Among US smokers with Peripheral Artery Disease
- 36% provided smoking cessation counseling or meds (Berger & Ladapo, 2017)
- Survey of 326 cardiologists in Spain (Dalmau, 2013)
  - 73% unfamiliar with cessation meds
  - 71% wanted to improve their tobacco treatment skills
- Survey of 610 cardiologists in Italy (Frisinghelli et al., 2015)
  - 45% regularly advised their patients to stop smoking
  - 72% believe cessation tools are lacking
  - 66% wanted to improve their tobacco treatment skills

This training is designed to meet the needs of cardiologists for effectively treating tobacco in practice

SMOKING CESSATION is a TREATMENT for CVD

- Standard treatments reduce the risk of death in patients with CVD by 15–35%
  - Aspirin = 15%
  - Beta blockers = 23%
  - ACE inhibitors = 23%
  - Statins = 29–35%

- Smoking cessation in patients with CVD reduces the risk of death by 36% and reduces the risk of future cardiac events by 50%

TREATING TOBACCO is a GOLD STANDARD TREATMENT

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Outcome</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Statins</td>
<td>Prevent 1 death over 5 years</td>
<td>107</td>
</tr>
<tr>
<td>Aspirin</td>
<td>Prevent 1 MI over 5 years</td>
<td>118</td>
</tr>
<tr>
<td>Antihypertensive therapy</td>
<td>Prevent 1 stroke, MI, death over 1 year</td>
<td>700</td>
</tr>
<tr>
<td>Cervical cancer screening</td>
<td>Prevent 1 death over 10 years</td>
<td>1140</td>
</tr>
<tr>
<td>MD 5 min advice to stop smoking</td>
<td>Prevent 1 premature death</td>
<td>80</td>
</tr>
<tr>
<td>+ cessation medication</td>
<td>Prevent 1 premature death</td>
<td>38-56</td>
</tr>
<tr>
<td>+ behavioral support</td>
<td>Prevent 1 premature death</td>
<td>16-40</td>
</tr>
</tbody>
</table>

NNT = Number Needed to Treat

Anthorison, 2006; Ann Intern Med; McQuay & Moore, 2009; Bandirolli, Gattes 2001; Ann Fam Phys; Cochrane Reviews by Stead, Bageton, et al., 2008; Stead, Perera, et al. 2012; Stead & Lancaster, 2012; Cahill et al., 2010; and USPSTF, 2009

OVERVIEW

- Module 1: Epidemiology of Tobacco Smoke
- Module 2: CVD Risks of Tobacco Smoke
- Module 3: Nicotine Addiction and Withdrawal
- Module 4: Changing Behavior: How You Can Help
- Module 5: Medications for Quitting Smoking

Optional 1: Forms of Tobacco
Optional 2: Addressing the Global Tobacco Epidemic

Module 1

EPIDEMIOLOGY OF TOBACCO SMOKE
SMOKING PREVALENCE by GENDER

FORMS of TOBACCO

- Globally, cigarettes are the most common form of tobacco consumed
- Substantial regional differences in the forms of tobacco
  - E.g., Smokeless is the main type used in South Asia; waterpipe use is common in the Middle East
- Attention to all forms of tobacco is needed
- Increasing in popularity are e-cigarettes

Electronic or E-Cigarettes (EC)

- Battery operated devices that deliver vaporized nicotine
  - Cartridges contain nicotine, flavoring agents + other chemicals
- Vary greatly in design, nicotine delivery & particulates
- Reported to increase arterial stiffness
- Increase HR and BP due to nicotine delivery
  - However, switching from cigarettes to ECs is associated with reduction in BP in hypertensive individuals
- Probable lower CV risk with EC relative to combustible cigarettes, though still unknown

CVD MORTALITY & TOBACCO USE

- Globally, 12% of all CVD deaths are attributable to tobacco use for adults 30+ years of age
  - Varies by region: Africa: 3%, Americas: 16%, Southeast Asia: 10%, Europe: 16%, Eastern Mediterranean: 7%, Western Pacific: 13%

DEATHS GLOBALLY from SECONDHAND SMOKE

- Secondhand smoke is tobacco smoke that is exhaled by smokers or given off by burning tobacco
- Secondhand smoke causes an estimated 605,000 premature deaths worldwide each year
- 87% of adult SHS deaths are due to ischaemic heart disease

Projected Deaths Caused by Tobacco Use During the 21st Century Total: 1 Billion

- Lower Respiratory Infections 17% 165,000 deaths
- Diets 2% >100 deaths
- Asthma 8% 17,000 deaths
- Lung cancer 8% 21,000 deaths
- Ischaemic heart disease 63% 379,000 deaths

What proportion of your practice is dedicated to the problem of tobacco?

