Smoking Cessation Research Review™

Making Education Easy

Issue 21 – 2016

In this issue:

- *Smoking increases risk of complications after THA/TKA*
- *Future regulatory options for e-cigs in NZ*
- *E-cigarette labelling noncompliant with EU/UK legislation*
- *Self-help booklets do not reduce relapse in short-term quitters*
- *Identifying intervention components for smoking cessation*
- *Extended medication helps maintain abstinence*
- N-*acetylcysteine may maintain smoking abstinence*
- *Perceived harm of e-cigs may impede switching*
- *Females rate nicotine e-cigs more highly than males*

Abbreviation used in this issue
THA/TKA = total hip/knee arthroplasty

CLICK HERE
to read previous issues of
Smoking Cessation Research Review

Welcome to issue 21 of Smoking Cessation Research Review.

The importance of providing smoking cessation support services within hospitals is illustrated by evidence from the Mayo Clinic linking current tobacco smoking to an increased risk of deep infection and implant revision after total joint arthroplasty.

A group of researchers from the University of Otago, Wellington, outline various potential regulatory options that the New Zealand Government could consider to ensure that e-cigarettes make a positive contribution to the achievement of the smokefree nation 2025 goal. Another investigation that we also discuss in this review reports that the majority of e-liquids and e-cigarettes manufacturers/distributors do not fully comply with currently enforced regulations in the UK.

Disappointingly, UK-based researchers report that a comprehensive self-help educational programme to teach people skills to identify and respond to high-risk situations for return to smoking did not reduce relapse following smoking cessation treatment. However, more promisingly, a study from the USA reports that extended medication (26 weeks) with nicotine patch or gum improves abstinence rates in adult smokers motivated to quit smoking.

We hope you enjoy the selection in this issue, and we welcome any comments or feedback.

Kind Regards,

Brent Caldwell
brentcaldwell@researchreview.co.nz

Natalie Walker
nataliewalker@researchreview.co.nz

Independent commentary by Dr Brent Caldwell.
Brent Caldwell is a Senior Research Fellow at Wellington Asthma Research Group, he is currently working on the Inhale 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 Honorary Associate Professor 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. **FOR FULL BIO CLICK HERE.**

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.

Current tobacco use is associated with higher rates of implant revision and deep infection after total hip or knee arthroplasty: a prospective cohort study

Authors: Singh JA et al.

Summary: In this study, postoperative complications were analysed from a cohort of patients who underwent primary total hip arthroplasty (THA) or total knee arthroplasty (TKA) at the Mayo Clinic from 2010–2013. Smokers were defined as patients who reported using cigarettes, cigars, pipes, or smokeless tobacco at the time of index THA or TKA; non-smokers were defined as former smokers or never-smokers. Of all 7926 study participants, 565 (7%) were current tobacco users. Compared to non-users, current tobacco users were more likely to be male ($p<0.001$), less likely to be obese ($p\leq0.008$), aged >60 years, have a Charlson score >0 or have undergone TKA rather than THA ($p<0.001$ each). The hazard ratios for deep infection (2.37; 95% CI, 1.19 to 4.72; p=0.01) and implant revision (1.78; 95% CI, 1.01 to 3.13; p 0.04) were higher in current tobacco users than in non-users. No significant differences were noted for periprosthetic fractures or superficial infections.

Comment (NW): It is well documented that current smokers are more likely to experience wound-related postoperative complications, but less is known about the effects of smoking on other surgical outcomes. The novel aspect of this study is that it highlights that current smokers undergoing hip or knee replacement are also at risk of 'adverse functional outcomes' that require additional surgical intervention – a costly exercise that patients and DHBs will want to avoid. This study provides yet another reason why smoking cessation support services within hospitals are so important.

Reference: BMC Medicine. 2015;13:283
Abstract

Potential new regulatory options for e-cigarettes in New Zealand

Authors: Wilson N et al.

Summary: This article explores various regulatory options that the New Zealand Government could consider for changing the regulation around nicotine-containing e-cigarettes, to ensure that these products could make a positive contribution to the achievement of the smokefree nation 2025 goal. Plausible options include: (1) a full free market for increasing access to e-cigarettes; (2) controlled increased access through: (a) pharmacy-only sales, (b) pharmacy-only plus sales by prescription via a registered health professional/access from 'licensed vapers'; (c) additional controls through non-profit supply/distribution (e.g. public hospital pharmacies); (3) increased restrictions compared with current (e.g. via a complete ban on self-imports and use). The article also considers mechanisms to improve product quality and safety, and argues that policy makers should take great care when regulating e-cigarettes, given the scientific uncertainty and the role of commercial vested interests amongst some participants in the e-cigarette domain (e.g. e-cigarette companies and some tobacco companies that own e-cigarette brands).

