

Smoking Cessation Research Review™

Making Education Easy

Issue 28 - 2017

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Abbreviations used in this issue

BID = twice daily
MRI = magnetic resonance imaging
NRT = nicotine replacement therapy
OR = odds ratio

Welcome to issue 28 of Smoking Cessation Research Review.

Findings from a large cross-sectional US-based survey underline the importance of the influence of gender in relation to smoking cessation. The data revealed a greater advantage of varenicline over transdermal nicotine patch for women compared to men. The study researchers recommend that clinicians consider varenicline as a first-line treatment for women who are trying to quit smoking.

In another paper, an analysis of data from the US 2014–2015 Tobacco Use Supplement-Current Population Survey has determined that the key to using e-cigarettes to quit smoking is to use them frequently. Among smokers making at least one quit attempt, success was more likely among those with at least 5 days use of e-cigarettes in the last month.

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

Kind regards,

Brent Caldwell

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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](#).**



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.

CHAMPIX® helps smokers quit with proven efficacy.^{1,2}

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Significantly greater odds of **quitting** with CHAMPIX vs NRT patch[†], bupropion or placebo at weeks 9-12.

Varenicline vs NRT patch (OR= 1.68 (1.46-1.93) p<0.0001); varenicline vs bupropion (OR= 1.75 (1.52-2.01) p<0.0001); varenicline vs placebo (OR= 3.61 (3.07-4.24) p<0.0001).^{1,2} [†]NRT patch was 21mg/day with taper, administered for 11 weeks.²

References: 1. CHAMPIX Data Sheet, Pfizer NZ. 2. Arnenelli RM, et al. Lancet. 2016; 387 (10037): 2507-2520. CHAMPIX® (varenicline tartrate) 0.5 mg and 1 mg tablets. 4.1 Therapeutic Indications: Aid to smoking cessation. 4.2 Dose and Method of Administration: 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 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. Patients should be treated for 12 weeks. An additional 12 weeks of treatment can be considered for patients who have successfully stopped smoking at the end of 12 weeks. A gradual approach to quitting smoking should be considered for patients who are not willing/able to quit abruptly. Patients should reduce smoking during the first 12 weeks and quit by the end of that treatment period. Patients should then continue for an additional 12 weeks for a total of 24 weeks. 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. 4.3 Contraindications: Hypersensitivity to varenicline or excipients. 4.4 Special Warnings and Precautions for Use: history of, or, underlying psychiatric illness; neuropsychiatric symptoms including changes in behaviour or thinking, anxiety, psychosis, mood swings, agitation, aggression, depressed mood, suicidal ideation and suicidal behaviour; patients and families should be advised that the patient should stop taking CHAMPIX and contact a health care professional immediately if such symptoms are observed; patients and families should be alerted to the need to monitor for the possible emergence of neuropsychiatric symptoms; 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. 4.8 Undesirable Effects: Smoking cessation/nicotine withdrawal symptoms. Most common: nausea, headache, insomnia, nasopharyngitis, abnormal dreams, abdominal pain, dizziness, constipation, fatigue, diarrhoea, flatulence, vomiting, dyspepsia, dysgeusia, irritability, influenza, anxiety, dry mouth, sleep disorder, back pain, increased appetite, somnolence. Post-marketing reports of neuropsychiatric symptoms, myocardial infarction, stroke. See Data Sheet for details. 7. Medicine Schedule: 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) or call 0800 736 363. ©Registered trademark. V10417 © Pfizer 2017. Pfizer New Zealand Limited, Level 1, Suite 1.4, Building B, 8 Nugent Street, Grafton, Auckland 1023, PO Box 3998, Auckland, New Zealand. Toll Free 0800 736 363. essence PF8486 DA1742EB PP-CHM-NZL-0088 09/17.



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Cigarette smoking is associated with amplified age-related volume loss in subcortical brain regions

Authors: Durazzo TC et al.

