

Smoking Cessation Research Review™

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Issue 4 – 2011

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Welcome to the fourth edition of Smoking Cessation Research Review.

This edition leads with an investigation that found cytisine to be an effective aid to smoking cessation, in a well-designed placebo-controlled trial that limited behavioural support and the number of follow-up sessions to a minimum to simulate, as much as possible, what might happen in a routine clinical situation. This successful outcome, combined with the lower price of cytisine compared with that of other smoking cessation pharmacotherapies may make it an affordable treatment option for smokers in low-income and middle-income countries, suggest the study authors.

Could mobile phones help smokers quit smoking? This innovative approach appears to be a very successful one, according to the UK-based txt2stop trial, which involved almost 6,000 people. The trial consisted of an automated smoking cessation programme that sent motivational and supportive text messages to smokers. Quit rates were doubled at 6 months amongst these smokers, compared to the control group, which simply received fortnightly text messages thanking them for participating in the trial.

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

Kind regards,

Dr Chris Tofield

Medical Advisor, Research Review

christofield@researchreview.co.nz

Placebo-controlled trial of cytisine for smoking cessation

Authors: West R et al

Summary: This UK-based, single-centre trial randomised adults who smoked ≥ 10 cigarettes per day to receive cytisine (n=370) or matching placebo (n=370) for 25 days; participants in both groups received a minimal amount of counselling during the study. The primary efficacy outcome, 12 months of sustained smoking abstinence after the end of treatment, was achieved by 8.4% (n=31) of the cytisine group and by 2.4% (n=9) of the placebo group (p=0.001). The 7-day point prevalence for abstinence at the 12-month follow-up was 13.2% in the cytisine group versus 7.3% in the placebo group (p=0.01). No serious adverse effects were reported with cytosine. Minor gastrointestinal adverse events, mostly consisting of stomach ache, dyspepsia, and nausea, were reported more frequently in the cytisine group.

Comment: Cytisine has been used in Eastern European countries to help people stop smoking since the 1960's. It acts in a similar way to nicotine by binding to nicotinic acetylcholine receptors in the ventral tegmental area of the midbrain, giving rise to dopamine release in the nucleus accumbens. However, cytisine is not a full agonist like nicotine and so does not have the same rewarding properties. It is, however, enough to reduce tobacco withdrawal symptoms, making quitting easier. The earliest published research reports suggested that this compound was effective in increasing long-term abstinence rates. However, these early studies suffered with methodological problems. This current study by West and colleagues is of high methodological quality and uses strict outcome measures. The results show that cytisine, compared to placebo, is effective in increasing long-term quit rates. Although cytisine is available in countries such as Bulgaria and Poland, we are unlikely to see it more widely available until regulatory authorities are satisfied that it is effective and safe. A large randomised controlled trial, comparing cytisine with nicotine replacement therapy, is currently underway in New Zealand. The results of this study will help determine whether this promising medicine will be a welcome addition to our toolkit for helping people stop smoking.

Reference: *N Engl J Med.* 2011;365(13):1193-200.

<http://www.nejm.org/doi/full/10.1056/NEJMoa1102035?query=TOC>

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¹ www.pharmac.govt.nz/Schedule/SAForms. R&A number 221110A.

Smoking and prostate cancer survival and recurrence

Authors: Kenfield SA et al

Summary: These researchers examined the relation between cigarette smoking and smoking cessation with overall, prostate cancer-specific, and cardiovascular disease (CVD) mortality and biochemical recurrence among men with prostate cancer. Data were analysed from 5,366 men diagnosed with prostate cancer between 1986 and 2006 in the US Health Professionals Follow-Up Study. A total of 1,630 deaths occurred, 524 (32%) due to prostate cancer, 416 (26%) due to CVD, and 878 biochemical recurrences. Multivariate analysis revealed that compared with never smokers, current smokers had an increased risk of prostate cancer mortality (HR, 1.61), as did current smokers with clinical stage T1 through T3 (HR, 1.80), a higher risk of recurrence (HR, 1.61), total mortality (HR, 2.28), and CVD mortality (HR, 2.13). In analyses adjusted for clinical stage and grade, current smokers had an increased risk of prostate cancer mortality (HR, 1.38), as did current smokers with clinical stage T1 through T3 (HR, 1.41); they also had an increased risk of biochemical recurrence (HR, 1.47). Current smokers of ≥ 40 pack-years vs never smokers had increased prostate cancer mortality (HR, 1.82) and biochemical recurrence (HR, 1.48). Compared with current smokers, those who had quit smoking for ≥ 10 years (HR, 0.60), or who had quit for < 10 years but smoked < 20 pack-years (HR, 0.64), had prostate cancer mortality risks similar to never smokers (HR, 0.61).

