Updates in the Treatment of Tobacco Use Disorder

PCSS-MAT; Smoking Cessation Leadership Center and American Psychiatric Association

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Disclosures

- Grant Support from Pfizer
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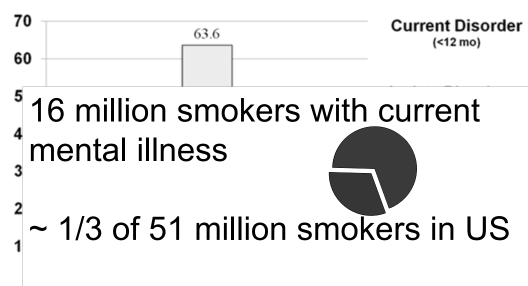
- Consultant and Speaker for American Lung Association

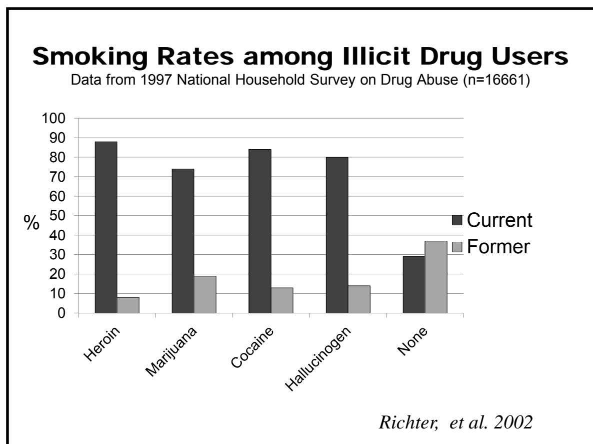
US Smoking Prevalence



16 million smokers with current mental illness

~ 1/3 of 51 million smokers in US

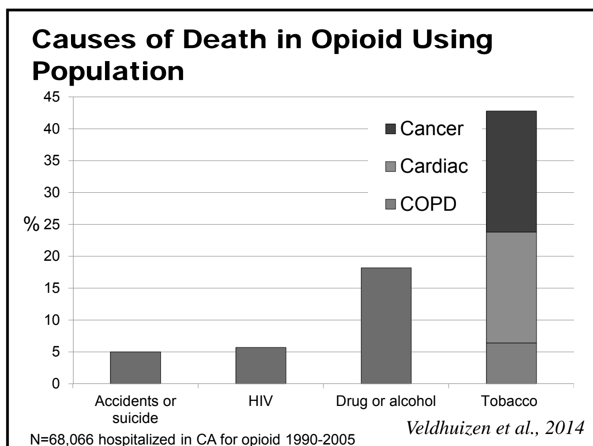
NCS-R 2001-2003; Diagnoses using CIDI
Lawrence et al, BMC Public Health 2009, 9:285

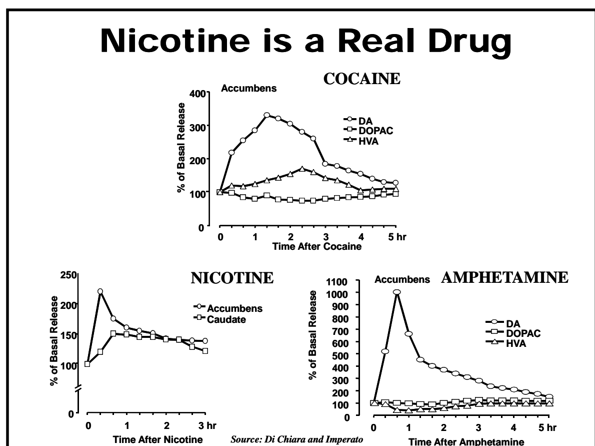


Smoking associated with Opioid Misuse

- **Smokers 3X more likely to have past-year prescription opioid misuse vs. never smokers (men and women)**
  Daily (AOR = 3.79); Intermittent (AOR = 3.12)
- **Daily Smokers ~ 5X more likely met criteria for past-year opioid abuse/dependence, vs. never smokers (men and women)**
  - Intermittent smokers ~ 3x
- **Daily smokers high nicotine dependence 2.5X more likely to have past-year prescription opioid abuse/dependence (men and women)**