Summary: In this study, 43 non-smokers and 40 smokers (all aged 22–70 years) underwent MRI interrogations of the bilateral total subcortical lobar white matter and subcortical nuclei volumes. The MRI findings demonstrated greater age-related volume loss amongst smokers compared with non-smokers in the bilateral subcortical lobar white matter, thalamus and cerebellar cortex, as well as in the corpus callosum and subdivisions. Greater cigarette quantity/exposure was linked to smaller volumes of the bilateral amygdala, nucleus accumbens, total corpus callosum and subcortical white matter.

Comment (NW): It is important to understanding the effects of chronic smoking on the brain, as it helps inform the development of effective smoking cessation medications. This study has some interesting findings, but a longitudinal study is required to prove causation, and more women need to be included.

Reference: *Drug Alcohol Depend.* 2017;177:228-36

[Abstract](#)

Gender differences in the real-world effectiveness of smoking cessation medications: Findings from the 2010–2011 Tobacco Use Supplement to the Current Population Survey

Authors: Smith PH et al.

Summary: These researchers used cross-sectional observational population data from the US 2010–2011 Tobacco Use Supplement to the Current Population Survey to generate propensity score-matched samples of smokers who quit either unassisted by medication, using only varenicline, or using only transdermal nicotine patch. Generalised estimating equations, adjusted for potential confounders, estimated gender differences in the comparative effectiveness of the different cessation options for achieving 30 days of abstinence. When stratified by gender, transdermal nicotine patch was significantly more effective than unassisted quit attempts for men (OR 1.37; 95% CI, 1.02 to 1.83; $p=0.03$), but not for women (OR 0.96; 95% CI, 0.71 to 1.31; $p=0.82$). In contrast, varenicline was significantly more effective than unassisted quit attempts for women (OR 1.63; 95% CI, 1.16 to 2.31; $p=0.005$), but not for men (OR 1.35; 95% CI, 0.94 to 1.96; $p=0.11$). Varenicline was also more effective than transdermal nicotine patch for women (OR 1.51; 95% CI, 0.12 to 2.05; $p=0.007$), but not for men (OR 0.92; 95% CI, 0.65 to 1.31; $p=0.64$). The only significant gender by medication interaction was for the comparison of varenicline to transdermal nicotine patch (OR 1.64; 95% CI, 1.04 to 2.61; $p=0.04$).

Comment (NW): Smoking prevalence tends to be higher in men than women, yet for a variety of reasons women are less successful at quitting smoking (e.g. there are differences in hepatic metabolism for women compared to men, which may explain differences in responses to smoking cessation medication). The findings from this cross-sectional study are consistent with trial data indicating that some smoking cessation medications work better for women than for men. Although not yet stated in the NZ smoking cessation guidelines, quitting success would be optimised if gender is considered when recommending/prescribing smoking cessation medication.

Reference: *Drug Alcohol Depend.* 2017;178:485-91

[Abstract](#)

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Lorcaserin for smoking cessation and associated weight gain: A randomized 12-week clinical trial

Authors: Shanahan WR et al.

Summary: This US multicentre trial enrolled 603 adult smokers with a BMI of 18.5–35 kg/m², averaging ≥ 10 cigarettes/day with no period of abstinence >3 months for the past year, and randomised them to lorcaserin 10 mg once daily (QD), 10 mg twice daily (BID) or placebo for 12 weeks; all participants underwent weekly standardised smoking cessation counselling sessions. The target quit date was day 15. The primary endpoint was carbon monoxide-confirmed continuous abstinence rates from weeks 9–12 (month 3). Continuous abstinence rates for month 3 were 5.6%, 8.7%, and 15.3% for the placebo, QD and BID groups, respectively (BID vs placebo: OR 3.02; 95% CI, 1.47 to 6.22; $p=0.0027$). At week 12, weight changes from baseline were -0.01 in the placebo group, -0.35 in the QD group and -0.98 kg in the BID group (BID vs placebo: $p=0.0004$), and $+0.73$, $+0.76$, and -0.41 kg, respectively, in those who achieved month 3 continuous abstinence.