Copyright © 1999-2017 The Regents of the University of California. All rights reserved. Updated July 2017.
Module 2
TOBACCO & SECONDHAND SMOKE: CARDIOVASCULAR DISEASE RISK

HEALTH CONSEQUENCES of SMOKING

Cardiovascular Diseases
- Coronary heart disease
- Heart failure
- Aortic aneurysm
- Cerebrovascular disease / stroke
- Peripheral arterial disease
- Sudden death
- Atherosclerosis
- Occlusion of bypass grafts & stents
- Poor surgical outcomes

Other
- Numerous cancers
- Pulmonary diseases
- Reproductive effects
- Eye disease
- Osteoporosis
- Type 2 diabetes
- Periodontitis
- Erectile dysfunction

Other
- Numerous cancers
- Pulmonary diseases
- Reproductive effects
- Eye disease
- Osteoporosis
- Type 2 diabetes
- Periodontitis
- Erectile dysfunction

BRITISH MALE DOCTORS’ STUDY: LIFE LOST

On average, life-long smokers lose 10 years of healthy life

Survival from age 35 for continuing cigarette smokers and lifelong non-smokers among UK male doctors born 1900-1930, with percentages alive at each decade of age.

Smokers lose > 10 years of life expectancy compared to never smokers

Jha et al. NEJM 2013;368: 341-350

BRITISH MALE DOCTORS’ STUDY: STOPPING SMOKING & YRS of LIFE GAINED

STOPPING WORKS: stopping smoking at ages 30, 40, 50, and 60 resulted in 10, 9, 6, and 3 years of life gained, respectively.


SECONDHAND SMOKE & CVD

- Second-hand smoke (SHS) causes premature death and disease in nonsmokers:
  - Immediate adverse effects on the CV system – same effects as active smoking
  - Increased risk for heart disease & lung cancer
  - Bans on smoking in public places reduce exposure to SHS and reduce heart attacks

There is no safe level of secondhand smoke


EFFECTS of SMOKING & SHS on the CARDIOVASCULAR SYSTEM

- Platelet activation
- Endothelial dysfunction
- Inflammation & infection
- Atherosclerosis
  - Low HDL levels
  - Platelet instability
  - Increased oxidized LDL
- Oxidative stress
- Decreased energy metabolism
- Coronary vasoconstriction
- Increased insulin resistance
- Outcome measures
  - Increased infarct size
  - Decreased heart rate variability
  - Increased arterial stiffness
  - Increased risk of coronary disease events

PATHOPHYSIOLOGICAL MECHANISMS of TOBACCO-RELATED CVD

OXIDANT CHEMICALS

OTHER COMBUSTION PRODUCTS

Inflammation

Reduced Oxygen Availability

Coronary Vasoconstriction

myocardial Ischemia

myocardial Infarction

Reduced Myocardial Oxygen Supply

Increased Myocardial Oxygen Demand

Increased heart rate

Increased blood pressure

Increased myocardial contractility

META-ANALYSIS of CHD RISK DUE to CHRONIC SHS among NEVER-SMOKERS

Overall RR = 1.78 for active smokers
Overall RR = 1.31 for passive smoking
Most of the SHS exposures were spousal

Long-term SHS exposure in the work or home is associated with a 30% increased risk for CHD in adult nonsmokers

HEAVY SHS EXPOSURE is LIKE BEING a LIGHT SMOKER

"Light passive" refers to the lowest quarter of cotinine concentration among nonsmokers (0-0.7 ng/ml), "heavy passive" to the upper three-quarters of cotinine concentration combined (0.8-14.0 ng/ml), "light active" to men smoking 1-9 cigarettes a day.

REDUCING SHS EXPOSURE REDUCES HOSPITAL ADMISSIONS for MI

Studies reporting reduction in hospital admissions for acute MI/acute coronary syndrome following smoke-free legislation

Copyright © 1999-2017 The Regents of the University of California. All rights reserved. Updated July 2017.
CHILDHOOD EXPOSURE to PARENTAL SMOKING

- Children with 1 smoking parent more likely to have elevated high-sensitivity C-reactive protein (hsCRP)
- CRP is a systemic inflammatory marker
- Elevated CRP is known to reflect the development of atherosclerosis and CVD


AFTER the LAST CIGARETTE...

<table>
<thead>
<tr>
<th>Time</th>
<th>Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 30 min</td>
<td>Blood pressure and pulse return to normal</td>
</tr>
<tr>
<td>8 hr</td>
<td>CO levels in blood return to normal</td>
</tr>
<tr>
<td>24 hr</td>
<td>Endothelial better, chance of heart attack decreases</td>
</tr>
<tr>
<td>48 hr</td>
<td>Nerve endings begin regrowth</td>
</tr>
<tr>
<td>72 hr</td>
<td>Breathing becomes easier, lung capacity increases</td>
</tr>
<tr>
<td>2-12 wks</td>
<td>Lung function increases 30%; circulation improves</td>
</tr>
<tr>
<td>1 year</td>
<td>Risk of CHD is half that of a smoker</td>
</tr>
<tr>
<td>3 years</td>
<td>MI risk is similar to that of never-smokers</td>
</tr>
<tr>
<td>5-15 years</td>
<td>Stroke risk reduced to that of never-smokers</td>
</tr>
</tbody>
</table>

WHY ADDRESS TOBACCO in CARDIOLOGY?

