

Smoking Cessation Research Review™

Making Education Easy

Issue 26 – 2017

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Welcome to issue 26 of Smoking Cessation Research Review.

A couple of studies demonstrate how to use the Internet to increase smoking cessation rates. One paper describes the successful use of a smartphone app for adult smoking cessation to increase engagement and quit rates, while the other paper demonstrates that delivering an integrated approach to medication provision and social network integration via an online programme can enhance adherence across all recommended components of an evidence-based smoking cessation programme (skills training, social support, and pharmacotherapy use).

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 was a Senior Research Fellow at Wellington Asthma Research Group, and worked 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. 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. **FOR FULL BIO [CLICK HERE](#).**



KINDLY SUPPORTED BY

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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.

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References: 1. Pharmac Special Authority Form [Click here](#). 2. Champix Data Sheet. **MINIMUM DATA SHEET: CHAMPIX®** (varenicline tartrate) 0.5 mg and 1 mg tablets. Indications: Aid to smoking cessation. **Contraindications:** Hypersensitivity to varenicline or excipients. **Precautions:** Neuropsychiatric symptoms: history of or underlying psychiatric illness, including changes in behaviour or thinking, anxiety, psychosis, mood swings, agitation, hallucinations, aggression, depressed mood, suicidal ideation and suicidal behaviour; patients and families to monitor; patients to stop taking CHAMPIX at first sign of symptoms and contact a health care professional immediately; ongoing follow-up until resolution. Seizures; hypersensitivity reactions; cardiovascular events; driving or operating machinery; alcohol consumption; pregnancy, lactation; severe renal impairment. See Data Sheet for details. **Adverse Effects:** Smoking cessation/nicotine withdrawal symptoms. Most common: nausea, headache, insomnia, nasopharyngitis, abnormal dreams, abdominal pain, constipation, fatigue, diarrhoea, flatulence, vomiting, dyspepsia, dysgeusia, dry mouth, sleep disorder, back pain, change in appetite, somnolence, weight increased, arthralgia, sinusitis, abdominal distension, rash, myalgia, dyspnoea, toothache, chest pain, gastroesophageal reflux disease, pruritis. Post-marketing reports of myocardial infarction, stroke. See Data Sheet for details. **Dosage and Administration:** Patients should set a date to quit smoking and start dosing 1-2 weeks before this date. Alternatively, patients can start treatment and quit smoking between days 8 and 35 of treatment. Days 1-3: 0.5 mg once daily. Days 4-7: 0.5 mg twice daily. Day 8 - end of treatment: 1 mg twice daily. Patients should be treated for 12 weeks. An additional 12 weeks of treatment can be considered for those who need additional support. Retreatment with varenicline is encouraged in patients who are motivated to quit and did not succeed with prior treatment or who relapsed. Dose tapering not required at end of treatment. Dose reduction is required for patients with severe renal impairment. Patients who cannot tolerate adverse effects may have the dose lowered temporarily or permanently. See Data Sheet for details. **Medicines Classification:** Prescription Medicine; CHAMPIX is fully funded under Special Authority. Before prescribing please review Data Sheet available from MEDSAFE (www.medsafe.govt.nz) or Pfizer New Zealand Ltd (www.pfizer.co.nz) Level 1, Suite 1.4, Building B, 8 Nugent St, Grafton, Auckland 1023 or call 0800 736 363. ®Registered trademark. V10115. P10135 March 2015.



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Association of long-term, low-intensity smoking with all-cause and cause-specific mortality in the National Institutes of Health–AARP Diet and Health Study

Authors: Inoue-Choi M et al.