Comment (NW): Lorcaserin is a selective serotonin agonist that acts as an appetite suppressant. Although approved as a weight loss medicine by the FDA, it is not yet available in New Zealand (but may be in the future). This trial highlights another indication for the medication, namely, smoking cessation. Given many smokers are concerned about weight gain if they quit smoking, the findings from this trial suggest lorcaserin may hold some appeal. A phase 2 trial ($n=300$) of lorcaserin 10mg BID plus 21/14/7 mg nicotine patch for 16 weeks is currently underway in the USA.

Reference: *Nicotine Tob Res.* 2017;19(8):944-51

[Abstract](#)

Feasibility of implementing a hospital-based “opt-out” tobacco-cessation service

Authors: Nahhas GJ et al.

Summary: This paper describes the outcomes of a policy implemented in 2014 by the Medical University of South Carolina requiring that all hospitalised patients who self-report using tobacco be referred to a tobacco-cessation treatment service. Between February 2014 and May 2015, 42,061 adults were admitted to the Medical University of South Carolina Hospital. 8,423 current cigarette smokers were identified; 5,843 eligible smokers were referred to the tobacco-cessation service, consisting of a bedside consult and phone follow-up at 3, 14, and 30 days after hospital discharge. One fulltime bedside counsellor was able to speak with 1,918 (32.8%) patients, of whom 96 (5%) denied currently smoking and 287 (14.9%) refused counselling. Reach at follow-up was achieved for 703 (55%) smokers who received bedside counselling and 1,613 (49%) who did not, yielding an overall follow-up reach rate of 60%. Of those reached by phone, 36.4% reported not smoking (51% vs 27% for those who did and did not receive bedside counselling, respectively). At the last known smoking status, the intent-to-treat abstinence rate was 13.5%.

Comment (NW): A proactive approach to providing smoking cessation support has been previously shown to increase the reach of and enrolment in smoking cessation services, including to Quitlines (see [Stoltzfus et al., J Smoking Cess.](#) 2011;6(2):133-7; and [Vidrine et al., JAMA Intern Med.](#) 2013;173(6):458-64). The NZ smoking cessation guidelines use the ABC approach: Advise patients to quit smoking, offer Brief advice around quitting, and provide Cessation support (by providing cessation medication, and/or referral to a cessation service). Health professionals would still be following these guidelines if they said to their patients “quitting smoking is so important to your health (Advise) I have referred you to Quitline (provide Cessation support). Someone from Quitline will be in touch soon.” Patients can opt out if they choose, when contacted by the service provider.

Reference: *Nicotine Tob Res.* 2017;19(8):937-43

[Abstract](#)

Young adult perceptions of the British American Tobacco New Zealand Agree/Disagree Plain Packaging Counter-Campaign

Authors: McCool J et al.

Summary: In 2012, British American Tobacco New Zealand (BATNZ) launched a mass media campaign branded "Agree/Disagree" as a response to the New Zealand government's plans to introduce plain packaging. This study explored young adults' perceptions of the campaign, as a way of assisting tobacco control policymakers in planning future interventions. Young adults living in the Auckland area were interviewed on what they knew about plain packaging of tobacco, the tobacco industry, and how they perceived specific advertisements included in the campaign. Perspectives from 12 interviews reflect the dominant discourse in New Zealand on the benefits of serving economic progress and international trade. Pervasive views about the campaigns reflected perceptions of the risk to the New Zealand image, trade, and economy. Concern was expressed about the potential for plain packaging to creep toward other products, such as alcohol.

Comment (NW): The findings from this qualitative study highlight how important it is to 1) understand generational viewpoints of messages put out by the tobacco industry, and 2) have in place appropriate counter-messages that resonate with each generation.

Reference: *Nicotine Tob Res.* 2017;19(10):1192-8

[Abstract](#)

The relationship of e-cigarette use to cigarette quit attempts and cessation: Insights from a large, nationally representative U.S. survey

Authors: Levy DT et al.

Summary: Using data from the US 2014–2015 Tobacco Use Supplement-Current Population Survey, these researchers examined the role of e-cigarettes in quit attempts and 3-month cigarette abstinence. The analysis revealed that having made a quit attempt was more likely among smokers using e-cigarettes than non-users. Among those making ≥ 1 quit attempt, success was lower among ever users, but higher among those with ≥ 5 days use of e-cigarettes in the last month. Quit attempts and quit success were both linearly related to the frequency of e-cigarette use.

