EPIDEMIOLOGY & IMPACT of TOBACCO USE in PEOPLE with MENTAL ILLNESS

TOBACCO USE in PSYCHIATRIC POPULATIONS

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

TRENDS in ADULT SMOKING, by SEX—United States, since 1955

SMOKING RATE by PSYCHIATRIC HISTORY

“90% of Schizophrenics Smoke”

- A meta-analysis of 42 studies on tobacco smoking among schizophrenia subjects found an average smoking prevalence of 62% (range=14-88%)
- Studies reporting higher smoking rates were more commonly cited in the research literature
  - A 10% increase in reported smoking prevalence was associated with a 61% increase in citation rate
  - This bias was mirrored on the Internet

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

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HEALTH CONSEQUENCES of SMOKING

- Cancers
  - Bladder/ureth/uterus
  - Blood (acute myeloid leukemia)
  - Cervix
  - Colon/rectum
  - Esophagus/stomach
  - Liver
  - Lung
  - Oropharynx/larynx
  - Pancreas

- Cardiovascular diseases
  - Aortic aneurysm
  - Coronary heart disease
  - Cerebrovascular disease
  - Peripheral vascular disease

- Reproductive effects
  - Reduced fertility in women
  - Poor pregnancy outcomes (e.g., congenital defects, low birth weight, preterm delivery)
  - Infant mortality

- Other: caner; diabetes type II; erectile dysfunction; impaired immune function; osteoporosis; periodontitis; postoperative complications; rheumatoid arthritis

SMOKING and SUBSTANCE USE

- Tobacco-related diseases account for 50% of deaths among individuals treated for alcohol dependence (Hurt et al., 1996)
- Death rate 4-5x greater for cigarette smoking vs. non-smoking 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)

TOBACCO KILLS PEOPLE with MENTAL ILLNESS

- Dying, on average, 15 years prematurely (Tam J, Warner KE, & Meza R, 2016)
- At greater risk of dying from CVD, respiratory illnesses, and cancer, than people without mental illness (e.g., Dalton et al., 2002; Himelhoch et al., 2004; Lichter et al., 2001)
- Tobacco use predicts future suicidal behavior
  - Independent of depressive symptoms, prior suicidal acts, and other substance use (Breslau et al., 2005; Oquendo et al., 2004)

COMPARATIVE CAUSES of ANNUAL DEATHS in the UNITED STATES

An estimated 8,700 compounds in tobacco smoke, including 72 proven or suspected human carcinogens

- Carbon monoxide
- Hydrogen cyanide
- Ammonia
- Benzene
- Formaldehyde

Componud in TOBACCO SMOKE

- Nicotine
- Nitrosamines
- Lead
- Cadmium
- Polonium-210

Nicotine is the addictive component of tobacco products, but it does NOT cause the ill health effects of tobacco use.

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**An EFFECTIVE MARKETING STRATEGY: “LIGHT” CIGARETTES**

The difference between Marlboro and Marlboro Lights...

- **an extra row of ventilation holes**

Image courtesy of Mayo Clinic Nicotine Dependence Center - Research Program / Dr. Richard D. Hurt
The Marlboro and Marlboro Lights logos are registered trademarks of Philip Morris USA

**“NO SAFE” LEVEL of SMOKING**

- Smoking even 1 to 4 cigarettes a day nearly triples the risk of death from heart disease
- Smokers who consume fewer cigarettes can reduce their risk of lung cancer, but still face a much larger risk of premature death or disability compared with people who quit

Source: Godtfredsen et al. (2005) JAMA, Bjartveit et al. (2005) Tobacco Control

**QUITTING: HEALTH BENEFITS**

- Time Since Quit Date
  - Circulation improves, walking becomes easier
  - Lung function increases
  - Excess risk of CHD decreases to half that of those who continue to smoke
  - Lung cancer death rate is similar to half that of those who continue to smoke
  - Risk of cancer of mouth, throat, esophagus, bladder, kidney, pancreas decreases
  - Risk of CHD is similar to that of people who have never smoked

**YEARS of SURVIVAL GAINED RELATIVE to CONTINUED SMOKING**

<table>
<thead>
<tr>
<th>Time Since Quit Date</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 month to 3 months</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1 to 9 months</td>
<td>6.3</td>
<td>7.7</td>
</tr>
<tr>
<td>1 year</td>
<td>8.9</td>
<td>9.6</td>
</tr>
<tr>
<td>5 years</td>
<td>11.1</td>
<td>13.3</td>
</tr>
<tr>
<td>10 years</td>
<td>12.4</td>
<td>15.1</td>
</tr>
<tr>
<td>More than 15 years</td>
<td>12.7</td>
<td>15.4</td>
</tr>
</tbody>
</table>

Source: DH Taylor et al., 2002 American Journal of Public Health

**TOBACCO IMPACTS TREATMENT**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Smoker, No NRT</th>
<th>Smoker, NRT</th>
<th>NonSmoker</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMA Discharge*</td>
<td>22%</td>
<td>10%</td>
<td>8%</td>
</tr>
<tr>
<td>Placed in Seclusion</td>
<td>17%</td>
<td>10%</td>
<td>8%</td>
</tr>
<tr>
<td>Ativan Prescription</td>
<td>83%</td>
<td>70%</td>
<td>69%</td>
</tr>
</tbody>
</table>


**TOBACCO USE ISOLATES and is COSTLY**

- 75% of psychiatric patients who smoke report smoking most or all of their cigarettes while alone (Prochaska et al., 2006).
- Median of $142.40 per month spent on cigarettes among an outpatient sample of smokers with schizophrenia (Steinberg et al., 2004)
  - 27% of their monthly incomes

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**FINANCIAL IMPACT of SMOKING**

Buying cigarettes every day for 50 years at $8.41 per pack (does not include interest)

<table>
<thead>
<tr>
<th>Packs per day</th>
<th>Dollars lost, in thousands</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.0</td>
<td>$306,900</td>
</tr>
<tr>
<td>1.5</td>
<td>$230,175</td>
</tr>
<tr>
<td>1.0</td>
<td>$153,450</td>
</tr>
</tbody>
</table>

Annual cost of smoking 1 pack per day: $3,069

*Average national cost, as of January 30, 2023. Campaign for Tobacco-Free Kids (2023).*

**ANNUAL SMOKING-ATTRIBUTABLE ECONOMIC COSTS**

- Health care expenditures: $132.5 billion
- Lost productivity costs due to premature mortality: $156.4 billion
- Total economic burden of smoking, per year: $288.9 billion

Societal costs: $19.16 per pack of cigarettes smoked


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**EPIDEMIOLOGY of TOBACCO USE: SUMMARY**

- Smoking prevalence is 2 to 4 times higher in individuals with a psychiatric history than that of the general population.
- Tobacco use adversely affects psychiatric treatment.
- Lifetime financial costs of buying cigarettes can exceed $200,000 for a heavy smoker.
- At any age, there are major health benefits to quitting smoking.

**PSYCHIATRIC MEDICATION INTERACTIONS with SMOKING**

Drugs that may have a decreased effect due to induction of CYP1A2:
- Bendamustine
- Caffeine
- Clozapine
- Erlotinib
- Fluvoxamine
- Trinotecan (clearance increased and systemic exposure decreased, due to increased glucuronidation of its active metabolite)

**PHARMACOKINETIC DRUG INTERACTIONS with TOBACCO SMOKE**

- Haloperidol
- Olanzapine
- Pirfenidone
- Rilpiciguat
- Ropinirole
- Tamsulosin

**GOOD PSYCHIATRIC CARE ≠ TOBACCO**

It is antithetical to provide patients with cigarettes as a form of reinforcement for taking their psychiatric medications.

