Treatment of Tobacco Use Disorder

Michael A Mitcheff, DO MBA CHCQM

Corporate Medical Director Wexford health sources

Panelist Project Echo Indiana University School of Medicine MAT/MOUD in Corrections

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Disclosures

- I have no relevant financial disclosures

Brief Biography

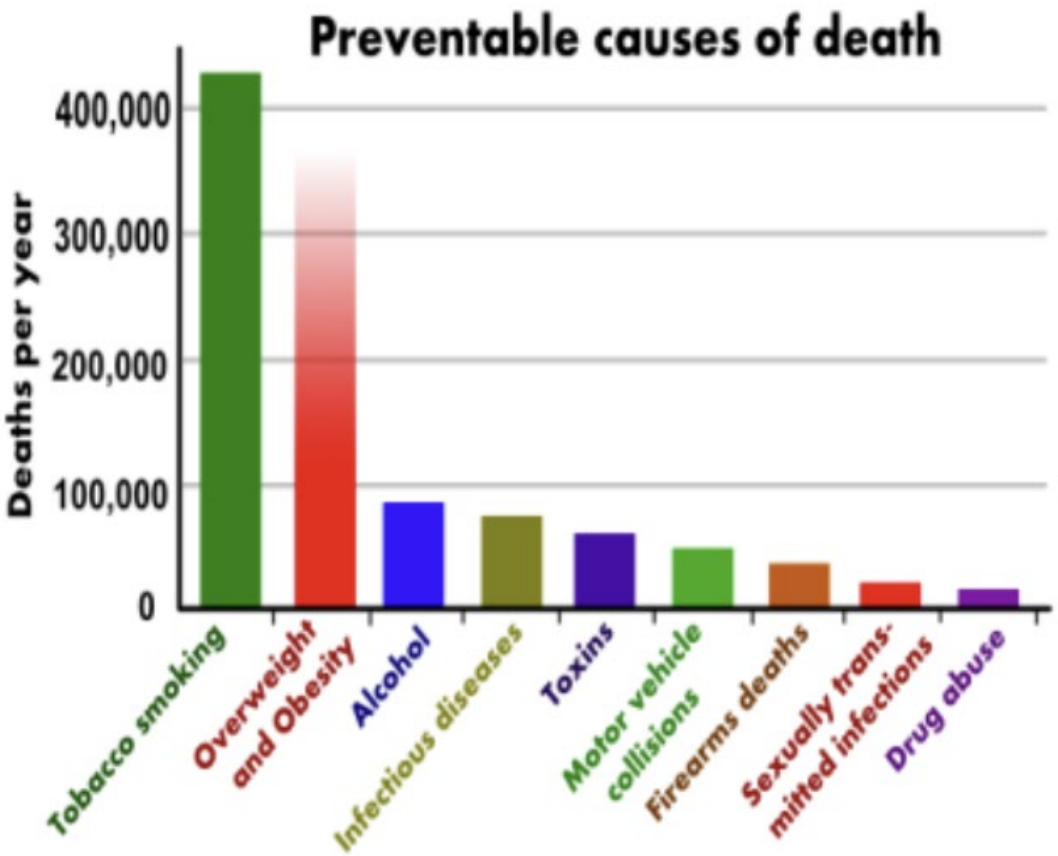
- Currently Corporate Medical Director Wexford health sources
- Currently supervising physician Workit health (telehealth addiction medicine platform)
- Former Chief Medical Officer Indiana Department of Correction
- Former Corporate Medical Director Advanced Correctional Healthcare
- Keynote speaker Mental Health America “removing the mask of addiction”
- Have been in Recovery from OUD for 25 years

Objectives

- Statement of Need: Although tobacco use rates are declining, smoking is still a leading cause of preventable death and rates are higher in low income and behavioral health populations.

- At the conclusion of this activity participants should be able to:
  - Recognize the effect of toxicity from combustible tobacco
  - Identify the available quick forms of clinical assessment, including the utility of the Time to First Cigarette measure (TTFC)
  - Demonstrate knowledge of pharmacotherapies for tobacco use disorder treatment, highlighting the safety and efficacy of each
  - Describe nicotine replacement treatment dosing and how to enhance its effectiveness in patients
  - Review the role of counseling in increasing the success of quit attempts and describe the Ask, Advise and Refer model for Primary Care

Tobacco= #1 cause of preventable deaths in the U.S.



30% of all cancer deaths

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

Equal opportunity health destroyer

Tobacco associated problems

- Smoking increases the risk for coronary heart disease 2 to 4 times
- Smoking increases the risk for stroke by 2 to 4 times
- 90% of all lung cancer deaths
- Poor wound healing, HTN, COPD, chronic bronchitis
- Smoking can damage nearly every organ of the body

DSM 5 criteria for Tobacco Use Disorder

The use of tobacco products has resulted in clinically significant impairment or distress, manifested by meeting at least two of the following within the past 12 months:

