

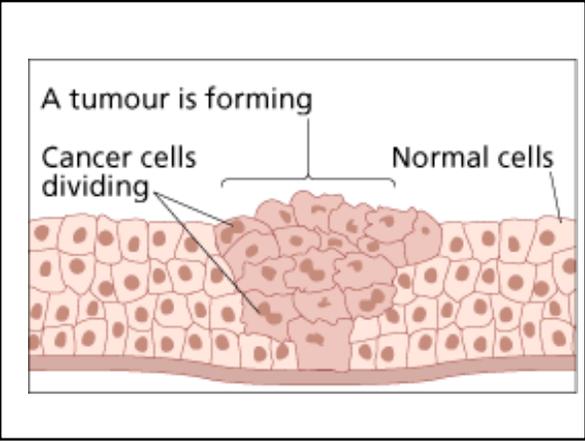
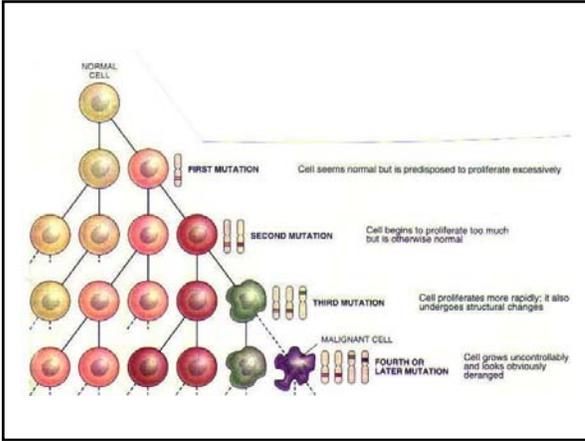
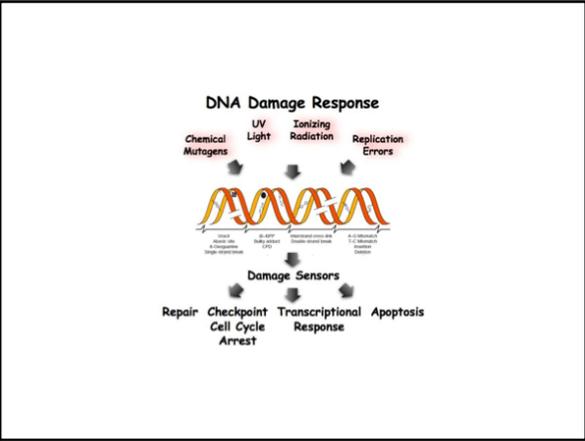
Lung Cancer Prevention

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www.tobaccoprogram.org



Objectives

- Describe the risk factors for developing lung cancer
- Explain strategies for prevention of lung cancer
- Review evidence-based strategies to treat the leading cause of lung cancer; tobacco dependence

Risk factors for Lung Cancer

- Radon exposure
 - Also other exposures
 - Asbestos, heavy metals, arsenic
- Pharmacological levels of beta-carotene (precursor to Vitamin A) in smokers
- Exposure to tobacco smoke
 - Environmental
 - Primary smoking



Radon

- Invisible radioactive gas released from the decay of uranium in rocks and soil
- Enters homes through cracks in floors, walls, or foundations, and collect indoors.
- Radon levels can be higher in homes that are well insulated, tightly sealed, and/or built on uranium-rich soil.
- Because of their closeness to the ground, basement and first floors typically have the highest radon levels.

Radon

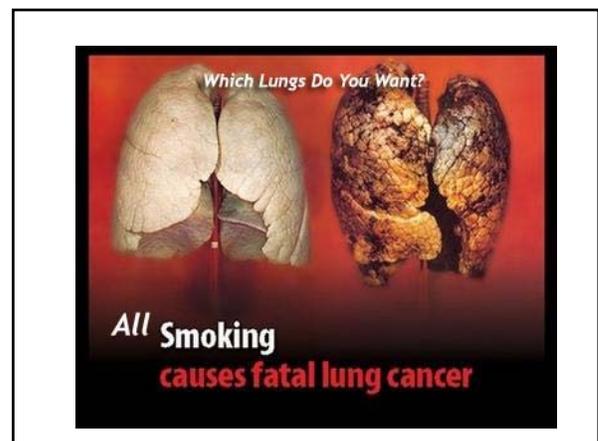
- When inhaled, these radioactive Radon particles can damage the cells that line the lung.
- Radon is the second leading cause of lung cancer in the United States, associated with 15,000 to 22,000 lung cancer deaths each year

Beta-carotene

- Pro-vitamin A
- Hypothesized to reduce cancer via anti-oxidant effects
- Meta-analysis of 100,000 subjects (Tanvetyanon; 2008) showed a 24% increase in lung cancer among current smokers who took beta-carotene

Health Effects of Environmental Tobacco Smoke

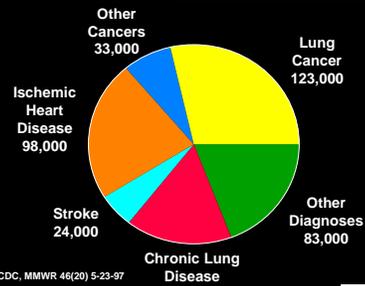
- Developmental
 - Low birthweight (40% increase)
 - SIDS (2,000 deaths per year)
- Respiratory
 - Childhood infections (bronchitis, ear) (150-300,000 /yr)
 - Asthma (400,000-1,000,000 exacerbations / yr)
- Cardiovascular
 - Heart disease (30% increase - 35-62,000 deaths /yr)
- Cancer
 - Lung (3,000 deaths per year)
 - Sinus
 - ? Cervix



Strategies for Reducing Risk of Lung Cancer

- Avoid radon exposure
 - Testing is the only way to know if your home has elevated radon levels.
 - EPA Web site: www.epa.gov/radon/index.html
- Avoid occupational exposures
- Avoid pharmacologic levels of beta-carotene if you are a smoker
- Avoid tobacco smoke exposure
- Smoking cessation

Over 430,000 deaths attributed to cigarette smoking annually



Source: CDC, MMWR 46(20) 5-23-97

Nearly one-third of all cancer deaths related to tobacco use

- **LUNG**
 - 90% of lung cancers related to tobacco use
- Cervix
- Bladder
- Kidney
- Mouth
- Larynx
- Esophagus
- Pancreas
- Acute Myelogenous Leukemia

Toxins in Tobacco Smoke

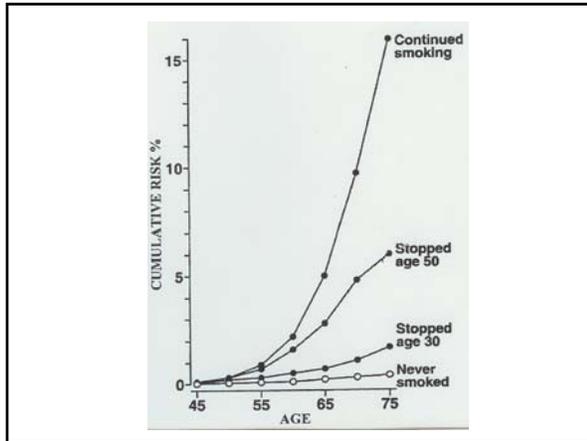
- Nicotine
- Carbon monoxide
- Carcinogens
 - Polycyclic aromatic hydrocarbons (PAH)
 - Benzopyrenes
 - 50,000 times as carcinogenic as saccharin
 - Nitrosamines
- Others
 - Ammonia (toilet bowl cleaner)
 - Hydrogen cyanide (gas chamber)
 - Sulfur dioxide (chemical bleach agent)
 - Formaldehyde (embalming fluid)
 - Arsenic (ant poison)
 - Cadmium (car batteries)
 - Acetone (nail polish remover)
 - Napthalene (moth balls)
 - Methane (swamp gas)

Consumers Underestimate Risks

- Only 29% of current smokers believe they have a higher than average risk of heart attack.
- Only 40% believe their risk of cancer is higher than average
 - Ayanian & Cleary, JAMA 218:1019

Average relative risk of cancer in smokers

- 15-30 x risk of lung cancer
- 10 x risk of laryngeal cancer
- 4-5 x risk of oral cancer
- 3 x risk of urinary tract cancer
- 2-4 x risk of pancreatic cancer
- About 2 x risk of other cancers (stomach, liver, cervix)



Benefits of Quitting

- Symptoms
 - Minutes-days: lower BP, lower carbon-monoxide, better stamina, smell/taste; lower heart attack risk
- Lung function
 - 2-4 weeks: respiratory infections decrease
 - 4-12 weeks: improved lung function
- Cardiovascular disease
 - 2-3 months: improved circulation
 - 1 year: 50% reduction for heart attack
 - 5 - 15 years: risk of heart attack and stroke equals never-smoker level
- Cancer
 - 10 years: risk of lung cancer reduced by half

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Nicotine Withdrawal

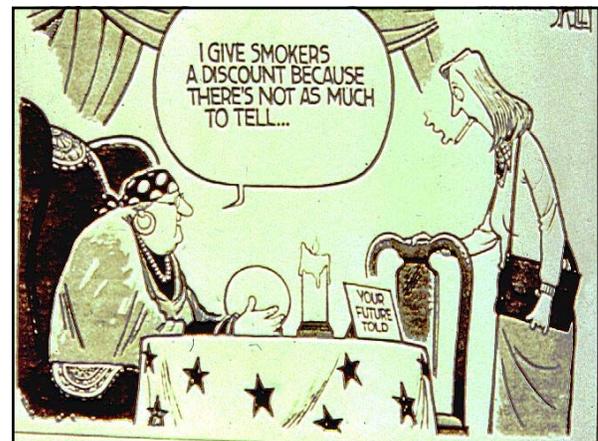
- Symptoms (4 or more)
 - Depressed mood
 - Insomnia
 - Irritability
 - Anxiety
 - Difficulty concentrating
 - Restlessness
 - Decreased heart rate
 - Increased appetite/weight gain

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Nicotine Withdrawal

- Predictors of dependence
 - Number of cigarettes per day
 - Time to first cigarette of the day
- Time course
 - Begins few hours after last dose
 - Usually peaks few days up to 1 week
 - Lasts about 4 weeks
 - "Cravings" last longer
 - 50% of former smokers report cravings at 6 months

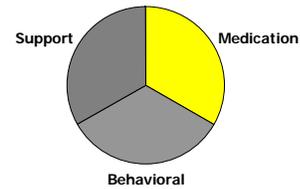
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Provider Intervention

- Public Health Service Guidelines (5 A's)
 - Ask
 - Advise
 - Assess
 - Assist
 - Arrange

Comprehensive Treatment



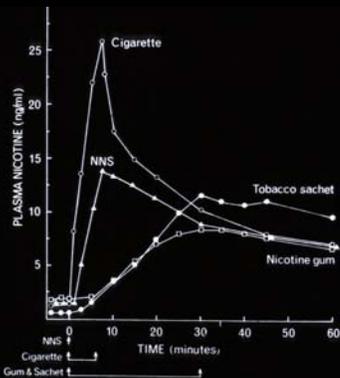
Cessation Medications

- Nicotine replacement
 - Patch
 - Gum
 - Oral inhaler
 - Nasal spray
 - Lozenge
- Non-nicotine medication
 - Bupropion (Zyban/Wellbutrin)
 - Varenicline (Chantix)

Current state of NRT - Beliefs

- Nicotine is a cause of Cancer
 - 53% Agree
 - 33% Disagree
 - 14% Don't know

(Cummings, 2004)



Nicotine Transdermal Patch (OTC)

- Use
 - Apply to clean skin (upper trunk/arms)
 - Try 24 hours (decrease morning cravings)
 - Rotate sites
 - Taper over weeks (4-6)
- Advantages
 - Place and forget
- Disadvantages
 - Passive (nothing to do when craving)
 - Local irritation (50%) – treat with steroid cream

Nicotine Gum (OTC)

- Use (2 or 4 mg dose based on consumption)
 - Chew and park (oral absorption)
 - As needed or fixed-schedule (every 1-2 hours, up to 24 pieces/day)
- Advantages
 - As needed use (active)
- Disadvantages
 - Don't eat/drink around use (decreased absorption)
 - Hard to chew – jaw pain
 - Nausea



Nicotine Lozenge (Commit®) (OTC)

- Dosing based on time to first cigarette (TTFC)
- Within 30 min = 4 mg
 - Over 30 min = 2 mg
 - Use 9-15 lozenges / day for 6 weeks then taper over next 6 weeks
 - 25% higher blood nicotine levels than gum, otherwise, similar to gum
 - Allow to dissolve / Don't chew



Nicotine Oral Inhaler (Rx)

- Use
 - Puff (oral absorption)
 - As needed or fixed-schedule (max 16 cartridges per day)
 - 1 cartridge lasts 30 minutes puffing
- Advantages
 - As needed use (active)
 - Oral/hand behavior
- Disadvantages
 - Throat irritation/cough (40%) – first few days
 - Visible



Nicotine Nasal Spray (Rx)

- Use
 - Spray (don't sniff/inhale)
 - As needed or fixed-schedule (1-2 doses per hour)
- Advantages
 - Rapid onset
 - As needed use (active)
- Disadvantages
 - Irritation (85%)
 - ? Dependence (20%)
 - Caution with sinusitis, rhinitis



Bupropion

- AKA:
 - Zyban®
 - Wellbutrin SR®
 - Wellbutrin XL®
- Dopaminergic and norepinephrine effects
- Reduces cravings, withdrawal

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Bupropion Use

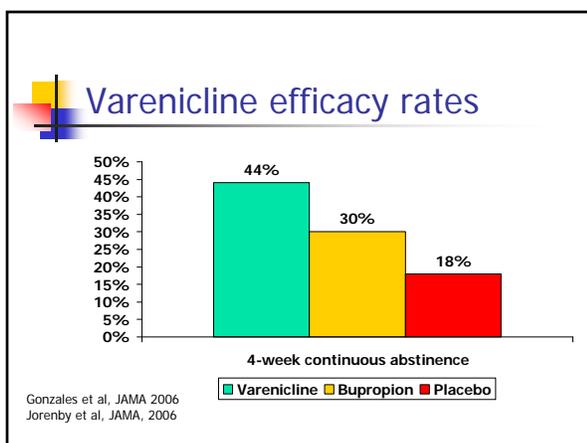
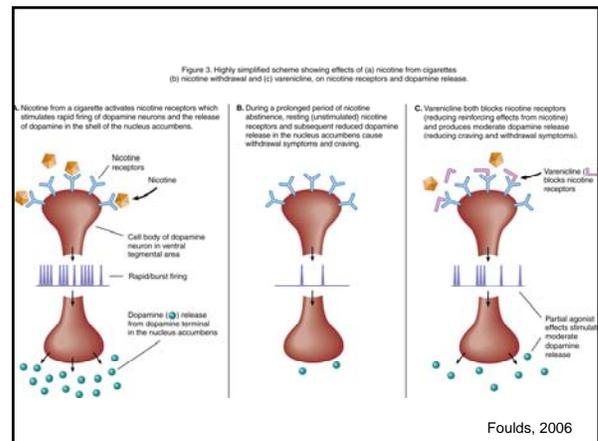
- Start 7-10 days prior to quit date
- Continue 7-12 weeks or longer (> 6 months)
- Contraindicated: seizure disorder, eating disorders, electrolyte abnormalities, MAO use
- Side effects:
 - Insomnia
 - Dry mouth
 - Headaches
 - Rash

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Varenicline (Chantix)

- Action at $\alpha_4\beta_2$ nicotine receptor
- Partial agonist/antagonist
- Releases lower amounts of dopamine into brain than nicotine
 - Reduces withdrawal
 - Not as addictive as nicotine
- Blocks nicotine from binding to receptor
 - Prevents reward of smoking

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Varenicline side effects

- Nausea 30%
 - 71% Mild
 - 26% Moderate
 - < 3% discontinued due to nausea
- Insomnia 18%
- Abnormal dreams 13%
- Constipation 8%

Gonzales et al, JAMA 2006
Jorenby et al, JAMA, 2006

Varenicline use

- Titrate dose up during week 1
- Set quit date on Day 8 of medication
- Avoid or reduce dose in renal disease
 - Exclusively excreted in urine
- Duration: 12-24 weeks or longer
 - 44 vs. 37% long-term abstinence with additional 12 weeks of treatment
- No data in pregnancy (Class C)
- No data under age 18

