



UW PACC

Psychiatry and Addictions Case Conference

UW Medicine | Psychiatry and Behavioral Sciences

UPDATE
TREATMENT OF TOBACCO USE
DISORDERS

MARK DUNCAN MD

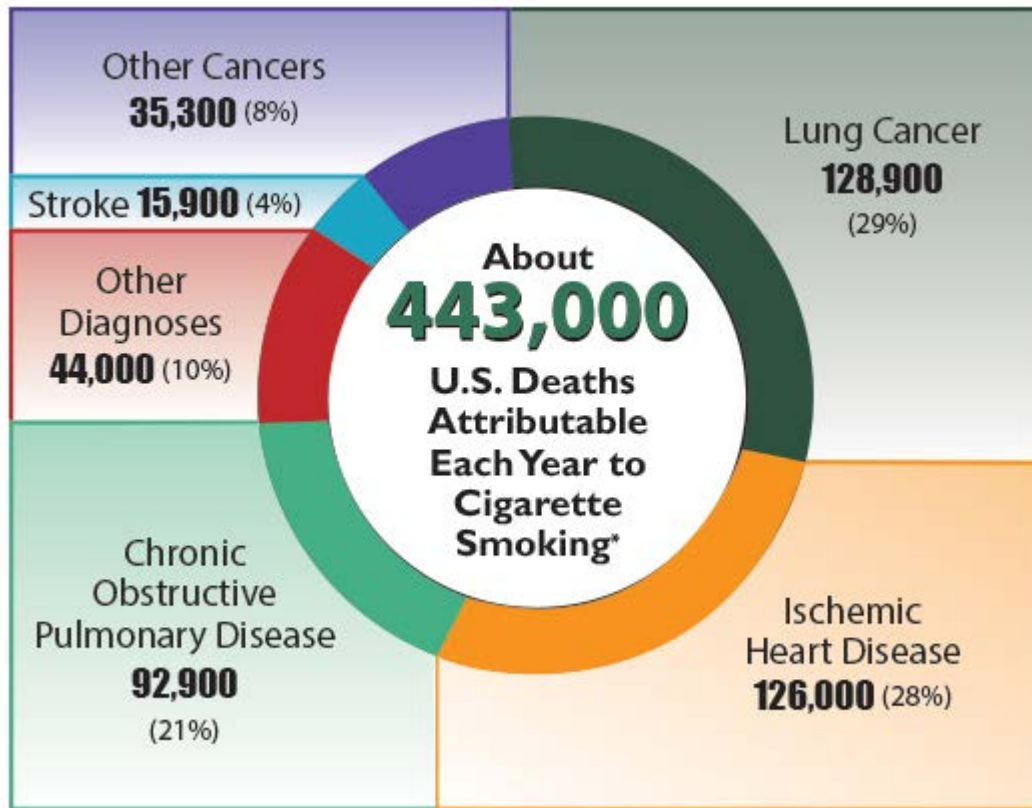
UNIVERSITY OF WASHINGTON



OBJECTIVES

1. Remind everyone that tobacco kills a lot of people
2. Provide update on treatment of tobacco disorders
3. Urge everyone to offer treatment

LEADING PREVENTABLE CAUSE OF PREMATURE DEATH IN THE US



[http://www.cdc.gov/tobacco/data_statistics/tables/health/attrdeaths/index.htm?utm_source=feedburner&utm_medium=feed&utm_campaign=Feed%3A+cdc%2FGELa+\(CDC+-+Smoking+and+Tobacco+Use+-+Main+Feed\)](http://www.cdc.gov/tobacco/data_statistics/tables/health/attrdeaths/index.htm?utm_source=feedburner&utm_medium=feed&utm_campaign=Feed%3A+cdc%2FGELa+(CDC+-+Smoking+and+Tobacco+Use+-+Main+Feed))