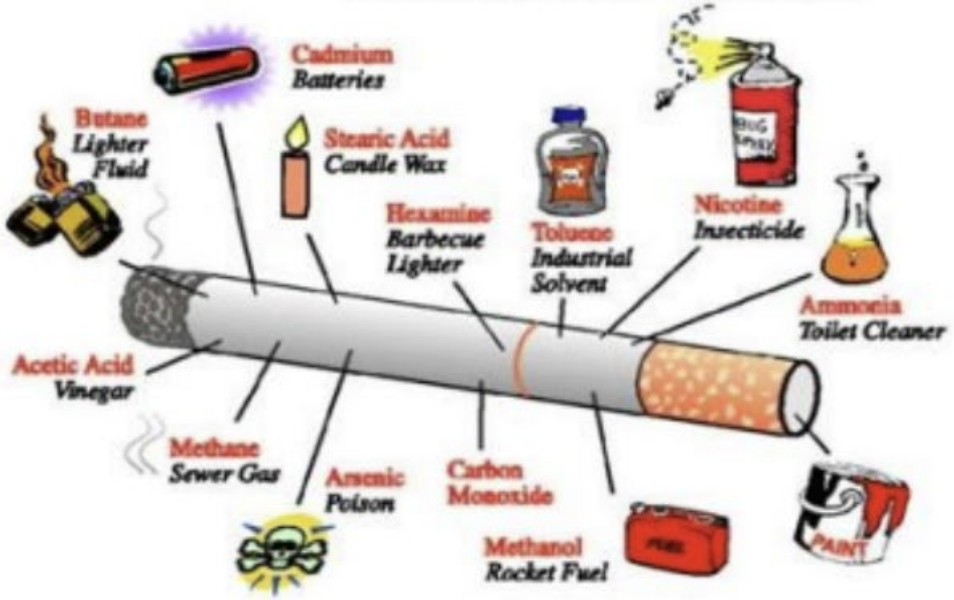
- Tobacco used for longer period of time or in larger amount than originally intended
- Unsuccessful efforts to quit or reduce use of tobacco
- Inordinate amount of time spent acquiring or using tobacco products
- Cravings for tobacco
- Failure to attend to responsibilities and obligations due to tobacco use
- Continued use despite adverse social or interpersonal consequences
- Forfeiture of social, occupational or recreational activities in favor of tobacco use
- Recurrent tobacco use in physically hazardous situations
- Continued use despite awareness of physical or psychological problems directly attributed to tobacco use
- Tolerance (need for increasing dose to get same effect or diminished effect from the same amount)
- Withdrawal symptoms upon cessation of use

AOAAM
The American Osteopathic Academy

The Smoke Kills!

- **Cigarette smoke > 7000 compounds**
  - Acetone, Cyanide, Carbon Monoxide, Formaldehyde
- **>65 Carcinogens**
  - Benzene, Nitrosamines

picture taken from nysmokefree.com



Sources of Tobacco toxins

Nicotine; nitrosamines

More than 600; Ammonia, cellulose acetate; flavors

Thousands; carbon monoxide; formaldehyde; benzene; arsenic, lead; polycyclic aromatic hydrocarbons

Improved Mental Health with smoking Cessation

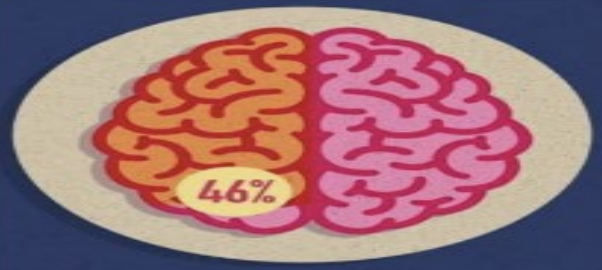
Meta-analysis 26 studies (gen pop and mental health)

Table 1| Effect of smoking cessation on mental health. Sensitivity analysis after removal of studies of low quality (mec
Newcastle-Ottawa scale)

Outcome	No of studies included	No of studies excluded	Standardised mean difference (95% CI)	
			Effect estimate	Original effect estimate
Anxiety	4	0	−0.37 (−0.70 to −0.03)	−0.37 (−0.70 to −0.03)
Depression	9	1	−0.29 (−0.42 to −0.15)	−0.25 (−0.37 to −0.12)
Mixed anxiety and depression	4	1	−0.36 (−0.58 to −0.14)	−0.31 (−0.47 to −0.14)
Psychological quality of life	4	4	0.17 (−0.02 to 0.35)	0.22 (0.09 to 0.36)
Positive affect	1	2	0.68 (0.24 to 1.12)	0.40 (0.09 to 0.71)
Stress	2	1	−0.23 (−0.39 to −0.07)	−0.27 (−0.40 to −0.13)

TOBACCO USE IS NOT AN EQUAL OPPORTUNITY KILLER.

THERE ARE UP TO **10X MORE TOBACCO ADS IN BLACK NEIGHBORHOODS** THAN IN OTHER NEIGHBORHOODS.