Summary: This analysis from the US National Cancer Institute reports on the effects of long-term, low-intensity smoking (≤ 10 cigarettes per day [CPD]) on all-cause and for cause-specific mortality, using data from 290,215 adults in the NIH-AARP Diet and Health Study. All participants were aged 59–82 years at study entry in 2004–2005. They were asked about their current and historical smoking behaviours during 9 periods (from <15 years to ≥ 70 years) across their lifetimes. Among current smokers, most who reported <1 or 1–10 CPD reported smoking substantially higher numbers of CPD earlier in their lives, yet 159 (9.1%) individuals reported smoking <1 CPD consistently in each age period that they smoked; 1493 (22.5%) reported smoking 1–10 CPD. In Cox proportional hazards regression analyses adjusted for sex, race/ethnicity, educational level, physical activity, and alcohol intake, low-intensity smoking over the lifetime was associated with a significantly higher risk of all-cause mortality compared with never smokers: 64% for consistent smokers of <1 CPD (HR, 1.64; 95% CI, 1.07 to 2.51) and 87% for those who smoked 1–10 CPD (HR, 1.87; 95% CI, 1.64–2.13). Associations were similar in women and men for all-cause mortality and were observed across a range of smoking-related causes of death, with an especially strong association with lung cancer (for <1 CPD: HR 9.12; 95% CI, 2.92 to 28.47, and for 1–10 CPD: HR 11.61; 95% CI, 8.25 to 16.35). Former smokers who had consistently smoked <1 or 1–10 CPD had progressively lower risks with a younger age at cessation: e.g. among those who quit at ≥ 50 years of age, HRs were 1.44 (95% CI, 1.12 to 1.85) for consistent smokers of <1 CPD and 1.42 (95% CI, 1.27 to 1.59) for consistent smokers of 1–10 CPD.

Comment (NW): The findings from this paper are important, as there is increasing evidence that the number of light and non-daily smokers (also referred to as social or intermittent smokers) in NZ is increasing. There is no definition of what a “light” smoker is – sometimes it’s smoking <1 pack per day, <5 , <10 , or <15 cigarettes per day, or 1–39 cigarettes per week. Some people are also referred to as “chippers” – people who consistently smoke ≤ 5 cigarettes per day on the days when they do smoke. Whatever the definition, the message is the same – “there is no risk-free level of exposure to tobacco smoke”.

Reference: *JAMA Intern Med.* 2017;177(1):87-95
[Abstract](#)

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Oral cancer risk factors in New Zealand

Authors: Yakin M et al.

Summary: This paper presents an overview of the main risk factors for oral and oropharyngeal cancers and their prevalence in New Zealand. Between 2000 and 2010, a total of 1916 cases of oral squamous cell carcinomas (OSCC) were reported, involving slightly more males than females (1.85:1), with an age-standardised incidence rate of 42 persons per 1,000,000 population. Average annual age-specific rates and the total number of cases of OSCC steadily increased with age; the highest incidence was in the 6th decade of life. Tobacco use is a key risk factor for the development of oral cancer: compared with non-smokers, the likelihood of developing oral cancers is 4 times higher in current smokers and 20 times higher in heavy smokers. The paper discusses the various risks of oral cancers associated with the different types of tobacco products: rolls (these include cigarettes, cigars and hand-rolled tobacco products), oral preparations (e.g. betel liquid, to which tobacco may also be added) and water-pipes. Alcohol is another major risk factor for oral cancer: compared with non-drinkers, regular and heavy alcohol drinkers are approximately 2.5 and 5 times more likely to develop oral cancers, respectively.

Comment (NW): Tobacco smoking and hazardous drinking tend to co-exist in individuals, and cluster in families and communities. For example, in the 2007/8 NZ Health survey, 33% of people that smoked also consumed alcohol at hazardous levels, compared to 13% of non-smokers. This paper highlights the serious implications of both these behaviours – “People who are heavy smokers and heavy drinkers are at a 48-fold risk of developing oral and pharyngeal cancers than non-smoking non-drinkers”. This is staggering. Two key areas are highlighted where more surveillance data are needed. First, approximately 10–20% of the world’s population consumes betel nut. Regular use of betel quid is common in many Indian, South East Asian and South Pacific countries (such as Papua New Guinea, Palau, The Marshall Islands, Vanuatu and the Solomon Islands). With increasing numbers of immigrants from these countries to NZ, we need to ensure all health professionals are asking patients from these cultures about prior betel nut use, and whether it was used with or without tobacco. Second, use of tobacco in water-pipes (also known as shisha, nargile and hookah) is a common practice in many Middle-Eastern countries, and shisha bars and lounges are becoming more common in some parts of NZ. All health professionals should also start to ask their patients about prior and current waterpipe use.

Reference: *N Z Med J.* 2017;130(1451):30-8

[Abstract](#)

Impact of smoking reduced nicotine content cigarettes on sensitivity to cigarette price: further results from a multi-site clinical trial

Authors: Smith TT et al.

