

## Addictions and Mental Health

Disparities in Tobacco Use and Cessation  
Ron Pohar, BScPharm

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## Disclosure

- **Potential for conflict(s) of interest:**
  - **Consulting Fees/Honoraria:** Pfizer, Johnson and Johnson, Mylan Pharma, Janssen, Leo Pharma

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## Impact of Smoking in Addictions and Mental Health

- Individuals with mental health disorders will die 10 to 20 years earlier than the general population.
- **Smoking** is the largest avoidable cause of premature death and disparities in health in this population.
- Disproportionate impact of tobacco-related harm seen in AMH is related to disproportionate consumption:
  - Individuals with mental health disorders consume 50% of all tobacco in the United States
  - No Canadian estimates are available

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## Smoking Prevalence According to Psychiatric Disorder

Disorder	Range
Major depression	36 to 80%
Bipolar mood disorder	51 to 70%
Schizophrenia	62 to 90%
Anxiety disorders	32 to 60%
Post-traumatic stress disorder	45 to 60%
Attention deficit hyperactivity disorder	38 to 42%
Alcohol abuse	34 to 93%
Other drug abuse	49 to 98%

Canadian general population smoking rate from CTADS 2017: 15%

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## Factors Associated With Tobacco Use in AMH

- Environmental and social-economic factors contribute to high smoking rates in addictions and mental health.
- Socioeconomic
  - Limited education, poverty, unemployment, peer pressure
- Environmental
  - Prevailing culture in AMH treatment
- Neurobiological factors
  - Self-medication (reduce stress, anxiety)
- Psychosocial factors
  - Source of pleasure – significant reward derived
  - Shared social activity

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## Canadian Action Network for the Advancement, Dissemination and Adoption of Practice-informed Tobacco Treatment (CAN-ADAPTT) Evidence Statement

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

▪ GRADE\*: 1A

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## Interventions in Individuals with Mental Illnesses

- Appropriate timing of the quit attempt must be evaluated
- Psychiatric symptoms should be stable
- No recent or planned changes in medications
- No urgent problems that take precedence

American Psychiatric Association. Practice guideline for the treatment of patients with substance use disorders. Second Edition, 2006.  
Fiore M, Bailey W, Cohen S, et al. Treating tobacco use and dependence: 2008 Update. Clinical Practice Guideline. Rockville, MD: US Department of Health and Human Services, 2008.

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## CAN-ADAPTT: First-Line Pharmacotherapies

- Nicotine Replacement Therapy (NRT)
- Bupropion SR
- Varenicline

CAN-ADAPTT. (2011). Canadian Smoking Cessation Clinical Practice Guideline. Toronto, Canada: Canadian Action Network for the Advancement, Dissemination and Adoption of Practice-informed Tobacco Treatment. Centre for Addiction and Mental Health.

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## NRT Options

- Patch
- Gum
- Lozenge
- Inhaler
- Mouth Spray
  
- Provide a "clean source" of nicotine thereby reducing withdrawal symptoms
- Typically have been used as monotherapies or combination therapy tailored to meet patient need and preference
- Prior to 2016, the majority of combination therapy was considered "off-label" and products carried warnings not to smoke while using NRT

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## Dosing of Combination NRT

- New licensing of NRT products does not provide guidance with respect to dosing of short and long acting NRT when used simultaneously.
- New labelling simply refers consumers to their healthcare providers for advice about using more than one type of NRT at the same time.
- Dosing algorithms for combination NRT vary across different jurisdictions, with some sources suggesting lower daily maximums with the short acting agent than when it is used as monotherapy.

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## NRT in Psychiatric Populations

- At best, the NRT patch replaces about 50% of nicotine
  - May need to increase beyond 21mg with heavy smokers
- For example, schizophrenia
  - Tend to be highly nicotine dependent
  - Smoke more heavily, generally prolonged duration of smoking
- "Heavily addicted smokers (> 25 cigarettes per day) may benefit from combining patch strengths so that they receive approximately 1 mg of nicotine for every cigarette smoked per day"

Reid RD, Pritchard G, Walker K, et al. Managing smoking cessation. CMAJ 2016.

