Helping pregnant smokers quit: a multi-centre randomised controlled trial of electronic cigarettes versus nicotine replacement therapy

Dunja Przulj,[1] Francesca Pesola,[1] Katie Myers Smith,[1*] Hayden McRobbie,[2] Tim Coleman,[3] Sarah Lewis,[3] Christopher Griffith,[1] Robert Walton,[1] Rachel Whitemore,[3] Miranda Clark,[3] Michael Ussher,[4] Lesley Sinclair,[5] Emily Seager,[1] Sue Cooper,[3] Linda Bauld,[5] Felix Naughton,[6] Peter Sasieni,[7] Isaac Manyonda[8] and Peter Hajek[1]

[1]Wolfson Institute of Population Health, Queen Mary University of London, London, UK
[2]National Drug and Alcohol Research Centre, University of New South Wales, Sydney, Australia
[3]School of Medicine, University of Nottingham, Nottingham, UK
[4]Population Health Research Institute, St George's University of London, London, UK; Institute of Social Marketing and Health, University of Stirling, Stirling, UK
[5]Usher Institute and SPECTRUM Consortium, Centre for Population Health Sciences, Old Medical School, Edinburgh, UK
[6]School of Health Sciences, University of East Anglia, Norwich, UK
[7]The Cancer Research UK and King's College London Cancer Prevention Trials Unit, King's College London, Institute of Psychiatry, London, UK
[8]St George's University Hospital NHS Foundation Trust, London, UK

[*]Corresponding author katie.smith@qmul.ac.uk

Disclosure of interests of authors

Full disclosure of interests: Completed ICMJE forms for all authors, including all related interests, are available in the toolkit on the NIHR Journals Library report publication page at https://doi.org/10.3310/AGTH6901.

Primary conflicts of interest: Linda Bauld is on the Public Health Research (PHR) Research Funding Board. Peter Hajek received research funding from and provided consultancy to Pfizer Inc. (New York, NY, USA). Hayden McRobbie received honoraria for speaking at smoking cessation meetings and attending advisory board meetings that have been organised by Pfizer Inc. Felix Naughton received consultancy fees from ResMed for a project that he led, designing an app that provided smoking behaviour change advice and connected to a novel inhaled nicotine replacement therapy device, although the company did not/does not make the nicotine device. Peter Sasieni is an unpaid chair of a Trial Steering Committee for Yorkshire Cancer Research (YESS) and holds Cancer Research UK grants and National Institute for Health and Care Research (NIHR) Clinical Trials Unit Support Funding. Lesley Sinclair was awarded funding for the Cessation in Pregnancy Incentives Trial (CPIT).

Published July 2023
DOI: 10.3310/AGTH6901

Scientific summary

Helping pregnant smokers quit: a multi-centre randomised controlled trial of electronic cigarettes versus nicotine replacement therapy

Health Technology Assessment 2023; Vol. 27: No. 13
DOI: 10.3310/AGTH6901

NIHR Journals Library www.journalslibrary.nihr.ac.uk

Scientific summary

Background

Pregnant smokers in the UK are routinely recommended nicotine patches (NPs), though their efficacy in this population is limited. Some pregnant smokers try spontaneously to reduce or stop smoking with the help of e-cigarettes (ECs), but safety and efficacy of such use are unknown. We compared NPs and ECs in a pragmatic multi-centre randomised controlled trial.

Setting

Twenty-three hospital sites across England, and one NHS Stop Smoking Service (SSS) in Scotland.

Participants

One thousand one hundred and forty pregnant daily smokers (12–24 weeks' gestation) motivated to stop smoking, with no strong preference for using NPs or ECs.

Interventions

Participants in the EC arm were posted a refillable EC device with two 10 ml bottles of tobacco-flavoured e-liquid (18 mg nicotine). Participants in the NP arm were posted a 2-week supply of 15 mg/16-hour NPs. Further supplies of both products were provided for up to 8 weeks, with participants encouraged to source further supplies themselves as needed. Participants in both arms received support calls prior to their target quit date (TQD), on the date, and weekly for the next 4 weeks.

Main outcome measures

The primary outcome was biochemically validated prolonged abstinence from smoking at the end of pregnancy (EOP). Three pre-specified sensitivity analyses were conducted: (1) a per-protocol analysis that excluded participants who did not start product use or never established contact with the study team; (2) multiple imputation of missing data; and (3) an analysis that excluded abstainers who were regularly using non-allocated products. Participants lost to follow-up or not providing biochemical validation were included as non-abstainers. Secondary outcomes included self-reported abstinence at different time points, treatment adherence and safety outcomes.

Randomisation

Participants were randomised (1:1) via a pre-programmed list generated by an independent statistician, comprising random permuted blocks. Research midwives conducted the randomisation over the internet via the study database application.

Results

Validation of smoking status via postal saliva sampling kits proved problematic, with only 55% of self-reported abstainers providing useable samples. Due to this, validated prolonged abstinence rates were low (6.8% vs. 4.4% in the EC and NP arms, respectively). The quit rates in the two study arms were not significantly different [risk ratio (RR) = 1.55, 95% confidence interval (CI) 0.95 to 2.53; Bayes factor (BF) = 2.7]. Multiple imputation and per-protocol sensitivity analyses generated the same results, but when abstainers regularly using non-allocated products were excluded, the difference became significant (6.8% vs. 3.6%, RR = 1.93, 95% CI 1.14 to 3.26; BF = 10). About 30% of the sample did not set a TQD. The uptake of support calls was low in both study arms (median sessions = 1), as was the initial allocated product use, though this was higher in the EC arm (39.9% vs. 22.5% using their products at 4 weeks, RR = 1.78, 95% CI 1.48 to 2.13). At the EOP, 33.8% versus 5.6% were using their allocated product in the EC versus NP arm (RR = 6.01, 95% CI 4.21 to 8.58). Regular use of ECs in the NP arm was more common than regular use of nicotine replacement products in the EC arm (17.8% vs. 2.8%).

