Treating Tobacco Use Disorder

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Land Acknowledgement

We respectfully acknowledge the land on which we work is the traditional territory of the Coast Salish Peoples, including the unceded homelands of xʷməθkwəy̓əm (Musqueam), Sḵwx̱wú7mesh (Squamish), and Səl̓ílwətaɬ (Tsleil-Waututh) Nations

Disclosures

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TEACH (Centre for Addiction and Mental Health)

Doctors of BC (Specialist Services Committee)

**No tobacco or electronic industry funding (past or current)*

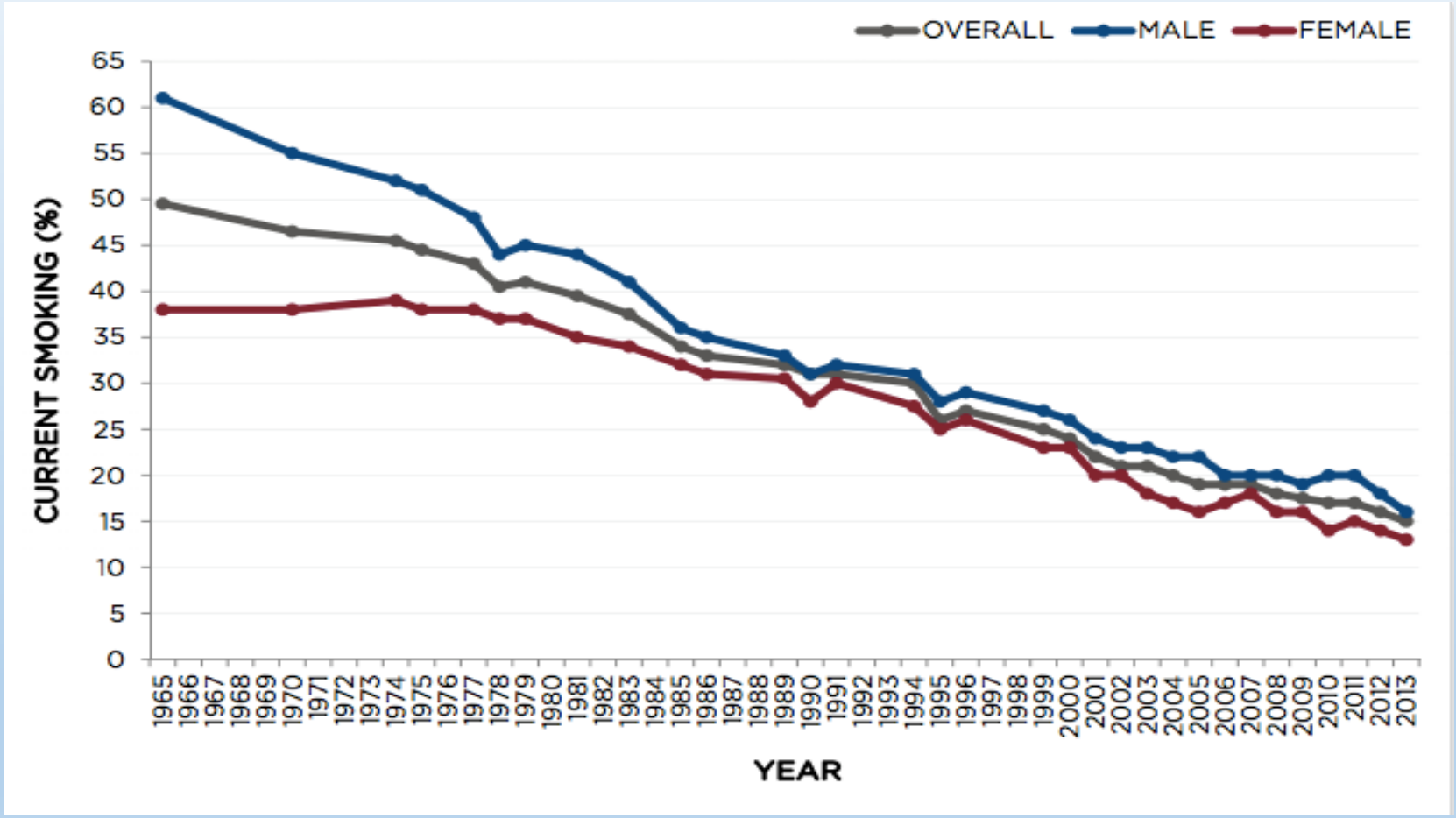
Mitigating Potential Bias

- *Content includes ALL smoking cessation medications*
- *Peer reviewed, published research*
- *Invitation to discuss or challenge content*

Learning Objectives

- *Review the neurobiology and treatment of TUD*
- *Understand the approach to those with concurrent disorders (including those with other substance use disorders)*
- *Consider the role of vaping and other new potential treatments*

Smoking Prevalence Trends in Canada



Reid JL et al. Tobacco Use in Canada: Patterns and Trends, 2015 Edition. Waterloo, ON: Propel Centre for Population Health Impact, University of Waterloo.

