



Smoking Cessation Research Review™

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Issue 6 – 2012

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Welcome to the sixth issue of Smoking Cessation Research Review.

The first study that we review for this issue reports that providing nicotine patches with behavioural counselling did not improve quit rates among pregnant women who smoked. The study authors suggest that guidelines for smoking cessation in pregnancy should be revised to encourage the use of only those interventions that have a secure evidence base – i.e., behavioural support. However, these findings have to be considered in the light of the low compliance rates with the therapy; only 7.2% of women who received nicotine patches and 2.8% of those who received placebo patches used them for >1 month.

The results of another study are controversial – the authors argue that nicotine replacement therapy (NRT) is ineffective for smoking cessation and that therefore public expenditure on NRT provision to smokers is a waste of resources. Instead, the researchers propose that funding be provided for those smoking interventions already proven to be effective, such as media campaigns, promotion of no smoking policies, and tobacco price increases.

We hope you find this edition stimulating reading, and we welcome any comments or feedback.

Kind regards,

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A randomized trial of nicotine-replacement therapy patches in pregnancy

Authors: Coleman T et al

Summary: This UK study enrolled 1050 women aged 16–50 years with pregnancies of 12–24 weeks' gestation and who smoked ≥ 5 cigarettes/day. All received behavioural cessation support and were randomly assigned to 8 weeks of treatment with active nicotine patches (15 mg per 16 hours; n=521) or matched placebo patches (n=529).

Comment: This is the largest study to date looking at the efficacy of NRT in pregnant women who smoke (this study compared 15mg, 16-hour nicotine patches with placebo patches). Like the few other studies on this topic, this one showed no advantage of using standard doses of NRT in pregnancy. The study was, however, plagued by low rates of adherence to treatment (similarly to the other NRT trials), with only 7% of woman using nicotine patches and 3% of woman on placebo patches using them for more than a month.

Data on pregnancy-related adverse events were also collected. There were no differences in the numbers of miscarriages, stillbirths, neonatal and postnatal deaths, low birth weight babies, preterm births, or admissions to a neonatal intensive care unit. The only significant difference was that nicotine patch users had higher rates of delivery by caesarean section (20.7%) compared to placebo users (15.3%). The authors believe this is likely to be a chance occurrence.

Although NRT has less risk than smoking, nicotine is not without risk in pregnancy. If there are a lack of data showing its efficacy should we be more discerning in its use? The authors of this study go further to say that there is a need for a trial of higher dose of NRT, but in the meantime we should provide interventions that do work, for example, behavioural support.

Reference: *N Engl J Med.* 2012;366(9):808-18.

<http://www.nejm.org/doi/pdf/10.1056/NEJMoa1109582>

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Fully funded under special authority²

A prospective cohort study challenging the effectiveness of population-based medical intervention for smoking cessation

Authors: Alpert HR et al

Summary: A cohort of 787 adult smokers in Massachusetts who had recently quit smoking were surveyed over three time periods: 2001–2002, 2003–2004, and 2005–2006. At each time period, about 25% of recent quitters reported to have relapsed. No difference in relapse rate was observed among those who used NRT for >6 weeks, with or without professional counselling. In addition, no difference in quitting success with use of NRT was observed for either heavy or light smokers.

Comment: This study received some media attention earlier this year, where it was cited as finding that NRT is no longer effective. Alpert and colleagues conducted an observational study where they followed smokers who had reported stopping smoking in the past 2 years. The researchers then measured the smoking relapse rate over the following year and found no difference between those who used NRT and those who did not. Nevertheless, this observation does not mean that NRT is ineffective.

Results from such studies need to be interpreted with some caution, as there may be other factors related to outcomes that could not be detected. There have been a number of studies that have observed lower quit rates in those who self-selected to use NRT than those who did not. However, it is known that those who choose to use NRT are more likely to have failed quit attempts in the past and more likely to be highly dependent, or addicted, smokers and therefore find quitting more difficult.

