

Smoking Cessation In Vulnerable Populations



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Janssen

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Context Research

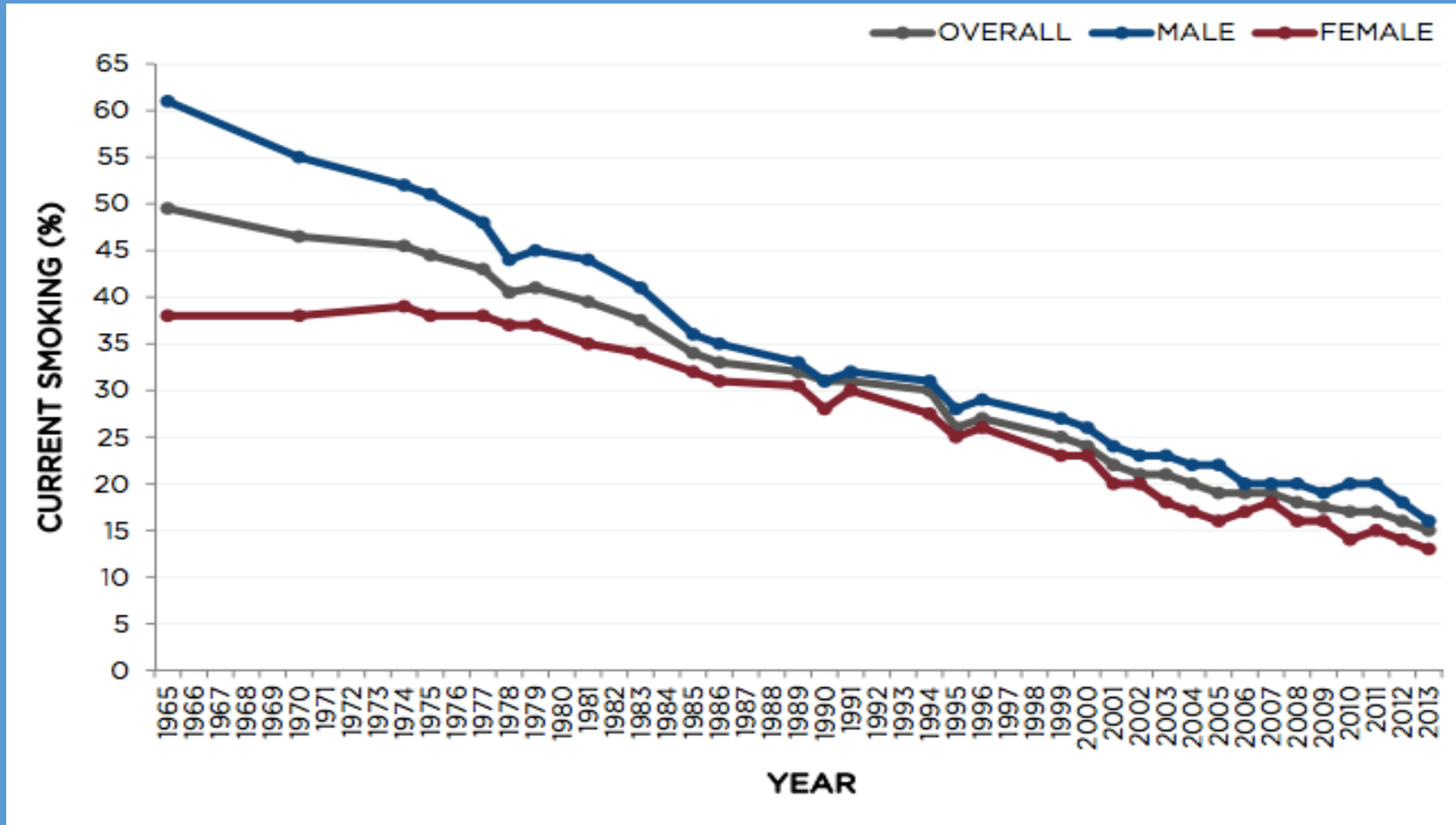
Mitigating Potential Bias

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

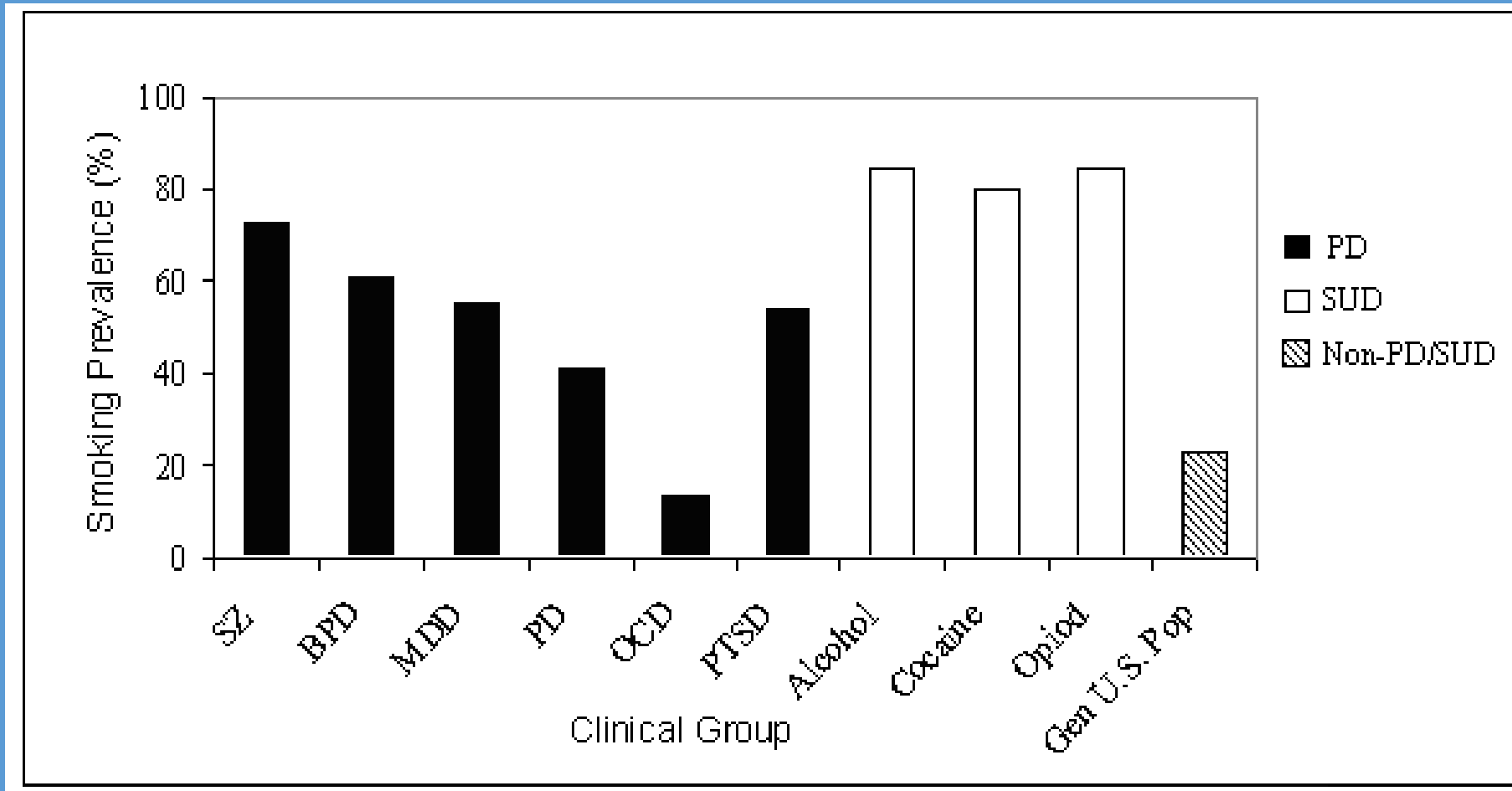
Learning Objectives

- *To recognize and challenge misconceptions relating to these populations and tobacco*
- *To increase confidence regarding tobacco treatment in these populations*
- *To become aware of specific “caveats” relating to tobacco treatment in these populations*

Smoking Prevalence Trends in Canada (1965-2013)



