

# TOBACCO

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# The ASAM Review Course of Addiction Medicine

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## Financial Disclosures

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None

# History

- Native American tribes cultivated and used tobacco for many different purposes for thousands of years before the arrival of the Europeans. <sup>1-2</sup>
- Tobacco became an important economic influence in the British American colonies and the early United States. <sup>1-2</sup>
- The World Health Organization estimates that 1/3 adults smoke, and because tobacco use is on the rise in developing countries, it is one of the few causes of death that is increasing. (CDC, 2005) <sup>3</sup>
- Nicotine and the reinforcing sensory stimulation associated with tobacco use are responsive for the compulsive use of tobacco in the form of cigarettes, bidis, cigars, pipes, snuff, chewing tobacco, etc.

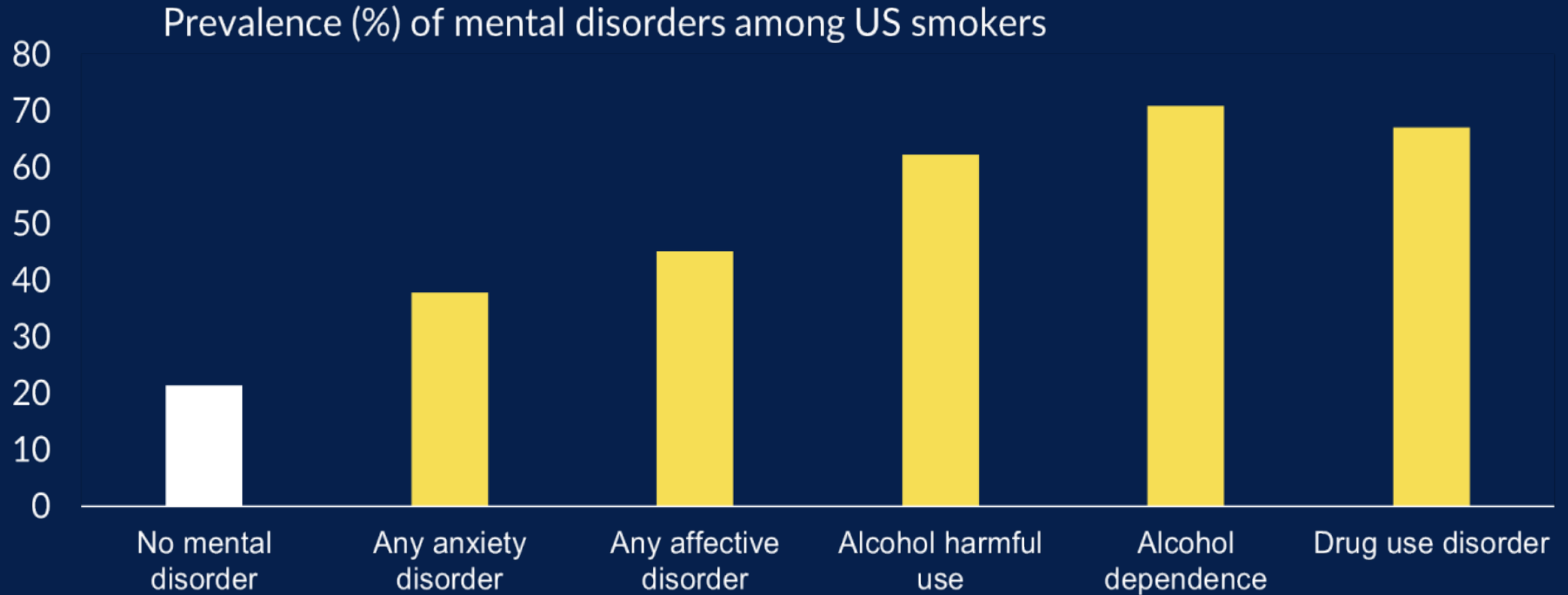
# Epidemiology of Tobacco

- Prevalence has declined in the US from 42% in 1965 to 14% in 2017 <sup>4,5</sup>
- Men are more likely to be smokers than women (15.8% vs. 12.2%) <sup>6</sup>
- >16 million Americans have smoking-related disease
- Accounts for 20% of coronary-artery disease <sup>7</sup>

# Morbidity and Mortality

- Leading cause of preventable death in the United States, accounting for about **440,000 premature deaths annually** <sup>8</sup>
  - **150K from CV disease**
  - **150K from cancer**
  - **150K from non-malignant pulmonary disease**
- Lost years of life: <sup>9</sup>
  - adult men: 13.2 yrs
  - adult women: 14.5 yrs

# Epidemiology



# Compounds in Tobacco Smoke

An estimated 4,800 compounds in tobacco smoke, including 11 proven human carcinogens <sup>11</sup>

## Gases <sup>12</sup>

- Carbon monoxide
- Hydrogen cyanide
- Ammonia
- Benzene
- Formaldehyde

## Particles <sup>12</sup>

- Nicotine
- Nitrosamines
- Lead
- Cadmium
- Polonium-120

Nicotine is the addictive component of tobacco products, but it does NOT cause the ill health effects of tobacco use.

# Health Consequences

- Smokers die 10 years earlier than non-smokers on average
- **Cancer:** oral cavity, pharynx, larynx, bladder, esophagus, cervix, kidney, lung, pancreas, stomach, liver, bowel, acute myeloid leukemia <sup>13</sup>
- **Cardiovascular disease, DM type II** <sup>14</sup>
- **COPD, Asthma** <sup>15</sup>
- Osteoporosis, cataracts and macular degeneration, early menopause, erectile dysfunction, gastric and duodenal ulcer disease, skin aging, periodontal disease <sup>16</sup>



# Tobacco Associated Problems

- Barrier to Recovery
- Financial Hardships
- More Employment Difficulties
- More Housing Difficulties
- Poorer Mental Health
- More Relapse to Drugs and Alcohol
- Social Stigma
- Poorer Appearance
- More Fires in Home

# Public Health Interventions <sup>17</sup>

- Anti-smoking advertisements
- Increasing taxes
- Age-restrictions
- Tobacco-free laws and policies
- Support for cessation

