers with diabetes.[6,7] Similarly, a higher risk for cardiovascular mortality and for total mortality, has also been identified among smokers with type 1 and type 2 DM.[6,7] Tobacco smoking may also increase the risk of microvascular diabetes complications, such as diabetic nephropathy, neuropathy and retinopathy, particularly amongst individuals with type 1 DM.[4,8] Conversely, smoking cessation is associated with better cardiometabolic profiles,[5] and a significant risk reduction for cardiovascular disease, mortality from cardiovascular disease, and total mortality amongst this population.[6,7] Smoking cessation for individuals with diabetes is one of the key recommendations of Malta's national diabetes strategy.[9]

Despite the importance of quitting smoking, having diabetes does not appear to motivate individuals to quit.[10,11] Durlach et al. estimated that on average 20% of individuals with type 2 DM and 30% of individuals with type 1 DM smoke.[4] Analysis of unpublished raw data from the Malta National Health Interview survey revealed that 17.4% of those who reported having diabetes also reported to smoke.[12] Smokers with diabetes may be less motivated to stop smoking due to a number of diabetes-related barriers and challenges to quitting. These include: concern about possible weight gain and poor glycaemic control, which may occur on quitting smoking;[5] comorbid anxiety and depression,[13,14] which can hinder efforts in quitting smoking;[15] and possibly increased nicotine metabolism associated with having diabetes, which increases nicotine addiction, making it harder for them to quit.[16,17]

While the need for providing tailored smoking cessation support to tackle these diabetes-related barriers and challenges to quitting has been emphasized,[4,8,11] evidence-based smoking cessation recommendations for individuals living with DM are still lacking. In a systematic review and meta-analysis, Nagrebetsky et al.[18] aimed to assess the effectiveness of intensive smoking cessation interventions, such as intensive behavioural support (e.g. intensive counselling) or interventions that combine behavioural support and pharmacotherapy, such as Nicotine Replacement Therapy (NRT), bupropion or varenicline, amongst individuals with DM for providing practice recommendations. However, the limited number of reviewed studies and the significant heterogeneity in the intervention tested and comparator group limited the authors from drawing conclusions regarding the efficacy of diabetes-specific smoking cessation interventions, and from providing practice recommendations. Based on the identified gap in evidence, further research on the development and evaluation of tailored smoking cessation interventions for individuals with diabetes has been recommended.[18]

Notwithstanding the lack of evidence-based smoking cessation recommendations for individuals with DM, evidence suggests that health professionals who care for individuals

with diabetes are less likely to advise their patients against smoking and support them towards quitting.[19,20] International and local literature suggest that diabetes clinicians and educators often prioritise other aspects of diabetes management over smoking cessation.[3,21–23] Diabetes educators have reported feeling inadequately prepared in discussing smoking cessation amongst individuals with diabetes, lacking motivation and time to do so.[3,24]

Given that the success of a proposed healthcare intervention, such as a smoking cessation intervention, is very much dependent on stakeholder engagement, patients and providers alike, investigating the feasibility and acceptability of a proposed intervention is crucial prior to further evaluation and implementation.[25] The feasibility and acceptability assessment of a proposed diabetes-specific smoking cessation intervention for undertaking a future large-scale randomised controlled trial is particularly advisable in view of the reported low recruitment, uptake and challenges encountered in two recent smoking cessation trials carried out amongst individuals with DM.[26,27] These smoking cessation trials, which were initiated prior to the COVID-19 pandemic, in 2018,[26] and after the declaration of the pandemic, in August 2020,[27] did not reach the target sample size and were later terminated due to lack of funding,[26] and following the recall of Varenicline which was required for the provision of the study intervention,[27] respectively. Conducting a feasibility study would help estimate the recruitment rate and study uptake, identify any potential challenges (along with mitigating factors), and assure the intervention's acceptability amongst patients and providers a priori, thus ensuring that the main trial targets can be met before proceeding with a larger, more expensive trial.[28]

Following the development of a unique multi-component smoking cessation intervention, based on evidence and theory, and tailored for people living with DM who smoke,[29–31] a feasibility study was proposed prior to a definitive evaluation. This feasibility study primarily aims to assess the feasibility of a large-scale randomised controlled trial, by

analysing the recruitment and study uptake, and the providers' perceived challenges and facilitators to implementation; and to assess the acceptability of the intervention, by analysing the participants' satisfaction with and perceived usefulness of the smoking cessation support provided, and the providers' feedback. The feasibility study also aims to compare the participants' satisfaction with and perceived usefulness of the smoking cessation support provided to standard care - the provision of general smoking cessation support; undergo a preliminary process evaluation, by assessing whether the intervention was delivered as intended and exploring the intervention's functioning; and determine the preliminary evidence of the intervention's effectiveness, by comparing the smoking cessation rates achieved in the intervention group to the control group (standard care). This study protocol reports the methods and analysis that will be undertaken.

METHODS AND ANALYSIS

This feasibility study is part of a doctoral research project titled, 'Development and Feasibility testing of a Multi-Component Smoking Cessation Intervention for Smokers Living with Diabetes Mellitus,' which is guided by the Medical Research Council (MRC) 2021 framework for the development and evaluation of complex interventions in healthcare.[25] The methods and analysis reported in this paper are according to the trial registration details available on ClinicalTrials.gov (NCT05920096). This protocol follows the Standard Protocol Items for Randomized Trials (SPIRIT) reporting guidelines (supplemental file 1).[32]

Design

An open-label, pragmatic, experimental design will be adopted. While a feasibility study may not need to be a randomised trial,[28] a comparative analysis of an alternative standard course of action, i.e., the provision of general smoking cessation support by the Health

Promotion and Disease Prevention Directorate (within the National Health Service), in terms of the outcomes, i.e. smoking cessation rates, and satisfaction with and perceived usefulness of the intervention provided, helps to provide more information to make decisions about progressing to the evaluation stage of the MRC framework, as part of the economic considerations.[25] Furthermore, in adopting the same design and protocol as would be adopted in a largescale randomised controlled trial, helps to assess the feasibility of undertaking the trial in the first place, by analysing the recruitment and study uptake and the successful delivery of the intervention, taking note of the resources utilised.[33] Given that healthcare interventions are highly dependent on the context in which they are tested, this study will take a pragmatic approach, assessing the feasibility of the intervention in the real world context;[25] in diabetes ambulatory care where formal diabetes education is locally provided.[9] An open-label design will also be adopted. The participants, who are likely to be aware of the National Health System's smoking cessation services, may be able to distinguish between the assigned arms. On the other hand, due to the pragmatic nature of the study, blinding the intervention providers will also not be possible. The Principal Investigator (PI), JG, who will be actively involved in recruiting and carrying out pre- and post-intervention assessments and data analyses, also cannot be blinded to treatment assignment. Nonetheless, being a feasibility study, blinding is not strictly required as there is no formal hypothesis testing.[28]

Study population

In Malta, all adults with type 1 DM are under the care of the diabetologists attending the diabetes outpatients/the Diabetes and Endocrine Centre (DEC) at the main acute public hospital in Malta, Mater Dei Hospital.[9] While individuals with type 2 DM may be seen in primary care, these are also to attend to the DEC when complications arise, or at prescribed time intervals, at least once annually.[9] In this study, participants will be recruited from the

DEC, and the adjacent Diabetes Education Unit (DEU), where formal diabetes education is provided.

Inclusion Criteria:

- Living with type 1 or type 2 diabetes and attending the DEU or the DEC at Mater Dei Hospital on an outpatient basis.
- Having smoked ≥100 cigarettes during his/her entire life and currently smoking.
- Being ≥ 18 years old.
- Speaking and understanding English or Maltese.
- Able to provide written informed consent.

Exclusion Criteria:

- Not being able to provide informed consent (due to dementia, a learning disability, or a psychological disorder).
- Being pregnant or breastfeeding.
- Unable to independently attend to the DEU and any of the health centres in which the Health Promotion and Disease Prevention Directorate provide smoking cessation support during the study period.
- Currently enrolled in another smoking cessation study/program or multi-behavioural program which also focuses on smoking cessation.
- Enrolment of the investigator or the research collaborators, and their family members.

Sample size

A power calculation to determine the sample size is not appropriate for a feasibility trial, as the purpose of a feasibility trial is not to establish efficacy.[34] However, the sample should be large enough to provide estimates of the parameters that are used to calculate the sample size

for definitive trials. For estimating the confidence intervals for feasibility outcomes, such as the recruitment rate and rate of consent to the study, and the compliance to the study protocol, Hertzog[35] suggests having 30 to 40 participants per group, while Teare et al.[36] recommend having 60 participants per group. However, ultimately the sample size decision must also take in consideration the resources required and time available.[36] Thus, this study aims to recruit between 80-100 participants in total.

Recruitment and randomisation

At the DEC, all new patients with type 1 or type 2 DM are screened for tobacco use by the diabetologists and advised to quit smoking. The diabetologists working at diabetes outpatients will thus be asked to identify smokers interesting in quitting and refer them to the PI for study recruitment. Additionally, the healthcare professionals working at the diabetic clinics at the DEC, such as the nurses and the podiatrists, and the diabetes specialist nurses (diabetes nurse educators) at the DEU, will also be asked to identify any interested smokers during their practice and to refer them to the study. Posters and flyers will also be present at the DEC so that participants can also self-refer to the study. To enhance recruitment, onsite visits will be held during which feedback on the recruitment process will be provided to all healthcare professionals.[37]

In 2022, there were 1,786 new patients (most of whom are individuals with type 1 or type 2 DM) who attended the diabetes outpatients (of whom 473 attended the DEU) at Mater Dei Hospital.[38] Of these, 17.4%, were likely to be smokers.[12] Assuming that the yearly population size is around 311 individuals, at a 95% CI, a sample size of 100 participants, would be sufficient to provide the above feasibility estimates at an acceptable margin of error of 8%.[39] Given that the consent rate for participating in smoking cessation trials was found to

be 66.4% (Interquartile Range, IQR: 42.7–85.2%),[40] it is anticipated that the target sample size will be achieved within a year.

The PI will screen all recruited patients by telephone to assess eligibility, inviting them to participate in the study. Eligible interested individuals will attend a pre-intervention assessment session for informed consent, during which the PI will randomly assign them to the intervention or control group and assess baseline characteristics. Participants will be randomly allocated to the intervention or control arm on a 1:1 ratio using a computer-generated random block length (in blocks of two and four), using the random allocation software by Saghaei.[41] The sequence will be prearranged before the study begins, with group assignments sealed in sequentially numbered opaque envelopes. The PI will assign the sequentially numbered opaque envelopes in the order they are met. The participants' characteristics will not be known prior to the assignment of the envelopes.

Participants are to receive the respective intervention within two weeks from assignment. Post-intervention evaluation will take place 12 weeks after the pre-intervention assessment session. Figure 1 displays the participant timeline for this study, based on the SPIRIT participant timeline figure.[32]

Pre-intervention assessment

In the pre-intervention assessment session, a baseline questionnaire will be used to collect information on the participants. This includes demographics, perceived health status, diabetes and smoking profiles, and anxiety and depression levels. Questions are based on the literature. Cigarette dependence, current motivation to stop smoking, which are part of the smoking profile, and anxiety and depression will be measured using established tools. Cigarette dependence will be measured using the Cigarette Dependence Scale-5 (CDS-5),[42] while motivation to stop smoking will be measured using the Motivation To Stop Scale

(MTSS).[43,44] Conversely, the Hospital Anxiety and Depression Scale (HADS),[45] will be used for screening for anxiety and depression. As part of the smoking profile section, exhaled carbon monoxide (eCO) will also be measured using the Bedfont piCO™ Smokerlyzer® to confirm smoking status.[46]

The baseline questionnaire is available in English and Maltese. Except for HADS,[45] which was already translated and validated into Maltese by Baldacchino, Bowman, & Buhagiar,[47] the CDS-5,[42] and the MTSS,[43,44] required translation and validity assessment. To ensure the content validity of the translated instruments, conceptual equivalence was established for these instruments by following the process outlined by Tang & Dixon.[48] Additionally, the CDS-5[42] was assessed for internal reliability using Cronbach's alpha. Based on the minimum sample size required,[49] 17 individuals living with type 1 or type 2 diabetes were invited to complete the Maltese version of the CDS-5 prior to participating to a smoking cessation programme. The Cronbach alpha score was high; 0.80. On eliminating the items one at a time from the analysis, the Cronbach alpha (and scale mean) remained relatively stable (supplemental file 2). All item-scale correlations were ≥0.4.

Interventions

Experimental intervention

Intervention development

The development of the intervention followed a three-stepped research process. Initially, a scoping review was undertaken to identify the most promising smoking cessation methods for persons living with diabetes, identifying any gaps in evidence.[30] This was followed by a systematic review and intervention component analysis of the identified most promising smoking cessation methods to identify their critical components.[29] Then a qualitative descriptive study was conducted to explore the needs of individuals with diabetes to quit

smoking, and their views of the identified promising smoking cessation components.[31] Based on the reviews and the qualitative descriptive study's findings and recommendations, a multi-component smoking cessation was developed and proposed to the diabetes specialist nurses working at the DEU.

Theoretical framework

The intervention is based on Information-Motivation-Behavioural Skills (IMB) model for achieving behaviour change,[50] and thus aims to:

- inform individuals with diabetes who smoke on the association between smoking and the diabetic complications and the benefits of quitting;
- motivate and encourage individuals to quit smoking and/or remain abstinent;
- support them in developing/using the appropriate behavioural skills to quit smoking and avoid relapse; and
- tackle any situational and individual characteristics (moderating factors) that can negatively influence smoking cessation, and negative health outcomes on quitting smoking, which can weaken adherence to the new behaviour via a feedback loop affecting the IMB constructs.

Figure 2 presents the theoretical framework of this intervention, outlining the strategies for addressing the IMB constructs (and any negative moderators and health outcomes)[50] for achieving and sustaining abstinence among individuals with DM.

Components of the intervention

The main components of this intervention include:

- Three to four (30-60 minutes) smoking cessation behavioural support sessions based on the 5A's (Ask, Advise, Assess, Assist and Arrange) and 5R's (Relevance, Risks,

Rewards, Roadblocks, and Repetition) algorithm[51] which will be provided by two diabetes specialist nurses at the DEU (figure 3);

- Three brief video clips (with English subtitles) featuring Bill from the Tips from Former Smokers' campaign, to raise awareness on the link between smoking and diabetes drawing on first-hand experience.[52] Bill was an individual with type 1 diabetes who suffered and died from tobacco associated diabetic complications (kidney failure, poor circulation, heart disease and blindness);[52] and
- A six-week supply of NRT based on the recommendations of Siahpush et al.[53] Six weekly packs of 25mgs 16-hour nicotine patch (tapered during the last two weeks; 15mg and 10mg, respectively) and/or four nicotine mouth sprays (1mg/spray; 150 sprays per bottle) for daily use if refraining from tobacco use, recommending the latter for breakthrough urges and/or to reduce withdrawal symptoms further.[54–56] The nicotine patches and mouth spray will be provided to those who smoke ≥10 cigarettes/day, while the mouth spray will be provided to those who smoke less.[54–56]

Additionally, participants are referred to psychological support if reporting experiencing depression or anxiety, or on further discussion with those identified as potential cases; a score of ≥11 on the anxiety/depression sub-scale on the HADS.[45,57,58] Participants are also offered a diabetic consultation by the nurse educator, and subsequent specialist/s referrals (if required) if reporting poor glycaemic control, or if they are concerned about diabetes management following a change in diet or weight gain on quitting smoking.

Nurses' training

The two diabetes specialist nurses had to be trained in smoking cessation prior to the study. A training programme, based on the successful training programme by Grech[59] (the PI), which followed the WHO toolkit for delivering the 5A's and 5R's for tobacco cessation,[51]

was developed and delivered by the PI to the nurses prior to the initial testing of the intervention in November 2022 and to the commencement of the feasibility study (July 2023). To help assess fidelity, all the sessions provided by the two nurses will be audio-recorded with consent.[60,61]

Intervention log

Additionally, the nurses will be asked to keep an intervention log to document the following information per participant for measuring compliance to the protocol, the resources utilised and any challenges encountered:[62]

- the number, and duration of the sessions provided (and the number of weeks during which the sessions are provided) and non-attendance, along with reasons;
- provision of the 5R's intervention at the first session;
- whether the participant opts not to see the informational video clips, along with reasons;
- whether the participant agrees to attempt to quit smoking (by setting a Target Quit Date, TQD) at their first session, and subsequent session, if still smoking), along with reasons for not wanting to;
- the amount of NRT provided, and returned;
- reported use of NRT, along with reasons if a participant reports not using it; and
- any problems encountered, such as side effects on using NRT, identified mental health issues, issues with managing diabetes, and any referrals, including reasons for refusing support.

As recommended by Hollands et al.,[63] NRT adherence will be assessed using a continuous outcome measure: the total days of NRT use, and the average number of times the nicotine spray is used per day. This assessment will cover the first week following the TQD (and the

subsequent TQD for those who agree to reattempt quitting), which should coincide with the follow-up session/s, and, as well as the next four weeks, coinciding with the final follow-up session.

Control intervention

The participants who are assigned to the control group will be actively referred to the Health Promotion and Disease Prevention Directorate's one-to-one smoking cessation service, which is provided within community health centres around Malta. The smoking cessation support provided is based on motivational interviewing and is delivered by trained tobacco cessation facilitators. The counselling sessions, lasting around 20 minutes each, are usually provided every fortnight, based on the individuals' needs.

The smoking cessation services coordinator will be asked to take note of the number of sessions provided (including the number of weeks during which the sessions are provided) and any dropouts (with reasons).

Post-intervention evaluation

End of study questionnaire

All participants will be invited to a post-intervention assessment session, held at 12 weeks follow-up in which they will be invited to fill in the end of study questionnaire, available in English and Maltese. In the questionnaire, participants will be asked about their quitting attempt and smoking status, about the support they received during the study period, and to rate their satisfaction with the smoking cessation intervention provided and their perceptions of its usefulness.

Smoking abstinence will be measured by following the recommendations by Piper et al.[64] Participants will be asked if, in the past seven days, they intentionally refrained from smoking

any combustible or non-combustible tobacco products and alternative products (seven-day point-prevalence abstinence). They will also be asked if they abstained from smoking for seven consecutive days (or more) during the study period (seven-day floating abstinence) or for at least one day or 24 hours (quit episode). Continuing smokers will be asked about their current tobacco use.

Biochemical verification of tobacco abstinence will be conducted for those reporting seven-day point-prevalence abstinence, based on the recommendations of Benowitz et al.[46] This will be carried out by using the same carbon monoxide monitor and by analysing a urine sample for cotinine exposure using a multilevel lateral flow immunoassays urine test strip with a nominal 200 ng/mL cutoff. Participants will be advised to stop using NRT prior to assessment, if possible.