Prevalence of Smoking: Psychiatric and Substance Use Disorders

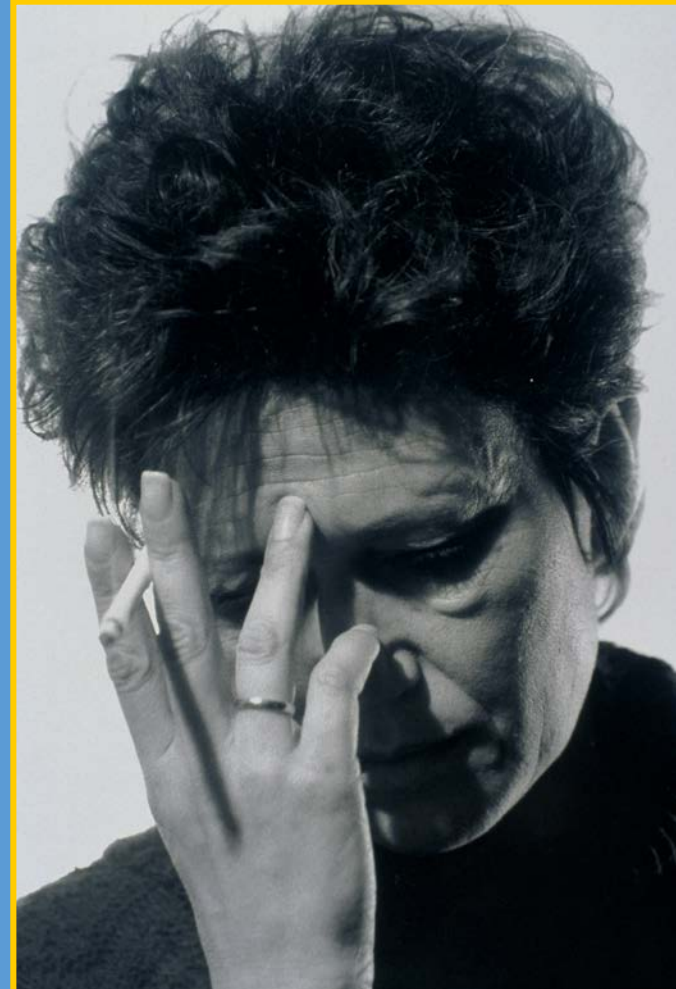


From Kalman, Morissette and George (2005), *Am. J. Addict.*, 14: 106-123

Smoking and Schizophrenia: Patient Perceived Benefits

- *Cigarette smoking in schizophrenia may be reinforcing because it may:*
 - *Improve psychiatric symptoms (self medication hypotheses)*
 - *Improve cognitive functioning*
 - *Reduce medication side effects*

Mental Health Service culture?



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*



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

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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 im-

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

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*

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...”*

Smoking and Psychotropic Drug Levels

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



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*

Cessation Treatment For Patients with PD/SUD

Summary Statement #2

Health care providers should offer **counseling and pharmacotherapy** treatment to persons who smoke and who have a mental illness and/or addiction to other substances.

GRADE: 1A

A 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

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 bupropion 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