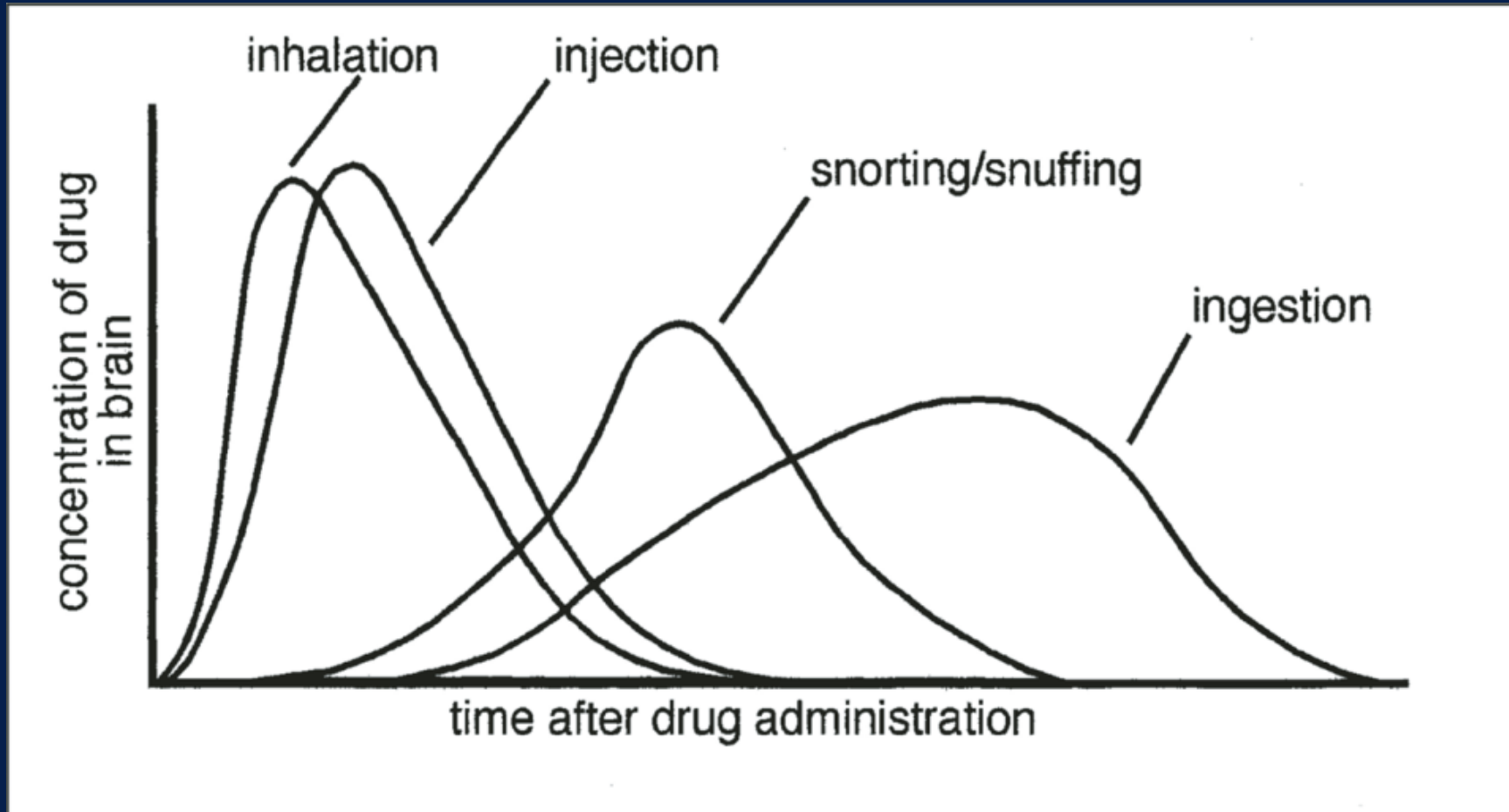
# Pharmacology of Nicotine

- Naturally occurring alkaloid <sup>3</sup>
- Triggers the release of a variety of neuroactive hormones
- Acts as a **nicotinic acetylcholine receptor (nAChR) agonist** <sup>3</sup>
- **Stimulant-like effect** in the CNS: enhances concentration, alertness, arousal <sup>3</sup>
- Increase of dopamine in brain's reward circuitry <sup>18</sup>
- Enters the CNS in rapidly after inhalation <sup>19</sup>
- Rapid effect on CNS contributes to reinforcement and dependence

# Routes of Use

- ◆ Nicotine and reinforcing sensory stimulation associated are responsible for the compulsive use of tobacco <sup>20-23</sup>
- ◆ Method of administration modifies the addictive potential associated with use <sup>24</sup>
- ◆ Compulsive use increases with rapid administration: smoking/vaping >> dermal patch, chewing

# Smoking is the Fastest Route of Drug Administration



# Nicotine

- ◆ Reaches the brain 20 seconds after inhalation + gradually increases occupancy of the nAChRs **over minutes** <sup>19</sup>
- ◆ Smoking 1 cigarette leads to significant occupancy of alpha4beta2 containing nAChRs **for >3 hrs** <sup>19</sup>
- ◆ The initial relatively rapid rate of rise of nicotine occurs within minutes, though levels of nicotine-bound receptors continue to rise slowly/are maintained for hours <sup>19</sup>
  - ◆ Rapid onset = allows smokers to control nicotine intake (by # of puffs, intensity of puffs, depth of inhalation)

# Pharmacology of Nicotine

- Half-life is 2 hours <sup>25-26</sup>
- Accumulation in various tissues throughout the body during the day <sup>27</sup>
- Continue to be release from tissues for 6-8 hours after smoking ceases during sleep <sup>25-26</sup>
- **Metabolized in the liver** via cytochrome P450 enzymes <sup>26</sup>
- Major metabolite is cotinine <sup>26</sup>
- Crosses placenta and is found is breast milk <sup>27</sup>

# Pharmacology

- ◆ Undergoes 1<sup>st</sup> pass metabolism <sup>26</sup>
- ◆ Oral bioavailability is 45% <sup>26</sup>
- ◆ Poorly absorbed from stomach 2/2 acidity of gastric fluid, but well absorbed in small intestine 2/2 alkaline environment <sup>26</sup>
- ◆ Renal clearance accounts for 2% to 35% (about 10%) of total nicotine clearance <sup>28</sup>
- ◆ Nicotine obtained via tobacco reaches high initial concentrations in arterial blood and lungs
  - ◆ Nicotine is then distributed to brain, storage adipose, muscle tissue from arterial blood
  - ◆ Avg steady-state concentration in body tissue is 2.6x that of the blood <sup>26</sup>