Summary: In this investigation, 839 adult smokers across the USA were randomised to receive cigarettes for 6 weeks that were either their usual brand or an investigational cigarette with 1 of 5 nicotine contents: 15.8 (primary control), 5.2, 2.4, 1.3, or 0.4 mg/g. All participants completed a Cigarette Purchase Task at baseline and at the week 6 post-randomisation visit. Compared with normal nicotine content controls, reducing nicotine content to the lowest level (0.4 mg/g) reduced the number of study cigarettes participants estimated they would smoke at a range of prices (mean reduction relative to 15.8 mg/g at a price of \$US4.00/pack: 9.50, 95% CI, 6.81 to 12.19), reduced the maximum amount of money allocated to study cigarettes and the price at which participants reported they would stop buying study cigarettes (median reduction relative to 15.8 mg/g, \$US8.21 (95% CI, 6.81 to 12.19) per day and \$0.44 (95% CI, 0.17 to 0.71) per cigarette, respectively), and also reduced the maximum amount of money allocated to usual brand cigarettes (median reduction relative to 15.8 mg/g: \$US4.39 95% CI, 1.88 to 6.90 per day).

Comment (NW): Nicotine reduction is a rapidly growing area of focus for tobacco control. Such a strategy is being considered in the absence of normal tobacco on the market and the increased availability of reduced harm products (e.g. NRT and e-cigarettes). There is strong trial evidence that very low nicotine cigarettes can reduce nicotine dependence and help people quit smoking. Research is now needed on the potential legal and regulatory barriers to implementing a nicotine reduction policy, as well as modelling of the likely population impact of such a policy on smoking prevalence and health. Furthermore, other policy around cigarette product modification (such as banning of menthol) is increasingly being considered by governments around the world (e.g. Canada).

Reference: *Addiction.* 2017;112(2):349-59

[Abstract](#)



Time spent reading this publication has been approved for CME for Royal New Zealand College of General Practitioners (RNZCGP) General Practice Educational Programme Stage 2 (GPEP2) and the Maintenance of Professional Standards (MOPS) purposes, provided that a Learning Reflection Form is completed. Please [CLICK HERE](#) to download your CPD MOPS Learning Reflection Form. One form per review read would be required.



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Tobacco retail outlet restrictions: health and cost impacts from multistate life-table modelling in a national population

Authors: Pearson AL et al.

Summary: These researchers modelled 4 tobacco outlet reduction interventions and used a multistate life-table model of 16 tobacco-related diseases, using national data by sex, age and ethnicity, to estimate quality-adjusted life years (QALYs) gained and net costs over the remainder of the 2011 New Zealand population's lifetime. At the end of the 10-year phase-in process, these tobacco outlet reductions reduced current tobacco outlets by >89%. The most effective intervention limited sales to half of liquor stores (and nowhere else) at 129,000 QALYs gained over the lifetime of the population (95% UI, 74,100 to 212,000, undiscounted). The interventions led to per capita QALY gains that were up to 5-fold higher for Māori compared with non-Māori and saved health system costs, with the largest saving for the liquor store only intervention: US\$1.23 billion (95% UI, \$0.70 to \$2.00 billion, undiscounted).

Comment (NW): This paper clearly shows that reducing the number of tobacco retailers will have a significant impact on reducing smoking prevalence in NZ, with clear health gains (particularly for Māori). [A complementary paper](#) looking at 623 smokers' perceptions of such policies found "policy scenarios in which tobacco was only sold at half the existing liquor stores or only at pharmacies were rated more likely to prevent youth smoking initiation, and at least as likely to help smokers to quit", relative to continued 10% annual tobacco tax increases. Although NZ has a smokefree 2025 goal, the government still has no clear plan on how to achieve this goal. This paper has identified some obvious policy options the government should consider moving forward, but the most benefit will be achieved if "a package of policies" is implemented.

Reference: *Tob Control*. 2016 Sep 22. [Epub ahead of print]

[Abstract](#)



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Nicotine, carcinogen, and toxin exposure in long-term e-cigarette and nicotine replacement therapy users: a cross-sectional study

Authors: Shahab L et al.