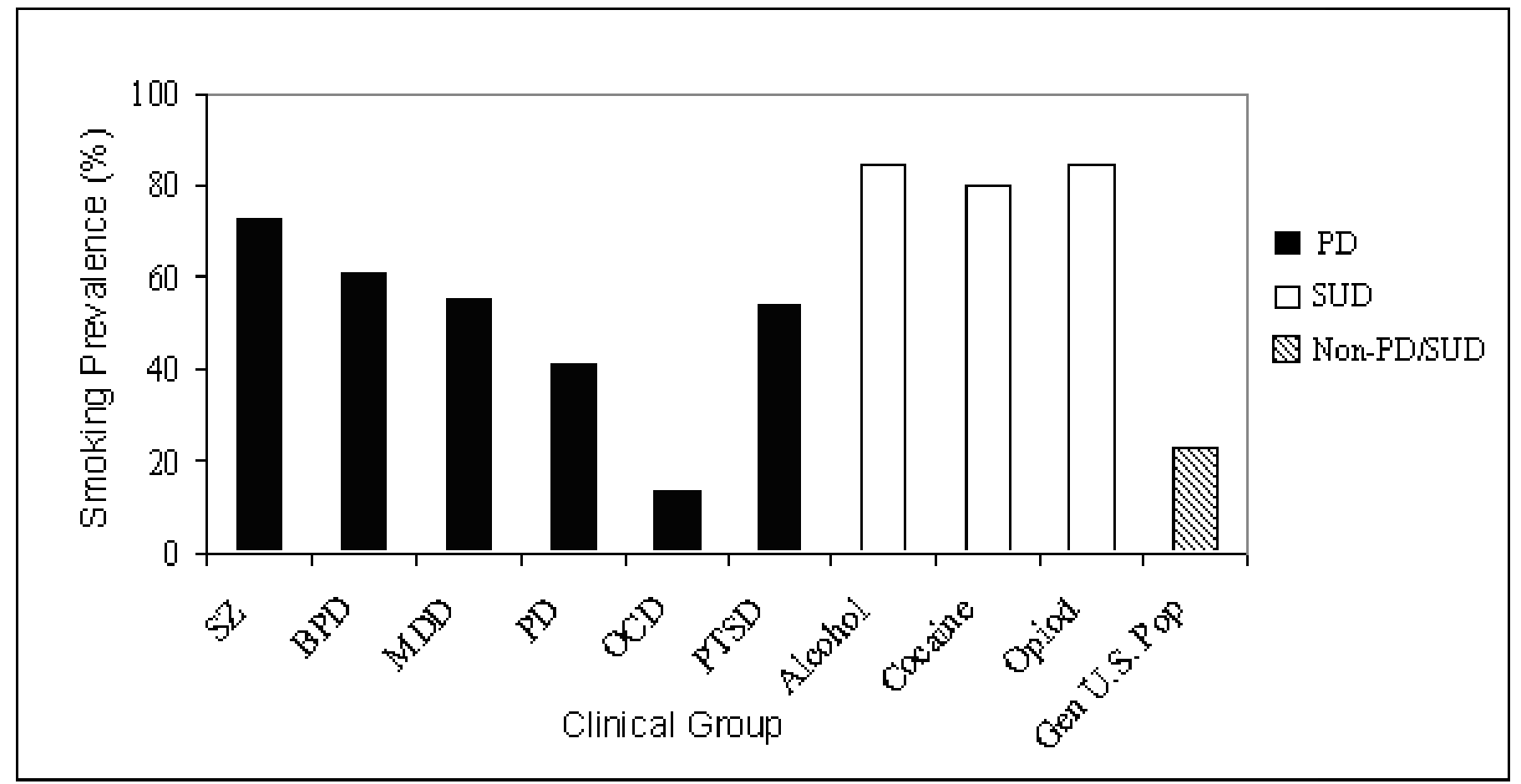
Disease Burden

- *The leading preventable cause of death in Canada*
- *37,000 smoking-attributable deaths per year*
- *1 in 2 smokers die prematurely from a smoking-related illness*

- *Persons with mental illness consume approximately 44% of all cigarettes smoked in the U.S*

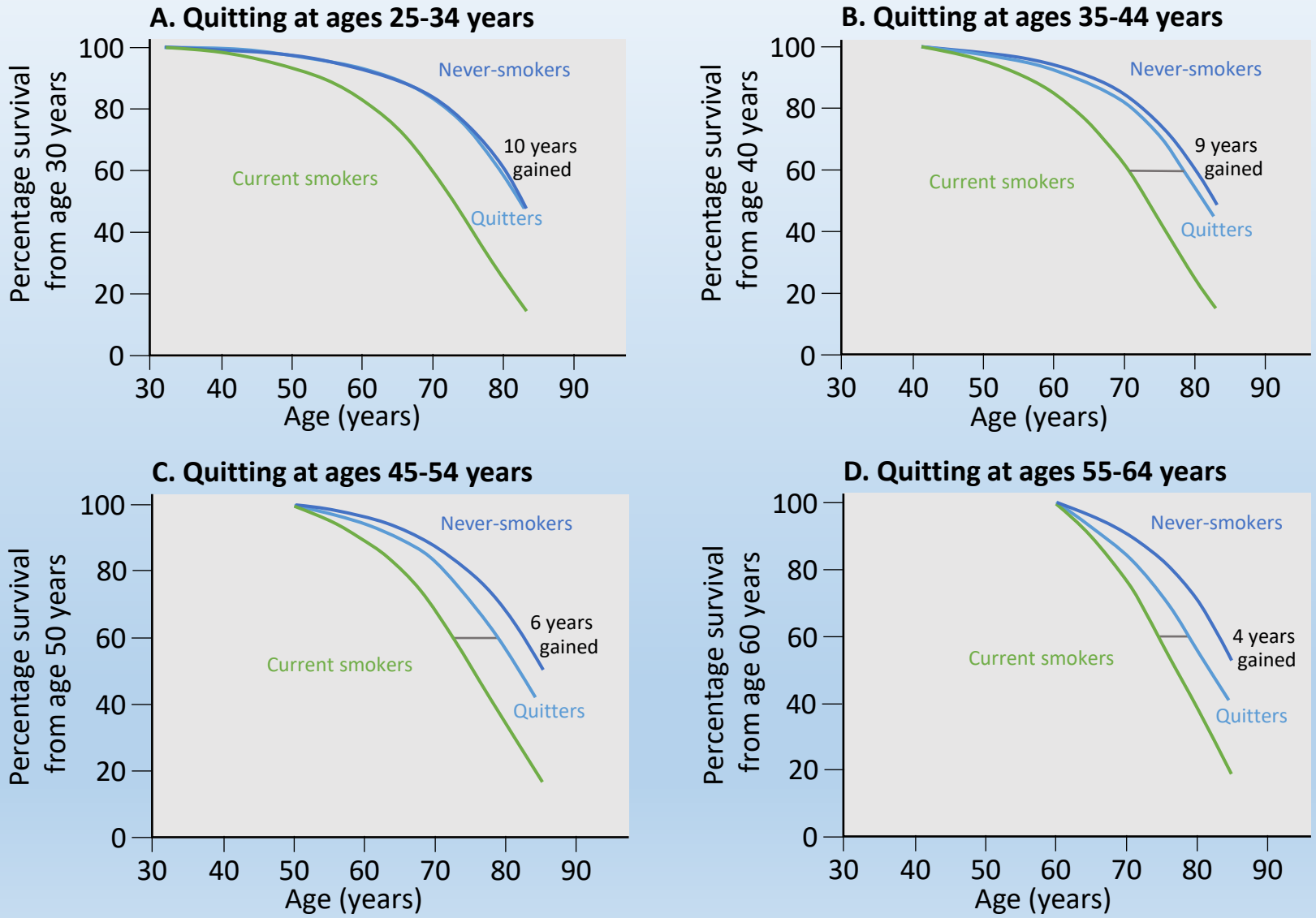
Doll R, et al. BMJ 2004; 328(7455):1519.
Lasser K, et al. JAMA 2000; 284(20):2606-10.
Canadian Cancer Society/National Cancer Institute of Canada. Canadian Cancer Statistics 2005. Available at: www.publications.gc.ca/collections/Collection/CS2-37-2005E.pdf.

Prevalence of Smoking: Psychiatric and Substance Use Disorders



Kalman, Morissette and George (2005), Am. J. Addict., 14: 106-123

The Benefits of Cessation



Jha P, et al. N Engl J Med 2013; 368(4):341-50.

Smoking and Schizophrenia: Patient Perceived Benefits

- *Improve psychiatric symptoms?*
- *Improve cognitive functioning?*
- *Reduce medication side effects*
- *"self-medication hypothesis"*

- *"shared genetic vulnerability hypothesis"*
- *Mental Health Service culture?*

Association Between Smoking Behavior and Cognitive Functioning in Patients With Psychosis, Siblings, and Healthy Control Subjects: Results From a Prospective 6-Year Follow-Up Study. Vermeulen JM et al. Am J Psychiatry. 2018 Nov 1

Williams et al. Addict Behav. 2004;29:1067-1083;

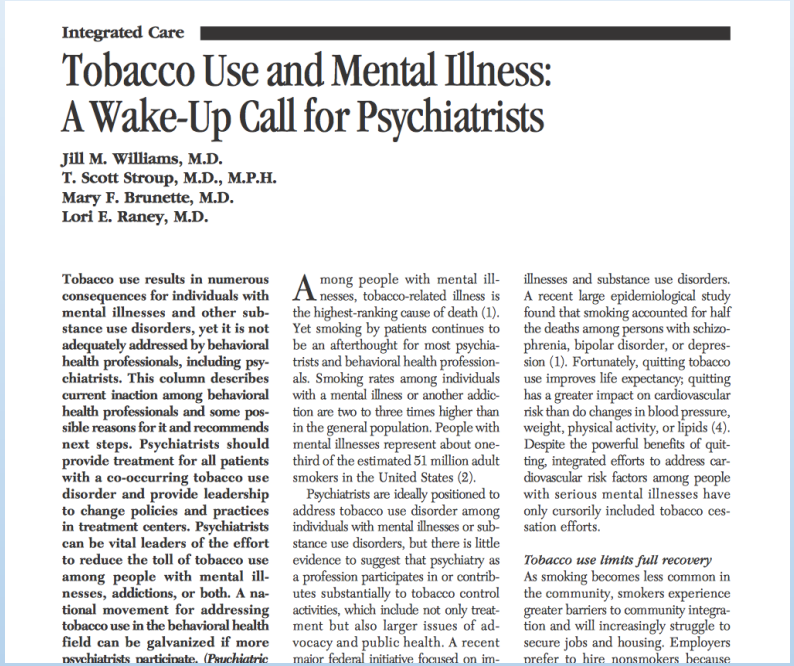
Management of Smoking in People with Psychiatric Disorders and SUD

- *Limited efforts to treat this population*
- *Providers rarely screen and mostly not trained*
- *Needs to be seen as a "co-occurring"disorder*
- *Integrated, intensive treatment*

Lasser K, Wesley BJ, Woolhandler S et al. Smoking and Mental Illness JAMA 2000

"A Wake Up Call For Psychiatrists": Reasons To Treat Tobacco Use

- *Tobacco use kills half our patients*
- *Tobacco use limits full recovery*
- *Tobacco use disorder is in the DSM*
- *Tobacco use has a negative impact on treatment*



Integrated Care

Tobacco Use and Mental Illness: A Wake-Up Call for Psychiatrists

Jill M. Williams, M.D.
T. Scott Stroup, M.D., M.P.H.
Mary F. Brunette, M.D.
Lori E. Raney, M.D.

