ACKNOWLEDGEMENTS

Karen Hudmon, DrPH, RPh and Rx for Change
California Tobacco Related Disease Research Program (#13KT-0152)
National Institute on Drug Abuse (#K23 DA018691 and #P50 DA09253
American Cancer Society (IRG# AC-08-04)
No commercial conflicts of interest

OVERVIEW

- Tobacco Use & Mental Illness
- Pharmacologic Effects of Nicotine & the Principles of Nicotine Addiction
- Treating Nicotine Dependence
- Working with Special Populations
TOBACCO USE in PSYCHIATRIC POPULATIONS

- Nicotine dependence – most prevalent substance use disorder among psychiatric patients
  - Smoking rates 2 to 4 x's that of the general population (Hughes, 1993; Poirier, 2002)

- The mentally ill comprise 44% to 46% of the US tobacco market (Lasser et al., 2000; Grant et al., 2004)
  - 175 billion cigarettes and $39 billion in annual sales (USDA, 2004)

SMOKING RATE by PSYCHIATRIC HISTORY

National Comorbidity Survey 1991-1992
Source: Lasser et al., 2000 JAMA

SMOKING in CALIFORNIA

<table>
<thead>
<tr>
<th>Inpatient Psychiatry</th>
<th>Outpatient Psychiatry</th>
<th>California Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cigarettes/day M(SD)</td>
<td>Cigarettes/day M(SD)</td>
<td>Cigarettes/day</td>
</tr>
<tr>
<td>45%</td>
<td>28%</td>
<td>14%</td>
</tr>
<tr>
<td>21 (15)</td>
<td>17 (12)</td>
<td>15</td>
</tr>
</tbody>
</table>

Acton, Prochaska, Kaplan, Small & Hall. (2001) Addict Behav

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WHY ADDRESS TOBACCO USE in PSYCHIATRIC POPULATIONS?

Prevent Death
Improve Health
Optimize Psychiatric Medication Effects
Reduce Isolation
Patient $ Savings

Tobacco Industry Profits
Interest groups/politicians supported by Tobacco Industry
Tax revenues

PHARMACOKINETIC DRUG INTERACTIONS with SMOKING

Drugs that may have a decreased effect due to induction of CYP1A2:

- Caffeine
- Clozapine (Clozaril™)
- Fluvoxamine (Luvox™)
- Haloperidol (Haldol™)
- Olanzapine (Zyprexa™)
- Phenothiazines (Thorazine, Trilafon, Prolixin, etc.)
- Propanolol
- Tertiary TCAs / cyclobenzaprine (Flexeril™)
- Thiothixene (Navane™)
- Other medications: estradiol, mexiletene, naproxen, phenacetin, riluzole, ropinirole, tacrine, theophyline, verapamil, r-warfarin (less active), zolmitriptan

Smoking cessation may reverse the effect.

FINANCIAL IMPACT of SMOKING

Buying cigarettes every day for 50 years @ $3.75/pack for generic or $5.25/pack for brand name. Money banked monthly, earning 5.5% interest.

<table>
<thead>
<tr>
<th>Packs per day</th>
<th>Hundreds of thousands of dollars lost</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>$1,004,196</td>
</tr>
<tr>
<td>1.5</td>
<td>$753,147</td>
</tr>
<tr>
<td>1</td>
<td>$502,098</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Category</th>
<th>Costs (Billions of Dollars)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ambulatory care</td>
<td>$27.2 billion</td>
</tr>
<tr>
<td>Hospital care</td>
<td>$17.2 billion</td>
</tr>
<tr>
<td>Nursing home</td>
<td>$18.4 billion</td>
</tr>
<tr>
<td>Prescription drugs</td>
<td>$6.4 billion</td>
</tr>
<tr>
<td>Medical care</td>
<td>$74.3 billion</td>
</tr>
<tr>
<td>Ambulatory care</td>
<td>$27.2 billion</td>
</tr>
<tr>
<td>Hospital care</td>
<td>$17.3 billion</td>
</tr>
<tr>
<td>Other care</td>
<td>$5.4 billion</td>
</tr>
<tr>
<td>Societal costs:</td>
<td>$7.65 per pack</td>
</tr>
<tr>
<td>Men</td>
<td>$40.5 billion</td>
</tr>
<tr>
<td>Women</td>
<td>$30.5 billion</td>
</tr>
</tbody>
</table>

