Updates in the Treatment of Tobacco Use Disorder

Jill M Williams, MD
Professor Psychiatry
Director, Division Addiction Psychiatry
Robert Wood Johnson Medical School

Disclosures

• Grant Support from Pfizer
• Consultant Pfizer
• Grant support from NCI, NIDA, NIMH, NJDMHAS, ABPN
• Consultant and Speaker for American Lung Association, Florida Council for Community Mental Health
Smokers with Behavioral Health Comorbidity (Mental Illness and Addiction) are Becoming a Sizeable Percentage of Smokers Left in the US
1/20/17

US Smoking Prevalence

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

Prevalence of Smoking Not Decreasing in those with Serious Mental Illness

Current Smoking among Adults Aged 18 or Older, by Past Month Serious Psychological Distress Status: NHIS, 1997 to 2011

It’s the Smoke that Kills

Cigarette smoke > 7000 compounds

Acetone, Cyanide, Carbon Monoxide, Formaldehyde

>65 Carcinogens

Benzene, Nitrosamines
Sources of Tobacco Toxins

- Nicotine; nitrosamines
- More than 600; Ammonia, cellulose acetate; flavors
- Thousands; carbon monoxide; formaldehyde; benzene; arsenic, lead; PAH

Smoking is the #1 Cause of Death in People with Mental Illness or Addiction
People with SMI die, on average, 25 years earlier than the general population.

National Association of State Mental Health Program Directors
Medical Directors Council, July 2006; Miller et al., 2006
Smoking Keeps Consumers from Achieving Recovery: Being Financially Stable, Getting Jobs, Securing Housing

Smokers Suffer Financial Consequences and Lower Quality of Life

N=68 smokers with schizophrenia on disability income

Smoke Free Housing

As much as 60% of airflow in multi-unit housing can come from other units.

SHS infiltrates through air ducts, cracks, stairwells, hallways, elevators, plumbing, electrical lines.

SHS is Class 1A carcinogen, in the same class as asbestos.


Tobacco Use May Worsen Behavioral Health Outcomes and Cessation Doesn’t Worsen BH Outcomes
**Suicide and Smoking**

Daily smoking →
predicts suicidal thoughts or attempt
(adjusted for prior depression, SUD, prior attempts; OR 1.82)

*Breslau et al., 2005; Ostacher et al., 2006; Altamura et al., 2006; Iancu et al., 2006; Cho et al., 2007; Oquendo et al., 2007; Riala et al., 2006; Moriya et al., 2006*

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**?? Benefits of Smoking**

**Cognition**

*Nicotine/ Nicotinic Receptors*
- ✓ Alzheimer's disease
- ✓ Attention deficit disorder
- ✓ Autism
- ✓ Schizophrenia

*Tobacco ≠ pharmacological treatment*

*Not a rationale for smoking*

**Depression**

*MAO Inhibitor Like Substance*
Improved Mental Health with Quitting Smoking

• Meta-analysis 26 studies (14 gen pop, 4 psychiatric, 3 physical conditions, 2 psychiatric or physical, 2 pregnant, 1 post-op)

Table 1 | Effect of smoking cessation on mental health. Sensitivity analysis after removal of studies of low quality (medium Newcastle-Ottawa scale)

<table>
<thead>
<tr>
<th>Outcome</th>
<th>No of studies included</th>
<th>No of studies excluded</th>
<th>Standardised mean difference (95% CI)</th>
<th>Effect estimate</th>
<th>Original effect estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety</td>
<td>4</td>
<td>0</td>
<td>-0.37 (-0.70 to -0.03)</td>
<td></td>
<td>-0.37 (-0.70 to -0.03)</td>
</tr>
<tr>
<td>Depression</td>
<td>9</td>
<td>1</td>
<td>-0.29 (-0.42 to -0.15)</td>
<td></td>
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</tr>
<tr>
<td>Mixed anxiety and depression</td>
<td>4</td>
<td>1</td>
<td>-0.36 (-0.58 to -0.14)</td>
<td></td>
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</tr>
<tr>
<td>Psychological quality of life</td>
<td>4</td>
<td>4</td>
<td>0.17 (-0.02 to 0.35)</td>
<td></td>
<td>0.17 (-0.02 to 0.35)</td>
</tr>
<tr>
<td>Positive affect</td>
<td>1</td>
<td>2</td>
<td>0.68 (0.24 to 1.12)</td>
<td></td>
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</tr>
<tr>
<td>Stress</td>
<td>2</td>
<td>1</td>
<td>-0.23 (-0.39 to -0.07)</td>
<td></td>
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</table>