Comment (BC): The 10% increase in abstinence for every extra day e-cigs were used and, the lack of efficacy of ever-use of e-cigs, suggests that if we can encourage smokers to keep trying different brands of e-cig until they find one that provides them with enough reward to motivate them to use it for an extended period of time; and teach smokers the ideal way to puff e-cigs to gain reward, their chances of long-term abstinence would be improved. By the way, since married people in this survey were significantly more likely to attempt to quit and remain quit for at least three months ($p < 0.001$ in Table 1), surely allowing Australian gay people the opportunity to marry would be an important step forwards in smoking cessation?

Reference: *Nicotine Tob Res.* 2017 Aug 21. [Epub ahead of print]

[Abstract](#)



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Changes in puffing topography and nicotine consumption depending on the power setting of electronic cigarettes

Authors: Farsalinos K et al.

Summary: These researchers measured changes in puffing topography and liquid consumption among e-cigarette users (vapers) while using different power settings in the e-cigarette battery device. Twenty-one experienced adult vapers were recruited. They used their own liquids and an atomiser and battery provided by the researchers in two 30-minute sessions in a randomised, crossover fashion, with the device power set at 6 W or 10 W. Puff number and puff duration were lower at 10 W (mean, 46 puffs and 3.8 s) compared to 6 W (mean, 57 puffs and 4.6 s). Liquid and nicotine consumption was higher at 10 W (mean, 373 mg and 4.2 mg, respectively) compared to 6 W (mean, 308 mg and 3.5 mg, respectively). Vapers reported more aerosol volume and ease of use at 10 W compared to 6 W.

Comment (BC): It is well known that more powerful batteries ensure that e-cigs deliver more nicotine, but this comes at the cost of transforming some of the nicotine into toxic substances like aldehydes. In the Methods section of this article, the authors stated that they chose to limit the high-strength battery to 10 W in order to avoid dry puffs. According to the internet, a dry puff is the result of using too high a voltage/wattage, which causes the nicotine to heat up too much, resulting in an awful taste and cough, and may cause e-cig liquid to deposit in the mouth. [Farsalinos and colleagues](#) have shown that acetaldehyde and dry puffs can be avoided, even when using 10 W, by using an atomiser with two wicks. Clearly, not all e-cigs are made equal, and smokers need to be given accurate information to avoid danger and ensure they do not have to puff more intensely or with large puff volumes, in order to make the experience more enjoyable.

Reference: *Nicotine Tob Res.* 2017 Oct 3. [Epub ahead of print]

[Abstract](#)

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Using elastic net penalized Cox proportional hazards regression to identify predictors of imminent smoking lapse

Authors: Suchting R et al.

Summary: Outcomes are reported from a secondary analysis of data from 92 smokers collected via smartphone-based ecological momentary assessment (EMA). All smokers were following a scheduled quit date. This analysis used elastic net-penalised Cox proportional hazards regression and model approximation via backward elimination to (1) optimise a predictive model of time to first lapse and (2) simplify that model to its core constituent predictors to maximise parsimony and generalisability. Elastic net proportional hazards regression selected 17 of 26 possible predictors from 2,065 EMAs to model time to first lapse. The strongest predictors of smoking lapse were environmental factors (i.e. having consumed alcohol in the past hour, being around and interacting with a smoker, and having cigarettes easily available). When the model was reduced using backward elimination, 5 predictors were retained, approximating to 93.9% of model fit. These retained predictors included the 3 mentioned above, as well as feeling irritable and being in areas where smoking is either discouraged or allowed (as opposed to not permitted).