BENEFITS OF STOPPING

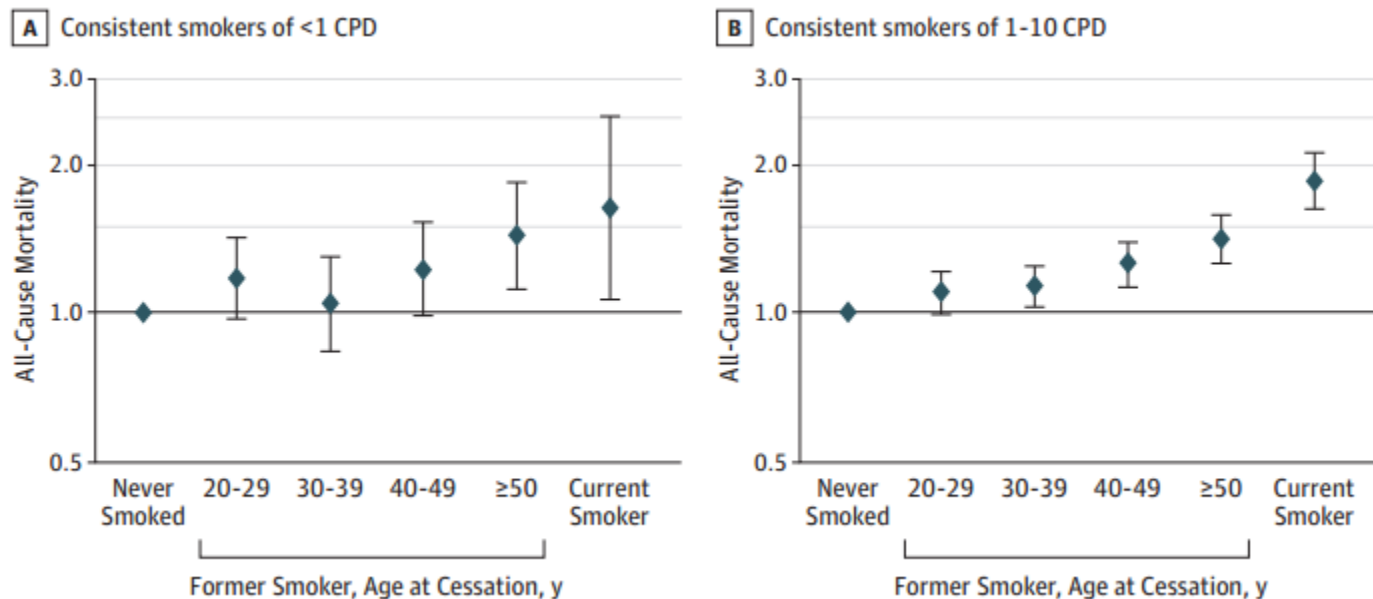
- Reduce CV risk after MI by $> 1/3$ over 5 years
- Reduce cancer risk
- Improve lung function
- Reduce risk of infections
- Decreased risk for DMII
- Reduce risk of hip fractures
- Decrease reproductive disorders
- Etc.

Smoking reduction vs cessation?

- Maybe helpful for heavy smokers-controversial
- Smokers often compensate

Association of Long-term, Low-Intensity Smoking With All-Cause and Cause-Specific Mortality in the National Institutes of Health–AARP Diet and Health Study

Maki Inoue-Choi, PhD, MS; Linda M. Liao, PhD, MPH; Carolyn Reyes-Guzman, PhD, MPH; Patricia Hartge, ScD; Neil Caporaso, MD; Neal D. Freedman, PhD, MPH



- Bottom-line: No safe level of smoking

SPECIAL POPULATIONS

- Psychiatric illness: no evidence that cessation worsens illness.
- Substance Use: no evidence cessation has a negative effect, often has positive effect.

McKelvey et al, Addictive Behaviors 2016; Apollonio et al, Cochranne 2016

Psychol Med. 2014 Sep;44(12):2523-35.

Smoking cessation is associated with **lower rates of mood/anxiety and alcohol use disorders.**

Cavazos-Rehg PA1, et al.

Abstract

BACKGROUND:

The psychological outcomes that accompany smoking cessation are not yet conclusive but positive outcomes could help to persuade quitting.

RESULTS:

Quitting predicted a decreased risk of mood/anxiety disorder [adjusted odds ratio (aOR) 0.6, 95% confidence interval (CI) 0.4-0.9] and alcohol disorder (aOR 0.7, 95% CI 0.5-0.99)

Among daily smokers quitting smoking predicted a decreased risk of drug use disorder (aOR 0.3, 95% CI 0.1-0.9).