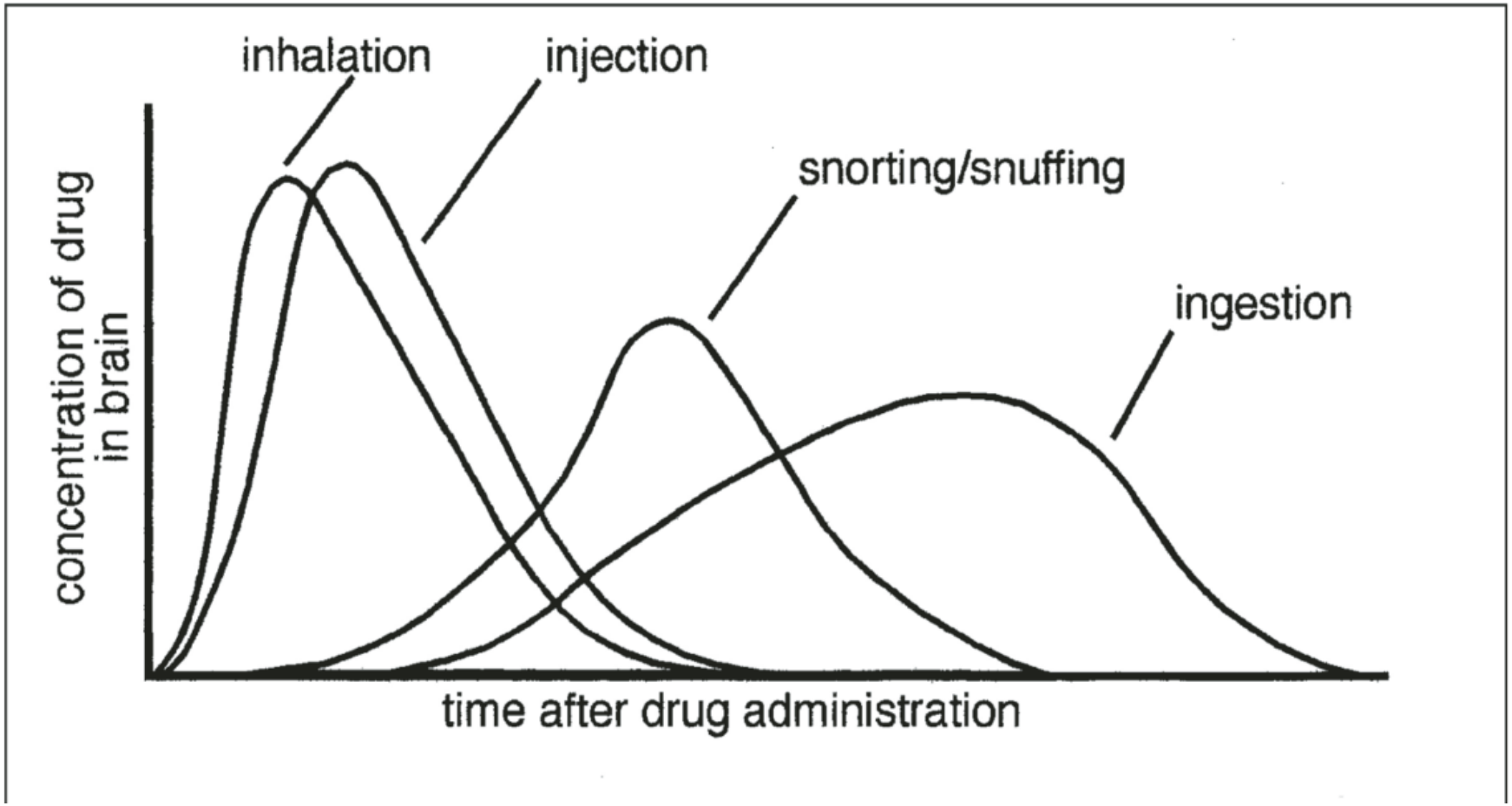
INDIVIDUALS WITH MENTAL ILLNESS **ACCOUNT FOR 46% OF CIGARETTES SOLD IN THE UNITED STATES.**

THERE ARE MORE TOBACCO RETAILERS NEAR SCHOOLS **IN LOW-INCOME AREAS THAN IN OTHER AREAS.**

LGBTQ YOUNG ADULTS, 18–24, ARE NEARLY **2X AS LIKELY TO SMOKE AS THEIR STRAIGHT PEERS.**

Pag

Smoking is the fastest route of administration



Best measure of Nicotine dependence severity

Heaviness of Smoking Index

- AM (upon awakening) Time to First Cigarette (TTFC)
  - ≤ 30 minutes = moderate
  - ≤ 5 minutes = severe
- Implications for Treatment Outcome
- Need for Medications
- Implications for dose

Assessment of Carbon Monoxide

- CO = product of combustion
- Expired CO in smokers
  - > 10 parts per million (ppm)
- Displaces oxygen on RBCs
- Strain on heart
  - Risk factor for CVD
- Can be assessed with a meter
- Reversible effect
  - Normal levels 2-3 days (0-3ppm)