**Tobacco use results in numerous consequences for individuals with mental illnesses and other substance use disorders, yet it is not adequately addressed by behavioral health professionals, including psychiatrists. This column describes current inaction among behavioral health professionals and some possible reasons for it and recommends next steps. Psychiatrists should provide treatment for all patients with a co-occurring tobacco use disorder and provide leadership to change policies and practices in treatment centers. Psychiatrists can be vital leaders of the effort to reduce the toll of tobacco use among people with mental illnesses, addictions, or both. A national movement for addressing tobacco use in the behavioral health field can be galvanized if more psychiatrists participate. (*Psychiatric*

Among people with mental illnesses, tobacco-related illness is the highest-ranking cause of death (1). Yet smoking by patients continues to be an afterthought for most psychiatrists and behavioral health professionals. Smoking rates among individuals with a mental illness or another addiction are two to three times higher than in the general population. People with mental illnesses represent about one-third of the estimated 51 million adult smokers in the United States (2).

Psychiatrists are ideally positioned to address tobacco use disorder among individuals with mental illnesses or substance use disorders, but there is little evidence to suggest that psychiatry as a profession participates in or contributes substantially to tobacco control activities, which include not only treatment but also larger issues of advocacy and public health. A recent major federal initiative focused on illnesses and substance use disorders. A recent large epidemiological study found that smoking accounted for half the deaths among persons with schizophrenia, bipolar disorder, or depression (1). Fortunately, quitting tobacco use improves life expectancy; quitting has a greater impact on cardiovascular risk than do changes in blood pressure, weight, physical activity, or lipids (4). Despite the powerful benefits of quitting, integrated efforts to address cardiovascular risk factors among people with serious mental illnesses have only cursorily included tobacco cessation efforts.

Tobacco use limits full recovery

As smoking becomes less common in the community, smokers experience greater barriers to community integration and will increasingly struggle to secure jobs and housing. Employers prefer to hire nonsmokers because

Callaghan RC; et al: Patterns of tobacco-related mortality among individuals diagnosed with schizophrenia, bipolar disorder, or depression. Journal of Psychiatric Research 2014
Allen MH; et al: Effect of nicotine replacement therapy on agitation in smokers with schizophrenia: a double-blind, randomized, placebo-controlled study. Am.Journal of Psychiatry 2011
Taylor G; et al: Change in mental health after smoking cessation: systematic review and meta-analysis. BMJ 2014

MHA Patients Want To Quit…..

- *Most smokers (80%) in a MMT population were “somewhat” or “very” interested in quitting.*
- *In an outpatient program for “alcohol abusers”, more than 75% were willing to consider stopping smoking.*
- *In substance dependent in-patients, 77% were “certain” they wanted to quit smoking.*
- *In SCZ, the majority were interested in attending a smoking cessation group and appeared to be motivated.*

Ellingstad TP et al (1999) Alcohol Abusers Who Want To Quit Smoking. Drug and Alcohol Dependence.
Richter KP et al.(2001) Tobacco Use and Quit Attempts Amongst Methadone Clients. AJPH
Irving, L M et al. (1994). Drug and alcohol inpatients' attitudes about smoking cessation. Journal of Substance Abuse
Addington J et al (1997) Readiness to stop smoking in schizophrenia. Can J Psychiatry

Smoking Cessation and Psychiatric Disorders

- *Change in mental health after smoking cessation: systematic review and meta-analysis. Taylor G et al BMJ 2014*

Changes in mental health after smoking cessation: systematic review

- *Investigate change in mental health after cessation v continuing to smoke*
- *Studies that assessed mental health before and after cessation*

- *"Smoking cessation is associated with REDUCED depression, anxiety and stress…IMPROVED positive mood and quality of life…effect equal for those with psychiatric disorders as without…"*

Taylor, Gemma et al. Change in mental health after smoking cessation: systematic review and meta-analysis BMJ 2014; 348 :g1151

Smoking and Psychotropic Drug Levels

- *Metabolized by CYP 1A2*
  - *Chlorpromazine*
  - *Haloperidol*
  - *Clozapine*
  - *Olanzapine*
  - *Caffeine*
- *Not Metabolized*
  - *Bupropion*
  - *Risperidone*
  - *Quetiapine*
  - *Ziprasidone*
  - *Aripiprazole*

Spina & de Leon Basic Clin Pharmacol Toxicol. 2007;100:4-22.

Smoking Cessation and Substance Use Disorders

- *Tobacco-free clients maintain longer periods of sobriety after inpatient treatment for alcohol/drug dependence than tobacco users.*

  Stuyt, 1997

- *Smoking cessation interventions result in effective drug and alcohol treatment outcomes, including reducing the risk of relapse and increasing long term sobriety.*

  Prochaska, 2004

- *Smoking and tobacco craving are strongly associated with the use of and craving for cocaine and heroin.*

  Epstein, 2010

Cessation Treatment For Patients with PD/SUD

"All smokers with psychiatric disorders, including substance use disorders, should be offered tobacco dependence treatment and clinicians must overcome their reluctance to treat this population"

- *Brief Intervention*
- *Individual, group and telephone counselling*
- *Pharmacotherapy*