# Pharmacology

- Once absorbed in bloodstream, nicotine has a volume of distribution of about 180 liters, with less than 5% of it binding to plasma proteins <sup>26</sup>
- Crosses placenta freely
- Found in the amniotic fluid and in the umbilical cord blood of neonates
- Found in breast milk at concentrations approximately 2x those found in blood

# Sex and Race on Metabolism

- ♦ Women metabolize nicotine faster than men, 2/2 estrogen effect on CYP2A6 <sup>29</sup>
  - ♦ Even faster during pregnancy
- ♦ Related to CYP2A6 gene variants, African Americans obtain on average 30% more nicotine per cigarette, and they clear nicotine and cotinine more slowly than Caucasians. <sup>30</sup>
- ♦ Chinese American have a lower nicotine intake per cigarette, and slower metabolism (vs. Caucasians or Hispanics) 2/2 having a higher prevalence of CYP2A6 alleles (associated with slow metabolism) <sup>31-32</sup>
  - ♦ Suggest why Chinese American smokers have lower rates of lung cancer than either African Americans or Caucasians <sup>31-32</sup>

# Biochemical Assessment

- ◆ Blood, salivary, and plasma cotinine can be used <sup>33,34</sup>
  - ◆ others include expired breath CO, blood carboxyhemoglobin, + plasma/salivary thiocyanate concentrations
- ◆ 16-hr  $\frac{1}{2}$  life of cotinine makes it useful as a plasma and salivary marker of nicotine intake <sup>35</sup>
- ◆ The gold standard for estimating daily nicotine intake from tobacco use is the sum of nicotine and its metabolites in urine. <sup>36</sup>
- ◆ Measurement of the minor tobacco alkaloids anabasine and anatabine in urine can be used as a biomarker of tobacco use in individuals who are using nicotine medications. <sup>37</sup>

# Drug Interactions from Tobacco Smoke

- Affects the pharmacokinetics or pharmacodynamic mechanisms
  - absorption, distribution, metabolism, or elimination
  - potentially causing **altered response or toxicity**
- Accelerates metabolism of many drugs, esp. those metabolize by CYP1A2 <sup>38</sup>
- Might increase CYP2E1 and inhibit CYP2A6 enzymatic activity <sup>38</sup>
- When smokes discontinue abruptly (i.e., when hospitalized) doses of such meds may need to be lowered to avoid toxicity <sup>38</sup>

# Drug Interactions from Tobacco Smoke

Drugs that may have a decreased effect due to induction of CYP1A2 by tobacco smoke: <sup>39</sup>

- Caffeine
- Clozapine
- Olanzapine
- Haloperidol
- Chlorpromazine
- Fluvoxamine
- Theophylline

# Quitting Smoking Effects on CYP1A2

- Risk for medication toxicity
  - May ↑ levels acutely
  - Consider dose adjustment
  - Clozapine toxicity
    - Seizures
  - Reduce caffeine intake
- **Nicotine (or NRT) Does Not** Change Medication Levels
  - Nicotine metabolized by **CYP2A6**

# Pharmacodynamic Interactions: OCPs

- Alter the expected response or action of a drug
- Combined OCPs (estrogen + progestin) w/ smoking is very important
  - Increased risk of serious cardiovascular effects (stroke, MI, thromboembolism) <sup>40</sup>
- Recommended that OCPs are **contraindicated** in women > 35 yrs old AND are a heavy smoker (>15cigs/day) <sup>40</sup>

# Pharmacodynamic Interactions

- Appear to enhance the procoagulant effect of **estrogens** <sup>41</sup>
- Results in *less sedation* from benzodiazepines and *less analgesia* from some opioids <sup>42</sup>
- Impairs the therapeutic effects of histamine H<sub>2</sub> -receptor antagonists used in treating **peptic ulcers** <sup>42</sup>
- Cutaneous vasoconstriction by nicotine can slow the rate of absorption of subcutaneously administered **insulin** <sup>43</sup>



# Pharmacologic Actions: CNS 44,45

- Acts on sympathetic system: increase BP, HR, cardiac output, and cutaneous vasoconstriction
- Causes muscle relaxation via stimulation of Renshaw cells, via inhibition of motor neurons
- Higher doses: produces ganglionic stimulation -> releases adrenal catecholamines
- Very high doses cause hypotension, slowing of HR

# Psychoactive Effects

- Causes arousal, relaxation, enhancement of mood/attention/rxn time <sup>46-48</sup>
- Results in relief of withdrawal sx of dependent smokers, rather than direct-enhancing effects <sup>46-48</sup>
  - Smokers may need regular doses of nicotine to feel normal rather than to enhance their capabilities/cognitive effects
- Psychoactive effects dependent on route, speed of administration, environmental factors
  - Subjective effects depend on pre-drug state, level of activity, genetics, history, expectancy <sup>49,50</sup>

# Genetic Predisposition

- GWAS: single nucleotide polymorphisms on... <sup>51</sup>
  - **CHRNA5-CHRNA3- CHRNA4 nAChR** subunit cluster on chromosome 15q25
    - associated w/ # of cigs/day, serum cotinine levels, lung cancer, peripheral artery disease, chronic lung dz
  - **CYP2A6**, primary enzyme responsible for the oxidation of nicotine and cotinine. <sup>52-53</sup>
    - Reduced function variants of the gene are associated with smoking fewer cigarettes per day and a lower risk of lung cancer
  - **Cell adhesion and ECM molecules** <sup>54</sup>
    - neural plasticity and learning are key determinants of individual differences in vulnerability to drug addictions
- Twin studies: <sup>55,56</sup>
  - monozygotic twins are more similar than dizygotic twins w/ smoking behavior
  - ½ of the total variance (28% to 84%) in smoking behavior are due to genetic effects
  - There is genetic influence on nicotine withdrawal symptoms as well

# Psychiatric Comorbidities

- **37%** of those w/ a mental illness are smokers vs. **20%** of smokers who do not carry a mental illness. <sup>57</sup>
- Those with Sz, depression, ADHD have **higher prevalence** of cig smoking compared with general population

## **Sz: 70-88% are smokers** <sup>58</sup>

- Diminished sensory gating to repeated stimuli, smoking can relieve negative sx (blunted affect, emotional withdrawal, lack of spontaneity)
- Smokers experience fewer side effects from antipsychotics (2/2 stimulating effects of nicotine), which might contribute to greater prevalence of smoking in ppl w/ Sz

