Implementing MAT Services for Tobacco Cessation in Integrated Care Settings
Innovation Community

Webinar #1

Slides for today’s webinar will be available on the CIHS website:
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mat_ic@nationalcouncilcommunities.org

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Disclaimer: The views, opinions, and content expressed in this presentation do not necessarily reflect the views, opinions, or policies of the Center for Mental Health Services (CMHS), the Substance Abuse and Mental Health Services Administration (SAMHSA), the Health Resources and Services Administration (HRSA), or the U.S. Department of Health and Human Services (HHS).
Setting the Stage: Today's Facilitator

Aaron Williams
Senior Director of Training and Technical Assistance for Substance Use
SAMHSA-HRSA Center for Integrated Health Solutions

Updates in the Treatment of Tobacco Use Disorder

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Director, Division Addiction Psychiatry
Robert Wood Johnson Medical School

Disclosures

• Grant Support from Pfizer
• Grant support from NCI, NIDA, NIMH, NJDMHAS, ABPN
• Consultant and Speaker for American Lung Association

51 Million Smokers in US Today
At least one third have a mental illness
~ 16 Million Smokers with Mental Illness

Why are Patients Not Quitting?

• Neurobiological
• Psychological
• Social & Environmental
• Spiritual & Advocacy
• Treatment System & Institutional
• Greater dependence
• Poor coping; low confidence
• Live with smokers
• No hope; No peers succeeding
• No access to help; Not encouraged to quit

Lawrence et al, BMC Public Health 2009, 9:288
Why are Patients Not Quitting?

- Neurobiological
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Tobacco Use Disorder

Many tobacco users are addicted (2 or more)
- withdrawal
- tolerance
- desire or efforts to cut down/control use
- great time spent in obtaining/using
- reduced occupational, recreational, social activities
- use despite problems (interpersonal; physical)
- larger amounts consumed than intended
- use when physically hazardous
- craving; strong urges to use

Tobacco Withdrawal

Emerge hours after last cigarette
Can last up to (4) weeks

Depressed mood
Insomnia
Irritability, frustration or anger
Anxiety
Difficulty concentrating
Restlessness
Increased appetite or weight gain

Heaviness of Smoking Index

Measure of Dependence

AM Time to first cigarette (TTFC)
- ≤ 30 minutes = moderate
- ≤ 5 minutes = severe

Implications for Treatment Outcome
Need for Medications
Implications for Dose

Smokers with depression smoke more cpd and are more dependent

Heatherton 1991
Smokers with SMI Have High Levels of Tobacco Dependence

80% Moderately to Severely Dependent

<table>
<thead>
<tr>
<th>Measure</th>
<th>SPD* (SMI)</th>
<th>Non-SPD*</th>
</tr>
</thead>
<tbody>
<tr>
<td>NDSS</td>
<td>49.7%</td>
<td>33.3%</td>
</tr>
<tr>
<td>FTND</td>
<td>57.6%</td>
<td>42.1%</td>
</tr>
<tr>
<td>TTFC ≤ 5 mins</td>
<td>29.2%</td>
<td>19.3%</td>
</tr>
</tbody>
</table>

*SPD by K6; NSDUH 2002

Williams et al., 2011; Hagman et al., 2008

Smokers in Addiction Treatment are Moderately to Severely Addicted to Nicotine

N=1882 smokers in NJ addictions treatment, 2001-2002;

Williams et al., 2005

Only 1 in 4 Mental Health Treatment Facilities Offers Quit Smoking Services


N-MHSS Report, Nov 2014

Pharmacological Treatment

Rationale
- Doubles chances of successful quit
- Cost-effective
- Reduce or eliminate withdrawal
- Lessen/delay weight gain
- Block reinforcing effects of nicotine

First-line Treatments (FDA Approved)

- **Nicotine Replacement Therapy**
- **Bupropion**
  - Zyban/ Wellbutrin
- **Varenicline**
  - Chantix

Counseling + Medications = Best treatment plan

Nicotine Replacement Therapy

- Can be combined with bupropion
- Can be combined with each other
- Has almost no contraindications
- Has no drug-drug interactions
- Safe enough to be OTC

- Scheduled better than PRN
- Use high enough dose
- Use for a long enough time period
Nicotine Safety
Smokers misinformed about safety/efficacy of nicotine
✓ Not a carcinogen
✓ Not a significant risk factor for cardiovascular events

Risk-benefit ratio supports nicotine replacement over using tobacco

FDA Labeling Updates
• No significant safety concerns associated with using more than one NRT
• No significant safety concerns associated with using NRT at the same time as a cigarette.
• Use longer than 12 weeks is safe

www.fda.gov/ForConsumers/ConsumerUpdates/ucm345087.htm April 2013; Facito et al., 2014

