Smoking Cessation in Cardiac Patients
University of Vermont
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Quinn R. Pack, MD, MSc, FACC, FAHA, FAACVPR
Associate Professor of Medicine
Non-Invasive and Preventive Cardiologist
Medical Director, Cardiac Rehabilitation and Wellness
University of Massachusetts Medical School – Baystate
Springfield, MA
Conflicts

- No conflicts of interest
- Will briefly discuss off-label use of NRT
- Grant Support
  - NHLBI grant #R01 HL156851-01 – Studying the implementation and effectiveness of a hospital-based tobacco treatment team
  - NIA grant #AG077179-01 – Comparing RPE and THRR on outcomes in cardiac rehabilitation
  - NHLBI grant #K23 HL135440- Studying the role of the hospital in improving cardiac rehabilitation uptake
“Giving up smoking is the easiest thing in the world. I know because I've done it thousands of times.”

- Mark Twain
March 2017

- 53 year-old man with chest pain and STEMI
  - PCI to mid-LAD was successful
  - Echo showed EF of 25-30% with anterior MI
  - Discharged 2.5 days later
  - Discharge meds: aspirin, clopidogrel, high-intensity statin, beta-blocker, ACEi, CR referral, even ... spironolactone

- Congratulations all around, nice work! 😊
The problem

- This man was a smoker.
- Discharged with:
  - no smoking cessation medications
  - no documented counseling
- PCP visit – 2 weeks later → nothing done
- Cardiac rehab – 3 weeks → given advice
- Cardiology – 6 weeks → prescribed varenicline
Special Communication

March 10, 2004

Actual Causes of Death in the United States, 2000

Ali H. Mokdad, PhD; James S. Marks, MD, MPH; Donna F. Stroup, PhD, MSc; et al

Author Affiliations


- #1: Tobacco: 485,000 deaths, (18.1%)
- #2: Poor diet & physical inactivity: 400,000 (16.6%)
- #3: Alcohol 85,000 (3.5%)
  - 2016: Opioid overdose – 68K
  - 2020: COVID – 375K
CV Mortality Decline

FIGURE 1. Age-adjusted death rates* for total cardiovascular disease, diseases of the heart, coronary heart disease, and stroke,† by year — United States, 1900–1996

*Per 100,000 population, standardized to 2000 U.S. standard population
†Excludes hypertension and peripheral arterial disease
Basification allows smoke to be inhaled – increasing nicotine delivery.
Smokers lose 11 years of life to their addiction!

Pirie et al., *Lancet* 2013; 381: 133–41

*Figure 5: All-cause mortality: Illustration of the effects of a 3-fold difference in annual death rates on mortality from age 35 years to age 80 years*
Interventionalist View of World

Figure 1. Decline in Deaths from Cardiovascular Disease in Relation to Scientific Advances.
Explaining the Decline in Coronary Heart Disease Mortality in England and Wales Between 1981 and 2000

Belgin Unal, MD, MPH; Julia Alison Critchley, DPhil; Simon Capewell, MD

Unal, Circulation 2004
2017 Smoking Rates
Tobacco Control in the Obama Era — Substantial Progress, Remaining Challenges

Michael C. Fiore, M.D., M.P.H., M.B.A.
Survey: Tobacco Related Diseases

❖ How many tobacco related diseases can you think of?
Tobacco Related CV-Diseases

- Sudden death
- Coronary artery disease (CABG, PCI)
- Myocardial Infarction
  - 50% of STEMI patients!
- Peripheral vascular disease
  - most important risk factor for in PAD
- Aneurysms (Thoracic, AAA, cerebral)
- Stroke
More Tobacco Related Diseases

- COPD (emphysema, chronic bronchitis)
- Asthma
- Pneumonia
- Osteoporosis
- Premature birth, pregnancy complications, miscarriage
- Peptic ulcer disease
- DVT
- PE
Tobacco Related Cancers

- Lung
- Throat, tongue, pharynx
- Esophageal, stomach
- Kidney, bladder
- Pancreas
- Cervical

The list goes on....
Addiction Severity

**Addiction, no order**
- Alcohol
- Caffeine
- Cocaine
- Heroin
- Marijuana
- Tobacco

**In Order, worst on top**
- Cocaine
- Tobacco
- Heroin
- Alcohol
- Marijuana
- Caffeine
Tobacco Addiction

- Former users agree, the only addiction harder to kick is cocaine. (Not heroin, marijuana, alcohol, caffeine)
  - In perspective, only 64,000 people died in 2016 from opioid overdose
- Should be viewed as a chronic disease
- I feel sorry for these people
Drug Delivery