- Smoking and SHS are independent and synergistically linked with other CVD risk factors
- Quitting smoking: improves survival, improves quality of life, reduces risk of future CVD events
- Reducing SHS: reduces hospitalizations for MI

TREATING TOBACCO is a GOLD STANDARD TREATMENT for CVD

NICOTINE ADDICTION AND WITHDRAWAL

TREATING TOBACCO is a GOLD STANDARD TREATMENT for CVD

Module 3

NICOTINE ADDICTION AND WITHDRAWAL

- Smoking and SHS are independent and synergistically linked with other CVD risk factors
- Quitting smoking: improves survival, improves quality of life, reduces risk of future CVD events
- Reducing SHS: reduces hospitalizations for MI

TREATING TOBACCO is a GOLD STANDARD TREATMENT for CVD

NICOTINE DISTRIBUTION

Nicotine reaches the brain within 11 seconds.

Henningsfeld et al. (1993). Drug Alcohol Depend 33:23–29

Copyright © 1999-2017 The Regents of the University of California. All rights reserved. Updated July 2017.
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
- β-Endorphin: Reduction of anxiety and tension
- GABA: Reduction of anxiety and tension


NICOTINE WITHDRAWAL EFFECTS

- Irritability/frustration/anger
- Anxiety
- Difficulty concentrating
- Restlessness/impatience
- Depressed mood/depression
- Insomnia
- Impaired performance
- Increased appetite/weight gain
- Cravings

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


NICOTINE ADDICTION CYCLE

- Physical dependence
  - Medications for cessation
  - Treatment of usage symptoms
  - Physical dependence
  - Treatment

- Behavioral dependence
  - Behavioral change program
  - The habit of using tobacco
  - Treatment
  - Medications for cessation

Treatment should address both the behavioral and physiologic aspects of dependence.


TOBACCO DEPENDENCE: A 2-PART PROBLEM

TOBACCO CESSATION REQUIRES BEHAVIOR CHANGE

- Fewer than 5% to 8% of people who quit without assistance are successful in quitting for > 1 year
- Few patients adequately PREPARE and PLAN for their quit attempt
- Many patients assume they can just “make themselves quit” when they are ready to do so
- Most patients expect a doctor to address tobacco with them and doing so can enhance rapport

Behavioral counseling is a key component of tobacco treatment.

Module 4

CHANGING BEHAVIOR: HOW YOU CAN HELP
With help from a clinician, the odds of quitting approximately double.

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.

**Type of Clinician**

- No clinician
- Self-help material
- Nonphysician clinician
- Physician clinician

**Estimated abstinence at 5+ months**

- No clinician: 1.0
- Self-help material: 1.1
- Nonphysician clinician: 1.7
- Physician clinician: 2.2

**N = 29 studies**


---

**STEP 1: ASK**

- **ASK** about tobacco use & exposure
  - “Do you, or does anyone in your household, ever smoke or use any type of tobacco?”
  - “Are you exposed to tobacco smoke at home, work, or in other public places?”
- **RECORD** tobacco use and secondhand smoke exposure in the medical record for all patients

**STEP 2: ADVISE**

- **ADVISE** tobacco users to quit and all patients to avoid secondhand smoke exposure
  - “As part of treatment for your heart health, it is critical that you quit smoking and avoid SHS.”
  - “Continued smoking after a heart attack more than doubles the chances of dying.”
  - “Avoid smoke at home, work, and in public.”

**STEP 3: ASSESS**

- **ASSESS** readiness to quit
  - Ask every tobacco user if they are willing to quit at this time
  - If willing to quit, provide resources and assistance
  - See STEP 4, **ASSIST**
  - If NOT willing to quit, assess benefits & barriers to quitting

For smokers who are not ready to quit, it is still worthwhile to advise them to quit AND to offer them assistance to do so

---

**THE 5 As**

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

Can occur over multiple treatment visits

**BRIEF CLINICIAN ADVICE MAKES a DIFFERENCE**
**NOT READY to QUIT: COUNSELING STRATEGIES**

- **Ask:** On scales from 1 (not at all) to 10 (extremely)
  - How important is it to you to quit smoking?
    - Why is it at X and not a 1? What would it take to get it to a 10?
  - How confident are you that you could quit right now?
    - Why is it at X and not a 1? What would it take to get it to a 10?

- **Foster understanding & rapport**
  - Keep the door open for future conversation and subsequent quit attempts


**STEP 4: ASSIST**

- **ASSIST** tobacco users with a quit plan
  - Discuss reasons for quitting and benefits of quitting
  - Review past quit attempts—what helped, what led to relapse
  - Discuss support from family, friends, and coworkers
  - Set a quit date—within 2 weeks
  - Advise making the home and car smoke-free
  - Encourage use of pharmacotherapy when not contraindicated
  - Anticipate challenges, particularly during the first few weeks
    - Nicotine withdrawal, stress-related smoking, other smokers, etc.

**STEP 5: ARRANGE**

- **ARRANGE** follow-up care
  - Status of attempt
    - Ask about support from friends, family, coworkers
    - Identify ongoing temptations and triggers for relapse (stress, negative affect, smokers, eating, alcohol, cravings)
  - Slips and relapse
    - Has the patient used tobacco at all—even a puff?
    - Cessation medication compliance, plans for termination
    - Is the regimen being followed?
    - Are withdrawal symptoms being alleviated?

- **Provide assistance throughout the quit attempt**

**IN the ABSENCE of TIME**

- **ASK** about smoking and secondhand smoke exposure
- **ADVISE** patients to quit smoking and/or avoid secondhand smoke
- **REFER** to treatment

Can take < 2 minutes to help a smoker

**5As for SMOKERS with ACUTE CORONARY SYNDROME**

- Hospitalized ACS patients not ready to quit smoking
- Randomized to 5As (n=155) or control (n=157)
- 5As group had significantly greater continuous abstinence verified by CO at:
  - Weeks 9-12: 28% vs. 18%
  - Week 24: 24% vs. 15%
- In those who did not quit, 5As greater reduction in cigarettes/day: -9.52±10.13 vs. -5.13±6.09

**MAKING A REFERRAL**

- **REFER** patients to other resources:
  - A doctor, nurse, pharmacist, or other health professional, for additional counseling
  - Self-help quit guide: [insert local guide, web link or if not available suggest a compatible guide from another jurisdiction]
  - Local cessation program: [insert program]
  - Local websites: [insert link]
  - Local quitline number: [insert link]
TECHNOLOGY MEDIATED TOBACCO TREATMENTS

- Scalable, tailored, engaging/interactive, accessible, social, low cost/free
  - Quitlines: 1-800-QUIT-NOW
  - Computer-assisted / Telemedicine
  - Web-based: smokefree.gov
  - Texting
  - Social media
  - Twitter, Facebook, WhatsApp
  - Smartphone apps

REFERRAL to QUITLINE

- Referring patients to a telephone quitline is:
  - Simple and easily integrated into routine care
  - Effective for supporting long-term quitting
- For info on country quitline availability:
  - WHO Country Profiles (offer assistance to quit section): http://www.who.int/tobacco/surveillance/policy/country_profile/en/index.html

Tobacco TX Apps

- 546 quit smoking apps in 2014 (Bricker 2014 Drug Alc Dep)
  - Downloads: 3.2 million in US and 14.3 million worldwide
  - Review of 225 Android quit smoking apps (Hoeppner 2015 NTR)
  - Most provided simplistic tools (e.g., calculators, trackers)
  - Use of tailoring was limited, though positively related to app popularity and user ratings
  - Numerous, but 4% of top 50 apps had scientific backing
  - Difficult to tell on app store which apps have been studied

TOBACCO DEPENDENCE: A 2-PART PROBLEM

Tobacco Dependence

- Behavioral
  - The habit of using tobacco
  - Treatment
  - Behavior change program
- Physiologic
  - Physical dependence
  - Treatment
  - Medications for cessation

Treatment should address both the behavioral and physiologic aspects of dependence.

PRACTICE the 5 As

- Review the handout: TOBACCO CESSATION COUNSELING GUIDESHEET – Patients with CVD
  - In pairs, practice the 5 As with one person acting as the patient then switch roles
  - After practicing the 5 As, try practicing the shorter version: Ask, Advise, Refer
  - Ask yourself: Do you feel confident in your skills?
Module 5
MEDICATIONS FOR QUITTING SMOKING

PHARMACOLOGIC METHODS*

- Nicotine replacement therapy (NRT)
  - WHO Model lists of essential medications includes nicotine gum and transdermal patch; additional formulations include lozenge, mouth spray, nasal spray, and inhaler
- Bupropion SR
- Varenicline
- Cytisine

* Not all medications are available in all settings

Provider and group counseling, websites and quitlines work, so use them

PLASMA VENOUS NICOTINE CONCENTRATIONS for NICOTINE-CONTAINING PRODUCTS

NICOTINE in NRT vs. SMOKING

- Absorbed more slowly (less acute effects)
- Absorbed via venous system
- No carbon monoxide! No oxidants!
- Attenuated sympathomimetic response
- Flat dose-response curve of nicotine and cardiovascular effects
- 7000+ other chemicals are not present