## **ADHD: 40% are smokers** <sup>59</sup>

- Associated with early initiation of regular cigarette smoking, even after controlling for confounding variables such as socioeconomic status, IQ, and psychiatric comorbidity
- transdermal patches improve the attentional symptoms of ADHD

# Best Measure of Nicotine Dependence Severity

## Heaviness of Smoking Index

- AM (upon awakening) Time to First Cigarette (TTFC) <sup>46</sup>
  - < 30 minutes = moderate
  - < 5 minutes = severe
- Implications for Treatment Outcome
- Need for Medications
- Implications for Dose

# Tobacco Tolerance

- Causes effects of individual cigarettes tend to lessen throughout the day.
- Overnight abstinence allows considerable, but not complete, re-sensitization of nicotinic receptors to non-desensitized states
- Populations of nAChR subtypes that begin to change as other molecular mechanisms involving neuroadaptations come into play after days and weeks of tobacco use <sup>47,48</sup>

# Tobacco Cravings

- Powerfully conditioned cues = cravings become associated with everyday events, become linked with mood
- High rates of relapse: <sup>49</sup>
  - Population surveys find that up to 75% of adults who smoke want to stop, but only 1/3 try to stop, and only 3% of those do without aids
  - 50% of individuals w/ past hx of MI, COPD, and other sequelae of smoking, revert to cig smoking days or weeks after leaving the hospital

# Tobacco Withdrawal

- Nicotine use is continued to avoid the negative sx associated with withdrawal (known as negative reinforcement)
- Majority of withdrawal sx are distressing, but not life-threatening
- Acute withdrawal sxs reach max. Intensity 24 - 48 hrs after cessation and then gradually diminish over weeks <sup>50,51</sup>
- Extrahypothalamic corticotropin-releasing factor (CRF-1) contributes to negative affect during withdrawal <sup>52</sup>
  - CRF released in central amygdala following nicotine withdrawal -> produces anxiety behavior
  - Pharmacological blockade of CRF1 receptors inhibits the anxiogenic effects in withdrawal



# Tobacco Withdrawal Symptoms <sup>53</sup>

Emerges hours after last cigarette

Can last up to (4) weeks

- Depressed mood
- Insomnia
- Irritability, frustration or anger
- Anxiety
- Difficulty concentrating
- Restlessness
- Increased appetite or weight gain

# MAO and Nicotine Dependence

- Cig smoking is associated w/ inhibition of monoamine oxidase A + B <sup>54-56</sup>
  - Not caused by nicotine itself, but the condensation products of acetaldehyde with biogenic amines, such as benzoquinones, 2-naphthylamine, harman, + others
- MAOs = metabolize catecholamines, including dopamine
- Rat studies: <sup>57</sup>
  - Pre-tx with MAO-I makes nicotine more rewarding and increases the likelihood and rate of acquisition of nicotine self-administration
  - Important consideration: anti-depressants also inhibit MAOs, therefore smoking-induced inhibition of MAO might contribute to the *perceived benefit* of smoking by some depressed patients

# Systemic Toxicities

- **Tobacco smoke** = carries volatile and particulate phases that contain substances that are primarily responsible for the human morbidity and mortality <sup>58</sup>
  - Volatile = 500 compounds (nitrogen, CO, carbon dioxide, ammonia, hydrogen cyanide, and benzene)
  - Particulates = >3,500 (alkaloids nornicotine, anabasine, anatabine, myosmine, nicotyrine, and nicotine)
- **Tar:** contains many carcinogens, including polynuclear aromatic hydrocarbons, N-nitrosamines, and aromatic amines <sup>58</sup>

# Toxicities: Pulmonary

- Causes imbalance between proteolytic and antiproteolytic forces in the lung <sup>59</sup>
- Heightens airway responsiveness
- High rates of COPD in tobacco smokers linked to: <sup>59</sup>
  - Exposure to tar, nitrogen oxides, hydrogen cyanide, and volatile aldehydes
  - These exposures results in oxidative stress and generation of superoxide radicals and hydrogen peroxide and lung damage
- Smokers with DNA damage from polynuclear aromatic hydrocarbons in the WBCs are 3x more likely to be dz with lung cancer than smokers with lower concentrations <sup>60</sup>

# Toxicities: Cardiovascular

- **Increased risk** of CV toxicity <sup>61</sup>
  - Related to exposure to oxidant chemicals and CO, + hydrogen cyanide, carbon disulfide, cadmium, and zinc
  - CO reduces oxygen delivery to the heart
  - Oxidant chemicals are primarily responsible for endothelial dysfunction, platelet activation, thrombosis, and coronary vasoconstriction

# Other Effects and Toxicities

- **For women:** <sup>62</sup>
  - lower levels of estrogen
  - earlier menopause
  - increased risk of osteoporosis
  - alkaloids in tobacco smoke decrease estrogen formation by inhibiting an aromatase enzyme in granulosa cells or placental tissue
- **Skin changes:** <sup>63</sup>
  - yellow staining of fingers
  - vasospasm and obliteration of small skin vessels
  - precancerous and squamous cell carcinomas on the lips and oral mucosa
  - enhanced facial skin wrinkling

# Predictors of Abstinence <sup>64-66</sup>

- Lower level of dependence
- Higher socioeconomic status: education, insured
- Older age
- Male gender
- No behavioral health comorbidity
- Fewer smokers in social networks
- Quit in first 7 days / # days quit
- **Use of cessation treatment**

# Why is it so hard to quit?

- Smoking a drug is highly addicting
- **Treatment options are limited**
  - Few medication types
  - Limited (brief) counseling support
  - No levels of care
- **Utilization of treatment is poor**
  - Most don't use counseling
  - Medications-too low dose, not enough time



# Treating Tobacco Use And Dependence

CLINICAL PRACTICE GUIDELINE  
2008 UPDATE

U.S. Department of  
Health and Human Services  
Public Health Service

## Brief Intervention

### 2As and R (Ask, Advise, and Refer)

- Do you use Tobacco?
  - How much? What kinds?
  - Document tobacco use at visits
- How do you feel about quitting?
- Can I give your name to someone to get more information?

# Why Not Quit For One Day?

## Or Six Hours?

- Save money
- Try free NRT
- Feel better
- Master a new skill
- Try other coping
- Not go outside in bad weather

You can be  
tobacco-free  
for one day!

Join the Great  
American Smokeout.