To investigate the participants' satisfaction with the intervention and their perceptions of its usefulness, the measures by Grech, Norman & Sammut for assessing the satisfaction and perceived usefulness of smoking cessation interventions among individuals with diabetes, will be utilised.[65] The satisfaction questionnaire consists of eight statements covering the main elements of smoking cessation interventions. It is rated by a 5-point Likert scale, ranging from (1) 'very unsatisfied' to (5) 'very satisfied.' The total score ranges from eight to 40. Conversely, the perceived usefulness questionnaire consists of 14 items, based on the Information-Motivation-Behavioural Skills (IMB) model of behaviour change. It is also rated by a 5-point Likert scale, ranging from (1) 'strongly disagree' to (5) 'strongly agree.' The total score ranges from 14 to 70. Three additional questions, asking participants to explain which aspects of the smoking cessation intervention they were most and least satisfied with, for suggestions for improvement, and whether they would recommend the intervention to others('yes' or 'no' option), complement these instruments. Both

questionnaires (in English and Maltese) were found to have a high internal consistency (>0.8).[65]

Semi-structured interviews

Additionally, the participants who are assigned the experimental intervention will be interviewed to obtain feedback on the study intervention, and to explore their quit attempt. The qualitative sample will consist of a smaller sample, for obtaining an in-depth understanding of the acceptability of the study and the mechanisms of the study intervention from different viewpoints,[60,62] selecting individuals who stop or do not stop smoking, attend or stop attending the study intervention; and use or do not use the NRT provided on attempting to quit smoking. In selecting participants, due consideration will also be made to sex, age, and the type of diabetes. The sample size will be based on the principle of 'data saturation,'[66] seeing saturation when new data collected repeats what was expressed in the previously collected data.[67] Given that no previous studies have explored the acceptability of a smoking cessation intervention among individuals with diabetes,[30] in estimating the required sample size, reference is made to the seminal study by Guest, Bunce, & Johnson,[68] in which saturation was relatively achieved after only 12 interviews. The estimate sample size was increased to 20 participants.

Semi-structured interviews will also be carried out with both nurses to obtain feedback on the study intervention and to explore the facilitators and challenges to implementation.

Patient and public involvement

Individuals living with DM were involved during both the developmental and the feasibility phases of this doctoral project. During the developmental phase, a qualitative descriptive study was conducted to explore the needs of individuals with DM to quit smoking, and their views of the identified promising smoking cessation components,[29–31] to guide the

development of the study intervention. Additionally, in November 2022, a pilot study was conducted to test and refine the intervention with a small sample of individuals with diabetes. Based on the feedback received, the study intervention was revised to include an additional follow-up session for those who report not quitting smoking, bringing the total to four sessions. Patients/public were not involved in the design or the conducting of this study. A summary of the study findings, presented in a simple factsheet with pictograms, will be offered to all participants.

Outcome measures

Primary feasibility and acceptability outcomes

Feasibility – recruitment parameters

The following outcomes will be measured during the study recruitment period:

- The monthly recruitment rate of eligible smokers interested in quitting (recruitment rate).
- The proportion of eligible smokers identified from each source of recruitment (DEU, DEC, and self-referral).
- The proportion of participants who consent to the study out of the total number of recruited eligible smokers, along with reasons for non-participation (consent rate).
- The recruitment duration in months.

Feasibility – compliance with the protocol, resources utilised and problems identified

These feasibility outcomes will be measured based on the information documented by the intervention providers during the intervention period:

- The proportion of participants who attend the scheduled sessions per group, along with reasons for not attending (participation rate).

- The proportion/number of participants in the intervention group who choose not to watch the informational video clips, along with their reasons.
- The proportion/number of participants in the intervention group who choose not to set a TQD at their first session (or subsequent session if still smoking), along with their reasons.
- The proportion of participants in the intervention group who use the nicotine patch and/or spray on their TQD, during the subsequent TQD for continuing smokers, and in their final follow-up period, along with reasons for not using it.
- The average percentage of days the nicotine patch and/or spray are used by participants in the intervention group during the first week after the TQD, the subsequent TQD for continuing smokers, and during the subsequent four weeks following one week from the TQD.
- The average daily usage of nicotine spray by participants in the intervention group during the first week after the TQD, the subsequent TQD for continuing smokers, and during the subsequent four weeks following one week from the TQD.
- The average number of sessions provided per participant per group.
- The average duration (in weeks) of smoking cessation support provided per participant per group.
- The average time (in minutes) taken to deliver the experimental intervention sessions.
- The proportion/number of participants from the intervention group who were provided with the 5R's intervention.
- The average amount of NRT provided per participant (taking note of any returned items).
- The number of problematic issues identified by the diabetes specialist nurses identified, such as reported adverse events while using NRT, and the number of

referrals to additional support services (e.g., psychotherapists). Participants who decline additional support will be documented, along with their reasons for refusal.

Feasibility – response rate at 12 weeks follow-up

- The proportion of participants attending their 12-week post-intervention evaluation session in both groups, with reasons for dropouts.

Feasibility – perceived challenges and facilitators to implementation

- The perceived challenges and facilitators to implementation as identified when conducting interviews with the diabetes specialist nurses at the end of the study.

Acceptability outcomes

The following acceptability outcomes will be measured based on information collected from participants in the intervention group during their post-intervention evaluation sessions (questionnaires and interviews), as well as interviews with diabetes specialist nurses at the end of the study.

- Participants' satisfaction with the intervention provided.
- Participants' perceived usefulness of the intervention provided.
- Nurses' satisfaction with the intervention.

Secondary outcomes

Secondary acceptability outcomes

The following outcomes will be measured based on the data collected from the end of study questionnaires.

- Group comparison of the participants' satisfaction with the smoking cessation support provided.

- Group comparison of the participants' perceived usefulness of the smoking cessation support provided.

Preliminary process evaluation

- Treatment fidelity of the experimental intervention. A random sample (20%) from all the audio recordings (all sessions provided) from both nurses will be selected, listened to, and cross-checked against a list outlining the intervention's action components (for each type of session) for calculating the level of adherence.[61] Any deviations from the study protocol will also be taken note of. An 80-100% level of adherence constitutes high fidelity, less than 80% medium fidelity, whereas ≤50% constitutes low fidelity.[61]
- Exploring the experimental intervention's functioning when conducting interviews with the participants.

Preliminary evidence of effectiveness

The following outcomes will also be measured, based on the data collected from the end of study questionnaires.

- Proportion of participants per group reporting a quit episode during their study period.
- Proportion of participants per group reporting a 7-day point prevalence abstinence at any time during the study period (floating abstinence).
- Proportion of participants per group reporting a 7-day point prevalence abstinence at follow-up, biochemically verified.
- The change in the average number of cigarettes smoked per day (amongst continuing smokers) per group at follow-up.

Data analysis plan

Quantitative data

Based on the recommendations for the analysis of pilot and feasibility studies, where a formal power calculation is not carried out, the data analyses will be descriptive in nature, and no statistical comparisons between the intervention and control groups will be undertaken.[69–71] Nonetheless, the feasibility and acceptability outcomes will be reported with 95% Confidence Intervals (CIs) to provide an estimate range of the said outcomes.[69–71]

Continuous data will be summarised using means (and standard deviations, SD) and 95% CIs, and medians (and interquartile range, IQR) for normally and non-normally distributed variables, respectively. For categorical data, frequencies and proportions/percentages will be used. Proportions/rates will also be reported with 95% CIs using the Clopper-Pearson "exact" interval, which is more conservative for estimating CIs when using binomial distributed data.[70,72]

Missing data

In line with standard smoking cessation research practice,[56,73,74] intention-to-treat analysis will be used for assessing effectiveness. Participants with missing smoking outcome data, i.e. those who drop out of the study or who are lost to follow-up, and participants whose abstinence cannot be biochemically verified, will be considered as continuing smokers or to have resumed smoking.[56,73,74] The baseline characteristics of those followed up and those lost to follow-up will be compared descriptively.

To calculate the satisfaction and perceived usefulness questionnaires' average scores, any missing data will be handled in accordance with the recommendations of Mirzaei et al.[75] In case of a missing data percentage of up to 10% (e.g. one item in the perceived usefulness questionnaire), the single imputation method will be conducted.[75] In case of a 10-40% missing data per questionnaire, missing data may be imputed if the Little test of missingness

determines that the missing values meet the specification of missing completely at random (MCAR).[75] In such case the recommended imputation method is multiple imputation (MI).[75,76] Given that it is not possible to confirm if the missing data are missing at random (MAR) or missing not at random (MNAR), no imputation will be carried out in such cases and these will be excluded from analyses.[75,76] However qualitative investigation (by inviting such participants to an interview) will be recommended.[75] The same principle applies to >40% missing data.[75]

Missing data in the intervention logs will not be imputed. The intervention logs will be frequently checked by the PI for their completeness and to ensure that they are being filled up in a timely manner.

Qualitative data

Qualitative data will be summarised by following the Applied Thematic Analysis (ATA) approach.[77] ATA has been described as a rigorous, primarily inductive method for describing and exploring the experiences of participants as accurately and comprehensively as possible.

To provide a further understanding of the acceptability of the study intervention and its' functioning as experienced by the study participants, the quantitative and qualitative data will be compared for confirming, disconfirming, or expanding each other. Ultimately, all findings derived from all sources will be synthesized to understand what needs to be modified to enhance the feasibility and acceptability of the study intervention, prior to a full-scale randomised trial.[62]

Criteria for proceeding to a future trial

The decision of whether to proceed to a future definitive trial will be based on the feasibility and acceptability data, i.e., the data on the recruitment and study uptake, and on the acceptability of the intervention. As stated earlier, the required sample should be recruited

within a year. Based on two previous studies; who similarly provided individuals with type 2 DM with a counselling session at baseline followed by a one-week and one-month follow-up (participation rates of 90% and 86.2%, respectively),[74] and who provided individuals with type 2 DM with weekly visits and varenicline for three months (reporting an approximate 30% attrition),[73] the uptake for this study, i.e., the participation rates, NRT usage (average percentage of days the nicotine patch and/or spray are used, at least during the first week after the TQD and the subsequent set TQD for continuing smokers), and follow-up response rates, should be not less than 70%. The participants from the intervention group should also rate the study intervention as satisfactory and useful, or above; an average score of 32 and 56, respectively. The intervention providers should also be satisfied with the intervention, finding it feasibility to introduce in practice for a definitive assessment. Not reaching these criteria does not necessarily indicate that a future definitive trial is unfeasible, however, modifications, informed from the qualitative findings, will be required prior to further testing and a definitive evaluation.

ETHICS AND DISSEMINATION

Before carrying out the study, permissions were sought from the authors of the tools that will be used, the recruiting stakeholders, the clinical chairperson, and the hospital administration. Ethical clearance was sought from the Faculty of Health Sciences Research Ethics Committee on behalf of the University Research Ethics Committee (UREC FORM V_15062020 8618). No ethical issues were foreseen, and the study was approved. The study started in August 2023 and is ongoing.

On indicating their interest to participate in the study, prospective participants will be verbally briefed on the study by the PI and provided with a detailed information letter and

consent form to sign. Participants will be informed that participation is voluntary and that they are free to withdraw from the study at any time, without the need to provide a reason. They will also be assured that refusing to participate or withdrawing from the study will not have any effect on their care whatsoever.

The participants in the intervention group will be encouraged to take the provided NRT on attempting to quitting smoking, however they are also free to refuse to take it. Often NRT may cause minor adverse reactions (for example, irritation of the site of use, the skin), however such adverse events can usually be minimised or avoided by applying the treatment correctly and so should not warrant treatment discontinuation.[78] On the other hand, on rare occasions, NRT may also cause non-ischaemic chest pain and palpitations but there is no evidence of an excess of serious cardiac problems, even in people with established cardiac disease.[78] In the very unlikely event of such a serious adverse event, NRT will be discontinued and participants will be seen by a doctor of their choice, free of charge.

Data will be securely stored in an encrypted computer, with access restricted to the PI. While the questionnaires used will be coded, to allow the comparison of the baseline characteristics of those followed up and those lost to follow-up, only the participants will be aware of their unique code, thus ensuring anonymity. The audio-recorded interviews will also be pseudonymised by the PI on transcription. These, and the audio-recorded experimental intervention sessions, which will only be listened to by the PI for quality assurance, will then be erased. The participants who do not quit smoking by the end of the study will be invited to attend to the Health Promotion and Disease Prevention Directorate's smoking cessation services.

The data supporting this research will be available from the corresponding author on reasonable request. The study results will be communicated and disseminated through

conference presentations at national and international conferences on general medicine, diabetes, public health, nursing and/or tobacco control. A publication is planned in a high-impact peer-reviewed journal. The study reporting will follow the CONSORT statement for the reporting of randomised pilot and feasibility trials.[79] Depending on the results, modifications to the study methods followed by further testing, or a definitive evaluation, will be proposed.

CRediT authorship contribution statement

JG: Conceptualization, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Visualization, Writing – Original Draft, Review & Editing.

CA and MG: Investigation, Resources, Writing – Review & Editing.

IJN and RS: Conceptualization, Supervision, Writing – Review & Editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. The authors declare no conflict of interest.

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REFERENCES

1. Boyko EJ, Magliano DJ, Karuranga S, et al. *IDF Diabetes Atlas*. 10th ed. International Diabetes Federation, 2021.

2. ElSayed NA, Aleppo G, Aroda VR, et al. Introduction and Methodology: Standards of Care in Diabetes — 2023. *Diabetes Care* 2023; 46: S1–S4.

3. Lotrean LM. Smoking Cessation In Patients With Diabetes. In: Behrakis P, Vardavas C, Papadakis S (eds) *Tobacco Cessation Guidelines for High-Risk Populations*. Athens, 2017, pp. 150–191.

4. Durlach V, Vergès B, Al-Salameh A, et al. Smoking and diabetes interplay: A comprehensive review and joint statement. *Diabetes Metab* 2022; 48: 101370.

5. Kar D, Gillies C, Zaccardi F, et al. Relationship of cardiometabolic parameters in non-smokers, current smokers, and quitters in diabetes: a systematic review and meta-analysis. *Cardiovasc Diabetol* 2016; 15: 158.

6. Pan A, Wang Y, Talaei M, et al. Relation of Smoking With Total Mortality and Cardiovascular Events Among Patients With Diabetes Mellitus: A Meta-Analysis and Systematic Review. *Circulation* 2015; 132: 1795–1804.

7. Qin R, Chen T, Lou Q, et al. Excess risk of mortality and cardiovascular events associated with smoking among patients with diabetes: Meta-analysis of observational prospective studies. *Int J Cardiol* 2013; 167: 342–350.

8. Campagna D, Alamo A, Di Pino A, et al. Smoking and diabetes: Dangerous liaisons and confusing relationships. *Diabetol Metab Syndr* 2019; 11: 85.

9. Calleja N, Azzopardi Muscat N, Reiff S, et al. *Diabetes: A National Public Health Priority A National Strategy for Diabetes 2016-2020*. Ministry for Health, Malta, 2016.

10. Holm M, Schiöler L, Andersson E, et al. Predictors of smoking cessation: A longitudinal study in a large cohort of smokers. *Respir Med* 2017; 132: 164–169.

11. Clement L, Gencer B, Muller O, et al. Smoking Cessation in People With and Without Diabetes After Acute Coronary Syndrome. *Nicotine Tob Res* 2023; 25: 58–65.

12. Directorate for Health Information and Research. *Data on smoking and diabetes [Unpublished raw data]*. 2023.

13. Smith KJ, Béland M, Clyde M, et al. Association of diabetes with anxiety: A systematic review and meta-analysis. *J Psychosom Res* 2013; 74: 89–99.

14. Rotella F, Mannucci E. Diabetes mellitus as a risk factor for depression. A meta-analysis of longitudinal studies. *Diabetes Res Clin Pract* 2013; 99: 98–104.

15. Richards CS, Cohen LM, Morrell HER, et al. Treating depressed and anxious smokers in smoking cessation programs. *J Consult Clin Psychol* 2013; 81: 263–273.

16. Keith RJ, Riggs DW, Conklin DJ, et al. Nicotine Metabolism in Adults With Type 2 Diabetes. *Nicotine Tob Res* 2019; 21: 846–849.

17. Yammine L, Kosten TR, Pimenova M, et al. Cigarette smoking, type 2 diabetes mellitus, and glucagon-like peptide-1 receptor agonists as a potential treatment for smokers with diabetes: An integrative review. *Diabetes Res Clin Pract* 2019; 149: 78–88.

18. Nagrebetsky A, Brettell R, Roberts N, et al. Smoking cessation in adults with diabetes: a systematic review and meta-analysis of data from randomised controlled trials. *BMJ Open* 2014; 4: e004107.

19. Sardana M, Tang Y, Magnani JW, et al. Practice-level Variation in Smoking Cessation Assistance Provided in the Cardiology Clinics: Insights From the NCDR PINNACLE Registry. *J Am Heart Assoc* 2019; 8: 1–9.

20. Bailey SR, Heintzman J, Jacob RL, et al. Disparities in Smoking Cessation Assistance in US Primary Care Clinics. *Am J Public Health* 2018; 108: 1082–1090.

21. Xu H, Luo J, Wu B. Self–reported diabetes education among Chinese middle–aged and older adults with diabetes. *J Glob Health* 2016; 6: 1–8.

22. Daly B, Kenealy T, Arroll B, et al. Do primary health care nurses address cardiovascular risk in diabetes patients? *Diabetes Res Clin Pract* 2014; 106: 212–220.

23. Camilleri T, Camilleri L, Midolo Y, et al. Empowering patients living with diabetes mellitus to cease smoking will improve lower limb perfusion. *J Addict Dis* 2021; 39: 74–80.

24. Jansink R, Braspenning J, van der Weijden T, et al. Primary care nurses struggle with lifestyle counseling in diabetes care: a qualitative analysis. *BMC Fam Pract* 2010; 11:

1–7.

25. Skivington K, Matthews L, Simpson SA, et al. A new framework for developing and evaluating complex interventions: update of Medical Research Council guidance. *Br Med J* 2021; 374: n2061.

26. Clair C, Augsburger A, Birrer P, et al. Assessing the efficacy and impact of a personalised smoking cessation intervention among type 2 diabetic smokers: study protocol for an open-label randomised controlled trial (DISCGO-RCT). *BMJ Open* 2020; 10: e040117.

27. Huang LC, Chang YT, Lin CL, et al. Effectiveness of Health Coaching in Smoking Cessation and Promoting the Use of Oral Smoking Cessation Drugs in Patients with Type 2 Diabetes: A Randomized Controlled Trial. *Int J Environ Res Public Health* 2023; 20: 4994.

28. Giangregorio LM, Thabane L. Pilot Studies And Feasibility Studies For Complex Interventions An Introduction. In: Richards DA, Rahm Hallberg I (eds) *Complex Interventions In Health An overivew of research methods*. London: Routledge/Taylor & Francis Group, 2015, pp. 127–135.

29. Grech J, Norman IJ, Sammut R. Effectiveness of intensive stand-alone smoking cessation interventions for individuals with diabetes: a systematic review and intervention component analysis. *Tob Induc Dis* 2023; 21: 57.

30. Grech J, Norman IJ, Sammut R. Helping smokers with diabetes quit: a scoping review of the interventions utilised, and the challenges and barriers to smoking cessation. *Prim Care Diabetes* 2023; 17: 119–128.

31. Grech J, Norman IJ, Sammut R. Development of a multi-component smoking

cessation intervention for individuals living with diabetes. *Tob Prev Cessat* 2023; 9: A20.

32. Chan AW, Tetzlaff JM, Gøtzsche PC, et al. SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials. *BMJ* 2013; 346: 1–42.

33. Gianregorio LM, Thabane L. Pilot Studies And Feasibility Studies For Complex Interventions. In: Richards DA, Rahm Hallberg I (eds) *Complex Interventions In Health An overview of research methods*. London: Routledge, 2015, pp. 127–135.