**Medical expenditures (1998)**

**Annual lost productivity costs (1997–2001)**

**CDC. MMWR 2002;51:300–303 and MMWR 2005;54:625-628.**

---

### WHY do INDIVIDUALS with MENTAL ILLNESS SMOKE?

- Smoking in adolescence is associated with psychiatric disorders in adulthood, including: panic disorder, GAD and agoraphobia, depression and suicidal behavior, substance use disorders, and schizophrenia (Breslau et al., 2004; Weiser et al., 2004; Goodman, 2000; Johnson et al., 2000).

---

### FACTORS ASSOCIATED with TOBACCO USE in the MENTALLY ILL

- **Psychological/Behavioral:**
  - Conditioning effects
  - Coping tool
  - Social interactions
  - Boredom

- **Biologic & Pharmacologic:**
  - Genetic predisposition
  - Alleviation of withdrawal
  - Pleasure effects
  - Weight control

- **Systemic & Treatment:**
  - Use of cigarettes for reinforcement
  - Failure to treat

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NEUROCHEMICAL and RELATED EFFECTS of NICOTINE

- Dopamine ➔ Pleasure, reward
- Norepinephrine ➔ Arousal, appetite suppression
- Acetylcholine ➔ Arousal, cognitive enhancement
- Glutamate ➔ Learning, memory enhancement
- β-Endorphin ➔ Reduction of anxiety and tension
- GABA ➔ Reduction of anxiety and tension
- Serotonin ➔ Mood modulation, appetite suppression

DOPAMINE REWARD PATHWAY

- Prefrontal cortex
- Nucleus accumbens
- Ventral tegmental area
- Amygdala
- Dopamine release
- Stimulation of nicotine receptors

State of Nicotine Withdrawal
Chronic Smoking Effects

CHRONIC ADMINISTRATION of NICOTINE: EFFECTS on the BRAIN

Human smokers have increased nicotine receptors in the prefrontal cortex.

Image courtesy of George Washington University / Dr. David C. Perry
Perry et al., J Pharmacol Exp Ther 1999;289:1545–1552.

GENETIC EFFECTS on NICOTINE METABOLISM

Nicotine

- 9.8% Nicotine
- 4.4% Nicotine-1'-N-oxide
- 4.2% Nornicotine

Cotinine

- 4.4% Nicotine-glucuronide
- 13.0% Cotinine
- 12.6% Cotinine-glucuronide
- 2.4% Cotinine-N-oxide

Trans-3' hydroxycotinine

- 4.2% Cotinine-glucuronide
- 9.8% Cotinine
- 4.4% Nicotine-1'-N-oxide
- 4.2% Nornicotine

Reprinted with permission, Benowitz et al., 1994.

Nicotine Addiction Cycle

Nicotine Withdrawal
A. Daily use of nicotine
B. Abrupt cessation/reduction followed within 24 hrs by 4+:
   1. Depressed mood
   2. Insomnia
   3. Irritability
   4. Anxiety
   5. Difficulty concentrating
   6. Decreased HR
   7. Increased appetite
C. Clinically significant impairment
D. Not due to GMC

Nicotine Dependence
- Maladaptive pattern of use with significant impairment manifested by 3+ in 12 mos:
  1. Tolerance
  2. Withdraw
  3. ↑ Use
  4. Unsuccessful efforts to stop
  5. Time investment
  6. Loss of important activities
  7. Continued use despite knowledge of physical or psychological problems

TOBACCO DEPENDENCE: A 2-PART PROBLEM

Tobacco Dependence

- **Physiological**
  - The addiction to nicotine
    - Treatment
    - Medications for cessation

- **Behavioral**
  - The habit of using tobacco
    - Treatment
    - Behavior change program

Treatment should address the physiological and the behavioral aspects of dependence.