**November 21<sup>st</sup>**



IQuit with AHEC.



[www.ahectobacco.com](http://www.ahectobacco.com)





# Quitline

1-800-QUIT-NOW

- Telephone counseling
- Toll-free / state funded
- Assessment
- 4 follow-up calls
- Good for transportation issues
- Scheduled calls from tobacco specialist
- Success rate in smoking cessation
- Many languages, free NRT

# Pharmacologic Treatments

- First line (FDA-approved): <sup>67</sup>
  - Nicotine replacement therapy (NRT)
  - Bupropion
  - Varenicline
- Second line (not FDA-approved): <sup>67</sup>
  - Nortriptyline

Counseling +  
Medications= Best  
Treatment Plan

# Nicotine Medications <sup>68</sup>

- Use high enough dose
- Scheduled better than PRN
- Use long enough time period
- Can be combined with bupropion
- Can be combined with each other
- Have almost no contraindications
- Have no drug-drug interactions
- Safe enough to be OTC

# Oral Nicotine Spray <sup>69,70</sup>

- Approved Sept 2019; OTC (Canada & Europe)
- Faster absorption
- 1-2 to two sprays (140/ container; each 1mg nic). Max 4/ hour, 64/ day (most 10-14/ day)
- No evidence product abuse
- Real world and efficacy trials 2X placebo
- Contains tiny amount ethanol. At 64 doses/d, <one tsp (~ 5ml) of wine with 12% alcohol)
- Side effects: hiccups, headache, nausea, mouth/throat irritation, dyspepsia, dizziness

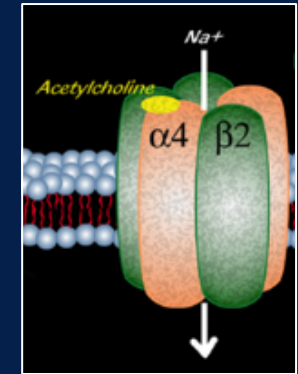
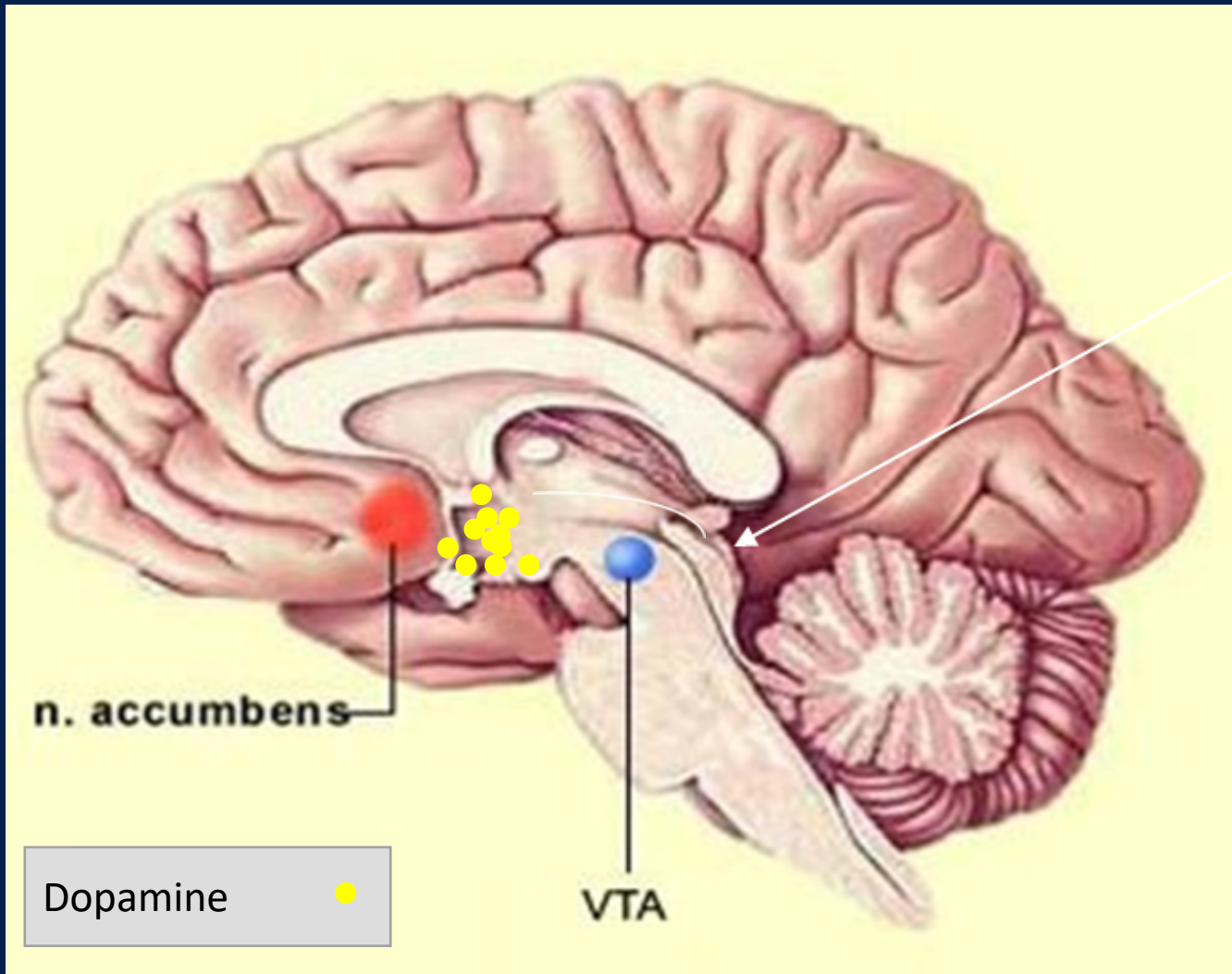
# Combination Therapies <sup>71,72</sup>

- Improve abstinence rates
- Decrease withdrawal
- Well tolerated

	OR
Patch + gum or spray	<b>1.9</b> (1.3-2.7)
Patch + bupropion	<b>1.3</b> (1.0-1.85)



# Varenicline: A selective $\alpha 4\beta 2$ nicotinic receptor partial agonist



Partial Agonist <sup>73</sup>

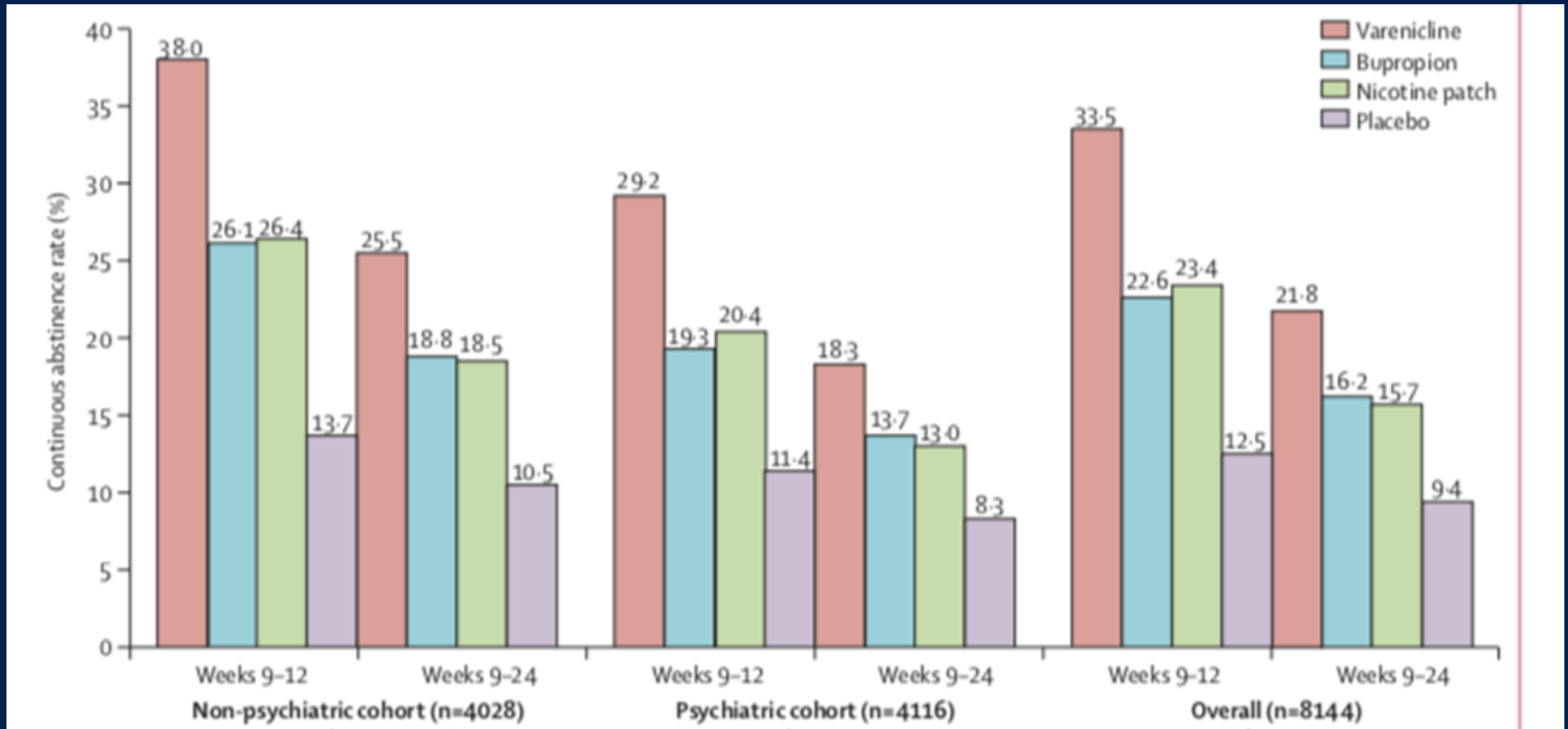
Partially stimulates receptor  
Some dopamine release  
Prevents withdrawal

“Antagonist”