Comment: Most New Zealanders who smoke are aware of at least a few of the many health risks associated with smoking. Lung cancer, for example, is commonly cited. However, the smoking-related risk of other cancers, such as those of the bladder and cervix, are less well known. Likewise, smoking increases the risk of prostate cancer, and this study shows that smoking at the time of diagnosis, compared to never smoking, increases the risk of recurrence of prostate cancer and mortality. However, mortality in those who had quit smoking (for 10 years or more, or less than 10 years in lighter smokers, at the time of diagnosis) was the same as never smokers. Interestingly, the risk of recurrence was unrelated to heaviness or length of time of smoking.

These findings represent another reason for men who smoke to quit.

Reference: *JAMA*. 2011;305(24):2548-55.

<http://jama.ama-assn.org/content/305/24/2548.abstract>

Association between smoking and risk of bladder cancer among men and women

Authors: Freedman ND et al

Summary: Data were analysed from 281,394 men and 186,134 women who had participated in the US National Institutes of Health-AARP Diet and Health Study and were followed-up between October 25, 1995, and December 31, 2006. During 4,518,941 person-years of follow-up, incident bladder cancer occurred in 3,896 men (144.0 per 100,000 person-years) and 627 women (34.5 per 100,000 person-years). Former smokers (119.8 per 100,000 person-years; HR, 2.22; number needed to harm [NNH], 1250) and current smokers (177.3 per 100,000 person-years; HR, 4.06; NNH, 727) had higher risks of bladder cancer than never smokers (39.8 per 100,000 person-years). In contrast, the summary risk estimate for current smoking in 7 previous studies (initiated between 1963 and 1987) was 2.94 ($F = 0.0\%$). The population attributable risks (PARs) for ever smoking were similar for men and women (0.50 and 0.52, respectively).

Comment: Carcinogens in tobacco smoking include substances such as tobacco-specific nitrosamines and beta-naphthylamine, the latter is a known carcinogen for bladder cancer. It is often said that smokers have a 3-fold increase in the risk of bladder cancer compared to never smokers. This large prospective cohort study showed that men and women who smoke have a 4-fold increase in risk of bladder cancer. So why the difference in risk between this and older studies? The authors hypothesise that changes in the constituents of cigarette smoke, including an increase in beta-naphthylamine, may be a causative factor.

In the past, PARs for tobacco smoking have been higher in men than women (50% vs. 20% respectively). In this case the PAR is the reduction in incidence of bladder cancer that would be expected if the population did not smoke. This study showed no difference in PARs between sexes (around 50% in both), possibly reflecting the equilibration of smoking prevalence in men and women. Reduction in the incidence of bladder cancer is just one of the many advantages of reducing smoking prevalence.

Reference: *JAMA*. 2011;306(7):737-45.

<http://jama.ama-assn.org/content/306/7/737.abstract>

The association between failed quit attempts and increased levels of psychological distress in smokers in a large New Zealand cohort

Authors: van der Deen FS et al

Summary: This investigation into the association of smoking status and quit status with psychological distress examined data from 18,525 adults surveyed over a single year of the Survey of Families, Income and Employment (SoFIE) conducted in New Zealand (2004/05). A total of 20% of the cohort were current smokers, 25% were ex-smokers and 55% were never smokers. Compared to never smokers, current smokers were much more likely to report high to very high levels of psychological distress (adjusted odds ratio [aOR] 1.45; 95% CI 1.24 to 1.69); the aOR was marginally significant for ex-smokers (1.18; 95% CI 1.00 to 1.39). Unsuccessful quitters had much higher levels of high to very high levels of psychological distress (16%) than any other group. Moreover, unsuccessful quitters were much more likely than long-term ex-smokers to experience high to very high levels of psychological distress (aOR 1.73; 95% CI 1.36 to 2.21).