- **Inhaled nicotine**
  - Lungs $\rightarrow$ LV $\rightarrow$ brain
  - Total transit time is about 7 seconds
  - Causes dopamine release (reward)
  - Faster than IV medicines
  - Faster than mucosal medicines (SL Nitro)
- This makes inhaled nicotine ideal for addictive potential
Nicotine Replacement Pharmacology

- With the exception of the nasal spray, NRT arrives too slowly to the brain to produce addictive reward potential.
Tobacco Addiction

- Tobacco dependence exhibits classic characteristics of drug/nicotine dependence
  - Causes physical dependence characterized by withdrawal symptoms upon cessation
  - Is psychoactive
  - Produces tolerance
  - Use persists despite consequences

Symptoms of Withdrawal

- Symptoms peak between 1-2 weeks:
  - Dysphoric or depressed mood
  - Insomnia
  - Irritability, frustration, or anger
  - Anxiety, difficulty concentrating
  - Restlessness
  - Decreased heart rate
  - Increased appetite or weight gain

- Can be observed in the hospital
Nicotine Cravings

- Are highly sensitive to environmental cues
  - Morning coffee and news
  - Driving in the car
  - Phone calls, meals, alcohol

- Cravings decrease with time from cessation

- For many smokers, cravings never completely go away, even decades later
Inpatient Smoking Cessation

- Urges to smoke are much lower in the hospital
  - “I won’t have a problem when I get home”
  - “I’m not having withdrawal”
  - “I already quit.”

- In truth, withdrawal peaks around 1-2 weeks after smoking cessation, usually long after hospital discharge.
Realities of Relapse

- Most smokers (80%) want to quit
- Most (65%) of smokers will relapse
- Median time to relapse is within 7 days
  - 5% of motivated patients relapse within 1 hour of discharge!
- Smoking cessation interventions should begin in the hospital

Riley, JCRP 2018; Colivicchi et al, Am J Cardiol. 2011;108:804-808; CMAJ March 2018
Cessation Meds after ACS

**In Hospital**
- Only 22% of patients get meds of any kind
- Hospital-dependent

**After Hospital**
- Only 7.0% got either varenicline or bupropion
- Clinician-dependent

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Pack et al, JAMA-IM 2017; Pagitipadi JAMA-Card 2017; Sardana, JAHA, 2019
“Tobacco use presents a rare confluence of circumstances:
• a highly significant health threat.
• a disinclination among clinicians to intervene consistently, and
• the presence of effective interventions.
Indeed, it is difficult to identify any other condition that presents such a mix of lethality, prevalence, and neglect, despite effective and readily available interventions.”

*Michael Fiore – 2008 Guidelines*
Fellows Clinic

- Two fellows – same day, both with patients with CAD
- “My patient has tried everything to quit smoking”

- Patient 1
  - Quit for 7 days on the 21mg patch then relapsed
  - Varenicline caused abnormal dreams

- Patient 2
  - Quit for 4 weeks on varenicline then relapsed
  - 14 mg patch was ineffective
  - 2 mg gum was ineffective
2018 ACC Expert Consensus Decision Pathway on Tobacco Cessation Treatment

A Report of the American College of Cardiology Task Force on Clinical Expert Consensus Documents
Key Points:

- Tobacco is a chronic relapsing disease
- Keep this on the problem list
- Second hand smoke is still a problem
Counseling

- Motivational interviewing
- Skills training
- Self-monitoring
- Stress management/mindfulness
- Alter environment to avoid triggers
## 5-Steps

### 5 A’s
- Ask
- Advise
- Assess Willingness
- Assist
- Arrange Follow-up

### 5 R’s
- Risks
- Rewards
- Roadblocks
- Relevance
- Repetition
Meds: Do they Work?

- Most smokers fail when trying to quit, but that doesn’t mean the medicines don’t help.
- From my perspective, the glass is half-full.

*PERCEPTION*

Is The Glass Half Empty or Half Full?  
It's A Glass of Water! Get Over It!
Nicotine Replacement Therapy (NRT)

- Nicotine is active ingredient
- Nicotine does not cause cancer or heart disease!
- Use of NRT doubles a patient’s chance of quitting
270 hospitals and 27,459 patients with AMI

17.8% got NRT in the first 2 days

After propensity matching and adjustment there was **no** difference in:

- Mortality (2.1% vs 2.3%, P=0.98)
- Length of stay (4.4 days vs 4.3, P=0.60)
- Cost ($10,502 vs. $10,428, P=0.57)
- Readmission (15.8% vs. 14.6% P=0.31)
Nicotine patch