NRT is certainly not a magic cure for people wanting to stop smoking. There is good evidence (see the Cochrane Systematic Review) that NRT increases quit rates when used alone and with behavioural support. However, once people stop using it (typically after 8–12 weeks) the rate of relapse back to smoking is similar to that seen in smokers who quit without treatment. Unfortunately, there are few interventions that are effective at preventing relapse.

Reference: *Tob Control*. 2012 Mar 23. [Epub ahead of print]

<http://tobaccocontrol.bmj.com/content/early/2012/01/03/tobaccocontrol-2011-050129>

Effect of offering different levels of support and free nicotine replacement therapy via an English national telephone quitline: randomised controlled trial

Authors: Ferguson J et al

Summary: Outcomes are reported from 2591 non-pregnant smokers aged ≥16 years who called a telephone quitline in England between February 2009 and February 2010 and agreed to set a quit date: 648 were each randomised to standard smoking cessation support, proactive support (repeat telephone calls from, and interaction with, cessation advisors), or proactive support with 6 weeks' free nicotine replacement therapy (NRT), and 647 were randomised to standard support with NRT. At 6 months, 17.7% (n=229) of those offered NRT reported smoking cessation compared with 20.1% (n=261) not offered such therapy (OR, 0.85), and 18.2% (n=236) offered proactive counselling reported smoking cessation compared with 19.6% (n=254) offered standard support (OR, 0.91).

Comment: This study compared the efficacy of two different telephone smoking cessation interventions (standard vs. proactive counselling) and within each arm, half of the smokers were offered NRT. The study showed that quit rates were similar across all groups; i.e. offering people free NRT or more intensive counselling did not increase quit rates over standard telephone support alone.

So is this another study showing that NRT is not effective? Well, the authors certainly don't make this conclusion and offer some possible explanations for their findings. One such explanation is that those offered standard care were also offered proactive contact and all were given advice on how to get effective treatment from the NHS Stop Smoking Service (SSS) – including how to access NRT. In fact, participants who were not offered NRT were more likely to use medicines prescribed by a health care professional or varenicline and to have attended a NHS SSS. Another is that those offered NRT did not use it correctly. The majority (72%) of people offered NRT requested the first 3-week supply but only 21% requested the second 3-week supply, which suggests to me that people did not use it for long enough. These *may* have undermined any anticipated benefit of NRT in the other groups. Regardless of these possible explanations, we cannot ignore that this well conducted trial showed that NRT did not add any benefit in this setting. However, this is not to say that we should stop using NRT to help smokers to quit, but to make sure that we can give the best start to people using these products. This includes helping people to understand the rationale of NRT (one does not simply slap on a patch and it 'starts working to stop you smoking') and know how to use it correctly.

Reference: *BMJ*. 2012;344:e1696.

<http://www.bmj.com/content/344/bmj.e1696>

The effectiveness of financial incentives for smoking cessation during pregnancy: is it from being paid or from the extra aid?

Authors: Mantzari E et al

Summary: This qualitative study explored the stop-smoking experiences of UK-based pregnant women who were incentivised for smoking cessation (n=20) and of pregnant smokers who were not incentivised for cessation (n=16). All women were offered standard NHS Stop-Smoking Services. When interviewed about their motivation to stop smoking and the factors they perceived as influencing their quitting efforts, both groups of women reported similar reasons for wanting to stop smoking during pregnancy. However, they described dissimilar experiences of the Stop-Smoking Services, which they perceived to have differentially influenced their quit attempts. The incentivised group used the services more than women who were not incentivised. In addition, they described the motivating experience of being monitored and receiving feedback on their progress. Non-incentivised women reported problems receiving the appropriate nicotine replacement therapy, which they described as having a detrimental effect on their quitting efforts.

Comment: There are data to show that financial incentives show promise in encouraging pregnant women who smoke to quit. The studies with the best outcomes generally used reward schemes that are contingent on abstinence, where woman stand to gain more if they remain smokefree. This qualitative study starts to unpick some of the reasons why incentive schemes might work and suggest here that women who are involved in such schemes are more likely to report greater engagement with stop smoking services, which may be the reason for their increased chances of quitting. Whatever the mechanism, these types of schemes deserve further research.