Fiore MC et al. Treating Tobacco Use and Dependence: 2008 US DHHS

Brief Smoking Cessation Intervention

ASK: about tobacco use

ADVISE: every tobacco user to quit

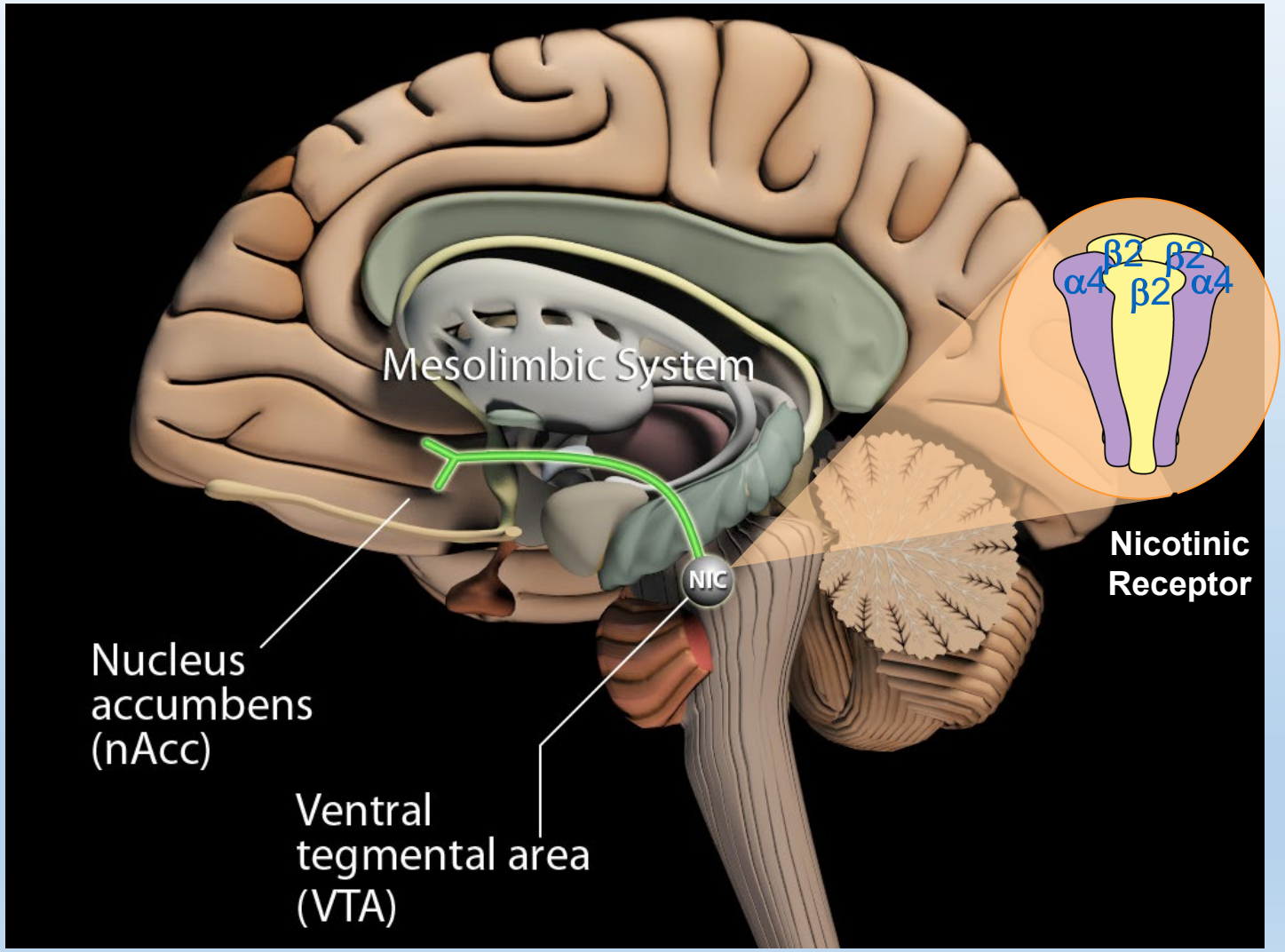
ASSESS: assess readiness to quit

ASSIST: self-help material
pharmacotherapy
counselling/quit lines

ARRANGE: follow up or referral

Fiore MC et al. *Treating Tobacco Use and Dependence: 2008 Update.* Clinical Practice Guideline.U.S. Department of Health and Human Services. Public Health Service. May 2008

Neurobiology of Tobacco Use Disorder



The Diagnostic and Statistical Manual of Mental Disorders (5th ed.; DSM–5; American Psychiatric Association [APA], 2013)

Pharmacologic Smoking Cessation Aids Available in Canada: Summary

Therapy	Route(s) of administration	Mechanism of action	Notes
Bupropion	Oral pill	Noradrenergic and/or dopaminergic*[1]	• Efficacious vs. placebo[2] • Proven safe & efficacious for patients with neuropsychiatric disorders[4,5]
Nicotine replacement therapy (NRT)	Transdermal patch, gum, inhaler, oral spray, lozenges	Delivers nicotine to the circulation via the venous system[2]	• Efficacious vs. placebo[2] • Most efficacious when two NRT modalities are combined[2] • Can be safely used in patients with underlying cardiovascular disease or neuropsychiatric disorders[6]
Varenicline	Oral pill	Stimulates and occupies the α4β2 nicotine receptor[3]	• Efficacious vs. placebo[2] • More efficacious than bupropion or single NRT[2] • Proven safe & efficacious for patients with neuropsychiatric disorders[4,5]

1. Valeant Canada LP. Zyban Product Monograph. Date of Preparation: July 25, 2016.
2. Cahill K, et al. Cochrane Database Syst Rev 2013; (5):CD009329.
3. Pfizer Canada Inc. Champix Product Monograph. Date of Revision: December 17, 2015.
4. Anthenelli RM, et al. Lancet 2016; 387(10037):2507-20.
5. Cinciripini PM, et al. JAMA Psychiatry 2013; 70(5):522-33.
6. Hubbard R, et al. Tob Control 2005; 14(6):416-21

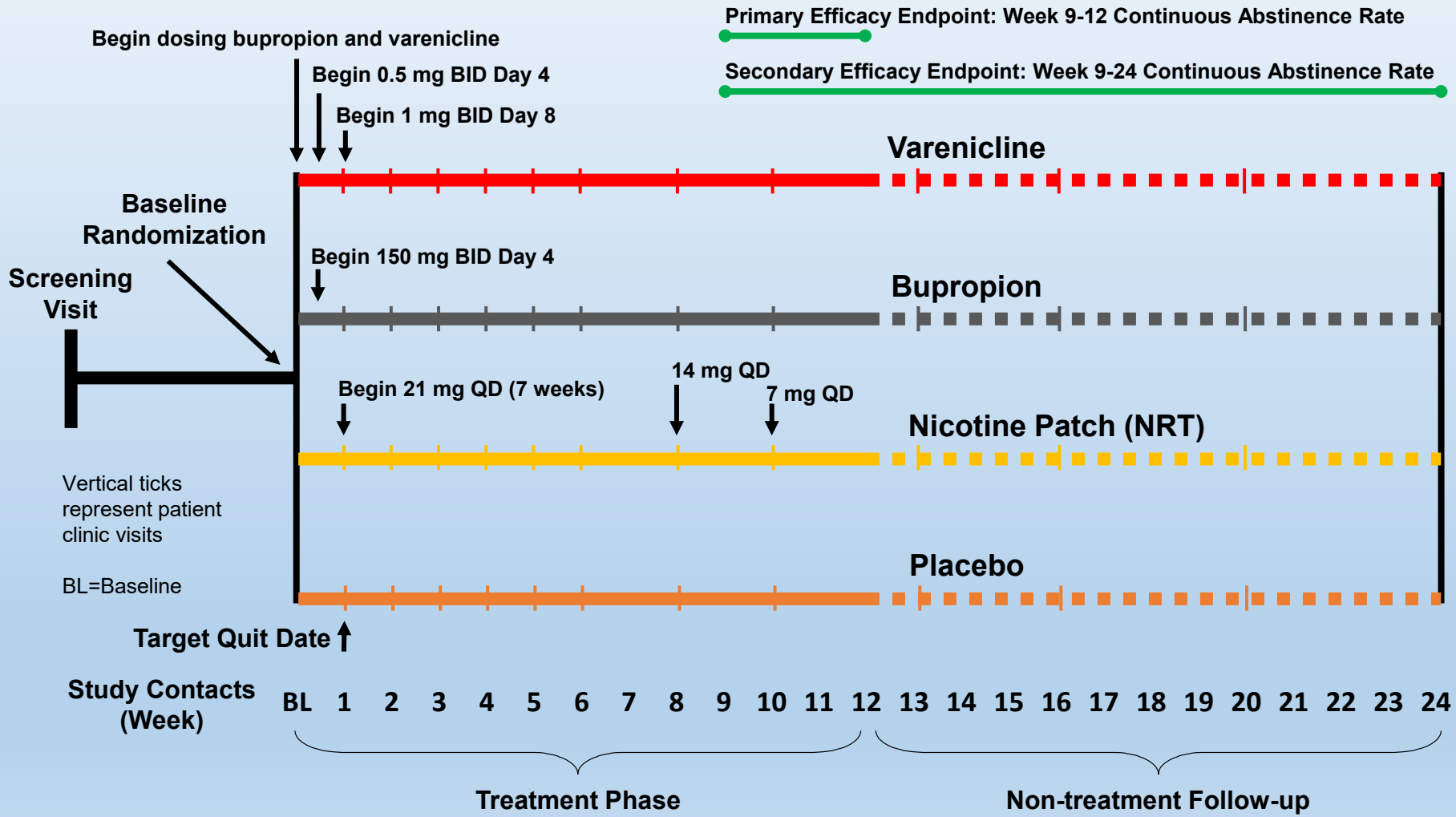
Efficacy of Cessation Therapies

- ***NRT** (combination)* *3.6 times more likely to quit**
- ***Varenicline*** *3.1 times more likely to quit**
- ***Bupropion*** *2.0 times more likely to quit**
- ***NRT** (patch alone)* *1.9 times more likely to quit**

**compared to placebo*

Agency for Healthcare Research and Quality (AHRQ). Available at: www.surgeongeneral.gov/tobacco/gdlnrefs.htm.