TREATING NICOTINE DEPENDENCE

*In terms of lives saved, quality of life, and cost-efficacy, treating smoking is considered the most important activity a clinician can do.*

-- John Hughes, MD
University of Vermont

TOBACCO TREATMENT GUIDELINES

- All patients ought to be screened for tobacco use, advised to quit, and offered intervention.
- All patients should be offered pharmacological treatment for quitting smoking, unless contraindicated.
- There is a dose response relationship with the amount of contact provided.


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CLINICIAN INTERVENTIONS

![Chart showing estimated abstinence rates at 5+ months for different types of clinicians.]

<table>
<thead>
<tr>
<th>Type of Clinician</th>
<th>Estimated Abstinence at 5+ months</th>
</tr>
</thead>
<tbody>
<tr>
<td>No clinician</td>
<td>1.0 (0.9, 1.3)</td>
</tr>
<tr>
<td>Self-help material</td>
<td>1.1 (1.0, 1.3)</td>
</tr>
<tr>
<td>Nonphysician clinician</td>
<td>1.7 (1.3, 2.1)</td>
</tr>
<tr>
<td>Physician clinician</td>
<td>2.2 (1.5, 3.2)</td>
</tr>
</tbody>
</table>


DOSE RESPONSE RELATIONSHIP of FOLLOW UP CARE

<table>
<thead>
<tr>
<th>Number of sessions</th>
<th>Estimated quit rate*</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 to 1</td>
<td>12.4%</td>
</tr>
<tr>
<td>2 to 3</td>
<td>16.3%</td>
</tr>
<tr>
<td>4 to 8</td>
<td>20.9%</td>
</tr>
<tr>
<td>More than 8</td>
<td>24.7%</td>
</tr>
</tbody>
</table>

* 5 months (or more) postcessation


NATIONAL CANCER INSTITUTE’S FIVE A’s for TREATING TOBACCO

- **ASK** about tobacco USE
- **ADVISE** tobacco users to QUIT
- **ASSESS** readiness to make a QUIT attempt
- **ASSIST** with the QUIT ATTEMPT
- **ARRANGE** FOLLOW-UP care

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Studying readiness to quit

**ASSESS READINESS TO QUIT**

Not Ready to Quit

- 6 months
- 30 days
- 6 months

Quit date

Preparation

- 30 days
- 6 months
+ 6 months

Ready to Quit

STUDIES of PSYCHIATRIC PATIENTS' READINESS to QUIT*

<table>
<thead>
<tr>
<th>Population</th>
<th>General Population</th>
<th>General Psych Outpts</th>
<th>Depressed Outpatients</th>
<th>Psych. Inpatients</th>
<th>General Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intend to quit in next 6 mo</td>
<td>40%</td>
<td>41%</td>
<td>55%</td>
<td>43%</td>
<td>51%</td>
</tr>
<tr>
<td>Intend to quit in next 30 days</td>
<td>20%</td>
<td>24%</td>
<td>24%</td>
<td>28%</td>
<td>20%</td>
</tr>
</tbody>
</table>

Smokers with mental illness are just as ready to quit smoking as the general population of smokers.

* No relationship between psychiatric symptom severity and readiness to quit

TAILOR TREATMENT to PATIENTS' READINESS to QUIT

- Does the patient now use tobacco?
- Yes
- No

- Is the patient now ready to quit?
- Yes
- No

- Did the patient once use tobacco?
- Yes
- No

- Promote motivation
- Provide treatment
- Prevent relapse*
- Encourage continued abstinence

*Relapse prevention interventions not necessary if patient has not used tobacco for many years and is not at risk for re-initiation.


