Evaluation of the impact of systematic delivery of cessation interventions on delivery of smoking cessation in secondary care

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Short title:	Exploring ways to help hospital patients stop smoking
Acronym:	*N/A*
Trial Registration:	http://www.controlled-trials.com/isrctn/
ISRCTN:	*insert when allocated*
REC reference:	*insert when allocated*
Trial Sponsor:	University of Nottingham
Funding Source:	National Institute for Health Research

TRIAL / STUDY PERSONNEL AND CONTACT DETAILS

Sponsor: Contact name	University of Nottingham Mr Paul Cartledge Head of Research Grants and Contracts Research Innovation Services King's Meadow Campus Lenton Lane Nottingham NG7 2NR
Chief investigator: (medical expert)	Name: Professor John Britton Phone: 0115 823 1708 Fax: 0115 823 1337 Email: j.britton@virgin.net
Co-investigators:	Dr Rachael Murray, Lecturer in Health Policy & Promotion, Professor Ann McNeill, Professor in Health Policy & Promotion
Trial / Study Statistician:	Dr Jo Leonardi-Bee, Lecturer in Medical Statistics Phone: 0115 823 1388 Fax: 0115 823 1337 Email: jo.leonardi-bee@nottingham.ac.uk
Trial / Study Coordinating Centre:	UK Centre for Tobacco Control Studies, Division of Epidemiology & Public Health, Clinical Sciences Building 2, City Hospital

SYNOPSIS

Title	Evaluation of the impact of systematic delivery of cessation interventions on delivery of smoking cessation in secondary care
Acronym	N/A
Short title	Exploring ways of helping hospital patients stop smoking
Chief Investigator	Professor John Britton
Objectives	To develop and test the effectiveness and cost-effectiveness of a systematic smoking intervention service that offers cessation treatment to all smokers admitted to the medical wards of an acute NHS Hospital who want to quit smoking.
Trial Configuration	Cluster randomised controlled trial
Setting	Nottingham City Hospital
Sample size estimate	About 300 people are discharged from the study wards each week. From a previous study in the same setting we know that about 25% of these are smokers. A trial with 9 wards per treatment group, recruiting for 6 months, or until 1300 smokers are recruited (whichever is sooner), in both intervention and usual care groups, which with allowance for clustering will provide over 90% power to detect a difference between 13% and 26% abstinence at 1 month at 5% significance.
Number of participants	1300 (650 intervention, 650 usual care)
Eligibility criteria	All current or recent (smoked within 28 days of admission) adult smokers admitted to one of eighteen wards at Nottingham City Hospital.
Description of interventions	For participants in the active intervention group, a cessation practitioner will deliver a brief cessation intervention and offer Nicotine Replacement Therapy and further 1:1 counselling. Participants in the control group will receive usual care. We will perform carbon monoxide validation at one and six months post discharge on participants from both groups to ascertain smoking status.
Duration of study	May 2010 – December 2012

Randomisation and blinding	Web-based randomisation stratified by number of discharges/week by a third party. Due to the nature of the trial, it is only possible to blind the trial statistician.
Outcome measures	The effectiveness and cost-effectiveness of the intervention One month post discharge quit rate Six month post discharge quit rate
Statistical methods	All analyses will be conducted based on intention to treat. Simple statistics, Mann Whitney U tests, and multilevel models will be used to compare the primary and secondary outcomes between the intervention and usual care control groups. Data will be analysed using STATA 11 MP.

ABBREVIATIONS

AE	Adverse Event
CI	Chief Investigator overall
CRF	Case Report Form
DAP	Data Analysis Plan
DMC	Data Monitoring Committee
EOT	End of Trial
GCP	Good Clinical Practice
ICF	Informed Consent Form
NHS	National Health Service
P/GIS	Parent / Guardian Information Sheet
PI	Principal Investigator at a local centre
PIS	Participant Information Sheet
REC	Research Ethics Committee
R&D	Research and Development department
SAE	Serious Adverse Event
SPC	Summary of Product Characteristics
TMG	Trial Management Group
TSG	Trial Steering Group