- Available as both prescription and OTC
- OR = 1.9 (1.7, 2.2) to quit

Common side effects
- Rash → rotate sites! Add 0.1% triamcinolone
- Bad dreams → lower the dose or remove patch at bedtime

Smoking on the Patch

- Smokers often mention old statements to not smoke on while on the nicotine patch.
- The FDA removed this warning in April 1, 2013.
Nicotine (under) replacement

- 22 mg patch replaces only 45-65% of baseline nicotine levels
- No toxicity at 44 mg
- 1 ppd ≠ 21 mg patch
  - Never use 7mg patch
  - Rare use 14 mg patch
- By extension
  - Rare use of 2mg gum or lozenge

Lawson, J Clin Pharm 1998
High-dose transdermal nicotine replacement for tobacco cessation

Laurie Brokowski, Jiahui Chen, and Sara Tanner

- 10 small trials (~1500 patients) with doses between 42 and 63 mg/day
- No serious side effects
- Favorable effects on short-term smoking cessation, but long-term effects were mixed
- Titration seems to be the key
- Note: Higher than 21 mg/day is an off-label use of NRT patch

Brokowski et al, AM J Health Syst Pharm. Apr 2014; 71 (8):634
Nicotine gum & lozenge

- Available OTC: 2 mg, 4 mg
- Gum OR = 1.5 (1.2, 1.7)*
- Lozenge OR = 2.0 (1.6, 2.5)**
- Ideal use
  - “Chew and park”
  - Avoid soda, coffee, OJ – acidic foods
- Common side effects
  - Hiccups, dyspepsia → don’t swallow

** Stead LF et al. Cochrane Database of Systematic Reviews, 2010.
Nicotine inhaler and nasal spray

- Available only by prescription
- OR = 2.1 (1.5, 2.9)

Notes:
- Nasal spray has addictive potential
- Inhaler is usually $$$

Bupropion SR

- Mechanism of action: blocks neural reuptake of dopamine and/or norepinephrine
- OR = 2.0 (1.8, 2.2)
- Quit on day 8
- Contraindicated in patients with h/o seizure or heavy alcohol
- Common side effect
  - insomnia, dry mouth

Varenicline

- Partial agonist actions at $\alpha_4\beta_2$ receptors
- Most effective agent on market
  - Starter pack
  - Continuing pack
  - Now generic
- Common side effects:
  - Nausea → take with food, reduce dose
  - Vivid dreams → dose daily or AM/noon instead of BID
Combination Therapy

- More effective than isolated therapy

- Common Permutations
  - Patch + Lozenge
  - Patch + Gum
  - Patch + Inhaler
  - Patch + Nasal spray
  - Bupropion + Lozenge
  - Bupropion + Gum
  - Varenicline + patch
  - Varenicline + patch + gum
Medications

“Pharmacotherapy ... should be encouraged for virtually all daily smokers.”

First line medications:
- Varenicline
- Patch and ad-lib NRT

Ideal:
- Varenicline + patch + lozenge

<table>
<thead>
<tr>
<th>Less effective</th>
<th>Effective</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Low-dose nicotine patch (7, 14 mg) or gum (2mg)</td>
<td>- Nicotine patch, adequately dosed and tailored (21 to 42 mg)</td>
</tr>
<tr>
<td>- 4 weeks of use</td>
<td>- Nicotine gum (4mg), lozenge (4mg), or inhaler</td>
</tr>
<tr>
<td>- Stopping medications with lapse</td>
<td>- Bupropion SR</td>
</tr>
<tr>
<td></td>
<td>- Continuing medication use even with lapses</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>More Effective</th>
<th>Most Effective</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Varenicline</td>
<td>- Varenicline + adequately dosed nicotine patch (21 to 42 mg)</td>
</tr>
<tr>
<td>- Combination nicotine replacement therapy (e.g. patch + gum)</td>
<td>- Varenicline + combination nicotine replacement therapy</td>
</tr>
<tr>
<td>- Bupropion + NRT</td>
<td>- Varenicline + bupropion</td>
</tr>
<tr>
<td>- 3 months of use</td>
<td>- 6 months of use</td>
</tr>
</tbody>
</table>

Table 1. Optimal prescribing practices for smoking cessation
Fellows Clinic

- Two fellows – same day, both with patients with CAD
- “My patient has tried everything to quit smoking”

**Patient 1**
- Quit for 7 days on the 21mg patch then relapsed
  - Rash - was not rotating skin site!
- Varenicline caused abnormal dreams
  - Dose only in the morning (1mg)
- Added counseling

**Patient 2**
- Quit for 4 weeks on varenicline then relapsed
  - Was prescribed only 4 weeks of medications. “Completed therapy”
- 14 mg patch/2 mg gum was ineffective
  - Never tried combination meds
  - Underdosing likely a problem
Cutting Down

- Factors that influence nicotine yield from a cigarette:
  - Puff volume
  - Depth of inhalation
  - Dilution with room air
  - Rate and intensity of puffing

- Often, cutting down does NOT change blood nicotine levels

Naiura et al, Psychopharmacology (2013) 230:261
Secondhand Smoke and Cardiovascular Risk

Smoking cessation, but not reduction, reduces cardiovascular disease incidence

Su-Min Jeong\textsuperscript{12}, Keun Hye Jeon\textsuperscript{21}, Dong Wook Shin\textsuperscript{1.3a}, Kyungdo Han\textsuperscript{4}, Dahye Kim\textsuperscript{5}, Sang Hyun Park\textsuperscript{8}, Mi Hee Cho\textsuperscript{6}, Cheol Min Lee\textsuperscript{7}, Ki-Woong Nam\textsuperscript{8}, and Seung Pyo Lee\textsuperscript{9}

- **898K smokers**
  - 3 waves
- **4 statuses**
  - Sustained quitter
  - Sustain smoker
  - Reduce by $<50\%$
  - Reduces by $>50\%$
  - Relapsed

Relapsed smoking was associated with increased risk of stroke and MI.
* No statistical significance
Change in mental health after smoking cessation: systematic review and meta-analysis

Gemma Taylor *doctoral researcher*¹², Ann McNeill *professor of tobacco addiction*²³, Alan Girling *reader in medical statistics*¹, Amanda Farley *lecturer in epidemiology*¹², Nicola Lindson-Hawley *research fellow*²⁴, Paul Aveyard *professor of behavioural medicine*²⁴

- 26 studies included
- Evaluated anxiety, depression, stress, quality of life, positive affect
- Smoking cessation consistently improved mental health

*BMJ* 2014;348
Mental Health

Effect size equivalent or larger than antidepressant medications
Neuropsychiatric safety and efficacy of varenicline, bupropion, and nicotine patch in smokers with and without psychiatric disorders (EAGLES): a double-blind, randomised, placebo-controlled clinical trial

Robert M Anthenelli, Neal L Benowitz, Robert West, Lisa St Aubin, Thomas McRae, David Lawrence, John Ascher, Cristina Russ, Alok Krishen, A Eden Evins

- 8,144 smokers, half with history of neuropsych disorders, currently stable
- 140 centers, 16 countries, 6-month follow-up
- Randomized to placebo, varenicline, bupropion, nicotine patch

Lancet, April 22, 2016
EAGLES Results

[Bar chart showing continuous abstinence rates for different treatments and cohorts over weeks 9-12 and 9-24.]
EAGLES – Psych Side Effects

FDA removed the Black Box warning from varenicline

Smoking cessation (not varenicline) is a risk factor for mental health problems
Long-term Nicotine Replacement Therapy
A Randomized Clinical Trial

Robert A. Schnoll, PhD; Patricia M. Goelz, MPH; Anna Veluz-Wilkins, MA; Sonja Blazekovic, BA.

- 525 smokers
  - 8 weeks NRT
  - 24 weeks NRT
  - 52 weeks NRT

- Outcomes
  - 21.7% vs 27.2% quit rates
  - OR 1.7, p = 0.04

- Treat for 3-6 mo

JAMA Intern Med, 2015; 175 (4):504
Weight Gain after Cessation

- **Weight gain**
  - Average is 8-12 lbs.
  - 15% increase in DMII

- **But, it is NOT all fat**
  - 28% is lean body mass!
  - ↑ bone density
  - ↑ muscle strength

- **Mortality decreases!**
  - Some weight gain is important

Optimal Treatment for Hospitalized Smokers

- Personalized counseling while hospitalized
- Varenicline and/or combination NRT at discharge
  - 6 months of medications
- Use of smokefree.gov or becomeanex.org
- Follow-up counseling within just a few days
- Cardiac rehab enrollment within 1 week
- Long-term medications and follow-up
Conceptual Model - STOP-NPT3 Trial

**Evidence Based Practice**
- Inpatient assessment and counseling
- Tailored smoking cessation medications in virtually all patients
- >1 month supportive counseling and follow-up

**Key Barriers**
- Low urgency, lack of time among clinicians
- Lack of clinician experience and confidence
  - Patient misconceptions about the value of medications
- Limited follow-up after discharge

**Implementation Strategies**
- Dedicated NPT3 team with clinical billing
- Direct prescription by the NPT3
- Medication adherence-based counseling
- Text-messages to sustain motivation and keep patients connected

