QuLIT – The Quit smoking Lung health Intervention Trial.

Study Protocol

V2 11-12-20

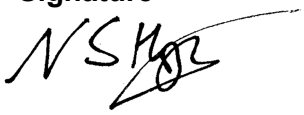
MAIN SPONSOR: Imperial College London
FUNDERS: Royal Marsden Partners
STUDY COORDINATION CENTRE: Royal Brompton Hospital

IRAS Project ID: 236191

REC reference:18/SC/0236:

ISRCTN: ISRCTN12455871

Protocol authorised by:

Name & Role	Date	Signature
Dr NS Hopkinson	11-12-20	

Study Management Group

Chief Investigator: Dr Nicholas Hopkinson n.hopkinson@ic.ac.uk
Reader in Respiratory Medicine, Imperial College London
Royal Brompton Campus
Fulham Rd, London SW3 6NP

Sponsor

Imperial College London is the main research Sponsor for this study. For further information regarding the sponsorship conditions, please contact the Head of Regulatory Compliance at:

Joint Research Compliance Office
Imperial College London & Imperial College Healthcare NHS Trust
2nd Floor Medical School Building
St Mary's Hospital
Praed Street
London
W2 1NY
Tel: 020759 41862

Funder

Royal Marsden Partners

This protocol describes the QuLIT study and provides information about procedures for entering participants. Every care was taken in its drafting, but corrections or amendments may be necessary. These will be circulated to investigators in the study. Problems relating to this study should be referred, in the first instance, to the Chief Investigator.

This study will adhere to the principles outlined in the NHS Research Governance Framework for Health and Social Care (2nd edition). It will be conducted in compliance with the protocol, the Data Protection Act and other regulatory requirements as appropriate.

Table of Contents

GLOSSARY OF ABBREVIATIONS

CO	Carbon monoxide
COPD	Chronic obstructive pulmonary disease
CAT	COPD assessment test
CT	Computerised tomography
PICOT	Patient group, intervention, comparator, outcome, time course
VBA	Very brief advice (about smoking cessation)

KEYWORDS

Smoking cessation, CT screening, lung cancer

STUDY SUMMARY

TITLE	The QuLIT study. Quit smoking Lung health Intervention Trial
DESIGN	An observational study comparing the effectiveness of two different smoking cessation strategies applied in a pseudo-randomised fashion. Smokers attending a lung health screening service, focussed on CT screening to detect early lung cancer will receive either (i) immediate smoking cessation input including pharmacotherapy or (ii) usual care, which will be advice and signposting to local services. Limited resources mean that a specialist smoking cessation practitioner will only be available on 5 days every fortnight so treatment allocation will depend on this (ie which day patients attend on).
AIMS	To evaluate the impact of additional smoking cessation support in the context of a lung cancer screening service.
Research question and outcome measures	Does the provision of additional immediate smoking cessation support translate into higher quit rates at 3 months, compared to signposting to smoking cessation services. Longer term outcomes (survival) will also be tracked in the context of the broader evaluation of the CT screening service. Impact of baseline characteristics and screening findings on quit attempts will also be evaluated.
POPULATION	Patients attending for lung health screening who are smokers and who wish to quit smoking. A minimum of 110 will be recruited but as many participants as possible within the screening programme will be involved to allow for subgroup analysis.
DURATION	3 years

Lay Summary

Smoking is a major cause of ill health including lung disease, health disease and cancer. It is important that the NHS makes use of the best approaches to help people to stop smoking. People with a history of smoking are now being offered screening by CT scan in order to detect early lung cancer so these can be treated and cured.
This screening program is also an opportunity to help people to quit smoking. The usual approach would be to direct individuals to NHS or local authority smoking cessation services. We want to see if a more intense approach, where smokers can see a smoking cessation counsellor immediately is more effective.
The counsellor will be available on half the days that the screening study is running. We will compare the outcomes on the different days by looking at smoking rates three months later. We aim to compare up to 500 smokers going through the screening programme who wish to quit.

1. INTRODUCTION

1.1 BACKGROUND

Smoking is the leading preventable cause of ill health and premature mortality in the UK. Smokers die on average 10 years earlier than non-smokers due to conditions including cardiovascular disease, cancer and COPD. Smoking cessation is therefore a high priority for the treatment and prevention of disease.