Zale et al., NTR 2014





Addressing Tobacco in SUD

- **TREATMENT** - No negative impact on SUD treatment
  - Same LOS
  - No worsening of craving or abstinence rates
- **POLICY** - No negative impact on SUD treatment
  - No early discharges
  - Clients interested in treatment
  - No reductions in admissions (NYOASAS)
- Smoking Cessation Interventions Provided during Addictions Treatment Associated with **A 25% INCREASED LIKELIHOOD OF LONG-TERM ABSTINENCE FROM ALCOHOL AND ILLICIT DRUGS**

Williams 2004; Reid et al., 2008; Prochaska JCCP 2004

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

DSM-5

Tobacco Withdrawal

Abrupt tobacco cessation or reduction

4 or more (in 24 hours)

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

DSM-5

Heaviness of Smoking Index

Measure of Dependence

Number of cigarettes per day (cpd)

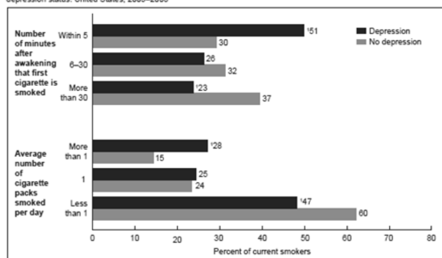
AM Time to first cigarette (TTFC)

≤ 30 minutes = moderate
≤ 5 minutes = severe

Heatherton 1991

Smokers with depression smoke more cpd and are more dependent

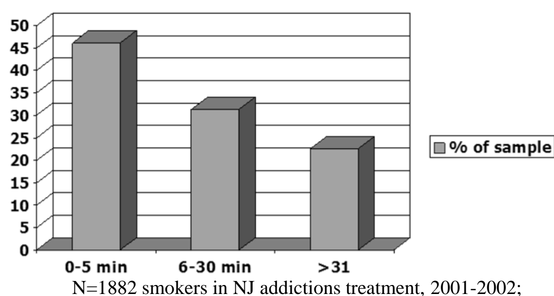
Figure 3. Percentage of current smokers aged 20 and over, by time of first cigarette and amount smoked per day, by depression status: United States, 2005–2008



¹Significantly different from no depression.

SOURCE: CDC/NCHS, National Health and Nutrition Examination Surveys, 2005–2008.

Smokers in Addiction Treatment are Moderately to Severely Addicted to Nicotine



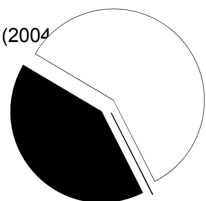
N=1882 smokers in NJ addictions treatment, 2001-2002;

Williams et al., 2005

Less than Half of US Substance Abuse Facilities Treat this Substance

National survey of 550 OSAT units (2004
- 88% response rate

41% offer smoking cessation counseling or pharmacotherapy



38% offer individual/group counseling
17% provide quit-smoking medication

Friedmann et al., JSAT 2008

Need for Pharmacotherapy in Tobacco Use and Behavioral Health

No reason not to use

NRT is not a “new drug”

First line treatment/ Recommended all smokers

Comfortable detox for temporary abstinence

Higher levels of nicotine dependence

Patients with SUD Quit Smoking Successfully

- H/o ETOH Just as likely to succeed in quitting smoking as other smokers
- Usual treatments effective
- Smokers learned skills in recovering from alcohol that helped them quit smoking

Hughes & Kalman, 2006

First-line Treatments
(FDA Approved)

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

Counseling + Medications = Best treatment plan

Pharmacological Treatment

Nicotine Replacement

- **Patch**
- **Gum**
- **Lozenge**

(Patch, Gum, Lozenge: **Available OTC but may be covered with prescription with state Medicaid**)