**Outcomes**

<table>
<thead>
<tr>
<th>Implementation</th>
<th>Effectiveness</th>
<th>Economic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guideline concordant medication use 7 days after d/c</td>
<td>Smoking cessation at 6 months</td>
<td>Cost-effectiveness (payers)</td>
</tr>
<tr>
<td>Satisfaction, adherence (patients)</td>
<td>Cigarettes per day</td>
<td>Cost-Revenue (hospitals)</td>
</tr>
<tr>
<td>Acceptability (clinicians)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sustainability (Administrators)</td>
<td></td>
<td>Hospitalization &amp; ER visits</td>
</tr>
</tbody>
</table>

**Mediator:** Medication prescription and use in the hospital and at discharge
STOP-NPT³ Trial Overview

- 424 hospitalized smokers with MI, HF, COPD, asthma
- 1:1 randomized
  - Control
  - NPT3 intervention
- Outcomes
  - Medication use at 7 days
  - Cessation at 6 months
  - Cost effectiveness
  - Acceptability
Vaccines are the only preventive health measure that is more cost-effective than smoking cessation.

Aboyans et al, Curr Opin Cardiol 2009 25:469–477
Thank you!

Quinn.PackMD@baystatehealth.org
Which statement is TRUE?

1. Smoking is no longer a significant health problem in the United States
2. Cutting down on cigarettes is a sign of reduced nicotine addiction
3. Lack of cravings while hospitalized predicts long-term success in quitting
4. Smoking cessation reduces a person’s stress levels
5. Nicotine patch can be addictive
Which statement is TRUE?

1. Varenicline use is a risk factor for suicide
2. Smoking while on the nicotine patch is unsafe
3. NRT is safe during the first 2 days of a heart attack
4. 21 mg nicotine patch is the maximal safe dose
5. Smoking cessation medications should not be combined
6. NRT should be tapered and discontinued with 1-2 months
Smoking & Cardiac Rehab

Smokers:
- More like to be referred
- Less likely to enroll
- More likely to drop out
- Relapse is related to drop out

Attendance
- Doubles the chance to stay quit long term

Table 3

<table>
<thead>
<tr>
<th>Attended CR(^a)</th>
<th>Yes</th>
<th>No</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remained abstinent from smoking(^a)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>26 (32%)</td>
<td>12 (15%)</td>
<td>38 (47%)</td>
</tr>
<tr>
<td>No</td>
<td>10 (12%)</td>
<td>33 (41%)</td>
<td>43 (53%)</td>
</tr>
<tr>
<td>Total</td>
<td>36 (44%)</td>
<td>45 (55%)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviation: CR, cardiac rehabilitation.
\(^a\)Assumes that those who did not complete follow-up (N = 19) did not attend CR and relapsed to smoking. If these patients are excluded, there is still a relationship between CR attendance and smoking cessation (OR: 3.0, P = .037).

Sochor, Am J Cards, 2015; Riley et al, JCRP 2019
Case – 2016

- 51 y/o woman with recent STEMI, PCI to D2, EF now 45%
- Now in clinic, still smoking
- Smoker, since age 12
  - What kinds of things should you ask about?
  - What do you want to know?
History

- PMH: Anxiety, no depression
- Social: No EtOH use, Stress OK, Finances OK
- Tobacco addiction:
  - 1st cigarette upon waking up
  - Previously a 2-3 ppd smoker, trying to cut down
- Limited prior success
  - Best attempt was with Bupropion (1 cig/day)
  - Varenicline made no difference
  - Smoked on the patch
Coaching

- Set quit date, in 1 week
- Quick follow-up after quit date
- Change AM routine (to help with 1st cig.)
- Tell friends, garner support, no alcohol
- In cardiac rehab (exercising)
- 1-800-QUIT-NOW
- What meds would you suggest?
Medications

- Bupropion SR 150 mg BID
- Nicotine patch 21 mg + 7 mg
- Nicotine inhaler, at least 3-4 times/day and PRN with urges
Short Term Pathophysiology

- Catecholamine release (sudden death)
- Hypercoagulability
- Hypoxia (carbon monoxide)
  - Carboxyhemoglobin can be 5-10%
- Coronary vasoconstriction
- Increased BP and HR
  - Increased myocardial work

Benowitz and Gourlay, JACC 1997; 29:1422-31
Long Term Pathophysiology

- Decreases HDL, increase VLDL
- Endothelial toxicity
- Oxidative Injury
- Neutrophil Activation (inflammation)
- Chronic hypercoagulability