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PATIENTS NOT READY to QUIT: CLINICIAN’S GOALS

- Building rapport
- Planting a seed to move patient forward
- Opening a door to facilitate further counseling
- Helping patients become more aware of their smoking behavior
- Providing education and establishing yourself as a resource

GOAL: Start thinking about quitting

PATIENTS READY to QUIT: CLINICIAN’S GOALS

- Thorough assessment of tobacco use & prior quit attempts
- Identify key triggers to smoke and anticipated barriers (stress, substance use, wt concerns)
- Develop a quit plan and set a quit date
  - Use of cognitive & behavioral strategies
- Incorporate pharmacological treatments as appropriate

GOAL: Achieve Cessation

RECENT QUITTERS: CLINICIAN’S GOALS

- Follow-up within 1 to 3 days after quit attempt
- Congratulate success!
- Assess:
  - Triggers for relapse and social support
  - Pharmacotherapy use and any problems
  - Prolonged withdrawal symptoms
  - Motivation level
- Encourage healthful alternative behaviors

GOAL: Remain tobacco-free

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STRESS MANAGEMENT

**The Myths**
- Smoking gets rid of all my stress
- I can’t relax without a cigarette

**The Facts**
- There will always be stress in one’s life
- There are many ways to relax without a cigarette

**Smokers confuse the relief of withdrawal with the feeling of relaxation**

**STRESS MANAGEMENT SUGGESTIONS:**
Deep breathing, shifting focus, taking a break

SOCIAL SUPPORT for QUITTING

- Key ingredients for successful quitting:
  - Social support as part of treatment (intra-treatment)
  - Social support outside of treatment (extra-treatment)

**PATIENTS SHOULD BE ADVISED TO:**
- Ask family, friends, and coworkers for support – ask them not to smoke around you and not to leave cigarettes out
- Get individual, group, or telephone counseling

Patients who receive social support and encouragement are more successful in quitting

ADDRESSING CONCERNS about POSTCESSATION WEIGHT GAIN

- Most quitters gain weight
  - Most gain < 10 pounds, but there is a wide range
- Discourage strict dieting while quitting
  - Recommend physical activity (e.g., walking, biking)
  - Encourage a healthy diet, planned meals, & high-fiber foods
  - Increase water intake
  - Chew sugarless gum
  - Select nonfood rewards
- Maintain patient on pharmacotherapy shown to delay weight gain
- Refer patient to a specialist or program

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**READINESS TO QUIT: A REVIEW**

<table>
<thead>
<tr>
<th>Not ready to quit</th>
<th>Recent quitter</th>
<th>Former tobacco user</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PROMOTE MOTIVATION</strong></td>
<td><strong>BEHAVIORAL COUNSELING</strong></td>
<td><strong>RELAPSE PREVENTION</strong></td>
</tr>
<tr>
<td>Ready to quit</td>
<td>Behavioral Counseling</td>
<td>Relapse Prevention</td>
</tr>
</tbody>
</table>

**PHARMACOTHERAPY**

“All patients attempting to quit should be encouraged to use effective pharmacotherapies for cessation except in the presence of special circumstances.”


**PHARMACOLOGIC METHODS**

- **First-Line (FDA Approved)**
  - Nicotine Replacement Therapy (NRT)
  - Bupropion (Zyban)
  - Varenicline (Chantix)
- **Second-line (evidence-based but not FDA approved)**
  - Nortriptyline
  - Clonidine
FDA APPROVALS: SMOKING CESSATION

<table>
<thead>
<tr>
<th>Year</th>
<th>Product</th>
<th>Prescription Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>1984</td>
<td>Rx nicotine gum</td>
<td></td>
</tr>
<tr>
<td>1991</td>
<td>Rx transdermal nicotine patch</td>
<td></td>
</tr>
<tr>
<td>1996</td>
<td>OTC nicotine gum &amp; patch; Rx nicotine nasal spray</td>
<td></td>
</tr>
<tr>
<td>1997</td>
<td>OTC nicotine lozenge; Rx nicotine inhaler; Rx bupropion SR</td>
<td></td>
</tr>
<tr>
<td>2002</td>
<td>Rx varenicline</td>
<td></td>
</tr>
<tr>
<td>2006</td>
<td>OTC nicotine lozenge</td>
<td></td>
</tr>
</tbody>
</table>

DRUGS IN DEVELOPMENT:
rimonabant, nicotine vaccine, etc.