34. Treweek S. Addressing Issues In Recruitment And Retention Using Feasibility And Pilot Trials. In: Richards DA, Rahm Hallberg I (eds) *Complex Interventions In Health An overivew of research methods*. New York: Routledge, 2015, pp. 155–165.

35. Hertzog MA. Considerations in Determining Sample Size for Pilot Studies. *Res Nurs Health* 2008; 31: 180–191.

36. Teare MD, Dimairo M, Shephard N, et al. Sample size requirements to estimate key design parameters from external pilot randomised controlled trials: a simulation study. *Trials* 2014; 15: 264.

37. Briel M, Olu KK, von Elm E, et al. A systematic review of discontinued trials suggested that most reasons for recruitment failure were preventable. *J Clin Epidemiol* 2016; 80: 8–15.

38. Clinical Performance Unit. *Hospital Activity Report: Annual Report 2022*. 2023.

39. Field A. *Discovering Statistics Using IBM SPSS Statistics*. 5th ed. London: Sage, 2017.

40. Bricca A, Swithenbank Z, Scott N, et al. Predictors of recruitment and retention in randomized controlled trials of behavioural smoking cessation interventions: a

systematic review and meta-regression analysis. *Addiction* 2022; 117: 299–311.

41. Saghaei M. Random allocation software for parallel group randomized trials. *BMC Med Res Methodol* 2004; 4: 1–6.

42. Etter JF, Houezec J Le, Perneger T V. A self-administered questionnaire to measure dependence on cigarettes: The cigarette dependence scale. *Neuropsychopharmacology* 2003; 28: 359–370.

43. Kotz D, Brown J, West R. Predictive validity of the Motivation To Stop Scale (MTSS): A single-item measure of motivation to stop smoking. *Drug Alcohol Depend* 2013; 128: 15–19.

44. Hummel K, Brown J, Willemsen MC, et al. External validation of the motivation to stop scale (MTSS): Findings from the international tobacco control (ITC) Netherlands survey. *Eur J Public Health* 2016; 27: 129–134.

45. Zigmond AS, Snalth RP. The Hospital Anxiety and Depression Scale. *Acta Psychiatr Scand* 1983; 67: 361–370.

46. Benowitz NL, Bernert JT, Foulds J, et al. Biochemical Verification of Tobacco Use and Abstinence: 2019 Update. *Nicotine Tob Res* 2020; 22: 1086–1097.

47. Baldacchino DR, Bowman GS, Buhagiar A. Reliability testing of the hospital anxiety and depression (HAD) scale in the English, Maltese and back-translation versions. *Int J Nurs Stud* 2002; 39: 207–214.

48. Tang ST, Dixon J. Instrument Translation and Evaluation of Equivalence and Psychometric Properties: The Chinese Sense of Coherence Scale. *J Nurs Meas* 2002; 10: 59–76.

49. Bujang MA, Omar ED, Baharum NA. A review on sample size determination for

Cronbach's alpha test: A simple guide for researchers. *Malaysian J Med Sci* 2018; 25: 85–99.

50. Fisher WA, Fisher JD, Harman JJ. The Information-Motivation-Behavioral Skills Model: A General Social Psychological Approach to Understanding and Promoting Health Behavior. In: Suls J (ed) *Social Psychological Foundations of Health and Illness*. Malden, MA: Blackwell Publishing, 2009, pp. 82–106.

51. World Health Organization. *Toolkit for delivering the 5A's and 5R's brief tobacco interventions in primary care*. Geneva: World Health Organization, 2014.

52. Centers for Disease Control and Prevention (CDC). Bill B.'s story, https://www.cdc.gov/tobacco/campaign/tips/stories/bill.html#bills-bio (2022, accessed 18 April 2022).

53. Siahpush M, Shaikh RA, McCarthy M, et al. Association between duration of use of pharmacotherapy and smoking cessation: Findings from a national survey. *BMJ Open* 2015; 5: 14–16.

54. Papadakis S. *Combination nicotine replacement therapy (NRT)*. 2021.

55. European Network for Smoking and Tobacco Prevention. *Guidelines for treating tobacco dependence*. Brussels: European Netwwork for Smoking and Tobacco Prevention, 2020.

56. Theodoulou A, Chepkin S, Ye W, et al. Different doses, durations and modes of delivery of nicotine replacement therapy for smoking cessation. *Cochrane Database Syst Rev* 2023; CD013308.

57. Snaith RP. The hospital anxiety and depression scale. *Health Qual Life Outcomes* 2003; 1: 6–9.

58. Bjelland I, Dahl AA, Haug TT, et al. The validity of the Hospital Anxiety and Depression Scale. *J Psychosom Res* 2002; 52: 69–77.

59. Grech J. Impact of a nurse-led brief tobacco cessation training program for healthcare professionals. *Public Health Nurs* 2021; 38: 869–878.

60. Moore GF, Audrey S, Barker M, et al. Process evaluation of complex interventions: Medical Research Council guidance. *BMJ* 2015; 350: 1–7.

61. Borrelli B. The assessment, monitoring, and enhancement of treatment fidelity in public health clinical trials. *J Public Health Dent* 2011; 71: 1–21.

62. Feeley N, Cossette S. Testing The Waters Piloting a complex intervention. In: Richards DA, Rahm Hallberg I (eds) *Complex Interventions In Health An overivew of research methods*. London: Routledge, 2015, pp. 166–174.

63. Hollands GJ, Naughton F, Farley A, et al. Interventions to increase adherence to medications for tobacco dependence. *Cochrane Database Syst Rev* 2019; 2019: CD009164.

64. Piper ME, Bullen C, Krishnan-Sarin S, et al. Defining and Measuring Abstinence in Clinical Trials of Smoking Cessation Interventions: An Updated Review. *Nicotine Tob Res* 2020; 22: 1098–1106.

65. Grech J, Norman IJ, Sammut R. Initial validation of the satisfaction and perceived usefulness questionnaires for evaluating smoking cessation interventions among individuals with diabetes. *Tob Prev Cessat* 2023; 9: A19.

66. Bradshaw C, Atkinson S, Doody O. Employing a Qualitative Description Approach in Health Care Research. *Glob Qual Nurs Res* 2017; 4: 1–8.

67. Saunders B, Sim J, Kingstone T, et al. Saturation in qualitative research: exploring its

conceptualization and operationalization. *Qual Quant* 2018; 52: 1893–1907.

68. Guest G, Bunce A, Johnson L. How Many Interviews Are Enough? An Experiment with Data Saturation and Variability. *Field methods* 2006; 18: 59–82.

69. Thabane L, Ma J, Chu R, et al. A tutorial on pilot studies: the what, why and how. *BMC Med Res Methodol* 2010; 10: 1–10.

70. Teresi JA, Yu X, Stewart AL, et al. Guidelines for Designing and Evaluating Feasibility Pilot Studies. *Med Care* 2022; 60: 95–103.

71. Lee EC, Whitehead AL, Jacques RM, et al. The statistical interpretation of pilot trials: should significance thresholds be reconsidered? *BMC Res Methodol* 2014; 14: 1–8.

72. Wallis S. Binomial confidence intervals and contingency tests: Mathematical fundamentals and the evaluation of alternative methods. *J Quant Linguist* 2013; 20: 178–208.

73. Russo C, Walicka M, Caponnetto P, et al. Efficacy and Safety of Varenicline for Smoking Cessation in Patients with Type 2 Diabetes: A Randomized Clinical Trial. *JAMA Netw Open* 2022; 5: E2217709.

74. Li WHC, Wang MP, Lam TH, et al. Brief intervention to promote smoking cessation and improve glycemic control in smokers with type 2 diabetes: a randomized controlled trial. *Sci Rep* 2017; 7: 45902.

75. Mirzaei A, Carter SR, Patanwala AE, et al. Missing data in surveys: Key concepts, approaches, and applications. *Res Soc Adm Pharm* 2022; 18: 2308–2316.

76. Heymans MW, Twisk JWR. Handling missing data in clinical research. *J Clin Epidemiol* 2022; 151: 185–188.

77. Guest G, MacQueen K, Namey E. *Applied Thematic Analysis*. Thousand Oaks: Sage Publications Inc., 2014.

78. Hartmann-Boyce J, Chepkin SC, Ye W, et al. Nicotine replacement therapy versus control for smoking cessation (Review). *Cochrane Database Syst Rev* 2018; CD000146.

79. Eldridge SM, Chan CL, Campbell MJ, et al. CONSORT 2010 statement: extension to randomised pilot and feasibility trials. *BMJ* 2016; 355: i5239.

Figure 1: Participant timeline for this feasibility trial (based on the SPIRIT figure)

	STUDY PERIOD				
	Enrolment	**Pre-intervention assessment**	**Post-allocation**	**Post-intervention assessment**	**End of study**
TIMEPOINT	**0**	**week$_0$**	***week$_1$ to week$_{12}$***	***week$_{12}$***	
ENROLMENT:					
Eligibility screen	X	X			
Informed consent	X	X			
Random allocation		X			
INTERVENTIONS:					
Experimental: Multi-component smoking cessation intervention			⟷		
Control: Health Promotion and Disease Prevention Directorate's one-to-one smoking cessation service			⟷		
ASSESSMENTS:					
Baseline characteristics		X			
Feasibility outcomes:					
Recruitment parameters	X	X			
Compliance with the protocol, resources utilised and problems identified			X		
Response rate at 12 weeks follow-up				X	
Perceived challenges and facilitators to implementation					X
Acceptability outcomes:					
Participants' satisfaction with and perceived usefulness of the intervention				X	
Nurses' satisfaction with the intervention					X
Treatment fidelity of the experimental intervention					X
Exploration of the experimental intervention's functioning				X	
Preliminary evidence of effectiveness				X	

Figure 2: The theoretical model of this intervention, outlining the strategies for addressing the IMB constructs for achieving and sustaining abstinence among individuals with DM

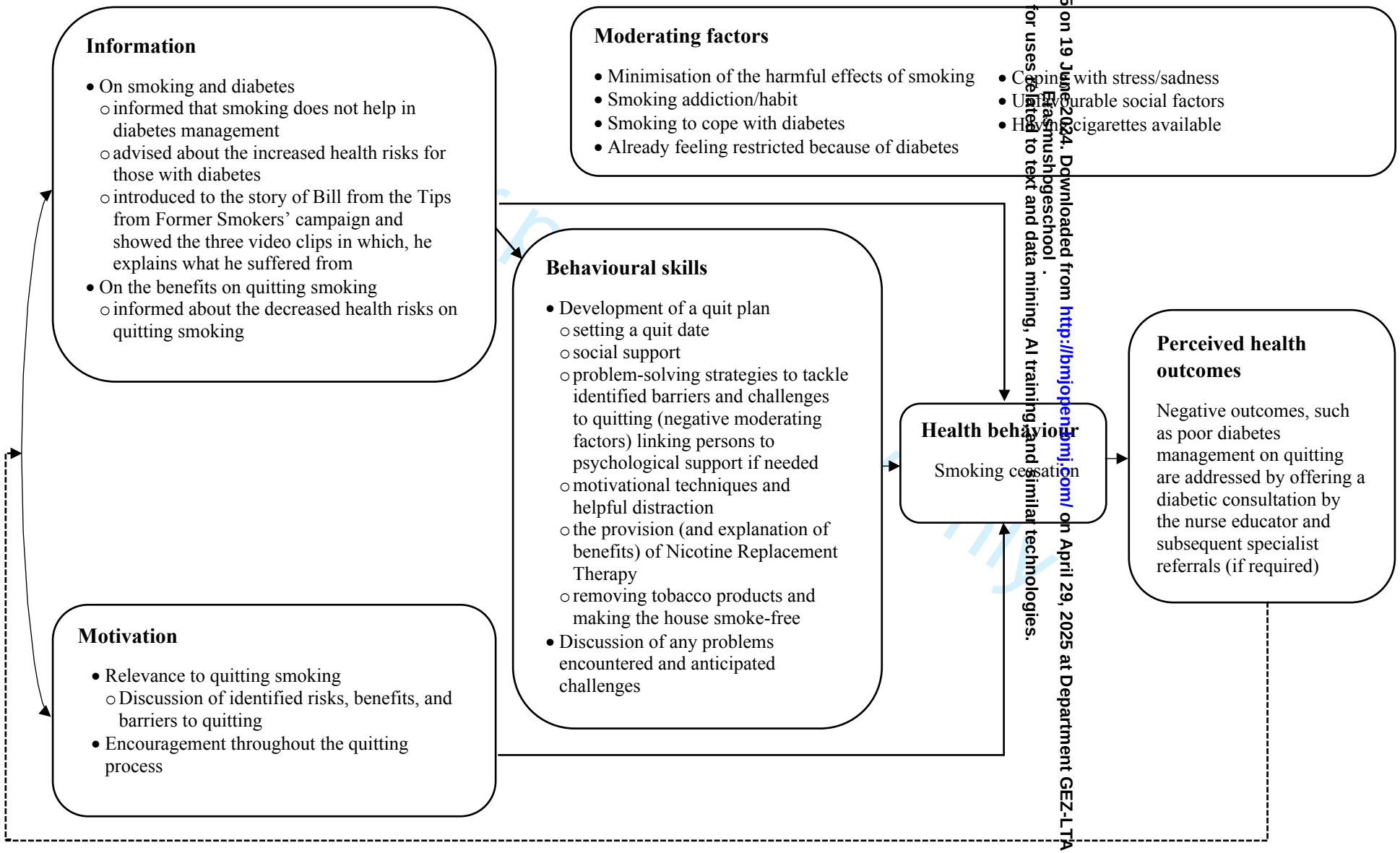
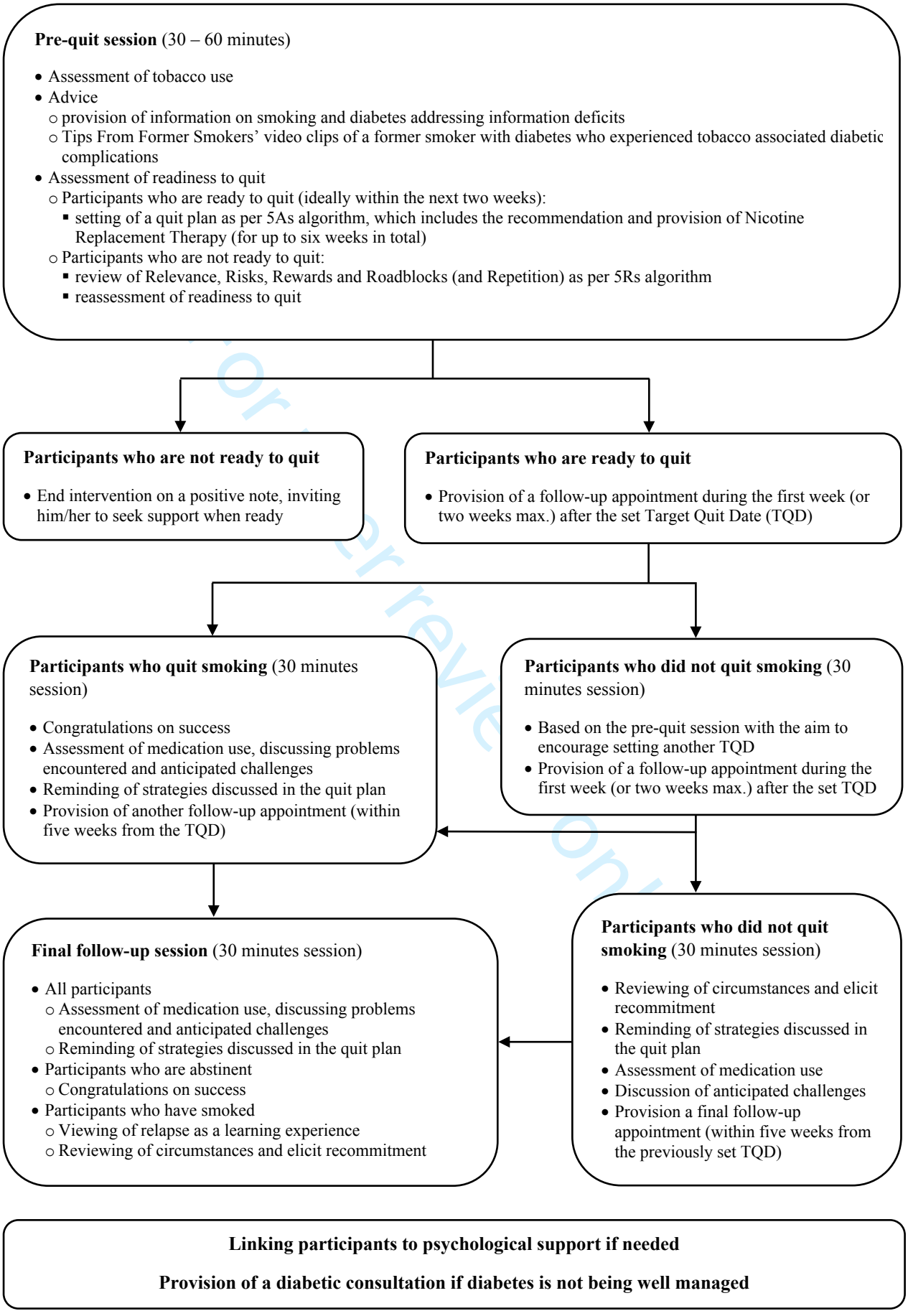


Figure 3: Study intervention algorithm based on the 5A's (and 5R's) framework for smoking cessation



Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRITreporting guidelines, and cite them as:

Chan A-W, Tetzlaff JM, Gøtzsche PC, Altman DG, Mann H, Berlin J, Dickersin K, Hróbjartsson A, Schulz KF, Parulekar WR, Krleža-Jerić K, Laupacis A, Moher D. SPIRIT 2013 Explanation and Elaboration: Guidance for protocols of clinical trials. BMJ. 2013;346:e7586

		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	#2a	Trial identifier and registry name. If not yet registered,	3, 7

		name of intended registry	
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	3, 7
Protocol version	#3	Date and version identifier	NA
Funding	#4	Sources and types of financial, material, and other support	27
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	1, 27
Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	1
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	27
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	NA

Introduction

Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4-7
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	7-8
Objectives	#7	Specific objectives or hypotheses	6-7
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	7-8, 11
Methods: Participants, interventions, and outcomes			
Study setting	#9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	8-9
Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg,	9

		surgeons, psychotherapists)	
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	12-14, 16
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	26
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	15-16
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	NA
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	19-22
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	11, 16, 18

Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	9-10
Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	10-11
Methods: Assignment of interventions (for controlled trials)			
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	11
Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	11
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	11

Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	8
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	NA
Methods: Data collection, management, and analysis			
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	11-12, 15-16
Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	NA
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values).	26

		Reference to where details of data management procedures can be found, if not in the protocol	
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	23
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	NA
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	23-24
Methods: Monitoring			
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	NA
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	NA
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial	15, 26

		conduct	
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	NA
Ethics and dissemination			
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	24
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	NA
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	11, 25
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	NA
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	26
Declaration of	#28	Financial and other competing interests for principal	27

interests		investigators for the overall trial and each study site	
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	26
Ancillary and post trial care	#30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	NA
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	26-27
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	NA
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	26
Appendices			
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	NA
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	NA

Cigarette Dependence Scale-5 (Maltese version) - Item-to-total statistics (*n*=17)

Cigarette Dependence Scale-5 items[a]	Scale mean if item deleted	Corrected item-total correlation	Cronbach's alpha if item deleted
Self-rated dependence, 0–100 score recoded to five categories	16.2	0.72	0.72
Cigarettes per day, five categories	16.0	0.40	0.85
Minutes to first cigarette, five categories	15.7	0.71	0.75
Quitting for good would be difficult.	15.9	0.65	0.76
An irresistible urge to smoke after a few hours.	15.5	0.63	0.76

a - original items in Maltese

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Assessing the feasibility and acceptability of a diabetes-specific nurse-led multi-component smoking cessation intervention in diabetes education: study protocol for an open-label pragmatic randomised controlled trial

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Assessing the feasibility and acceptability of a diabetes-specific nurse-led multi-component smoking cessation intervention in diabetes education: study protocol for an open-label pragmatic randomised controlled trial

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ABSTRACT

Introduction Smoking cessation is an essential, but often overlooked aspect of diabetes management. Despite the need for tailored smoking cessation support for individuals with diabetes, evidence of effective interventions for this cohort is limited. Additionally, individuals with diabetes do not easily adopt such interventions, resulting in low uptake and abstinence rates. This protocol describes a study that aims to assess the feasibility and acceptability of a unique smoking cessation intervention, based on the best evidence, theory, and the needs of individuals with diabetes, among patients and service providers, the diabetes nurse educators.