Reference: *BMC Pregnancy Childbirth*. 2012;12(1):24.

<http://www.biomedcentral.com/1471-2393/12/24/abstract>

Brief opportunistic smoking cessation interventions: a systematic review and meta-analysis to compare advice to quit and offer of assistance

Authors: Aveyard P et al

Summary: These researchers investigated the effects of opportunistic brief physician advice to stop smoking and offer of assistance on incidence of attempts to stop and quit success in smokers not selected by motivation to quit, in this analysis of data on quit attempts and quit success in 13 trials from the Cochrane Reviews of physician advice for smoking cessation, nicotine replacement therapy, varenicline and bupropion.

Comment: The authors of this systematic review have untangled the literature on brief interventions (e.g., the ABC approach) to look at the effect of brief advice and offering assistance to quitting. Advice to quit on medical grounds significantly increased the frequency of quit attempts by 24%. However, making an offer of treatment (e.g., offering a prescription for smoking cessation medicines or referral to a behavioural support programme), regardless of assessing readiness to quit, motivates an **additional 40–60%** of people.

The authors estimate that some 20% of smokers will go on to make a quit attempt in a 6-month period following a GP visit. If all smokers were given brief advice to quit then the proportion of smokers making a quit attempt would increase to 25%. This can be further increased (by 40%) to 35% if this advice to quit is followed up with an offer of support to quit. Furthermore, people seem to be willing to accept this offer.

There is no need to assess readiness to quit. Aveyard and colleagues cite data from a large smoking cessation study that assessed readiness to quit.¹ Most smokers (89%) in this study did not express a desire to quit in the near future, however, they were offered treatment and 24% joined the smoking cessation programme being offered and 37% quit. Of the 11% that were motivated to quit, 52% took up the offer of treatment and 27% quit. These results suggest that healthcare professionals can make a difference, even in those that may not be thinking of quitting anytime soon.

1. Pisinger C, et al. It is possible to help smokers in early motivational stages to quit. *The Inter99 study*. *Prev Med*. 2005;40(3):278–84.

Reference: *Addiction*. 2011 Dec 16. [Epub ahead of print]

<http://onlinelibrary.wiley.com/doi/10.1111/j.1360-0443.2011.03770.x/abstract>

A selective reversible monoamine oxidase B inhibitor in smoking cessation: effects on its own and in association with transdermal nicotine patch

Authors: Berlin I et al

Summary: This study assessed the efficacy and safety of the selective, reversible monoamine oxidase B (MAO-B) inhibitor EVT302, alone or co-administered with nicotine patch (NP) therapy, in smoking cessation. Smokers (≥ 10 cigarettes/day) received either EVT302 (n=145) or placebo (n=145), or EVT302 (n=61) or placebo (n=61) with open-label NP 21 mg/day for 8 weeks. End-of-treatment 4-week continuous abstinence rates were 15.2% for placebo, 17.2% for EVT302, 26.8% for NP + placebo and 32.8% for NP + EVT302. There was no difference between EVT302 and placebo either alone (adjusted OR, 1.45) or when co-administered with NP.

Comment: Tobacco smoke is known to contain monoamine oxidase inhibitors (MAOIs) that inhibit degradation of dopamine and may potentiate the addictive effects of nicotine. In theory, providing someone with a MAOI (e.g., selegiline) when quitting smoking may be helpful, and may be even more helpful when combined with a nicotine replacement therapy. However, the evidence to date has not given any support to the use of MAOIs in smoking cessation and the findings from this study confirm this lack of effect.

Reference: *Psychopharmacology (Berl)*. 2012 Mar 27. [Epub ahead of print]

<http://www.springerlink.com/content/v82224876u577u31/?MJD=MP>

Independent commentary by Dr Hayden McRobbie,

Senior Lecturer in the School of Public Health and Psychosocial Studies, Auckland University of Technology and Honorary Senior Lecturer in the School of Population Health at the University of Auckland. He is also a Reader in Public Health Interventions within the UK Centre for Tobacco Control Studies, Queen Mary University of London.

