Nicotine replacement treatment, e-cigarettes and an online behavioural intervention to reduce relapse in recent ex-smokers: a multinational four-arm RCT

Hayden J McRobbie,[1,2] Anna Phillips-Waller,[1*] Catherine El Zerbi,[3] Ann McNeill,[3] Peter Hajek,[1] Francesca Pesola,[3] James Balmford,[4†] Stuart G Ferguson,[5] Lin Li,[6] Sarah Lewis,[7] Ryan J Courtney,[2] Coral Gartner,[8] Linda Bauld[9] and Ron Borland[6]

[1]Health and Lifestyle Research Unit, Queen Mary University of London, London, UK
[2]National Drug and Alcohol Research Centre, University of New South Wales, Randwick, NSW, Australia
[3]Cancer Prevention Group, School of Cancer & Pharmaceutical Sciences, Faculty of Medicine and Life Sciences, King's College London, London, UK
[4]Institute of Medical Biometry and Statistics, Faculty of Medicine and Medical Center, University of Freiburg, Freiburg im Breisgau, Germany
[5]College of Health and Medicine, University of Tasmania, Hobart, TAS, Australia
[6]Melbourne School of Psychological Sciences, University of Melbourne, Melbourne, VIC, Australia
[7]Clinical Sciences Building, University of Nottingham, Nottingham City Hospital, Nottingham, UK
[8]School of Public Health, Faculty of Medicine, University of Queensland, St Lucia, QLD, Australia
[9]Usher Institute, University of Edinburgh, Edinburgh, UK

*Corresponding author a.phillips-waller@qmul.ac.uk
†In memoriam

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Scientific summary

Reducing relapse in recent ex-smokers

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Scientific summary

Background

Most efforts to stop smoking that are initially successful end in relapse. Extended stop smoking medication use can help prevent relapse, but uptake and long-term use are low. Fast-acting nicotine replacement products, such as nicotine mouth spray, lozenges and electronic cigarettes, can be used opportunistically in relapse situations, which may be a more promising (and more economical) approach. Regarding behavioural interventions, although most approaches have been found to be ineffective, a recent trial of an online Structured Planning and Prompting Protocol started at the beginning of the quit attempt reduced relapse between 1 and 26 weeks.

Objectives

We planned to determine if the Structured Planning and Prompting Protocol plus interactive texting, or a provision of fast-acting nicotine products to use in emergencies, or the combination of the two approaches, reduced relapse rates at 12 months post quit date compared with usual care. In addition, we aimed to determine the feasibility and acceptability of the interventions and their cost-effectiveness. The trial also included a qualitative and ecological momentary assessment substudy to explore the relapse process and barriers to and facilitators of relapse prevention. Owing to delays in setting up the online intervention as a result of technical and regulatory issues, problems with recruiting from Australian quitlines and English service restructuring affecting recruitment, the trial was curtailed at 6 months' follow-up with a reduced sample size. Therefore, the revised (prespecified) objective was whether or not the number of interventions received (i.e. none, one or two) affected relapse rates at 6 months post quit date.

Design

A multicentre randomised controlled trial.

Participants and setting

Originally, we planned to recruit 1400 recent ex-smokers, with 700 participants recruited from English stop smoking services and 700 participants from Australian quitlines. However, because of the issues described, only 234 participants were randomised ($n = 131$ in Australia and $n = 103$ in England). Initially, participants were to be recruited when they had achieved at least 4 weeks of abstinence, but, later, participants in Australia were recruited from 1 week post quit date via social media and St Vincent's Hospital Melbourne, Fitzroy, VIC, Australia.

Study arms

There were four study arms.

1. A fast-acting nicotine product of the participant's choice (e.g. nicotine mouth spray, lozenge or electronic cigarette) to use if they were at risk of relapse, accompanied by static text messages.

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2. A Structured Planning and Prompting Protocol, for which participants received access to the online protocol that offers training in strategies to deal with temptations to smoke and provides motivational input. This was combined with intensive interactive text messaging.
3. Provision of a nicotine product and Structured Planning and Prompting Protocol interventions.
4. Static text messages added to usual care, typically comprising access to stop smoking medications used during the quit attempt for up to 3 months.

Participants in all arms who were recruited through English stop smoking services and Australian quitlines also had access to their usual care alongside their allocated intervention.

Procedures

Participants referred to the study were contacted by the study team to confirm eligibility, obtain consent and collect baseline data via online surveys or telephone. Participants were randomised to one of the four study arms following completion of the baseline survey. Participants in the nicotine product arm received their products by post plus a series of static text messages (a maximum of 33 messages sent over 4 months). The Structured Planning and Prompting Protocol arm participants completed an online assessment that generated tailored advice. Participants could complete new assessments for updated advice at any time. In addition, participants received a minimum of 55 interactive text messages over 6 months that were tailored to their assessment responses. The usual-care group received the same static messages as the nicotine product arm. Participants were followed up online or by telephone at 3 and 6 months. Ninety-four participants from the main study were also recruited to take part in a qualitative interview substudy. The interviews took approximately 30 minutes and were conducted by telephone. The interviews were conducted following both the 3- and 6-month follow-ups and included participants who had lapsed, relapsed or remained abstinent from each of the study arms. Data on the feasibility, acceptability, use and perceived impact of study interventions were collected. At around 8–12 weeks post quit date, 79 participants from the main study took part in an ecological momentary assessment substudy, which involved 4 weeks' monitoring of the use and relationship to cravings and slips of the two interventions using a handheld electronic diary.