Summary: This UK investigation compared exposure to nicotine, tobacco-related carcinogens, and toxins among smokers of combustible cigarettes only, former smokers with long-term (≥6 months) e-cigarette use only, former smokers with long-term NRT use only, and long-term dual combustible cigarette–e-cigarette or combustible cigarette–NRT users (36 to 37 subjects per group; total number = 181). Urine and saliva samples from all participants were analysed for biomarkers of nicotine, tobacco-specific N-nitrosamines (TSNAs) and volatile organic compounds (VOCs). In analyses controlling for potential confounders, there were no clear between-group differences in salivary or urinary biomarkers of nicotine intake. The e-cigarette–only and NRT–only users had significantly lower metabolite levels for TSNAs (including the carcinogenic metabolite 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol [NNAL]) and VOCs (including metabolites of the toxins acrolein; acrylamide; acrylonitrile; 1,3-butadiene; and ethylene oxide) than combustible cigarette–only, dual combustible cigarette–e-cigarette, or dual combustible cigarette–NRT users. NNAL levels were significantly lower in the e-cigarette–only group compared with all other groups. TSNA and VOC metabolite levels did not differ much at all amongst combustible cigarette–only, dual combustible cigarette–NRT, and dual combustible cigarette–e-cigarette users.

Comment (BC): Not only does this research provide further evidence of the safety of the use of NRT and e-cigarettes, the fact that there was no significant difference in urine nicotine levels between groups suggests the possibility that if smokers are able to use NRT or e-cigarettes in such a way that they absorb the same nicotine as when they smoked, then they will be more likely to continue to use the NRT and e-cigarettes for long enough to remain abstinent. It is essential to coach smokers on how to best use and enjoy their NRT and e-cigarettes so they can gain enough nicotine from them. It is vital to inform smokers that dual use of NRT/e-cigs and smoking still exposes them to substantial harm.

Reference: *Ann Intern Med*. 2017;166(6):390-400

[Abstract](#)

Single-arm trial of the second version of an acceptance & commitment therapy smartphone application for smoking cessation

Authors: Bricker JB et al.

Summary: [In 2014, these researchers reported](#) that an innovative smartphone-delivered acceptance and commitment therapy (ACT) application (app) for adult smoking cessation (SmartQuit1.0) is feasible to deliver and shows higher engagement and promising quit rates compared with an app following US Clinical Practice Guidelines. The researchers subsequently revised this app (SmartQuit2.0) and tested it for participant receptivity, short-term cessation and reduction in a cohort of 99 adults, all of whom were followed-up at 2 months (85% retention). High proportions of participants said they were satisfied with SmartQuit2.0 (84% vs 59% for SmartQuit1.0), would recommend it to a friend (73% vs 48% for SmartQuit1.0), and considered the ACT exercises useful for quitting (81% vs 44% for SmartQuit1.0). At the 2-month follow-up, quit rates were similar to those with SmartQuit1.0 for 7-day point prevalence (21% vs 23%, respectively) and 30-day point prevalence (11% vs 13% for SmartQuit1.0), although more SmartQuit2.0 participants reduced their smoking frequency (75% vs 57% for SmartQuit1.0). Among programme completers (24% of total sample), the quit rates were 33% for 7-day point prevalence, 28% for 30-day point prevalence, and 88% of participants reduced their smoking frequency.

Comment (BC): Cellphone apps have been shown to be effective at helping smokers to quit, so it is such a good idea to deliver a psychological intervention this way. Several studies have demonstrated that Acceptance & Commitment Therapy has advantages over Cognitive Behavioural Therapy for smoking cessation; imagine how effective this app might be if it were combined with NRT? If you are interested in learning more about this technique, I can recommend "Acceptance and Commitment Therapy: An Experiential Approach to Behavioral Change" by Hayes, Strosahl, and Wilson, published by The Guilford Press – it is very readable and gives practical examples.

Reference: *Drug Alcohol Depend*. 2017;170:37-42

[Abstract](#)

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Research Review publications are intended for New Zealand health professionals.

Improving adherence to smoking cessation treatment: Intervention effects in a Web-based randomized trial

Authors: Graham AL et al.

Summary: Outcomes are reported from an internet-based smoking cessation intervention involving 5290 adult US smokers who were randomised to 1 of 4 approaches: (1) an interactive, evidence-based smoking cessation website (WEB) alone; (2) WEB plus a social network (SN) intervention designed to integrate participants into the online community (WEB+SN); (3) WEB plus free NRT (WEB+NRT); or (4) the combination of all treatments (WEB+SN+NRT). At 3 months, WEB+SN+NRT was associated with the highest level of adherence amongst all 4 interventions, as assessed by website utilisation metrics, use of practical counselling skills training components, intra-treatment social support, and NRT use. It was the only intervention to promote the sending of private messages and the viewing of community pages over WEB alone. Both social network arms outperformed WEB on most metrics of online community engagement and both NRT arms had higher levels of medication use compared with WEB alone.