CONCLUSIONS:

There is no support in our data for the concern that smoking cessation would result in smokers' increased risk of some mental disorders. **To the contrary, our data suggest that smoking cessation is associated with risk reduction for mood/anxiety or alcohol use disorder, even among smokers who have had a pre-existing disorder.**

TREATMENT UPDATES

THE “5 A’S” MODEL

- **Ask**
 - Frequency
 - Products
 - Previous quit attempts
 - Readiness to quit
- **Advise to quit**
 - < 5 min
 - At every encounter
 - Modest effectiveness, BUT STILL EFFECTIVE
 - Patients are satisfied
- **Assess Readiness to change**
- **Assist**
 - Help with a quit plan (and date)
 - Provide practical problem solving
 - Manage withdrawal symptoms
 - Combined behavioral and pharmacological treatments most effective
 - Insurances are required to cover treatments

ARRANGE FOLLOW-UP

- **The week following their quit date**
 - Assess med adherence and any problems
- **Relapse prevention**
 - Good to follow closely over **first 3 months** due to high rates of relapse during this time (22%)
 - Long term follow-up needed
 - 35-40% will relapse between 1-5 years
 - **Pharmacotherapy for up to 18 months can be helpful**
 - No evidence to support any specific behavioral interventions for relapse prevention.
 - Best bet to focus on identifying and resolving triggers
- **Relapse?**
 - Make another attempt
 - What worked before?
 - More intense treatment?
 - **Specialty clinic**

QUITTING: BEHAVIORAL

CBT

- Counseling to avoid triggers and deal with situations that may tempt smoking
- Self monitoring
- Reduction in cigarettes prior to quit date
- Identifying triggers
- Problem solving
- ACE
 - Avoid-high-risk environments
 - Change-alter high-risk environment
 - Escape-plan how to excuse oneself

Coping with Urges

- Behavioral distraction-engage in repetitive or simple activities
- Cognitive distraction-think about what needs to be done
- Food and drink-drink a glass of water or have a snack
- Oral fixation-gum
- Positive self-talk and visualization
- Benefits of quitting



QUITTING: BEHAVIORAL

- Group or Individual therapy is effective
 - Individual: brief interventions work
 - Group: informational meetings, self-monitoring, tapering instructions, work on coping skills
- Telephone counseling
 - Proactive-calls from counselors to smokers work better
 - 2008 Australian study of GPs n=771
 - 12 month follow-up OR =2.86 (6.5% vs 2.6%)
 - Reactive-calls to quit lines-not better than self-help literature
 - 1-800-QUIT-NOW
 - Have the patient check their insurance plan for specifics
 - <http://www.doh.wa.gov/YouandYourFamily/Tobacco/HowtoQuit>

FDA APPROVED MEDICATIONS & 1ST LINE TREATMENT

- Nicotine Replacement Therapy
- Varenicline
- Bupropion

NICOTINE REPLACEMENT THERAPY

- Can increase quit rates vs placebo 2 fold
- **Combination therapy** -better then monotherapy for effectiveness
 - (RR 1.34, 95% CI 1.18 to 1.51)
 - Long-acting patch for baseline withdrawal symptoms
 - Short-acting for cravings or withdrawal symptoms prn
 - **Start on quit date**

TRANSDERMAL NICOTINE PATCH

- 24 hour relief, several hours to peak
- >10 cigg/day (1/2 pack)
 - 21mg/day x 6 weeks, 14mg/day x 2 weeks, 7mg/day x 2 weeks
- <10 cigg/day or <45kg
 - 14mg/day
- Start on quit day!
- Rotate patch site daily, non-hairy site
- Can remove patch at night to avoid potential insomnia or vivid dreams
- Longer then 6 weeks of use may be helpful
- Cost without insurance per patch (21mg): \$25.98

Equate Step Two Clear Transdermal System Nicotine Patches, 14mg

★★★★☆ 31 reviews Q&A By: Equate Walmart #: 004079679



SHORT-ACTING NICOTINE REPLACEMENT

- To control cravings: Gum
 - >25 cigarettes/day → 4mg dose
 - <25 cigarettes/day → 2mg dose
 - Peak levels 20 minutes
 - 1st 6 weeks: Use Q1 to 2 hours prn for cravings
 - 2nd 6 weeks: gradually reduce use
 - Avoid acidic beverages: lower pH reduces absorption
 - **“Chew and Park”**
 - If chewed too rapidly, nicotine is not absorbed and it is swallowed, where it is metabolized by the liver