Comment: It is known that levels of stress typically decrease in people who successfully quit smoking. Similar changes can be seen in levels of anxiety and depression. This cohort study looked at levels of psychological distress (PD) in four different groups – long-term ex-smokers; recent ex-smokers; unsuccessful quitters; and never smokers. Results show that current smokers were significantly more likely to report greater levels of PD than never smokers. Unsuccessful quitters show greater levels of PD than any other group. As would be expected, unsuccessful quitters were more likely to be from deprived backgrounds; however, after adjusting for these factors these smokers still had higher levels of PD. Data from this study also suggest that levels of PD decrease over time when people quit.

The authors suggest that the heightened PD could be alleviated by interventions that raise the odds of quitting smoking. A tailored approach could also be taken whereby those with already high levels of PD are recommended more intensive smoking cessation interventions. In addition, people can be reassured that stress will decrease the longer they go without smoking.

Reference: *BMC Public Health*. 2011;11:598.

<http://www.biomedcentral.com/1471-2458/11/598/abstract>

Smoking cessation support delivered via mobile phone text messaging (txt2stop): a single-blind, randomised trial

Authors: Free C et al

Summary: This UK trial randomly allocated smokers willing to make a quit attempt to the txt2stop programme (n=2,915) or a control group (n=2,885). The txt2stop group received motivational messages and behavioural-change support, whereas the control group received text messages unrelated to quitting. Data were available from 5,524 participants for the primary outcome (biochemically verified continuous abstinence at 6 months) and revealed that continuous abstinence was significantly increased in the txt2stop group (10.7% txt2stop vs 4.9% control, relative risk [RR] 2.20; $p < 0.0001$). Outcomes were similar when participants that were lost to follow-up were treated as smokers (268 [9%] of 2,911 txt2stop vs 124 [4%] of 2,881 control [RR 2.14; $p < 0.0001$]) and when they were excluded (268 [10%] of 2,735 txt2stop vs 124 [4%] of 2,789 control [2.20; $p < 0.0001$]).

Comment: Previous studies involving mobile-phone interventions have shown promising but unconvincing results. The results of this study tip the balance in favour of such interventions helping people quit smoking long term. Free and colleagues randomised 5,800 people who smoke to a text-based smoking cessation intervention (receiving 5e text messages per day for 5 weeks and then 3 per week for the following 26 weeks) or to a control group that received fortnightly text messages unrelated to quitting. Participants were followed up at 6 months and those who reported being abstinent had a saliva sample collected for cotinine analysis to verify smoking status.

Strict outcome measures were used and only those who reported being continuously abstinent for 6 months and had a salivary cotinine of < 7 ng/ml were considered to be abstinent. The results show those who received the txt2stop intervention were twice as likely to be abstinent at 6 months (11% versus 5%). This was a well-conducted and large study, giving us confidence in the effect of this simple and low-cost intervention.

Reference: *Lancet*. 2011;378(9785):49-55.

[http://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(11\)60701-0/abstract](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(11)60701-0/abstract)

Effects of smoking cessation on pain in older adults

Authors: Shi Y et al

Summary: This analysis of longitudinal biennial survey data from 1992 through 2006 collated by the nationally representative US Health and Retirement Study, involving adults aged >50 years, sought to determine the association between smoking cessation and changes in pain symptoms. In multivariate analyses, among the 4,695 smokers who reported no pain or mild pain at enrolment, no association was seen between smoking status and exacerbation of pain (odds ratio [OR]: 0.95; 95% CI 0.84 to 1.08). Among the 1,118 smokers who reported moderate to severe pain at enrolment, no association was seen between smoking status and improvement of pain (OR 0.87; 95% CI 0.70 to 1.08).

Comment: There is an association between smoking and pain. People who smoke are said to report higher levels of pain and often use smoking as a way of coping. There is often a worry that when people who smoke are forced to abstain (e.g. post-operatively in hospital) their perceived level of pain will be greater. This, in theory, may be due to the loss of mild analgesic properties of nicotine and the occurrence of tobacco withdrawal symptoms may add to the discomfort.

