Welcome to the eleventh issue of Smoking Cessation Research Review.

The results of an American study that we discuss in this issue have relevance for New Zealand prisons. The study describes how a behavioural intervention provided to inmates prior to release decreases relapse to smoking after their release from a smoke-free prison – forced tobacco abstinence alone during incarceration has little impact on postrelease smoking status.

In another study, combining nicotine patches with varenicline had no beneficial or detrimental effect on urges to smoke, withdrawal discomfort, abstinence rates, or adverse effects profile.

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

Kind Regards,
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In this issue:
- Relapse to smoking after release from a smoke-free prison
- NRT + varenicline: lack of synergy
- Delivering smoking cessation counselling in the ED
- Mass intervention approach assists quitting
- e-cigarettes decrease cigarette consumption
- Wide support for rigorous tobacco control measures
- Varenicline + adjuvant therapy may improve quit rates
- Cigarette smoking and risk of breast cancer
- Use and acceptability of e-cigarettes in NZ
- Pharmacological interventions for smoking cessation

Abbreviations used in this issue
ED = emergency department
NRT = nicotine replacement therapy

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HELP KIWIS BECOME SMOKEFREE NOW AND NZ CAN BE SMOKEFREE BY 2025.

At 12 weeks, smokers are 4x more likely to quit with Champix than if they had taken placebo^”

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**Is a combination of varenicline and nicotine patch more effective in helping smokers quit than varenicline alone?**

**Authors:** Hajek P et al

**Summary:** 117 subjects seeking help to stop smoking were randomly allocated to varenicline plus placebo patch or varenicline plus nicotine patch (15 mg/16 hour). Varenicline was started one week prior to the target quit date (TQD), patch use started on the TQD. Rates of medication use were high for both groups during the first week after the TQD (92%). Combination treatment was not associated with any increase in nausea or other adverse effects. It had no overall effect on urges to smoke or on other withdrawal symptoms and did not improve biochemically-validated abstinence rates at 1 week and 4 weeks post-TQD (69% vs 59%; p=0.28 and 60% vs 59%; p=0.01, in the nicotine patch and placebo patch arm, respectively), or self-reported abstinence rates at 12 weeks (36% vs 29%; p=0.39).

**Comment (NW):** One approach to enhance quit rates is to combine pharmacotherapies that have different modes of action, e.g. combining a slow delivery long-acting NRT (patch) with a fast delivery short-acting NRT (oral or nasal NRT) increases quit rates over and above a single type of NRT. It is known that nAChR partial agonists (like varenicline) do not saturate all nicotine receptors and smokers may get better relief from withdrawal and craving symptoms if they use a nAChR partial agonist in combination with NRT. Unfortunately, the results of this trial do not support this hypothesis, although the authors acknowledge that this proof of concept trial may have been too small to detect the true difference. Before completely dismissing this intervention, we must await the results of a much larger trial (n=544) currently underway in South Africa comparing 12 weeks of standard varenicline treatment combined with 15mg NRT patch (with the patch offered two weeks prior to the target quit date) to varenicline alone.

**Reference:** BMC Med 2013;11:1140
http://www.biomedcentral.com/1741-7015/11/140

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**The Emergency Department Action in Smoking Cessation (EDASC) trial: impact on cessation outcomes**

**Authors:** Katz DA et al

**Summary:** This US study evaluated the effectiveness of an emergency nurse-initiated intervention targeting the delivery of smoking cessation counselling based on the 5As framework (ask-advises-assist-arrange). The study also assessed emergency department (ED) nurses’ and physicians’ perceptions of smoking cessation counselling. A total of 789 adult smokers (≥5 cigarettes/day) were recruited upon presentation to two EDs. The intervention focused on improving delivery of the 5As by ED nurses and physicians and included face-to-face training and an online tutorial, use of a charting/reminder tool, fax referral of motivated smokers to the state tobacco quitline for proactive telephone counselling, and group feedback to ED staff. Telephone interviews of 650 smokers soon after the ED visit revealed that a greater proportion had been asked about smoking by an ED nurse (68% vs 53%), assessed for willingness to quit (31% vs 9%), assisted in quitting (23% vs 6%) and had arrangements for follow-up cessation counselling (7% vs 1%) during the intervention compared to the baseline period. Survey feedback revealed a significant improvement in ED nurses’ self-efficacy and role satisfaction in cessation counselling post-intervention, although there was little change in their attitudes (i.e. “pros” and “cons”) towards smoking cessation.