Nicotine Patch
Slow onset of action
Continuous nicotine delivery
24 or 16 hour dosing
No strict tapering or timeline
Easy, good compliance
OTC
Side effects - skin reaction, insomnia

“Oral” Forms of Nicotine
Dose frequently – every 1-2 hours
Slow, buccal absorption
Acidic foods ↓ absorption
Mild side effects - mouth, throat burning
GI upset if swallowed

New Directions For Use

Cardiovascular Review
• No increase in serious cardiovascular disease events in those who use NRT (compared to ongoing smoking)
• No increased cardiovascular disease events with bupropion
• No evidence that varenicline linked to increased heart and circulatory problems

Sharma et al., Curr Cardiology Reports (Review) 2015
**Cardiovascular Review**

**SUMMARY:**

- Low risk of harm
- Benefits outweigh low risk of serious adverse CVS events associated with use of tobacco treatment medications

Sharma et al., Curr Cardiology Reports (Review) 2015

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**Smoking with NRT**

- Relatively safe
- Harm Reduction
- Less reinforcing effects
- Withdrawal of treatment = punishment for relapsing

LeHouezec et al., 2011; Kozlowski et al., 2007; Zapawa 2011

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**Cut Down To Quit (CDTQ)**

- NRT gum and inhaler previously licensed in the UK for quitting have recently been granted a new licensed indication called ’cut down to quit’ (CDTQ).
- Approach for smokers unwilling or unable to stop smoking in the short term
- Gradually cut down smoking over an extended period while taking NRT
- Is it safe and effective?

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**NRT Assisted Reduction**

- Meta-analysis of 2767 smokers who declared no intention to quit smoking in the short term
- NRT (gum, inhaler) or placebo for 6-18 months
- 6.75% of smokers receiving NRT had sustained abstinence for six months, twice more than those receiving placebo
- No statistically significant differences in adverse events, except nausea (more common with NRT)
- Estimated to be cost-effective compared to not quitting

Wang et al., 2008; Moore et al., 2009

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**Bupropion SR**

- Zyban/ Wellbutrin
- Nonsedating, activating antidepressant with effects on NE and DA systems
- 150mg to 300mg daily (SR or XL)
- Start 10-14 days prior to quit date
- Contraindicated in h/o seizures or bulimia
- Effect independent of depression and alcohol use
- Less weight gain with 300mg than placebo

Slemmer et al. 2000; Hughes et al., 2007; Hayford et al., 1999

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**Combination Therapies**

- Improve abstinence rates
- Decrease withdrawal
- Well tolerated

<table>
<thead>
<tr>
<th>Combined Therapy</th>
<th>Odds Ratio (95% CI)</th>
</tr>
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<tbody>
<tr>
<td>Patch + gum or spray</td>
<td>1.9 (1.3 – 2.7)</td>
</tr>
<tr>
<td>Patch + bupropion</td>
<td>1.3 (1.0 – 1.8)</td>
</tr>
</tbody>
</table>

Fiore 2008
Varenicline: a selective a4B2 nicotinic receptor partial agonist

Varenicline

Partial Agonist
- Partially stimulates receptor
- Some DA release at NAcc
- Prevents withdrawal

“Antagonist”
- Blocks nicotine binding a4B2

No drug-drug interactions
Excreted by kidney (urine)

Varenicline Labeling Updates

- Warning
  - Observe patients for serious neuropsychiatric symptoms including changes in behavior, agitation, depressed mood, suicidal thoughts or behavior
  - Worsening of preexisting psychiatric illness
  - Causal relationship not established

Effectiveness of First Line Medications

Results from meta-analyses comparing to placebo (6 month F/U)

<table>
<thead>
<tr>
<th>Medication</th>
<th>No. Studies</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nic. Patch (6-14 wks)</td>
<td>32</td>
<td>1.9</td>
<td>1.7-2.2</td>
</tr>
<tr>
<td>Nic. Gum (6-14 wks)</td>
<td>15</td>
<td>1.5</td>
<td>1.2-1.7</td>
</tr>
<tr>
<td>Nic. Inhaler</td>
<td>6</td>
<td>2.1</td>
<td>1.5-2.9</td>
</tr>
<tr>
<td>Nic. Spray</td>
<td>4</td>
<td>2.3</td>
<td>1.7-3.0</td>
</tr>
<tr>
<td>Bupropion</td>
<td>26</td>
<td>2.0</td>
<td>1.8-2.2</td>
</tr>
<tr>
<td>Varenicline (2mg/day)</td>
<td>5</td>
<td>3.1</td>
<td>2.5-3.8</td>
</tr>
</tbody>
</table>