Measures and outcomes

The original plan was to collect outcome data at 3, 6 and 12 months post quit date, with biochemical validation of self-reported abstinence at 12 months. However, because of the curtailment of the study, outcome data were collected at only 3 and 6 months. All revised outcomes were prespecified in the statistical analysis plan, which was drafted prior to data download and analysis.

Original primary outcome

The original primary outcome was relapse rate in each study arm. Relapse was defined as smoking on at least 7 consecutive days or any smoking in the last month at the 12-month follow-up. Participants lost to follow-up were assumed to have relapsed.

Curtailed primary outcome

The curtailed primary outcome was relapse rate in arms that received no intervention (i.e. usual care), one intervention (i.e. the Structured Planning and Prompting Protocol or a nicotine product) and two interventions (i.e. Structured Planning and Prompting Protocol plus a nicotine product) at 6 months. Relapse was defined as smoking on at least 7 consecutive days or any smoking in the last month at the 6-month follow-up. Participants lost to follow-up were assumed to have relapsed.

Original secondary outcomes

The original secondary outcomes were sustained abstinence using different criteria to the primary outcome (e.g. point prevalence and shorter-term period prevalence outcomes); sustained reduction in cigarette consumption; evaluations of likely mechanisms of effect, focusing on strategies that were encouraged and participant perceptions of effect (e.g. participant ratings and data from the ecological momentary assessment/qualitative substudies); dose–response effects; cost-effectiveness; effects of intervention components by country and by demographic; and adverse events.

Curtailed secondary outcomes

The curtailed secondary outcomes were sustained (i.e. no more than five cigarettes smoked since 2 weeks post quit date) and point prevalence (i.e. no smoking in the past 7 days) abstinence at 3 and 6 months; nicotine product preferences (e.g. electronic cigarette or nicotine replacement treatment); product use at 6 months (i.e. frequency of use of nicotine, number of assessments completed for the Structured Planning and Prompting Protocol, number of text messages read); use of coping strategies (i.e. prespecified list with yes/no answers based on the Structured Planning and Prompting Protocol strategies, plus ecological momentary assessment data); adverse events (free text); participant ratings (e.g. five-point scale from very useful to very useless); and qualitative feedback on the interventions.

Sample size

In our original sample size calculations we expected that 70% of participants would relapse by 12 months in usual care, that each relapse prevention intervention would reduce the rate to 58% and that the combination of the two interventions would result in a 48% relapse rate. Assuming no interaction and comparisons between those who received (two arms) and those who did not receive (two arms) each intervention individually, 257 participants were needed per arm to detect this difference (90% power, alpha = 0.025, two-sided). We aimed to recruit 300 participants in each arm, with an additional 50 participants per arm for the ecological momentary assessment substudy. However, with our reduced sample size of 234 participants, we used an alternative (prespecified) approach that compared the number of interventions [i.e. no intervention (usual care), one intervention (Structured Planning and Prompting Protocol or a nicotine product) or two interventions (Structured Planning and Prompting Protocol plus a nicotine product)] and avoided multiple testing. Using one-tailed alpha = 0.05, the sample size afforded 78% power to detect the differences in relapse rates as estimated above. Ninety-four participants were recruited for the qualitative substudy and 79 participants were recruited for the ecological momentary assessment substudy.

Results

The 6-month relapse rate was 60.0% (95% confidence interval 47% to 71%) in the usual-care arm, 43.5% (95% confidence interval 35% to 53%) in those receiving one intervention [nicotine replacement treatment 44.8% (95% confidence interval 33% to 58%); Structured Planning and Prompting Protocol 42.1% (95% confidence interval 30% to 55%)] and 49.2% (95% confidence interval 37% to 62%) in those receiving two interventions ($p = 0.11$). The secondary outcome of sustained abstinence rate at 6 months was 41.7% in the usual-care arm, 54.8% in the arm receiving one intervention (nicotine replacement treatment 53.5%, Structured Planning and Prompting Protocol 56.1%) and 50.9% in the arm receiving two interventions ($p = 0.17$). In the two study arms that were offered a nicotine product, electronic cigarettes were chosen more frequently than nicotine replacement treatment in Australia (71.0% vs. 29.0%; $p = 0.001$), but not in England (54.0% vs. 46.0%; $p = 0.57$). Most participants tried their products and 23.1% were still using them daily at 6 months (26.8% using electronic cigarettes and 17.1% using nicotine replacement treatment). The Structured Planning and Prompting Protocol received positive ratings (somewhat or very useful) from 63.0% of participants who provided the ratings at 6 months, regardless of whether or not the nicotine product intervention was added to

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the Structured Planning and Prompting Protocol. Eighty-six per cent of participants allocated to the Structured Planning and Prompting Protocol completed at least one assessment and > 60% of participants in the Structured Planning and Prompting Protocol arms also reported that they read the online advice, at least briefly. Overall, the site was rarely revisited and coping strategies imparted by the Structured Planning and Prompting Protocol were used with similar frequency in all study arms. Only one participant used the Structured Planning and Prompting Protocol interactive texting feature. Tailored and static text messages received virtually identical ratings. The qualitative study suggested that access to the Structured Planning and Prompting Protocol intervention could be simplified.

Limitations

The inability to recruit sufficient participants resulted in a lack of power to detect clinically relevant differences. Self-reported abstinence was not biochemically validated. The intervention started after a period of abstinence, perhaps reducing the perceived relevance of interventions offered to participants. The study included some smokers who were abstinent for only 7 days during their hospital stay.

Conclusions

Adherence to nicotine products was high, and the online intervention was appreciated but not widely used. There was a trend in favour of single treatments (when compared with usual care), but it did not reach statistical significance and the two interventions combined did not seem to be effective. The study is underpowered and so further evaluation is warranted.

Trial registration

This trial is registered as ISRCTN11111428.

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