**Comment (NW):** Attendance at an ED, irrespective of presenting condition, offers a ‘teachable moment’ around being smokefree (be that as a household and/or as a personal state). However, how to give interrogated brief cessation advice within a busy and stressful ED environment is difficult. This study has shown that a brief intervention based on the 5As (which is similar to NZ’s ABC smoking cessation support) can be successfully integrated into an ED environment if sufficient resources are provided (in this instance it was nursing time), plus if people are receptive. Make use of the time people spend sitting around a waiting room. Even in people who smoke but are unmotivated to quit, a brief cessation intervention can elicit more spontaneous quitting behaviour. Research is currently being undertaken by the University of Auckland, in conjunction with Starship Children’s Hospital ED, specifically looking at this issue in families of children presenting with acute respiratory illness.

**Reference:** Acad Emerg Med 2012;19(4):409-20

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**Reach and effectiveness of mailed nicotine replacement therapy for smokers: 6-month outcomes in a naturalistic exploratory study**

**Authors:** Zawertailo L et al

**Summary:** These researchers provided 14,000 treatments of 5 weeks in duration of either nicotine patch (n=10,000) or nicotine gum (n=4000) to all eligible adult smokers in Ontario, Canada, who called a toll-free number to register with the STOP (Smoking Treatment for Ontario Patients) Study and receive a single brief intervention. The aim of this study was to determine the effectiveness of free nicotine replacement therapy (NRT), brief advice and self-help materials on quit attempts and 6-month quit rates in motivated smokers. 16,405 callers were assessed and 13,143 eligible participants were mailed a treatment package with 5 weeks of NRT (choice of patch or gum), self-help and community resource materials. At 6 months, complete follow-up data were available for 2601 participants, 21.4% of whom self-reported as being abstinent. In contrast, 11.6% quit rates were reported by a concurrent no-intervention cohort of Ontario smokers matched for eligibility (rate ratio of 1.84). Thirty-day point prevalence rates were 17.8% and 9.8% for the intervention and no-intervention cohorts, respectively (rate ratio 1.81).

**Comment (NW):** This simple but effective study supports similar research undertaken in NZ within primary care, which showed that sending a smoker an unsolicited personalised letter from their GP giving written quit advice plus information about direct support and access to subsidised NRT (via an enclosed Quitcard), can prompt a quit attempt in almost 10% of recipients regardless of their motivation to quit. More efforts need to be made in NZ to utilise such mass intervention approaches that could be repeated at regular intervals.

**Reference:** Tob Control 2013;22(3):e4
http://tobaccocontrol.bmj.com/content/early/2012/04/10/tobaccocontrol-2011-050303

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**Smoking Cessation Research Review**

**Independent commentary by Brent Caldwell.**

Brent Caldwell is a Senior Research Fellow at Wellington Asthma Research Group, he is currently working on the Whistle Study. His main research interest is in identifying and testing improved smoking cessation methods, with a particular focus on clinical trials of new smoking cessation pharmacotherapies.

**Independent commentary by Dr Natalie Walker.**

Dr Natalie Walker is an epidemiologist and leader of the Addiction Research programme at the National Institute for Health Innovation, University of Auckland. Natalie joined the University in 1995, and completed a PhD in cardiovascular epidemiology in 2000. Natalie currently holds a Heart Foundation Douglas Senior Fellowship in Heart Health (Prevention). Her primary area of interest is the conduct of phase III, community-based, clinical trials, particularly in the fields of smoking cessation, alcohol consumption, and heart health. She is a member of the Society for Research on Nicotine and Tobacco, and a board member of ASH.

Research Review publications are intended for New Zealand health professionals.

**Disclosure Statement:** Natalie Walker has provided consultancy to the manufacturers of smoking cessation medications, received honoraria for speaking at a research meeting and received benefits in kind and travel support from a manufacturer of smoking cessation medications. Natalie has also undertaken two trials of very low nicotine content cigarettes, which were purchased from two different tobacco companies. The companies concerned had no role in development of the study design, data collection, data analysis, data interpretation, or writing of the trial publications.
Support for a tobacco endgame and increased regulation of the tobacco industry among New Zealand smokers: results from a National Survey

Authors: Edwards R et al

Summary: Survey results are reported from 2299 adult smokers participating in the New Zealand arm of the International Tobacco Control Policy Evaluation Survey during 2007–2009. Responses indicated that the majority (65%) supported greater regulation of the tobacco industry and 59% supported more government action on tobacco. Almost half (46%) supported a ban on cigarette sales in 10 years’ time, provided effective nicotine substitutes were available. In multivariate analyses adjusted for potential confounders, Maori ethnicity, experience of financial stress and greater awareness about the harms of smoking were all found to be significantly associated with support for greater tobacco company regulation. Factors significantly associated with support for a ban on tobacco sales in 10 years’ time included increasing area-based deprivation level, increasing intention to quit and greater concern about the health effects of smoking.