NRT PATCH REDUCES EXERCISE-INDUCED MYOCARDIAL ISCHEMIA in SMOKERS with CAD

Smokers with CAD using nicotine patches: within subject design

NRT POSES NO CARDIOVASCULAR RISK

The safety of NRT in CVD patients is supported by data from RCTs, efficacy studies, observational data, and physiologic studies

Joseph et al., Prog in CVD, 2003

Use of NRT is not associated with any increase in the risk of MI, stroke, or death. N=33,247

Hubbard et al., Tob Control, 2005

High dose nicotine treatment, even with concomitant smoking, caused no short-term adverse effects on the cardiovascular system

TRANSDERMAL NICOTINE PATCH

**ADVANTAGES**
- The patch provides consistent nicotine levels
- The patch is easy to use and conceal
- Fewer compliance issues are associated with the patch

**DISADVANTAGES**
- Patients cannot acutely titrate the dose
- Allergic reactions to adhesive may occur
- Vivid/disturbing dreams may occur with nocturnal patch use (can remove before sleep)

---

PATIENT EDUCATION: NICOTINE PATCH

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

---

NICOTINE GUM & LOZENGE

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

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

---

NICOTINE INHALER

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

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

---

NICOTINE NASAL SPRAY

**ADVANTAGES**
- Most rapidly absorbed form of nicotine replacement
- Patients can easily titrate therapy to rapidly manage withdrawal symptoms

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

---

* Dosing of 1 mg ~ 1 cpd less accurate in light smokers and dual users
* Sneezing/rhinorrhea go away after 1 wk
** The data on higher dependence are not definitive and are based on small trials
**BUPROPION SR**

**ADVANTAGES**
- Easy to use
- Can be used with NRT or varenicline
- May delay cessation-related weight gain
- May be beneficial in patients with coexisting depression

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

---

**BUPROPION: MECHANISM of ACTION**

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

---

**BUPROPION SR: DOSING for SMOKING CESSATION**

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

**Then, if tolerated...**
- 150 mg po bid x 7–12 weeks

**If 300 mg is not well tolerated...**
- Reduce dose to 150 mg and reassure that 150 mg dose is still efficacious (Swan et al., 2003)

*Patients should begin therapy one week PRIOR to quitting to assure therapeutic plasma levels of drug are achieved when patient is no longer smoking.*

---

**BUPROPION USE in PATIENTS with CVD: EFFICACY & SAFETY**

- Study of 629 patients with stable, documented CVD (other than HTN alone) diagnosed for > 3 months
  - 49% MI, 42% cardiac procedure, 35% stable angina, 33% PVD, 6% CHF
- Randomized to 7 weeks bupropion or placebo
- Monitored over 52 weeks
- Multisite trial funded by GSK

**Tonstad et al. (2003). Euro Heart J; 24:946-55.**

---

**CONTINUOUS ABSTINENCE RATES: BUPROPION vs. PLACEBO**

<table>
<thead>
<tr>
<th>Week</th>
<th>Dose</th>
<th>Bupropion</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wk 4-7</td>
<td>19%</td>
<td>34%</td>
<td>27%</td>
</tr>
<tr>
<td>Wk 4-12</td>
<td>15%</td>
<td>27%</td>
<td>22%</td>
</tr>
<tr>
<td>Wk 4-26</td>
<td>11%</td>
<td>22%</td>
<td>9%</td>
</tr>
<tr>
<td>Wk 4-52</td>
<td>9%</td>
<td>15%</td>
<td>12%</td>
</tr>
</tbody>
</table>

* p < 0.001 for group comparisons at all time points

**Tonstad et al. (2003). Euro Heart J; 24:946-55.**

---

**BUPROPION: ADVERSE EVENTS**

- Most frequent events in the bupropion group:
  - Insomnia (24%), dry mouth (18%), nausea (13%), headache (11%), dizziness (8%), constipation (5%), sweating (5%)
  - Discontinued due to AE: 5% on bupropion vs. 6% on placebo
  - No impact on vital signs such as blood pressure
  - SAEs occurred in 2.6% on bupropion vs. 1.3% on placebo
  - No reported depression, suicidality, or abnormal behavior
  - CV events 1.2% bupropion vs. 0.6% placebo
  - Deaths 0.6% bupropion or placebo
  - Comparable attrition on placebo (6%) and bupropion (5%)

Varenicline

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

Disadvantages
- Common side effects:
  - Nausea (in up to 33% of patients)
  - Sleep disturbances (vivid, abnormal dreams)
  - Constipation
  - Flatulence
  - Vomiting

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: 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

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
- Angioedema and hypersensitivity reactions
- Serious skin reactions

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

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

<table>
<thead>
<tr>
<th>Treatment Day</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days 1–3</td>
<td>0.5 mg qd</td>
</tr>
<tr>
<td>Days 4–7</td>
<td>0.5 mg bid</td>
</tr>
<tr>
<td>Day 8 – week 12</td>
<td>1 mg bid</td>
</tr>
</tbody>
</table>

Varenicline use in patients with CVD: efficacy & safety
- Study of 714 patients with stable, documented CVD (other than hypertension alone) diagnosed for > 2 months
  - 51% angina, 49% MI, 49% coronary revascularization
  - Randomized to 12 weeks varenicline or placebo
  - Monitored over 52 weeks
  - Multisite trial funded by Pfizer, Inc.

CONTINUOUS ABSTINENCE RATES: VARENICLINE vs. PLACEBO


VARENICLINE: ADVERSE EVENTS

- Most frequent events in the varenicline group:
  - Nausea (30%), headache (13%), insomnia (12%), vomiting (8%), and abnormal dreams (8%)
  - Discontinued due to AE: 10% on varenicline vs. 4% on placebo
- SAEs occurred in 6.5% on varenicline vs. 6% on placebo
  - No reported depression, suicidality, or abnormal behavior
  - CV events 7% varenicline vs. 6% placebo
  - CV deaths 0.3% varenicline vs. 0.6% placebo
- Greater attrition on placebo (20%) vs. varenicline (15%)

VARENICLINE & CV RISK

- 3 meta-analyses on varenicline and CV risk
- Differential conclusions
- If any risk at all, it is small
- “These events were uncommon in both the Chantix and placebo groups, and the increased risk was not statistically significant” – US FDA

Singh et al (2011) CMAJ
Prochaska & Hilton (2012) BMJ
Chantix product label

VARENICLINE & CV RISK

- Randomized to varenicline or NRT for smoking cessation (n=188)
- At 3 months decreased CO, oxidative stress markers, and augmentation index (Aix)
- CO levels and endothelial covering measurement had greater improvement with varenicline than NRT

Ikonomidis et al. (2017) Atherosclerosis

“No evidence of any increased risk of CV or neuropsychiatric adverse events in smokers using varenicline or bupropion when compared with NRT users. On the contrary, some events were associated with a reduced risk, including the events with the highest noted incidences (e.g., depression and ischemic heart disease).”

CYTISINE

ADVANTAGES
- Partial nicotine receptor agonist; mechanisms may be similar to varenicline
- Lower cost medication
  - US$6-15 full course treatment in E. Europe
- Emerging evidence of effectiveness

DISADVANTAGES
- Fewer trials
- Evidence of adverse gastrointestinal events, nausea, and headache

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

Data adapted from Cahill et al. (2012), Cochrane Database Syst Rev; Stead et al. (2012), Cochrane Database Syst Rev; Hughes et al. (2014), Cochrane Database Syst Rev
### COMBINATION TREATMENTS

**Long Acting**
- Pick 1 or 2 from here
  - Nicotine patch
  - Bupropion

**Short Acting**
- Plus 1 or 2 from here
  - Nicotine gum
  - Nicotine lozenge
  - Nicotine nasal spray

*Combination of varenicline and NRT is exploratory, no trials to support its efficacy to date but initial evidence indicates well tolerated.

---

### TREATMENT EFFICACY

**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 (1.8–2.4)</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 (2.4–3.5)</td>
</tr>
</tbody>
</table>

*Includes nicotine nasal spray, lozenge, and inhaler

---

### TREATMENT TIMELINES

<table>
<thead>
<tr>
<th>Bupropion</th>
<th>NRT</th>
<th>BUPR+NRT</th>
<th>Varenicline</th>
</tr>
</thead>
<tbody>
<tr>
<td>150 mg</td>
<td>300 mg</td>
<td>Patch and consider prn gum/lozenge</td>
<td>1 mg bid</td>
</tr>
<tr>
<td>150 mg</td>
<td>300 mg</td>
<td>Patch and consider prn gum/lozenge</td>
<td>1 mg bid</td>
</tr>
</tbody>
</table>

---

### COVERAGE for MEDICATIONS

- Some countries/jurisdictions may provide coverage for smoking cessation medications
- Insert local data on any financial coverage available for smoking cessation medications if available

---

### TOBACCO CESSATION TRIALS in HOSPITALIZED PATIENTS

- Greater quit rates among hospitalized patients
  - Admitted with CVD, RR=1.42
  - Provided on-unit counselling with follow-up support for >1 mo after discharge, RR=1.37
  - Provided NRT, RR=1.54
  - No effect found for less intense interventions
  - Insufficient evidence for adding bupropion (3 trials) or varenicline (2 trials)

---

### RELAPSE following MI HOSPITALIZATION

- Most patients return to smoking within 6 months following an MI hospitalization
- Patients more likely to stay smoke-free if...
  - Hospital has a cessation program
  - Patient referred for cardiac rehab
  - Less depressive symptoms during hospitalization

---


---

TREATING TOBACCO DEPENDENCE in HOSPITALIZED CVD PATIENTS

- Quit rates: intervention (42%) vs. usual care (34%)
- Patients more likely to quit if treatment provided:
  - 6+ interactions: OR = 1.67
  - Greater duration & intensity: OR = 3.17
  - Concurrent use of NRT or bupropion: OR = 2.13

Behavioral smoking cessation interventions initiated during hospitalization result in a significantly higher quit rate compared to usual smoking cessation advice.