Methods and analysis This is an open-label pragmatic randomised controlled trial. Between 80 and 100 individuals with type 1 or type 2 diabetes who smoke will be recruited from the diabetes outpatients at the main acute public hospital in Malta, starting in August 2023. Participants will be randomly assigned (1:1 ratio) to the intervention or control arm for 12 weeks. The experimental intervention will consist of three to four smoking cessation behavioural support sessions based on the 5A's (Ask, Advise, Assess, Assist and Arrange) algorithm, and a six-week supply of Nicotine Replacement Therapy. The control intervention will consist of an active referral to the Maltese National Health Service's one-to-one smoking cessation support service, which is based on motivational interviewing. The primary feasibility and acceptability outcomes include the recruitment and participation rates, resources utilised, problems identified by the nurses, the nurses' perceived challenges and facilitators to implementation, and the nurses and patients' acceptability of the study intervention. Data analyses will be descriptive and no statistical comparisons between the randomised groups will be conducted.

Ethics and dissemination Ethical clearance was obtained from the Faculty of Health Sciences Research Ethics Committee, University of Malta. The study results will be disseminated through conference presentations and a publication in a peer-reviewed journal.

Trial Registration Number ClinicalTrials.gov NCT05920096

Keywords Diabetes Mellitus; Tobacco Use Cessation; Clinical Trial; Healthcare Acceptability; Feasibility Studies; Information Motivation Behavioral Skills Model; Counselling; Smoking Cessation Agents; 5A's Framework

Strengths and limitations of this study

- This paper outlines the study protocol of a feasibility trial, an overlooked, but critical step in the development and evaluation of smoking cessation interventions among individuals with diabetes, in preparation for a future definitive evaluation.
- Since healthcare interventions are highly context-dependent, this study will adopt a pragmatic approach, assessing the feasibility of the intervention in the real-world context of diabetes ambulatory care, where formal diabetes education is provided locally.
- A unique multi-component smoking cessation intervention based on evidence, theory, and the needs of individuals living with diabetes is described to allow its replication.
- This is a feasibility trial and is not powered to determine the effectiveness of the intervention.

INTRODUCTION

Diabetes mellitus (DM) is a major public health concern both worldwide and in the Maltese context. DM, characterised by chronically elevated blood glucose levels that lead to the development of various macro- and micro-vascular complications, thus increasing the risk of morbidity and death, is estimated to affect approximately one in every ten adults aged 20 to 79 worldwide.[1] While the European region has the second-lowest diabetes prevalence (at 9.2%; 95% Confidence Interval, CI: 7.1-10.4), Malta, a European country, has a high diabetes prevalence, estimated at 11.2% (95% CI: 8.7-13.8).[1]

Individuals living with DM require medical care, self-management education, and support that goes beyond glucose management. Tobacco cessation is an essential, but often overlooked aspect of diabetes management.[2] In persons with DM, tobacco smoking, likely mediated by the effects of nicotine, appears to contribute to greater insulin resistance,[3–6] worsened beta-cell function and impaired insulin secretion,[3,4] glucolipotoxicity and dyslipidaemia.[3–6] This exacerbates both macro- and micro-vascular complications of DM. Both individuals with type 1 and type 2 DM who smoke are at approximately 50% higher risk of adverse cardiovascular events, such as coronary heart disease and stroke, compared to non-smokers with diabetes.[7,8] Similarly, a higher risk for cardiovascular mortality and total mortality, has also been identified among smokers with type 1 and type 2 DM.[7,8] Tobacco smoking may also increase the risk of microvascular diabetes complications, such as diabetic nephropathy, neuropathy, and retinopathy, particularly amongst individuals with type 1 DM.[4,9] Furthermore, individuals with DM who smoke experience a 1.65-fold increase in the risk of diabetic foot amputations.[10] Conversely, smoking cessation is associated with significant health benefits, including improved cardiometabolic profiles,[3] and a notable reduction in the risk for cardiovascular disease, cardiovascular mortality, and overall

mortality amongst this population.[7,8] Smoking cessation for individuals with diabetes is one of the key recommendations of Malta's national diabetes strategy.[11]

Despite the importance of quitting smoking, having diabetes does not appear to motivate individuals to quit.[12,13] Durlach et al. estimated that on average 20% of individuals with type 2 DM and 30% of individuals with type 1 DM smoke.[4] Analysis of unpublished raw data from the Malta National Health Interview survey revealed that 17.4% of those who reported having diabetes also reported being a smoker (Unpublished data on smoking and diabetes; Directorate for Health Information and Research, 2023). Smokers with diabetes may be less motivated to stop smoking due to several diabetes-related barriers and challenges to quitting. These include: concern about possible weight gain and poor glycaemic control, which may occur on quitting smoking;[3] comorbid anxiety and depression,[14,15] which can hinder efforts in quitting smoking;[16] and possibly increased nicotine metabolism associated with having diabetes, which increases nicotine addiction, making it harder for them to quit.[17,18]

While the need for providing tailored smoking cessation support to tackle these diabetes-related barriers and challenges to quitting has been emphasized,[4,9,13] evidence-based smoking cessation recommendations for individuals living with DM are still lacking. Nagrebetsky et al.'s systematic review and meta-analysis aimed to assess the effectiveness of intensive smoking cessation interventions, such as intensive behavioural support (e.g. intensive counselling) or interventions that combine behavioural support and pharmacotherapy, such as Nicotine Replacement Therapy (NRT), bupropion or varenicline, amongst individuals with DM.[19] However, the limited number of reviewed studies and the significant heterogeneity in the intervention tested and comparator group limited the authors' conclusions regarding the efficacy of diabetes-specific smoking cessation interventions, and from providing practice recommendations.

Grech and colleagues, who recently updated Nagrebetsky et al.'s systematic review and included an intervention component analysis, found that intensive smoking cessation interventions, comprising three to four sessions, each lasting more than 20 minutes, were more likely to be associated with smoking cessation compared to brief interventions or those consisting of fewer sessions.[20] However, inconsistent findings limited their ability to make comprehensive recommendations for practice, particularly concerning the use of specific behavioural interventions and smoking cessation pharmacotherapy.[20] Given the identified gap in evidence, further research on the development and evaluation of tailored smoking cessation interventions for individuals with diabetes has been recommended.[19,20]

Notwithstanding the limited evidence-based smoking cessation recommendations for individuals with DM, evidence suggests that health professionals who care for individuals with diabetes are less likely to advise their patients against smoking and support them towards quitting, compared to health professionals who treat individuals without diabetes.[21,22] International and local literature suggest that diabetes clinicians and educators often prioritise other aspects of diabetes management over smoking cessation.[2,23–25] Diabetes educators have reported feeling inadequately prepared to discuss smoking cessation with individuals with diabetes, lacking motivation and time to do so.[2,26]

Given that the success of a proposed healthcare intervention, such as a smoking cessation intervention, is very much dependent on stakeholder engagement, patients, and providers alike, investigating the feasibility and acceptability of a proposed intervention is crucial prior to further evaluation and implementation.[27] The feasibility and acceptability assessment of a proposed diabetes-specific smoking cessation intervention for undertaking a future large-scale randomised controlled trial is particularly advisable in view of the reported low recruitment, uptake and challenges encountered in two recent smoking cessation trials carried

out amongst individuals with DM.[28,29] These trials, which were initiated before the COVID-19 pandemic, in 2018,[28] and after the declaration of the pandemic, in August 2020,[29] did not reach the target sample size and were later terminated due to lack of funding,[28] and following the recall of Varenicline which was one element of the study intervention,[29] respectively. Conducting a feasibility study will help estimate the recruitment rate and study uptake, identify potential challenges (along with mitigating factors), and assure the intervention's acceptability amongst patients and providers a priori, thus ensuring that the main trial targets can be met before proceeding with a larger, definitive trial.[30]

In summary, following the development of a unique multi-component smoking cessation intervention, based on best evidence and theory, and tailored for people living with DM who smoke,[20,31,32] a feasibility study was proposed prior to a definitive evaluation. This study aims to assess the feasibility of a definitive randomised controlled trial, by analysing the recruitment and study uptake, the perceived challenges and facilitators to implementation among service providers, and the acceptability of the intervention. This will involve analysing participants' and providers' satisfaction with the smoking cessation support provided, as well as participants' perceived usefulness of the intervention. The feasibility study also aims to: compare the participants' satisfaction with and perceived usefulness of the smoking cessation support provided to standard care (the provision of general smoking cessation support); undertake a preliminary process evaluation, by assessing whether the intervention was delivered as intended and exploring the intervention's functioning; and determine the preliminary evidence of the intervention's effectiveness, by comparing the smoking cessation rates achieved in the intervention group to the control group (standard care).

METHODS AND ANALYSIS

This feasibility study is part of a research project titled, 'Development and Feasibility testing of a Multi-Component Smoking Cessation Intervention for Smokers Living with Diabetes Mellitus,' which is guided by the Medical Research Council (MRC) 2021 framework for the development and evaluation of complex interventions in healthcare.[27] The methods and analysis reported in this paper match the trial registration details available on ClinicalTrials.gov (NCT05920096). This protocol follows the Standard Protocol Items for Randomized Trials (SPIRIT) reporting guidelines (supplemental file 1).[33]

Design

An open-label, pragmatic, experimental design will be adopted. While a feasibility study may not need to be a randomised trial,[30] a comparative analysis of an alternative standard course of action, (i.e., the provision of general smoking cessation support by the Health Promotion and Disease Prevention Directorate, within the Maltese National Health Service), in terms of the outcomes, (i.e. smoking cessation rates, and satisfaction with and perceived usefulness of the intervention provided), will provide sufficient information to make decisions about progressing to the evaluation stage of the MRC framework.[27] Furthermore, adopting the same design and protocol as would be adopted in a larger scale randomised controlled trial, will help assess the feasibility of undertaking the trial, by analysing the recruitment and study uptake and the successful delivery of the intervention, taking note of the resources utilised.[34] Given that healthcare interventions are highly dependent on the context in which they are tested, this study will adopt a pragmatic approach, assessing the feasibility of the intervention in the real-world context;[27] in diabetes ambulatory care where formal diabetes education is provided locally.[11] An open-label design will be adopted. The participants, who are likely to be aware of the Maltese National

Health System's smoking cessation services, may be able to distinguish between the assigned arms and hence will not be blind to treatment. On the other hand, due to the pragmatic nature of the study, blinding the intervention providers will also not be possible. The Principal Investigator (PI), JG, who will be actively involved in recruiting and carrying out pre- and post-intervention assessments and data analyses, also cannot be blinded to treatment assignment. However, being a feasibility study, blinding is not strictly required as there is no formal hypothesis testing.[30] Nonetheless, as explained below, the 7-day point prevalence abstinence at follow-up will be objectively measured to minimise bias.[35] Furthermore, the questionnaires used during the pre- and post-intervention assessments will be coded to avoid participant identification.

Study population

In Malta, all adults with type 1 DM are under the care of the diabetologists attending the diabetes outpatients/the Diabetes and Endocrine Centre (DEC) at the main acute public hospital in Malta, Mater Dei Hospital.[11] While individuals with type 2 DM may be seen in primary care, they also attend the DEC when complications arise, or at prescribed time intervals, at least once annually.[11] In this study, participants will be recruited from the DEC, and the adjacent Diabetes Education Unit (DEU), where formal diabetes education is provided.

Inclusion Criteria:

- Documented diagnosis of type 1 or type 2 diabetes (meeting the diagnostic criteria of the American Diabetes Association, ADA)[36] and attending the DEU or the DEC at Mater Dei Hospital on an outpatient basis.
- Having smoked at least 100 cigarettes in one's lifetime and currently smoking.
- Being ≥ 18 years of age.

- Speaking and understanding English or Maltese.
- Able to provide written informed consent.

Exclusion Criteria:

- Not being able to provide informed consent (due to dementia, a learning disability, or a psychological disorder).
- Being pregnant or breastfeeding.
- Unable to independently attend to the DEU and any of the health centres in which the Health Promotion and Disease Prevention Directorate provide smoking cessation support during the study period.
- Currently enrolled in another smoking cessation study/program or multi-behavioural program which also focuses on smoking cessation.
- Enrolment of the investigator or the research collaborators, and their family members.

Sample size

A power calculation to determine the sample size is not appropriate for a feasibility trial, as the purpose of a feasibility trial is not to establish efficacy.[37] However, the sample should be large enough to provide estimates of the parameters that are used to calculate the sample size for definitive trials. For estimating the confidence intervals for feasibility outcomes, such as the recruitment rate and rate of consent to the study, and the compliance to the study protocol, Hertzog[38] suggests having 30 to 40 participants per group, while Teare et al.[39] recommend having 60 participants per group. However, ultimately the sample size decision must also take into consideration the resources required and time available.[39] Thus, this study aims to recruit a minimum of 80 and a maximum of 100 participants.

Recruitment and randomisation

At the DEC, all new patients with type 1 or type 2 DM are screened for tobacco use by diabetologists and advised to quit smoking. As part of the study's pragmatic approach to assess the feasibility of providing smoking cessation support in diabetes practice, the diabetologists working at the diabetes outpatients will be asked to identify smokers who are interested in quitting and to refer them to the PI for study recruitment. Additionally, the healthcare professionals working at the diabetic clinics at the DEC, such as the nurses and the podiatrists, and the diabetes specialist nurses (diabetes nurse educators) at the DEU, will also be asked to identify any interested smokers during their practice and to refer them to the study. Posters and flyers will also be present at the DEC so that participants can also self-refer to the study. To enhance recruitment, onsite visits will be held during which feedback on the recruitment process will be provided to all healthcare professionals.[40] No additional strategies, such as offering patient incentives, will be employed, as they would limit the feasibility study's capacity to truly assess the need for smoking cessation support within diabetes practice.

In 2022, there were 1,786 new patients (most of whom are individuals with type 1 or type 2 DM) who attended the diabetes outpatients (of whom 473 attended the DEU) at Mater Dei Hospital.[41] Of these, 17.4%, were likely to be smokers (Unpublished data on smoking and diabetes; Directorate for Health Information and Research, 2023). Assuming a yearly population size of approximately 311 individuals, a sample size of 100 (or 80) participants, with a 95% confidence interval, would be sufficient to provide the aforementioned feasibility estimates with an acceptable margin of error of 8% (or 10%).[42] Given that the consent rate for participating in smoking cessation trials was found to be 66.4% (Interquartile Range, IQR: 42.7–85.2%),[43] it is anticipated that the target sample size of 80 or 100 participants will be achieved within one year.

The PI will screen all recruited patients by telephone to assess eligibility, inviting them to participate in the study. Eligible interested individuals will attend a pre-intervention assessment session for informed consent, during which the PI will randomly assign them to the intervention or control group and assess baseline characteristics. Participants will be randomly allocated to the intervention or control arm on a 1:1 ratio using a computer-generated random block length (in blocks of two and four), using the random allocation software by Saghaei.[44] The sequence will be prearranged before the study begins, with group assignments sealed in sequentially numbered opaque envelopes. The PI will assign the sequentially numbered opaque envelopes in the order they are met. The participants' characteristics will not be known before the assignment of the envelopes.

Participants are to receive the respective intervention within two weeks from the assignment. Post-intervention evaluation will take place 12 weeks after the pre-intervention assessment session. Figure 1 displays the participant timeline for this study, based on the SPIRIT participant timeline figure.[33]

Pre-intervention assessment

In the pre-intervention assessment session, a baseline questionnaire will be used to collect information on the participants. This questionnaire will collect demographic data, perceived health status, diabetes and smoking profiles, and anxiety and depression levels. Questions are based on the literature. Cigarette dependence, current motivation to stop smoking, which are part of the smoking profile, and anxiety and depression will be measured using well-established validated questionnaire scales. Cigarette dependence will be measured using the Cigarette Dependence Scale-5 (CDS-5),[45] while motivation to stop smoking will be measured using the Motivation To Stop Scale (MTSS).[46,47] Conversely, the Hospital Anxiety and Depression Scale (HADS),[48] will be used for screening for anxiety and

depression. As part of the smoking profile section, exhaled carbon monoxide (eCO) will also be measured using the Bedfont piCO™ Smokerlyzer® to confirm smoking status.[49]

The baseline questionnaire will be made available to participants in English and Maltese. Except for HADS,[48] which was already translated and validated into Maltese by Baldacchino, Bowman, & Buhagiar,[50] the CDS-5,[45] and the MTSS,[46,47] required translation and validity assessment. To ensure the content validity of the translated instruments, conceptual equivalence was established for these instruments by following the process outlined by Tang & Dixon.[51] Additionally, the CDS-5[45] was assessed for internal reliability using Cronbach's alpha. Based on the minimum sample size required,[52] 17 individuals living with type 1 or type 2 diabetes were invited to complete the Maltese version of the CDS-5 prior to participating in a smoking cessation programme. The Cronbach alpha score was high; 0.80. On eliminating the items one at a time from the analysis, the Cronbach alpha (and scale mean) remained relatively stable (supplemental file 2). All item-scale correlations were ≥0.4.

Interventions

Experimental intervention

Intervention development

The development of the intervention followed a three-stepped research process. Initially, a scoping review was undertaken to identify the most promising smoking cessation methods for persons living with diabetes, identifying any gaps in evidence.[31] This was followed by a systematic review and intervention component analysis of the identified most promising smoking cessation methods to identify their critical components.[20] Then a qualitative descriptive study was conducted to explore the needs of individuals with diabetes to quit smoking, and their views of the identified promising smoking cessation components.[32]

Based on the reviews and the qualitative descriptive study's findings and recommendations, a multi-component smoking cessation was developed and proposed to the diabetes specialist nurses working at the DEU.

Theoretical framework

The intervention is based on Information-Motivation-Behavioural Skills (IMB) model for achieving behaviour change,[53] and thus aims to:

- inform individuals with diabetes who smoke on the association between smoking and diabetic complications and the benefits of quitting;
- motivate and encourage individuals to quit smoking and/or remain abstinent;
- support them in developing/using the appropriate behavioural skills to quit smoking and avoid relapse; and
- tackle any situational and individual characteristics (moderating factors) that can negatively influence smoking cessation, and negative health outcomes on quitting smoking, which can weaken adherence to the new behaviour via a feedback loop affecting the IMB constructs.