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TRIAL / STUDY BACKGROUND INFORMATION AND RATIONALE

Smoking is the largest avoidable cause of death, disability and social inequality in life expectancy in the UK. Half of all regular cigarette smokers die from a disease caused by their smoking, typically losing about 10 years of life [1]. Smoking currently kills about 100,000 people [2], and causes about 360,000 hospital admissions and over 1 million GP consultations [3] in the UK each year. Passive smoking kills an estimated 12,000 people each year [4], and we estimate that one million children aged under 5 live with parents or carers who smoke, putting them at risk of cot death, lung infection, ear disease and asthma due to passive smoking in the home. Smoking is most prevalent among the most disadvantaged in society [5] and in a recent study from Scotland, had a greater impact on life expectancy than poverty [6]. Smoking is thus a problem of vast importance to the NHS, and it is therefore important to develop more effective ways of drawing smokers into quitting and helping them to succeed. This trial is proposed to address some of these needs by developing new approaches to providing a cessation service in secondary care.

Provision and uptake of NHS stop smoking services (SSS) throughout the UK has improved dramatically over the past decade [7], but still only about 10% of smokers use them [8], and integration of systematic service delivery into routine care, particularly in secondary care, remains poor [9]. Few clinicians or other health professionals have been trained to intervene effectively in smoking, and knowledge and understanding of the mechanisms underlying nicotine addiction, and of the drug and behavioural interventions that can be used to support cessation, is low. Supporting cessation is also time consuming, and although important is often consequently neglected in the face of more immediate and pressing demands on staff in the context of busy acute medical units. Attempts to encourage routing cessation intervention by existing medical staff in the acute setting have failed to achieve lasting change. Thus, whilst hospital admission is a major opportunity to promote smoking cessation [10], and many hospitals now provide cessation advice for planned admissions, delivery of effective interventions for acute admissions remains piecemeal and scant [9]. As a result, few of the estimated 4 million smokers admitted to hospital in the UK each year receive effective cessation support. It is therefore important to develop methods to ensure that behavioural support and pharmacotherapy are offered to all smokers in hospital.

Smoking cessation interventions are effective but not difficult to deliver, and since their success depends at least as much on the personality and empathy as the clinical experience of the person delivering the intervention, there is no reason why these interventions cannot be delivered effectively by non-clinical staff. The present proposal is made to test the coverage and cessation rates achieved by introducing a systematic, counsellor-led smoking cessation service offering behavioural support with delegated NRT prescribing in a typical hospital setting.

TRIAL / STUDY OBJECTIVES AND PURPOSE

PURPOSE

To develop and test the effectiveness and cost-effectiveness of a systematic smoking intervention service that offers treatment to all smokers admitted to the medical wards of an acute NHS Trust who want to quit smoking.

A service is currently offered to relevant patients and we now wish to test the delivery of a new service by randomising certain wards to receive the new service. The study is therefore not a service evaluation and should be categorised as research.

PRIMARY OBJECTIVES

To compare participants in intervention and usual care groups by assessing the proportion of all smokers admitted to hospital with validated cessation one month after discharge

SECONDARY OBJECTIVES

In each of the intervention and usual care groups, we will assess the proportion of smokers who:
- accept behavioural support and/or pharmacotherapy
- are discharged on cessation therapy and have post-discharge support arranged
- receive post-discharge support from SSS
- remain abstinent from smoking at discharge

- remain abstinent from smoking 6 months after discharge

We will also assess the cost effectiveness of the service.

NB: The effectiveness and efficacy of any medication (nicotine replacement therapy and/or buproprion/varenicline) used in the study is not being assessed.

TRIAL / STUDY DESIGN

TRIAL / STUDY CONFIGURATION

Cluster randomised controlled trial

Primary endpoint

The proportion of all smokers admitted to hospital with validated cessation one month after discharge.

Secondary endpoint

The proportion of smokers:
- offered cessation counselling and pharmacotherapy as an inpatient
- who accept cessation counselling and pharmacotherapy as an inpatient
- who remain abstinent from smoking with CO validation at discharge
- who leave hospital with an active prescription for a smoking cessation therapy
- who are discharged on cessation therapy and have post-discharge support arranged
- who receive post-discharge support from SSS
- who remain abstinent from smoking, with CO validation, at 6 months

Safety endpoints

All suspected adverse effects thought to be related or potentially related to any component of the cessation interventions delivered will be recorded.

