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Nicotine patch preloading for smoking cessation: The Preloading Trial

Submission date
27/04/2012

Recruitment status
No longer recruiting

Registration date
27/04/2012

Overall study status
Completed

Last Edited
18/12/2019

Condition category
Mental and Behavioural Disorders

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Smokers find stopping difficult because when they try they suffer urges to smoke, which compel them to smoke again. Pharmacotherapy for smoking cessation reduces the intensity and frequency of these urges to smoke, but does not abolish them entirely and consequently most quitters will be back to smoking by the end of their treatment. Better treatments are therefore necessary. One possibility is wearing a nicotine patch prior to stopping smoking (preloading), and there is promising evidence that this would enhance success rates. The mechanism is not fully clear, but the most likely explanation relates to unlearning the learned association between smoking and pharmacological reward of cigarettes, principally derived from nicotine. There is good evidence that wearing a patch while smoking is safe and well tolerated and the MHRA have removed prohibitions on doing so. Therefore we aim to establish how well nicotine patch preloading works when combined with standard NHS smoking cessation treatment, in comparison to standard NHS treatment alone.

Who can participate?
Smokers who are willing to give up smoking in four weeks time, and are 18 years of age or older. Participants will be recruited through their GP practice or through their local NHS stop smoking service clinic.

What does the study involve?
We will provide smokers in the active treatment arm with 21mg nicotine patches for 4 weeks prior to quit day. We will advise people to smoke as often as normal while wearing the patch to undermine reward from 'forced' smoked cigarettes. They will also be referred for standard NHS stop smoking service treatment (which comprises behavioural support and pharmacotherapies). Participants in the control/coping arm will be provided with a minimal behavioural intervention aimed at identifying smoking cues and ways to deal with these after quit day, and will also be referred for standard NHS stop smoking service treatment. Follow-ups will take place 1 week, 4 weeks, 6 months and 12 months after each participant's quit day. The primary outcome will be six month validated prolonged abstinence. Additional abstinence outcomes will be 4 week and 12 month prolonged abstinence, and point prevalence 4 week, 6 month and 12 month

abstinence. Markers of potential mediators, such as changes in carbon monoxide and cigarettes per day, aversion, dependence, smoking reward, urges to smoke, confidence in quitting and motivation to change will also be measured. A health economic analysis will be carried out.

What are the possible benefits and risks of participating?
By utilising standard NHS support for smoking cessation smokers can increase their chances of quitting smoking by four times more than when quitting alone, therefore we hope that taking part in the trial will benefit smokers by increasing their chances of success in quitting. There are no real risks of participation, however, a minimal extra amount of time and effort may need to be put into participating in the trial in comparison to standard NHS treatment alone (due to the need to complete more questionnaires, and undertake additional clinic visits and follow-ups).

Where is the study run from?
All participants will be recruited within the UK, from one of the four research centres recruiting for the study (Birmingham, Bristol, London, Nottingham). Target recruitment is split equally between the four centres (approx 450 in each centre). Birmingham, Bristol and Nottingham will recruit through primary care practices and conduct clinic visits from these practices. London will recruit through and conduct clinics from an existing NHS smoking cessation service clinic.

When is the study starting and how long is it expected to run for?
March 2012 to August 2016

Who is funding the study?
National Institute for Health Research (NIHR) Health Technology Assessment (HTA), UK.

Who is the main contact?
Prof Paul Aveyard
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Contact information

Type(s)
Scientific

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Additional identifiers

Protocol serial number
11918; HTA 09/110/01

Study information

Scientific Title
An open label pragmatic randomised controlled trial of nicotine patch preloading for smoking cessation

Acronym
The Preloading Trial

Study objectives
The evidence for the efficacy of preloading using nicotine replacement therapy is inconclusive. Therefore a hypothesis is not specified, however our research question is: Is four weeks of nicotine patch treatment before quitting smoking alongside standard NHS stop smoking service treatment more effective than standard NHS stop smoking service treatment alone?

Ethics approval required
Old ethics approval format

Ethics approval(s)
ref: 12/EM/0014

Study design
Randomised controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Tobacco smoking; smoking cessation; nicotine addiction

Interventions
Active treatment arm: daily 24hr use of 21mg nicotine transdermal patches over a four week period prior to participants quitting smoking.
Control arm: no pharmacotherapy. Minimal behavioural intervention encouraging participants to explore their cues to smoke and ways to counter these following their quit day.
Both arms will also receive the same standard NHS Stop Smoking Service treatment to help them quit smoking (comprising behavioural support and pharmacotherapy as standard)

Intervention Type
Other

Phase
Phase IV

Primary outcome(s)
Current secondary outcome measure (as of 24/01/2018):
Six month prolonged abstinence, measured by the Russell standard criteria i.e. a grace period of 2 weeks, followed by smoking fewer than 5 cigarettes thereafter to six months and biochemically confirmed by an exhaled CO of <10ppm or a salivary cotinine <14ng/ml. This is assessed in the same way as all smoking-related outcomes, namely by participant self-report confirmed biochemically.