PLASMA NICOTINE CONCENTRATIONS for NICOTINE-CONTAINING PRODUCTS

- Cigarette
- Moist snuff
- Nasal spray
- Inhaler
- Lozenge (2mg)
- Gum (2mg)
- Patch

ADVANTAGES
- Provides consistent nicotine levels
- Easy to use and conceal
- Fewer compliance issues

DISADVANTAGES
- Patients cannot titrate the dose
- Allergic reactions to adhesive may occur
- Taking patch off to sleep may lead to morning nicotine cravings
PATIENT EDUCATION: Nicotine Patch

- Apply patch to hairless area -- new location daily
- Water will not harm the nicotine patch if it is applied correctly; patients may bathe, swim, shower, or exercise while wearing the patch
- Do not cut patches to adjust dose
  - Nicotine may evaporate from cut edges
  - Patch may be less effective
- Keep new and used patches out of the reach of children and pets

NICOTINE GUM & LOZENGE

ADVANTAGES
- Patients can titrate therapy to manage withdrawal symptoms
- May satisfy oral cravings
- May delay weight gain

DISADVANTAGES
- Gastrointestinal side effects may be bothersome
- Gum may be socially unacceptable and difficult to use with dentures
- Patients must use proper chewing technique to minimize adverse effects

PATIENT EDUCATION: Nicotine Gum & Lozenge

- Chew and “park” gum
- To improve chances of quitting, use at least nine pieces of the gum or lozenge daily
- The effectiveness of nicotine gum and lozenge may be reduced by some foods and beverages:
  - Coffee
  - Juices
  - Wine
  - Soft drinks

Do NOT eat or drink for 15 minutes BEFORE or while using nicotine gum or lozenge.
NICOTINE INHALER

**ADVANTAGES**
- Patients can easily titrate therapy to manage withdrawal symptoms.
- The inhaler mimics hand-to-mouth ritual of smoking.

**DISADVANTAGES**
- Initial throat or mouth irritation can be bothersome.
- Cartridges should not be stored in very warm conditions or used in very cold conditions.
- Patients with underlying bronchospastic disease must use the inhaler with caution.

NICOTINE NASAL SPRAY

**ADVANTAGES**
- Most rapidly absorbed form of nicotine replacement
- Patients can easily titrate therapy to rapidly manage withdrawal symptoms
- Demonstrated use with smokers with schizophrenia

**DISADVANTAGES**
- Nasal/throat irritation may be bothersome
- Dependence can result
- Patients must wait 5 min before driving or operating heavy machinery

COMBINATION NRT

Long-acting formulation (patch)
- Produces relatively constant levels of nicotine
  **PLUS**

Short-acting formulation (gum, lozenge, inhaler, nasal spray)
- Allows for acute dose titration as needed for withdrawal symptoms

**Reserve for patients unable to quit using monotherapy**

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**BUPROPION SR**

**ADVANTAGES**
- Easy to use
- Can be used with NRT
- May be beneficial in patients with depression

**DISADVANTAGES**
- Should be avoided in patients with an increased risk for seizures
- Side effect profile:
  - Common: dry mouth, anxiety, insomnia (avoid bedtime dosing)
  - Less Common: tremor, skin rash

**BUPROPION: MECHANISM OF ACTION**

- Atypical antidepressant thought to affect levels of various brain neurotransmitters
  - Dopamine
  - Norepinephrine
- Clinical effects
  - ↓ craving for cigarettes
  - ↓ symptoms of nicotine withdrawal

**VARENICLINE**

**ADVANTAGES**
- Oral formulation with twice-a-day dosing
- Offers a new mechanism of action for persons who previously failed using other medications
- Early industry-sponsored trials suggest this agent is superior to bupropion SR

**DISADVANTAGES**
- Common side effects:
  - Nausea (in up to 33% of pts)
  - Sleep disturbances (insomnia, abnormal dreams)
  - Constipation
  - Flatulence
  - Vomiting

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**VARENICLINE: MECHANISM of ACTION**

- Binds with high affinity and selectivity at α₄β₂ neuronal nicotinic acetylcholine receptors
- Stimulates low-level agonist activity
- Competitively inhibits binding of nicotine
- Clinical effects
  - ↓ symptoms of nicotine withdrawal
  - Blocks dopaminergic stimulation responsible for reinforcement & reward associated with smoking

**VARENICLINE: PHARMACOKINETICS**

**Absorption:** Virtually complete after oral administration; not affected by food

**Metabolism:** Undergoes minimal hepatic metabolism

**Elimination:** Primarily renal through glomerular filtration and active tubular secretion; 92% excreted unchanged in urine

**Half-life:** 24 hours

**VARENICLINE: DOSING**

Patients should begin therapy 1 week PRIOR to their quit date. The dose is gradually increased to minimize treatment-related nausea and insomnia.