Comment (BC): It is very encouraging to know that use of a combination of a website, social networks, NRT, and online counselling tools, improves adherence to treatment. Sadly, we have to wait for the authors to publish the effects of adherence on abstinence. Their protocol states they will report the primary outcome of self-reported 30-day point prevalence abstinence measured at 9 months, which will give a good estimate of the effect size and its durability. The beauty of this intervention is that it is automated and can inexpensively reach a large population, and is something to which we could confidently refer smokers. Nearly four million New Zealanders have access to the internet, so this service would be accessible for many smokers, whether by computer or smartphone.

Reference: *Nicotine Tob Res.* 2017;19(3):324-32

[Abstract](#)

Depression among current, former, and never smokers from 2005 to 2013: The hidden role of disparities in depression in the ongoing tobacco epidemic

Authors: Goodwin RD et al.

Summary: This paper reports annual prevalence rates of depression among current, former (past 12-month) and lifetime non-smokers in the USA from 2005 to 2013, using data from the National Household Survey on Drug Use (NSDUH), an annual cross-sectional study of persons aged ≥ 12 years ($n=496,805$). The analyses indicate a significant increase in depression between 2005 and 2013 in all 3 study groups. Notably, while there was an increase in depression prevalence amongst current smokers overall, increases were even more substantial among former and never smokers. Re-analysis and stratification of the data by age, gender, and household income revealed marked temporal changes: (1) current smokers aged 12–17 years experienced a significant increase in depression rates, from 16% in 2005 to 22% in 2013 ($p=0.0002$) and the prevalence was consistently more than twice as high as that of never smokers; (2) depression increased among male smokers (6.19% to 7.82%; $p=0.0099$); (3) depression increased significantly among smokers in the highest income group (6.36% to 8.91%; $p=0.0400$). The data also revealed that the prevalence of depression among current smokers was consistently twice as high as among former and never smokers.

Comment (BC): Depression is well known to cause relapse and is a common symptom of the nicotine withdrawal syndrome. We can help prevent depression from acting as a barrier to quitting, by being alert to the presence of depression, treating it, and by reassuring patients that a meta-analysis by Taylor et al. ([BMJ. 2014;348:g1151](#)) showed that contrary to popular belief, once the short-term withdrawal symptoms have subsided, depression and anxiety is less common in those who have quit, than smokers who continue to smoke. Advising depressed smokers to exercise may help their affect as well as help them quit, because some studies have shown exercise aids smoking cessation, possibly by increasing self-efficacy, and some studies have found that depression is ameliorated by exercise.

Reference: *Drug Alcohol Depend.* 2017;173:191-9

[Abstract](#)

Concurrent e-cigarette use during tobacco dependence treatment in primary care settings: association with smoking cessation at three and six months

Authors: Zawertailo L et al.

Summary: This Canadian trial recruited smokers accessing standard smoking cessation treatment (NRT plus behavioural counselling) through 187 primary care clinics across Ontario. The trial offered free, individualised dosing of NRT and a maximum of 26 weeks of brief behavioural counselling. At 3 months' follow-up, approximately one-fifth (18%) of the 6526 participants reported using an e-cigarette while in treatment. The majority of e-cigarette users (78.2%) reported using an e-cigarette for smoking cessation. In logistic regression analyses adjusted for covariates including severity of tobacco dependence, gender, and age, the researchers found a negative association between e-cigarette use and abstinence at 3 months' follow-up (adjusted OR 0.706; 95% CI, 0.607 to 0.820; $p<0.001$) and 6 months' follow-up (adjusted OR 0.502; 95% CI, 0.393 to 0.640; $p<0.001$).

Comment (BC): It never ceases to amaze me how often the results of trials are misinterpreted, particularly by the authors of the studies themselves. Just because the authors controlled for potential confounders like nicotine dependence, age and gender does not mean that they have removed the effect of all factors that could potentially confound the association between use of e-cigarettes and poorer abstinence. We should be alert to the fact that self-selecting to use e-cigs may be a sign that a patient is having difficulty with quitting/remaining abstinent, and offer them further assistance. The people who chose to use e-cigs in this trial may have had other risk factors for relapse, which the authors did not adjust for, such as: lower socio-economic smokers are more likely to use e-cigs and more likely to relapse, greater anxiety sensitivity and anxiety and depressive symptoms, which are predictive of early smoking lapse and relapse.

Reference: *Nicotine Tob Res.* 2017;19(2):183-9

[Abstract](#)

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