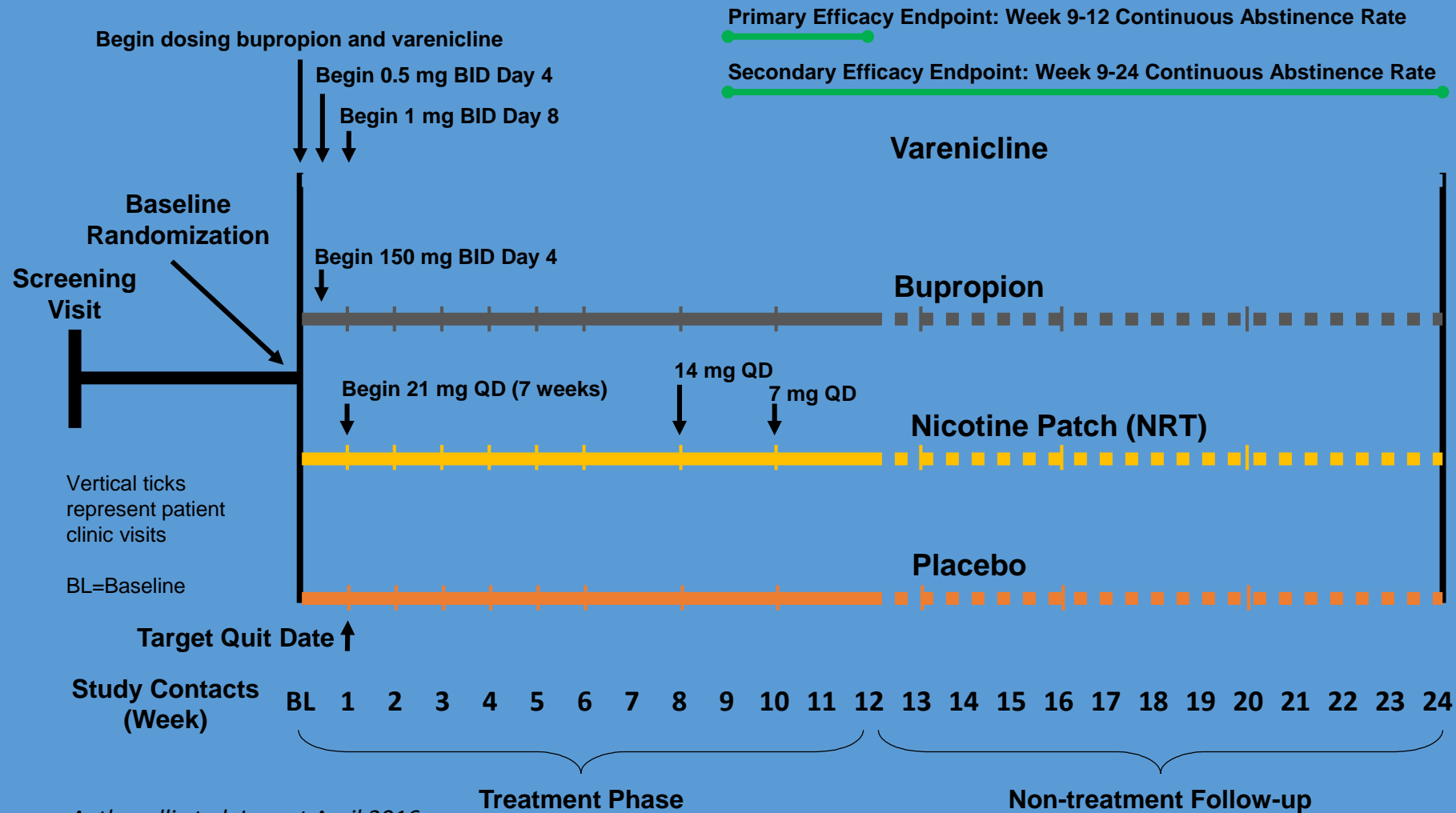
FDA Proposed Label Changes

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

EAGLES Study Design

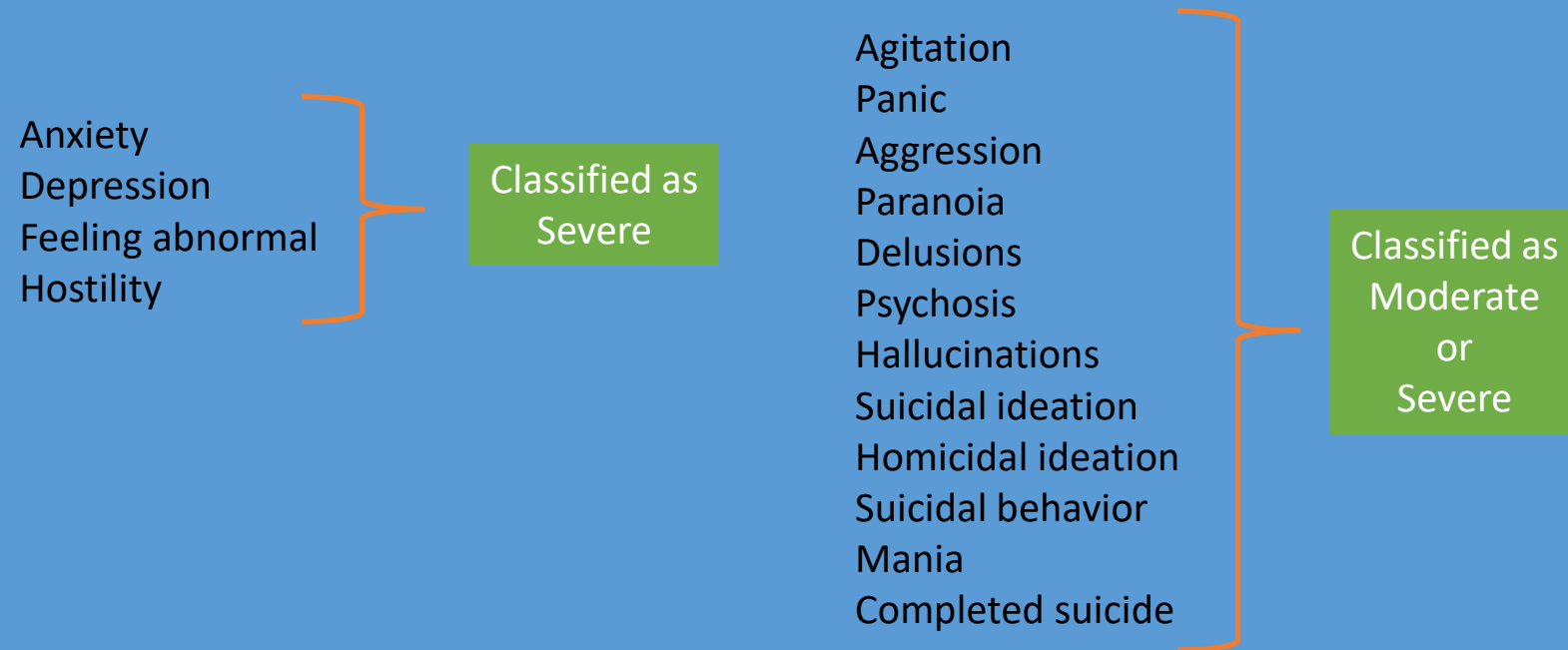
- **Main Objectives**
 - **Safety:** Characterize the neuropsychiatric safety profiles of varenicline and bupropion vs. placebo in subjects with and without a diagnosis of psychiatric disorder
 - **Efficacy:** Compare smoking abstinence rates of varenicline and bupropion relative to placebo in subjects with and without a diagnosis of psychiatric disorder
- **Design:** Randomized, double-blind, 24-week, and NRT and placebo-controlled
 - **Four Treatment Arms:** varenicline, bupropion, nicotine patch (NRT), placebo
 - Primary comparisons: varenicline vs. placebo and bupropion vs. placebo
 - Nicotine replacement therapy (NRT) was used as an active control
 - Triple dummy design: all 3 active study drugs were blinded
 - 12 weeks of active treatment followed by 12 weeks of non-treatment follow-up
 - All participants received counseling of up to 10 minutes at each clinic visit
 - **Targeted Sample Size: 8000 total randomized subjects**
 - 2000 per treatment arm, including 1000 with and 1000 without psychiatric disorder

EAGLES Study Diagram



Key Endpoints

Primary Outcome Measure: The percentage of subjects reporting at least one of the following Neuropsychiatric (NPS) adverse events (AEs) during treatment and up to 30 days after last dose:



Main Efficacy Measure: CO-confirmed 4-week continuous abstinence rates (CAR) for Weeks 9-12