Figure 2 presents the theoretical framework of this intervention, outlining the strategies for addressing the IMB constructs (and any negative moderators and health outcomes)[53] for achieving and sustaining abstinence among individuals with DM.

Components of the intervention

The main components of this intervention include:

- Three to four (30-60 minutes) smoking cessation behavioural support sessions based on the 5A's (Ask, Advise, Assess, Assist, and Arrange) and 5R's (Relevance, Risks,

Rewards, Roadblocks, and Repetition) algorithm[54] which will be provided by two diabetes specialist nurses at the DEU (figure 3);

- Three brief video clips (with English subtitles) featuring Bill from the Tips from Former Smokers' campaign, to raise awareness on the link between smoking and diabetes drawing on first-hand experience.[55] Bill was an individual with type 1 diabetes who suffered and died from tobacco-associated diabetic complications (kidney failure, poor circulation, heart disease, and blindness);[55] and
- A six-week supply of NRT based on the recommendations of Siahpush et al.[56]

Despite the increasing evidence demonstrating the effectiveness of nicotine electronic cigarettes (e-cigarettes) for smoking cessation compared to NRT,[57,58] participants in this study will not be provided with e-cigarettes to address their nicotine dependence. This is because in Malta, in line with the World Health Organisation's recommendations,[59] and that of other organisations, including the ADA,[60,61] the use of e-cigarettes is not recommended for smoking cessation in clinical practice. The decision to provide NRT instead of e-cigarettes is also based on the observation that individuals who quit smoking using e-cigarettes tend to continue using them, unlike those who use NRT,[5,57,62,63] possibly leading to permanent nicotine dependence,[62] and the associated ill-health effects previously mentioned. Consistent with the literature, combination NRT, i.e. the daily combination of the (16-hour) nicotine patch and a fast-acting nicotine product will be provided to individuals who smoke ≥10 cigarettes per day, while a fast-acting nicotine product will be provided to those who smoke fewer.[60,64,65] The nicotine mouth spray was selected as the preferred fast-acting nicotine product due to its faster absorption rate compared to other options like gum or lozenges, resulting in quicker relief of cravings.[66,67] While mild adverse effects, such as hiccups and burning of the

throat/tongue, tend to be more common when using the mouth spray, this was still deemed the treatment of preference amongst those who had used it.[68,69] Additionally, in the systematic review and meta-analysis by Theodoulou et al.,[65] no significant difference in quit rates was identified between participant-selected and clinician-selected NRT. Participants will be provided with six weekly packs of 25mgs 16-hour nicotine patch (tapered during the last two weeks; 15mg and 10mg, respectively) and/or four nicotine mouth sprays (1mg/spray; 150 sprays per bottle) for daily use if refraining from tobacco use, recommending the latter for breakthrough urges and/or to reduce withdrawal symptoms further.[60,64,65]

Additionally, participants will be referred for psychological support if reporting experiencing depression or anxiety, or on further discussion with those identified as potential cases; a score of ≥11 on the anxiety/depression sub-scale on the HADS.[48,70,71] Participants will also be offered a diabetic consultation by the nurse educator if reporting poor glycaemic control, or if they are concerned about diabetes management following a change in diet or weight gain on quitting smoking. Subsequent referrals to specialists, such as dietitians and diabetologists at the DEC, will be provided as needed.

Nurses' training

The two diabetes specialist nurses have been trained in smoking cessation prior to the study. A training programme, based on the successful training programme by Grech[72] (the PI), which followed the WHO toolkit for delivering the 5A's and 5R's for tobacco cessation,[54] was developed and delivered by the PI to the nurses prior to the initial testing of the intervention in November 2022 and to the commencement of the feasibility study (July 2023). To help assess fidelity, all the sessions provided by the two nurses will be audio-recorded with consent.[73,74]

Intervention log

Additionally, the nurses will be asked to keep an intervention log to document the following information per participant for measuring compliance to the protocol, the resources utilised and any challenges encountered:[75]

- the number, and duration of the sessions provided (and the number of weeks during which the sessions are provided) and non-attendance, along with reasons;
- provision of the 5R's intervention at the first session;
- whether the participant opts not to see the informational video clips, along with reasons;
- whether the participant agrees to attempt to quit smoking (by setting a Target Quit Date, TQD) at their first session, and subsequent session, if still smoking), along with reasons for not wanting to;
- the amount of NRT provided, and returned;
- reported use of NRT, along with reasons if a participant reports not using it; and
- any problems encountered, such as side effects on using NRT, identified mental health issues, issues with managing diabetes, and any referrals, including reasons for refusing support.

As recommended by Hollands et al.,[76] NRT adherence will be assessed using a continuous outcome measure: the total days of NRT use, and the average number of times the nicotine spray is used per day. This assessment will cover the first week following the TQD (and the subsequent TQD for those who agree to reattempt quitting), which should coincide with the follow-up session/s, and, as well as the next four weeks, coinciding with the final follow-up session.

Control intervention

The participants who are assigned to the control group will be actively referred to the Health Promotion and Disease Prevention Directorate's one-to-one smoking cessation service, which is provided within community health centres around Malta. The smoking cessation support provided is based on motivational interviewing and is delivered by trained tobacco cessation facilitators. The counselling sessions, lasting around 20 minutes each, are usually provided every fortnight, based on the individuals' needs.

The smoking cessation services coordinator will be asked to take note of the number of sessions provided (including the number of weeks during which the sessions are provided) and any dropouts (with reasons).

Post-intervention evaluation

End of study questionnaire

All participants will be invited to a post-intervention assessment session, held at 12 weeks follow-up in which they will be invited to fill in the end-of-study questionnaire, available in English or Maltese. In the questionnaire, participants will be asked about their quitting attempt and smoking status, about the support they received during the study period, and to rate their satisfaction with the smoking cessation intervention provided and their perceptions of its usefulness.

Smoking abstinence will be measured by following the recommendations by Piper et al.[77] Participants will be asked if, in the past seven days, they intentionally refrained from smoking any combustible or non-combustible tobacco products and alternative products (seven-day point-prevalence abstinence). They will also be asked if they abstained from smoking for seven consecutive days (or more) during the study period (seven-day floating abstinence) or for at least one day or 24 hours (quit episode). Continuing smokers will be asked about their current tobacco use.

Biochemical verification of tobacco abstinence will be conducted for those reporting seven-day point-prevalence abstinence, based on the recommendations of Benowitz et al.[49] This will be carried out by using the same carbon monoxide monitor and additionally by analysing a urine sample for cotinine exposure using a multilevel lateral flow immunoassays urine test strip with a nominal 200 ng/mL cutoff. The latter will help to confirm abstinence from both combustible and non-combustible tobacco sources and the use of alternative products, e.g. e-cigarettes. Participants will be advised to discontinue the use of NRT prior to assessment, if possible, as cotinine can also be detected in urine because of NRT use.

To investigate the participants' satisfaction with the intervention and their perceptions of its usefulness, the measures by Grech, Norman & Sammut for assessing the satisfaction and perceived usefulness of smoking cessation interventions among individuals with diabetes, will be utilised.[78] The satisfaction questionnaire consists of eight statements covering the main elements of smoking cessation interventions. It is rated by a 5-point Likert scale, ranging from (1) 'very unsatisfied' to (5) 'very satisfied.' The total score ranges from eight to 40. Conversely, the perceived usefulness questionnaire consists of 14 items, based on the Information-Motivation-Behavioural Skills (IMB) model of behaviour change. It is also rated by a 5-point Likert scale, ranging from (1) 'strongly disagree' to (5) 'strongly agree.' The total score ranges from 14 to 70. Four additional questions, asking participants to explain which aspects of the smoking cessation intervention they were most and least satisfied with, suggestions for improvement, and whether they would recommend the intervention to others ('yes' or 'no' option), complement these instruments. Both questionnaires (in English and Maltese) were found to have a high internal consistency (>0.8).[78]

Semi-structured interviews

Additionally, the participants who are assigned the experimental intervention will be interviewed to obtain feedback on the study intervention and to explore their quit attempt. The qualitative sample will consist of a purposeful sample, for obtaining an in-depth understanding of the acceptability of the study and the mechanisms of the study intervention from different viewpoints,[73,75] selecting individuals who stop or do not stop smoking, attend or stop attending the study intervention; and use or do not use the NRT provided on attempting to quit smoking. In selecting participants, due consideration will also be made to sex, age, and the type of diabetes. The sample size will be based on the principle of 'data saturation,'[79] seeing saturation when new data collected repeats what was expressed in the previously collected data.[80] Given that no previous studies have explored the acceptability of a smoking cessation intervention among individuals with diabetes,[31] in estimating the required sample size, reference is made to the seminal study by Guest, Bunce, & Johnson,[81] in which saturation was relatively achieved after only 12 interviews. The estimated sample size was increased to 20 participants.

Semi-structured interviews will also be carried out with both nurses to obtain feedback on the study intervention and to explore the facilitators and challenges to implementation.

Patient and public involvement

Individuals living with DM were involved during both the development and in planning feasibility testing of the intervention. During the developmental phase, a qualitative descriptive study was conducted to explore the needs of individuals with DM to quit smoking, and their views of the identified promising smoking cessation components,[20,31,32] to guide the development of the study intervention. Additionally, in November 2022, a pilot study was conducted to test and refine the intervention with a small sample of individuals with diabetes.[78] Based on the feedback received from both patients

and providers, the study intervention was revised to include an additional follow-up session for those who report not quitting smoking, bringing the total to four sessions. Patients/public were not involved in the design or the conducting of this study. A summary of the study findings, presented in a simple factsheet with pictograms, will be offered to all participants.

Outcome measures

Primary feasibility and acceptability outcomes

Feasibility – recruitment parameters

The following outcomes will be measured during the study recruitment period:

- The monthly recruitment rate of eligible smokers interested in quitting (recruitment rate).
- The proportion of eligible smokers identified from each source of recruitment (DEU, DEC, and self-referral).
- The proportion of participants who consent to the study out of the total number of recruited eligible smokers, along with reasons for non-participation (consent rate).
- The recruitment duration in months.

Feasibility – compliance with the protocol, resources utilised, and problems identified

These feasibility outcomes will be measured based on the information documented by the intervention providers during the intervention period:

- The proportion of participants who attend the scheduled sessions per group, along with reasons for not attending (participation rate).
- The proportion/number of participants in the intervention group who choose not to watch the informational video clips, along with their reasons.

- The proportion/number of participants in the intervention group who choose not to set a TQD at their first session (or subsequent session if still smoking), along with their reasons.
- The proportion of participants in the intervention group who use the nicotine patch and/or spray on their TQD, during the subsequent TQD for continuing smokers, and in their final follow-up period, along with reasons for not using it.
- The average percentage of days the nicotine patch and/or spray are used by participants in the intervention group during the first week after the TQD, the subsequent TQD for continuing smokers, and during the subsequent four weeks following one week from the TQD.
- The average daily usage of nicotine spray by participants in the intervention group during the first week after the TQD, the subsequent TQD for continuing smokers, and during the subsequent four weeks following one week from the TQD.
- The average number of sessions provided per participant per group.
- The average duration (in weeks) of smoking cessation support provided per participant per group.
- The average time (in minutes) taken to deliver the experimental intervention sessions.
- The proportion/number of participants from the intervention group who were provided with the 5R's intervention.
- The average amount of NRT provided per participant (taking note of any returned items).
- The number of problematic issues identified by the diabetes specialist nurses, such as reported adverse events while using NRT, and the number of referrals to additional support services (e.g., psychotherapists). Participants who decline additional support will be documented, along with their reasons for refusal.

Feasibility – response rate at 12 weeks follow-up

- The proportion of participants attending their 12-week post-intervention evaluation session in both groups, with reasons for dropouts.

Feasibility – perceived challenges and facilitators to implementation

- The perceived challenges and facilitators to implementation as identified when conducting interviews with the diabetes specialist nurses at the end of the study.

Acceptability outcomes

The following acceptability outcomes will be measured based on information collected from participants in the intervention group during their post-intervention evaluation sessions (questionnaires and interviews), as well as interviews with diabetes specialist nurses at the end of the study.

- Participants' satisfaction with the intervention provided.
- Participants' perceived usefulness of the intervention provided.
- Nurses' satisfaction with the intervention.

Secondary outcomes

Secondary acceptability outcomes

The following outcomes will be measured based on the data collected from the end-of-study questionnaires.

- Group comparison of the participants' satisfaction with the smoking cessation support provided.
- Group comparison of the participants' perceived usefulness of the smoking cessation support provided.

Preliminary process evaluation

- Treatment fidelity of the experimental intervention. A random sample (20%) from all the audio recordings (all sessions provided) from both nurses will be selected, listened to, and cross-checked against a list outlining the intervention's action components (for each type of session) for calculating the level of adherence.[74] Any deviations from the study protocol will also be taken note of. An 80-100% level of adherence constitutes high fidelity, less than 80% medium fidelity, whereas ≤50% constitutes low fidelity.[74]
- Exploring the experimental intervention's functioning when conducting interviews with the participants.

Preliminary evidence of effectiveness

The following outcomes will also be measured, based on the data collected from the end-of-study questionnaires.

- Proportion of participants per group reporting a quit episode during their study period.
- Proportion of participants per group reporting a 7-day point prevalence abstinence at any time during the study period (floating abstinence).
- Proportion of participants per group reporting a 7-day point prevalence abstinence at follow-up, biochemically verified.
- The change in the average number of cigarettes smoked per day (amongst continuing smokers) per group at follow-up.

Data analysis plan

Quantitative data

Based on the recommendations for the analysis of pilot and feasibility studies, where a formal power calculation is not carried out, the data analyses will be descriptive in nature, and no statistical comparisons between the intervention and control groups will be undertaken.[82–84] Nonetheless, the feasibility and acceptability outcomes will be reported with 95% Confidence Intervals (CIs) to provide an estimated range of the said outcomes.[82–84]

Continuous data will be summarised using means (and standard deviations, SD) and 95% CIs, and medians (and interquartile range, IQR) for normally and non-normally distributed variables, respectively. For categorical data, frequencies and proportions/percentages will be used. Proportions/rates will also be reported with 95% CIs using the Clopper-Pearson "exact" interval, which is more conservative for estimating CIs when using binomial distributed data.[83,85]

Missing data

In line with standard smoking cessation research practice,[65,86,87] intention-to-treat analysis will be used for assessing effectiveness. Participants with missing smoking outcome data, i.e. those who drop out of the study or who are lost to follow-up, and participants whose abstinence cannot be biochemically verified, will be considered as continuing smokers or to have resumed smoking.[65,86,87] The baseline characteristics of those followed up and those lost to follow-up will be compared descriptively.

To calculate the satisfaction and perceived usefulness questionnaires' average scores, any missing data will be handled in accordance with the recommendations of Mirzaei et al.[88] In case of a missing data percentage of up to 10% (e.g. one item in the perceived usefulness questionnaire), the single imputation method will be conducted.[88] In the case of 10-40% missing data per questionnaire, missing data may be imputed if the Little test of missingness determines that the missing values meet the specification of missing completely at random

(MCAR).[88] In such a case the recommended imputation method is multiple imputation (MI).[88,89] Given that it is not possible to confirm if the missing data are missing at random (MAR) or missing not at random (MNAR), no imputation will be carried out in such cases and these will be excluded from analyses.[88,89] However qualitative investigation (by inviting such participants to an interview) will be recommended.[88] The same principle applies to >40% of missing data.[88]

Missing data in the intervention logs will not be imputed. The intervention logs will be frequently checked by the PI for their completeness and to ensure that they are being filled up in a timely manner.

Qualitative data

Qualitative data will be summarised by following the Applied Thematic Analysis (ATA) approach.[90] ATA has been described as a rigorous, primarily inductive method for describing and exploring the experiences of participants as accurately and comprehensively as possible.

To provide a further understanding of the acceptability of the study intervention and its' functioning as experienced by the study participants, the quantitative and qualitative data will be compared to confirm, disconfirm, or expand each other. Ultimately, all findings derived from all sources will be synthesized to understand what needs to be modified to enhance the feasibility and acceptability of the study intervention, prior to a full-scale randomised trial.[75]

Criteria for proceeding to a future trial

The decision of whether to proceed to a future definitive trial will be based on the feasibility and acceptability data, i.e., the data on the recruitment and study uptake, and the acceptability of the intervention. As stated earlier, the required sample should be recruited within a year.

Based on two previous studies; who similarly provided individuals with type 2 DM with a counselling session at baseline followed by a one-week and one-month follow-up (participation rates of 90% and 86.2%, respectively),[87] and who provided individuals with type 2 DM with weekly visits and varenicline for three months (reporting an approximate 30% attrition),[86] the uptake for this study, i.e., the participation rates, NRT usage (average percentage of days the nicotine patch and/or spray are used, at least during the first week after the TQD and the subsequent set TQD for continuing smokers), and follow-up response rates, should be not less than 70%. The participants from the intervention group should also rate the study intervention as satisfactory and useful, or above; with an average score of 32 and 56, respectively. The intervention providers should also be satisfied with the intervention, finding it feasible to introduce it in practice for a definitive assessment. Not reaching these criteria does not necessarily indicate that a future definitive trial is unfeasible, however, modifications, informed from the qualitative findings, will be required before further testing and a definitive evaluation.

ETHICS AND DISSEMINATION

Before carrying out the study, permissions were sought from the authors of the tools that will be used, the recruiting stakeholders, the clinical chairperson, and the hospital administration. Ethical clearance was sought from the Faculty of Health Sciences Research Ethics Committee on behalf of the University Research Ethics Committee (UREC FORM V_15062020 8618). No ethical issues were foreseen, and the study was approved. The study started in August 2023 and is ongoing.

On indicating their interest to participate in the study, prospective participants will be verbally briefed on the study by the PI and provided with a detailed information letter and

consent form to sign (supplemental files 3 and 4). The participants and the nurses (intervention providers) who participate in the interviews at the end of the study will also receive an information letter and consent form to sign (supplemental files 5-8). Participants will be informed that participation is voluntary and that they are free to withdraw from the study at any time, without the need to provide a reason. They will also be assured that refusing to participate or withdrawing from the study will not have any effect on their care whatsoever.

The participants in the intervention group will be encouraged to take the provided NRT in attempting to quit smoking, however, they are also free to refuse to take it. Often NRT may cause minor adverse reactions (for example, irritation of the site of use, the skin), however, such adverse events can usually be minimised or avoided by applying the treatment correctly and so should not warrant treatment discontinuation.[91] On the other hand, on rare occasions, NRT may also cause non-ischaemic chest pain and palpitations but there is no evidence of an excess of serious cardiac problems, even in people with established cardiac disease.[91] In the unlikely event of such a serious adverse event, NRT will be discontinued and participants will be seen by a doctor of their choice, free of charge.

Data will be securely stored in an encrypted computer, with access restricted to the PI. While the questionnaires used will be coded, to allow the comparison of the baseline characteristics of those followed up and those lost to follow-up, only the participants will be aware of their unique code, thus ensuring anonymity. The audio-recorded interviews will also be pseudonymised by the PI on transcription. These, and the audio-recorded experimental intervention sessions, which will only be listened to by the PI for quality assurance, will then be erased. The participants who do not quit smoking by the end of the study will be invited to attend the Health Promotion and Disease Prevention Directorate's smoking cessation services.