**TOBACCO CESSATION can be a cost effective component of MENTAL HEALTH TREATMENT**

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CASE REPORTS of MEDICATION INTOXICATION FOLLOWING CESSATION

- Patients treated with CYP1A2 substrate antipsychotics should regularly be monitored with regard to their smoking consumption in order to adjust doses in cases of a reduction or increase in smoking
- Tobacco and cannabis smoking cessation can lead to intoxication with clozapine or olanzapine

DRUG INTERACTION: TOBACCO SMOKE and CAFFEINE

- Constituents in tobacco smoke induce CYP1A2 enzymes, which metabolize caffeine
  - Caffeine levels increase ~56% upon quitting
- Challenges:
  - Nicotine withdrawal effects might be enhanced by increased caffeine levels
  - Insomnia can be due to ↑ caffeine levels or a side effect of a smoking cessation drug (e.g., varenicline or bupropion)
  - Decrease caffeine intake by about half when quitting
  - For individuals with a typical bedtime, suggest eliminating caffeine by early afternoon

PHARMACODYNAMIC DRUG INTERACTIONS with TOBACCO SMOKE

Smokers who use combined hormonal contraceptives have an increased risk of serious cardiovascular adverse effects:
- Stroke
- Myocardial infarction
- Thromboembolism

This interaction does not decrease the efficacy of hormonal contraceptives.

Women who are 35 years of age or older AND smoke at least 15 cigarettes per day are at significantly elevated risk.

DRUG INTERACTIONS with TOBACCO SMOKE: SUMMARY

Clinicians should be aware of their patients' smoking status:
- Clinically significant interactions result the combustion products of tobacco smoke, not from nicotine.
- Constituents in tobacco smoke (e.g., polycyclic aromatic hydrocarbons; PAHs) may enhance the metabolism of other drugs, resulting in an altered pharmacologic response.
- Changes in smoking status might alter the clinical response to the treatment of a wide variety of conditions.
- Drug interactions with smoking should be considered when patients start smoking, quit smoking, or markedly alter their levels of smoking.

FACTORS ASSOCIATED with TOBACCO USE & MENTAL ILLNESS

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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 INDIVIDUALS with MENTAL ILLNESS

Individual
- Sociodemographics
- Genetic predisposition
- Coexisting medical conditions

Pharmacology
- Alliation of withdrawal symptoms
- Weight control
- Pleasure, mood modulation

Environment
- Tobacco advertising
- Conditioned stimuli
- Social interactions

NEUROCHEMICAL and RELATED EFFECTS of NICOTINE

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

BIOLOGY of NICOTINE ADDICTION: ROLE of DOPAMINE

Nicotine stimulates dopamine release

Pleasurable feelings

Repeat administration

Tolerance develops

Nicotine addiction is not just a bad habit.

Discontinuation leads to withdrawal symptoms.

DOPAMINE REWARD PATHWAY

Prefrontal cortex

Dopamine release

Stimulation of nicotine receptors

Nucleus accumbens

Ventral tegmental area

Nicotine enters brain

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

**Chronic Smoking Effects**

Nicotine receptor


**State of Nicotine Withdrawal**

Nicotine receptor


---

**NICOTINE ADDICTION CYCLE**

Plasma nicotine concentration (ng/ml)


**NICOTINE WITHDRAWAL SYMPTOMS: Time Course**

Most symptoms manifest within the first 1–2 days, peak within the first week, and subside within 2–4 weeks.

<table>
<thead>
<tr>
<th>Time</th>
<th>Symptom</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 week</td>
<td>Irritability/Frustration/Anger</td>
<td></td>
</tr>
<tr>
<td>1 week</td>
<td>Anxiety</td>
<td></td>
</tr>
<tr>
<td>1 week</td>
<td>Difficulty concentrating</td>
<td></td>
</tr>
<tr>
<td>1 week</td>
<td>Restlessness/Impatience</td>
<td></td>
</tr>
<tr>
<td>1 week</td>
<td>Depressed mood/Depression</td>
<td></td>
</tr>
<tr>
<td>1 week</td>
<td>Insomnia</td>
<td></td>
</tr>
<tr>
<td>1 week</td>
<td>Increased appetite</td>
<td></td>
</tr>
<tr>
<td>1 week</td>
<td>Weight gain</td>
<td></td>
</tr>
<tr>
<td>1 week</td>
<td>Cravings</td>
<td></td>
</tr>
<tr>
<td>6 months</td>
<td>Can persist for months to years after quitting</td>
<td></td>
</tr>
</tbody>
</table>

**GENETIC EFFECTS on NICOTINE METABOLISM**

Reprinted with permission, Benowitz et al., 1994.

**WHAT IS ADDICTION?**

“Compulsive drug use, without medical purpose, in the face of negative consequences”

Alan I. Leshner, Ph.D.
Former Director, National Institute on Drug Abuse
National Institutes of Health

Nicotine addiction is a chronic condition with a biological basis.
**MODEL of ADDICTION**

**Impulse control disorders**
- Impulsive acts
  - Regret / guilt / self-reproach
  - Pleasure / relief / gratification
- Anxiety / stress
  - Relief of anxiety / relief of stress

**Compulsive disorders**
- Obsessions
  - Tension / arousal
- Repetitive behaviors

**Positive Reinforcement**
- Pleasure / relief / gratification

**Negative Reinforcement**
- Regret / guilt / self-reproach
- Tension / arousal

Source: GF Koob et al. (2004). Neuroscience and Biobehavioral Reviews

---

**DSM-V TOBACCO-RELATED DISORDERS**

**Tobacco Use Disorder**
A problematic pattern of tobacco use leading to clinically significant impairment or distress, as manifested by 2 of the following within a 12-month period:
1. Tolerance
2. Persistent desire to use
3. Use
4. Unsuccessful efforts to stop
5. Time investment
6. Continued use despite knowledge of physical or psychological problems
7. Tobacco use continued even through physical or psychological problems occurring from tobacco use

**Nicotine Withdrawal**
- A. Daily use
- B. Abrupt cessation/reduction followed within 24 hrs by 4+
  1. Depressed mood
  2. Insomnia
  3. Irritability
  4. Anxiety
  5. Difficulty concentrating
  6. Increased appetite
  7. Restlessness
- C. Clinically significant
- D. Not due to other mental disorders or medical conditions

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**SYSTEMIC and TREATMENT FACTORS**

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**PSYCHIATRISTS in PRACTICE**
(Himelhoch & Daumit, 2003)
- 1992-96 Nat’l Ambulatory Medical Care Survey
  - 23% of psychiatric visits dropped from analysis because patient smoking status unknown
  - For patients identified as smokers (N=1610)
    - Cessation counseling offered at 12% of visits
    - Nicotine Dependence not diagnosed at any visit
    - Nicotine replacement therapy never prescribed

---

**2005 AAMC PRACTICE SURVEY: 801 PSYCHIATRISTS**
- 62% Ask about tobacco
- 44% Assess readiness to quit
- 62% Advise cessation
- Assist:
  - NRT (23%), other Rx (20%)
  - Cessation materials (13%)
  - 14% Arrange follow up
  - 11% Refer to others

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### PSYCHIATRY RESIDENTS’ (N=105) ENGAGEMENT in the 5-As

<table>
<thead>
<tr>
<th>Activity</th>
<th>Never or Rarely</th>
<th>Sometimes</th>
<th>Often</th>
<th>Other or Always</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ask about smoking</td>
<td>18%</td>
<td>30%</td>
<td>32%</td>
<td>50%</td>
</tr>
<tr>
<td>Advise to quit</td>
<td>18%</td>
<td>32%</td>
<td>20%</td>
<td>30%</td>
</tr>
<tr>
<td>Assess readiness to quit</td>
<td>49%</td>
<td>26%</td>
<td>17%</td>
<td>16%</td>
</tr>
<tr>
<td>Assist with quitting</td>
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<td>20%</td>
<td>18%</td>
<td>39%</td>
</tr>
<tr>
<td>Arrange follow-up</td>
<td>18%</td>
<td>34%</td>
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Source: Prochaska, Fromont et al., 2005 Ascd Psychiatr

### TOBACCO INDUSTRY’S INTERESTS

- **1950s–1980s:** Beliefs that patients with schizophrenia, who smoke at high rates, immune to cancer

### TOBACCO INDUSTRY’S INTERESTS

- **1960s–1970s:** TI funded research on psychosomatic causes of cancer
  - Proposed those who denied or repressed grief were more likely to develop cancer than those who expressed emotion
  - "Longterm schizophrenics, outwardly calm, have no capacity for the repression of significant emotional events and no need to contain emotional conflict"
  - Ultimately came under scrutiny for its “scientific integrity”

### Legacy Tobacco Documents

- Digital online library
- 15+ million documents (92+ million pages) from the major tobacco companies
- Related to their advertising, manufacturing, marketing, sales, and scientific research activities
- Located at: http://legacy.library.ucsf.edu

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**I am therefore requesting a donation of approximately 5,000 cigarettes a week (8 per day for each of the 100 patients without funds). Any help you can give would be much appreciated.**

Sincerely yours,

[Signature]

Dr. E. A. Jones

Department of Health, Education, and Welfare
National Institute of Mental Health
Washington, DC
August 4, 1980

**I am writing to request a donation of cigarettes for long-term psychiatric patients...because of recent changes in the DHHS regulations, Saint Elizabeth Hospital can no longer purchase cigarettes for them.**

---

**TOBACCO INDUSTRY’S INTERESTS**

- **1950s–1980s:** Beliefs that patients with schizophrenia, who smoke at high rates, immune to cancer

---

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</tbody>
</table>

Source: Prochaska, Fromont et al., 2005 Ascd Psychiatr
TOBACCO INDUSTRY’S INTERESTS

- 1964 & 1997: TI denied funding of 2 proposals to examine high rates of cancer in smokers with mental illness
  - 1964 proposal “denied in principle but referred to the study group on the psychophysiological aspects of smoking.”
  - Questioned whether some other kind of use could profitably be made of his data collection methods.


Nicotine: helping those who help themselves?

LD 463 - An Act to Exempt Substance Abuse and Psychiatric Patients from the Prohibition against Smoking in Hospitals

HOSPITAL SMOKING BANS

ICAOH ultimately “yielded to massive pressure from mental patients and their families, relaxing a policy that called on hospitals to ban smoking.”
CONTRIBUTING FACTORS: SUMMARY

- Tobacco products are effective delivery systems for the highly addictive drug nicotine.
- Nicotine activates the dopamine reward pathway in the brain, which reinforces continued tobacco use.
- Nicotine dependence and withdrawal are DSM-V psychiatric disorders.
- Tobacco dependence involves biological, psychological, social, systemic and treatment factors requiring a long-term multifaceted treatment approach.
**TOBACCO DEPENDENCE: A 2-PART PROBLEM**

<table>
<thead>
<tr>
<th>Physiological</th>
<th>Behavioral</th>
</tr>
</thead>
<tbody>
<tr>
<td>The addiction to nicotine</td>
<td>The habit of using tobacco</td>
</tr>
<tr>
<td>Treatment</td>
<td>Treatment</td>
</tr>
<tr>
<td>Medications for cessation</td>
<td>Behavior change program</td>
</tr>
</tbody>
</table>

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

---

**RECOMMENDATIONS to TREAT TOBACCO USE in PSYCHIATRY**

*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
Professor of Psychiatry
University of Vermont

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**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

---

**EFFECTS of CLINICIAN INTERVENTIONS**

With help from a clinician, the odds of quitting approximately doubles.

Compared to patients who receive no assistance from a clinician, patients who receive assistance are 1.7–2.2 times as likely to quit successfully for 5 or more months.

---

**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) post-cessation

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WHY MENTAL HEALTH PROVIDERS?

- Often the clinician for whom contact is the most frequent and who knows the patient best
- Able to combine psychopharmacological and behavioral/counseling treatment
- Trained in substance abuse treatment
- Able to identify and address any changes in psychiatric symptoms during the quit attempt

Failure to address tobacco use tactically implies that quitting is not important or that the patient is not worth helping.

The 5 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

The 5 A’s: ASK

- Ask about tobacco use; with a tone that conveys sensitivity, concern and is non-judgmental:
  - “Do you smoke or use other types of tobacco or nicotine, such as e-cigarettes?”
  - “It’s important for us to have this information so we can check for potential interactions between tobacco smoke and your other medicines.”
  - “We ask all of our patients, because tobacco smoke can affect how some medicines work.”
  - “We care about your health, and we have resources to help our patients quit smoking.”
  - “Has there been any change in your smoking status?”

The 5 A’s: ADVISE

- Advise tobacco users to quit (clear, strong, personalized):
  - “Quitting smoking is the most important thing you can do to protect your health now and in the future.”
  - “I have training to help my patients quit, and when you are ready, I can work with you to design a specialized treatment plan.”

52% of psychiatric patients who smoke report never having been advised to quit by a mental healthcare provider (Prochaska et al., 2005)

The 5 A’s: ASSESS and ASSIST

- **ASSESS** readiness to make a quit attempt
- **ASSIST** with the quit attempt
  - Not ready to quit: enhance motivation (the 5 R’s)
  - Ready to quit: design a treatment plan
  - Recently quit: relapse prevention

READINESS to QUIT

- Not ready to quit
- Recently quit
- Behaviors counseling
- Relapse prevention

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

**READYNESS to QUIT SMOKING***

<table>
<thead>
<tr>
<th>Category</th>
<th>Readiness to Quit in 6 mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>General Population</td>
<td>40%  20%</td>
</tr>
<tr>
<td>General Psych Outpts</td>
<td>42%  28%</td>
</tr>
<tr>
<td>Depressed Outpatients</td>
<td>55%  24%</td>
</tr>
<tr>
<td>Psych. Inpatients</td>
<td>61%  24%</td>
</tr>
<tr>
<td>Methadone Clients</td>
<td>48%  22%</td>
</tr>
</tbody>
</table>

* No relationship between psychiatric symptom severity and readiness to quit

**ASSIST: TAILOR TREATMENT to PATIENTS’ READINESS to QUIT**

- **Assess: Readiness to quit**
  - Does the patient now use tobacco?
  - Is the patient now ready to quit?
  - Did the patient once use tobacco?

**Stage 1: NOT READY to QUIT**

**Stage 1: Not ready to quit**

**Goal:** Start thinking about quitting.

- Some patients are aware of the need to quit.
- Patients struggle with ambivalence about change.
- Patients are not ready to change, yet.
- Pros of continued tobacco use outweigh the cons.

**ASSIST: NOT READY to QUIT**

**Stage 1: Not ready to quit**

**DO**
- Strongly advise to quit
- Provide information
- Ask noninvasive questions; identify reasons for tobacco use
- Raise awareness of health consequences/concerns
- Demonstrate empathy, foster communication
- Leave decision up to patient

**DON’T**
- Persuade
- “Cheerlead”
- Tell patient how bad tobacco is, in a judgmental manner
- Provide a treatment plan

**SUMMARY:**

**Patients not yet READY to QUIT**

- Clinician goals include –
  - 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

---

**RAISING AWARENESS: TOBACCO USE MOOD LOG**

- Use the Mood Log to raise patients’ awareness of their tobacco use
- For each day, patient should record # of cigarettes smoked, # of pleasant activities, and provide a mood rating.
- Review log sheets with patient to identify relationship between smoking, activities / isolation, and mood

Is patient’s tobacco use associated with isolation and poorer mood?

---

CASE 1: Vera

- 48 year old divorced woman
- Dual diagnosis treatment facility
- Bipolar disorder, alcohol dependence, h/c crack cocaine dependence
- Smokes 1.5 packs/day
- “I'll likely die with a cigarette in my mouth”

ASSIST: 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

ASSIST: READY to QUIT

STAGE 2: Ready to quit

Ready to quit in the next month
- Patients are aware of the need to, and the benefits of, making the behavioral change.
- Patients are getting ready to take action.

GOAL: Achieve cessation.

STRATEGIES for PATIENTS READY to QUIT

- Key Questions to Ask:
  - Why do you want to quit now?
  - How confident are you that you’ll be able to quit?
  - Have you quit in the past? What worked for you then?
  - What are key triggers for you with smoking?
  - How do stress and your mood play into your smoking?
  - Who can support you with quitting?
  - What concerns do you have about quitting? (withdrawal symptoms, weight gain, coping with stress)
  - How can we work together to manage your anxiety (or other psychiatric symptoms) during the quitting process?

STRATEGIES for PATIENTS READY to QUIT

DOs
- Discuss and develop coping strategies
- Offer pharmacological treatment, unless contraindicated
- Set a quit date!
- Schedule follow up visit

COPING with QUITTING

Cognitive Coping Strategies
- Review commitment to quit
- Distractive thinking
- Positive self-talk
- Relaxation through imagery
- Mental rehearsal and visualization

Remind yourself that urges are brief.
COPING with QUITTING (cont’d)

Cognitive Coping Strategies: Examples

- Thinking about cigarettes doesn't mean you have to smoke one:
  - "Just because you think about something doesn't mean you have to do it!"
  - Tell yourself, "It's just a thought," or "I am in control."
- As soon as you get up in the morning, look in the mirror and say to yourself:
  - "I am proud that I made it through another day without tobacco."
- Reframe how you think about yourself:
  - Begin thinking of yourself as a non-smoker, instead of as a struggling quitter

Behavioral Coping Strategies

- Control your environment
  - Tobacco-free home and workplace
  - Remove cues to tobacco use; actively avoid trigger situations
  - Modify behaviors that you associate with tobacco: when, what, where, how, with whom
- Substitutes for smoking
  - Water, sugar-free chewing gum or hard candies (oral substitutes)
  - Minimize stress where possible, obtain social support, take a break, and alleviate withdrawal symptoms

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

The FIVE A’s: ARRANGE

ARRANGE follow-up care
- Follow-up in person or via phone within 1 to 3 days after quit attempt
- Congratulate success
- Address lapses “let a slip slide”
- Assess pharmacotherapy use and problems

CASE 6: Mr. Brooks

- 58 year old divorced male, unemployed
- PTSD clinic at Veteran’s Hospital
- PTSD, h/o polysubstance abuse, chronic pain
- Smokes 1.5 packs per day
- Interested in quitting
**ASSIST: TAILOR TREATMENT to PATIENTS’ READINESS to QUIT**

Does the patient now use tobacco?

- **Yes**

  - Is the patient now ready to quit?
    - **Yes**
      - Provide treatment
      - Prevent relapse*
      - Encourage continued abstinence
    - **No**
      - Promote motivation

- **No**

  - Did the patient once use tobacco?
    - **Yes**
      - Prevent relapse*
      - Encourage continued abstinence
    - **No**

*Relapse prevention interventions and motivation if patient has not avoided tobacco for many years and is not at risk for an intervention.


---

**ASSESSING READINESS to QUIT (cont’d)**

**STAGE 3: Recent quitter**

Actively trying to quit for good

- Patients have quit using tobacco sometime in the past 6 months and are taking steps to increase their success.
- Withdrawal symptoms occur.
- Patients are at risk for relapse.

**GOAL:** Remain tobacco-free for at least 6 months.

---

**STRATEGIES for RECENT QUITTERS**

**DOs**

- Praise progress - solicit commitment to quit for good
- Evaluate current quit attempt:
  - Status of attempt
  - "Slips" or relapse
  - Medication use, plans for discontinuation
- Ask about social support
- Identify temptations and triggers for relapse
  - Negative affect, smokers, eating, alcohol, cravings, stress
- Encourage healthful alternative behaviors to replace tobacco use
- Offer tips for relapse prevention

---

**RELAPSE PREVENTION for LONG-TERM QUITTERS**

**Relapse Prevention**

- Congratulate success!
- Encourage continued abstinence
  - Discuss benefits of quitting, problems encountered, successes achieved, and potential barriers to continued abstinence
  - Ask about strong or prolonged withdrawal symptoms (change dose, combine or extend use of medications)
- Promote smoke-free environments
- Schedule additional follow-up as needed

---

**SMOKING CESSATION and WEIGHT GAIN CONCERNS**

**SMOKING CESSATION & WEIGHT GAIN**

- Weight gain a major impediment to quitting smoking, particularly among women
  - Average weight gain: men=6 lbs, women=8 lbs
  - Major weight gain (>28 lbs) occurred in <15%
- Risk factors for post-cessation weight gain
  - African American race, younger age (<55 yrs), heavier smokers (>15 cigarettes/day)
- At baseline smokers weigh less than nonsmokers, they weigh nearly the same after quitting

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ADDRESSING CONCERNS about POST CESSATION WEIGHT GAIN

**Weight Gain**
- Discourage strict dieting while quitting
- Encourage healthy diet and meal planning
- Suggest increasing water intake or chewing sugarless gum
- Recommend selection of nonfood rewards
- When fear of weight gain is a barrier to quitting
  - Consider pharmacotherapy with evidence of delaying weight gain (bupropion SR or 4-mg nicotine gum or lozenge)
  - Assist patient with weight maintenance or refer patient to specialist or program

ASSIST: TAILOR TREATMENT to PATIENTS’ READINESS to QUIT

**READINESS to QUIT: A REVIEW**

<table>
<thead>
<tr>
<th>Quit date</th>
<th>Not ready to quit</th>
<th>Ready to quit</th>
<th>Recent quitter</th>
<th>Former tobacco user</th>
</tr>
</thead>
<tbody>
<tr>
<td>- 30 days</td>
<td>Enhance motivation</td>
<td>The 5 A's</td>
<td>Behavioral counseling</td>
<td>Pharmacotherapy</td>
</tr>
<tr>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>6 months</td>
<td>+ 6 months</td>
<td>Ready to quit</td>
<td>Behavioral counseling</td>
<td>Pharmacotherapy The 5 A's</td>
</tr>
<tr>
<td>Does the patient now use tobacco? Yes No</td>
<td>Is the patient now ready to quit? Yes No</td>
<td>Did the patient once use tobacco? Yes No</td>
<td>Encourage continued abstinence</td>
<td></td>
</tr>
</tbody>
</table>

INTEGRATING TOBACCO TREATMENT into PSYCHOTHERAPY

Quotes from Psychodynamically Trained Faculty
- “Attention to substance abuse is part of psychotherapy and how we address self-defeating, self-destructive behaviors and examine resistance to change and support change.”
- “Ideally, link to the central pathology – ‘When people are depressed they don’t take very good care of themselves. I want to help you take as good care of yourself as possible.’”
- If the patient says he needs to smoke to deal with psychiatric symptoms I would respond, ‘Wow, you must have a lot of stress and anxiety if you need to take a cancer-causing agent to deal with it. I think we really need to look at your level of stress. It should be a real priority.’

BRIEF COUNSELING: ASK, ADVISE, REFER

- ASK about tobacco USE
- ADVISE tobacco users to QUIT
- REFER to other resources

Patient receives assistance from other resources, with follow-up counseling arranged

ASSIST
ARRANGE

BRIEF COUNSELING: ASK, ADVISE, REFER (cont’d)

- Brief interventions have been shown to be effective
- In the absence of time or expertise:
  - Ask, advise, and refer to other resources, such as local group programs or the toll-free quitline
  - 1-800-QUIT-NOW

This brief intervention can be achieved in less than 1 minute.
**CESSATION COUNSELING: SUMMARY**

- Routinely identify tobacco users (ASK)
- Strongly ADVISE patients to quit
- ASSESS stage at each contact
- Tailor intervention messages (ASSIST)
  - Be a good listener
  - Minimal intervention in absence of time for more intensive intervention
- ARRANGE follow-up
  - Use the referral process, if needed

**MEDICATIONS for CESSATION**

**PHARMACOTHERAPY**

"Clinicians should encourage all patients attempting to quit to use effective medications for tobacco dependence treatment, except where contraindicated or for specific populations* for which there is insufficient evidence of effectiveness."

*Includes pregnant women, smokeless tobacco users, light smokers, and adolescents.

Medications significantly improve success rates.

**FDA-APPROVED MEDICATIONS for CESSATION**

- Nicotine polacrilex gum*
  - Nicorette (OTC)
  - Generic nicotine gum (OTC)
- Nicotine lozenge*
  - Nicorette (OTC)
  - Generic nicotine lozenge (OTC)
- Nicotine transdermal patch*
  - Habitrol (OTC)
  - NicoDerm CQ (OTC)
  - Generic nicotine patches (OTC)
- Nicotine inhaler *,**
  - Nicotrol (Rx)
- Nicotine nasal spray *
  - Nicotrol NS (Rx)
- Bupropion SR
  - Generic (Rx)
- Varenicline
  - Generic (Rx)

* Nicotine replacement therapy (NRT) products
** Discontinued by Pfizer in 2013

Recommended treatment is behavioral counseling.

**TIMELINE for MEDICATIONS and ENDS***

1984 OTC nicotine gum and patch; Rx nicotine nasal spray
1991 Rx nicotine nasal spray; Rx bupropion SR
1996 Rx transdermal nicotine patch
1997 Nicotine inhaler; Rx varenicline
2002 Rx varenicline
2006 e-cigarettes sold in US
2007 Nicotine inhaler discontinued
2023 Electronic Nicotine Delivery Systems

* Electronic Nicotine Delivery Systems

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NICOTINE REPLACEMENT THERAPY (NRT) RATIONALE for USE

- Reduces physical withdrawal from nicotine
- Eliminates the immediate, reinforcing effects of nicotine that is rapidly absorbed via tobacco smoke
- Allows patient to focus on behavioral and psychological aspects of tobacco cessation

NRT products approximately doubles quit rates.

PLASMA NICOTINE CONCENTRATIONS for NICOTINE-CONTAINING PRODUCTS

NRT: PRECAUTIONS

- Patients with underlying cardiovascular disease
  - Recent myocardial infarction (within past 2 weeks)
  - Serious arrhythmias
  - Serious or worsening angina

NRT products may be appropriate for these patients if they are under medical supervision.

NICOTINE GUM

Nicorette; generics

- Resin complex
  - Nicotine
  - Polacrilin
- Sugar-free chewing gum base
- Contains buffering agents to enhance buccal absorption of nicotine
- Available: 2 mg, 4 mg; original, cinnamon, fruit, and mint (various) flavors

NICOTINE LOZENGE

Nicorette Lozenge, Nicorette Mini Lozenge; generics

- Nicotine polacrilex formulation
  - Delivers ~25% more nicotine than equivalent gum dose
- Sugar-free mint, cherry flavors
- Contains buffering agents to enhance buccal absorption of nicotine
- Available: 2 mg, 4 mg

NICOTINE GUM & LOZENGE: DOSING

Dose based on the “time to first cigarette” (TTFC) as an indicator of nicotine dependence

Use the 2 mg gum/lozenge:
If first cigarette of the day is smoked more than 30 minutes after waking

Use the 4 mg gum/lozenge:
If first cigarette of the day is smoked within 30 minutes of waking

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NICOTINE GUM & LOZENGE: DOSING (cont’d)

Recommended Usage Schedule

<table>
<thead>
<tr>
<th>Weeks 1–6</th>
<th>Weeks 7–9</th>
<th>Weeks 10–12</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 piece q 1–2 h</td>
<td>1 piece q 2–4 h</td>
<td>1 piece q 4–8 h</td>
</tr>
</tbody>
</table>

NICOTINE GUM: DIRECTIONS FOR USE

- Chew slowly
- Stop chewing at first sign of peppery taste or tingling sensation
- Chew again when peppery taste or tingle fades
- Park between cheek and gum

NICOTINE LOZENGE: DIRECTIONS for USE

- Place in mouth and allow to dissolve slowly (nicotine release may cause warm, tingling sensation)
- Do not chew or swallow
- Occasionally rotate to different areas of the mouth
- Lozenges will dissolve completely in about 20–30 minutes

NICOTINE GUM/LOZENGE: ADDITIONAL PATIENT EDUCATION

- To improve chances of quitting, use at least nine pieces daily during the first 6 weeks
- The gum/lozenge will not provide the same rapid satisfaction that smoking provides
- The effectiveness of the nicotine gum/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 the nicotine gum or lozenge.

NICOTINE GUM/LOZENGE: ADD’L PATIENT EDUCATION (cont’d)

- Chewing the lozenge or using incorrect gum chewing technique can cause excessive and rapid release of nicotine, resulting in:
  - Lightheadedness/dizziness
  - Nausea and vomiting
  - Hiccups
  - Irritation of throat and mouth

NICOTINE GUM/LOZENGE: ADD’L PATIENT EDUCATION (cont’d)

- Adverse effects of nicotine gum and lozenge:
  - Mouth and throat irritation
  - Hiccups
  - Gastrointestinal complaints (dyspepsia, nausea)

- Adverse effects associated with nicotine gum:
  - Jaw muscle ache
  - May stick to dental work
**ADVANTAGES**
- Might serve as an oral substitute for tobacco
- Might delay weight gain
- Can be titrated to manage withdrawal symptoms
- Can be used in combination with other agents to manage situational urges
- Relatively inexpensive

**DISADVANTAGES**
- Need for frequent dosing can compromise adherence
- Gastrointestinal adverse effects (nausea, hiccups, and dyspepsia) may be bothersome
- Specific to nicotine gum:
  - Might be problematic for patients with significant dental work
  - Proper chewing technique is necessary for effectiveness and to minimize adverse effects
  - Chewing might not be acceptable or desirable for some patients

---

**NICOTINE GUM/LOZENGE: SUMMARY**

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**TRANSDERMAL NICOTINE PATCH**
Habitrol; NicoDerm CQ; generic

- Continuous (24-hour) nicotine delivery system
- Nicotine is well absorbed across the skin
- Transdermal delivery to systemic circulation avoids hepatic first-pass metabolism
- Plasma nicotine levels are lower and fluctuate less than with smoking

---

**TRANSDERMAL NICOTINE PATCH: DOSING**

<table>
<thead>
<tr>
<th>Product</th>
<th>Light Smoker</th>
<th>Heavy Smoker</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>≤10 cigarettes/day</td>
<td>&gt;10 cigarettes/day</td>
</tr>
<tr>
<td>NicolDerm CQ</td>
<td>Step 2 (14 mg x 6 weeks) Step 3 (7 mg x 2 weeks)</td>
<td>Step 1 (21 mg x 6 weeks) Step 2 (14 mg x 2 weeks) Step 3 (7 mg x 2 weeks)</td>
</tr>
<tr>
<td>Habitrol</td>
<td>Step 2 (14 mg x 6 weeks) Step 3 (7 mg x 2 weeks)</td>
<td>&gt;10 cigarettes/day Step 1 (21 mg x 4 weeks) Step 2 (14 mg x 2 weeks) Step 3 (7 mg x 2 weeks)</td>
</tr>
<tr>
<td>Generic</td>
<td>Step 2 (14 mg x 6 weeks) Step 3 (7 mg x 2 weeks)</td>
<td></td>
</tr>
</tbody>
</table>

---

**TRANSDERMAL NICOTINE PATCH: DIRECTIONS for USE**

- Choose an area of skin on the upper body or upper outer part of the arm
- Make sure skin is clean, dry, hairless, and not irritated
- Apply patch to different area each day
- Do not use same area again for at least 1 week

---

**TRANSDERMAL NICOTINE PATCH: DIRECTIONS for USE (cont’d)**

- Remove protective liner and apply adhesive side of patch to skin
- Peel off remaining protective covering
- Press firmly with palm of hand for 10 seconds
- Make sure patch sticks well to skin, especially around edges

---

**TRANSDERMAL NICOTINE PATCH: DIRECTIONS for USE (cont’d)**

- Wash hands: Nicotine on hands can get into eyes or nose and cause stinging or redness
- Do not leave patch on skin for more than 24 hours—doing so may lead to skin irritation
- Adhesive remaining on skin may be removed with rubbing alcohol or acetone
- Dispose of used patch by folding it onto itself, completely covering adhesive area

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TRANSDERMAL NICOTINE PATCH: ADDITIONAL PATIENT EDUCATION

- 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
  - Can unpredictably effect nicotine delivery
  - Patch may be less effective
- Keep new and used patches out of the reach of children and pets
- Remove patch before MRI procedures

TRANSDERMAL NICOTINE PATCH: ADD’L PATIENT EDUCATION (cont’d)

- After patch removal, skin may appear red for 24 hours
  - If skin stays red more than 4 days or if it swells or a rash appears, contact health care provider—do not apply new patch
- Local skin reactions (redness, burning, itching)
  - Usually caused by adhesive
  - Up to 50% of patients experience this reaction
  - Fewer than 5% of patients discontinue therapy
  - Avoid use in patients with dermatologic conditions (e.g., psoriasis, eczema, atopic dermatitis)

TRANSDERMAL NICOTINE PATCH: SUMMARY

ADVANTAGES

- Once-daily dosing associated with fewer adherence problems
- Of all NRT products, its use is least obvious to others
- Can be used in combination with other agents; delivers consistent nicotine levels over 24 hrs
- Relatively inexpensive

DISADVANTAGES

- When used as monotherapy, cannot be titrated to acutely manage withdrawal symptoms
- Not recommended for use by patients with dermatologic conditions (e.g., psoriasis, eczema, atopic dermatitis)

NICOTINE NASAL SPRAY

Nicotrol NS

- Aqueous solution of nicotine in a 10-ml spray bottle
- Each metered dose actuation delivers
  - 50 mcL spray
  - 0.5 mg nicotine
  - ~100 doses/bottle
- Rapid absorption across nasal mucosa

NICOTINE NASAL SPRAY: DOSING & ADMINISTRATION

- One dose = 1 mg nicotine
  (2 sprays, one 0.5 mg spray in each nostril)
- Start with 1–2 doses per hour
- Increase as needed to maximum dosage of 5 doses per hour or 40 mg (80 sprays; ~½ bottle) daily
- At least 8 doses daily for the first 6–8 weeks
- Termination:
  - Gradual tapering over an additional 4–6 weeks
  - Recommended maximum duration of therapy is 3 months

Common adverse effects include:

- Irritation at the patch application site (generally within the first hour)
  - Mild itching
  - Burning
  - Tingling
- Sleep disturbances
  - Abnormal or vivid dreams
  - Insomnia

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NICOTINE NASAL SPRAY: DIRECTIONS for USE

- Press in circles on sides of bottle and pull to remove cap

NICOTINE NASAL SPRAY: DIRECTIONS for USE (cont’d)

- Prime the pump (before first use)
  - Re-prime (1–2 sprays) if spray not used for 24 hours
- Blow nose (if not clear)
- Tilt head back slightly and insert tip of bottle into nostril as far as comfortable
- Breathe through mouth, and spray once in each nostril
- Do not sniff or inhale while spraying

NICOTINE NASAL SPRAY: DIRECTIONS for USE (cont’d)

- If nose runs, gently sniff to keep nasal spray in nose
- Wait 2–3 minutes before blowing nose
- Avoid contact with skin, eyes, and mouth
  - If contact occurs, rinse with water immediately
  - Nicotine is absorbed through skin and mucous membranes

NICOTINE NASAL SPRAY: ADDITIONAL PATIENT EDUCATION

- What to expect (first week):
  - Hot peppery feeling in back of throat or nose
  - Sneezing
  - Coughing
  - Watery eyes
  - Runny nose
- Adverse effects should lessen over a few days
  - Regular use during the first week will help in development of tolerance to the irritant effects of the spray
  - If adverse effects persist after a week, contact health care provider and consider alternative treatment

NICOTINE NASAL SPRAY: SUMMARY

<table>
<thead>
<tr>
<th>ADVANTAGES</th>
<th>DISADVANTAGES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Can be titrated to rapidly manage withdrawal symptoms</td>
<td>Need for frequent dosing can compromise adherence</td>
</tr>
<tr>
<td>Can be used in combination with other agents to manage situational urges</td>
<td>Nasal administration might not be acceptable/desirable for some patients; nasal irritation often problematic</td>
</tr>
<tr>
<td></td>
<td>Not recommended for use by patients with chronic nasal disorders or severe reactive airway disease</td>
</tr>
<tr>
<td></td>
<td>Cost of treatment</td>
</tr>
</tbody>
</table>

NRT: REDUCTION of DOSE

- Dose tapering is not required when discontinuing treatment
- Strategies for discontinuing use:
  - Use lower dose patch/gum/lozenge
  - Chew gum for 10–15 min instead of 30 min
  - Reduce the number of pieces used daily
  - Substitute ordinary chewing gum/lozenge for NRT

If patients experience significant withdrawal symptoms during tapering or discontinuing NRT, increase the dose and consider extending treatment.
**BUPROPION SR**

**Generics**

- Non-nicotine cessation aid
- Mechanism of action: atypical antidepressant thought to affect levels of various brain neurotransmitters
  - Dopamine
  - Norepinephrine
- Clinical effects
  - ↓ craving for cigarettes
  - ↓ symptoms of nicotine withdrawal

---

**BUPROPION: PHARMACOKINETICS**

**Absorption**
- Bioavailability: 5–20%

**Metabolism**
- Undergoes extensive hepatic metabolism (CYP2B6)

**Elimination**
- Urine (87%) and feces (10%)

**Half-life**
- Bupropion (21 hours); metabolites (20–37 hours)

---

**BUPROPION: CONTRAINDICATIONS**

- Seizure disorder
- Current or prior diagnosis of bulimia or anorexia nervosa
- Abrupt discontinuation of alcohol, benzodiazepines, barbiturates and antiepileptic drugs
- Use of MAO inhibitors (within 14 days of initiating or discontinuing therapy)

---

**BUPROPION: WARNINGS and PRECAUTIONS**

- Neuropsychiatric symptoms and suicide risk
  - Changes in mood (including depression and mania)
  - Psychosis/hallucinations/paranoia/delusions
  - Homicidal ideation
  - Aggression/hostility/anxiety/panic
  - Suicidal ideation, suicide attempt, completed suicide

**FDA boxed warning removed Dec 2016**

Advis patients to stop taking bupropion SR and contact a health care provider immediately if symptoms such as agitation, depressed mood, or changes in behavior or thinking that are not typical are observed or if the patient develops suicidal ideation or suicidal behavior.

---

**BUPROPION SR: DOSING**

To ensure therapeutic plasma levels of the drug are achieved, begin therapy 1 to 2 weeks PRIOR to the quit date.

**Initial treatment**
- 150 mg po q AM for 3 days

**Then...**
- 150 mg po bid for 7–12 weeks
- Doses must be administered at least 8 hours apart
- Tapering not necessary when discontinuing therapy

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BUPROPION: ADVERSE EFFECTS

Common adverse effects include the following:
- Insomnia (avoid bedtime dosing)
- Dry mouth
- Nausea

Less common but reported effects:
- Anxiety/difficulty concentrating
- Constipation
- Tremor
- Skin rash

BUPROPION USE in OTHER PSYCHIATRIC DISORDERS

- Bupropion commonly used for treating ADHD in patients with comorbid substance abuse (off label use)
- Bupropion for smoking cessation found to be well tolerated in patients with schizophrenia who are stabilized on an adequate antipsychotic regime.
- With bipolar disorder, bupropion suggested to have lower risk of activation of hypomanic state relative to other antidepressants. Consider using a lower dose (150 mg) in selected cases. Monitor closely.

BUPROPION SR: SUMMARY

ADVANTAGES
- Oral dosing is simple and associated with fewer adherence problems
- Might delay weight gain
- Bupropion might be beneficial in patients with depression
- Can be used in combination with NRT agents
- Relatively inexpensive

DISADVANTAGES
- Seizure risk is increased
- Several contraindications and precautions preclude use in some patients
- Patients should be monitored for neuropsychiatric symptoms

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 (~90%) after oral administration; not affected by food

Metabolism
- Undergoes minimal metabolism

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

Half-life
- 24 hours
**VARENICLINE: WARNINGS and PRECAUTIONS**

- Neuropsychiatric symptoms and suicide risk
  - Changes in mood (including depression and mania)
  - Psychosis/hallucinations/paranoia/delusions
  - Homicidal ideation
  - Aggression/hostility/anxiety/panic
  - Suicidal ideation, suicide attempt, completed suicide

Advising patients to stop taking varenicline and contact a health care provider immediately if symptoms such as agitation, depressed mood, or changes in behavior or thinking that are not typical are observed or if the patient develops suicidal ideation or suicidal behavior.

**FDA boxed warning removed Dec 2016**

**VARENICLINE: WARNINGS and PRECAUTIONS (cont’d)**

In some patients, use of varenicline has been associated with:
- Seizures
- Enhanced effects of alcohol
- Accidental injury
- Cardiovascular events
- Somnambulism
- Angioedema and hypersensitivity reactions
- Serious skin reactions

These are rare events and most have not been causally linked to varenicline use.

**VARENCLINE: STANDARD 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>Initial dose titration</th>
<th>Treatment Day</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 1 to day 3</td>
<td>0.5 mg qd</td>
<td></td>
</tr>
<tr>
<td>Day 4 to day 7</td>
<td>0.5 mg bid</td>
<td></td>
</tr>
<tr>
<td>Day 8 to end of treatment*</td>
<td>1 mg bid</td>
<td></td>
</tr>
</tbody>
</table>

* Up to 12 weeks

**VARENICLINE QUIT APPROACHES**

**FIXED QUIT approach**
- Set quit date for 1 week after starting varenicline
- Continue treatment for 12 weeks

**FLEXIBLE QUIT approach**
- Start taking varenicline and pick a quit date between 8 to 35 days from treatment initiation
- Continue treatment for 12 weeks

**GRADUAL QUIT approach**
- Start taking varenicline and reduce smoking by 50% within the first 4 weeks, an additional 50% in the next 4 weeks, and continue until complete abstinence by 12 weeks

Images from: https://www.pfizerpro.com/products/tenax/tenax-quit-approaches

**VARENICLINE: ADVERSE EFFECTS**

Common adverse effects include the following:
- Nausea
- Insomnia
- Abnormal dreams
- Headache

Less common adverse effects:
- Gastrointestinal (flatulence, constipation)
- Taste alteration

**VARENICLINE: ADDITIONAL PATIENT EDUCATION**

- Doses should be taken after eating, with a full glass of water
- Nausea and insomnia are usually temporary side effects
  - If symptoms persist, notify your health care provider
- May experience vivid, unusual or strange dreams during treatment
- Use caution driving, drinking alcohol, and operating machinery until effects of quitting smoking with varenicline are known

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Varenicline: Summary

Advantages
- Oral dosing is simple and associated with fewer adherence problems
- Offers a different mechanism of action for persons who have failed other agents
- Most effective agent for cessation when used as monotherapy

Disadvantages
- Cost of treatment
- Patients should be monitored for potential neuropsychiatric symptoms

Varenicline and Bupropion SR: Safety

The "EAGLES study": FDA-mandated clinical trial
- 8,144 participants (4,116 with a psychiatric disorder)
- 140 multinational centers
- 24-week, double-blind; active and placebo-controlled:
  - Varenicline: standard dosing, 12 wks
  - Bupropion SR: standard dosing, 12 wks
  - Nicotine patch: 21 mg/day with standard taper, 12 wks
  - Placebo: 12 wks
- All arms: 13 counseling visits, 11 telephone calls
- Follow-up through 24 wks; outcome = continuous abstinence

The "EAGLES" Study: Safety Data

Incidence of Moderate or Severe Neuropsychiatric Adverse Events

<table>
<thead>
<tr>
<th>Patient cohort</th>
<th>Varenicline</th>
<th>Bupropion SR</th>
<th>Nicotine patch</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-psychiatric</td>
<td>1.3%</td>
<td>2.2%</td>
<td>2.5%</td>
<td>2.4%</td>
</tr>
<tr>
<td>Psychiatric</td>
<td>6.5%</td>
<td>6.7%</td>
<td>5.2%</td>
<td>4.9%</td>
</tr>
</tbody>
</table>

No significant differences in neuropsychiatric events by treatment arm

The "EAGLES" Study: Efficacy Data (Weeks 9-24)

Continuous abstinence

<table>
<thead>
<tr>
<th>Patient cohort</th>
<th>Varenicline</th>
<th>Bupropion SR</th>
<th>Nicotine patch</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-psychiatric</td>
<td>25.5%</td>
<td>18.8%</td>
<td>18.5%</td>
<td>10.5%</td>
</tr>
<tr>
<td>Psychiatric</td>
<td>18.3%</td>
<td>13.7%</td>
<td>13.0%</td>
<td>8.3%</td>
</tr>
</tbody>
</table>

Highest efficacy with varenicline
**COMBINATION PHARMACOTHERAPY**

Combination NRT [first-line, recommended treatment approach]

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

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

**Other combinations [evidence less compelling]**

- Bupropion + NRT
- Varenicline + NRT
- Varenicline + Bupropion SR

---

**TREATMENT OPTIONS**

Multiple Treatment Comparison Meta-Analysis

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nicotine gum vs Placebo</td>
<td>1.7 (1.5–1.9)</td>
</tr>
<tr>
<td>Bupropion SR vs Placebo</td>
<td>1.9 (1.6–2.1)</td>
</tr>
<tr>
<td>Nicotine patch vs Placebo</td>
<td>1.9 (1.7–2.1)</td>
</tr>
<tr>
<td>Other NRT vs Placebo</td>
<td>2.0 (1.6–2.4)</td>
</tr>
<tr>
<td>Combination NRT vs Placebo</td>
<td>2.7 (2.1–3.7)</td>
</tr>
<tr>
<td>Varenicline vs Placebo</td>
<td>2.9 (2.6–3.5)</td>
</tr>
</tbody>
</table>

*Includes nicotine nasal spray, lozenge, and inhaler

**Strong evidence that combination NRT and varenicline are more effective than bupropion SR or NRT monotherapy**

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**COMBINATION NRT: TREATMENT REGIMENS**

**Nicotine patch**

Dose: 21 mg/day x 4–6 weeks → 14 mg/day x 2 weeks → 7 mg/day x 2 weeks

**PLUS**

- Nicotine gum or lozenge (2 mg/4 mg; based on TTFC)
  - Dose: Use 1 piece q 1–2 hours as needed
  - and/or

- Nicotine nasal spray (0.5 mg/spray)
  - Dose: Use 1 spray in each nostril q 1–2 hours as needed

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**ESSENTIAL QUESTION for SELECTION of NRT PRODUCT(s)**

“Would it be a challenge for you to take a medication frequently throughout the day (e.g., a minimum of 8 or 9 times)?”

- With the exception of the nicotine patch, all NRT formulations require frequent dosing throughout the day.
- If patient is unable to adhere to the recommended dosing, these products should be ruled out as monotherapy because they will be ineffective.

---

**ADHERENCE IS KEY to QUITTING**

- Promote adherence with prescribed regimen(s)
- Select the correct strength of medication
- Use daily (according to a fixed schedule, NOT as needed)
- Complete the recommended duration of therapy
- Consider telling the patient:
  - “If used correctly, the medicines will make you more comfortable while quitting.”
  - “Medicines work best when taken regularly, to prevent withdrawal symptoms before they occur. If you wait until you’re already craving a cigarette, it will be too late. The medicines don’t work as fast as inhaled nicotine from a cigarette.”

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“Drugs don’t work... in patients who don’t take them.”

*C. Everett Koop, M.D., former U.S. Surgeon General*

Medication adherence should be addressed at each encounter.

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**COMPARATIVE DAILY COSTS**

of PHARMACOTHERAPY

<table>
<thead>
<tr>
<th>Drug</th>
<th>WHAC*</th>
<th>Generic</th>
<th>Average daily cost ($/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gum Lozenge Patch</td>
<td>$5.48</td>
<td>$1.90</td>
<td>$0.00 - $2.00</td>
</tr>
<tr>
<td>Nasal spray</td>
<td>$4.20</td>
<td>$1.99</td>
<td>$2.00 - $4.00</td>
</tr>
<tr>
<td>Inhaler Bupropion SR</td>
<td>$3.49</td>
<td>$1.52</td>
<td>$4.00 - $6.00</td>
</tr>
<tr>
<td>Varenicline</td>
<td>$10.63</td>
<td>$0.72</td>
<td>$6.00 - $8.00</td>
</tr>
<tr>
<td>NRT combination</td>
<td>$18.06</td>
<td>$13.76</td>
<td>$8.00 - $10.00</td>
</tr>
<tr>
<td>Discontinued</td>
<td></td>
<td>$17.72</td>
<td>$10.00 - $12.00</td>
</tr>
</tbody>
</table>

** Discontinued in 2023.

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**SUMMARY**

- To maximize success, interventions should include behavioral counseling and one or more medications.
- Encourage the use of effective medications by all patients attempting to quit smoking.
- Exceptions include medical contraindications or specific populations for which there is insufficient evidence of effectiveness.
- First-line medications that reliably increase long-term smoking cessation rates:
  - Bupropion SR
  - Nicotine replacement therapy (as monotherapy or combination therapy)
  - Varenicline
- Varenicline and combination NRT demonstrate the highest efficacy.