There is evidence that participation in a lung cancer screening programme is associated with greater quit rates(1). This suggests that this is an important opportunity for stop smoking interventions, however the best strategy for delivering these is not clear and evidence as to the relative effectiveness and value of interventions is needed to guide commissioners of healthcare. A recent consensus review of research questions around CT screening for lung cancer identified this as an important question(2).

In particular we do not know if the addition of immediate smoking cessation interventions will produce a better outcome than a standard “signposting to service” model.

2. STUDY OBJECTIVES

To answer the following PICOT question: In people who smoke attending a lung cancer CT screening programme, does the provision of immediate smoking cessation support including pharmacotherapy compared to signposting to a smoking cessation service improve quit rates at 3 months.

Primary outcome will be quit rate at three months following the initial screening visit in people who express the wish to quit smoking compared between the two arms

Secondary outcomes:
Quit rate in all participants.
Mortality at one and three years (available as part of the routine evaluation of the screening protocol)

Exploratory outcomes
Does the impact of the smoking cessation interventions differ in different baseline groups including (i) those with new abnormal findings (e.g. spirometry) (ii) in those with or without an abnormal CT finding that requires further follow up.
Numbers of individuals who are smoking and who wish to quit will also be documented to provide guidance for service development and resource requirements.

3. STUDY DESIGN

The study is a pseudo-randomised controlled study embedded within the evaluation of a clinical service to deliver lung health screening which focusses on CT screening for lung cancer. As part of the clinical service individuals will receive a range if investigations and will be followed up, including their smoking status as part of the evaluation of the services value/impact.

The study will compare two possible forms of smoking cessation service delivery in the context of this screening service. These are *signposting to smoking cessation* or *immediate access*).

Limited clinical resources mean that a specialist smoking cessation practitioner will only be available on 5 days every fortnight so treatment allocation will depend on this.

Broader evaluation of the CT screening programme as a clinical service will include longer term outcomes.

4. PARTICIPANT ENTRY

4.1 PRE-REGISTRATION EVALUATIONS

Participants will have been invited to attend a lung health check including a CT scan based on their risk score (smoking history, co-morbidities, age).

4.2 INCLUSION CRITERIA

All screening participants who attend a lung health session.
Only those who express a wish to quit smoking will be included in the primary endpoint analysis

4.3 EXCLUSION CRITERIA

Non smokers

5. ASSESSMENT AND FOLLOW-UP

Baseline measures: The clinical service for all individuals attending the screening programme will include the following measures administered by the clinical team as part of the routine assessment of Lung Health.

(i) Brief questionnaire about symptoms
(ii) CAT score. The COPD assessment test score is a measure of respiratory symptom burden.
(iii) Spirometry. Measured according to national guidance.
(iv) Smoking history (age started, when had last cigarette, average daily consumption, use of e-cigarettes, use of other inhaled illicit drugs.
(v) Smoking status
(vi) Having been advised of the health benefits of quitting, does the person wish to quit smoking?

Usual care: all participants will be asked about smoking status and advised to quit in accordance with Very Brief Advice (VBA) as outlined by the National Centre for Stop Smoking Training (NCSST). Signposting intervention will make use of the London stop smoking portal https://london.stopsmokingportal.com/ to show participants how to contact a local stop smoking service.

Immediate intervention: Smokers will be offered the chance to have an immediate appointment with a smoking cessation practitioner which will include the availability of immediate pharmacotherapy. The preference will be for using a 12 week course of varenicline as this is the most effective agent to support smoking cessation (3), but dual NRT will also be available if patients prefer.

Smokers will be contacted three months after the appointment by telephone and asked about quit attempts and smoking status.
(i) Current smoking
(ii) Quit attempts made
(iii) All participants who are still smoking will be given further advice to quit smoking.