EAGLES Study Diagram



Anthenelli RM, et al. Lancet 2016; 387(10037):2507-20.

Safety: Neuropsychiatric AE Composite Endpoint

Cohort	Participants with Events n/N, %			
	Varenicline	Bupropion	NRT	Placebo
Non-Psychiatric	13/990 **1.3%**	22/989 **2.2%**	25/1006 **2.5%**	24/999 **2.4%**
Psychiatric	67/1026 **6.5%**	68/1017 **6.7%**	53/1016* **5.2%**	50/1015 **4.9%**
Overall (both cohorts)	80/2016 **4.0%**	90/2006 **4.5%**	78/2022 **3.9%**	74/2014 **3.7%**

AEs reported during treatment and ≤30 days after last dose.

** One additional participant (Psychiatric/NRT group) who reported suicidal ideation was identified after clinical database lock and was not included in the analysis*

Anthenelli RM, et al. Lancet 2016; 387(10037):2507-20.

Authors' Conclusions

- *Neuropsychiatric Safety*
  - *The EAGLES trial provides evidence that varenicline and bupropion do not pose a neuropsychiatric safety risk*
  - *These drugs can be used safely by smokers without a history of psychiatric disorders and by smokers with stable psychiatric disease*

- *Efficacy*
  - *Varenicline, bupropion, and NRT transdermal patches are more effective than placebo in aiding smoking cessation in patients with and without a history of psychiatric disorder*
  - *Varenicline is more effective than bupropion and NRT in psychiatric and non-psychiatric cohorts*

Anthenelli RM, et al. Lancet 2016; 387(10037):2507-20.

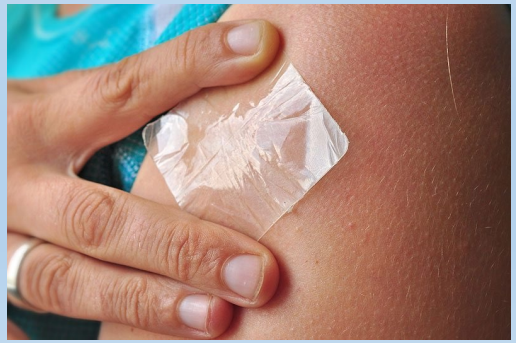
NRT Combinations

- *Common to combine patch + gum/lozenge/inhaler/oral spray*
- *More efficacious than monotherapy*
- *Considered safe (FDA 2013)*

1.Mills E.J. et al. Comparison of high-dose and combination NRT, varenicline and buproprion for smoking cessation: a systematic review and multiple treatment analysis. Ann Med 2012 Sep; 44(6): 588-97
2. Cahill K et al. Pharmacological interventions for smoking cessation: an overview and meta-analysis. Cochrane Database Syst. Rev 2013 May 31

FDA Proposed Label Changes

- *NRT use permitted whilst still smoking*
- *Use of multiple NRT products allowable*
- *Safe to extend treatment beyond label recommendation*



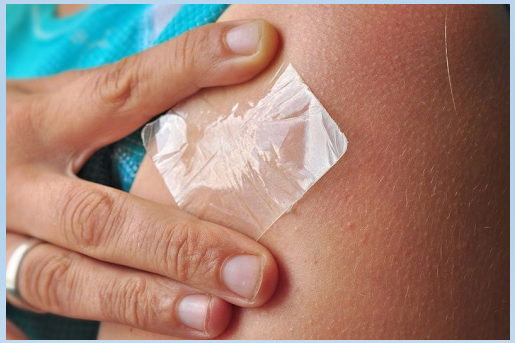
Food and Drug Administration (2013b). Nicotine replacement therapy labels may change. FDA Consumer Health Information. Silver Spring, MD: U. S. Department of Health and Human Services.

BC Smoking Cessation Program

- *BC Smoking Cessation Program since Sept 2011*
- *12 weeks per year of NRT or Varenicline /Zyban*
- *Consider SA for extension/change*
- *Process changed Jan 1st 2016 (no 811 call, more options)*

An Alternative Approach To Cessation: "Reduce to Quit"

- *Reducing cigarettes pre-quit day, and abrupt cessation approaches produce similar quit rates*
- *Patients should be given the choice to quit via either approach*
- *Reduction approaches can include the use of pre-quit nicotine replacement therapy (NRT)*
- *Cigarette smoking and concurrent NRT does not pose increased risk*



Lindson N, et al. Cochrane Database Syst Rev 2010 Mar 17; (3):CD008033.
U.S. Food and Drug Administration (FDA). Nicotine replacement therapy labels may change. 2013. Available at: www.fda.gov/ForConsumers/ConsumerUpdates/ucm345087.htm.

Cytisine(cytisinicline)

- ***Cytisine*** *(which inspired the development of varenicline) is a partial agonist of the* $\alpha_4\beta_2$ *NicAch receptor*
- *high-certainty evidence suggesting that nicotine e-cigarettes (EC), varenicline and* ***cytisine*** *were associated with the greatest chances of quitting tobacco smoking at six months or longer*
- *Used in eastern Europe for smoking cessation since the 1960's*
- *"natural health product" in Canada (prescription not required)*
- *Cost-effective but complex dosing regimen*

Lindson N et al Pharmacological and electronic cigarette interventions for smoking cessation in adults: component network meta-analyses. Cochrane Database of Systematic Reviews 2023, Issue 9. Art. No.: CD015226. DOI: 10.1002/14651858.CD015226.pub2.

Practical Approaches to Behavioural Counselling

- *Provide thoughtful, non-judgmental strategic advice and tactical suggestions to optimize cessation success*

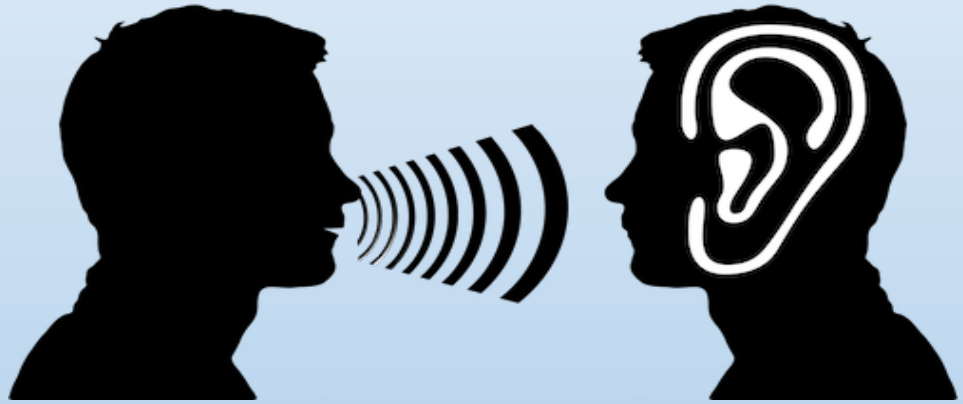
  - *Avoid situations, circumstances and settings associated with smoking*
  - *Secure the support of family and friends*
  - *Deal with withdrawal and cravings:*
    - ***THE 4 D's: DEEP BREATHS! DRINK WATER! DISTRACTION! DELAY!***

  - *Motivational interviewing: "the treatment of choice for ambivalence"*

University of Ottawa Heart Institute, Ottawa Model for Smoking Cessation.