SHORT-ACTING NICOTINE REPLACEMENT

- To control cravings: Lozenge
 - 4mg dose for smokers who smoke < 30minutes of awakening
 - 2mg dose for all others
 - Dose 1 lozenge q1-2 hours x 6 wks
 - Reduce after that x 6 weeks
 - Max 5 lozenges q6hr or 20 in a day
 - Use: place in mouth and allow to dissolve over 30 minutes
 - AE: abd pain, N/V, diarrhea, HA, palpitations



SHORT-ACTING NICOTINE REPLACEMENT: (FOR CRAVINGS)

- Nasal spray
 - Most rapid onset (10 min) of short-acting meds
 - 1-2 sprays/hour x 3 months. Max dose is 10 sprays per hour (80/day)
 - Limited in clinical use due to side effects → nasal and throat irritation, rhinitis, sneezing, and tearing
- Mouth spray
 - 1mg/spray
 - 1-2 sprays/hour, max 4/hour
- Sublingual tablets
- Inhaler



SHORT-ACTING NICOTINE REPLACEMENT: (FOR CRAVINGS)

- Nasal spray
- Mouth spray
- Sublingual tablets
 - 2mg tablet
 - Dissolves over 30min
- Inhaler
 - Can also address some of the behavioral and sensory aspects of smoking
 - Plasma levels are 1/3 of those achieved with a cigarette
 - Dose: 6-16 cartridges/day x 6-12 weeks
 - Reduce dose over next 12 weeks



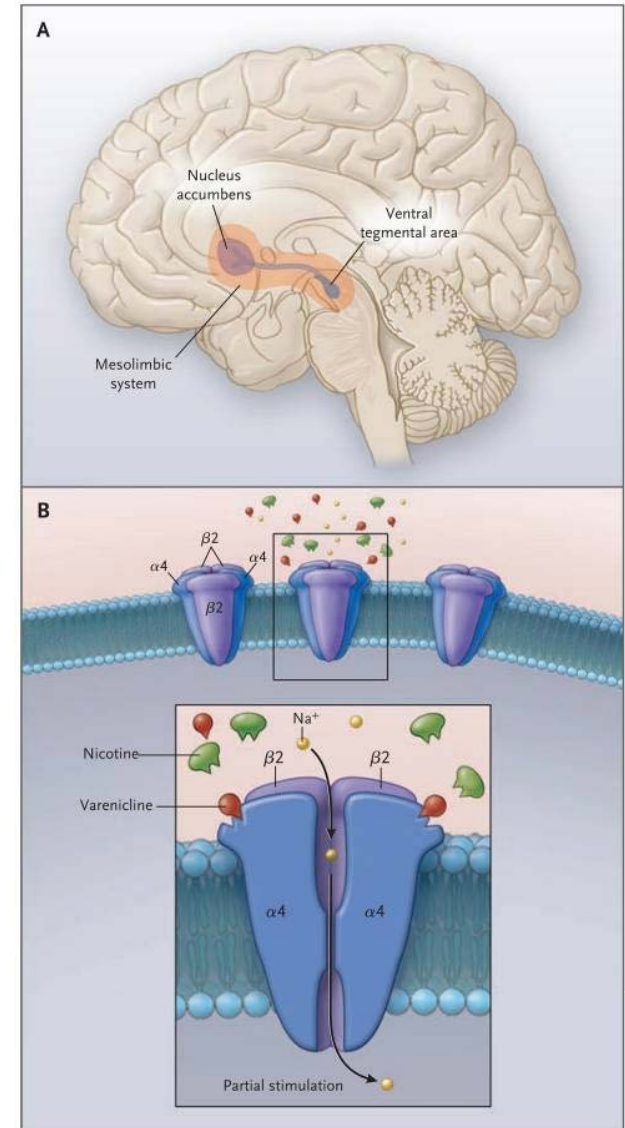
NICOTINE REPLACEMENT TREATMENT

- Nicotine dependence rarely occurs during treatment
- Can titrate to decrease side effects

- Safe to use in stable CV disease (i.e. no recent ACS)
- After acute coronary syndrome?
 - No differences in adverse outcomes between those using it or not
 - Usually start as outpatient

VARENICLINE

- **MOA: partial agonist at $\alpha 4\beta 2$ subunit of nicotinic Ach receptor**
 - Partial stimulation leads to reduction of withdrawal
 - Binds with high affinity to subunit and blocks the nicotine from binding
- **Efficacy**
 - 2013 meta-analysis
 - RR 2.27 95% CI 2.02-2.5
- **Start 1 a week before their planned quit day**
 - Could start 4 weeks before (47 vs 21%)
- **Dose: 0.5mg x 3 days, 0.5mg bid x 4 days, and then 1mg bid for rest of 12 weeks**
 - May continue for another 12 weeks (71 vs 50%)
- **Main side effect: nausea, insomnia, abnl dreams**
- **Pharmacokinetics**
 - **Mostly through kidney, dose reduction needed in renal insufficiency**



VARENICLINE: NEUROPSYCHIATRIC

- Likely minimal impact
 - 2009 FDA Postmarket Review, The smoking cessation aids varenicline (marketed as Chantix) and Bupropion (marketed as Zyban and Generics)
 - Review of 3249 FDA case reports from 1998 to 2010 of suicidal/self-injurious behavior and depression
 - Varenicline associated with 90%
 - Bupropion associated with 7%
 - NRT associated with 3%
 - Possible over-reported
 - 2010 Tonstad, S., et al., Psychiatric adverse events in randomized, double-blind, placebo-controlled clinical trials of varenicline: a pooled analysis.
 - 10 RCTs of 5096 smokers → No association between Varenicline and incidence of psychiatric disorders (10.7% vs 9.7% RR of 1.02 (95% CI 0.86, 1.22) or adverse events (anxiety, depression, mood disturbances)
 - Trials excluded those with a history of depression or other psychiatric disorders
 - Not sufficiently powered
 - 2013 Thomas, K.H., et al., Smoking cessation treatment and risk of depression, suicide, and self harm in the Clinical Practice Research Datalink: prospective cohort study
 - Prospective cohort study in 349 Primary Care clinics in England with 119, 546 patients from 2006-2011
 - There was NO evidence that Varenicline led to higher risks of fatal or non-fatal self harm or treated depression
- Bottom-line: consider using in stable psychiatric illness, no SA

VARENICLINE: CARDIOVASCULAR

2011 FDA advisory that Varenicline may increase the risk of CV events in patients with known CVD.

- 2010 RCT by Rigotti, N.A., et al., of 714 smoking patients with stable CVD
- Non-significant results vs placebo
 - Increase in non-fatal MI (2 vs 0.9%)
 - Increase need for coronary revascularization (2.3 vs 0.9%)
 - Decrease in all-cause mortality (0.6 vs 1.4%)

2011 Meta-analysis by Singh S., et al., of 14 double-blind RCTs

- Increase in risk of serious CV events compared to placebo (1.06 vs 0.82%)
- Excluded trials with no CV event

2012 Metanalysis by Prochaska, J.J., et al., of 22 trials of serious cardiovascular adverse events with Varenicline

- Rates of treatment emergent, cardiovascular serious adverse events were 0.63% (34/5431) in the varenicline groups and 0.47% (18/3801) in the placebo groups.
 - Results were not significant

2012 Cohort study by Svanstrom, H.B., et al., with 35,852 showed no increase risk of major cardiovascular events in smokers who took bupropion vs Varenicline

- Bottom-line: no problem to use in stable cardiovascular disease, but should provide precautions and monitor w/in 1 wk

VARENICLINE: ACCIDENTS

- A review by the Institute for Safe Medication Practices (non-profit medicine safety group) found a **high rate of accidental injuries** from road accidents and falls in patients taking Varenicline
- FDA has issued a **warning** about possible impairment when operating **heavy machinery**
- FAA **prohibits pilots and air traffic controllers** from taking Varenicline

BUPROPION

- May act as a partial nicotine antagonist and reduces rewarding effects of cigarettes
- Administration
 - Start 7 days before quit date to achieve steady state
 - Target dose is SR 150mg bid
 - SR 150mg qday is an option for those who can't tolerate bid
 - Duration: 12 weeks, although this can be continued
 - 1 year?
 - Delayed smoking relapse vs placebo (55 vs 42%) and led to less weight gain (3.8 vs 5.6kg)
- Safety
 - Safe for smokers with stable CVD and COPD
 - Monitor for neuropsych symptoms

COMPARATIVE EFFICACY

- **Varenicline vs NRT**

- Varenicline vs Patch

- **Mixed results**

- Cochrane Meta-analysis did not show a difference
 - Aubin, H.J., et al., Varenicline versus transdermal nicotine patch for smoking cessation: results from a randomised open-label trial. *Thorax*, 2008. 63(8): p. 717-24.
 - » N=757, at 4 weeks: abstinence rates at the end of treatment (V-56 vs P-43 %)
 - » Difference did not persist at 52 weeks
 - » Varenicline reduced craving, w/d symptoms, and smoking satisfaction vs NRT

- Varenicline vs Combined NRT

- **Few trials looking at this**

- *Kaduri, P., et al., Real-World Effectiveness of Varenicline Versus Nicotine Replacement Therapy in Patients With and Without Psychiatric Disorders. J Addict Med, 2015.*
 - Retrospective chart review, Varenicline=98 or NRT=98 (72% on combined therapy)
 - At a specialty tobacco treatment clinic
 - **Varenicline was more effective than NRT** (33 vs 18% quit rates)

COMPARATIVE EFFICACY

- **Varenicline vs Bupropion**

- Gonzales, D., et al., Varenicline, an alpha4beta2 nicotinic acetylcholine receptor partial agonist, vs sustained-release bupropion and placebo for smoking cessation: a randomized controlled trial. JAMA, 2006. 296(1): p. 47-55.
- Jorenby, D.E., et al., Efficacy of varenicline, an alpha4beta2 nicotinic acetylcholine receptor partial agonist, vs placebo or sustained-release bupropion for smoking cessation: a randomized controlled trial. JAMA, 2006. 296(1): p. 56-63..
 - N=2052, Varenicline vs Bupropion SR vs Placebo x 12 weeks
 - Continuous abstinence from wk 9-52: V-72% vs B-16% vs P-9%

- **Bupropion vs NRT**

- Bupropion monotherapy appears as effective as NRT

COMBINATION TREATMENT: IF FAILED WITH MONOTHERAPY

- **Bupropion and NRT**
 - More effective than bupropion alone
 - Not more effective than NRT alone
- **Bupropion and Varenicline**
 - May be more effective than Varenicline alone
 - At one year the difference between combined therapy and Varenicline alone was not significant
- **NRT (patch) and Varenicline**
 - More effective than Varenicline alone at end of treatment and 6 months later
- **Combined NRT and Bupropion**
 - Non-significant trend towards higher rates of abstinence

SPECIAL GROUPS

- Depressed patients
 - No evidence that bupropion is any more helpful in treating nicotine addiction in currently depressed patients
 - It may be more helpful in patients with past depression
- Schizophrenia
 - Bupropion-typically considered first-line
 - Varenicline: both safe and effective
 - Effective maintenance treatment for up to 1 year
 - Although people are still careful
- Bipolar
 - NRT considered first line
 - Varenicline also considered
 - Effective maintenance treatment for up to 1 year

RELAPSE PREVENTION & EXT MED?

- Longer treatment episodes are helpful
 - 15-35% success with treatment
- Current evidence
 - 26wks more helpful vs 8 wks of NRT
 - 1 year of Varenicline use in patients with Schizophrenia

e-Cigarettes

- Designed to deliver nicotine without tobacco



Good or Bad?



e-Cigarettes: current findings

- Content

- Propylene glycol, glycerol → mostly safe
- Impurities and toxicants in liquid → not safe, but safer than tobacco
- Nicotine delivered varies

****Long term effects of these additives are unknown****

- Adverse effects: mouth and throat irritation, increase in blood pressure
 - More serious: exploding cartridge, lipid pneumonia, afib in elderly pt
 - CV: increased heart rate
 - Resp: increased resistance after 5 min of use, but deemed not clinically significant
 - Nicotine poisoning: 1 report of a child death after drinking e-liquid
 - Less calls to poison control than for tobacco exposure



e-Cigarettes

- Effect on smoking behavior
 - Reduces cravings and withdrawal
 - Hand-to-mouth ritual
 - Mixed evidence for reduction and cessation
- Public Health
 - Appeal to youth
 - Renormalization?
 - WA state: must be 18yo and over