For full bio [CLICK HERE](#).

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The relationship of major depressive disorder and gender to changes in smoking for current and former smokers: Longitudinal evaluation in the U.S. population

Authors: Weinberger AH et al

Summary: Changes in smoking were compared for current and former smokers with and without current and lifetime major depressive disorder (MDD), in this analysis of two waves of data from the National Institute on Alcohol Abuse and Alcoholism's National Epidemiologic Survey on Alcohol and Related Conditions (Wave 1, 2001–2002; Wave 2, 2004–2005). Study participants comprised 11,973 adults (aged ≥ 18 years) classified as current or former daily smokers at Wave 1 and Wave 2.

Comment: The relationship between depression and smoking is well known. People with depression are more likely to smoke than those without, and people who smoke are more likely to have a history of depressive disorder than never-smokers. Data from this study show that people with a current or history of major depressive disorder are less likely to quit smoking and for those patients who have managed to stop, a current major depressive disorder puts them at risk of relapse.

However, it is important to remember that many, if not most, people with mental health illness want to quit smoking. These people are often very highly tobacco-dependent and can find quitting difficult. Multi-session behavioural support, supplemented with pharmacotherapy, is recommended.

Reference: *Addiction*. 2012 Mar 19. [Epub ahead of print]

<http://onlinelibrary.wiley.com/doi/10.1111/j.1360-0443.2012.03889.x/abstract>

Prevalence of video game use, cigarette smoking, and acceptability of a video game-based smoking cessation intervention among online adults

Authors: Raiff BR et al

Summary: Outcomes are reported from an online survey completed by 499 participants, nearly half of whom reported smoking cigarettes and 74.5% of the smokers reported playing video games. More smokers than nonsmokers played video games and smokers reported playing more recently, for longer durations each week, and were more likely to play social games than nonsmokers. Most participants (63.7%), including those who worked as health care professionals, believed that a video game-based contingency management intervention would motivate smokers to quit and would recommend such an intervention to someone trying to quit (67.9%).

Comment: Novel smoking cessation interventions are on the horizon. This study reports on the potential of video game-based stop smoking interventions. You may be wondering how a video game might help someone to quit. The authors cite four video games that have been developed for the purposes of smoking cessation and prevention – with names like Blast 'n Quit, Smoke Rings and Nicot. The latter, which involves players crushing virtual cigarettes, has been tested in a randomised controlled trial and showed some promise. Whilst searching the internet for video-game interventions I found a prototype smartphone application that involves a 'reverse tamagotchi' concept where your aim is to kill your virtual nicotine monster. Other games utilise contingency management, where you can earn virtual rewards when remaining smokefree.

The findings from this study show that the sample surveyed thought that video game-based stop smoking interventions could motivate smokers to quit. Such interventions may be a particularly promising way to access our young people who smoke.

Reference: *Nicotine Tob Res*. 2012 Mar 15. [Epub ahead of print]

<http://ntr.oxfordjournals.org/content/early/2012/03/15/ntr.nts079.short?rss=1>

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Explaining the stress-inducing effects of nicotine to cigarette smokers

Authors: Parrott AC, Murphy RS

Summary: These researchers developed an explanatory leaflet to explain the deprivation reversal model to tobacco smokers and assessed its usefulness with 82 cigarette smokers. The leaflet significantly enhanced smokers' understanding, which was maintained 1 week later.

Comment: The authors of this paper tackle the belief that many smokers hold – that smoking relieves stress. For many smokers this is their experience and it is sometimes difficult to convince them otherwise. What many people don't realize is that it is the cigarette that has made them feel more stressed (and more depressed) in the first place. What smokers experience is the negative reinforcement of tobacco dependence; when they abstain they experience withdrawal symptoms, which can be stressful for many. When they then have a cigarette, they feel much better again. However, they are only experiencing alleviation of withdrawal, not alleviation of stress per se. I often try and communicate this message to people who are quitting smoking and who are often worried that they will become more stressed.