Blocks nicotine binding



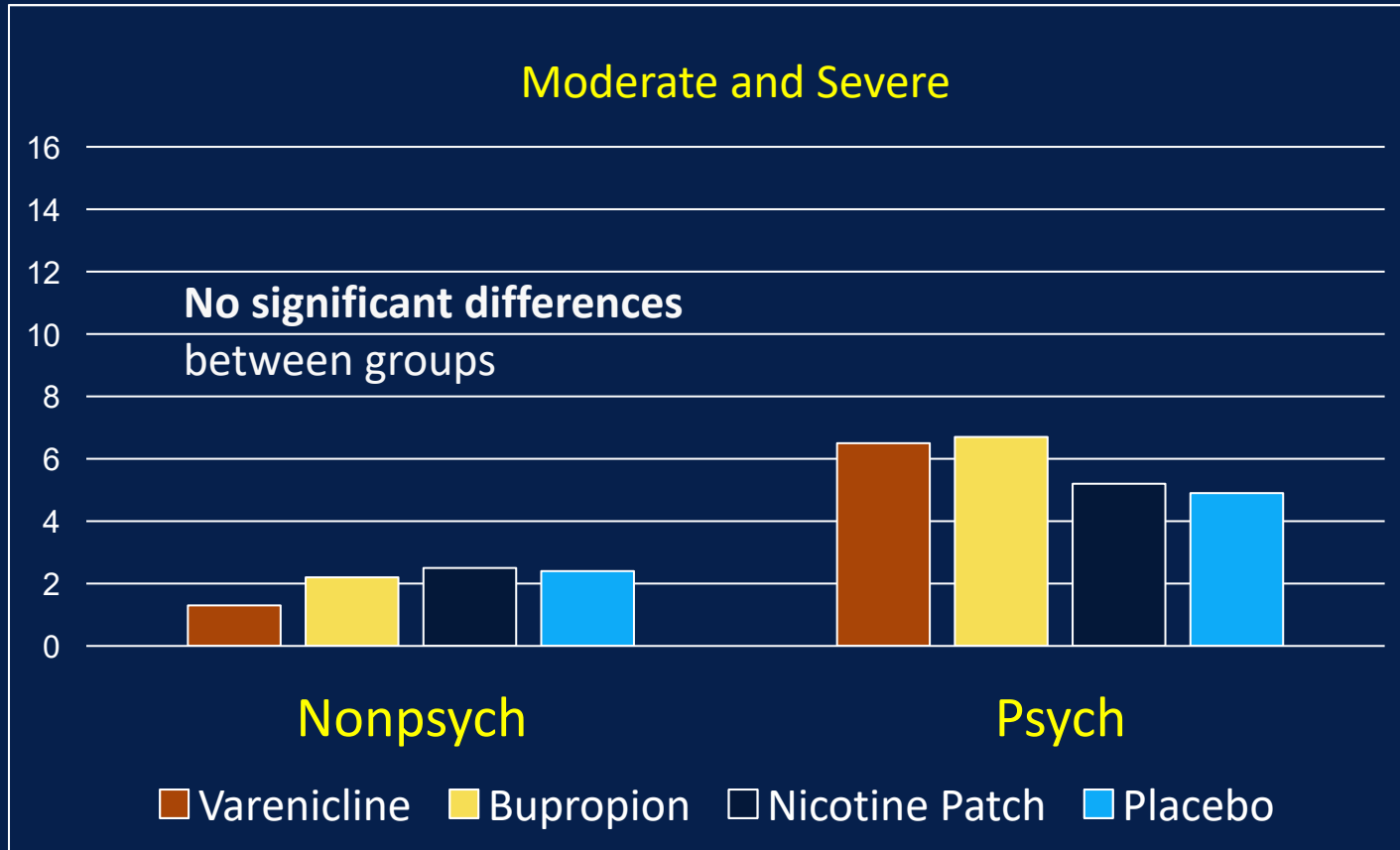
# EAGLES study <sup>74</sup>



# Results from 2013 <sup>75</sup>Cochrane Review

Medication	Versus Placebo OR (95% Credible Interval)	Versus other medication OR (95% Credible Interval)
NRT	1.84 (1.71-1.99)	Combination outperformed single formulations
Bupropion	1.82 (1.60-2.06)	NRT: 0.99 (0.86-1.13)
Varenicline	2.88 (2.40-3.47)	Nicotine patches: 1.51 (1.22-1.87) Nicotine gums: 1.72 (1.38-2.13) Other NRT: 1.42 (1.12-1.79) Combination NRT: 1.06 (0.75-1.48)

# Neuropsychiatric Adverse Events



FDA Approves Removal of Boxed Warning Regarding Serious Neuropsychiatric Events from CHANTIX<sup>®</sup> (varenicline) Labeling<sup>90</sup>

Based on a U.S. Food and Drug Administration (FDA) review of a large clinical trial that we required the drug companies to conduct, we have determined the risk of serious side effects on mood, behavior, or thinking with the stop-smoking medicines Chantix (varenicline) and Zyban (bupropion) is lower than previously suspected. The results of the trial confirm that the benefits of stopping smoking outweigh the risks of these medicines

(December 2016)<sup>76</sup>

Varenicline ↑ Side effects: Nausea, insomnia, abnormal dreams, headaches

# Summary of Treatment

- All tobacco users should be offered treatment to try to stop
- Counseling + Medications = Best treatment plan
- Better outcomes
  - Education to use medication effectively
  - Combinations of NRT or Varenicline as first line
  - Longer durations (6 mos) effective for relapse prevention

# Gender Issues

- In any given quit-attempt, women are less likely to successfully quit smoking than men <sup>77</sup>
  - Negative affect/ depression/ socioeconomic issues/ less likely meds
- Women in placebo group less likely than men to quit
- Varenicline was more effective than TNP for women (OR=1.51; 95%CI=0.12,2.05; p=0.007) but not men (OR=0.92; 95%CI=0.65,1.31; p=0.64). <sup>78</sup>
- The advantage of varenicline over bupropion SR and TN is greater for women than men
- Clinical trials and epidemiologic studies

# Combination Therapy Of Varenicline and Bupropion

- Meta Analysis: 4 RCTs with 1230 smokers.
- Compared with varenicline, combination treatment with varenicline and bupropion could significantly improve the abstinence rate at the end of treatment (RR 1.153, 95% CI 1.019 to 1.305,  $P = 0.024$ ).<sup>79</sup>

# Combination Therapy Of Varenicline and Bupropion

- The benefit existed at 6 months follow-up (RR 1.231, 95% CI 1.017 to 1.490,  $P = 0.033$ ), and was mainly concentrated in highly dependent smokers (RR 1.631, 95% CI 1.290 to 2.061,  $P < 0.001$ ) and heavy smokers (RR 1.515, 95% CI 1.226 to 1.873,  $P < 0.001$ )<sup>79</sup>
- For safety outcomes, the combination treatment was associated with more anxiety (RR 1.717, 95% CI 1.176 to 2.505,  $P = 0.005$ ) and insomnia (RR 1.268, 95% CI 1.076 to 1.494,  $P = 0.005$ ) symptoms vs varenicline monotherapy.<sup>79</sup>

# Medication Interaction Tobacco Treatments <sup>79</sup>

<b>Nicotine</b>	<b>CYP<sub>2</sub>A6</b>	<b>None</b>
<b>Bupropion</b>	<b>CYP<sub>2</sub>B6 CYP<sub>2</sub>D6 inhibitor</b>	<b>Many</b>
<b>Varenicline</b>	<b>Excreted in urine</b>	<b>None</b>



# Special Population: Pregnancy

In 2016, 7.2% of US women who gave birth smoked cigarettes during pregnancy.<sup>80</sup>

## Smoking in pregnancy ↑ risks of:

- Spontaneous pregnancy loss
- Placenta abruption
- Ectopic pregnancy
- Placenta previa
- Preterm rupture of membranes
- Low birth weight
- Sudden infant death syndrome
- Low milk volume production and shorter duration of lactation