<table>
<thead>
<tr>
<th>Treatment Day</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial dose titration</td>
<td></td>
</tr>
<tr>
<td>Days 1-3</td>
<td>0.5 mg qd</td>
</tr>
<tr>
<td>Days 4-7</td>
<td>0.5 mg bid</td>
</tr>
<tr>
<td>Day 8 - Week 12</td>
<td>1 mg bid</td>
</tr>
</tbody>
</table>

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LONG-TERM (≥6 month) QUIT RATES for AVAILABLE CESSATION MEDICATIONS

<table>
<thead>
<tr>
<th>Medication</th>
<th>Percent Quit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nicotine gum</td>
<td>19.5%</td>
</tr>
<tr>
<td>Nicotine patch</td>
<td>14.6%</td>
</tr>
<tr>
<td>Nicotine lozenge</td>
<td>16.4%</td>
</tr>
<tr>
<td>Nicotine nasal spray</td>
<td>11.5%</td>
</tr>
<tr>
<td>Nicotine inhaler</td>
<td>5.1%</td>
</tr>
<tr>
<td>Bupropion</td>
<td>10.2%</td>
</tr>
<tr>
<td>Varenicline</td>
<td>8.8%</td>
</tr>
</tbody>
</table>


COMBINATION THERAPY: PATCH PLUS BUPROPION SR

<table>
<thead>
<tr>
<th>Treatment</th>
<th>% Abstinence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo</td>
<td>15.6%</td>
</tr>
<tr>
<td>NRT Patch</td>
<td>16.4%</td>
</tr>
<tr>
<td>Bupropion</td>
<td>30.3%</td>
</tr>
<tr>
<td>Both</td>
<td>35.5%</td>
</tr>
</tbody>
</table>

Odds Ratio:
- Placebo vs NRT Patch: 1.1
- Placebo vs Bupropion: 2.3
- Placebo vs Both: 2.7

* p<.001 compared with placebo


NORTRIPTYLINE (second-line)

ADVANTAGES
- Effective treatment for smoking cessation and depression
- Can combine with NRT
- Useful in patients with chronic pain, insomnia, and anxiety
- Inexpensive
- One of the best tolerated TCAs

DISADVANTAGES
- Seizure risk is increased as in all antidepressants
- May require blood level monitoring and EKG
- Dangerous in overdose
- Side-effect profile:
  - Dry mouth, orthostatic hypotension, cardiac arrhythmia, constipation, urinary retention, sexual dysfunction, sedation, etc.

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NORTRIPTYLINE: DOSING for SMOKING CESSATION

- Begin treatment 4 weeks prior to quit date at 25 mg q HS
- Increase as tolerated by 25 mg per week up to 75 - 100 mg to reach therapeutic blood levels of 50 - 150 ng/ml
- Continue for 7 weeks with a 1-week taper (12 weeks total)

Source: Hughes, Stead & Lancaster (2005). NTR

CLONIDINE (second-line)

ADVANTAGES
- Inexpensive
- Good for patients who are anxious or have insomnia
- Consider for patients with contraindications to antidepressants
- Consider for patients with hypertension
- Second-line treatment for ADHD and opioid withdrawal

DISADVANTAGES
- Fewer efficacy studies
- Medication interactions
- Side-effect profile:
  - Decreased HR, sedation, orthostatic hypotension, dizziness, dry mouth

CLONIDINE: DOSING for SMOKING CESSATION

- Usually in the range of 0.1 – 0.4 mg/day in divided TID or QID or 0.2 mg patch (TTS-2) q week
- Some patients may require more
- Initiate clonidine therapy 48 to 72 hours before quit attempt