Stopping rules and discontinuation

No interim analyses of the data are planned; no stopping rules for the trial have been formulated.

RANDOMIZATION AND BLINDING

Web-based randomisation will be undertaken by a statistician in the Division of Epidemiology and Public Health who is independent from all other aspects of study analysis. . The 18 medical wards will be randomised to intervention or usual care groups. Randomisation will be at ward level, stratified by number of discharges per week (low discharge: less than 10 discharges per week; higher discharge: 10 or more discharges per week), using a computer generated random numbers list. The randomisation will be communicated to the Chief Investigator (JB) and thence to study staff delivering the intervention. It is not possible to blind the participants or the baseline data collectors to the intervention allocations, due to the nature of the intervention; however the follow-up outcome assessors, the trial statistician, and all statistical analyses will be blind to the intervention allocation.

Maintenance of randomisation codes and procedures for breaking code

As the trial is unblinded, no procedures for breaking randomisation codes will be required.

TRIAL MANAGEMENT

The trial will be overseen by a Trial Steering Group who will meet regularly to monitor trial progress. This group shall consist of the chief investigator, trial statistician and two other members of the research team.

DURATION OF THE TRIAL / STUDY AND PARTICIPANT INVOLVEMENT

All current and recent adult smokers admitted to one of the eighteen specialist medical wards at Nottingham City Hospital will be provided with information about the trial during the course of their inpatient stay. For those willing to take part, those in the usual care group will have self-reported smoking status recorded, and exhaled carbon monoxide levels measured, at a time close to discharge. In all who are well enough to continue to participate, smoking status will be assessed one and six months following discharge.

Nine wards will be randomised to usual care, and patients on these wards will receive whatever smoking interventions are currently offered. For most smokers this will be brief advice delivered at the time of admission. Smokers in the intervention group will all be seen by a trained cessation practitioner with delegated power to prescribe nicotine replacement therapy (NRT), who will provide immediate brief advice to quit, prescribe NRT, and offer further one to one counselling throughout the duration of their inpatient stay. For smokers in whom NRT is contraindicated, the practitioner will arrange an alternative therapy (bupropion or varenicline) if appropriate and this will be following discussion with the relevant supervising clinician. One and six month follow ups will be made either by home visit or at the time of a pre-arranged hospital outpatient visit. The duration of the trial for each participant will be 6 months plus the period of inpatient stay.

End of the Trial

The study will end recruitment at the end of the six month recruitment period, and will close following completion of the last six month post discharge follow up.

SELECTION AND WITHDRAWAL OF PARTICIPANTS

Recruitment

All adults admitted to any of the 18 medical wards at Nottingham City Hospital who are self-reported smokers at time of admission, or report smoking regularly until the onset of the episode causing admission (if not more than 28 days prior to admission) will be eligible to participate. All patients admitted to the study wards will be provided with an information sheet explaining the study during the course of their inpatient stay. If any patient wishes to receive the service, but does not wish to be included in the study, we will ensure their data is not used in the study analysis. Their personal details will be recorded for clinical care only, and not used in the research analysis.
If needed, the hospital interpreter and translator services will be available to assist with discussion of the study, the participant information sheets, and consent forms, but the consent forms and information sheets will not be available printed in other languages.

Inclusion criteria

All adult patients admitted to one of the eighteen medical wards at the Nottingham City Hospital for a medical condition or illness who are current smokers, or smoked regularly until the onset of the acute illness causing admission, or recent smokers (smoked within 28 days prior to admission), will be defined as smokers and eligible to participate.

Exclusion criteria

Patients will be excluded from the study analysis if they do not consent to participate in the trial, or are too ill to understand the information and consent forms. All other smokers will be eligible for inclusion. Prescribing will be undertaken by discussion with supervising clinicians. The default will however be to prescribe NRT if it seems otherwise more likely than not that the patient will smoke.

Expected duration of participant participation

Study participants will be participating in the study for the period of admission with follow up for 6 months post discharge.

Removal of participants from therapy or assessments

No routine therapy, assessment or any other aspect of care will be affected in any way by participation in the study.