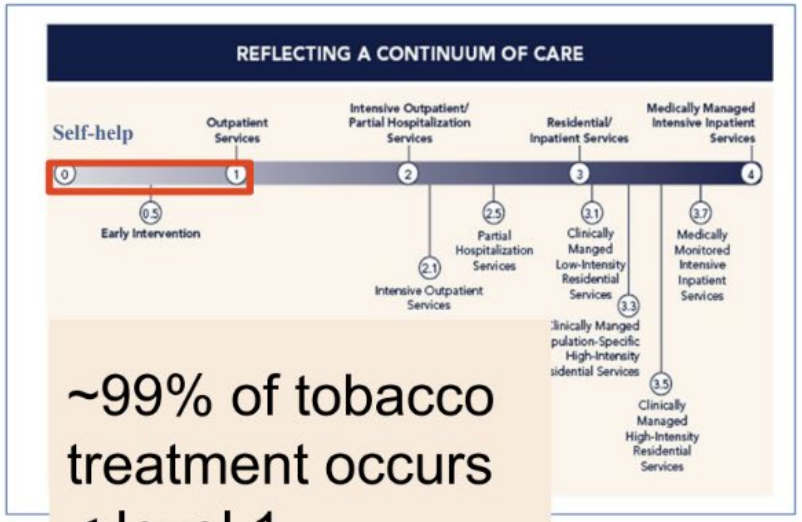
Tobacco withdrawal symptoms

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

Limited access to TUD treatment

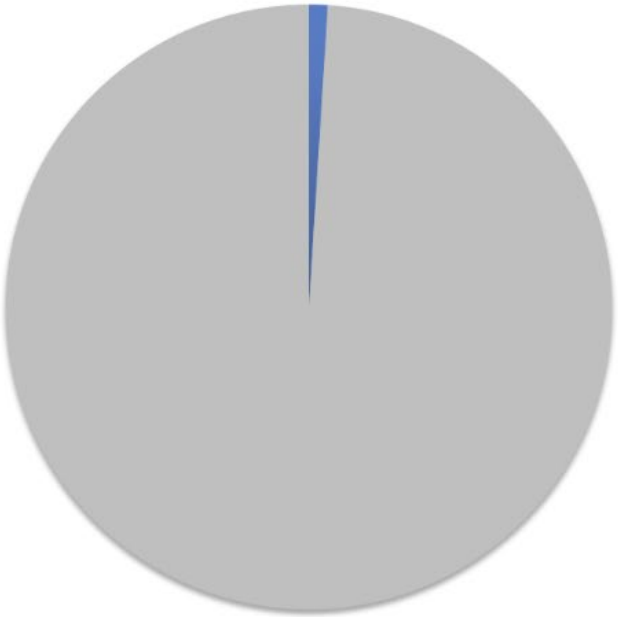
ASAM Levels of Care for SUD



~99% of tobacco treatment occurs ≤ level 1

Williams et al., JAM, 2016

1% Use Quitlines



Lichtenstein et al, 2010

Limited access to TUD treatment

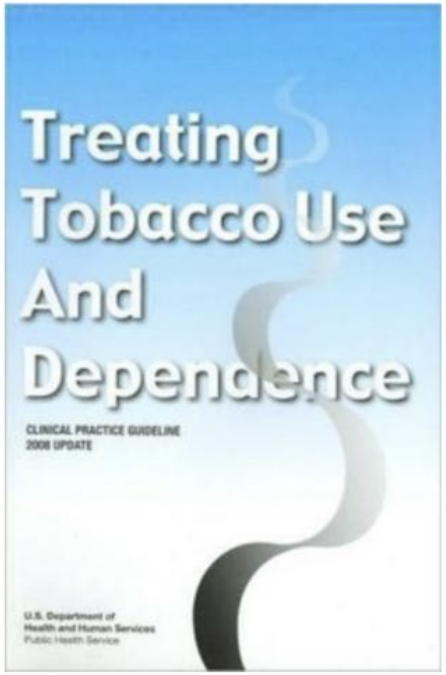
Tobacco Related Policies and Practices (2016 data)

Mental health treatment facilities (%)	Substance abuse treatment facilities (%)	
48.9	64.0	Reported screening patients for tobacco use
37.6	47.4	Offered tobacco cessation counseling
25.2	26.2	Offered nicotine replacement therapy
21.5	20.3	Offered non-nicotine cessation medications
48.6	34.5	Had a smoke free campus policy

Brief interventions

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?



Treatment for TUD works!

- Brief Assessment
- Counseling + Medications
- Approach like a Co-occurring Disorder
- “Treatment” not “Cessation”

Hard to Quit

- 55% make a serious quit attempt/year (>1d)
- <5% ultimately successful on a given quit attempt without treatment
- 6 month quit rates usually ~ 25% with 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

Predictors of success

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

Counseling + Medications = Best Treatment Plan

Effectiveness of meds or counseling alone vs. combination

Treatment	No of Studies	Est Odds Ratio (95%cl)	Estimated Quit Rate (%)
Medication alone	8	1.0	22
Meds plus counseling	39	**1.4** (1.2-1.6)	28

Treatment	No of Studies	Est Odds Ratio (95%cl)	Estimated Quit Rate (%)
Counseling alone	11	1.0	15
Meds plus counseling	13	**1.5** (1.3-2.1)	22

Psychosocial Treatment

Individual or Group

- Skills training
- Relapse prevention
- Problem solving
- Coping skills
- Stress management

✓Change cognitions about smoking

✓Reinforce nonsmoking

✓Avoid high risk situations

Quitline

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

1-800-QUIT-NOW

We can help you draw the line.