Taylor et al, BMJ, 2014

Addressing Tobacco in SUD

TREATMENT - No negative impact on SUD treatment

– Same LOS
– No worsening of craving or abstinence rates

Smoking Cessation Interventions Provided during Addictions Treatment Associated with **25% INCREASED LIKELIHOOD OF LONG-TERM ABSTINENCE FROM ALCOHOL AND ILLICIT DRUGS**

Brown 2012; Williams 2004; Prochaska JCCP 2004
Tobacco Use Disorder is a Behavioral Health Condition in the DSM-5

Activation of the reward pathway by addictive drugs

Tobacco Dependence is in the DSM-5
**Tobacco Use Disorder**

Most 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 activities
- use despite problems
- larger amounts consumed than intended
- Craving; strong urges to use  

*DSM-5*

**Tobacco Withdrawal**

**4 or more**

Depressed mood  
Insomnia  
Irritability, frustration or anger  
Anxiety  
Difficulty concentrating  
Restlessness  
Increased appetite or weight gain
Tobacco Use is Still Part of Behavioral Health Culture and We’re not Doing Enough

and Treatment Works

Mental health and chemical dependency counselor Joan Ayala. Joan has a dual diagnosis of mental illness and addiction. During her lifelong battle she has learned coping skills to sustain her and end her addiction and cope with her mental illness.

USA TODAY; December 22, 2014
Smokers with MI or SMI
Reduced Quitting over Lifetime

Former Smokers (%)

- SMI
- non-SMI
- MI
- non-MI

mental illness = anxiety, MDE, PTSD, psychoses, bipolar, drug dependence
SMI= measured by K6
Hagman 2007; McClave 2010; Lasser 2000; Pratt & Brody 2010

Ex = N x S

Exsmokers = (# trying to quit) x (success of attempts)

R West, 2013
<table>
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<th>Why are Patients Not Quitting?</th>
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<td><strong>Psychological</strong></td>
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<td><strong>Social &amp; Environmental</strong></td>
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<td><strong>Spiritual &amp; Advocacy</strong></td>
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<td><strong>Treatment System &amp; Institutional</strong></td>
</tr>
<tr>
<td>Greater dependence</td>
</tr>
<tr>
<td>Poor coping; low confidence</td>
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<tr>
<td>Live with smokers</td>
</tr>
<tr>
<td>No hope; No peers succeeding</td>
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<td>No access to help; Not encouraged to quit</td>
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<tr>
<td>No hope; No peers succeeding</td>
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<td>Limited access to help</td>
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**Heaviness of Smoking Index**
Measure of Dependence

Number of cigarettes per day (cpd)

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

Heatherton 1991

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**Smokers with depression smoke more cpd and are more dependent**

Figure 3. Percentage of current smokers aged 20 and over, by time of first cigarette and amount smoked per day, by depression status: United States, 2005–2006

![Bar chart showing the percentage of current smokers aged 20 and over, by time of first cigarette and amount smoked per day, by depression status: United States, 2005–2006.](source)

Significantly different from no depression.

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 ≤ 5mins</td>
<td>29.2%</td>
<td>19.3%</td>
</tr>
</tbody>
</table>

*SPD by K6; NSDUH 2002

Smokers in Addiction Treatment are Moderately to Severely Addicted to Nicotine

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

Williams et al., 2005
Individuals with schizophrenia highly addicted

**4 minute Nicotine Boost (ng/mL)**

25.2 vs. 11.1; p<0.01

**Greater nicotine intake per cigarette**

*Williams NTR 2010*

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


*N-MHSS Report, Nov 2014*
State Hospital Smoking Survey

2011; 206 Hospitals Surveyed; 80% response rate
Almost 80% no-smoking on premises
Less than 35% treatment

Less than Half of US Substance Abuse Facilities Treat this Substance

– 88% response rate
41% offer smoking cessation counseling or pharmacotherapy
38% offer individual/group counseling
17% provide quit-smoking medication
### Which Approach to Take

