UPDATE
TREATMENT OF TOBACCO USE DISORDERS
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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

About 443,000 U.S. Deaths Attributable Each Year to Cigarette Smoking

- Lung Cancer: 128,900 (29%)
- Ischemic Heart Disease: 126,000 (28%)
- Chronic Obstructive Pulmonary Disease: 92,900 (21%)
- Other Diagnoses: 44,000 (10%)
- Stroke: 15,900 (4%)
- Other Cancers: 35,300 (8%)

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
• 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
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.
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 than 6 weeks of use may be helpful

• Cost without insurance per patch (21mg): $25.98
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 < 30 minutes 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 α4β2 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: NEUROSPYCHIATRIC

• 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
    • 10 RCTs of 5096 smokers \( \rightarrow \) 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
    • 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
        » 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
        - 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**
  
    • 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

Wu et al, Addiction 2016
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

Schlam et al, Addiction 2016; Evins et al, JAMA 2014
- 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 then 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, lipoid 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 then for tobacco exposure
- **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