The data supporting this research will be available from the corresponding author upon reasonable request. The study results will be communicated and disseminated through conference presentations at national and international conferences on general medicine, diabetes, public health, nursing, and/or tobacco control. A publication is planned in a high-impact peer-reviewed journal. The study reporting will follow the CONSORT statement for the reporting of randomised pilot and feasibility trials.[92] Depending on the results, modifications to the study methods followed by further testing, or a definitive evaluation, will be proposed.

CRediT authorship contribution statement

JG: Conceptualization, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Visualization, Writing – Original Draft, Review & Editing.

CA and MG: Investigation, Resources, Writing – Review & Editing.

IN and RS: Conceptualization, Supervision, Writing – Review & Editing.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. The authors declare no conflict of interest.

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REFERENCES

1 Boyko EJ, Magliano DJ, Karuranga S, *et al. IDF Diabetes Atlas*. 10th ed. International Diabetes Federation 2021.

2 Lotrean LM. Smoking Cessation In Patients With Diabetes. In: Behrakis P, Vardavas C, Papadakis S, eds. *Tobacco Cessation Guidelines for High-Risk Populations*. Athens 2017:150–91.

3 Kar D, Gillies C, Zaccardi F, *et al.* Relationship of cardiometabolic parameters in non-smokers, current smokers, and quitters in diabetes: a systematic review and meta-analysis. *Cardiovasc Diabetol*. 2016;15:158.

4 Durlach V, Vergès B, Al-Salameh A, *et al.* Smoking and diabetes interplay: A comprehensive review and joint statement. *Diabetes Metab*. 2022;48:101370.

5 Kos K. Smoking cessation, weight gain, and cardiovascular risk. *Lancet Diabetes Endocrinol*. 2020;8:93–5.

6 Kos K. Cardiometabolic Morbidity and Mortality with Smoking Cessation, Review of Recommendations for People with Diabetes and Obesity. *Curr Diab Rep*. 2020;20:82.

7 Pan A, Wang Y, Talaei M, *et al.* Relation of Smoking With Total Mortality and Cardiovascular Events Among Patients With Diabetes Mellitus: A Meta-Analysis and Systematic Review. *Circulation*. 2015;132:1795–804.

8 Qin R, Chen T, Lou Q, *et al.* Excess risk of mortality and cardiovascular events associated with smoking among patients with diabetes: Meta-analysis of observational prospective studies. *Int J Cardiol*. 2013;167:342–50.

9 Campagna D, Alamo A, Di Pino A, *et al.* Smoking and diabetes: Dangerous liaisons and confusing relationships. *Diabetol Metab Syndr*. 2019;11:85.

10 Liu M, Zhang W, Yan Z, *et al.* Smoking increases the risk of diabetic foot amputation: A meta-analysis. *Exp Ther Med*. 2018;15:1680–5.

11 Calleja N, Azzopardi Muscat N, Reiff S, *et al. Diabetes: A National Public Health Priority A National Strategy for Diabetes 2016-2020*. Ministry for Health, Malta 2016.

12 Holm M, Schiöler L, Andersson E, *et al.* Predictors of smoking cessation: A longitudinal study in a large cohort of smokers. *Respir Med*. 2017;132:164–9.

13 Clement L, Gencer B, Muller O, *et al.* Smoking Cessation in People With and Without Diabetes After Acute Coronary Syndrome. *Nicotine Tob Res*. 2023;25:58–65.

14 Smith KJ, Béland M, Clyde M, *et al.* Association of diabetes with anxiety: A systematic review and meta-analysis. *J Psychosom Res*. 2013;74:89–99.

15 Rotella F, Mannucci E. Diabetes mellitus as a risk factor for depression. A meta-analysis of longitudinal studies. *Diabetes Res Clin Pract*. 2013;99:98–104.

16 Richards CS, Cohen LM, Morrell HER, *et al.* Treating depressed and anxious smokers in smoking cessation programs. *J Consult Clin Psychol*. 2013;81:263–73.

17 Keith RJ, Riggs DW, Conklin DJ, *et al.* Nicotine Metabolism in Adults With Type 2 Diabetes. *Nicotine Tob Res*. 2019;21:846–9.

18 Yammine L, Kosten TR, Pimenova M, *et al.* Cigarette smoking, type 2 diabetes mellitus, and glucagon-like peptide-1 receptor agonists as a potential treatment for smokers with diabetes: An integrative review. *Diabetes Res Clin Pract*. 2019;149:78–88.

19 Nagrebetsky A, Brettell R, Roberts N, *et al.* Smoking cessation in adults with diabetes: a systematic review and meta-analysis of data from randomised controlled trials. *BMJ Open*. 2014;4:e004107.

20 Grech J, Norman IJ, Sammut R. Effectiveness of intensive stand-alone smoking cessation interventions for individuals with diabetes: a systematic review and intervention component analysis. *Tob Induc Dis*. 2023;21:57.

21 Sardana M, Tang Y, Magnani JW, *et al.* Practice-level Variation in Smoking Cessation Assistance Provided in the Cardiology Clinics: Insights From the NCDR PINNACLE Registry. *J Am Heart Assoc*. 2019;8:1–9.

22 Bailey SR, Heintzman J, Jacob RL, *et al.* Disparities in Smoking Cessation Assistance in US Primary Care Clinics. *Am J Public Health*. 2018;108:1082–90.

23 Xu H, Luo J, Wu B. Self–reported diabetes education among Chinese middle–aged and older adults with diabetes. *J Glob Health*. 2016;6:1–8.

24 Daly B, Kenealy T, Arroll B, *et al.* Do primary health care nurses address cardiovascular risk in diabetes patients? *Diabetes Res Clin Pract*. 2014;106:212–20.

25 Camilleri T, Camilleri L, Midolo Y, *et al.* Empowering patients living with diabetes mellitus to cease smoking will improve lower limb perfusion. *J Addict Dis*. 2021;39:74–80.

26 Jansink R, Braspenning J, van der Weijden T, *et al.* Primary care nurses struggle with lifestyle counseling in diabetes care: a qualitative analysis. *BMC Fam Pract*. 2010;11:1–7.

27 Skivington K, Matthews L, Simpson SA, *et al.* A new framework for developing and evaluating complex interventions: update of Medical Research Council guidance. *Br Med J*. 2021;374:n2061.

28 Clair C, Augsburger A, Birrer P, *et al.* Assessing the efficacy and impact of a personalised smoking cessation intervention among type 2 diabetic smokers: study protocol for an open-label randomised controlled trial (DISCGO-RCT). *BMJ Open*. 2020;10:e040117.

29 Huang LC, Chang YT, Lin CL, *et al.* Effectiveness of Health Coaching in Smoking Cessation and Promoting the Use of Oral Smoking Cessation Drugs in Patients with Type 2 Diabetes: A Randomized Controlled Trial. *Int J Environ Res Public Health*. 2023;20:4994.

30 Giangregorio LM, Thabane L. Pilot Studies And Feasibility Studies For Complex Interventions An Introduction. In: Richards DA, Rahm Hallberg I, eds. *Complex Interventions In Health An overivew of research methods*. London: Routledge/Taylor & Francis Group 2015:127–35. https://doi.org/10.4324/9780203794982

31 Grech J, Norman IJ, Sammut R. Helping smokers with diabetes quit: a scoping review of the interventions utilised, and the challenges and barriers to smoking cessation. *Prim Care Diabetes*. 2023;17:119–28.

32 Grech J, Norman IJ, Sammut R. Exploring the smoking cessation needs of individuals with diabetes using the Information-Motivation-Behavior skills model. *Tob Prev Cessat*. 2024;10:10.18332/tpc/181366.

33 Chan AW, Tetzlaff JM, Gøtzsche PC, *et al.* SPIRIT 2013 explanation and elaboration: guidance for protocols of clinical trials. *BMJ*. 2013;346:1–42.

34 Gianregorio LM, Thabane L. Pilot Studies And Feasibility Studies For Complex Interventions. In: Richards DA, Rahm Hallberg I, eds. *Complex Interventions In Health An overview of research methods*. London: Routledge 2015:127–35. https://doi.org/10.4324/9780203794982

35 Kahan BC, Cro S, Doré CJ, *et al.* Reducing bias in open-label trials where blinded outcome assessment is not feasible: Strategies from two randomised trials. *Trials*. 2014;15:456.

36 American Diabetes Association Professional Practice Committee. 2. Diagnosis and Classification of Diabetes: Standards of Care in Diabetes—2024. *Diabetes Care*. 2024;47:S20–42.

37 Treweek S. Addressing Issues In Recruitment And Retention Using Feasibility And Pilot Trials. In: Richards DA, Rahm Hallberg I, eds. *Complex Interventions In Health An overivew of research methods*. New York: Routledge 2015:155–65. https://doi.org/10.4324/9780203794982

38 Hertzog MA. Considerations in Determining Sample Size for Pilot Studies. *Res Nurs*

Health. 2008;31:180–91.

39 Teare MD, Dimairo M, Shephard N, *et al.* Sample size requirements to estimate key design parameters from external pilot randomised controlled trials: a simulation study. *Trials*. 2014;15:264.

40 Briel M, Olu KK, von Elm E, *et al.* A systematic review of discontinued trials suggested that most reasons for recruitment failure were preventable. *J Clin Epidemiol*. 2016;80:8–15.

41 Clinical Performance Unit. Hospital Activity Report: Annual Report 2022. 2023.

42 Field A. *Discovering Statistics Using IBM SPSS Statistics*. 5th ed. London: Sage 2017.

43 Bricca A, Swithenbank Z, Scott N, *et al.* Predictors of recruitment and retention in randomized controlled trials of behavioural smoking cessation interventions: a systematic review and meta-regression analysis. *Addiction*. 2022;117:299–311.

44 Saghaei M. Random allocation software for parallel group randomized trials. *BMC Med Res Methodol*. 2004;4:1–6.

45 Etter JF, Houezec J Le, Perneger T V. A self-administered questionnaire to measure dependence on cigarettes: The cigarette dependence scale. *Neuropsychopharmacology*. 2003;28:359–70.

46 Kotz D, Brown J, West R. Predictive validity of the Motivation To Stop Scale (MTSS): A single-item measure of motivation to stop smoking. *Drug Alcohol Depend*. 2013;128:15–9.

47 Hummel K, Brown J, Willemsen MC, *et al.* External validation of the motivation to stop scale (MTSS): Findings from the international tobacco control (ITC) Netherlands survey. *Eur J Public Health*. 2016;27:129–34.

48 Zigmond AS, Snalth RP. The Hospital Anxiety and Depression Scale. *Acta Psychiatr Scand*. 1983;67:361–70.

49 Benowitz NL, Bernert JT, Foulds J, *et al.* Biochemical Verification of Tobacco Use and Abstinence: 2019 Update. *Nicotine Tob Res*. 2020;22:1086–97.

50 Baldacchino DR, Bowman GS, Buhagiar A. Reliability testing of the hospital anxiety and depression (HAD) scale in the English, Maltese and back-translation versions. *Int J Nurs Stud*. 2002;39:207–14.

51 Tang ST, Dixon J. Instrument Translation and Evaluation of Equivalence and Psychometric Properties: The Chinese Sense of Coherence Scale. *J Nurs Meas*. 2002;10:59–76.

52 Bujang MA, Omar ED, Baharum NA. A review on sample size determination for Cronbach's alpha test: A simple guide for researchers. *Malaysian J Med Sci*. 2018;25:85–99.

53 Fisher WA, Fisher JD, Harman JJ. The Information-Motivation-Behavioral Skills Model: A General Social Psychological Approach to Understanding and Promoting Health Behavior. In: Suls J, ed. *Social Psychological Foundations of Health and Illness*. Malden, MA: Blackwell Publishing 2009:82–106. https://doi.org/10.1002/9780470753552.ch4

54 World Health Organization. *Toolkit for delivering the 5A's and 5R's brief tobacco interventions in primary care*. Geneva: World Health Organization 2014.

55 Centers for Disease Control and Prevention (CDC). Bill B.'s story. 2022. https://www.cdc.gov/tobacco/campaign/tips/stories/bill.html#bills-bio (accessed 18 April 2022)

56 Siahpush M, Shaikh RA, McCarthy M, *et al.* Association between duration of use of pharmacotherapy and smoking cessation: Findings from a national survey. *BMJ Open*. 2015;5:14–6.

57 Lindson N, Butler AR, McRobbie H, *et al.* Electronic cigarettes for smoking cessation. *Cochrane Database Syst Rev*. 2024;1:CD010216.

58 Lindson N, Theodoulou A, Ordóñez-mena J, *et al.* Pharmacological and electronic cigarette interventions for smoking cessation in adults: component network meta-analyses. *Cochrane Database Syst Rev*. 2023;9:CD015226.

59 World Health Organisation (WHO). Call to action on electronic cigarettes. 2023. https://www.who.int/publications/m/item/technical-note-on-call-to-action-on-electronic-cigarettes (accessed 8 March 2024)

60 European Network for Smoking and Tobacco Prevention. *Guidelines for treating tobacco dependence*. Brussels: European Netwwork for Smoking and Tobacco Prevention 2020.

61 American Diabetes Association Professional Practice Committee. 5. Facilitating Positive Health Behaviors and Well-being to Improve Health Outcomes: Standards of Care in Diabetes—2024. *Diabetes Care*. 2024;47:S77–110.

62 Hanewinkel R, Niederberger K, Pedersen A, *et al.* E-cigarettes and nicotine abstinence: a meta-analysis of randomised controlled trials. *Eur Respir Rev*. 2022;31:210215.

63 Butler AR, Lindson N, Fanshawe TR, *et al.* Longer-term use of electronic cigarettes when provided as a stop smoking aid: Systematic review with meta-analyses. *Prev Med (Baltim)*. 2022;165:107182.

64 Papadakis S. Combination nicotine replacement therapy (NRT). 2021. https://www.ncsct.co.uk/library/view/pdf/Combination NRT 2021.pdf (accessed 8 March 2024)

65 Theodoulou A, Chepkin S, Ye W, *et al.* Different doses, durations and modes of delivery of nicotine replacement therapy for smoking cessation. *Cochrane Database Syst Rev*. 2023;CD013308.

66 McRobbie H, Thornley S, Bullen C, *et al.* A randomized trial of the effects of two novel nicotine replacement therapies on tobacco withdrawal symptoms and user satisfaction. *Addiction*. 2010;105:1290–8.

67 Hansson A, Hajek P, Perfekt R, *et al.* Effects of nicotine mouth spray on urges to smoke, a randomised clinical trial. *BMJ Open*. 2012;2:1–6.

68 Bolliger CT, Van Biljon X, Axelsson A. A nicotine mouth spray for smoking cessation: A pilot study of preference, safety and efficacy. *Respiration*. 2007;74:196–201.

69 Tønnesen P, Lauri H, Perfekt R, *et al.* Efficacy of a nicotine mouth spray in smoking cessation: A randomised, double-blind trial. *Eur Respir J*. 2012;40:548–54.

70 Snaith RP. The hospital anxiety and depression scale. *Health Qual Life Outcomes*. 2003;1:6–9.

71 Bjelland I, Dahl AA, Haug TT, *et al.* The validity of the Hospital Anxiety and Depression Scale. *J Psychosom Res*. 2002;52:69–77.

72 Grech J. Impact of a nurse-led brief tobacco cessation training program for healthcare professionals. *Public Health Nurs*. 2021;38:869–78.

73 Moore GF, Audrey S, Barker M, *et al.* Process evaluation of complex interventions:

Medical Research Council guidance. *BMJ*. 2015;350:1–7.

74 Borrelli B. The assessment, monitoring, and enhancement of treatment fidelity in public health clinical trials. *J Public Health Dent*. 2011;71:1–21.

75 Feeley N, Cossette S. Testing The Waters Piloting a complex intervention. In: Richards DA, Rahm Hallberg I, eds. *Complex Interventions In Health An overivew of research methods*. London: Routledge 2015:166–74. https://doi.org/10.4324/9780203794982

76 Hollands GJ, Naughton F, Farley A, *et al.* Interventions to increase adherence to medications for tobacco dependence. *Cochrane Database Syst Rev*. 2019;2019:CD009164.

77 Piper ME, Bullen C, Krishnan-Sarin S, *et al.* Defining and Measuring Abstinence in Clinical Trials of Smoking Cessation Interventions: An Updated Review. *Nicotine Tob Res*. 2020;22:1098–106.

78 Grech J, Norman IJ, Sammut R. Initial validation of measures assessing satisfaction and perceived usefulness of smoking cessation interventions among individuals with diabetes. *Public Heal Pract*. 2024;7:100487.

79 Bradshaw C, Atkinson S, Doody O. Employing a Qualitative Description Approach in Health Care Research. *Glob Qual Nurs Res*. 2017;4:1–8.

80 Saunders B, Sim J, Kingstone T, *et al.* Saturation in qualitative research: exploring its conceptualization and operationalization. *Qual Quant*. 2018;52:1893–907.

81 Guest G, Bunce A, Johnson L. How Many Interviews Are Enough? An Experiment with Data Saturation and Variability. *Field methods*. 2006;18:59–82.

82 Thabane L, Ma J, Chu R, *et al.* A tutorial on pilot studies: the what, why and how.

BMC Med Res Methodol. 2010;10:1–10.

83 Teresi JA, Yu X, Stewart AL, *et al.* Guidelines for Designing and Evaluating Feasibility Pilot Studies. *Med Care*. 2022;60:95–103.

84 Lee EC, Whitehead AL, Jacques RM, *et al.* The statistical interpretation of pilot trials: should significance thresholds be reconsidered? *BMC Res Methodol*. 2014;14:1–8.

85 Wallis S. Binomial confidence intervals and contingency tests: Mathematical fundamentals and the evaluation of alternative methods. *J Quant Linguist*. 2013;20:178–208.

86 Russo C, Walicka M, Caponnetto P, *et al.* Efficacy and Safety of Varenicline for Smoking Cessation in Patients with Type 2 Diabetes: A Randomized Clinical Trial. *JAMA Netw Open*. 2022;5:E2217709.

87 Li WHC, Wang MP, Lam TH, *et al.* Brief intervention to promote smoking cessation and improve glycemic control in smokers with type 2 diabetes: a randomized controlled trial. *Sci Rep*. 2017;7:45902.

88 Mirzaei A, Carter SR, Patanwala AE, *et al.* Missing data in surveys: Key concepts, approaches, and applications. *Res Soc Adm Pharm*. 2022;18:2308–16.

89 Heymans MW, Twisk JWR. Handling missing data in clinical research. *J Clin Epidemiol*. 2022;151:185–8.

90 Guest G, MacQueen K, Namey E. *Applied Thematic Analysis*. Thousand Oaks: Sage Publications Inc. 2014. https://doi.org/10.4135/9781483384436

91 Hartmann-Boyce J, Chepkin SC, Ye W, *et al.* Nicotine replacement therapy versus control for smoking cessation (Review). *Cochrane Database Syst Rev*. 2018;CD000146.

92 Eldridge SM, Chan CL, Campbell MJ, *et al.* CONSORT 2010 statement: extension to randomised pilot and feasibility trials. *BMJ*. 2016;355:i5239.