Varenicline recent issues

- Serious neuropsychiatric symptoms have occurred in patients taking varenicline. These symptoms include changes in behavior, agitation, depressed mood, suicidal ideation, and attempted and completed suicide.
- Patients should discontinue varenicline if these symptoms develop and contact their doctor

Varenicline safety update

- UK study (Gunnell, 2009) - 80,000 smokers prescribed smoking cessation medications by their primary care doctor
- Compared with smokers using NRT, results for varenicline:
 - Suicide (Hazard ratio (HR)=1.12; 95% CI=0.67-1.88)
 - Depression (HR=0.88; 0.77-1.00)

Varenicline Safety Update

- Pooled analysis of psychiatric adverse events in clinical trials (Tonstad, 2010)
- 10 RCT's
- 5096 subjects (active and placebo)
- Excluded current psychiatric disease
- Rates of all psychiatric AE's (apart from sleep disturbances)
 - 10.7% varenicline
 - 9.7% placebo
- Relative risk of specific AE's
 - Anxiety: RR 0.86 (0.67-1.12)
 - Depressed mood: RR 1.42 (0.96-2.08)
 - Other mood disorders: RR 1.21 (0.79-1.83)
 - Sleep disturbances: RR 1.70 (1.50-1.92)
- No suicidal ideation or behavior in all 10 RCT's on varenicline
 - 1 completed suicide in an open label study (on varenicline)

Arrange: follow-up

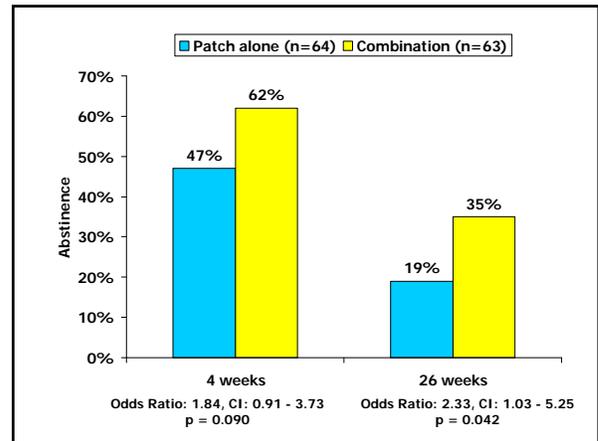
- Need good clinical follow-up for all treated smokers (regardless of medication used)
 - Depressed mood is a withdrawal symptom
 - Tobacco treatment not a quick-fix

Combination Medications

- "Long-acting" (Patch/Bupropion) + "Short-acting" (Gum/Inh/Nasal/Lozngge)
 - Evidence that combined forms of NRT are more effective than single agents
 - Evidence that NRT plus Bupropion is better than either alone
- No trial data on combining varenicline

Efficacy of Medications (Fiore, 2008)

Medication	Odds Ratio	Abstinence rate
Placebo	1.0	13.8%
Varenicline	3.1	33.2%
Nicotine nasal spray	2.3	26.7%
Nicotine inhaler	2.1	24.8%
Bupropion SR	2.0	24.2%
Nicotine patch	1.9	23.4%
Nicotine gum	1.5	19.0%
Long term Patch + Gum/Spray	3.6	36.5%
Patch + Bupropion SR	2.5	28.9%



Factors in choosing medication

- Efficacy
- Medical comorbidity
- Adverse effects
- Previous experience
 - Patient and provider
- Patient preference
- Cost/access

Summary – What we know about medications

- NO magic pills
- NRT, bupropion, varenicline are all good first line choices for treatment
 - Varenicline may be better as single agent
 - However, ongoing evaluation of risk/benefit
- Combining multiple NRT's or NRT + bupropion may have advantages
 - Not recommending varenicline combos at this time

Tobacco Dependence as a Chronic Disease

- Tobacco dependence demonstrates features of a chronic disease:
 - Long-term disorder
 - Periods of relapse and remission
 - Requires ongoing rather than acute care
- "Quick-fix" is not appropriate
 - need availability of ongoing treatment

Steinberg, *Ann Int Med*; 148(7):554-7; 2008

