Feasibility RCT of nicotine preloading for stopping smoking in pregnancy: a new approach to cessation

Section 1 – Project Details

Rationale

Smoking in pregnancy is the biggest avoidable cause of perinatal morbidity and mortality in the developed world. There aren’t many proven, effective interventions for helping pregnant smokers to stop. Nicotine replacement therapy (NRT) improves cessation rates when used by non-pregnant smokers [1] but in pregnancy it has at best, borderline efficacy. [2] The standard method for using NRT is to set a quit date and on that day to start using NRT and to not smoke. ‘Nicotine preloading’ is a new way of using NRT in which smokers use NRT when still smoking in the lead up to their quit dates, then after this they continue on NRT but stop smoking. Although they aren’t specifically instructed to do so, when smokers use NRT as ‘preloading’ they smoke fewer cigarettes and experience fewer cravings or urges to smoke; reduced craving is probably what makes preloading more effective than the usual way of using NRT.

Our team worked on the world’s largest trial of nicotine preloading; this NIHR HTA-funded RCT enrolled 1786 participants and contributes substantially to what is known about preloading efficacy. [3] An HTA monograph describing complete trial findings will soon be published but we can reveal key details here. The Preloading Study found that, after adjustment for varenicline use, preloading increased cessation rates. This suggests that using NRT for preloading before quit attempts in which NRT is used as a cessation treatment is very likely to be more effective than using NRT without preloading. Trial participants were allocated to Preloading or a behavioural control and after their quit dates were allowed to choose cessation treatments. Preloading group ‘quitters’ were more likely to choose NRT for cessation whereas those in the control group were more likely to choose varenicline which is more effective for cessation than NRT; this biased the trial against finding an independent effect of NRT Preloading. However, varenicline isn’t licensed in pregnancy, so pregnant ‘quitters’ can only use NRT; as such Preloading before NRT use in pregnancy has great potential for increasing NRT cessation rates. As NRT is the mainstay of NHS treatment for smoking in pregnancy, preloading could enhance the cost-effectiveness of smoking cessation support delivered across the NHS.

Pregnant women can be reluctant to use medication; previously we showed that even amongst those who use NRT, some women severely restrict NRT use due to concerns about potential fetal harms. [4] [5] Hence, to persuade pregnant women to use NRT before they have stopped smoking will require NRT preloading to be accompanied by counselling which addresses women’s concerns and reassures them that preloading is likely to be safer than smoking. In this studentship a counselling and nicotine preloading intervention for pregnant smokers will be developed, refined and possibly tested for feasibility and acceptability in a pilot RCT. The intervention’s ultimate aim will be to increase pregnant smokers chances of permanently stopping smoking.
Aims

1. To develop and refine a prototype counselling and nicotine preloading intervention for pregnant smokers
2. To assess the feasibility, acceptability and safety of the refined intervention, piloting measures and procedures for use in a definitive RCT
3. To estimate potential intervention efficacy

Objectives 2 & 3 will be achieved through either qualitative and cohorts studies alone or by using these approaches followed by a small RCT. Actual methods used will depend on the time required for objective 1.

Methodology

Qualitative work will investigate pregnant smokers’ concerns about nicotine preloading and using established methods, a prototype counselling and nicotine preloading intervention will be developed and delivered to a cohort pregnant smokers. With feedback the intervention will be refined and the process will be iteratively repeated as necessary, until the intervention is considered ‘refined’. Safety will be assessed by comparing nicotine exposure when smoking with that when preloading. During cohort study(ies) measures for use in an RCT will be developed and refined and a non-randomised estimate for the likely efficacy of a counselling and preloading intervention. If time allows, the feasibility of randomisation will be assessed in a pilot RCT.

Benefits and suitability as a PhD project

The student will develop a new therapeutic intervention for smoking in pregnancy which could easily be incorporated into the NHS. Hence (s)he would be well placed to secure fellowship funding to conduct a further pilot or definitive RCT(s) and the work would be of intense, global interest.

(S)he would be well supported; we are leaders in the conduct of smoking cessation trials in pregnancy and are completing a project to improve counselling used in NHS smoking cessation support for pregnant smokers. Also we are starting an NIHR programme to develop and test a different intervention for cessation in pregnancy using similar methods.

Key References

Section 2 – Training Provision

In addition to training provided by the Graduate School, the student will be able to assess formal training opportunities offered by three organisations to which supervisors are affiliated:

UK Centre for Tobacco and Alcohol Studies (UKCTAS), [http://ukctas.net/](http://ukctas.net/)


NIHR National School for Primary Care Research, [http://www.spcr.nihr.ac.uk/](http://www.spcr.nihr.ac.uk/)

At the outset of the studentship, a formal assessment of the student’s training requirements will be made and relevant courses or opportunities for experiential learning will be identified. The Smoking in Pregnancy research group has statistics, health psychology, applied health services research, economics, qualitative research and systematic review expertise, so the student will have ready access to colleagues conversant in a range of methodologies. There will be particular synergy with a NIHR research programme which supervisors started from July 2017. This programme will investigate ways of improving pregnant smokers’ adherence with NRT as used currently in the NHS (i.e. without preloading). Early programme studies are focussing on finding ways to counsel women such that any concerns about NRT use are countered and pregnant quitters are persuaded to use NRT for longer in their quit attempts. Consequently, the student will have a cohort of colleagues working on similar issues from which he or she can learn; however, both sets of studies are distinct enough for separate outcomes to be produced.

[https://www.nottingham.ac.uk/research/groups/tobaccoandalcohol/smoking-in-pregnancy/index.aspx](https://www.nottingham.ac.uk/research/groups/tobaccoandalcohol/smoking-in-pregnancy/index.aspx)