Maximizing Social Support

- Intra-treatment support
  - GROUP members
  - Clinician
- Extra-treatment
  - Friends
  - Family
  - Self-help
  - Internet

Both ↑ success in making a quit attempt

Pharmacological Treatment

- Rationale
  - Cost-effective
  - Reduce or eliminate withdrawal
  - Lessen/delay weight gain
  - Block reinforcing effects of nicotine

Increases chances of successful quit 2-3X

First Line FDA approved treatments

- **Nicotine Replacement Therapy**
- **Bupropion**
  - Zyban/Wellbutrin
- **Varenicline**
  - Chantix

Counseling + Medications = Best treatment plan

Pharmacological Treatment

- Nicotine Replacement Therapy (NRT)
  - Patch
  - Gum
  - Lozenge

  Available OTC, but may be covered with prescription with state Medicaid*

  - Inhaler
  - Nasal Spray

Nicotine Medications

- 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

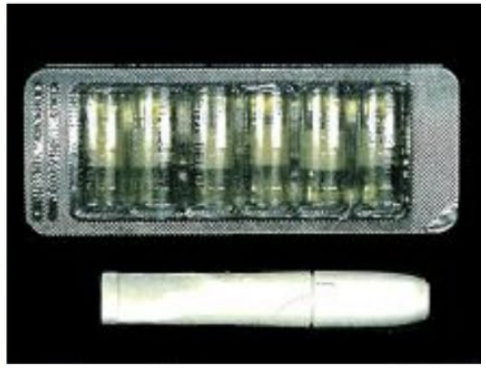
FDA labeling updates

- No significant safety concerns associated with using more than one NRT
- No significant safety concerns associated with using NRT at the same time as a cigarette.
- Use longer than 12 weeks is safe

Summary:

- Low risk of harm
- Benefits outweigh low risk of serious adverse cardiovascular events associated with use of tobacco treatment medications

Nicotine oral medications

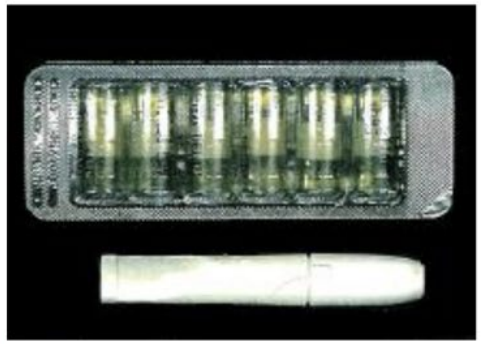


- Dose frequently – every 1-2 hours
- Slow, buccal absorption
- Acidic foods ↓ absorption
- Mild side effects – mouth, throat burning
- GI upset if swallowed (bite and park gum)
- Rx for Nicotine Inhaler

Prescription Nicotine

- **Nicotine Nasal Spray**
  - Rapid delivery though nasal mucosa
  - Most side effects (nasal irritation, rhinitis, coughing, watering eyes)
  - 2 sprays = 1 dose; up to 40 doses/day
  - Some dependence liability

- **Nicotine Inhaler**
  - 6-16 cartridges/day
  - Puff for 20-30 minutes
  - Oral puffer
  - Acidic beverages decrease absorption
  - Mild side effects – throat irritation or coughing



Smoking with NRT

- Relatively safe (nausea)
- Harm reduction
- Less reinforcing effects
- Withdrawal of treatment = punishment for relapsing
- In unmotivated smokers, 7% quit

Combination therapy

- Improve abstinence rates
- Decrease withdrawal
- Well tolerated

	OR
Patch + gum or spray	**1.9** (1.3-2.7)
Patch + bupropion	**1.3** (1.0-1.85)

Varenicline and NRT **NOT** recommend

Nicotine Patch

- Slow onset of action
- Continuous nicotine delivery
- 24 or 16 hour dosing
- Usual dose 21 mg/day
- Easy, good compliance
- No strict tapering or timeline
- Side effects – skin reaction, insomnia
- OTC

Nicotine Gum

- Nicotine Replacement (Agonist Therapy)
- Reduces nicotine withdrawal: anxiety, anger/irritability, depression, poor concentration
- Effect on craving is minimal
- 2- or 4-mg gum; use over 30 min
- Use 4-mg dose for heavy smokers (>25 cigarettes daily)
- Dosing: 1 piece every 1 hr better than prn for craving
- 50-90% nicotine released, depending on chewing rate

Nicotine Gum

- Nicotine absorbed through buccal mucosa
- Peak concentrations in 15-30 min (compared to 1-2 min for cigarette

smoking)

- Avoid acidic foods/beverages (e.g. coffee, juices, soda) as these

decrease absorption of nicotine

- Pregnancy Class (risk versus benefit):

Gum, lozenge, nasal spray Class C

Patch is Class D

Nicotine Gum

- Length of treatment is up to 12 weeks
- Approximate Costs:
- $48/2 mg gum
- $63/4 mg gum
- Boxes with 100-170 pieces
- Abstinence rate: NRTs increase quit rates by 50-70% (Stead et al. 2012), to 6.8%

sustained abstinence at 6 months (Moore et al. 2009)