Previous primary outcome measure
Six month prolonged abstinence, measured according to the Russell standard criteria, i.e. a grace period of 2 weeks, followed by smoking fewer than 5 cigarettes thereafter and biochemically confirmed by an exhaled CO of <10ppm

Key secondary outcome(s))
Current secondary outcome measures (as of 24/01/2018):
1. Russell standard abstinence at 4 weeks and 12 months, measured and defined analogously. They also comprise seven-day point prevalence, meaning total abstinence by self-report for the seven preceding days confirmed biochemically, as in the Russell standard measures.
2. Adverse events (adverse health states reported by the participant that occurred for the first time between baseline and the second assessment) are self-reported in response to enquiry by the trial staff at one week after baseline and one week after quit day (approximately 5 weeks after baseline). We will also assess some adverse events that may indicate an excess dose of nicotine by a self-completion questionnaire one week after baseline.
3. Costs of behavioural support and NRT, in order to calculate cost/lifetime quitter, the cost/life year gained and the cost/quality adjusted life year, and health service use.
4. Potential mediators of the preloading effect will be measured at baseline, one week later in the pre-quit period, and one week after quit day by self-completion questionnaire:
4.1 Positive reinforcement: modified Cigarette Evaluation Questionnaire (mCEQ) satisfaction subscale and noticing whether cigarettes were more or less enjoyable than previously.
4.2 Negative reinforcement: mCEQ reward subscale.
4.3 Drive to smoke: self-reported change in urge strength and frequency of urges to smoke combined assessed using the Mood and Physical Symptoms Scale Craving subscale (MPSS-C), smoking stereotypy taken from the Nicotine Dependence Syndrome Scale, the mCEQ craving question, and a question used by Hajek and colleagues in a similar trial that asked participants to rate their urge to smoke compared with usual.
4.4 Cigarette consumption: cigarettes per day, and exhaled carbon monoxide.
4.5 Symptoms of addiction: modified score on the Fagerstrom Test for Cigarette Dependence-modified by removing cigarette consumption from the scale to ensure it was distinct from cigarette consumption.
4.6 Medication adherence: days of use of post-quit day medication measured at the +1week visit.
4.7 Confidence ‘How high would you rate your chances of giving up smoking for good at this attempt?’ on a 5-point scale (not at all, to extremely).
4.8 Nausea and aversion: we assessed nausea using the mean of two questions derived from themes from our participant interviews in a previous trial. These were ‘over the past week how nauseous have you felt when you have seen cigarettes or lighters’ and ‘Over the past week how nauseous have you felt when you have smelt cigarette smoke?’ on 5-point scales from not at all to extremely. Aversion was measured using the aversion subscale of the mCEQ.

Previous secondary outcome measures
1. Efficacy - abstinence measured according to Russell standard at four weeks and 12 months post-quit, and 7-day point prevalence, biochemically confirmed abstinence at 4 weeks, 6 and 12 months post-quit.
2. Side-effects of NRT patch use and symptoms of nicotine overdose (such as nausea, watering mouth) at each contact.
3. Costs of behavioural support and NRT, in order to calculate cost/lifetime quitter, the cost/life year gained and the cost/quality adjusted life year, and health service use.

Completion date
30/08/2016

Eligibility

Key inclusion criteria
1. Smokers (defined as regular smokers of cigarettes, cigars, and tobacco cigarettes combined with marijuana)
2. Aged ≥18 years of age
3. Smokers who, in the judgement of the trial researcher, would be suitable for preloading
4. Seeking NHS support to stop smoking and willing to quit in 4 weeks
5. Able to understand and consent to, and willing to comply with, study procedures

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
1792

Key exclusion criteria
1. Pregnant or breastfeeding
2. Extensive dermatitis/other skin disorder that precludes patch use
3. Acute coronary syndrome or stroke within the past three weeks
4. Active phaeocromocytoma
5. Uncontrolled hyperthyroidism

Date of first enrolment
13/08/2012

Date of final enrolment
01/03/2014

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
University of Birmingham
Birmingham
United Kingdom
B15 2TT

Sponsor information

Organisation
University of Birmingham (UK)

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Government

Funder Name
Health Technology Assessment Programme

Alternative Name(s)
NIHR Health Technology Assessment Programme, Health Technology Assessment (HTA), HTA

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location

United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	13/06/2018		Yes	No
Results article	results	01/08/2018		Yes	No
Protocol article	protocol	22/07/2014		Yes	No
HRA research summary			28/06/2023	No	No
Other publications	analysis of pre-loading	01/12/2018	18/12/2019	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes