Treatment of Nicotine Addiction in Primary Care

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Disclosure

- Speakers Bureau Reckitt Benckiser
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Objectives

- Definitions
- Epidemiology
- Public Health & Policies
- Intervention Strategies
- Role of the Physician
- Outlook
DEFINITIONS
Definitions

- Addiction is a primary, chronic, neurobiological disease, with genetic, psychosocial, and environmental factors influencing the development and manifestations.
- It is characterized by behaviors that include one or more of the following:
  - impaired control over drug use
  - compulsive use
  - continued use despite harm
  - craving

American Society of Addiction Medicine, 2001
Updated Definition

- Addiction is a primary, chronic disease of brain reward, motivation, memory and related circuitry.
- Dysfunction in these circuits leads to characteristic biological, psychological, social and spiritual manifestations.
- This is reflected in an individual pathologically pursuing reward and/or relief by substance use and other behaviors.
Is Nicotine Addictive?

- Of primary importance to its addictive nature are findings that nicotine activates reward pathways—the brain circuitry that regulates feelings of pleasure.

- A key brain chemical involved in mediating the desire to consume drugs is the neurotransmitter dopamine, and research has shown that nicotine increases levels of dopamine in the reward circuits.
Is Nicotine Addictive?

- This reaction is similar to that seen with other drugs of abuse and is thought to underlie the pleasurable sensations experienced by many smokers.

- For many tobacco users, long-term brain changes induced by continued nicotine exposure result in addiction.
Is Nicotine Addictive?

- Cigarette smoking triggers marked decrease in the levels of monoamine oxidase (MAO), an important enzyme that is responsible for the breakdown of dopamine.
- Nicotine itself does not dramatically alter MAO levels.
- The decrease in two forms of MAO (A and B) results in higher dopamine levels and may be another reason that smokers continue to smoke—to sustain the high dopamine levels that lead to the desire for repeated drug use.
Is Nicotine Addictive?

- Cigarette smoking produces a rapid distribution of nicotine to the brain, with drug levels peaking within 10 seconds of inhalation.
- Acute effects of nicotine dissipate quickly, as do the associated feelings of reward, which causes the smoker to continue dosing to maintain the drug’s pleasurable effects and prevent withdrawal.
Is Nicotine Addictive?

- Nicotine withdrawal symptoms include irritability, craving, depression, anxiety, cognitive and attention deficits, sleep disturbances, and increased appetite.
- Symptoms may begin within a few hours after the last cigarette, quickly driving people back to tobacco use.
- Symptoms peak within the first few days of smoking cessation and usually subside within a few weeks. For some people, however, symptoms may persist for months.
Is Nicotine Addictive?

- Behavioral factors can also affect the severity of withdrawal symptoms.
- For some people, the feel, smell, and sight of a cigarette and the ritual of obtaining, handling, lighting, and smoking the cigarette are all associated with the pleasurable effects of smoking and can make withdrawal or craving worse.
Aspects of Nicotine Addiction

Social

Behavioral

Psychological

Physical/Biochemical

Nicotine Dependence

"Don't you know how bad those things are for you?"
Epidemiology
How Prevalent Is The Problem?

• Tobacco use, primarily cigarette smoking, is the leading cause of preventable morbidity and mortality in the United States.

• Tobacco use kills approximately 440,000 Americans every year.

• One in every five U.S. deaths.

• 70.9 million Americans aged 12 or older reported current use of tobacco.
Pregnancy

- Smoking has adverse effects on unborn child
- 20-30% of smoking women quit in pregnancy
- Smoking cessation programmes are effective
- NRT is assumed to be safe
- Bupropion and varenicline are contra-indicated

- Post-partum follow up reduces the 70% relapse rate

Pregnancy is often a trigger for quitting

Adolescent Smoking

- Nearly all smokers begin as adolescents
- 75% become daily smokers by 20 y.o.
- Higher daily consumption, lower quit rate
- Female > Male

Affective and Cognitive Components

- Vulnerable subset: loss of autonomy with a few cigs
  also - greater withdrawal problems
- Relationship to maternal smoking during pregnancy?
Adolescents

- Address the issues that matter to the teenager
- Brief interventions are likely to be effective
- Pharmacotherapies are not licensed in teenagers

Teenagers care about the immediate benefits to their appearance, well being and financial status rather more than future health gains

Mental health

• Psychotic disorders are associated with three times the risk being a heavy smokers (35% vs 9%)
• Smoking may alleviate symptoms of psychosis
• Smoking and depression are related
• The antidepressants, bupropion and nortriptyline are effective in assisting smoking cessation
• Bupropion interacts with other antidepressants

People with mental health problems are more likely to smoke than those without mental illness
Intervention Strategies
I TOLD YOU
CIGARS WERE
BAD FOR YOU!
The cycle of change

Ambivalent to cessation

- Move them closer to a cessation attempt
- Understand how you can help

Be a positive partner
Let them describe their doubts – and fear of failing
Identify how to plan a quit attempt
Offer the ongoing medical support

Adapted from Prochaska JO, DiClemente CC. J Consult Clin Psychol 1983; 51
The cycle of change

Ready to make a cessation attempt

- Provide support for a quit attempt

Be supportive and enthusiastic!
Give time to planning the attempt
Set a quit date
Discuss problems of withdrawal

Adapted from Prochaska JO, DiClemente CC. J Consult Clin Psychol 1983; 51
The cycle of change

Action! a cessation attempt

- Be available to support the quit attempt

Congratulate!
Arrange review (even if relapse)

Adapted from Prochaska JO, DiClemente CC. J Consult Clin Psychol 1983; 51
Behavioral Interventions

- Self-help materials
- Brief Advice
- Counseling
- Exercise
Self-Help Materials

• Appear to increase long-term abstinence ~1.5-fold relative to no intervention\textsuperscript{1}
• May be tailored to individual or type
• Should be available in office and provided to all smokers

Source: \textsuperscript{1}Lancaster T, Stead LF. *Cochrane Database Syst Rev.* 2005(3):CD001118.
Brief Advice (<3 Min)

- May be offered by clinician or nurse
- Should include firm quit recommendation and call attention to health outcomes and practical issues
- Increases odds of quitting ~1.7-fold compared to no advice\(^1\)
- Absolute benefit appears greater for motivated patients

Individual Counseling

- Improves quit rates for adults\(^1\)
- Recommended by US Public Health Service for adolescents
- May be more effective than team-based counseling\(^2\)
- When possible, should be >10 minutes, face-to-face, with trained specialist\(^3\)

Sources:  
Elements of a Counseling Intervention

- Discuss previous quit experiences
- Anticipate challenges
- Assess patient’s household environment
- Provide patient with options for dealing with nicotine withdrawal
- Suggest abstaining from alcohol during quit attempt
"Gasp! - New nicotine patch...New nicotine patch..."
Pharmacotherapy

Pharmacotherapy + behavioural counselling improves long-term quit rates

Smokers of 10 or more cigarettes a day who are ready to stop should be encouraged to use pharmacological support as a cessation aid

Aveyard P, West R. Managing smoking cessation. BMJ 2007;335;37-41
Nicotine replacement

- Begin NRT on the quit date, (apply patches the night before)
- Use a dose that controls the withdrawal symptoms
- NRT provides levels of nicotine well below smoking
- Prescribe in blocks of two weeks
- Arrange follow up to provide support
- Use a full dose for 6 to 8 weeks then stop
  or reduce the dose gradually over 4 weeks.

NRT increases the odds of quitting about 1.5 to 2 fold

NRT: Nicotine patches

- Patches provide a slow, consistent release of nicotine throughout the day
- Available in various shapes and sizes,
- Common side effects with patches include skin sensitivity and irritation

NRT increases the odds of quitting about 1.5 to 2 fold

NRT: Nicotine nasal spray

- Nasal sprays more closely mimic nicotine from cigarettes
- Common side effects with nasal sprays include nasal and throat irritation, coughing and oral burning

NRT increases the odds of quitting about 1.5 to 2 fold

NRT: Nicotine gum

- Instruct the patient to ‘chew and park’
- Absorption may be impaired by coffee and some acidic drinks
- Common side effects with gum include gastrointestinal disturbances and jaw pain
- Dentures may be a problem!

NRT increases the odds of quitting about 1.5 to 2 fold

NRT: Nicotine lozenges

- Nicotine tablets deliver 2-mg or 4-mg dosages of nicotine over 30-minutes
- Common side effects with gum include burning sensations in the mouth, sore throat, coughing, dry lips, and mouth ulcers

NRT increases the odds of quitting about 1.5 to 2 fold

**Bupropion**

- Begin bupropion a week before the quit date
- Normal dose 150mg bd, (reduce in elderly, liver/renal disease)
- Contra-indicated in patients with epilepsy, anorexia nervosa, bulimia, bipolar disorder or severe liver disease.
- The most common side effects are insomnia (up to 30%), dry mouth (10-15%), headache (10%), nausea (10%), constipation (10%), and agitation (5-10%)
- Interaction with antidepressants, antipsychotics and anti-arrhythmics

Bupropion increases the odds of quitting about 2 fold

Nortryptiline

- Tri-cyclic antidepressant
- Not licensed for smoking cessation
- Low cost
- Side-effects include sedation, dry mouth, light-headedness, cardiac arrhythmia
- Contra-indicated after recent myocardial infarction

Nortryptiline increases the odds of quitting about 2 fold

Varenicline

• Begin varenicline a week before the quit date, increasing dose gradually.
• Alleviates withdrawal symptoms, reduces urge to smoke
• Common side effects include: nausea (30%), insomnia, (14%), abnormal dreams (13%), headache (13%), constipation (9%), gas (6%) and vomiting (5%).
• Contra-indicated in pregnancy
• New drug

Varenicline increases the odds of quitting about 2.5 fold

SIDE EFFECTS

- Neuropsychiatric side effects with varenicline were first publicly reported by the Food and Drug Administration (FDA) on November 20, 2007.

- In a public health advisory issued on February 1, 2008, the agency stated, “As FDA's review of the data has progressed it has become increasingly likely that the severe changes in mood and behavior may be related to Chantix.”

Side Effects

- On June 16, 2011, the FDA issued a safety announcement that Chantix may be associated with a "a small, increased risk of certain cardiovascular adverse events in patients who have cardiovascular disease."

- On July 4, 2011, four scientists published a review of double-blind studies stating that the use of varenicline carries an increased risk of serious adverse cardiovascular events compared with placebo.

"FDA Drug Safety Communication: Chantix (varenicline) may increase the risk of certain cardiovascular adverse events in patients with cardiovascular disease". 06/16/2011

Changing Morbidity
Cardiovascular Diseases
HIV Disease: Changing Paradigm

- Reduced mortality

- Chronic disease
  - PLWH/AIDS living longer, healthier and more productive lives

- Changing morbidity/mortality
  - Cancer, CVD, diabetes, liver disease, etc.
Myocardial infarction Among Patients with HIV Infection

Holmberg et al. Trends in rates of myocardial infarction among patients with HIV
Acute Myocardial Infarction
NY: Discharges among PLWHA

Source: SPARCS database, NYSDOH
“Cigarette smoking is the most important modifiable cardiovascular risk factor among HIV-infected patients.”

“Cessation of smoking is more likely to reduce cardiovascular risk than either the choice of antiretroviral therapy or the use of any lipid-lowering therapy.”

Women: Cigarette Smoking and HIV Prognosis in the HAART Era

Cumulative percentage remaining free from an AIDS-defining condition, by smoking status before HAART initiation

Impact of Cigarette Smoking on Mortality and QOL Among PLWHA

- 867 HIV+ from Veterans Aging Cohort 3 Site Study
- 63% current smokers, 22% former smokers
- Current smokers had highest VL (compared to former or never smokers. p=.001)
- Smoking was strongly associated with increased respiratory symptoms (cough, dyspnea), noninfectious pulmonary disease (COPD &/or asthma), and bacterial pneumonia

Impact of Cigarette Smoking on Mortality

After adjusting for age, race/ethnicity, baseline CD4 cell count, VL, hemoglobin, illegal drug/alcohol use, mortality was significantly increased in current smokers compared with never smokers (hazard ratio [HR] 1.99, 95% CI 1.03 to 3.86).

Cigarette Smoking and Quality Of Live (QOL)

Human Immunodeficiency Virus Infection, AIDS, and Smoking Cessation: The Time is Now

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Treatments for persons who are infected with human immunodeficiency virus (HIV) or who have developed AIDS have advanced to the point where death is no longer the inevitable outcome of diagnosis. Combination antiretroviral therapy has made HIV infection less of a terminal condition and more of a medically manageable chronic disease. Thus, efforts to improve the health status and quality of life of HIV-infected persons have become one of the highest treatment priorities for the next decade. Cigarette smoking is highly prevalent among HIV-infected persons, and quitting smoking would greatly improve the health status of these individuals. However, to date, no studies have evaluated the efficacy of a smoking-cessation intervention specifically tailored to this population. This article reviews the evidence and rationale for advancing smoking-cessation treatments specifically tailored to the needs of HIV-infected persons and provides recommendations for future treatment studies.
How Serious is the Problem?

- Prevalence of smoking among people with HIV --- estimated to be **higher** than among the general population
- New England clinics: More than 70% of HIV+ smoke
- Swiss HIV Cohort Study
  - 72% are current/former smokers
  - 96% among IDUs


Smoking And Mental Health
Serious Mental Illness

Reduced Cessation
- Schizophrenia/Schizoaffective disorder
- Bipolar disorder
- PTSD
- Alcohol use disorder
Smoking and Schizophrenia

- High prevalence of smoking (about 90%, OR = 5.9)
- Highly nicotine dependent (FTND = 7 or higher)
- Nicotine produces cognitive or other benefit
- Smoking ameliorates medication side effects (e.g., lower rates of neuroleptic-induced Parkinsonism)
Smoking and Schizophrenia (Continued)

- Smokers with schizophrenia take in more nicotine per cigarette than smokers without this disorder.
- Higher levels of positive symptoms and decreased negative symptoms.
- Ad libitum smoking increases after initiation of haloperidol.
- SCZ tend to smoke less on clozapine.
Smoking & Bipolar Disorder

- High prevalence of smoking: 61-80%
- Findings are inconsistent regarding the prevalence of smoking between bipolar disorder with and without psychotic features
- Bupropion is contraindicated
- Quit rates are comparable to general population and durable
- Quit rates enhanced with CBT
Smoking and Depression

- The prevalence of smoking: 37-60%
- Leads to more severe nicotine withdrawal symptoms
  - High risk for relapse in first week
  - Female > Male
- **30% risk of relapse to MDE after quitting if past history present**
- Depressed smokers have higher suicide rates than depressed nonsmokers
  (Bruce, 1994; Lohr, 1992; Yassa, 1987)
Smoking and Depression (Continued)

- NRT alone insufficient treatment for smokers with current and/or past MDD
- Combining NRT with non-NRT pharmacotherapy appear to be promising for smokers with depression (Ait-Daoud et al., 2006)
- CBT that emphasizes group cohesion and social support appears to be particularly effective for depressed smokers with or without alcohol dependence
Smoking and Anxiety

- The prevalence of smoking: About 35-50%
- Smokers have greater anxiety and panic symptoms than non-smokers
- Heavy smoking in adolescent is associated with higher risk of developing Agoraphobia, GAD, and Panic Disorder
- PTSD:
  - Increased risk for relapse in first two weeks of quit attempt
  - Increased the risk of smoking and nicotine dependence
  - lower rates for quitting smoking & remission from nicotine dependence
  - Stopping smoking not associated with worsening of PTSD
  - Bupropion tolerated and effective treatment
SSRIs and Smokers with Anxiety Disorder

- No benefit for smoking cessation
- Can reduce likelihood of emergent anxiety and panic during quit attempt
- Bupropion is not appropriate as only medication
- Can be combined with NRT/Bupropion
- Can be combined with varnicline
Smoking and Alcohol Dependence

- High prevalence of smoking: 80-95%
- Two studies reporting similar outcomes of NRT in alcoholics compared with non-alcoholics (e.g., Grant et al., Alcohol, 2007)
- Tobacco dependence treatment does not cause abstinent alcoholics to relapse (Hughes & Callas, 2003)
- Smoking cessation reduces the risk of alcohol relapse (Sobell et al., 1995)
Smoking and Alcohol Dependence (Continued)

- Bupropion added to nicotine patch did not improve smoking outcomes
- Topiramate group was significantly more likely to become abstinent (OR = 4.46) compared with placebo group (Johnson et al., 2003)
- Topiramate group reported more weight loss compared with placebo group (44% vs. 18%)
Benefits of Treating Tobacco Dependence in Mental Healthcare Settings

- Emerging evidence shows that morbidity is reduced
- May enhance abstinence from other substances
- Reduced financial burden
- Increased self-confidence
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Summary

- Smoking cessation confers numerous well-established health benefits.
- Physicians should initially assess a smoker’s degree of nicotine addiction.
- A proactive intervention strategy that includes counseling and/or pharmacotherapy should be tailored to the patient.
- Physicians must individualize and personalize therapy and debunk smoking myths.
- Relapse is common among smokers who try to quit.
“If smoking relaxes you, then don’t quit. Being dead is very relaxing.”
Conclusions

- Tobacco use is a major public health threat.
- Pharmacotherapy works and is relatively safe
- Many options now available
- Expectation Management important.
- Be patient and compassionate.
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