Comment (NW): Governments and members of the tobacco control community around the world are struggling with whether e-cigarettes need to be regulated in any way – there are many views and opinions (often quite polarised). The struggle is that there is little good quality data (and a lot of poor quality data) on which to base any decision, and so many views are opinion-based. I suspect there would have been more acceptance of these nicotine-delivery devices if they had been promoted under a different name and were created by a pharmaceutical company. This paper offers some future regulatory options for e-cigarettes. There are other options as well, but these are a good starting point for discussion.

Reference: N Z Med J. 2015;128(1425):88-96
Abstract

Labelling of electronic cigarettes: regulations and current practice

Authors: Buonocore F et al.

Summary: This paper describes compliance of marketed e-liquids and e-cigarettes with current European Union and UK legislation. From May 2016, safe handling and disposal of liquids and cartridges will be regulated by European Community Directives (ECDs) 2001/83/EC and 93/42/EEC, or 2014/40/EU if marketed as tobacco-related products. Currently, manufacturers and distributors must abide by the Chemical (Hazard Information and Packaging for Supply) Regulations 2009 (CHIP) or Classification, Labelling and Packaging Regulations (CLP), the latter replacing CHIP in June 2015. This evaluation included 21 e-liquid brands and 9 e-cigarette brands. There was evidence of non-compliance in relation to the CHIP/CLP toxic (13%) and environmental (37%) pictograms, tactile warning (23%), nominal amount of solution (30%), and supplier contact telephone number and address (40%). None of the evaluated e-cigarettes displayed information on the correct disposal/recycling of batteries in line with the ECD 2006/66/EC.

Comment (NW): Since the arrival of e-cigarettes the scientific community has raised concerns over the safety and general poor quality of many of the devices. In 2013, the Medicines and Healthcare Products Regulatory Agency (MHRA) in the UK announced that e-cigarettes will be fully regulated by 2016, and until such time various other rules and regulations are in force that e-cigarettes are expected to comply with to ensure their safe handling and disposal. This paper highlights that the majority of e-cigarettes reviewed didn't comply with any of the current and proposed regulation. Furthermore, enforcement of the regulations is likely to be difficult for local authorities given the large on-line e-cigarette market. I'm sure the scenario is no different in New Zealand.

Reference: Tob Control. 2016 Jan 20. [Epub ahead of print]
Abstract

Self-help educational booklets for the prevention of smoking relapse following smoking cessation treatment: a randomized controlled trial

Authors: Maskrey V et al.

Summary: This study recruited people who stopped smoking for 4 weeks after receiving behavioural and pharmacological cessation treatment in smoking cessation clinics in the UK. The experimental group (n=703) was mailed 8 booklets, each of which taught readers how to resist urges to smoke. The control group (n=704) received a leaflet currently used in practice. There were no statistically significant between-group differences in prolonged carbon monoxide-verified abstinence from months 4 to 12 (36.9% vs 38.6%; odds ratio [OR] 0.93, 95% CI, 0.75 to 1.16; p=0.524). In addition, there were no significant differences between the groups in any secondary outcomes, which included 7-day self-reported abstinence at 3 and 12 months. However, people who reported knowing risky situations for relapse and using strategies to handle urges to smoke were less likely to relapse.

Comment (NW): Often we focus more on supporting people to quit smoking and less on helping to prevent relapse back to smoking. Few clinical trials have focussed on relapse prevention, which is why it's so nice to see this paper. A large trial, a low-cost and simple behavioural intervention, and reasonably good compliance with having read the material – unfortunately, no effect was observed. This finding is consistent with that reached by a Cochrane review on the topic – namely, there is "*insufficient evidence to support the use of any specific behavioural intervention to help smokers who have successfully quit for a short time to avoid relapse*".

Reference: Addiction. 2015;110(12):2006-14
Abstract

Identifying effective intervention components for smoking cessation: a factorial screening experiment

Authors: Piper ME et al.

Summary: This study was conducted in southern Wisconsin, USA, and involved 637 adult smokers (55% women, 88% white) motivated to quit smoking who visited primary care clinics. The researchers evaluated six intervention components intended to help smokers to attain and maintain abstinence in their quit smoking attempts: (1) preparation nicotine patch versus none; (2) preparation nicotine gum versus none; (3) preparation counselling versus none; (4) intensive cessation in-person counselling versus minimal; (5) intensive cessation telephone counselling versus minimal; and (6) 16 versus 8 weeks of combination nicotine replacement therapy (NRT; nicotine patch + nicotine gum). The primary outcome was 7-day self-reported point-prevalence abstinence at 16 weeks. Preparation counselling significantly improved abstinence rates at week 16 (p=0.04), while both forms of preparation NRT interacted synergistically with intensive cessation in-person counselling (p<0.05). In contrast, intensive cessation phone counselling combined with intensive cessation in-person counselling interacted antagonistically (p<0.05); smoking abstinence rates were higher when these components were used separately than when they were combined.

Comment (BC): Although the results are presented very confidently, this is just a hypothesis-generating trial, woefully underpowered, so that none of its findings would remain statistically significant after correcting for multiple comparisons. Very interesting that face-to-face counselling plus telephone counselling resulted in lower quit rates than either intervention on its own. This could be due to the combination being too burdensome on patients, or perhaps the two services gave conflicting advice? I eagerly await further trials to see if the results of this trial are replicated.

Reference: Addiction. 2016;111(1):129-41
Abstract

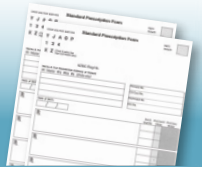
Comparative effectiveness of intervention components for producing long-term abstinence from smoking: a factorial screening experiment

Authors: Schlam TR et al.

Summary: As with the previous trial, this study was undertaken in Wisconsin, USA, and recruited smokers during primary care visits who were motivated to quit. Of the 544 participants, 59% were women and 86% were white. These researchers assessed five intervention components designed to help smokers attain and maintain abstinence: (1) extended medication (26 vs 8 weeks of nicotine patch + nicotine gum); (2) maintenance (phone) counselling versus none; (3) medication adherence counseling versus none; (4) automated (medication) adherence calls versus none; and (5) electronic medication monitoring with feedback and counselling versus electronic medication monitoring alone. The primary outcome was 7-day self-reported point-prevalence abstinence 1 year after the target quit day. Extended medication was the only intervention that resulted in a main effect. Twenty-six versus 8 weeks of medication improved point-prevalence abstinence rates (43% vs 34% at 6 months; 34% vs 27% at 1 year; p=0.01 for both). There were four interaction effects at 1 year, showing that an intervention component's effectiveness depended upon the components with which it was combined.

Comment (BC): It is interesting that this trial found that extended treatment (26 weeks cf. 8 weeks) with patch or gum was effective, whereas the previous trial by Piper and colleagues that I reviewed in this issue of *Smoking Cessation Research Review*, which compared 16 weeks cf. 8 weeks, found no improvement in abstinence. In my experience, New Zealand smokers are very keen to discontinue NRT earlier than recommended; this provides further evidence that we can use to encourage smokers to use long-term NRT. The study by Piper et al. was terribly underpowered, and would require very small p-values due to multiple comparisons. An example of why it is important to adjust for multiple comparisons can be seen by the non-intuitive finding in Piper's study of a p=0.02 interaction, suggesting that people who receive medication adherence counselling plus an electronic medication dispenser had lower abstinence than those who received just one or other of those interventions.

Reference: Addiction. 2016;111(1):142-55
Abstract



The effects of *N*-Acetylcysteine on frontostriatal resting-state functional connectivity, withdrawal symptoms and smoking abstinence: A double-blind, placebo-controlled fMRI pilot study

Authors: Froeliger B et al.

Summary: This study examined the effects of *N*-acetylcysteine on frontostriatal resting-state functional connectivity (rsFC), nicotine-withdrawal symptoms and maintaining abstinence in a cohort of 16 healthy adult, non-treatment seeking smokers (mean age 36.5 years; mean 15.8 cigarettes/day; mean 15.7 years/smoking). Participants received either 2400 mg *N*-acetylcysteine (1200 mg twice daily; n=8) or placebo (n=8) over 3½ days of monetary-incentivised smoking abstinence. On each abstinent day, mood and craving were measured and participants were tested for exhaled carbon monoxide levels. On day 4, participants were subjected to functional magnetic resonance imaging (fMRI) scanning. Compared with placebo, *N*-acetylcysteine helped to maintain abstinence, reduce craving and produce a higher positive affect (all p values <0.01), and was associated with stronger rsFC between the ventral striatal nodes, medial prefrontal cortex and precuneus-key default mode network nodes, and the cerebellum (p<0.025).