TRIAL / STUDY TREATMENT AND REGIMEN

Intervention wards:
On the intervention wards, a trained cessation counsellor with delegated power to prescribe NRT will check all inpatient records on a daily basis (Monday to Friday) to identify all documented smokers (smoking status is normally recorded on an admission proforma completed on the Emergency Admissions Unit), and to ascertain smoking status of those with missing data. Smokers will then be seen individually, given brief advice to quit, and offered help to do so in accordance with current NIHCE management guidelines [11]. All who are willing to make a quit attempt will be given one-to-one counselling by the counsellor, tailored as appropriate to the cause of their admission to hospital, and offered NRT. If

accepted and not contraindicated, NRT will be prescribed, by delegated prescribing by the cessation practitioner, as combination slow (16 hour, 15mg skin patches given daily) and fast (gum, lozenges, inhaler or spray according to preference) acting preparations, using the patch continually, and the fast acting NRT as required in advance of regular cigarette times or at times of craving. Participants who decline NRT will be offered varenicline or bupropion, and if accepted their clinician requested to confirm that no contra-indications apply and to prescribe the treatment. Smokers with acute contraindications to NRT (such as acute coronary insufficiency or stroke) who are unable to smoke will have NRT or other therapy withheld until their acute condition has stabilised, and/or they experience craving to smoke. A decision to prescribe for these individuals, and for those with relative contraindications such as pregnancy, will then be made in conjunction with their supervising clinician. The general approach will be to provide NRT or other therapy for all smokers from the point at which it is judged more likely than not that the patient will otherwise smoke. Behavioural support will then continue to be given by the counsellor on repeated occasions as appropriate and as acceptable to the patient throughout the admission. Follow-up behavioural support after discharge will be arranged with the appropriate local Stop Smoking Service (SSS). So far as can be achieved and in accordance with accepted good practice and current NHS Stop Smoking Service guidance all participants who accepted cessation support will be contacted at least once within a month of discharge by a study cessation counsellor to inquire about current smoking status and offer further support if needed.

On the day before or of discharge, or the Friday before a planned weekend discharge, the counsellor will seek consent from all smokers (whether or not cessation support has been accepted) for a measurement of exhaled carbon monoxide, and for further contact to ascertain smoking status (and in those who report that they have not smoked, a further carbon monoxide measure) at around one month and six months after discharge. Smoking status will be established if possible by telephone, or letter, and carbon monoxide measurement either by home visit or in conjunction with a routine outpatient visit according to convenience.

Usual care wards:
On the day before or of discharge, or the Friday before a planned weekend discharge, a cessation counsellor will check the hospital notes of those admitted to usual care wards to ascertain and clarify smoking status in relation to the above inclusion criteria. Patients who are documented as smokers or recent smokers (within 28 days of hospital admission) or whom smoking status is unknown, will be provided with a letter from their consultant, informing them of the study, this will be presented by a member of the nursing staff and will include an information sheet. This sheet will have contact details of the research team. Patients will be made aware that smoking cessation support will be delivered in accordance with existing usual care on the wards., and seek consent from all smokers for a measurement of exhaled carbon monoxide, and for further contact to ascertain smoking status (and in those who report that they have not smoked, a further carbon monoxide measure) as in the intervention group, at around one month and six months after discharge. Smoking status will be established if possible by telephone, or letter, and carbon monoxide measurement either by home visit or in conjunction with a routine outpatient visit according to convenience.

Any other smoking cessation interventions will be provided in accordance with the usual management practice of the supervising clinicians and without influence from the research team.

Compliance

Self-reported use of NRT or other therapy will be recorded at the time of measurement of smoking status, at discharge, 1 and 6 months. All behavioural support interventions will also thus be documented from those giving consent, thus providing a measure of the typical level of input accepted by smokers admitted to the intervention wards

Criteria for terminating trial

In the unlikely event of a disproportionate number of adverse events occurring in the active (intervention) group, which will be reported according to NHS procedures, the Trial Steering Group will assess whether to temporary or definitively halt the trial.

STATISTICS

General Considerations

A full analysis strategy will be developed independently of the trial database, before undertaking any analysis, after the start of randomisation. No analyses will be conducted until the strategy has been approved by the Chief Investigator and the Trial Steering Group by signing and dating a copy of this strategy. Analyses will be performed while blind to assignment status.