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**RESEARCH on TOBACCO & DEPRESSION**

- Most of the research has been conducted with people with a history of MDD, in free-standing smoking clinics.
  - Greater tobacco abstinence with increased psychological support (Hall et al., 1994; Brown et al., 2001).
  - Individuals with recurrent MDD may be especially helped by CBT—mood management approaches.
  - Individuals with a history of MDD may have more difficulty quitting and more severe withdrawal symptoms than those without MDD.

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**OVERVIEW**

- Tobacco Treatment
  - Smoking Outcomes
  - Co-occurring Disorders
  - Integration
- Tobacco Prevention

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**TREATING SPECIAL POPULATIONS**

**READINESS to QUIT SMOKING**

- No relationship between psychiatric symptom severity and readiness to quit.

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TREATING TOBACCO DEPENDENCE in SMOKERS with DEPRESSION

322 smokers with depression recruited from four outpatient psychiatry clinics

- Stepped Care Intervention
  - Stage-based expert system counseling
  - Nicotine patch
  - 6 session individual counseling

Brief Contact Control

Hall et al. 2006. Am J Public Health

ABSTINENCE RATES by TREATMENT CONDITION

- 7 day prevalence
  - 14% intervention, 12% control at 3 months
  - 18% intervention, 15% control at 6 months
  - 21% intervention, 19% control at 12 months
  - 25% intervention, 25% control at 18 months

p<.05 for group comparison

TREATING SMOKERS with SCHIZOPHRENIA

- Treatments tailored for smokers with schizophrenia no more effective than standard programs (George et al., 2000)
- Atypical antipsychotics associated with greater cessation than typical antipsychotics

TREATMENT of PSYCHIATRIC INPATIENTS

- Using the same model...
  - Tobacco cessation treatment initiated during psychiatric hospitalization
  - 224 patients enrolled
  - Full range of psychiatric diagnoses
  - 79% recruitment rate
  - >80% retention at 18 months
  - 7-day point prevalence tobacco abstinence was higher in intervention (motivational tobacco cessation and NRT) than patients who received usual care
  - NO relationship between psychiatric severity and efficacy

DEPRESSION SEVERITY & TOBACCO TREATMENT OUTCOME

- NO RELATIONSHIP
  - Depression severity, as measured by the Beck Depression Inventory-II, was unrelated to participants' likelihood of quitting smoking
  - Among intervention participants, depression severity was unrelated to their likelihood of accepting cessation counseling and nicotine patch

TWO RCTS of TOBACCO TREATMENT in PATIENTS with SCHIZOPHRENIA

George et al. (2002) - Bupropion vs. Placebo
Evins et al. (2005) - Bupropion vs. Placebo

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VARENICLINE USE with INDIVIDUALS with SCHIZOPHRENIA

- Evins et al. (2008): Open-label case series reported 13 of 19 patients (68%) with schizophrenia quit smoking at the end of treatment
- Evins et al. (2014): Open-label trial of varenicline and CBT vs. placebo and CBT
  - 60% abstinence from tobacco for ≥7 days in varenicline group vs. 19% in placebo after 40 weeks

DOES ABSTINENCE from TOBACCO CAUSE RECURRENT of PSYCHIATRIC DISORDERS?

- Case studies suggesting MDE recurrence after quitting smoking among those with a history of depression
- Glassman, 2001: MDE recurrence in 6% (n=2) of those smoking vs. 31% (n=13) of those abstinent
  - Differential loss to follow-up: 5% (n= 2/44) of quitters missing vs. 39% (n= 22/56) of continued smokers
- Tsoh, 2001: N=308, no difference in rate of MDE among abstinent vs. smoking participants
  - Difference in rate of MDE by depression history: 10% among those with no MDD history vs. 24% if MDD+ history

Depression is a remitting and relapsing disorder

MENTAL HEALTH OUTCOMES: SMOKERS WITH DEPRESSION TREATED for TOBACCO

- Among depressed patients who quit smoking:
  - No increase in suicidality
    - Quit: 0% vs Smoking: 1-4%
  - No increase in psych hospitalization
    - Quit: 0-1% vs Smoking: 2-3%
  - Comparable improvement in % of days with emotional problems
  - No difference in use of marijuana, stimulants or opiates
  - Less alcohol use among those who quit smoking

TOBACCO CESSATION & SCHIZOPHRENIA SYMPTOMS

- Tobacco abstinence (1-wk) not associated with worsening of:
  - Attention, verbal learning/memory, working memory, or executive function/inhibition, or clinical symptoms of schizophrenia (Evins et al., 2005)
- Bupropion: decreased the negative symptoms of schizophrenia (Evins et al. 2005, George et al. 2002)
- Varenicline: no worsening of clinical symptoms and a trend toward improved cognitive function (Evins et al., 2009)

INTEGRATING TOBACCO TREATMENT within PTSD SERVICES

- RCT with 66 clients from VA Medical Center
- Integrated care (IC)
  - Manualized treatment delivered by PTSD clinician and case manager (3-hr training)
  - Behavioral counseling once a week for 5 weeks + 1 follow-up
  - Bupropion, nicotine patch, gum, spray
- Usual care (UC): referral to VA smoking cessation clinic

INTEGRATING TOBACCO TREATMENT within PTSD SERVICES

- Cessation Medication Use
  - Integrated Intervention: 94%
  - Usual Care: 64%
- Counseling Sessions Attended
  - Integrated Intervention: M=5.5
  - Usual Care: M=2.6
- At all assessments, the odds of abstinence were 5 times greater for integrated care vs. usual care

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### SUMMARY: TOBACCO TREATMENT in PSYCHIATRIC PATIENTS

- In general, currently available interventions show effectiveness
- Wide range of abstinence rates, with unknown determinants
- Evidence of deleterious effect on psychiatric symptoms or recurrence is weak
- Integration into mental health treatment settings increases abstinence rates

### TOBACCO CESSATION DURING ADDICTIONS TREATMENT or RECOVERY

- Meta-analysis of 19 trials
  - 12 in treatment; 7 in recovery
- Findings: Tobacco Cessation
  - In Treatment Studies: Post treatment abstinence rates were intervention=12% vs. control=3%
  - In Recovery Studies: Post treatment abstinence rates were intervention=38% vs. control=22%
  - No significant effect for tobacco cessation at long-term follow-up (> 6 months)

### SUMMARY: TOBACCO TREATMENT for SUBSTANCE ABUSING PATIENTS

- In general, currently available interventions show some effectiveness, at least for the short-term
- Range of abstinence rates, with unknown determinants
- Weak evidence of deleterious effect on abstinence from illicit drugs and alcohol
- Disorder specific data may eventually allow better tailoring of treatments

### DOES ABSTINENCE from TOBACCO CAUSE RELAPSE to ALCOHOL and ILLICIT DRUGS?

- At > 6 months follow-up, tobacco treatment with individuals in addictions treatment was associated with a 25% increased abstinence from alcohol and illicit drugs (Prochaska et al., 2004).

  **Caveat:** One well done study (N=499) of concurrent versus delayed treatment reported (Joseph et al., 2004):
  - Comparable smoking abstinence rates at 18 months (12.4% versus 13.7%)
  - Lower 6-month prolonged alcohol abstinence rates among those offered concurrent compared to delayed tobacco cessation treatment; NS at 12 and 18-months

### PREVENTION

- Problem of identification and developmental sequence, with a few exceptions:
  - ADHD
    - ADHD diagnosed prior to initiation of smoking
    - Smoking rates 2 to 3 times higher for adolescents with vs. without ADHD
    - Adults with childhood history of ADHD may have more difficulty in quitting smoking (Humfleet et al., 2005)
  - Children of parents with addiction problems
    - Sons more likely to be recent smokers than the general population (Schukit et al. 2004)

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PREVENTION

- Drug Abuse Treatment Settings
  - Prospective study, N=649
    - At 12-month follow-up, 13% of the 395 baseline smokers reported quitting smoking and 12% of the 254 baseline nonsmokers reported starting/relapsing to smoking

Kohn et al. (2003) Drug Alc Dep

“Those who deliver mental health care often pride themselves on treating the whole patient, on seeing the big picture, and on not being bound by financial irrationality or by the biases of their culture; yet many fail to treat nicotine dependence. They forget that when their patient dies of a smoking-related disease, their patient has died of a psychiatric illness they failed to treat.”

- John Hughes 1997