Reference: Tobacco Control 22(e1):e86-e93
http://tobaccocontrol.bmj.com/content/early/2012/04/24/tobaccocontrol-2011-050324

Effectiveness of coadministration of varenicline, bupropion, and serotonin reuptake inhibitors in a smoking cessation program in the real-life setting

Authors: Issa JS et al

Summary: This study involved 427 patients in a specific cardiovascular smoking cessation service who were treated with varenicline for 12 weeks as monotherapy or in combination with pharmacotherapy. Patients were followed for 52 weeks. At each medical visit, the patients were evaluated and in those experiencing mood changes after varenicline use, serotonin reuptake inhibitors (SRIs) were prescribed. Bupropion was added for those who failed to achieve complete tobacco abstinence in 2 or 3 weeks after starting varenicline use or if the patient presented uncomfortable abstinence symptoms. At 52 weeks, continuous abstinence rates by regimen were: varenicline monotherapy (32.1%), varenicline + bupropion (55.0%), varenicline + SRI (50.6%), and varenicline + bupropion + SRI (57.7%). In a multivariate analysis of successful treatment predictors, compared with varenicline monotherapy, using bupropion + SRI adjuvant treatment was associated with an odds ratio of 5.05 for a successful treatment response after 1-year follow-up, while patients who used bupropion or SRI had ORs of 3.21 and 3.58, respectively.

Comment (BC): Although the majority of New Zealand smokers support the goals of the SmokeFree2025 Vision, it is important to note that this support was predicated on increased availability of effective nicotine substitutes. Simply reducing the supply of tobacco (which would inevitably increase its price) would not be supported by smokers, and would be punitive. Tobacco addiction, like all addictions, is a “primary, chronic disease of brain reward, motivation, memory and related circuitry”, it is a physical disease, and requires physical chemical therapies. Greater access to more effective nicotine delivery devices is essential to give smokers a genuine replacement for their cigarettes.

http://ntr.oxfordjournals.org/content/15/6/1146.abstract

Efficiency and safety of an electronic cigarette (ECLAT) as tobacco cigarettes substitute: a prospective 12-month randomized control design study

Authors: Caponnetto P et al

Summary: 12-month outcomes are reported from ECLAT, a prospective randomised, controlled trial designed to evaluate smoking reduction/abstinence in 300 smokers not intending to quit experimenting with two different nicotine strengths of a popular electronic cigarette (e-cigarette) model (‘Categoria’; Arbi Group Srl, Italy) compared to its non-nicotine choice. Group A (n=100) received 7.2 mg nicotine cartridges for 12 weeks; Group B (n=100) received 7.2 mg nicotine cartridges for 6 weeks then 5.4 mg nicotine cartridges for a further 6 weeks; Group C (n=100) received no-nicotine cartridges for 12 weeks. Declines in cig/day use and exhaled carbon monoxide (eCO) levels were observed upon 9 study visits in all participants (p<0.001 vs baseline), with no consistent between-group differences. Smoking reduction was documented in 22.3% and 10.3% at weeks 12 and 52, respectively; corresponding values for complete abstinence from smoking were 10.7% and 8.7%, respectively. A substantial decrease in adverse events from baseline was observed and acceptance of the product under investigation was satisfactory.

Comment (NW): It is important to note that this is a proof of concept trial and as such, was not powered to detect any differences between the groups. Consequently, ‘too small a sample size’ may be one of the explanations for why the initial statistically significant difference in abstinence observed at 12 weeks (end of treatment), was not sustained at 6 and 12 months. The findings should not, however, be ignored – this is the first trial to show that e-cigarettes (irrespective of whether they contain nicotine or not) can help people unmotivated to quit to stop smoking. What remains unanswered is whether quit rates are higher than those using no intervention. Furthermore, in smokers who are motivated to quit it is not known what the effect is of using e-cigarettes (nicotine and non-nicotine) compared to proven smoking cessation treatments (e.g. NRT) on short and long-term abstinence. A well-powered, e-cigarette smoking cessation trial currently underway at the University of Auckland will be able to answer the latter question – results are due out in September.