Data files can be transferred into a range of statistical packages for analysis including SPSS, STATA, SAS and S-Plus.

Brief Analysis Plan

The primary analysis will compare intervention with usual care groups based on intention-to-treat. The intention-to-treat population is defined as all patients who agreed to participate. Participants for whom smoking status is unknown will be assumed to have relapsed into smoking in the group to which they were randomised. Per protocol analysis will also be conducted, where the population is defined as all participants who agreed to participate, who received the intervention their ward were assigned to and assumes relapse to smoking in those with missing follow-up data. Participants who did not receive the intervention their ward was assigned to will be excluded from the analysis.

The primary analysis will be pragmatic. We will initially perform simple summary statistics to calculate the percentage of patients from each ward achieving the primary and secondary outcomes, and compare these between intervention groups using the Mann-Whitney U test. We will compare the primary outcome between the intervention groups using a multi-level model where patients are nested within wards by including a contrast for active versus usual care, clustered for ward using a random effect, and adjusted for age, sex, quantity smoked per day at baseline by including them as fixed covariates in the model. We will perform an assessment of the validity of the model assumptions, including fitting wards as fixed effects. Further analyses will also be conducted to assess the robustness of the conclusions to missing primary outcome data.

Statistical signficance will be determined as <5% for the primary outcome and <1% for secondary outcomes. All analyses will be conducted using STATA 11 MP.

Sample size and justification

About 300 people are discharged from the 18 study wards each week. From a previous study in the same setting we know that about 25% of these are smokers, and of the approximately 50% of smokers who participated in a cessation trial about 26% of those receiving usual care (13% of all smokers) had quit at one month [25]. We aim to offer effective cessation care to all smokers, and expect this to at least double the proportion of quitters at 1 month after discharge to 26%. The respective expected proportions at 6 months are about 10 and 17% [12].

A trial with 9 wards per treatment group, recruiting for approximately 6 months, will, (taking into account a small proportion who do not wish to, or are too ill to take part), study approximately 1300 smokers in both active and usual care groups, which with allowance for clustering will provide over 90% power to detect a difference between 13% and 26% abstinence at 1 month at 5% significance.

Primary outcome measure

The proportion of all smokers admitted to hospital with validated cessation one month after discharge.

Secondary outcome measures

The proportion of smokers:
- offered cessation counselling and pharmacotherapy as an inpatient
- who accept cessation counselling and pharmacotherapy as an inpatient
- who remain abstinent from smoking with CO validation at discharge
- who leave hospital with an active prescription for a smoking cessation therapy
- who are discharged on cessation therapy and have post-discharge support arranged
- who receive post-discharge support from Stop Smoking Services (e.g. New Leaf)
- who remain abstinent from smoking, with CO validation, at 6 months

Assessment of efficacy

Abstinence from smoking at one month
Abstinence from smoking at six months

Assessment of safety

We will document all suspected adverse events in the intervention group.

Procedures for missing, unused and spurious data

Departures from randomised intervention protocols and withdrawals from intervention will be reported. Loss to follow-up will be reported for primary and secondary outcome data at discharge, one month post discharge, and six months post discharge.

Definition of populations analysed

Intention –to-Treat Population
All analysis will be based on the intention-to-treat principle, including all patients who agreed to participate and assuming relapse to smoking in those with missing follow-up data.

Per Protocol PopulationThe per protocol population is defined as all participants who agreed to participate, who received the intervention their ward were assigned to and assuming relapse to smoking in those with missing follow-up data. Participants who did not receive the intervention their ward was assigned to will be excluded from the analysis.

ADVERSE EVENTS

Potential adverse events from NRT, varenicline and bupropion have previously been well documented and will be discussed with participants in accordance with usual clinical practice at the time of prescription. All prescribing will be carried out in line with guidance in the British National Formulary. If any adverse event that could be related to cessation therapy occurs, management and decisions on continued treatment will be delivered by the supervising clinicians. However the safety profile of NRT in particular, and of cessation therapies in general when used in accordance with BNF guidance, is extremely good. Major adverse events are therefore unlikely.

All adverse events relating to the intervention will be reported according to local NHS procedures. The research team will not collect data on adverse events and these will not be reported to the REC

Participant removal from the study due to adverse events

Any participant who experiences an adverse event may be withdrawn from the study at the discretion of the Investigator.