- **Inhaler**
- **Nasal Spray**

Bupropion

Varenicline

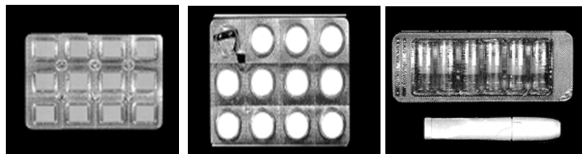
Nicotine Medications

- **Not a carcinogen**
- Use high enough dose
- Scheduled better than PRN
- Use long enough time period
- Can be combined with bupropion
- Can be combined with each other
- Have almost no contraindications
- Have no drug-drug interactions
- Safe enough to be OTC

Nicotine Patch

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

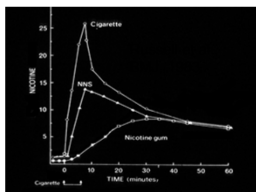
Oral Forms of Nicotine



Dose frequently – every 1-2 hours
Slow, buccal absorption
Acidic foods ↓ absorption
Mild side effects- mouth, throat burning
GI upset if swallowed (bite and park gum)
Rx for Nicotine Inhaler

Nicotine Nasal Spray

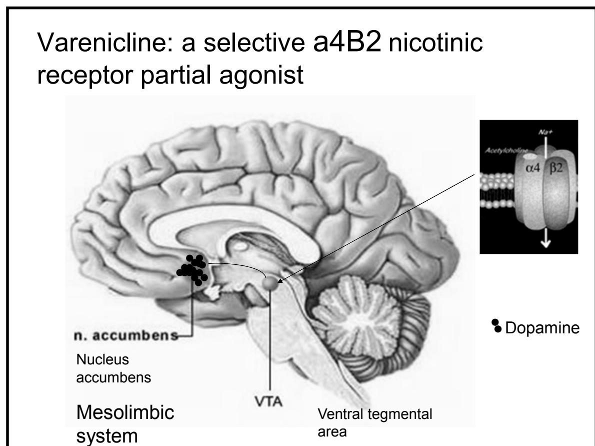
- Rapid delivery though nasal mucosa
- Most side effects (nasal irritation, rhinitis, coughing, watering eyes)
- 2 sprays= 1 dose; up to 40 doses/day
- Some dependence liability
- Rx needed



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

APRIL2013
www.fda.gov/ForConsumers/ConsumerUpdates/ucm345087.htm



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)

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

PHS Clinical Practice Guideline 2008 Update

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
- Clinical trials (N>5000; SI rate = placebo)
- Sleep disturbance/ vivid dream

http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/ucm106540.htm

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

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

Combination Therapies

Improve abstinence rates
Decrease withdrawal
Well tolerated

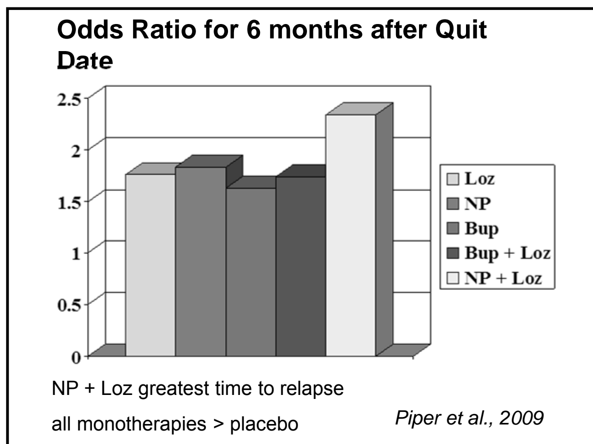
	OR
Patch + gum or spray	1.9 (1.3 – 2.7)
Patch+ bupropion	1.3 (1.0 – 1.8)

Fiore 2008

A randomized placebo-controlled clinical trial of five smoking cessation pharmacotherapies