Varenicline and Neuropsychiatric Side Effects

- Meta analysis: 39 RCT (10,761 participants)
- Study: not sponsored by Pfizer
- Industry and non-industry funded studies

- No increased risk of suicide
- No increased risk of suicidal ideation
- No increased risk of depression
- No increased risk of irritability
- No increased risk of aggression
- Increased risk of sleep disorders
- Increased risk of insomnia
- Increased risk of abnormal dreams
- Reduced risk of anxiety

Thomas et al., 2015; BMJ

Varenicline, Bupropion, Nicotine Patch Smokers with and without Psych Disorders (EAGLES)

- 8144 (4416 psych and 4028, non psych by SCID)
- Triple dummy (DB-PC) x 12 weeks
  - 21mg patch taper
  - Varenicline mg BID
  - Bupropion 150 BID
- Largest smoking cessation study
- 33% lifetime suicidal ideation (12% behavior); 50% on psych meds
  - 70% depression/ bipolar
  - 20% anxiety d/o
  - 10% psychotic
  - 1% personality disorder
- Brief weekly counseling
- Funded Pfizer and Glaxo (GSK)

Neuropsychiatric Safety and Efficacy

Authenelli et al., Lancet 2016
Varenicline superior to BUP and NP overall and in psych and non psych cohorts

Anthenelli et al., Lancet 2016

**Neuropsychiatric Composite**
- Anxiety/ Panic
- Depression
- Feeling abnormal
- Hostility
- Agitation
- Aggression
- Delusions
- Hallucinations/ Paranoia/ Psychosis
- Homicidal ideation
- Mania
- Suicidal ideation or behavior

Anthenelli et al., Lancet 2016

**Rates of Neuropsychiatric Adverse Events**

Anthenelli et al., Lancet 2016

**Maintenance Varenicline**
Greater abstinence at 1 year

Evins et al., 2014; Pachas et al., 2012

**Need for Pharmacotherapy in Tobacco Users w/MI and SUD**
- No reason not to use
- NRT is not a “new drug”
- First line treatment/ Recommended all Comfortable detox for temporary abstinence
- Higher levels of nicotine dependence
- Withdrawal within hours of last tobacco use

**Medication Interactions with Tobacco Smoke**
- Smoking ↑ P450 enzyme system
- Polynuclear aromatic hydrocarbons (tar)
- ↑ 1A2 isoenzyme activity
- Smoking ↑ metabolism of meds – ↓ serum levels
- Smokers on higher medication doses
Drugs Reduced by Smoking

Antipsychotics
- Olanzapine (Zyprexa)
- Clozapine (Clozaril)
- Fluphenazine, Haloperidol, Chlorpromazine, Perphenazine

Antidepressants
- Amitriptyline, doxepin, clomipramine, desipramine, imipramine, Fluvoxemine (Luvox)

Others
- Caffeine, theophylline, warfarin, propranolol, acetaminophen

Desai et al., 2001; Zevin & Benowitz 1999

Quitting Smoking

- Risk for medication toxicity
- May ↑ levels acutely
- Consider dose adjustment
- Clozapine toxicity – Seizures
- Reduce caffeine intake

Nicotine (or NRT) Does Not Change Medication Levels

Nicotine metabolized by CYP2A6

Medication Interaction Tobacco Treatments

- Nicotine CYP2A6 None
- Bupropion CYP2B6 Many CYP2D6 inhibitor
- Varenicline Excreted in urine None

Electronic Nicotine Delivery System (ENDS)
- Made by Big Tobacco
- Safer than cigarette does not mean safe
- Not regulated in sales or advertising
- Not proven effective for cessation
- Risk of re-normalizing smoking behavior

Conclusions

Treatments increase the success rates and should be used in all smokers
Nicotine treatments are effective and well tolerated
Combinations improve outcomes
Varenicline greater efficacy than prior monotherapy treatments
Important tobacco smoke interactions at CYP1A2

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Questions?
8-Month Activity Schedule

- 5-monthly didactic webinars
  - April 27th 3:00PM Est
  - May TBD
  - June, TBD
  - July TBD
  - August TBD
- 3 months of Individual coaching calls: April, May, June
- Group Calls: July, August
- August Close out Webinar

Questions?

Thank you for joining us today. Please take a moment to provide your feedback by completing the survey at the end of today's webinar.

If you have additional questions/comments please send them to:

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Madhana Pandian – madhanap@thenationalcouncil.org