The authors designed a simple leaflet that communicated this messages – summarised at the end with five key messages – quit straight to the point “(1) There are no real mood benefits to nicotine, (2) Instead the nicotine habit makes cigarette smokers feel more stressed and depressed, (3) So if you are a smoker – then quit now, (4) It will be tough for a few weeks, (5) But after a few months you will feel better – both physically and mentally.”

Reference: *Hum Psychopharmacol.* 2012;27(2):150-5.

<http://onlinelibrary.wiley.com/doi/10.1002/hup.1247/abstract>

A Simple Offer

We knew brief medical advice to quit smoking increases quit attempts (by 24% actually).

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Systematic biases in cross-sectional community studies may underestimate the effectiveness of stop-smoking medications

Authors: Borland R et al

Summary: These researchers analysed data from the International Tobacco Control 4-country cohort study to examine the relationship between stop-smoking medications (SSMs; e.g., varenicline, bupropion, and over-the-counter nicotine replacement therapies), level of nicotine addiction, and the reported date since the start of participants' (n=1,101) most recent quit attempt.

Comment: A number of retrospective studies have found unassisted quitting to be more effective than assisted quit attempts. This finding may, in part, be biased by the ability of people to recall their quit attempts. Borland and colleagues explored differences in recall of quit attempts and level of addiction in those who tried to quit with help (used some sort of smoking cessation medicine) versus those that did not in a large sample of smokers from the International Tobacco Control Project. Essentially, those people who tried to quit with help were more likely to remember their quit attempt than those who tried to quit without (i.e., people who tried without help were less likely to recall quit attempts, so it would appear that those who are trying with help are failing more often). Of course, once you finally manage to quit there is no recall bias. Another important finding was that those who chose to use medicines to help them quit were more dependent smokers.

Reference: *Nicotine Tob Res.* 2012 Feb 7. [Epub ahead of print]

<http://ntr.oxfordjournals.org/content/early/2012/02/07/ntr.nts002.short?rss=1>

How much unsuccessful quitting activity is going on among adult smokers? Data from the International Tobacco Control Four Country cohort survey

Authors: Borland R et al

Summary: Data were analysed from 21,613 smokers recruited across 7 waves of the International Tobacco Control Policy Evaluation Four Country Survey (Australia, Canada, the UK and the US) to document the amount of quitting, length of quit attempts and prevalence of plans and serious thought about quitting among smokers. Around 40% of smokers report attempts to quit in a given year and report an average of 2 attempts. Based on free recall, this translates to an average annual quit attempt rate of 0.82 attempts per smoker. Estimates derived only from the preceding month to adjust for recall bias indicate an annual rate of approximately one attempt per smoker. There is a high prevalence of quit-related activity, with more than a third of smokers reporting thoughts or actions related to quitting in a given month. More than half the surveyed smokers eventually succeeded in quitting for at least 1 month, and a majority of these for over 6 months.

Comment: You often hear that the average number of quit attempts people make before they finally succeed is 14. You may not be surprised to hear that it is probably many more than this. In another paper by Ron Borland and colleagues it is estimated that the average smoker makes about 1 quit attempt every year. Therefore, your average 45-year-old smoker who started in their teenage years would have made over 25 unsuccessful quit attempts. The authors also raise an interesting point – should we be encouraging smokers to try less often but put in more effort to increase the chances of a successful attempt, or should we go with the approach where we encourage people to 'just keep on trying'?

A positive finding of this study was that many quit attempts last for at least a month. The key challenge is then to help these people stay stopped. More research on interventions designed to prevent relapse is urgently needed.

Reference: *Addiction.* 2012;107(3):673-82.

<http://onlinelibrary.wiley.com/doi/10.1111/j.1360-0443.2011.03685.x/abstract>

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