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## Neuropsychiatric safety and efficacy of varenicline, bupropion, and nicotine patch in smokers with and without psychiatric disorders (EAGLES):

**A double-blind, randomised, placebo-controlled clinical trial.**

Arterelli RM, et al. Lancet 2016 Apr 22. doi: 10.1016/S0140-6736(16)30272-0 [Epub ahead of print]

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## 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

Arthurs RM, et al. Lancet 2016 Apr 22. doi: 10.1016/S0140-6736(16)30272-0 [Epub ahead of print]

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## Study Design

- Randomized (1:1:1:1), double-blind, placebo-controlled and active-controlled trial
  - Nicotine patch (21 mg with taper) – Active control
  - Varenicline (1mg BID)
  - Bupropion (150mg BID)
  - Placebo
- 12 weeks treatment followed by 12 weeks of non-treatment follow up
- Also received 10 minutes of counselling at each visit
- **8,144 total randomized participants**
  - 4,028 included in the non-psychiatric cohort
  - 4,116 included in the psychiatric cohort
  - Within each cohort, between 1,001-1,033 participants were randomized to each active therapy or placebo
- Study Sites: 140 centers in 16 countries on 5 continents

Arthurs RM, et al. Lancet 2016 Apr 22. doi: 10.1016/S0140-6736(16)30272-0 [Epub ahead of print]

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## Primary Endpoint: Neuropsychiatric AE Composite Endpoint

Cohort	Number (percentage) of subjects with ≥1 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 moderate

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**Primary NPS AE Endpoint:  
Risk Differences Between Treatment groups**

Comparison	Non-Psychiatric Cohort Risk Difference (95% CI)	Psychiatric Cohort
Varenicline vs placebo	-1.28 (-2.4 to -0.15)*	1.59 (-0.42 to 3.59)
Bupropion vs placebo	-0.08 (-1.37 to 1.21)	1.78 (-0.24 to 3.81)
NRT vs placebo	-0.21 (-1.54 to 1.12)	0.37 (-1.53 to 2.26)
Varenicline vs NRT	-1.07 (-2.21 to 0.08)	1.22 (-0.81 to 3.25)
Bupropion vs NRT	0.13 (-1.19 to 1.45)	1.42 (-0.63 to 3.46)
Varenicline vs Bupropion	-1.19 (-2.30 to -0.09)*	-0.20 (-2.34 to 1.95)

\* P <0.05

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**Authors' Conclusions**

- Safety
  - This study did not show a significant increase in neuropsychiatric adverse events attributable to varenicline or bupropion relative to nicotine patch or placebo.
- Efficacy
  - Varenicline was more effective than placebo, nicotine patch, and bupropion in helping smokers achieve abstinence
  - Bupropion and nicotine patch were more effective than placebo.

Arrhenelli RM, et al. Lancet 2016 Apr 22; doi: 10.1016/S0140-6736(16)30272-0 [Epub ahead of print]

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**Monograph Changes Based on EAGLES**

- Removal of "black box" type warnings about neuropsychiatric adverse effects in varenicline product monographs by the EMA, FDA and most recently Health Canada in February 2017.
- Health Canada removed statement that thorough consideration should be given to a trial of NRT prior to prescribing varenicline.

[http://www.accessdata.fda.gov/drugsatfda\\_docs/nda/2015/021109Orig1s01AMD\\_x.pdf](http://www.accessdata.fda.gov/drugsatfda_docs/nda/2015/021109Orig1s01AMD_x.pdf) EMA - 15/0011-2016eb2017.

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### Challenges to Achieving 5% Smoking Prevalence by 2035 in AMH

- Patient-related factors
  - Long histories of tobacco use
  - More severe tobacco dependence (physical and emotional)
  - Demonstrate higher levels of stress and low mood
    - Use of tobacco to cope with stress
    - Difficulties coping with withdrawal symptoms
- Socio-economic factors
  - Can limit ability to participate in programs
  - Can limit access to pharmacotherapy

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### Challenges to Achieving 5% Smoking Prevalence by 2035 in AMH

- System/provider related factors
  - Acceptability of smoking/norms
  - Provider misconceptions of low motivation to quit
  - Inadequate support to quit provided by health professionals
  - Provider time
  - Lack of translation of newer evidence into practice

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### Achieving 5% Target by 2035

- Need for training and support of health care providers
  - Reduce misconceptions and change norms
  - Improve confidence
  - Latest evidence of medication efficacy and safety into practice
- Improved coverage for pharmacotherapy
  - Multiple quit attempts required
  - Higher dosages of NRT required
  - Longer duration of therapy
    - To support abstinence
    - To support long-term reduction
- Providing onsite delivery of programs and support

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- Tobacco Cessation Pharmacology for Mental Health



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