Aziz et al. (2009). Int J Cardiology.
Meta-analysis of 11 RCTs (N=2751), 1990-2007

OTTAWA MODEL for SMOKING CESSATION (OMSC)

Initial consultation, cessation medications, patient education, 8 automated telephone follow-ups, with nurse consultation by phone if relapse. 30.5% abstinence rate

- Reduced ED visits and hospital re-admissions, both smoking and non-smoking related
- Reduced mortality at 1 year
- Cost per Quality Adjusted Life Year (QALY): $68

Mullen KA et al. (2016) Tobacco Control
Mullen KA et al. (2015) Tobacco Control

TOBACCO CESSATION TREATMENT in PATIENTS with CHD

- Positive long-term treatment effect: OR = 1.22
  - Brief interventions: OR = 1.01 (not significant)
  - Self-help: OR = 1.22
  - Telephone support: OR = 1.21
  - Behavioral therapies: OR = 1.23
  - Intense interventions (follow-up >1 mo): OR = 1.28

Behavioral smoking cessation interventions in patients with CHD are effective in promoting abstinence at 1 year, provided they are of sufficient duration.

Meta-analysis, 40 trials (N=2677), 1974-2013

SMOKE-FREE HOMES & WORKPLACES

- Smoke-free homes and workplaces protect people from SHS and help smokers quit

Mills et al. (2008). Nicotine Tob Res.
Calvillo et al. (2010) Cochrane

FUNDAMENTAL PRINCIPLE

Treat smoking in exactly the same way that you would manage any other cardiovascular disease risk factor

A. Pipe (2013) The Ottawa Model of Smoking Cessation

TOBACCO TREATMENTS with DEMONSTRATED EFFICACY

- Physician Advice
- Formal Smoking Cessation Programs
  - Individual Counselling
  - Web and telephone
  - Group Programs
  - Texting interventions
- Medications
  - NRT
  - Bupropion
  - Varenicline
  - Cytisine*

* Not available in the US
TOBACCO TREATMENTS LACKING EVIDENCE of EFFICACY

- SSRIs and SNRI
- Anxiolytics:
  - Sedative, hypnotics, buspirone
- Homeopathic treatments
- Hypnotherapy
- Herbal supplements
- Lobeline
- Massage therapy
- Acupuncture
- Laser therapy
- Nicotine Anonymous
- E-cigarettes

WHAT IF...
a patient asks you about your use of tobacco?

THE HEALTH PROFESSIONAL

- Be a non-tobacco using role model
- Advocate for programs to support health professionals to quit using tobacco
- Advocate for tobacco-free hospitals and worksites
- Refuse funding from the tobacco industry

THE CARDIOLOGY TEAM’S RESPONSIBILITY

The cardiology team has a professional obligation to address tobacco use & exposure

ADDRESSING TOBACCO USE & EXPOSURE is an ESSENTIAL COMPONENT of CVD TREATMENT for ALL PATIENTS

SET REALISTIC EXPECTATIONS

- It’s a learning process. Reframe success!
- With each attempt, the patient learns new strategies for addressing triggers to use
- Longer prior quit attempts predict future success!

MAKE a COMMITMENT...

Address tobacco use and secondhand smoke exposure with all patients.
At a minimum, commit to incorporating brief tobacco interventions as part of routine patient care:

Ask, Advise, and Refer

Become an advocate for smoke-free hospitals and clinics, workplaces, and public places.
If you smoke, set a quit date and get help with quitting

Copyright © 1999-2017 The Regents of the University of California. All rights reserved. Updated July 2017.
Cardiologists have an Important Responsibility

- Refuse collaboration and funding from the Tobacco Industry
- Be non-tobacco using role models
- Advise tobacco users to quit and tell all patients to avoid SHS
- Approach tobacco use as a chronic disease; document smoking status
- Help reduce premature mortality from CVD by 25% by 2025
- Ensure cessation support is accessible
- Provide medical students with the skills and motivation to treat tobacco use
- Support smoke-free healthcare and educational facilities

Forms of Tobacco

- Manufactured and roll-your-own (RYO) cigarettes
- Smokeless tobacco
- Other forms of smoked tobacco
  - Clove cigarettes (kreteks)
  - Bidis
  - Waterpipes
- Electronic cigarettes
  - E-cigarettes are devices that deliver nicotine and are not a form of tobacco