Principles of Motivational Interviewing

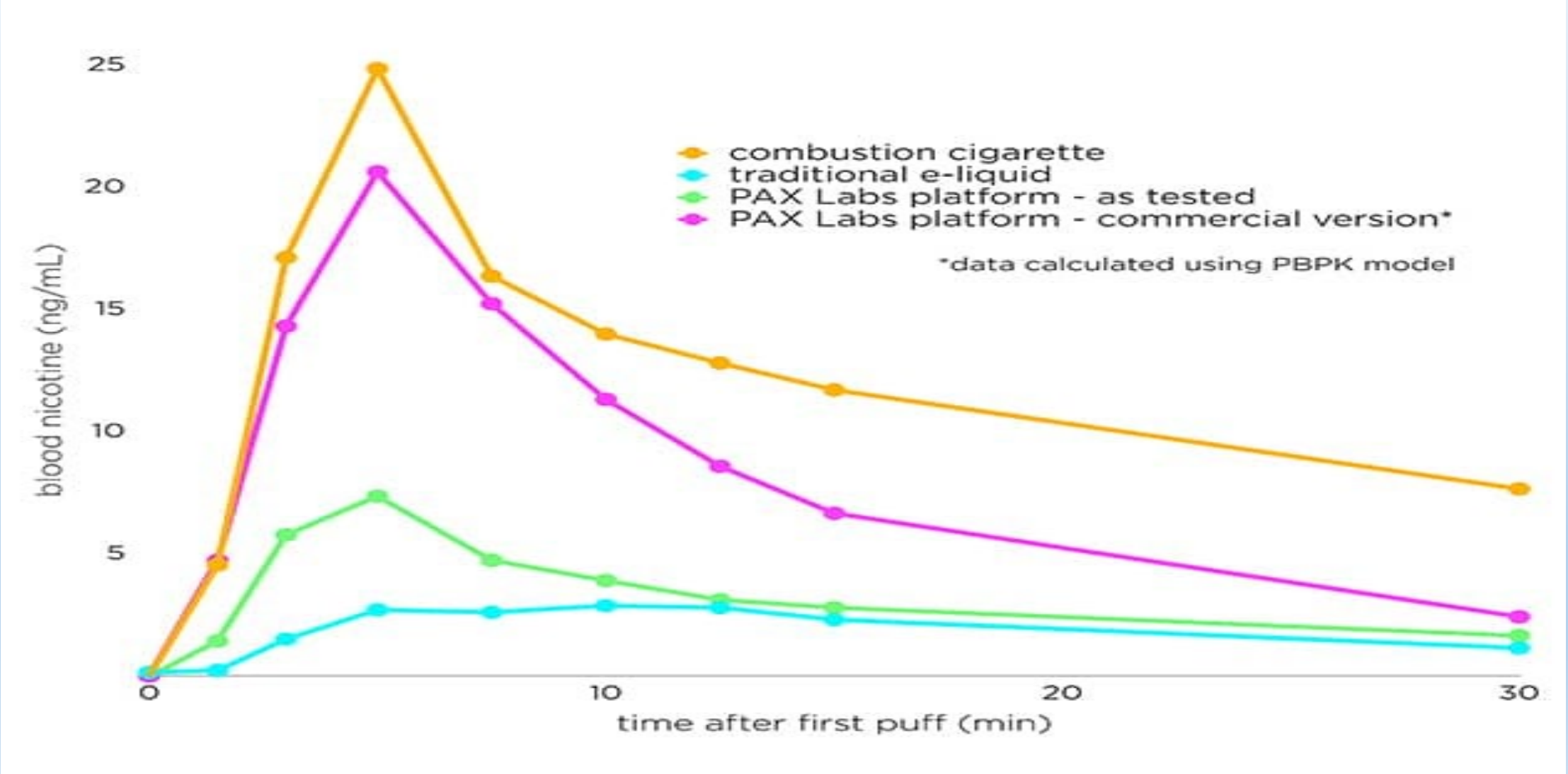
- Express Empathy
- Develop Discrepancy
- Roll with Resistance
- Support Self Efficacy



Miller, W. R., & Rollnick, S. (1991). Motivational Interviewing Preparing People to Change Addictive Behavior

Electronic Nicotine Delivery Systems (ENDS)?

Electronic Cigarettes for Smoking Cessation



ENDS for Cessation?

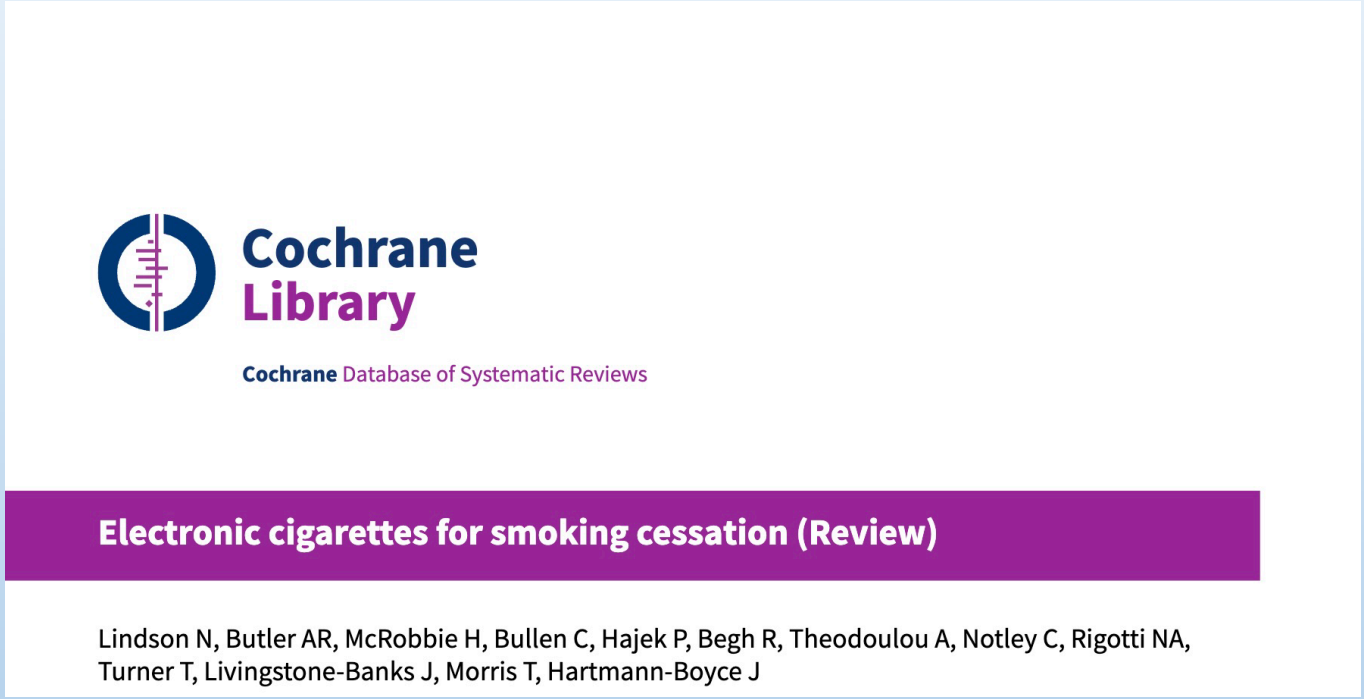
A Randomized Trial of E-Cigarettes versus Nicotine Replacement Therapy

- *n=886, randomised to ENDS or NRT*
- *Primary outcome: sustained abstinence for 12mos (biochemically confirmed)*
- *ENDS v NRT abstinence rate: 18% v 9.9% (RR 1.83)*
- *At 52w, 80% using ENDS v 9% NRT*

- ***"E-cigarettes were more effective for smoking cessation than nicotine-replacement therapy, when both products were accompanied by behavioral support"***

- *Hajek P, Phillips-Waller A, Przulj D, et al. A randomized trial of e-cigarettes versus nicotine-replacement therapy. N Engl J Med 2019;380:629-637*

ENDS for Cessation?