Figure legend

Figure 1 – Participant timeline for this feasibility study

Figure 2 – The theoretical model of the study's intervention

Figure 3 – Study intervention algorithm

Figure 1: Participant timeline for this feasibility trial (based on the SPIRIT figure)

	STUDY PERIOD				
	Enrolment	**Pre-intervention assessment**	**Post-allocation**	**Post-intervention assessment**	**End of study**
TIMEPOINT	**0**	**week$_0$**	***week$_1$ to week$_{12}$***	***week$_{12}$***	
ENROLMENT:					
Eligibility screen	X	X			
Informed consent	X	X			
Random allocation		X			
INTERVENTIONS:					
Experimental: Multi-component smoking cessation intervention			⟷		
Control: Health Promotion and Disease Prevention Directorate's one-to-one smoking cessation service			⟷		
ASSESSMENTS:					
Baseline characteristics		X			
Feasibility outcomes:					
Recruitment parameters	X	X			
Compliance with the protocol, resources utilised and problems identified			X		
Response rate at 12 weeks follow-up				X	
Perceived challenges and facilitators to implementation					X
Acceptability outcomes:					
Participants' satisfaction with and perceived usefulness of the intervention				X	
Nurses' satisfaction with the intervention					X
Treatment fidelity of the experimental intervention					X
Exploration of the experimental intervention's functioning				X	
Preliminary evidence of effectiveness				X	

Figure 2: The theoretical model of this intervention, outlining the strategies for addressing the IMB constructs for achieving and sustaining abstinence among individuals with DM

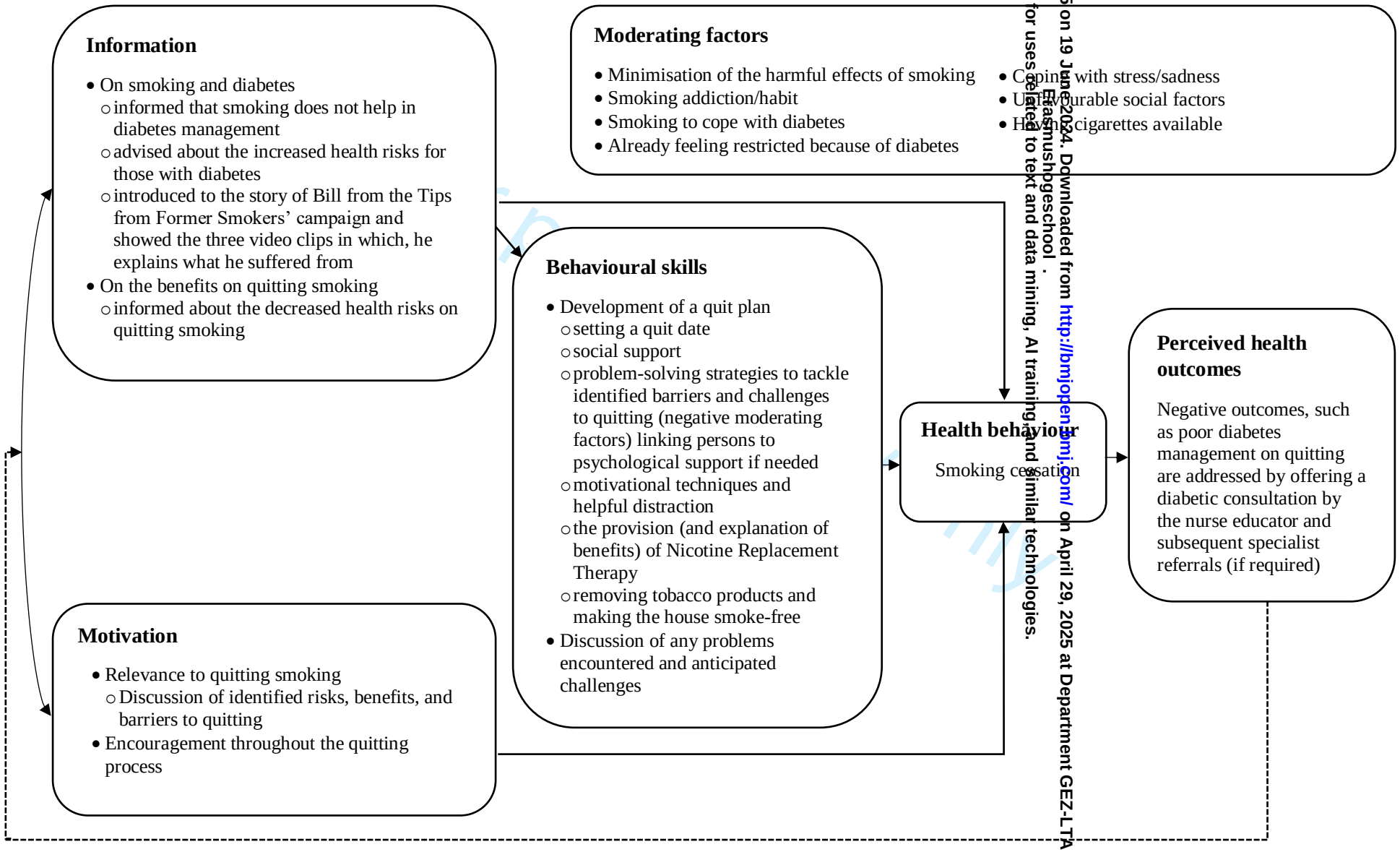
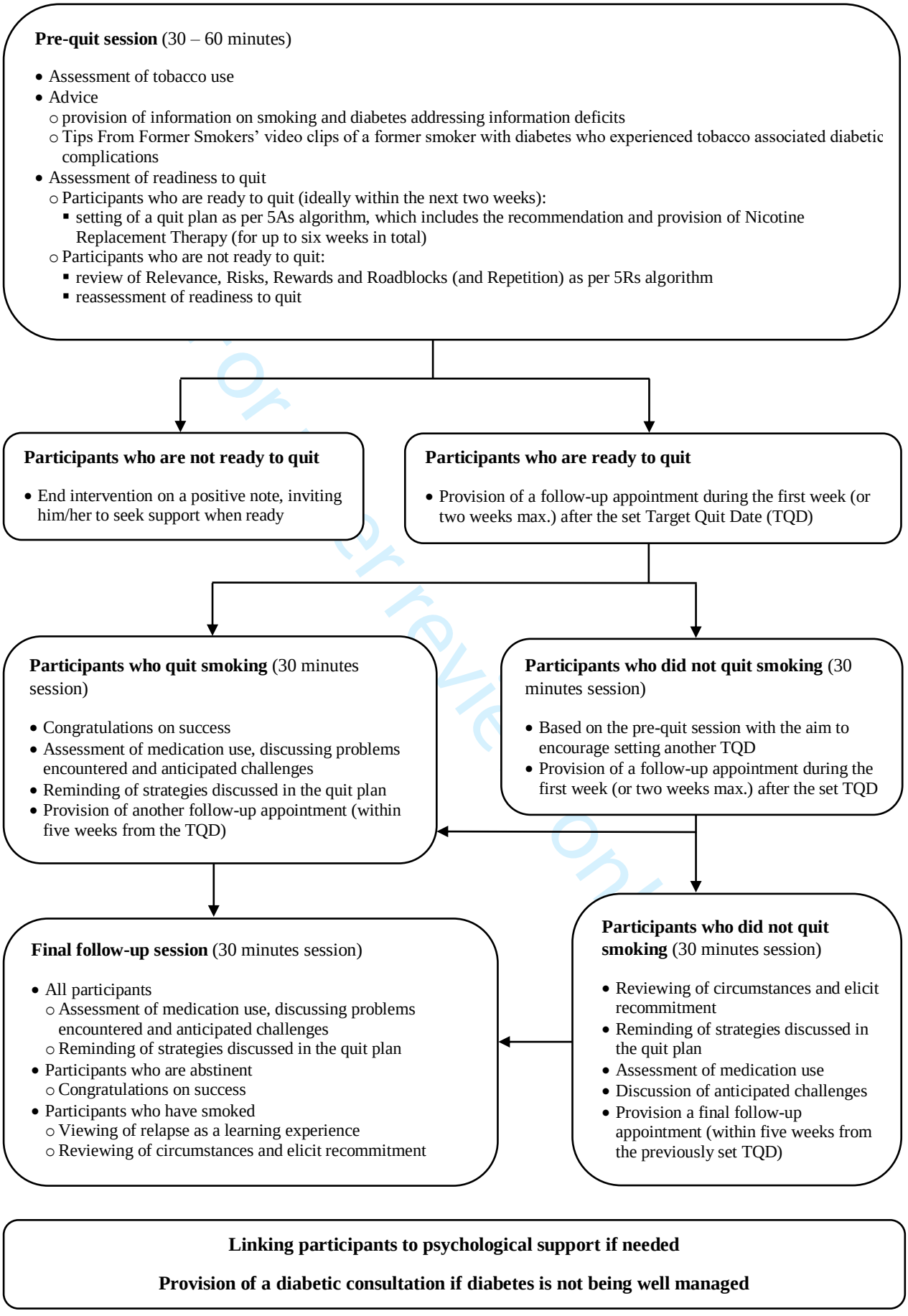


Figure 3: Study intervention algorithm based on the 5A's (and 5R's) framework for smoking cessation



Reporting checklist for protocol of a clinical trial.

Based on the SPIRIT guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the SPIRITreporting guidelines, and cite them as:

Chan A-W, Tetzlaff JM, Gøtzsche PC, Altman DG, Mann H, Berlin J, Dickersin K, Hróbjartsson A, Schulz KF, Parulekar WR, Krleža-Jerić K, Laupacis A, Moher D. SPIRIT 2013 Explanation and Elaboration: Guidance for protocols of clinical trials. BMJ. 2013;346:e7586

		Reporting Item	Page Number
Administrative information			
Title	#1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	#2a	Trial identifier and registry name. If not yet registered, name of intended registry	3, 8
Trial registration: data set	#2b	All items from the World Health Organization Trial Registration Data Set	3, 8
Protocol version	#3	Date and version identifier	NA
Funding	#4	Sources and types of financial, material, and other support	29
Roles and responsibilities: contributorship	#5a	Names, affiliations, and roles of protocol contributors	1, 28-29

Roles and responsibilities: sponsor contact information	#5b	Name and contact information for the trial sponsor	1
Roles and responsibilities: sponsor and funder	#5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	29
Roles and responsibilities: committees	#5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	NA
Introduction			
Background and rationale	#6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4-7
Background and rationale: choice of comparators	#6b	Explanation for choice of comparators	8
Objectives	#7	Specific objectives or hypotheses	7
Trial design	#8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, non-inferiority, exploratory)	8-9, 11
Methods: Participants, interventions, and outcomes			
Study setting	#9	Description of study settings (eg, community clinic,	9

		academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	
Eligibility criteria	#10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	9-10
Interventions: description	#11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	13-18
Interventions: modifications	#11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving / worsening disease)	27-28
Interventions: adherance	#11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return; laboratory tests)	16-18
Interventions: concomitant care	#11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	NA
Outcomes	#12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	20-24
Participant timeline	#13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	12, 18-19
Sample size	#14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	10

Recruitment	#15	Strategies for achieving adequate participant enrolment to reach target sample size	10-11
Methods: Assignment of interventions (for controlled trials)			
Allocation: sequence generation	#16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	11-12
Allocation concealment mechanism	#16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	11-12
Allocation: implementation	#16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	11-12-9
Blinding (masking)	#17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	8
Blinding (masking): emergency unblinding	#17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	NA
Methods: Data collection, management, and analysis			
Data collection plan	#18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a	12-13, 16-20

		description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	
Data collection plan: retention	#18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	NA
Data management	#19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	9, 28
Statistics: outcomes	#20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	24-25
Statistics: additional analyses	#20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	NA
Statistics: analysis population and missing data	#20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	25
Methods: Monitoring			
Data monitoring: formal committee	#21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	NA
Data monitoring: interim analysis	#21b	Description of any interim analyses and stopping guidelines, including who will have access to these	NA

		interim results and make the final decision to terminate the trial	
Harms	#22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	17, 27-28
Auditing	#23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	NA
Ethics and dissemination			
Research ethics approval	#24	Plans for seeking research ethics committee / institutional review board (REC / IRB) approval	27
Protocol amendments	#25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC / IRBs, trial participants, trial registries, journals, regulators)	NA
Consent or assent	#26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	11, 27
Consent or assent: ancillary studies	#26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	NA
Confidentiality	#27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	9, 28
Declaration of interests	#28	Financial and other competing interests for principal investigators for the overall trial and each study site	29
Data access	#29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	28
Ancillary and post	#30	Provisions, if any, for ancillary and post-trial care,	NA

trial care		and for compensation to those who suffer harm from trial participation	
Dissemination policy: trial results	#31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	26-27
Dissemination policy: authorship	#31b	Authorship eligibility guidelines and any intended use of professional writers	NA
Dissemination policy: reproducible research	#31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	28
Appendices			
Informed consent materials	#32	Model consent form and other related documentation given to participants and authorised surrogates	Supplemental files 3 and 4
Biological specimens	#33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	NA

Cigarette Dependence Scale-5 (Maltese version) - Item-to-total statistics (*n*=17)

Cigarette Dependence Scale-5 items[a]	Scale mean if item deleted	Corrected item-total correlation	Cronbach's alpha if item deleted
Self-rated dependence, 0–100 score recoded to five categories	16.2	0.72	0.72
Cigarettes per day, five categories	16.0	0.40	0.85
Minutes to first cigarette, five categories	15.7	0.71	0.75
Quitting for good would be difficult.	15.9	0.65	0.76
An irresistible urge to smoke after a few hours.	15.5	0.63	0.76

a - original items in Maltese

L-Università ta' Malta

Participants` Information Sheet

Dear Participant,

My name is Joseph Grech and I am currently reading for a Doctor of Philosophy (Ph.D.) in Nursing at the University of Malta. As part of my Ph.D. project, I am conducting a research study entitled, **"Development and feasibility testing of a multi-component smoking cessation intervention for smokers living with diabetes mellitus: a randomised feasibility study"**. This study aims to evaluate the feasibility and acceptability of a multi-component smoking cessation intervention among individuals with diabetes. While this study will help you to evaluate your smoking habits and assist you in quitting smoking, your feedback will help me ensure the applicability of this smoking cessation intervention for use amongst individuals with diabetes. You will only be asked to share data that is necessary for this research. All data collected from this research shall be used solely for this study.

You are being invited to participate in a randomized feasibility study lasting twelve weeks, where you will be allocated at random either to the multi-component smoking cessation intervention and the provision of nicotine replacement therapy – the nicotine patch and/or spray for daily use for up to six weeks, or to standard care (referral to the Health Promotion and Disease Prevention Directorate's one to one smoking cessation counselling sessions), both of which will help you to re-consider your smoking habits and support you to quit smoking, free of charge. The multi-component smoking cessation intervention will be provided by the nurses (Ms. Moira Grixti or Ms. Catherine Azzopardi) at the Diabetes Education Unit at Mater Dei Hospital. Each session should not take longer than one hour. The Health Promotion and Disease Prevention Directorate's one to one smoking cessation counselling sessions are usually provided within the Primary Health Care Department's health centres. Each session should not take longer than half an hour. Before being allocated to the smoking cessation interventions or standard care you will be provided with a personal unique code, unknown to the researcher and anyone else. You will have to refer to this code in filling in the study's baseline questionnaire (on your personal characteristics, your health status, your diabetes and smoking profiles, and your feelings in the past week), and the questionnaire at the end of the study period (on your smoking habit, about the support you have received during the study period, and your views and opinions of the provided intervention). Each questionnaire should not take you more than 20 minutes to fill in. You will also be asked to take a simple, easy, and non-invasive exhaled carbon monoxide test, to measure how much carbon monoxide is in your body at baseline. If you quit smoking, you will also be asked to take the carbon monoxide test again and to provide a urine sample which will be assessed for traces of nicotine to confirm smoking abstinence. Unless you have any objections, the provision of the multi-component smoking cessation intervention will be audio recorded. This will help ensure the integrity of the intervention provided. Following this study, you may be invited to participate to a follow-up interview.

Participation in this study does not expose you to any risks. If you fail to quit smoking, the service of a smoking cessation advisor from the Health Promotion and Disease Prevention Directorate is available at no financial cost on your part, by calling the National Quitline 8007 3333. Participation in this study is completely voluntary and you are free to accept or refuse to take part without giving a reason. Refusing to participate will not have any impact or negative consequences on your care. While if assigned to the group where you are provided with nicotine replacement therapy you are encouraged to take this on quitting smoking, you are also free to refuse without giving a reason. In the very unlikely event of an adverse event, you are to inform the researcher who will ensure that you are seen by a doctor of your choice free of charge. You may also withdraw from the study at any time without giving a reason and this will not bear any negative repercussions on you or your care. Any data collected by the researcher from your end, unless this cannot be identified, i.e. anonymized data, will hence be erased. In the case of having been allocated to standard care, you may also want to inform the Health Promotion and Disease Prevention Directorate about your decision so that they can erase any personal data that they may have collected on their behalf. All personal data collected by the researcher will only be accessed by the researcher. The audio-recordings (of the provision of the multi-component smoking cessation intervention) will be provided to the researcher on a password protected encrypted USB and stored on the researcher`s personal computer that is also password protected and in an encrypted format. A random selection of these audio-recordings will be listened to and assessed for treatment integrity by the researcher. I can assure you that confidentiality will be maintained throughout the study and that your identity and personal information will not be revealed in the thesis and any publications, reports, and presentations arising from this research. Any personal data in hard-copy form, such as the consent forms will be placed in a locked cupboard.

A copy of the information sheet and consent form will be provided for future reference. As a participant, you have the right, under the General Data Protection Regulation (GDPR) and national legislation that implements and further specifies the relevant provisions of said regulation, to access, rectify, and where applicable ask for the data concerning you to be erased. Anonymous results from this research study will be published in my Ph.D. thesis and may be published in academic journals or reported at conferences or to health service organisations. Some of the things you may write in the questionnaire may be used as direct quotes in publications or conferences, but your confidentiality and anonymity will be maintained, and it will not be possible to identify you. A summary of the results of this research study will be offered to all participants who show interest. Once this research study is completed, the audio-recordings will be erased. The consent forms will be destroyed within two years from the completion of my Ph.D. project.

This study has been approved by the Research Ethics Committee of the Faculty of Health Sciences at the University of Malta.

Thank you for your time and consideration. Should you have any questions or concerns do not hesitate to contact me on **9980 2504** or by e-mail joseph.grech.02@um.edu.mt or my supervisor **Prof. Roberta Sammut** on **2340 1831** or roberta.sammut@um.edu.mt or my co-supervisor **Prof. Ian James Norman** on **+44 (0)207 848 3020** or ian.j.norman@kcl.ac.uk.

Yours Sincerely,

Mr. Joseph Grech
Researcher
Tel: 9980 2504
joseph.grech.02@um.edu.mt

Prof. Roberta Sammut
Research Supervisor
Tel. 2340 1831
roberta.sammut@um.edu.mt

Prof. Ian James Norman
Research Co-supervisor
Tel. +44 (0)207 848 3020
ian.j.norman@kcl.ac.uk

Participants` Consent Form

Development and feasibility testing of a multi-component smoking cessation intervention for smokers living with diabetes mellitus: a randomised feasibility study

I, the undersigned, give my consent to take part in the study conducted by Mr. Joseph Grech. The purpose of this document is to specify the terms of my participation in this research study.