This study assessed the association between pain and smoking cessation in a cohort of older adults followed for 14 years. The investigators found that there was no association, positive or negative, between pain and smoking cessation. Factors such as not being depressed or having better health were better predictors of improvement of pain. Pain is a potential barrier for quitting, however, people can be reassured that pain will not worsen when they quit smoking.

Reference: Nicotine Tob Res. 2011;13(10):919-25.

<http://ntr.oxfordjournals.org/content/13/10/919.abstract>

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Competitions and incentives for smoking cessation

Authors: Cahill K, Perera R

Summary: This Cochrane Systematic Review included 19 studies (more than 4,500 smokers) that assessed the effects of competitions and incentives on long-term quit rates. The main outcome measure was abstinence from smoking for ≥ 6 months from the start of the intervention. Only one study, the largest in the review and covering 878 smokers, demonstrated significantly higher quit rates for the incentives group than for the control group beyond the 6-month assessment. This trial referred its participants to local smoking cessation services, and offered substantial cash payments (up to US\$750) for prolonged abstinence. No clear evidence was found in the remaining 18 trials to show that participants who committed their own money to the programme did better than those who did not, or that contingent rewards enhanced success rates over fixed payment schedules. There was some evidence that recruitment rates may be improved by rewarding participation, which may be expected to deliver higher absolute numbers of successful quitters, conclude the researchers.

Comment: Why not simply pay people to stop smoking instead of spending money on smoking cessation services? Well, the data presented in this Cochrane Systematic Review suggests that there is currently no evidence for this approach. Whilst incentives can promote abstinence, the effect generally disappears once payments stop. Only one of the 19 studies included showed any benefit on long-term quit rates, however, this was a large and well-conducted study. The investigators randomised workers at General Electric workplaces to an intervention where participants could 'earn' up to US\$750 if they completed a smoking cessation programme and sustained abstinence at 9 or 12 months. At this time point, more people in the intervention managed to quit compared to control (14.7% vs. 5.0%; $p < 0.001$) and this difference was still evident at 6 months after the final payment (9.4% vs. 3.6% $p = 0.001$). The other area where incentives may have a role to play is in helping pregnant women who smoke to quit. In fact, in the Cochrane review for smoking cessation interventions in pregnancy, financial incentives seemed to be the most effective, although there are several methodological limitations of these positive studies. In conclusion, there is currently little evidence to support the use of financial incentives for smoking cessation, however, this intervention shows enough promise to warrant further investigation.

Reference: Cochrane Database Syst Rev. 2011 Apr 13;(4):CD004307.

<http://www2.cochrane.org/reviews/en/ab004307.html>

Longitudinal study of smoking cessation before pregnancy and children's cognitive abilities at 56 months of age

Authors: Heinonen K et al

Summary: Outcomes are reported from a Finnish cohort of 1,019 children born at term and free of any major impairment who underwent cognitive assessment (child's general reasoning, visual-motor integration, verbal competence, and language comprehension) at 56 months of age. In analyses adjusted for potential confounders, compared with children of never smokers, children whose mothers smoked >10 cigarettes per day before pregnancy but none during pregnancy performed less well in general reasoning and in language comprehension tests, by 12.07 (95% CI 4.07 to 20.08) and 11.23 (95% CI 2.81 to 19.66) age-standardised points, respectively.

Comment: There is an inverse relationship between maternal cigarette consumption and cognitive abilities in children. This may be due to the effect of nicotine on the developing central nervous system. This study followed up 1,019 children, born at term, 4–5 years later to assess cognitive abilities (CAbs). Children with mothers who smoked more than 10 cigarettes per day before or during pregnancy had significantly lower CAbs than children with non-smoking mothers. Mothers who smoked <10 cigarettes per day, but quit during pregnancy had children with normal CAbs. However, for heavier smokers (>10 cigarettes per day), quitting during pregnancy made little difference to CAbs in their children.

These data should not be interpreted as showing no benefit of quitting during pregnancy for heavier smokers as there are many other health benefits of quitting before and during pregnancy. However, as the authors suggest, there is a need to target women of childbearing age and help them to quit smoking.