Comment (BC): This evidence that *N*-acetylcysteine influences neural pathways involved in drug abuse, increases short-term abstinence, and improves withdrawal symptoms and mood is really exciting! *N*-acetylcysteine does not occur in nature, and is known to cause nausea; hopefully, future randomised controlled trials find that it is both effective and tolerable. Great to know that there are still some potentially more effective therapies out there.

Reference: Drug Alcohol Depend. 2015;156:234-42
Abstract

Perceived relative harm of electronic cigarettes over time and impact on subsequent use. A survey with 1-year and 2-year follow-ups

Authors: Brose LS et al.

Summary: Data are reported from a web-based survey of British smokers and ex-smokers followed annually in 2012, 2013 and 2014; of 4553 respondents in 2012, 44% and 31% responded in 2013 and 2014, respectively. The study assessed perception of the relative harm of electronic (e)-cigarettes versus tobacco cigarettes at all three waves, as well as e-cigarette use and smoking status. Perceived relative harm changed significantly over time (p<0.001); the proportion perceiving e-cigarettes to be less harmful than cigarettes decreased from 2013 to 2014 (p<0.001). Previous perception of e-cigarettes as less harmful, having tried e-cigarettes and having stopped smoking between waves predicted perceiving e-cigarettes as less harmful than cigarettes. In multivariate analysis adjusting for demographics and smoking status, accurately perceiving e-cigarettes as less harmful than cigarettes predicted subsequent use of e-cigarettes (OR 1.39; 95% CI, 1.08 to 1.80; p=0.011).

Comment (BC): The finding that people who believe electronic cigarettes are less harmful than cigarettes, and had greater satisfaction from trying an electronic cigarette, were more likely to change their smoking habits and have lower scores on the Fagerström test for nicotine dependence (FTND), would not surprise me had they been able to continue to use nicotine electronic cigarettes to help them quit, but subjects in this trial only used nicotine electronic cigarettes once. Perhaps the biological mechanism behind this observation is that smokers for whom the amount of satisfaction they get from their brand of cigarette is not so dependent on its sensory and psychological effects, that they can readily gain satisfaction from an alternative nicotine device with different sensory effects, are more able to forgo the pleasure of their own brand and are therefore better able to quit. Although definitive evidence of the safety of electronic cigarettes is required, surely we know enough to suggest that theoretically electronic cigarettes are unlikely to be more dangerous than smoking, or any harder to quit than smoking, so would we really be worse off if all smokers switched to electronic cigarettes?

Reference: Drug Alcohol Depend. 2015;157:106-11
Abstract

Gender differences in satisfaction ratings for nicotine electronic cigarettes by first-time users

Authors: Grace RC et al.

Summary: In this study, 357 New Zealand smokers with no intention to quit were interviewed in November-December 2012 and tried a nicotine e-cigarette (NEC) for the first time, which they rated in addition to their own-brand tobacco for satisfaction on a 10-point visual analogue scale. NECs were rated 83.3% as highly as own-brand tobacco for liking and satisfaction. Females rated NECs more highly than males. On 1 January 2013, the tobacco excise tax was increased by 10% and the participants were contacted again in February-March 2013. Of the 227 people who agreed to be re-interviewed, 37.8% said they had cut back or made a change in their smoking habit and 7% had quit in February-March 2013. In multivariate analyses that controlled for demographic variables, factory-made versus roll-your-own tobacco preference, and addiction scores, positive NEC satisfaction ratings predicted changes in smoking habit and reductions in nicotine dependence.

Comment (BC): The fact that favourable first impressions of e-cigarettes resulted in a higher odds of reducing or quitting smoking and reduced FTND score suggests that the current ultra-conservative official approach to nicotine-containing cigarettes, which is hardly going to engender good impressions of e-cigarettes among New Zealand smokers, is destroying the opportunity for e-cigarettes to help people change their smoking habits.

Reference: Addict Behav. 2015;50:140-3
Abstract