American Cigarettes

- Most common form of tobacco used in U.S.
- Sold in packs (20 cigarettes/pack)
- Total nicotine content, per cigarette: Average 13.5 mg (range, 11.9 to 14.5 mg)
- Machine-measured nicotine yield:

<table>
<thead>
<tr>
<th>Type of cigarette</th>
<th>Yield per cigarette</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full-flavor (regular)</td>
<td>1.1 mg</td>
</tr>
<tr>
<td>Light</td>
<td>0.8 mg</td>
</tr>
<tr>
<td>Ultra-light</td>
<td>0.4 mg</td>
</tr>
<tr>
<td>Average (all brands)</td>
<td>0.9 mg</td>
</tr>
</tbody>
</table>

- Smoker’s nicotine yield, per cigarette: 1-2 mg

Smokeless Tobacco

- Prevalence of smokeless tobacco use and the type used varies widely by region and gender
  - Over 25 types of smokeless used globally
- Smokeless products used both orally and nasally
- Dual Users = people may use both smokeless and smoked tobacco
- Nicotine exposure comparable to smokers with physical dependence and withdrawal symptoms

Health Consequences of Smokeless Tobacco Use

- Periodontal effects
  - Gingival recession
  - Bone attachment loss
  - Dental caries
- Oral leukoplakia
- Cancer
  - Oral cancer
  - Pharyngeal cancer
- Cardiovascular
  - Fatal MI (13% more likely)
  - Fatal stroke (40% more likely)
CLOVE CIGARETTES (KRETEKS)
- Mixture of tobacco and cloves
- From Indonesia
- Two times the tar and nicotine content of standard cigarettes

BIDIS
- Primarily used in India and other Southeast Asian countries
- Small, hand-rolled cigarettes
- Deliver 3-fold higher levels of carbon monoxide and nicotine and 5-fold higher levels of tar when compared to standard cigarettes

WATERPIPE SMOKING
- Also known as Shisha, Narghile, Goza, Hookah
- Tobacco flavored with fruit pulp, honey, and molasses
- Nicotine, tar and carbon monoxide levels comparable to or higher than those in cigarette smoke

CIGARS
- Estimated 13.3 million cigar smokers in the U.S. in 2009 (5% of people 12 yrs or older)
- Tobacco content of cigars varies greatly
- One cigar can deliver enough nicotine to establish and maintain dependence
- Use of small cigars (cigarillos) carries same risk as cigarettes

PIPE TOBACCO
- Pipe smokers have an increased risk of death due to:
  - Cancer (lung, oral cavity, esophagus, larynx)
  - COPD
- Risk of tobacco-related death:
  - Cigarettes > pipes ≈ cigars

POtentially reduced-exposure products (PREPs)
- Tobacco formulations altered to minimize exposure to harmful chemicals in tobacco
  - Cigarette-like delivery devices
    - Eclipse, Heatbar
  - Oral noncombustible tobacco products
    - Ariva, Marlboro Snus, Stonewall, Camel Snus
- No evidence to prove that PREPs reduce the risk of developing tobacco-related disease
SUMMARY: FORMS of TOBACCO

- Prevalence of different forms of tobacco use differs across countries and locales, and often by gender
- Safety/efficacy of e-cigarettes is not established
- Attention to all forms of tobacco is needed

WHO FRAMEWORK CONVENTION on TOBACCO CONTROL (FCTC)

- First global public health treaty
  - Developed to address the tobacco epidemic
  - Seeks to reduce the demand and supply of tobacco
- Adopted by the World Health Assembly in 2003
  - In force February of 2005
  - Currently, 181 countries are parties to the FCTC

FCTC DEMAND ARTICLES 6-14

- Price and tax measures
- Protection from SHS
- Tobacco product regulation
- Education, training, communication, and public awareness
- Tobacco advertising, promotion and sponsorship
- Packaging and labelling
- Tobacco dependence and cessation

FRAMEWORK CONVENTION ALLIANCE

- The FCA is a civil society alliance made up of 350 organizations working to support the development, ratification, and implementation of the FCTC
- FCA Mission: "to help develop and implement the FCTC as the basis for effective global tobacco control."

NON-COMMUNICABLE DISEASES (NCD) ALLIANCE

- 2011 United Nations High-Level Meeting on NCDs
- Agreed to tackle world’s major NCDs
- World Heart Day: Sept 29th
- NCD Alliance: http://www.ncdalliance.org/
  - Aims to put non-communicable disease, including CVD on the global agenda
  - Tobacco is risk factor shared by main NCDs
  - Strategic Plan 2016-2020
  - Obtained an NCD target as part of 2030 Agenda for Sustainable Development – Reduce premature mortality from NCD’s by 33%
"If we do not act decisively, a hundred years from now our grandchildren and their children will look back and seriously question how people claiming to be committed to public health and social justice allowed the tobacco epidemic to unfold unchecked."