Source: Gourlay, Stead, & Benowitz. (2005). Cochrane Reviews
COMPARATIVE DAILY COSTS of PHARMACOTHERAPY

<table>
<thead>
<tr>
<th>Product</th>
<th>Cost per day, in U.S. dollars</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clonidine</td>
<td>$3.75 (generic) $5.00 in CA</td>
</tr>
<tr>
<td>Nortriptyline</td>
<td>$4.00</td>
</tr>
<tr>
<td>Bupropion SR</td>
<td>$2.24 (generic)</td>
</tr>
<tr>
<td>Chantix</td>
<td>$1.13 (generic)</td>
</tr>
<tr>
<td>Inhaler</td>
<td>$0.14 (generic)</td>
</tr>
<tr>
<td>Nasal spray</td>
<td>$4.00</td>
</tr>
<tr>
<td>Gum</td>
<td>$3.07</td>
</tr>
<tr>
<td>Cigarettes (1 PPD)</td>
<td>$5.88</td>
</tr>
<tr>
<td>Nicotine Vaccine</td>
<td></td>
</tr>
<tr>
<td>Rimonabant</td>
<td>Approved obesity treatment in European Union</td>
</tr>
<tr>
<td></td>
<td>FDA approval for obesity expected in late 2006</td>
</tr>
<tr>
<td></td>
<td>FDA non-approval for smoking cessation</td>
</tr>
<tr>
<td>NicVAX (Nabi)</td>
<td>NicQb (Cytos AG) in Phase II Trials</td>
</tr>
<tr>
<td></td>
<td>Goal to prevent relapses after quitting</td>
</tr>
</tbody>
</table>

EMERGING TECHNOLOGIES

- Rimonabant
  - Approved obesity treatment in European Union
  - FDA approval for obesity expected in late 2006
  - FDA non-approval for smoking cessation

- Nicotine Vaccine
  - 3 companies in development (Japanese, US, Swiss)
    - NicVAX (Nabi) and NicQb (Cytos AG) in Phase II Trials
    - Goal to prevent relapses after quitting

SPECIAL POPULATIONS
TOBACCO USE in PREGNANCY

- Health complications to the fetus:
  - Low birth weight
  - Breakthrough bleeding
  - Miscarriage / death of the fetus
  - Placenta previa
  - Abruptio placenta
  - Premature rupture of membranes
  - Premature birth
- Fetal blood holds onto CO more strongly than oxygen leading to growth retardation and asphyxiation

TREATING the PREGNANT SMOKER

- Comprehensive psychosocial and behavioral intervention that includes pregnancy-specific materials
  - Pregnancy Toll-free Quitline: 1-866-66-START
- If pt unable to quit without pharmacological treatment, NRT may be prescribed at any point in the pregnancy.
- Bupropion and varenicline currently not recommended (Category C drugs). Use only if clearly indicated.


AFTER DELIVERY

- Relapse prevention is critical. Nonsmoking in the mother (and father) important for avoiding infant exposure to secondhand smoke to prevent SIDs and childhood asthma.
- Promote breastfeeding in all cases, even for mothers who smoke or use NRT.
- Bupropion and varenicline not currently recommended for smoking cessation with breastfeeding women.

Source: Melvin & Gaffney, 2004 Nicotine & Tobacco Research

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SMOKING and SUBSTANCE USE

- Tobacco-related diseases account for 50% of deaths among individuals treated for alcohol dependence (Hurt et al., 1996)
- Death rate 4-times greater for cigarette smoking vs. nonsmoking long-term drug abusers (Hser, 1994)
- Health consequences of tobacco and other drug use synergistic: 50% greater than sum of each individually (Bien & Burge, 1990)

A META-ANALYSIS of SMOKING CESSATION INTERVENTIONS with INDIVIDUALS in SUBSTANCE ABUSE TREATMENT or RECOVERY

Judith Prochaska, PhD, MPH
Kevin Delucchi, PhD & Sharon Hall, PhD
University of California, San Francisco
Supported by TRDRP #11FT-0013 and NIDA #PS0 DA09253
JCCP 2004