"There is high-certainty evidence that ECs with nicotine increase quit rates compared to NRT…"

Lindson N, et al. Electronic cigarettes for smoking cessation. Cochrane Database of Systematic Reviews 2024, Issue 1. Art. No.: CD010216. DOI: 10.1002/14651858.CD010216.pub8.

ENDS for Cessation?

Lower-Risk Nicotine Use Guidelines

E-cigarettes: Cessation Recommendation #5b: E-cigarettes with nicotine may be an effective cessation aid for people who use combustible tobacco.	Moderate	Conditional	1. Systematic reviews and RCTs provide some evidence of the effectiveness of e-cigarettes as a cessation aid. 2. More frequent use (i.e.: daily) of e-cigarettes is associated with an increase in cessation outcomes. 3. People who use combustible nicotine products should try to quit using approved smoking cessation treatments first. If they are unable or unwilling to quit, e-cigarettes can be considered. **Considerations** • E-cigarettes as a cessation aid may be most effective when combined with behavioural counselling. • Smokers should be advised to switch completely from combusted tobacco to e-cigarettes and to use e-cigarettes when they would normally have smoked tobacco cigarettes. • There is no evidence for a specific device type or amount of nicotine that is most effective for cessation. • Switching completely to e-cigarettes will significantly reduce the harms associated with combusted tobacco. However, smokers should be advised that harms associated with long-term e-cigarette use are currently unknown. • Continued use of e-cigarettes may reduce risk of relapse to combustible tobacco.

Lower-Risk Nicotine Use Guidelines CAMH 2022

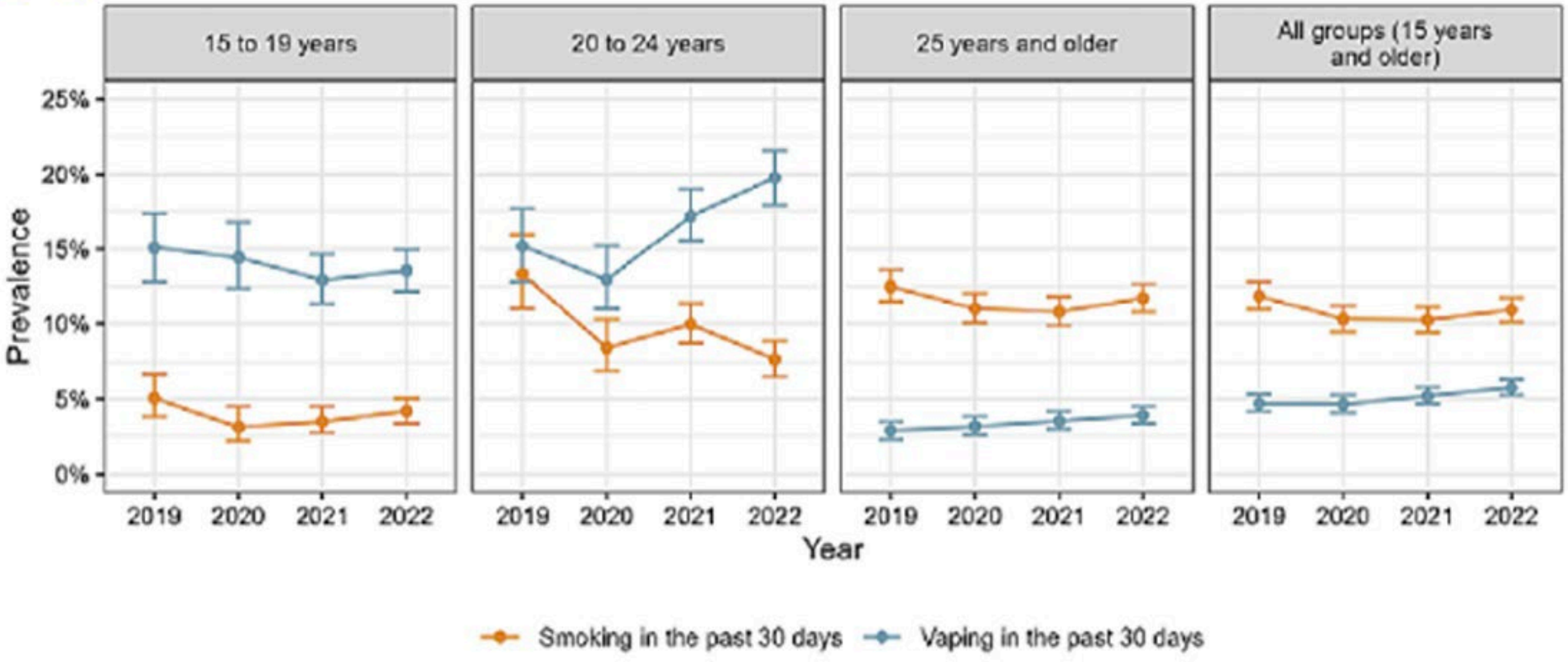
ENDS for Cessation?

"Clinicians should be prepared to have a risk–benefit discussion about e-cigarettes....the evidence has brought e-cigarettes to a tipping point. The burden of tobacco-related disease is too big for potential solutions such as e-cigarettes to be ignored"