Risks to researchers

1. Risk of cross-infection
Cessation counsellors who have direct contact with patients may be at risk of cross-infection,but will receive the necessary immunisations via occupational health clearance.

2. Risk of aggressive/abusive behaviour
If any participant becomes aggressive or abusive on the ward, clinical and security staff will be on hand to assist the member of staff, and the participant will be made clear that aggressive and/or abusive behaviour will not be tolerated within the hospital.

3. Risk of lone working
In some cases, a carbon monoxide measure will be taken from participants. Where possible, this will be taken during a routine hospital visit, but on the occasion where a home visit is necessary, the researcher will be accompanied by another member of the research team and (where this is not possible) follow the procedures in the University of Nottingham Lone Worker Policy (available at: http://www.nottingham.ac.uk/safety/guides.htm#L). If conducting the visit alone, the researcher will inform a colleague of the time of the visit, and agree to telephone the colleague at the end of the visit. In the case of not receiving a phone call from the researcher around the pre-arranged time, the relevant colleague can investigate. At all times, lone researchers will carry a mobile phone.

ETHICAL AND REGULATORY ASPECTS

ETHICS COMMITTEE AND REGULATORY APPROVALS

The trial will not be initiated before the protocol, informed consent forms and participant and GP information sheets have received approval / favourable opinion from the Research Ethics Committee (REC), and the respective National Health Service (NHS) Research & Development (R&D) department. Should a protocol amendment be made that requires REC approval, the changes in the protocol will not be instituted until the amendment and revised informed consent forms and participant and GP information sheets (if appropriate) have been reviewed and received approval / favourable opinion from the REC and R&D departments. A protocol amendment intended to eliminate an apparent immediate hazard to participants may be implemented immediately providing that the REC are notified as soon as possible and an approval is requested. Minor protocol amendments only for logistical or administrative changes may be implemented immediately; and the REC will be informed.

The trial will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, 1996; the principles of Good Clinical Practice, and the Department of Health Research Governance Framework for Health and Social care, 2005.

INFORMED CONSENT AND PARTICIPANT INFORMATION

The process for obtaining participant informed consent or assent and parent / guardian informed consent will be in accordance with the REC guidance, and Good Clinical Practice (GCP) and any other regulatory requirements that might be introduced. The investigator or their nominee and the participant or other legally authorised representative shall both sign and date the Informed Consent Form before the person can participate in the study.

The participant will receive a copy of the signed and dated forms and the original will be retained in the Trial Master File. A second copy will be filed in the participant's medical notes and a signed and dated note made in the notes that informed consent was obtained for the trial.

The decision regarding participation in the study is entirely voluntary. The investigator or their nominee shall emphasize to them that consent regarding study participation may be withdrawn at any time without penalty or affecting the quality or quantity of their future medical care, or loss of benefits to which the participant is otherwise entitled. No trial-specific interventions will be done before informed consent has been obtained.

The investigator will inform the participant of any relevant information that becomes available during the course of the study, and will discuss with them, whether they wish to continue with the study. If applicable they will be asked to sign revised consent forms.

If the Informed Consent Form is amended during the study, the investigator shall follow all applicable regulatory requirements pertaining to approval of the amended Informed Consent Form by the REC and use of the amended form (including for ongoing participants).

RECORDS

Case Report Forms

Each participant will be assigned a trial identity code number, allocated at randomisation, for use on CRFs other trial documents and the electronic database. The documents and database will also use their initials (of first and last names separated by a hyphen or a middle name initial when available) and date of birth (dd/mm/yy).

CRFs will be treated as confidential documents and held securely in accordance with regulations. The investigator will make a separate confidential record of the participant's name, date of birth, local hospital number or NHS number, and Participant Trial Number (the Trial Recruitment Log), to permit identification of all participants enrolled in the trial, for use in follow-up.
CRFs shall be restricted to those personnel approved by the Chief or local Principal Investigator and recorded on the 'Trial Delegation Log.'

All paper forms shall be filled in using black ballpoint pen. Errors shall be lined out but not obliterated by using correction fluid and the correction inserted, initialled and dated.
The Chief or local Principal Investigator shall sign a declaration ensuring accuracy of data recorded in the CRF.