## Special Population: Pregnancy <sup>80</sup>

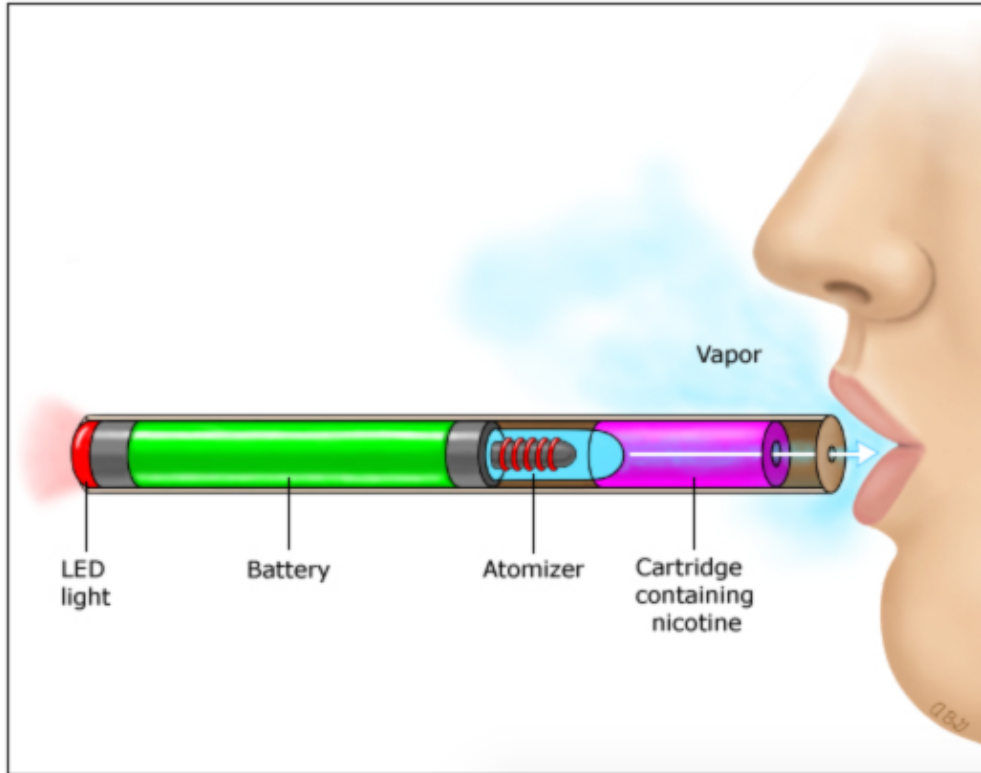
- More likely to quit smoking in pregnancy
- Initiate intervention before conception
- Continue interventions during prenatal care visits
- Counseling is the first-line of treatment
- NRT or bupropion are acceptable second-line options (data lacking but supported by experts committees)
- Limited information regarding safety of varenicline

# Special Population: Adolescents

- Early intervention is important
- **Counseling is the first-line** of treatment
- If counseling fails **NRT is an acceptable** options
- Insufficient data regarding bupropion and varenicline

# E-Cigarettes

- Battery-operated device
- Heats liquid containing nicotine
- Creates vapor that is inhaled
- Entered US market in 2006 <sup>81</sup>



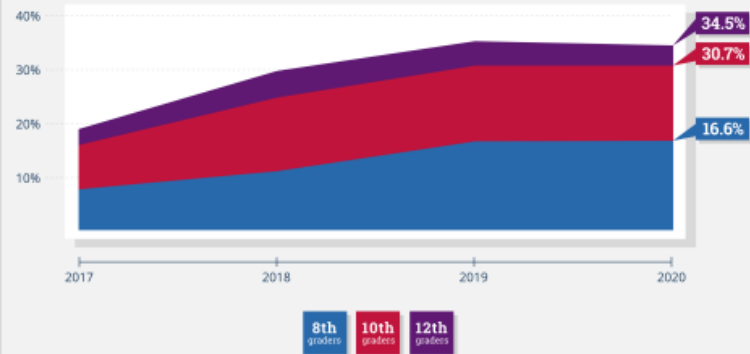
# Chemicals in Electronic Cigarettes

82,83

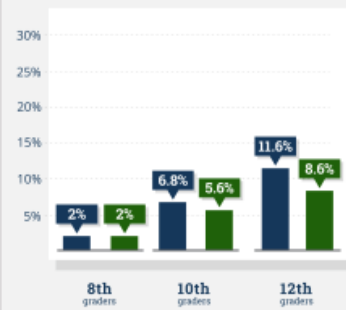
- Propylene glycol, ethylene glycol and glycerin
- Nicotine
- Flavors (sweeteners)
- Most chemicals found at or below 1% of levels in tobacco smoke, and far below safety limits for occupational exposure.
  - Metals (cadmium, chromium, lead, manganese and nickel)
  - Formaldehyde
  - Other carcinogens
  - Solvents
  - Tobacco alkaloids

## Surge of Nicotine Vaping Levels Off, but Remains High

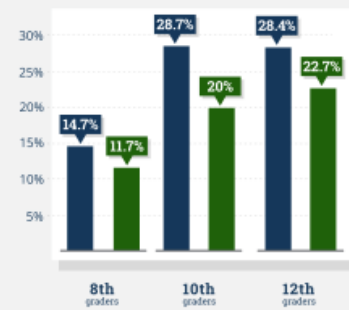
Past-Year Nicotine Vaping Held Steady



Daily or Near-Daily Nicotine Vaping



Past-Year JUUL Use Dropped Significantly Among Older Grades



2019 2020



# Vaping and Youth

- “Vaping” = nicotine, marijuana, just flavoring since 2017
- Increased dramatically in 2018 <sup>84</sup>
  - Nicotine vaping largest ↑ ever recorded for any substance in the 44 years of MTF (2017-2018)
    - 30% of 12th graders vaping nicotine (↑ 11%)
  - Marijuana vaping increased (1-3%) among 8, 10, 12th graders  
4%, 12% and 13%
  - Just flavoring increased among 8, 10, 12th graders
    - 15%, 25% and 26%

# Association of Electronic Cigarette Use With Subsequent Initiation of Tobacco Cigarettes in US Youths

- Prospective cohort (6123=N), mean age 13.4
- Cigarette use at wave 3 was higher among prior e-cigarette users (20.5%) vs no prior tobacco (3.8%).<sup>85</sup>
- Prior e-cigarette use was associated with more than 4 times the odds of ever cigarette use (odds ratio, 4.09; 95%CI, 2.97-5.63) and nearly 3 times the odds of current cigarette use (odds ratio, 2.75; 95%CI, 1.60-4.73) vs no prior tobacco use.
- Supports that e-cigarette use is associated with increased risk for cigarette initiation and use, particularly among low-risk youths.



# E-cigarette or Vaping Associated Lung Injury (EVALI) <sup>86</sup>

- Lung injury cases associated with e-cigarette, or vaping, to CDC
- **Vitamin E acetate** -bronchoalveolar lavage (BAL) fluid samples
- Thickening agent in THC-containing e-cigarette
- **Most (86%) involved THC products**; some (11%) nicotine alone
- 70% of patients are male; 79% are < 35 years old

# E-Cigarettes

- More frequently used by Americans than other FDA-approved treatments for smoking cessation
- Safer than combustible products, but long-term effects are unknown
- Controversial whether e-cigarette should be used as a first line of treatment, although this is common in UK

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