Tobacco Dependence as a Chronic Disease

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Disclosure

• I conducted Tobacco Treatment seminars at Pfizer-sponsored conferences in Brazil, Chile and Mexico
• I did not receive any direct honorarium from Pfizer or Mayo Clinic
• Pfizer reimbursed Mayo Clinic for my services
Objectives

1. Discuss current prevalence of tobacco use
2. Describe the rationale of treating tobacco dependence as a chronic disease
3. Describe the relationship of tobacco use to cardiovascular disease, chronic lung disease, and cancer
4. Discuss the USPHS Clinical Practice Guideline 2008 Update; recommendations for smoking cessation

Everybody knows smoking is bad, well how bad is it?
The Cigarette Death Epidemic in Perspective-USA

Tobacco Deaths

- Tobacco is the only consumer product proven to kill more than half of its regular users
- 443,000 deaths annually in USA
- 5 million deaths worldwide every year
  - ½ of these deaths in developing world (China, India)
  - ½ in industrialized countries
Scenarios for future deaths from tobacco

Source: Peto et al

Scenarios: Impact of Treatment

Source: Peto et al
Future Tobacco Deaths
By 2025

• 10 million deaths every year
• 7 million in developing world – Asia
• Will eventually kill 650 million smokers – 10% of current world population

Worldwide toll of cigarettes

• 80% of deaths in developing countries—(i.e. China and India)
• China has more than 300 million smokers
  – Largest worldwide population of male smokers (65% Chinese males)
• India 110 million smokers
• USA 50 million (largest female population of smokers in the world)
USA prevalence of smoking
CDC data (2009)

- U.S. adults >age 18—20.6%
- Males —23.5%
- Females -17.9%
- Persons below federal poverty level 31.1%
- Education level:
  - no high school diploma 28.5%
  - Graduate degree 5.6%
  - (ref: MMWR –Sept. 7,2010)

Prevalence by age group

- Age: 18-24   men 28%   women 15.6%
- Age 25-44   men 26.5%  women 21.5%
- Age 45-64   men 24.5%  women 19.5%
- Age >65     men 9.5%   women 9.5%
Regional differences

- Midwest 23.1%
- South 21.8%
- West 16.4%
- Highest prevalence: Kentucky 25.7% and West Virginia 25.6%; Oklahoma 25.5%
- Lowest Utah 9.8%; California 12.9%; Massachusetts 15%
- New York 18.1%

Prevalence of adult cigarette smoking by state –2009

ref: MMWR Sept. 10, 2010
Ethnic groups

- Asians 12%
- Hispanics 14.5%
- Non-Hispanic blacks 21.3%
- Non-Hispanic white 22.1%
- Multiracial 29.5%
- American Indians/Alaska natives 23.2%

Trends

- California prevalence declined 40% between 1998-2006 → lung cancer incidence in California declined 4 X faster than rest of USA
- Maine, New York, and Washington 45-60% reduction in youth smoking with comprehensive statewide programs
Prevalence of smoking–Health Professionals
(survey of 2,804 health professionals)
• Nurses 13%
• Primary Care physicians: 1.7%
• Emergency Med physicians: 5.7%
• Psychiatry 3.2%
• Dentists 5.8%; Dental hygienist 5.3%
  • Ref: (E.K. Tong et el;NTR volu 12, no. 7 , July, 2010)

Cigarettes
• Tobacco smoke – complex mixture of 4,000 chemicals with over 60 known carcinogens
• Cigarette smoking – responsible for 1 in 5 deaths in USA (>400,000 deaths/year)
• 1965 to 2009 – Decline in adult smoking rate, 41% to 20.6% (MMWR; Sept. 7, 2010)
• Recent decrease in youth smoking
• 2005- Lowest consumption of cigarettes in USA in 50 years
• BUT—no further decrease since 2005!!
Chronic Disease Rationale

- Tobacco Dependence should be considered a chronic disease similar to Diabetes and Hypertension (USPHS guidelines 2000)
- Smoker goes through “process of quitting”
  - Stages of pre contemplation, contemplation
- Associated with frequent lapses, relapses

Stages of Change-Prochasky

- Pre contemplation=no serious consideration of quitting
- Contemplation=planning to quit in near future
- Preparation=quit date set
- Action=recently quit
- Maintenance=quit > 6 months
Rationale

- Clinicians should address this problem with each patient visit as with other medical problems
- Patients should be educated to understand smoking cessation is a process and the risk of relapse is lifelong
- May be similar to Alcoholic Anonymous framework.

Cigarettes and Tobacco Dependence

- Cigarette smoke – complex mixture of 4,000 chemicals with over 60 known carcinogens
- Most efficient delivery device for nicotine that exists-better than intravenous
- Cigarette manufacturers have modified cigarettes to maximize nicotine delivery to the brain. (pH change)
- High doses of arterial nicotine cause upregulation of the nicotinic acetylcholine receptors
- Genetic factors influence tobacco dependence
- Left untreated 60% of smokers die from a tobacco-caused disease

Hurt RD, Robertson CR JAMA 280:1173, 1998
438,000 Deaths Attributable to Cigarette Smoking
United States

- Leading cause of death in the USA
- Most of decline in incidence is because of ↓ smoking rate
- ~100,000 CVD deaths due to smoking and >35% occur before age 65
- 2-6X ↑ risk of sudden death in smokers
- Over 1.6 million coronary procedures/year
Smoking Effects on Cardiovascular System

- **Cigarette Smoking & Vascular Events**
  - Hypercoagulability
  - Increased myocardial work
  - CO effects
  - Catecholamine release
  - Vasoconstriction

- **Cigarette Smoking & Atherosclerosis**
  - Lipids
  - Endothelial Function
  - Oxidant Injury
  - Thrombosis
  - Blood viscosity

Cardiovascular Disease Related to Cigarette Smoking

- Coronary Artery Disease
- Sudden Death
- Stroke
- Atherosclerotic Vascular Disease
- Abdominal Aortic Aneurysms

US SURGEON GENERAL’S REPORT: 2004

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Sudden Cardiac Death in CAD Patients

- 3122 patients with known CAD and moderate hypercholesterolemia
- 8.2 years mean follow-up
- 12% current smokers, 58% ex-smokers, 30% nonsmokers
- Current smokers ↑ risk of sudden cardiac death (RR 2.47; 95% CI 1.46-4.19)
- Ex-smokers not different than nonsmokers for SCD (RR 1.06; 95% CI 0.70-1.62)


INTERHEART: Odds of MI according to number of cigarettes smoked

Lancet. 2004;364:937-52
Leading Causes of Death in USA
1970-2002

Figure 1. Trends in Age-Standardized Death Rates for the 6 Leading Causes of Death in the United States, 1970-2002

Jemal, A et al, JAMA 294:1255, 2005
Respiratory Diseases Related to Cigarette Smoking

- COPD
- Acute respiratory disease
- Reduced lung function in infants
- Cough, phlegm, wheezing, dyspnea
- Poor asthma control
- Premature onset and accelerated age-related decline in lung function

Emphysema

Normal

US SURGEON GENERAL’S REPORT: 2004
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COPD
Chronic Obstructive Pulmonary Disease

- 3rd leading cause of death in USA
  - 80% of COPD deaths due to smoking
  - Death rate for COPD 10 times higher among current smokers

- 3 types:
  Chronic bronchitis, Emphysema, Asthma
  - Decreased airflow
  - Reduced ability to bring oxygen to the body
  - Shortness of breath
  - Can lead to disability and death

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Smoking: Asthma Severity

- Compared with Never Smokers and Ex-smokers, Current Smokers reported
  - Significantly more attacks of breathlessness
  - Significantly higher severity scores

\[ \text{Severity Score}^c \]

<table>
<thead>
<tr>
<th></th>
<th>Never Smokers</th>
<th>Ex-smokers</th>
<th>Current Smokers</th>
</tr>
</thead>
<tbody>
<tr>
<td>At rest in the last 12 months.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Relationship between attacks of breathlessness</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severity score for asthma was established using an a priori decisional tree.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strength of the relationship between severity score and smoking. The 3 classes were coded 1, 2, and 3 for quantitative analysis. Severity score was adjusted for age, sex, and educational level.</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


FEV1, Smoking, and Stopping Smoking

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Smoking and Tuberculosis

- Smoking is a risk factor for the development of pulmonary TB

<table>
<thead>
<tr>
<th>Nonsmokers</th>
<th>Current Smokers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Odds Ratio (95% CI)</td>
<td></td>
</tr>
</tbody>
</table>

*The ratio of the odds of development of disease in exposed persons to the odds of development of disease in nonexposed persons. Crude OR was adjusted for age. To minimize the effect of other confounders the study population was restricted to men aged 20 to 50 years only.

TB=tuberculosis.


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Tobacco Smoke: Role in Carcinogenesis

Carcinogenicity of Tobacco Smoke

- Tobacco smoke contains more than 4000 chemicals
- More than 60 carcinogens are in cigarette smoke

**Tobacco Smoke Constituents**

- Arsenic
- Benzene
- Benzo[a]pyrene
- Cadmium
- Chromium VI
- Cresol
- Formaldehyde
- Lead
- Nitrosamines
- Phenol
- Polonium 210
- Polycyclic aromatic hydrocarbons
- Vinyl chloride

**Medical Complications of Tobacco**

- Cigarette smoking – 30% of all cancer deaths (>180,000 in 2005)
- Risk of cancer death 2 x higher in smokers and 4 x higher in heavy smokers
- Smoking causally linked to cancers of lung, larynx, oral cavity, esophagus, pancreas, bladder, kidney, stomach, and uterine cervix
Smoking and Lung Cancer

Lung Cancer

• Leading cause of cancer death in men and women in USA. About 15% of smokers will develop lung cancer
• 2008 – 215,000 new cases and 161,800 deaths
• Smoking causes 90% of lung cancers and increases risks of all four major cell types.
• Cigar and pipe smoking associated with increased risk
• 5-year survival for non-SCLC is 15%. Varies with race and gender.
• Reduced risk with stopping smoking
Lung Cancer: Leading Cause of Cancer Death in Women

Annual Age-adjusted Cancer Death Rates among Males for Selected Cancers, U.S. 1930-2005

Risk of Lung Cancer

- Current smokers have a higher risk of developing lung cancer than ex-smokers or nonsmokers

*The relative likelihood of experiencing a particular event or the effect of an explanatory variable on the hazard or risk of an event.

Risk of Lung Cancer

- The risk of developing lung cancer is directly related to the amount smoked.

<table>
<thead>
<tr>
<th>Pack/Years</th>
<th>Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never Smokers</td>
<td>&lt;30</td>
</tr>
<tr>
<td>&lt;30</td>
<td>1.0</td>
</tr>
<tr>
<td>30 to &lt;60</td>
<td>2.9</td>
</tr>
<tr>
<td>≥60</td>
<td>9.0</td>
</tr>
</tbody>
</table>

Pack/year was calculated by multiplying the average number of cigarettes smoked daily by the number of years smoked and dividing the product by 20.

*The relative likelihood of experiencing a particular event or the effect of an explanatory variable on the hazard or risk of an event.


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COPD: Risk for Lung Cancer

- When evaluated long-term, diagnosis of COPD is a predictor of lung cancer development.

Kaplan-Meier curves for incident lung cancer.
Adjusted for age, race, sex, education, smoking status, pack-years, and years since regular smoking.

Summary: Smoking and Lung Cancer

• Risk of lung cancer increases with
  – Quantity and duration of smoking
  – Diagnosis and severity of COPD
  – Severity of lung function
  – Quantity and duration of environmental tobacco smoke exposure

• Risk of lung cancer and lung cancer death decreases with
  – Duration of abstinence
  – Age at cessation
Impact of Smoking Cessation on Mortality: Men

- Risk of death from lung cancer progressively decreases with increased duration of abstinence.

*The combined risks from aggregate exposures to multiple agents or stressors.


Smoking Cessation: Effects on Mortality

CHD=coronary heart disease; CVD=cardiovascular disease.

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Smoking Cessation: Lung Cancer Risk Reduction

- Lung cancer risk declines with increased duration of abstinence and approaches that of nonsmokers

<table>
<thead>
<tr>
<th>Relative Risk (95% CI)</th>
<th>Current Smokers</th>
<th>Recent Ex-smokers</th>
<th>Distant Ex-smokers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nonsmokers</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Current Smokers</td>
<td>3.4</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recent Ex-smokers^b</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distant Ex-smokers^c</td>
<td></td>
<td></td>
<td>3.4</td>
</tr>
</tbody>
</table>

Adjusted for age, physical activity, education, body mass index, waist circumference, alcohol use, and fruit consumption.

^The probability of an event (developing a disease) occurring in exposed people compared with the probability of the event in nonexposed people.

^Recent ex-smoker (quit ≤5 years at baseline).

^Distant ex-smoker (quit >5 years at baseline).

Ebbert et al. J Clin Oncol. 2003;21(5);921-926.

Other Health Effects

- Periodontal Disease
- Adverse Surgical Outcomes
  - Poor Wound Healing
  - Respiratory complications
- Cataracts
- Hip Fractures
- Low Bone Density
- Peptic Ulcer Disease

Periodontal Disease and Gum Recession

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Reproductive Effects of Cigarette Smoking

- Decreased fertility
- Low birth weights
- Premature rupture of membranes
- Placenta praevia
- Placenta abruption
- Preterm delivery
- SIDS

US SURGEON GENERAL’S REPORT: 2004

Smoking and Macular Degeneration

- Population-based longitudinal cohort (N=4926) of Wisconsin people age 43-84
- Eye examination every 5 years for 15 years
- Macular degeneration status determined by stereoscopic color fundus photographs
- Smokers had ↑ risk of age-related macular degeneration (OR 1.47; CI 1.09-1.99; p=0.01) and progression (OR 1.43; CI 1.05-1.94 p=0.02)

Skin Effects of Smoking
Premature Wrinkling

123 nonsmokers, 160 current smokers, and 67 past smokers ages 20-69

Standardized assessment of crow’s feet wrinkling

Severe wrinkling – current smokers > past smokers > nonsmokers

↑ severe wrinkling with ↑ pack years of smoking


Skin Effects of Smoking
Free Radicals

Tobacco smoke contains >10^14 free radicals/puff

Free radicals are toxic and highly reactive molecules

- Deplete antioxidants
- Promote carcinogenic transformation
- Damage protein & lipids
- Alter enzyme activity, membrane receptors, and protein transporters

Smoking 52 Y/O Twin


Nonsmoking 52 Y/O Twin

USPHS Clinical Practice Guideline- 2008

- JCAHO requires intervention for smokers with diagnosis of MI, pneumonia, and CHF.
- Telephone quit lines now provide wide access to treatment.
- 7 First-line medications are now available.

USPHS Clinical Practice Guideline- 2008

- Tobacco dependence is a chronic disease that often requires repeated interventions.
- Clinicians and healthcare systems must consistently identify and document tobacco use status and treat every tobacco user.
- Every patient willing to make a quit attempt should be offered counseling and medication.
- Brief tobacco dependence treatment is effective. Every tobacco using patient should be offered at least brief treatment.
USPHS Clinical Practice Guideline- 2008

• Combination of counseling and medication is more effective than either alone. Both should be routinely offered.

• Telephone quit line counseling is effective and has broad reach. Clinicians and healthcare systems should ensure patient access and promote their use.

• Motivational treatments increase future quit attempts among some smokers unwilling to make a quit attempt.

• Tobacco dependence treatments are clinically effective and highly cost effective. Insurers and health plans should include counseling and medications identified by the Guideline as effective.

USPHS Clinical Practice Guideline- changes --2008

• Stronger evidence that counseling is an effective tobacco use treatment strategy.
• Counseling adds significantly to the approved medications.
• Telephone quit line counseling is an effective intervention with broad reach.
• Counseling increases tobacco abstinence in adolescent smokers.
USPHS Clinical Practice Guideline- 2008

• 5 A’s (Ask, Advise, Assess, Assist, Arrange)
• 5 R’s =??
• Vital sign
• Every physician responsibility

How are we doing with the 5 A’s

• Ask –87%-99.5%
• Advise: 65%-95%
• Assess: 38%-85%
• Assist 16%-63%
• Arrange 1.3%-23.1%

– Ref: E, K. Tong et al; NTR, vol 12, No. 7 (July 2010, p. 724
5 R’s

- RELEVANCE: Tailor advice and discussion to each patient
- RISKS: Outline risks of continued smoking
- REWARDS: Outline benefits of stopping
- ROAD BLOCKS: Identify barriers
- REPETITION: Reinforce the motivational message at each visit

USPHS Clinical Practice Guideline - Motivational Interviewing

- Principles spelled out in Guideline:
  - Express empathy
  - Roll with resistance
  - Support self-efficacy
USPHS Clinical Practice Guideline - 2008

• First line
  – nicotine gum
  – nicotine patch
  – nicotine lozenge
  – nicotine nasal spray
  – nicotine inhaler
  – bupropion
  – varenicline
  – combination of medications

• Second line
  – clonidine, nortriptyline

USPHS Clinical Practice Guideline - 2008

• All smokers trying to quit should be encouraged to use effective pharmacotherapies except:
  – Presence of contraindications.
  – Populations where there is insufficient evidence of efficacy—pregnant smokers, ST users, light smokers(<10 CPD), and adolescents.

• Choice of 1st line medication guided by:
  – Clinician familiarity with medications
  – Patient preference/previous experience
  – Patient characteristics
  – Withdrawal symptom relief
USPHS Clinical Practice Guideline- 2008

- Tobacco-user identification system in every clinic.
- Education, resources and feedback to promote provider intervention.
- Dedicated staff to provide tobacco dependence treatment.
- Hospital policies that support and provide inpatient tobacco dependence treatment services.
- Include tobacco dependence treatment as a paid or covered service for all subscribers.

Mayo Clinic Nicotine Dependence Center

- Established April 1988
- Outpatients- Individual counseling by TTS.
- Inpatients- Hospital nurse Tobacco Use Intervention Protocol and Nurse Practitioner TTS
- Residential treatment program
Mayo Nicotine Dependence Center

- 8 day multicomponent treatment in a residential unit
- Tobacco-free protected milieu
- Daily physician and counselor rounds
- Group and individual therapy and education sessions
- Tailored pharmacotherapy
- Proactive follow-up for relapse prevention


Mayo Nicotine Dependence Center

- Individual outpatient counseling: 23-27%
- Individual bedside counseling: 32%
- Residential treatment: 52%

Croghan IT et al, Addict Behav 34:61, 2009
Summary

• Tobacco-related diseases are the most important preventable cause of death worldwide
• Tobacco dependence should be viewed as a chronic disease
• Most smokers want to quit
• New treatments -- counseling techniques and new medications are available

“It Is A Disease

“Not a Bad Person with a Bad Habit, but a Good Person with a Difficult Disease”

--Tom Gauvin, NDC Counselor