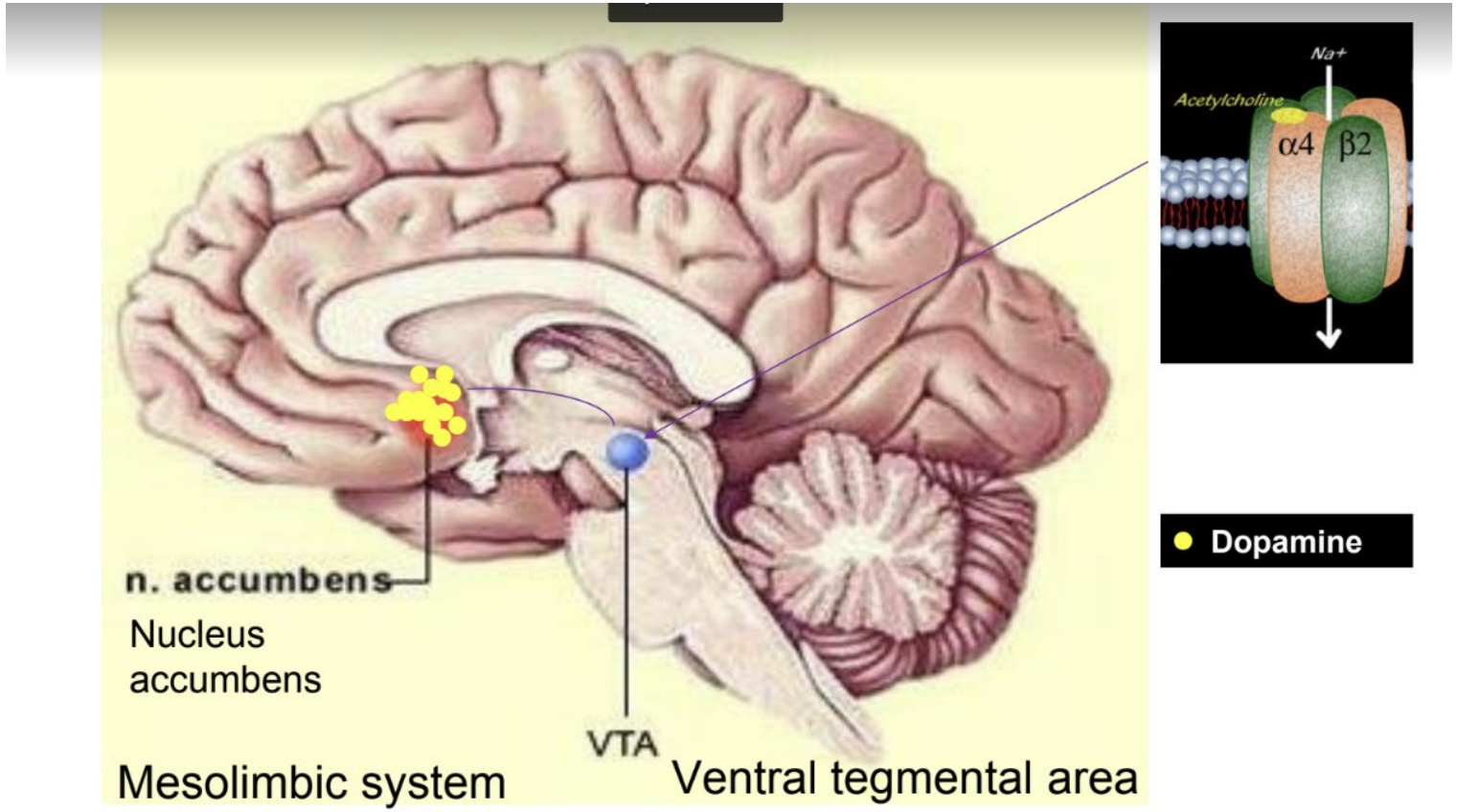
Bupropion SR (Zyban or Wellbutrin)

- Effective at 150 to 300mg daily
- Nonsedating, activating antidepressant with effects on NE and DA systems
- Start 10-14 days prior to quit date
- Side effects- headache, insomnia
- Contraindicated in h/o seizures or bulimia/ anorexia
- Noncompetitive nicotinic receptor antagonist
- Similar efficacy to NRT
- Effect independent of depression
- Less weight gain with 300mg than placebo

Varenicline (chantix)

- a4B2 partial nicotinic agonist
- No drug-drug interactions
- Excreted by kidney (urine)
- Only precaution in severe kidney disease (reduced dose)

Varenicline: A selective a4B2 nicotinic receptor partial agonist



Varenicline

- **Partial Agonist**
  - Partially stimulates receptor
  - Some dopamine release at nucleus accumbens
  - Prevents withdrawal
- **“Antagonist”**
  - Blocks nicotine binding a4B2

Most common Varenicline side effects

- Nausea
- Insomnia
- Abnormal dreams
- Constipation
- Flatulence
- Vomiting

Dosed twice a day with food to reduce nausea

Increasing dose in week one to 1mg BID

Effectiveness of First Line Medications

Results from meta-analyses comparing to placebo (6 month F/U)

Medication	No. Studies	OR	95% CI
Nic. Patch (6-14 wks)	32	**1.9**	1.7-2.2
Nic. Gum (6-14 wks)	15	**1.5**	1.2-1.7
Nic. Inhaler	6	**2.1**	1.5-2.9
Nic. Spray	4	**2.3**	1.7-3.0
Bupropion	26	**2.0**	1.8-2.2
Varenicline (2mg/day)	5	**3.1**	2.5-3.8

Varenicline and neuropsychiatric side effects

- Meta analysis 39 RCT (10,761 participants)
- Study not sponsored by Pfizer
- Industry and non-industry funded studies

- **No** increased risk of suicide
- **No** increased risk of suicidal ideation
- **No** increased risk of depression
- **No** increased risk of irritability
- **No** increased risk of aggression
- Increased risk of sleep disorders
- Increased risk of insomnia
- Increased risk of abnormal dreams
- Reduced risk of anxiety

- Warning (OLD)
- Reported from case reports of individuals taking varenicline
- Observe patients for serious neuropsychiatric symptoms including changes in behavior, agitation, depressed mood, suicidal thoughts or behavior

Thomas et al., 2015; BMJ

PCSS MAT TRAINING
PROVIDERS' CLINICAL SUPPORT SYSTEM
For Medication Assisted Treatment

Neuropsychiatric Composite side effect measure

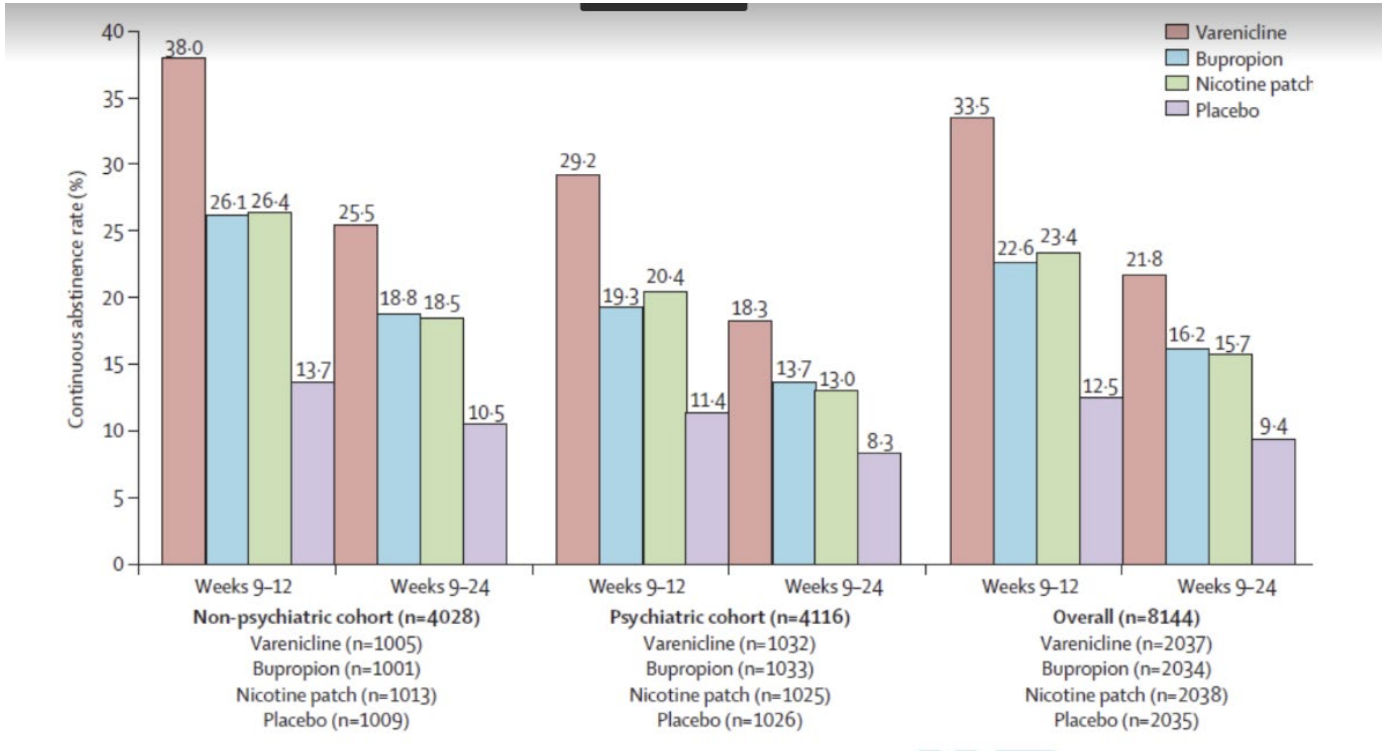
- Anxiety/panic
- Depression
- Feeling abnormal
- Hostility
- Agitation
- Aggression
- Delusions
- Hallucinations/paranoia/psychosis
- Homicidal ideation
- Mania
- Suicidal ideation or behavior