Source documents

Source documents shall be filed at the investigator's site and may include but are not limited to, consent forms, current medical records, laboratory results and pharmacy records. A CRF may also completely serve as its own source data. Only trial staff as listed on the Delegation Log shall have access to trial documentation other than the regulatory requirements listed below.

Direct access to source data / documents

The CRF and all source documents, including progress notes and copies of laboratory and medical test results shall made be available at all times for review by the Chief Investigator, Sponsor's designee and inspection by relevant regulatory authorities.

DATA PROTECTION

All trial staff and investigators will endeavour to protect the rights of the trial's participants to privacy and informed consent, and will adhere to the Data Protection Act, 1998. The CRF will only collect the minimum required information for the purposes of the trial. CRFs will be held securely, in C118 in the Clinical Sciences Building at City Hospital. Access to the information will be limited to the trial staff and investigators and relevant regulatory authorities (see above). Computer held data including the trial database will be held securely and password protected on a University of Nottingham computer. All data will be stored on a secure dedicated web server. Data files will be password protected and electronically archived by the trial statistician using a 12 character password. Access will be restricted by user identifiers and passwords (encrypted using a one way encryption method).
Information about the trial in the participant's medical records / hospital notes will be treated confidentially in the same way as all other confidential medical information.

Electronic data will be backed up every 24 hours to both local and remote media in encrypted format.

QUALITY ASSURANCE & AUDIT

INSURANCE AND INDEMNITY

Insurance and indemnity for trial participants and trial staff is covered within the NHS Indemnity Arrangements for clinical negligence claims in the NHS, issued under cover of HSG (96)48. There are no special compensation arrangements, but trial participants may have recourse through the NHS complaints procedures.

The University of Nottingham has taken out an insurance policy to provide indemnity in the event of a successful litigious claim for proven non-negligent harm.

TRIAL CONDUCT

Trial conduct will be subject to systems audit of the Trial Master File for inclusion of essential documents; permissions to conduct the trial; Trial Delegation Log; CVs of trial staff and training received; local document control procedures; consent procedures and recruitment logs; adherence to procedures defined in the protocol (e.g. inclusion / exclusion criteria, correct randomisation, timeliness of visits); adverse event recording and reporting; and accountability of trial materials.
A designated member of the research team, or where required, a nominated designee of the Sponsor, shall carry out a site systems audit at least yearly and an audit report shall be made to the Trial Steering Group.

TRIAL DATA

Monitoring of trial data shall include confirmation of informed consent; source data verification; data storage and data transfer procedures; local quality control checks and procedures, back-up and disaster recovery of any local databases and validation of data manipulation. The Trial Coordinator, or where required, a nominated designee of the Sponsor, shall carry out monitoring of trial data as an ongoing activity.

Entries on CRFs will be verified by inspection against the source data (normally patient notes and pharmacy records). A sample of CRFs (10%) will be checked on a regular basis for verification of all entries made. In addition the subsequent capture of the data on the trial database will be checked. Where corrections are required these will carry a full audit trail and justification.

Trial data and evidence of monitoring and systems audits will be made available for inspection by REC as required.

RECORD RETENTION AND ARCHIVING

In compliance with the ICH/GCP guidelines, regulations and in accordance with the University of Nottingham Research Code of Conduct, the Chief or local Principal Investigator will maintain all records and documents regarding the conduct of the study. These will be retained for at least 7 years or for longer if required. If the responsible investigator is no longer able to maintain the study records, a second person will be nominated to take over this responsibility.
The Trial Master File and trial documents held by the Chief Investigator on behalf of the Sponsor shall be finally archived at secure archive facilities at the University of Nottingham. This archive shall include all trial databases and associated meta-data encryption codes.

DISCONTINUATION OF THE TRIAL BY THE SPONSOR

The Sponsor reserves the right to discontinue this trial at any time for failure to meet expected enrolment goals, for safety or any other administrative reasons. The Sponsor shall take advice from the Trial Steering Group as appropriate in making this decision.

STATEMENT OF CONFIDENTIALITY

Individual participant medical information obtained as a result of this study are considered confidential and disclosure to third parties is prohibited with the exceptions noted above.
Participant confidentiality will be further ensured by utilising identification code numbers to correspond to treatment data in the computer files.