<table>
<thead>
<tr>
<th>Implement current evidence based practices?</th>
<th>Develop tailored approaches?</th>
</tr>
</thead>
<tbody>
<tr>
<td>✓ Public health model</td>
<td>✓ Clinical/ co-occurring treatment model</td>
</tr>
<tr>
<td>✓ Primary care</td>
<td>✓ Behavioral health</td>
</tr>
<tr>
<td>✓ Brief strategies</td>
<td>✓ Face to face</td>
</tr>
<tr>
<td>✓ Limited insurance coverage</td>
<td>✓ Longer treatment</td>
</tr>
<tr>
<td>✓ Telephone counseling</td>
<td>✓ Expanded Medicaid and Medicare coverage for treatment</td>
</tr>
</tbody>
</table>

### Treatment for Tobacco Use Disorder Works

- Brief Assessment
- Counseling + Medications
- Approach like a Co-occurring Disorder
First-line Treatments  
(FDA Approved)

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

Counseling + Medications =  
Best treatment plan

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<table>
<thead>
<tr>
<th>Treatment</th>
<th>Number</th>
<th>Est Odds Ratio (95%CI)</th>
<th>Estimated Quit Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medication alone</td>
<td>8</td>
<td>1.0</td>
<td>22</td>
</tr>
<tr>
<td><strong>Meds plus Counseling</strong></td>
<td>39</td>
<td><strong>1.4</strong> (1.2-1.6)</td>
<td>28</td>
</tr>
</tbody>
</table>

Meta-analysis (2008)  
Effectiveness of meds or counseling alone vs combination

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<th>Number</th>
<th>Est Odds Ratio (95%CI)</th>
<th>Estimated Quit Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Counseling alone</td>
<td>11</td>
<td>1.0</td>
<td>15</td>
</tr>
<tr>
<td><strong>Meds plus Counseling</strong></td>
<td>13</td>
<td><strong>1.5</strong> (1.3-2.1)</td>
<td>22</td>
</tr>
</tbody>
</table>

2008 PHS Guideline Update
Pharmacological Treatment

Nicotine Replacement
- Patch
- Gum
- Lozenge
- Inhaler
- Nasal Spray

Bupropion

Varenicline

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

APRIL 2013 www.fda.gov/ForConsumers/ConsumerUpdates/ucm345087.htm
New Directions For Use

Bupropion SR

- Effective at 150 to 300mg daily
- Nonsedating, activating antidepressant with effects on NE and DA systems
- Start 10-14 days prior to quit date
- Side effects- headache, insomnia
- Contraindicated in h/o seizures or bulimia
- Noncompetitive nicotinic receptor antagonist
- Similar efficacy to NRT
- Effect independent of depression
- Less weight gain with 300mg than placebo

Slemmer 2000
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)
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>

PHS Clinical Practice Guideline 2008 Update

Varenicline Labeling Updates

- **Warning (Reported with Chantix)**
  - 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**
- **Clinical trials** (N>5000; SI rate = placebo)
  - Sleep disturbance/ vivid dream

www.PfizerPRO.com/chantix
Neuropsychiatric Safety and Efficacy
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)

Anthenelli et al., Lancet 2016

Varenicline superior to BUP and NP overall and in psych and nonpsych 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

VAR ➤ Side effects: Nausea, insomnia, abnormal dreams, headache

Anthenelli et al., Lancet 2016
Rates of Neuropsychiatric Adverse Events

VAR → Side effects: Nausea, insomnia, abnormal dreams, headache

Anthenelli et al., Lancet 2016

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FDA Approves Removal Of Boxed Warning Regarding Serious Neuropsychiatric Events From CHANTIX® (varenicline) Labeling

- Based on a U.S. Food and Drug Administration (FDA) review of a large clinical trial that we required the drug companies to conduct, we have determined the risk of serious side effects on mood, behavior, or thinking with the stop-smoking medicines Chantix (varenicline) and Zyban (bupropion) is lower than previously suspected. The results of the trial confirm that the benefits of stopping smoking outweigh the risks of these medicines (December 2016)

http://www.fda.gov/Drugs/DrugSafety/ucm532221.htm
Combination Therapies

 Improve abstinence rates
 Decrease withdrawal
 Well tolerated

<table>
<thead>
<tr>
<th>Treatment</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patch + gum or spray</td>
<td>1.9</td>
<td>(1.3 - 2.7)</td>
</tr>
<tr>
<td>Patch + bupropion</td>
<td>1.3</td>
<td>(1.0 - 1.8)</td>
</tr>
</tbody>
</table>

Fiore 2008

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 other monotherapy treatments

jill.williams@rutgers.edu