http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0066317

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Dr Simon Meech, Dee Street Medical Centre, Mt Maunganui and Dr Alastair McDonald, Mercury Bay Medical Centre, Whitianga who both won an iPad mini 32GB with WiFi plus cellular by subscribing to www.researchreview.co.nz

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Cigarette smoking and risk of breast cancer in a New Zealand multi-ethnic case-control study

Authors: McKenzie F et al

Summary: This investigation sought to determine the effect of smoking behaviours on the risk of breast cancer among three ethnic groups of New Zealand women. 1799 breast cancer cases (302 Māori, 70 Pacific, 1427 non-Māori/non-Pacific) registered on the New Zealand Cancer Registry between 2005 and 2007 were matched with 2540 controls (746 Māori, 191 Pacific, 1603 non-Māori/non-Pacific) by ethnicity and 5-year age-group. No clear association was observed between smoking and breast cancer for non-Māori/non-Pacific women, although non-Māori/non-Pacific ex-smokers were at significantly higher risk of breast cancer when smoking duration was >20 years, and this remained significant in the fully adjusted model (OR 1.31). Māori showed more consistent increased risk of breast cancer with increasing duration among current smokers (<20 years OR 1.61; 20+ years OR 2.03). Among all ethnic groups, the data clearly showed that shorter duration since smoking cessation was associated with increased likelihood of breast cancer.

Comment (BC): The fact that smoking at any stage is a particularly strong risk factor for breast cancer among Māori women could be used by clinicians and health promoters to encourage Māori women to quit smoking. Other studies have suggested that the amount smoked prior to first childbirth has a long-lasting effect on risk of breast cancer, and that breast-feeding has a protective effect, which may explain the high impact of smoking on breast cancer risk among Māori in this study, and suggests that public health interventions should focus on young Māori women before they become pregnant.

http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0063132

The use and acceptability of electronic cigarettes among New Zealand smokers

Authors: Li J et al

Summary: Responses were analysed from 840 current smokers and recent quitters aged ≥18 years participating in the New Zealand Smoking Monitor (NZSM), a 33-item telephone-based survey undertaken in 2011 and 2013 that was designed to elucidate New Zealanders’ use, perceptions and views on the acceptability of e-cigarettes. Few respondents (7%) reported having purchased an e-cigarette. One-third of respondents (n=158) believed Zealanders’ use, perceptions and views on the acceptability of e-cigarettes. Few respondents (7%) reported having purchased an e-cigarette. One-third of respondents (n=158) believed e-cigarettes were safer than tobacco cigarettes, and could help people quit smoking tobacco. Forty-one percent considered it acceptable to use e-cigarettes as a replacement product and 58% as a cessation aid. Responses differed by ethnicity, age and household income.

Comment (BC): Although there is insufficient evidence about the efficacy and safety of e-cigarettes, it is unlikely that they would cause harm. Pulmonary delivery is required to replicate smoking’s rapid rewarding delivery of nicotine to the brain. However, the pulmonary nicotine dose depends greatly on the brand of e-cig and whether it is puffed often enough for it to form sufficiently small particles. The interest of low-income smokers in switching to e-cigs if they were cheaper than smoking provides an ideal opportunity for promoting e-cig-assisted smoking cessation, if e-cigs are proven to be safe and effective.


Pharmacological interventions for smoking cessation: an overview and network meta-analysis

Authors: Cahill J et al

Summary: This overview of 12 treatment-specific Cochrane reviews involved 267 randomised trials (101,804 participants). The effectiveness of nicotine replacement therapy (NRT), bupropion and varenicline were compared with each other and with placebo in achieving long-term abstinence (>6 months). Other therapies were also investigated for effectiveness, and the results are reported in the article. It also examined the risks of adverse and serious adverse events relating to each treatment, and found that the current evidence does not mitigate the use of any of the treatments.

Comment (BC): Varenicline monotherapy and the combination of patch plus other NRT produce the highest abstinence rates. If smokers have contraindications or tolerability issues with one of these treatments, they could use the other and have equal chance of success. Smokers who cannot tolerate varenicline or nicotine patches should be offered the other nicotine replacement therapies to use as monotherapy or in combination with each other, bearing in mind that nicotine gum was the least effective. Alternatively, they could use nortriptyline if they can tolerate it, or bupropion with only a marginally smaller chance of abstinence, and cytisine when it becomes available.

Reference: Cochrane Database Syst Rev 2013;5:CD009329

A Simple Offer

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

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