OVERALL SMOKING CESSATION RATES

<table>
<thead>
<tr>
<th>7-day PPY</th>
<th>In Treatment</th>
<th>In Recovery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Post-Treatment</td>
<td>18 studies</td>
<td>15 studies</td>
</tr>
<tr>
<td>3%</td>
<td>6%</td>
<td>3%</td>
</tr>
<tr>
<td>12%</td>
<td>7%</td>
<td>12%</td>
</tr>
<tr>
<td>38%</td>
<td>15%</td>
<td>38%</td>
</tr>
<tr>
<td>28%</td>
<td>20%</td>
<td>28%</td>
</tr>
</tbody>
</table>

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TREATING SMOKERS with SUBSTANCE USE DISORDERS

- Significant treatment effects for quitting smoking at post-treatment, but not at long-term follow up (> 6 months)
- At long-term follow up, evidence of improved sobriety among intervention participants
- 25% greater odds of being sober if exposed to the tobacco cessation intervention

Source: Prochaska et al., 2004. JCCP. Meta-analysis

TREATMENT of DEPRESSED PSYCHIATRIC OUTPATIENTS for CI GARETTE SMOKING

Sharon Hall, PhD, Janice Tsoh, PhD, Judith Prochaska, PhD, MPH, Stuart Eisendrath, MD, Joseph Rossi, PhD, Colleen Redding, PhD, Amy Rosen, PsyD, Marc Meisner, MD, Gary Humfleet, PhD, & Julie Gorecki, MA

University of California, San Francisco

Supported by NIDA #P50 DA09253

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**STUDY DESIGN**

- 322 depressed smokers recruited from four outpatient psychiatry clinics
- **Stepped Care Intervention**
  - Stage-based expert system counseling
  - Nicotine patch
  - 6 session individual CBT counseling
  - Bupropion available
- **Brief Contact Control**
- Primary outcome:
  - 7 day PPA @ 12 & 18 months, CO verified

**ABSTINENCE RATES by TREATMENT CONDITION**

<table>
<thead>
<tr>
<th>Month</th>
<th>Intervention</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>12%</td>
<td>16%</td>
</tr>
<tr>
<td>6</td>
<td>20%</td>
<td>21%</td>
</tr>
<tr>
<td>12</td>
<td>25%</td>
<td>19%</td>
</tr>
<tr>
<td>18</td>
<td>18%</td>
<td>12%</td>
</tr>
</tbody>
</table>

**MENTAL HEALTH OUTCOMES**

- Among depressed smokers who quit:
  - No increase in suicidality
    - Quit: 0% vs Smoking: 1-4%
  - No increase in psych hospitalization
    - Quit: 0-1% vs. Smoking: 2-3%
  - Comparable improvements in BDI and STAXI scores and % of days with emotional problems
TREATING SMOKERS with SCHIZOPHRENIA

- Treatments tailored for smokers with schizophrenia no more effective than standard cessation programs (George et al., 2000)
  - Atypical antipsychotics (clozapine) associated with greater cessation than typicals
- Tobacco abstinence (1-wk) not associated with:
  - Worsening of attention, verbal learning/memory, working memory, or executive function/inhibition nor worsening of clinical symptoms in individuals with schizophrenia (Evins et al., 2005)

SUMMARY: TOBACCO TREATMENTS with DEMONSTRATED EFFICACY

- Physician advice and counseling
- NRT, bupropion, varenicline, nortriptyline, clonidine
- Telephone counseling:
  - 1-800-NO-BUTTS (CA toll-free quit line)
  - 1-800-QUIT-NOW (national toll-free quit line)
- Group programs
- Aversion therapy
- Hypnotherapy
TOBACCO TREATMENTS LACKING EVIDENCE of EFFICACY

- SSRIs and SNRI
- Anxiolytics:
  - Sedative, hypnotics, buspirone
- Homeopathic treatments
- Herbal supplements
- Lobeline
- Massage Therapy
- Acupuncture
- Nicotine Anonymous

SET REALISTIC EXPECTATIONS

Most quit attempts are not “successful”:

- It’s a learning process. Reframe success!
- Most people make multiple quit attempts before they are successful.
- Longer prior quit attempts predict future success.

Source: Legacy Tobacco Documents