Editorial, N Engl J Med 390;7 nejm.org February 15, 2024

Youth Vaping in Canada

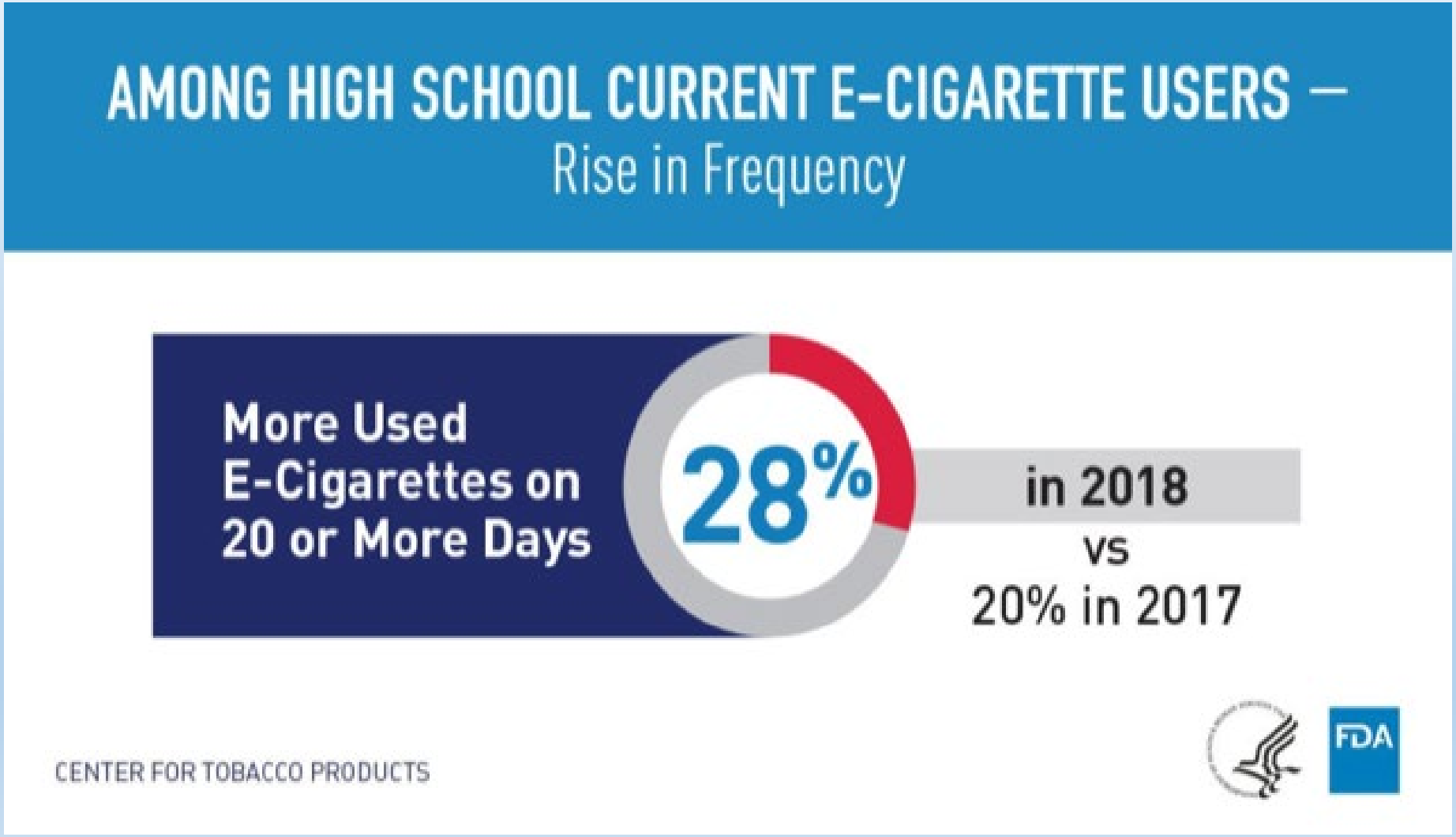
Infographic 1 – Cigarette smoking and vaping in the 30 days before the survey, by age group, 2019 to 2022



Note: Error bars indicate the 95% confidence intervals of the prevalence estimates.

Source: Canadian Tobacco and Nicotine Survey, 2019 to 2022.

Youth Vaping



Repetitive transcranial magnetic (rTMS) stimulation for smoking cessation

- Evidence for rTMS for smoking cessation is increasing
- One rTMS coil has recently received regulatory approval
- Implementation and dissemination into clinical practice requires planning and preparation.
- Accessibility, technological, economical, and social challenges remain to be addressed.
- Real-world effectiveness studies are needed

Victor M. Tang et al. Repetitive transcranial magnetic stimulation for smoking cessation: Next steps for translation and implementation into clinical practice, Psychiatry Research,Volume 326,2023,

Repetitive transcranial magnetic (rTMS) stimulation for smoking cessation

- 262 chronic smokers meeting DSM-5 criteria for TUD
- 3/52 daily bilateral active or sham rTMS to the lateral prefrontal and insular cortices (+ once weekly 3/52)
- CQR until Week 18 was ***19.4%*** (active) and ***8.7%*** (sham) rTMS (p=0.017)

- 1st large multicenter RCT of brain stimulation in addiction medicine (leading to clearance by the US FDA for rTMS as an aid in smoking cessation)

Zangen, A. et al. Repetitive transcranial magnetic stimulation for smoking cessation: a pivotal multicenter double-blind randomized controlled trial. World Psychiatry, 20: 397-404. https://doi.org/10.1002/wps.20905

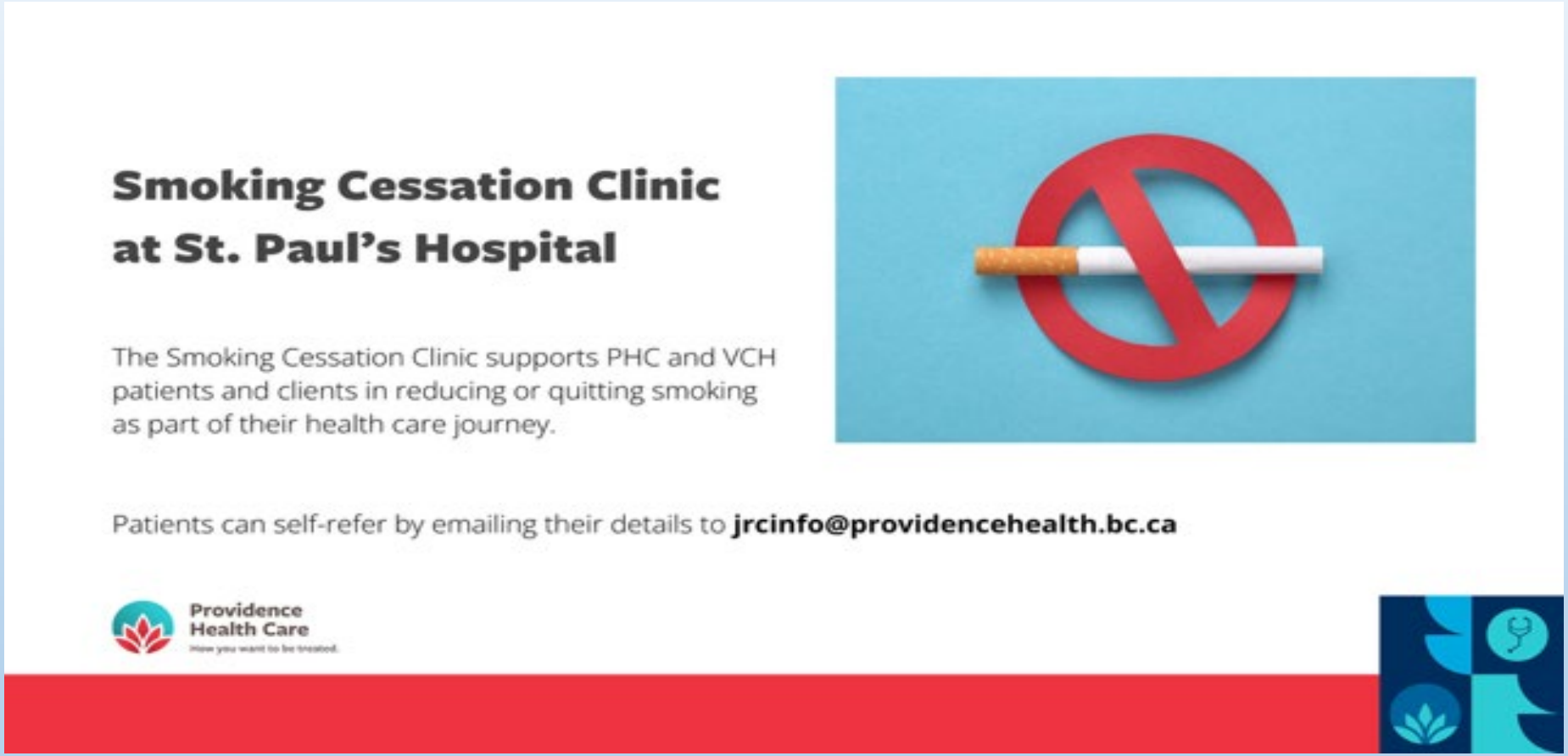
Smoking Addiction Treatment

About Smoking Addiction | Treatment Options | Efficacy | Safety | Treatment Protocol

Introducing

BrainsWay Deep Transcranial Magnetic Stimulation (Deep TMS™) is a safe and effective aid for short-term smoking cessation in adults, representing the first FDA clearance in the

Questions?



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