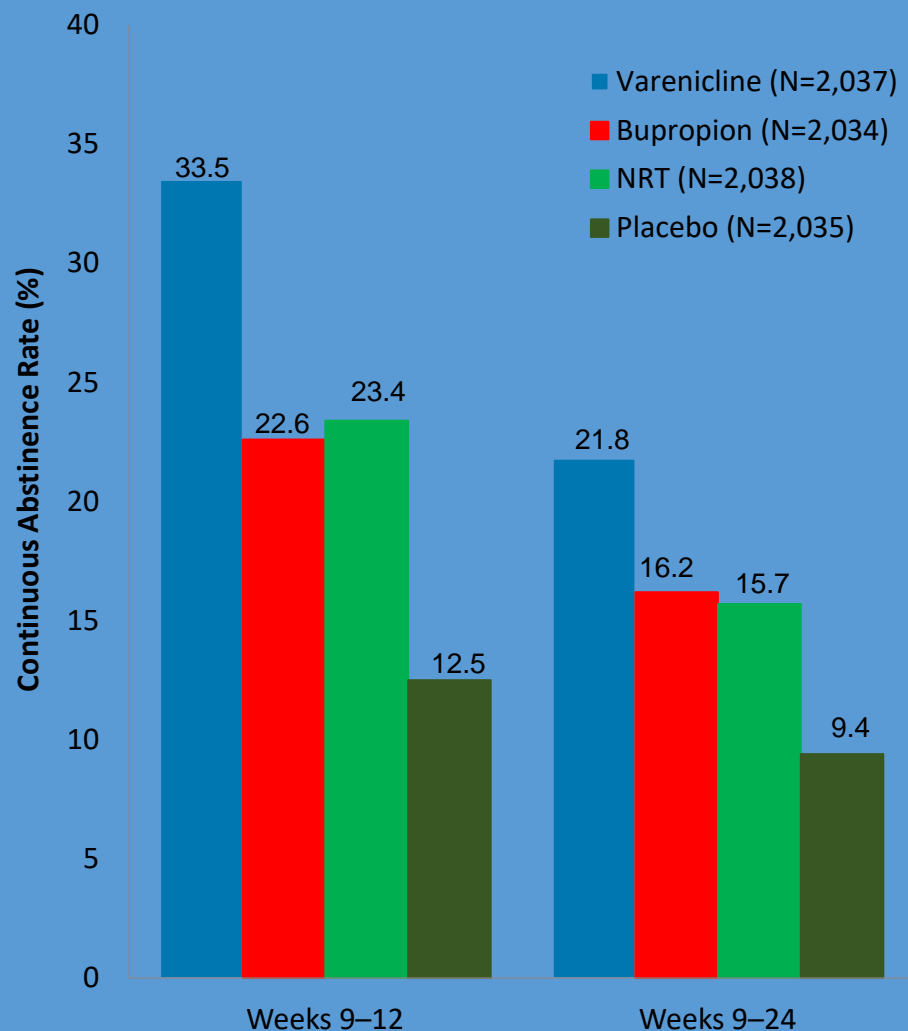
Primary Outcome Measure: Neuropsychiatric AE Composite Endpoint

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

Efficacy: Continuous Abstinence Rates (CARs) All Treated Subjects (Both Cohorts Pooled)



Odds Ratios* CAR Weeks 9-12 Main Efficacy Measure	
	OR (95% CI)
Varenicline vs. placebo*	3.61 (3.07-4.24)
Bupropion vs. placebo*	2.07 (1.75-2.45)
NRT vs. placebo	2.15 (1.82-2.54)
Varenicline vs. NRT	1.68 (1.46, 1.93)
Bupropion vs. NRT	0.96 (0.83, 1.11)
Varenicline vs. bupropion	1.75 (1.52, 2.01)

Odds Ratios* CAR Weeks 9-24	
	OR (95% CI)
Varenicline vs. placebo*	2.74 (2.28-3.30)
Bupropion vs. placebo*	1.89 (1.56-2.29)
NRT vs. placebo	1.81 (1.49, 2.19)
Varenicline vs. NRT	1.52 (1.29, 1.78)
Bupropion vs. NRT	1.04 (0.88, 1.24)
Varenicline vs. bupropion	1.45 (1.24, 1.70)

* Primary comparisons

Authors' Limitations

- *Findings may not generalize to smokers with untreated or unstable psychiatric disease*
- *Light smokers not included*
- *Smokers with imminent suicidality risk were excluded*
- *Low power for rare NPS events*

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*

Efficacy of Varenicline + NRT Patch v Varenicline alone

- *n=435, multicentre, RCT*
- *12 weeks Rx + 12 weeks f/u*
- *CAR Wk 9-12: 55.4% v 40.9% (OR 1.85)*

- *Conclusion: Var/NRT more effective than Var alone.
No difference in adverse events (except skin rash)*

Electronic Nicotine Delivery Systems (ENDS)



Electronic Nicotine Delivery Systems (ENDS)

- *E-cigarettes...*
 - *Are not currently marketed as cessation products at all*
 - *Are not regulated or approved for sale in Canada*
 - *Have not been fully evaluated for their efficacy as smoking cessation therapies*
 - *Have not been fully evaluated for their safety*
 - *Formaldehyde-releasing molecules can be formed²*



Electronic Nicotine Delivery Systems (ENDS)

- *“The USPSTF concludes that the current evidence is insufficient to recommend ENDS for tobacco cessation in adults... recommends that clinicians direct patients who smoke tobacco to other cessation interventions with established effectiveness and safety”*
- *“estimates show e-cigarettes are 95% less harmful than normal cigarettes, and when supported by a smoking cessation service, help most smokers to quit tobacco altogether.”*

What's New in Tobacco Control