1. I have been given written and verbal information about the purpose of the study and all questions have been answered.
2. I understand that I have been invited to participate in a randomized feasibility study lasting twelve weeks, which evaluates the feasibility and acceptability of a multi-component smoking cessation intervention among individuals with diabetes. I am aware that I will be allocated at random either to the multi-component smoking cessation intervention and the provision of nicotine replacement therapy – the nicotine patch and/or spray for daily use for up to six weeks, or to standard care (referral to the Health Promotion and Disease Prevention Directorate's one to one smoking cessation counselling sessions), all of which will help me to re-consider my smoking habits and support me to quit smoking, free of charge.
3. I understand that the multi-component smoking cessation intervention will be provided by the nurses (Ms. Moira Grixti or Ms. Catherine Azzopardi) at the Diabetes Education Unit at Mater Dei Hospital. I also understand that each session should not take longer than one hour. I am aware that the Health Promotion and Disease Prevention Directorate's one to one smoking cessation counselling sessions are usually provided every fortnight within the Primary Health Care Department's health centres. I am also aware that each session should not take longer than half an hour.
4. I am also aware that I will be invited to fill in a questionnaire on my personal characteristics, my health status, my diabetes and smoking profiles, and my feelings in the past week on enrollment to the study, and another questionnaire on my smoking habit, about the support I have received during the study period, and my views and opinions of the provided intervention at the end of the study, as part of this research study. I understand that the questionnaires are anonymous and only I will be aware of my personal identifier through the participant's code, which I will refer to in filling in the questionnaires. I also understand that I should not take more than 20 minutes to fill in each questionnaire. I am aware that I will be invited to take a simple, easy, non-invasive exhaled carbon monoxide test at baseline. I am also aware that if I quit smoking, I will

also be asked to take the carbon monoxide test and provide a urine sample which will be assessed for traces of nicotine to confirm smoking abstinence. I am also aware that the provision of the multi-component smoking cessation intervention will be audio recorded. I understand that following this study I may be invited to participate to a follow-up interview.

5. I also understand that the researcher is the only person who has access to any personal data collected from his end. I also understand that the audio-recordings (of the provision of the multi-component smoking cessation intervention) will be provided to the researcher on a password protected encrypted USB and will be stored on the researcher`s personal computer that is also password protected and in an encrypted format. I am aware that a random selection of these audio-recordings will be listened to and assessed for treatment integrity by the researcher. I understand that any personal data in hard-copy form, such as the consent forms will be placed in a locked cupboard.
6. I am aware that my identity and personal information will not be revealed in the researcher's Ph.D. thesis and any publications, reports, and presentations arising from this research.
7. I understand that participation in this study does not expose me to any risks. I am aware that if I fail to quit smoking, the service of a smoking cessation advisor from the Health Promotion and Disease Prevention Directorate is available at no financial cost on my part, by calling the National Quitline 8007 3333. I am also aware that if I am assigned to the group where I am provided with nicotine replacement therapy, I will be encouraged to take this on quitting smoking, however I am also free to refuse without giving a reason. I am also aware that in the very unlikely event of an adverse event, I am to inform the researcher who will ensure that I am seen by a doctor of my choice free of charge.
8. I understand that I am free to accept, refuse, or stop participation at any time without giving any reason. This will have no negative repercussions on myself or my care. Furthermore, I also understand that any data collected from my end, unless this cannot be identified, e.g. is anonymised, will be erased.
9. I am aware that in the case of having been allocated to standard care, I will have to inform the Health Promotion and Disease Prevention Directorate about my decision so that they can erase any personal data that they may have collected on their behalf.
10. I also understand that my contribution will serve Mr. Joseph Grech to ensure the applicability of this smoking cessation intervention for use amongst individuals with diabetes.
11. I am aware that under the General Data Protection Regulation (GDPR) and national legislation that implements and further specifies the relevant provisions of said regulation, I have the right to access, rectify, and where applicable ask for the data concerning me to be erased.

12. I am also aware that anonymous results from this research study will be published in the researcher's Ph.D. thesis and may be published in academic journals or reported at conferences or to health service organisations.
13. I understand that some of the things I may write in the questionnaires may be used as direct quotes in publications or conferences, but my confidentiality and anonymity will be maintained, and it will not be possible to identify me.
14. I am aware that a summary of the results of this research study will be offered if I show interest (see below).
15. I understand that once the study is completed, the audio-recordings will be erased. I am aware that any personal details, i.e. the consent forms, will be destroyed within two years from completion of the Ph.D. project.
16. I am also aware that I will be provided with a copy of the information letter and consent form for future reference.
17. I have read and understood the points and statements of this form. I have had all the questions answered to my satisfaction, and I agree to participate in this study.

Participant: _____

Signature: _____

Date: _____

Mr. Joseph Grech	Prof. Roberta Sammut	Prof. Ian James Norman
Researcher	Research Supervisor	Research Co-supervisor
Tel: 9980 2504	**Tel. 2340 1831**	**Tel. +44 (0)207 848 3020**
joseph.grech.02@um.edu.mt	**roberta.sammut@um.edu.mt**	**ian.j.norman@kcl.ac.uk**

Please note:

Please leave your mobile phone number so that we can contact you with the date, time, and place of your first smoking cessation session. At the end of the intervention, you may also be invited to participate in a follow-up interview:

_____

If you agree to be contacted to be provided with a summary of the results of this research study, please tick this box ☐

Treatment allocation (for office use only) ☐

L-Università ta' Malta

Participants` Information Sheet

Dear Participant,

My name is Joseph Grech and I am currently reading for a Doctor of Philosophy (Ph.D.) in Nursing at the University of Malta. As part of my Ph.D. project, I am conducting a follow-up interview on the research study entitled, **"Development and feasibility testing of a multi-component smoking cessation intervention for smokers living with diabetes mellitus: a randomised feasibility study"**, to which you participated. This study aims to explore the feasibility and acceptability of this smoking cessation intervention amongst individuals with diabetes. Your insight will help us ensure the applicability of the multi-component smoking cessation intervention for use amongst individuals with diabetes. You will only be asked to share data that is necessary for this research. All data collected from this research shall be used solely for this study.

You are being invited to participate in an interview exploring your views, preferences, barriers and suggestions on the smoking cessation intervention and on your quitting attempt experience. The interview should not take more than 40 minutes and will be held at one of the Faculty of Health Science's approved and identified training sites at a time and date most suitable for you. Unless you have any objections, the interview will be audio-recorded. You are not obliged to answer all the questions and may withdraw from the study at any time without giving a reason. Withdrawal from the study will not have any negative repercussions on you or your care. Furthermore, any data collected from your end, unless this cannot be identified, e.g. has been already anonymised, will be erased. I can assure you that confidentiality will be maintained throughout the study and that your identity and personal information will not be revealed in the thesis and any publications, reports, and presentations arising from this research. All data collected will be pseudonymised meaning that the transcript of the audio recording will be protected by a code system and that this data will be stored securely and separately from any personal data (audio-recording and consent forms). This data may only be accessed by the researcher. The academic supervisors and the examiners will typically have access to coded data only. There may be exceptional circumstances which allow the supervisors to have access to the audio-recording too, for verification purposes (if you would like to know who accessed your data, please contact me as per the details below). The audio-recording and transcript will be stored on the researcher`s personal computer that is password protected and in an encrypted format. The consent forms, will be placed in a locked cupboard.

Participation in this study does not expose you to any risks. If you are still interested in quitting smoking, the service of a smoking cessation advisor from the Health Promotion and Disease Prevention Directorate, is available at no financial cost on your part, by calling the National Quitline 8007 3333.

Participation in this study is completely voluntary and you are free to accept or refuse to take part without giving a reason. A copy of the information sheet and consent form will be provided for future reference. As a participant, you have the right, under the General Data Protection Regulation (GDPR) and national legislation that implements and further specifies the relevant provisions of said regulation, to access, rectify, and where applicable ask for the data concerning you to be erased. Once this research study is completed, the audio-recording will be erased and data will be retained only in anonymous form. Anonymous results from this research study will be published in my Ph.D. thesis and may be published in academic journals or reported at conferences or to health service organisations. Some of the things you say may be used as direct quotes in publications or conferences, but your confidentiality and anonymity will be maintained, and it will not be possible to identify you. A summary of the results of this research study will be offered to all participants who show interest. The consent forms will be destroyed within two years from the completion of my Ph.D. project.

This study has been approved by the Research Ethics Committee of the Faculty of Health Sciences at the University of Malta.

Thank you for your time and consideration. Should you have any questions or concerns do not hesitate to contact me on **9980 2504** or by e-mail joseph.grech.02@um.edu.mt or my supervisor **Dr. Roberta Sammut** on **2340 1831** or roberta.sammut@um.edu.mt or my co-supervisor **Prof. Ian James Norman** on **+44 (0)207 848 3020** or ian.j.norman@kcl.ac.uk.

Yours Sincerely,

Mr. Joseph Grech	**Prof. Roberta Sammut**	**Prof. Ian James Norman**
Researcher	Research Supervisor	Research Co-supervisor
Tel: 9980 2504	**Tel. 2340 1831**	**Tel. +44 (0)207 848 3020**
joseph.grech.02@um.edu.mt	**roberta.sammut@um.edu.mt**	**ian.j.norman@kcl.ac.uk**

L-Università ta' Malta

Participants` Consent Form

Development and feasibility testing of a multi-component smoking cessation intervention for smokers living with diabetes mellitus: a randomised feasibility study (a follow-up interview)

I, the undersigned, give my consent to take part in the study conducted by Mr. Joseph Grech. The purpose of this document is to specify the terms of my participation in this research study.

1. I have been given written and verbal information about the purpose of the study and all questions have been answered.
2. I understand that I have been invited to participate in an interview, in which the researcher will ask questions to explore the feasibility and acceptability of this smoking cessation intervention amongst individuals with diabetes.
3. I am aware that the interview will not take longer than 40 minutes. I understand that the interview is to be conducted at one of the Faculty of Health Science's approved and identified training sites in a place and at a time that is convenient for me.
4. I am aware that the interview will be audio-recorded and transcribed (written down as it has been spoken).
5. I am also aware that the transcript will be coded, and that this data will be stored securely and separately from any personal data (audio-recording and consent forms).
6. I understand that the researcher is the only person who has access to this data. The academic supervisors and examiners will typically have access to coded data only. I am aware that there may be exceptional circumstances which allow the supervisors to have access to the audio-recording too, for verification purposes. I understand that if I would like to know who accessed my data, I can contact the researcher as per the details below.
7. I am also aware that the audio-recording and the transcript will be stored on the researcher`s personal computer that is password protected and in an encrypted format. The consent forms will be placed in a locked cupboard.
8. I am also aware that my identity and personal information will not be revealed in the researcher's Ph.D. thesis and any publications, reports, and presentations arising from this research.
9. I understand that I am free to accept, refuse, or stop participation at any time without giving any reason. This will have no negative repercussions on myself or my care.

Furthermore, I also understand that any data collected from my end, unless this cannot be identified, e.g. is anonymised, will be erased.

10. I also understand that my contribution will serve Mr. Joseph Grech ensure the applicability of this smoking cessation intervention for use amongst individuals with diabetes.
11. I also understand that participating in this study does not expose me to any risks. I am aware that if I am still interested in quitting smoking, the service of a smoking cessation advisor from the Health Promotion and Disease Prevention Directorate is available at no financial cost on my part, by calling the National Quitline 8007 3333.
12. I am aware that under the General Data Protection Regulation (GDPR) and national legislation that implements and further specifies the relevant provisions of said regulation, I have the right to access, rectify, and where applicable ask for the data concerning me to be erased.
13. I understand that once the study is completed, the audio-recording will be erased, and data will only be retained in anonymous form. I am aware that anonymous results from this research study will be published in the researcher's Ph.D. thesis and may be published in academic journals or reported at conferences or to health service organisations.
14. I understand that some of the things I say may be used as direct quotes in publications or conferences, but my confidentiality and anonymity will be maintained, and it will not be possible to identify me.
15. I am aware that a summary of the results of this research study will be offered if I show interest (see below).
16. I am also aware that any personal details, i.e. the consent forms, will be destroyed within two years from completion of the Ph.D. project.
17. I am also aware that I will be provided with a copy of the information letter and consent form for future reference.
18. I have read and understood the points and statements of this form. I have had all the questions answered to my satisfaction, and I agree to participate in this study.

Participant: _____

Signature: _____

Date: _____



Mr. Joseph Grech	**Prof. Roberta Sammut**	**Prof. Ian James Norman**
Researcher	Research Supervisor	Research Co-supervisor
Tel: 9980 2504	**Tel. 2340 1831**	**Tel. +44 (0)207 848 3020**
joseph.grech.02@um.edu.mt	**roberta.sammut@um.edu.mt**	**ian.j.norman@kcl.ac.uk**

Please note:
If you agree to be contacted to be provided with a summary of the results of this research study please provide your telephone/mobile number here:

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L-Università ta' Malta

Intervention Providers` Information Sheet

Dear Nurse,

My name is Joseph Grech and I am currently reading for a Doctor of Philosophy (Ph.D.) in Nursing at the University of Malta. As part of my Ph.D. project, I am conducting a follow-up interview on the research study entitled, **"Development and feasibility testing of a multi-component smoking cessation intervention for smokers living with diabetes mellitus: a randomised feasibility study"**, to which you participated. This study aims to explore the feasibility and acceptability of delivering this smoking cessation intervention amongst individuals with diabetes. Your insight will help us ensure the applicability of this diabetes practice nurse-led cessation intervention for use amongst individuals with diabetes in practice. You will only be asked to share data that is necessary for this research. All data collected from this research shall be used solely for this study.

You are being invited to participate in an interview exploring your views, and suggestions on the smoking cessation intervention and your perceived challenges and facilitators to implementing this smoking cessation intervention in practice. The interview should not take more than 40 minutes and will be held at one of the Faculty of Health Science's approved and identified training sites at a time and date most suitable for you. Unless you have any objections, the interview will be audio-recorded. You are not obliged to answer all the questions and may withdraw from the study at any time without giving a reason. Withdrawal from the study will not have any negative repercussions whatsoever. Furthermore, any data collected from your end, unless this cannot be identified, e.g. has been already anonymised, will be erased. I can assure you that confidentiality will be maintained throughout the study and that your identity and personal information will not be linked to your responses and revealed in the thesis and any publications, reports, and presentations arising from this research. All data collected will be pseudonymised meaning that the transcript of the audio recording will be protected by a code system and that this data will be stored securely and separately from any personal data (audio-recording and consent forms). This data may only be accessed by the researcher. The academic supervisors and the examiners will typically have access to coded data only. There may be exceptional circumstances which allow the supervisors to have access to the audio-recording too, for verification purposes (if you would like to know who accessed your data, please contact me as per the details below). The audio-recording and transcript will be stored on the researcher`s personal computer that is password protected and in an encrypted format. The consent forms, will be placed in a locked cupboard.

Participation in this study does not expose you to any risks. Participation is completely voluntary and you are free to accept or refuse to take part without giving a reason. A copy of the information sheet and consent form will be provided for future reference. As a participant, you

have the right, under the General Data Protection Regulation (GDPR) and national legislation that implements and further specifies the relevant provisions of said regulation, to access, rectify, and where applicable ask for the data concerning you to be erased. Once this research study is completed, the audio-recording will be erased and data will be retained only in anonymous form. Anonymous results from this research study will be published in my Ph.D. thesis and may be published in academic journals or reported at conferences or to health service organisations. Some of the things you say may be used as direct quotes in publications or conferences, but your confidentiality and anonymity will be maintained, and it will not be possible to identify you. A summary of the results of this research study will be offered to all participants who show interest. The consent forms will be destroyed within two years from the completion of my Ph.D. project.

This study has been approved by the Research Ethics Committee of the Faculty of Health Sciences at the University of Malta.

Thank you for your time and consideration. Should you have any questions or concerns do not hesitate to contact me on **9980 2504** or by e-mail joseph.grech.02@um.edu.mt or my supervisor **Dr. Roberta Sammut** on **2340 1831** or roberta.sammut@um.edu.mt or my co-supervisor **Prof. Ian James Norman** on **+44 (0)207 848 3020** or ian.j.norman@kcl.ac.uk.

Yours Sincerely,

Mr. Joseph Grech	Prof. Roberta Sammut	Prof. Ian James Norman
Researcher	Research Supervisor	Research Co-supervisor
Tel: 9980 2504	**Tel. 2340 1831**	**Tel. +44 (0)207 848 3020**
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Intervention Providers` Consent Form

Development and feasibility testing of a multi-component smoking cessation intervention for smokers living with diabetes mellitus: a randomised feasibility study (a follow-up interview)

I, the undersigned, give my consent to take part in the study conducted by Mr. Joseph Grech. The purpose of this document is to specify the terms of my participation in this research study.

1. I have been given written and verbal information about the purpose of the study and all questions have been answered.
2. I understand that I have been invited to participate in an interview, in which the researcher will ask questions to explore the feasibility and acceptability of delivering this smoking cessation intervention amongst individuals with diabetes.
3. I am aware that the interview will not take longer than 40 minutes. I understand that the interview is to be conducted at one of the Faculty of Health Science's approved and identified training sites in a place and at a time that is convenient for me.
4. I am aware that the interview will be audio-recorded and transcribed (written down as it has been spoken).
5. I am also aware that the transcript will be coded, and that this data will be stored securely and separately from any personal data (audio-recording and consent forms).
6. I understand that the researcher is the only person who has access to this data. The academic supervisors and examiners will typically have access to coded data only. I am aware that there may be exceptional circumstances which allow the supervisors to have access to the audio-recording too, for verification purposes. I understand that if I would like to know who accessed my data, I can contact the researcher as per the details below.
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9. I understand that I am free to accept, refuse, or stop participation at any time without giving any reason. This will have no negative repercussions on myself. Furthermore, I also

understand that any data collected from my end, unless this cannot be identified, e.g. is anonymised, will be erased.

10. I also understand that my contribution will help Mr. Joseph Grech ensure the applicability of this diabetes practice nurse-led smoking cessation intervention for use amongst individuals with diabetes in practice.
11. I also understand that participating in this study does not expose me to any risks.
12. I am aware that under the General Data Protection Regulation (GDPR) and national legislation that implements and further specifies the relevant provisions of said regulation, I have the right to access, rectify, and where applicable ask for the data concerning me to be erased.
13. I understand that once the study is completed, the audio-recording will be erased, and data will only be retained in anonymous form. I am aware that anonymous results from this research study will be published in the researcher's Ph.D. thesis and may be published in academic journals or reported at conferences or to health service organisations.
14. I understand that some of the things I say may be used as direct quotes in publications or conferences, but my confidentiality and anonymity will be maintained, and it will not be possible to identify me.
15. I am aware that a summary of the results of this research study will be offered if I show interest (see below).
16. I am also aware that any personal details, i.e. the consent forms, will be destroyed within two years from completion of the Ph.D. project.
17. I am also aware that I will be provided with a copy of the information letter and consent form for future reference.
18. I have read and understood the points and statements of this form. I have had all the questions answered to my satisfaction, and I agree to participate in this study.

Participant: _____

Signature: _____

Date: _____

Mr. Joseph Grech
Researcher
Tel: 9980 2504
joseph.grech.02@um.edu.mt

Prof. Roberta Sammut
Research Supervisor
Tel. 2340 1831
roberta.sammut@um.edu.mt

Prof. Ian James Norman
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Please note:
If you agree to be contacted to be provided with a summary of the results of this research study please provide your telephone/mobile number here:

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