Reference: Early Hum Dev. 2011;87(5):353-9.

<http://www.earlyhumandev.com/article/S0378-3782%2811%2900130-7/abstract>



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Use of nicotine replacement after a smoking lapse

Author: Hughes JR

Summary: This US-based investigation considered information from 24 treatment smoking cessation programs or providers, treatment protocols, directors of quitlines and state programs, published treatment texts, and self-help manuals, books, and Internet sites, as to continued use of nicotine replacement therapy (NRT) post-relapse. The investigation also included responses from 101 current smokers who had attempted to stop smoking in the last 3 months and lapsed while using NRT, who were surveyed by an Internet consumer database (www.zoomerang.com). Most programs and providers (67%) did not discuss use of NRT post-lapse, and only 8% recommended continuing NRT post-lapse. Among recent quitters using NRT, about one-fourth (27%) stopped NRT on the day of the lapse, and one-fourth (25%) used NRT for only 1 or 2 days post-lapse. Most (73%) reported that use of NRT post-lapse was helpful.

Comment: Most people using NRT who lapse stop treatment. Possible reasons for this are a belief that smoking and using NRT concurrently is dangerous, and the abstinence violation effect (a lapse is seen as a failure and so people return to smoking). There are data to suggest that using NRT following a smoking lapse can prevent progression to full-blown relapse and people should be strongly encouraged to continue using NRT. However, the results of this survey suggest that this advice is not routinely given. Hughes makes an interesting, and perhaps obvious, comparison to treatments for other drug dependencies, e.g. clinicians would usually increase methadone dose in opioid-dependent people who relapse, and not stop treatment. People using NRT should be routinely advised to use it correctly, in sufficient doses, for long enough, and to carry on using it even if they slip.

Reference: *Nicotine Tob Res.* 2011 Sep 8. [Epub ahead of print]

<http://ntr.oxfordjournals.org/content/early/2011/09/08/ntr.ntr208.abstract>

Cessation assistance reported by smokers in 15 countries participating in the International Tobacco Control (ITC) policy evaluation surveys

Authors: Borland R et al

Summary: Data are reported from the 2007 survey wave of the International Tobacco Control Policy Evaluation Project surveys of smokers in Australia, Canada, China, France, Germany, Ireland, Malaysia, Mexico, Netherlands, New Zealand, South Korea, Thailand, UK, Uruguay and the USA. Self-reported prevalence rates of quit attempts in the last year varied from under 20% to over 50% across countries. Similarly, there was wide variation across countries in reporting of visiting health professionals in the last year (<20% to over 70%), and among those who did, provision of advice to quit also varied greatly. The levels and types of help reported varied markedly. Use of medication was generally more common than use of behavioural support, except where medications are not readily available.

Comment: This paper presents more data from the International Tobacco Control (ITC) Project and compares cessation support utilised by smokers across 15 countries. In 2007, the proportion of New Zealand smokers who have ever tried to quit was relatively low (60%) compared to other countries such as Australia, Canada, and the UK (all between 80–90%). However, the proportion that had tried to quit in the last year (40%) was similar, suggesting a recent increase in quit attempts. The highest level of advice from a health care professional was seen in the USA (around 50%), while approximately 25% of New Zealand smokers reported receiving advice from healthcare professionals. Use of smoking cessation medication in New Zealand was relatively low (around 25% versus 45% in Australia), especially considering the subsidy scheme that was in operation at the time. However, availability of low-cost treatments does not necessarily translate into high uptake.

New Zealand has seen a number of important changes in smoking cessation since 2007, e.g. a national health target 'Better help for smokers to quit' was introduced in 2009. The aims of this are to prompt more quit attempts and use of effective treatments. Future surveys will show whether we have been able to achieve these aims.

Reference: *Addiction.* 2011 Aug 28. [Epub ahead of print]

<http://onlinelibrary.wiley.com/doi/10.1111/j.1360-0443.2011.03636.x/abstract>

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 Senior Clinical Research Fellow post within the UK Centre for Tobacco Control Studies Queen Mary University of London.

Conflict of interest statement: Dr McRobbie has received research funding from, and provided consultancy to, manufacturers of smoking cessation medications.

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