Comment (BC): Although this study found that smokers were more likely to lapse if they consumed alcohol in the past hour, spent time with other smokers, had cigarettes easily available, felt irritable, and were in areas where smoking was not banned, this does not necessarily mean that we should advise smokers to completely avoid those situations, because it is impossible to avoid them for the rest of one's life and, unless one has extinguished the salience of those cues by experiencing those cues without smoking, then they will retain their salience, and if one experiences cues, even a long time after avoiding them, they will still have the potential to wreak havoc on one's resolve to remain abstinent. Perhaps being made aware of the threats to abstinence, and using more NRT when those threats are encountered, would help?

Reference: *Nicotine Tob Res.* 2017 Sep 7. [Epub ahead of print]

[Abstract](#)

Comparing perceived effectiveness of FDA-proposed cigarette packaging graphic health warnings between sexual and gender minorities and heterosexual adults

Authors: Tan ASL et al.

Summary: These researchers analysed data from a project conducted in 2013–2014 involving 1,200 adults residing in 3 Massachusetts communities, with an oversample from low socioeconomic status groups. The project examined whether perceived effectiveness of graphic health warnings on cigarette packaging differs by gender and sexual orientation. Participants viewed and rated the effectiveness of 9 graphic health warnings proposed by the US FDA in 2012. Female heterosexuals rated graphic health warnings as more effective than male heterosexual, lesbian, and transgender and other gender respondents. Views did not differ significantly between female and male heterosexuals versus gay, male bisexual, or female bisexual respondents. Differences by gender and sexual orientation were consistent across all 9 graphic health warnings. Higher perceived effectiveness was significantly correlated with certain graphic health warnings, older age, being African-American (vs white), being Hispanic (vs non-Hispanic), having less than high school education (vs associate degree or higher), and being a current smoker (vs being a non-smoker).

Comment (BC): This study enrolled very few lesbians, and even fewer gay men, so it was limited in its ability to detect a difference in effectiveness of graphic health warnings between queer and straight smokers. This may explain why it found so few differences. Interestingly, the estimate for current smokers versus former smokers (regardless of sexual orientation) was -0.125 ($p=0.033$), which equates to an OR of 0.88, so the warnings were perceived to be less effective by current smokers than ex-smokers – oh dear! A search of Medline found plenty of studies that identified the high prevalence of smoking amongst queer people, but no research on interventions tailored to queer people. What are the chances of getting such a study funded by the HRC?

Reference: *Cancer Causes Control.* 2017;28(10):1143-55

[Abstract](#)

Trends in utilization of smoking cessation agents before and after the passage of FDA boxed warning in the United States

Authors: Shah D et al.

Summary: This analysis examined the trends in bupropion and varenicline use before and after the passage in 2009 of US FDA black box warnings (BBWs) for these smoking cessation agents following reports of adverse neuropsychiatric events. Data were retrospectively analysed from the Medical Expenditure Panel Survey (2007–2014) relating to adult smokers who were advised by their physicians to stop smoking. Varenicline use significantly declined from 22.1% in 2007 to 9.23% in 2014 ($p<0.001$). In the logistic (adjusted OR 0.36; 95% CI, 0.22 to 0.58) and piecewise regression analyses (OR 0.64; 95% CI, 0.41 to 0.99), smokers who were advised to quit smoking by their physicians were less likely to use varenicline in the immediate post-BBW period as compared to the pre-BBW period. The use of varenicline remained significantly lower in the late post-BBW period (adjusted OR 0.45; 95% CI, 0.31 to 0.64) as compared to the pre-BBW period, although piecewise regression analysis revealed a stable trend in use (OR 0.90; 95% CI, 0.75 to 1.06). No significant differences in bupropion use were observed between the pre- and post-BBW periods.

Comment (BC): This study highlights the need for doctors and patients to have good information about the safety of smoking cessation products, to encourage them to prescribe them and use them, respectively. It is greatly reassuring that the rate of use of varenicline returned to normal once more time had elapsed since varenicline's BBW, so people are able to 'get used' to new threats if they've been exposed to them or been aware of them for long enough. We need to reassure our patients that NRT, varenicline, e-cigs, and bupropion are much safer than many of the things we do every day, and are certainly safer in the long run than continuing to smoke.

Reference: *Drug Alcohol Depend.* 2017;177:187-93

[Abstract](#)

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