Rates of adverse birth outcomes were similar in the two study arms, apart from the EC arm having fewer infants with low birthweight than the NP arm (<2500 g) (9.6% vs. 14.8%, RR = 0.65, 95% CI 0.47 to 0.90; BF = 10.3).

Limitations

Return rates of posted saliva samples were low, resulting in low validated quit rates and reduced power to detect a difference between the two study arms. The 2019 outbreak of a lung disease in young vapers in the USA caused by illicit marijuana products but widely reported as due to nicotine vaping led some participants to stop using ECs and return to smoking. Treatment adherence was low, with a substantial proportion of participants not using the help on offer sufficiently enough to test its benefits. The finding that nicotine use does not affect birthweight only concerns nicotine use in late pregnancy, because all participants smoked in early pregnancy.

Conclusions

ECs were not significantly more effective than NPs in the primary analysis, but their effect appears to have been masked by EC use in the NP arm. When this was controlled for, ECs were almost twice as effective than NPs in all abstinence outcomes. ECs did not pose more risks to birth outcomes assessed in this study than NPs and may have reduced the incidence of low birthweight. In pregnant smokers seeking help, ECs are probably more effective than NPs and do not pose any additional risks to women or their infants.

Future work

If specialist SSSs add ECs to their offer to pregnant smokers, routine monitoring of birth outcomes in women using NPs and ECs would provide further important information.

Trial registration

This trial is registered as ISRCTN62025374 and Eudract 2017-001237-65.

Funding

This project was funded by the National Institute for Health and Care Research (NIHR) Health Technology Assemsent programme and will be published in full in *Health Technology Assessment*; Vol. 27, No. 13. See the NIHR Journals Library website for further project information.

Health Technology Assessment

ISSN 1366-5278 (Print)

ISSN 2046-4924 (Online)

Impact factor: 4.014

Launched in 1997, *Health Technology Assessment* (HTA) has an impact factor of 4.014 and is ranked 27th (out of 108 titles) in the 'Health Care Sciences & Services' category of the Clarivate 2021 Journal Citation Reports (Science Edition). It is also indexed by MEDLINE, CINAHL (EBSCO Information Services, Ipswich, MA, USA), Embase (Elsevier, Amsterdam, the Netherlands), NCBI Bookshelf, DOAJ, Europe PMC, the Cochrane Library (John Wiley & Sons, Inc., Hoboken, NJ, USA), INAHTA, the British Nursing Index (ProQuest LLC, Ann Arbor, MI, USA), Ulrichsweb™ (ProQuest LLC, Ann Arbor, MI, USA) and the Science Citation Index Expanded™ (Clarivate™, Philadelphia, PA, USA).

This journal is a member of and subscribes to the principles of the Committee on Publication Ethics (COPE) (www.publicationethics.org/).

Editorial contact: journals.library@nihr.ac.uk

The full HTA archive is freely available to view online at www.journalslibrary.nihr.ac.uk/hta.

Criteria for inclusion in the *Health Technology Assessment* journal
Reports are published in *Health Technology Assessment* (HTA) if (1) they have resulted from work for the HTA programme, and (2) they are of a sufficiently high scientific quality as assessed by the reviewers and editors.

Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

HTA programme

Health Technology Assessment (HTA) research is undertaken where some evidence already exists to show that a technology can be effective and this needs to be compared to the current standard intervention to see which works best. Research can evaluate any intervention used in the treatment, prevention or diagnosis of disease, provided the study outcomes lead to findings that have the potential to be of direct benefit to NHS patients. Technologies in this context mean any method used to promote health; prevent and treat disease; and improve rehabilitation or long-term care. They are not confined to new drugs and include any intervention used in the treatment, prevention or diagnosis of disease.

The journal is indexed in NHS Evidence via its abstracts included in MEDLINE and its Technology Assessment Reports inform National Institute for Health and Care Excellence (NICE) guidance. HTA research is also an important source of evidence for National Screening Committee (NSC) policy decisions.

This report

The research reported in this issue of the journal was funded by the HTA programme as project number 15/57/85. The contractual start date was in May 2017. The draft report began editorial review in October 2021 and was accepted for publication in September 2022. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the reviewers for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

This report presents independent research funded by the National Institute for Health and Care Research (NIHR). The views and opinions expressed by authors in this publication are those of the authors and do not necessarily reflect those of the NHS, the NIHR, the HTA programme or the Department of Health and Social Care. If there are verbatim quotations included in this publication the views and opinions expressed by the interviewees are those of the interviewees and do not necessarily reflect those of the authors, those of the NHS, the NIHR, the HTA programme or the Department of Health and Social Care.

Published by the NIHR Journals Library (www.journalslibrary.nihr.ac.uk), produced by Newgen Digitalworks Pvt Ltd, Chennai, India (www.newgen.co).