- 1504 smokers
- 5 treatments and 5 placebo groups
  - nicotine lozenge
  - nicotine patch
  - bupropion SR
  - nicotine patch + nicotine lozenge
  - bupropion + nicotine lozenge

Piper et al., 2009



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

Varenicline- Major Depression

- 525 past h/o or stable, treated MDE; ≥10 cpd
- MADRS, HAM, C-SSRS, SBQ
- 73% on antidepressants (SSRI or SNRI)

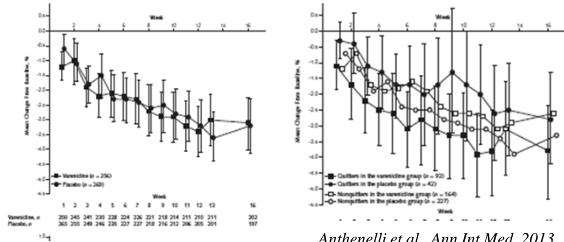
- VAR More effective vs placebo
- Week 12 CAR: 35.9% vs 15.6% for placebo (OR 3.35; p<0.001)
- 24 and 52 week outcomes also significant

Anthenelli et al., Ann Int Med, 2013

No Worsening of Depression Scores

No difference in AEs (abnormal dreams, anxiety, agitation, restlessness, SI)

MADRS total scores mean change from baseline; Slight improvement in depression and anxiety in both groups



Anthenelli et al., Ann Int Med, 2013

Studies in Methadone Maintenance

- 4 RCTs
- Motivated to quit/ reduce
- 35% patients quit on quit date
- Reduced quit rates from Varenicline or NRT
  (10% 7dPP 12 weeks)
- Lower medication adherance
- High rates personality disorders (poor emotion regulation)

Cahill et al., 2011; Tsukahara et al., 2010; DeDios 2014; Stein 2013; Cooperman in press

Other Medications

With Efficacy Data but not FDA Approved
Nortripytyline
Clonidine
Cytisine (not available in US)

Not Shown to be Effective
SSRIs
Naltrexone

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, acetominophen

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 CYP2D6 inhibitor	Many
• Varenicline	Excreted in urine	None

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Conclusions

Tobacco number one cause of death – mental health and addictions

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

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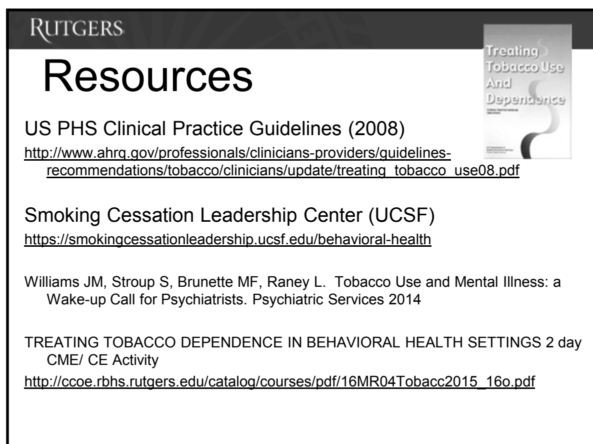
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Resources

US PHS Clinical Practice Guidelines (2008)

http://www.ahrq.gov/professionals/clinicians-providers/guidelines-recommendations/tobacco/clinicians/update/treating_tobacco_use08.pdf

Smoking Cessation Leadership Center (UCSF)

https://smokingcessationleadership.ucsf.edu/behavioral-health

Williams JM, Stroup S, Brunette MF, Raney L. Tobacco Use and Mental Illness: a Wake-up Call for Psychiatrists. Psychiatric Services 2014

TREATING TOBACCO DEPENDENCE IN BEHAVIORAL HEALTH SETTINGS 2 day CME/ CE Activity

http://ccoe.rbhs.rutgers.edu/catalog/courses/pdf/16MR04Tobacc2015_16o.pdf