In addition, participants in the lung health screening will be invited to take part in longer interviews to help understand participant experience of the programme. Verbal consent will be recorded for taking part and also for recording of the interviews.
The interview will include open ended questions about participation in the screening, attitudes to health, to smoking and to smoking cessation.
Recordings will be transcribed and analysed thematically using NVivo software.
It will be made clear to participants that they can stop at any time. If any issues come up that are distressing these will be dealt with in a sensitive way and followed up appropriately (e.g. signposting to online information, PALS, advice to contact the appropriate healthcare professional.

7. STATISTICS AND DATA ANALYSIS

Sample size Assuming, based on the EAGLES trial(3), a 38% quit rate on the pharmacology arm and a 14% rate in the UK Lung Cancer Screening Study(1), the control arm a superiority study would require 88 participants (1:1 randomisation) to have 90% power at a 5% significance level [calculator at sealedenvelope.com]. Allowing for a 20% dropout we would need to recruit 110 individuals who wish to quit smoking to answer the direct comparison.

However, to improve power of exploratory analyses which compare different sub-groups (e.g. those with or without airflow obstruction on spirometry) we will recruit as many participants in the screening programme as possible.

Long term survival analysis will be based on intention to treat.

Data and all appropriate documentation will be stored for a minimum of 10 years after the completion of the study, including the follow-up period.

8. REGULATORY ISSUES

8.1 ETHICS APPROVAL

The Study Coordination Centre has obtained approval from the South Central – Oxford C Research Ethics Committee (REC) and Health Research Authority (HRA). REC reference:18/SC/0236.

The study must also receive confirmation of capacity and capability from each participating NHS Trust before accepting participants into the study or any research activity is carried out. The study will be conducted in accordance with the recommendations for physicians involved in research on human subjects adopted by the 18th World Medical Assembly, Helsinki 1964 and later revisions.

8.2 CONSENT

The study is effectively a cluster randomised (by day) evaluation of two possible clinical services.

For logistical reasons (high throughput of patients each day) and intervention fidelity reasons (a prolonged discussion about smoking cessation would itself be an intervention) individual patient consent will not be sought.

Because the targeted lung health check / lung cancer screening process is a clinical project intended to maximise uptake a patient information sheet about research projects is not

included as this might deter participation. The information sheet remains available to participants in the screening project or clinicians if they enquire.

8.3 CONFIDENTIALITY

The Chief Investigator will preserve the confidentiality of participants taking part in the study and is registered under the Data Protection Act.

8.4 INDEMNITY

Imperial College London holds negligent harm and non-negligent harm insurance policies which apply to this study.

8.5 SPONSOR

Imperial College London will act as the main Sponsor for this study. Delegated responsibilities will be assigned to the NHS trusts taking part in this study.

8.6 FUNDING

Royal Marsden Partners are funding this study.

8.7 AUDITS

The study may be subject to inspection and audit by Imperial College London under their remit as sponsor and other regulatory bodies to ensure adherence to GCP and the UK Policy Framework for Health and Social Care Research.

9. PUBLICATION POLICY

Anonymised, aggregate results will be published in open access medical journals

10. REFERENCES

1. Brain K, Carter B, Lifford KJ, Burke O, Devaraj A, Baldwin DR, Duffy S, Field JK. Impact of low-dose CT screening on smoking cessation among high-risk participants in the UK Lung Cancer Screening Trial. *Thorax* 2017; 72: 912-918.
2. Kathuria H, Detterbeck FC, Fathi JT, Fennig K, Gould MK, Jolicoeur DG, Land SR, Massetti GM, Mazzone PJ, Silvestri GA, Slatore CG, Smith RA, Vachani A, Zeliadt SB, Wiener RS. Stakeholder Research Priorities for Smoking Cessation Interventions within Lung Cancer Screening Programs. An Official American Thoracic Society Research Statement. *American Journal of Respiratory and Critical Care Medicine* 2017; 196: 1202-1212.
3. Anthenelli RM, Benowitz NL, West R, St Aubin L, McRae T, Lawrence D, Ascher J, Russ C, Krishen A, Evins AE. Neuropsychiatric safety and efficacy of varenicline, bupropion, and nicotine patch in smokers with and without psychiatric disorders (EAGLES): a double-blind, randomised, placebo-controlled clinical trial. *The Lancet* 2016; 387: 2507-2520.

Schematic of QuLIT study flow