Such medical information may be given to the participant's medical team and all appropriate medical personnel responsible for the participant's welfare.

Data generated as a result of this trial will be available for inspection on request by the participating physicians, the University of Nottingham representatives, the REC, local R&D Departments and the regulatory authorities.

PUBLICATION AND DISSEMINATION POLICY

The results of the study will be published in a peer-reviewed journal, and presented at relevant conferences. A presentation giving the study findings will be made to staff at the City Hospital.

USER AND PUBLIC INVOLVEMENT

Wayne Sherwood is a past user of local cessation, primary and secondary care services for smoking and a member of the British Lung Foundation Breathe Easy group in Nottingham (a network providing support for people living with a lung condition), and is a co-applicant. He has commented on the proposal and will work with us on across the trial. Carole McCulloch is manager of the Aspley/Bells Lane Partnership Group in Nottingham working to improve her local community (which has one of the highest smoking prevalences in the country) and has previously carried out surveys with local adolescents (on carrying knives) and the elderly (on local issues). She is a smoker and is keen to help reduce smoking rates in her local area. Both individuals will provide input to study documentation and will be informed as the trial progresses.
Professor Ann McNeill will provide continued support and mentorship for lay people throughout the trial.

STUDY FINANCES

Funding source

This study is funded by the National Institute for Health Research as part of a programme grant.

Participant stipends and payments

Participants will not be paid to participate in the trial. Travel expenses will be offered for any hospital visits in excess of usual care.

SIGNATURE PAGES

Signatories to Protocol:

Chief Investigator: (name)_____

Signature:_____

Date: _____

Co- investigator: (name) _____

Signature:_____

Date: _____

Trial Statistician: (name)_____

Signature:_____

Date: _____

REFERENCES

(1) Doll R, Peto R, Boreham J, Sutherland I. Mortality in relation to smoking: 50 years' observations on male British doctors. Br Med J 2004 Jun 26;328(7455):1519-33.

(2) Twigg L, Moon G, Walker S. The smoking epidemic in England. London: Health Development Agency; 2004.

(3) Royal College of Physicians. Nicotine Addiction in Britain. A report of the Tobacco Advisory Group of the Royal College of Physicians. London: Royal College of Physicians of London; 2000.

(4) Jamrozik K. Estimate of deaths attributable to passive smoking among UK adults: database analysis. Br Med J 2005 Apr 9;330(7495):812-7.

(5) Robinson S, Lader D. Smoking and drinking among adults, 2007. Newport: Office for National Statistics; 2009.

(6) Gruer L, Hart CL, Gordon DS, Watt GCM. Effect of tobacco smoking on survival of men and women by social position: a 28 year cohort study. Br Med J 2009 Feb 17;338(feb17_2):b480.

(7) The Information Centre. Statistics on NHS Stop Smoking Services in England, April 2007 to March 2008. The Information Centre, Lifestyles Statistics 2008. Available from: URL: http://www.ic.nhs.uk/webfiles/publications/Stop%20smoking%20ANNUAL%20bulletins/SSS0708/SSS%202007-08%20final%20format%20v2.pdf

(8) Lader D. Smoking-related behaviour and attitudes, 2007. Cardiff: Office for National Statistics; 2008.

(9) Royal College of Physicians. Going smoke-free: the medical case for clean air in the home, at work and in public places. A report on passive smoking by the Tobacco Advisory Group of the Royal College of Physicians. London: RCP; 2005.

(10) Freund M, Campbell E, Paul C, McElduff P, Walsh RA, Sakrouge R, et al. Smoking care provision in hospitals: A review of prevalence. Nicotine Tob Res 2008 May;10(5):757-74.

(11) Brief interventions and referral for smoking cessation in primary care and other settings. NICE Public Health guidance.
National Institute for Health & Clinical Excellence (NICE). March 2006
Available at: http://guidance.nice.org.uk/PH1

(12) Molyneux A, Lewis S, Leivers U, Anderton A, Antoniak M, Brackenridge A, et al. Clinical trial comparing nicotine replacement therapy (NRT) plus brief counselling, brief counselling alone, and minimal intervention on smoking cessation in hospital inpatients. Thorax 2003 Jun;58(6):484-8.