Neuropsychiatric safety and efficacy

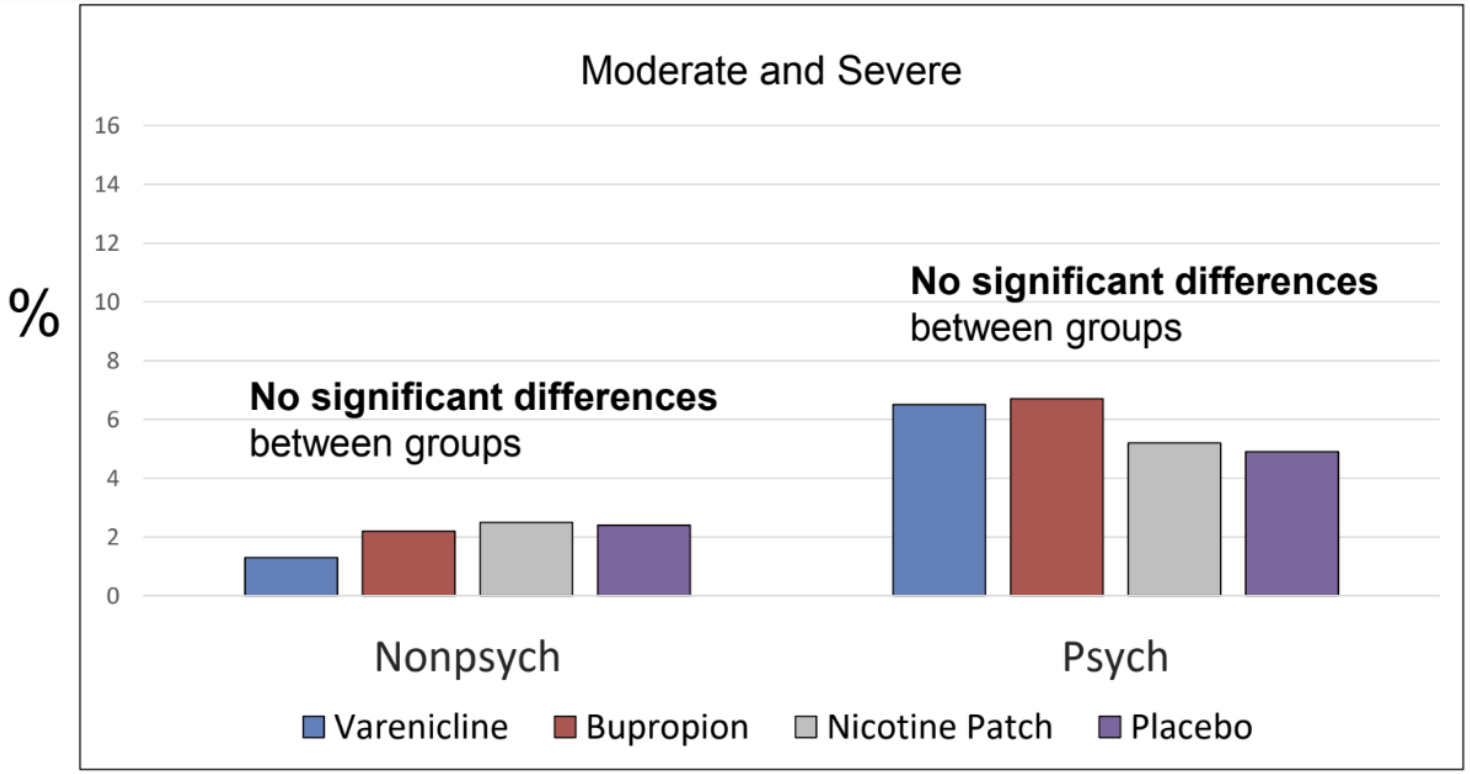
Varenicline, Bupropion, Nicotine Patch Smokers with and without Psych Disorders (EAGLES)

- 8144 (4416 psych and 4028, non psych by SCID)
- Triple dummy (DB-PC) x 12 weeks
  - Nicotine patch 21mg (NP)
  - Varenicline 1 mg BID
  - Bupropion 150 mg BID (BUP)
- Largest smoking cessation study
- 33% lifetime suicidal ideation (12% behavior); 50% on psych meds
  - 70% depression/ bipolar
  - 20% anxiety d/o
  - 10% psychotic
  - 1% personality disorder
- Brief weekly counseling
- Funded Pfizer and Glaxo (GSK)

Varenicline superior to BUP and NP in psych and non psych cohorts



Rates of neuropsychiatric adverse events



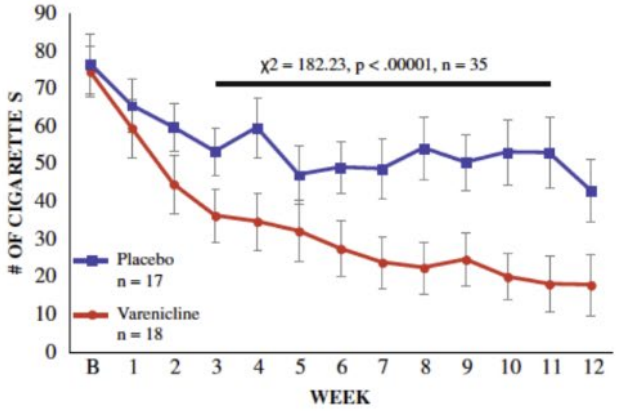
Varenicline ↑ Side effects: Nausea, insomnia, abnormal dreams, headaches

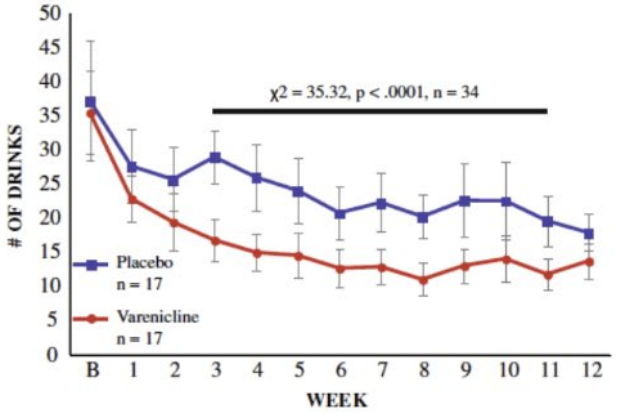
FDA Approves **Removal** of Boxed Warning Regarding Serious Neuropsychiatric Events from CHANTIX® (varenicline) Labeling

- 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)

Varenicline and Alcohol

- a4B2 may modulate rewarding effects of alcohol
- Varenicline reduces alcohol consumption and craving
  - In heavy drinkers
  - In smokers trying to quit smoking
  - In lab studies of animals and humans

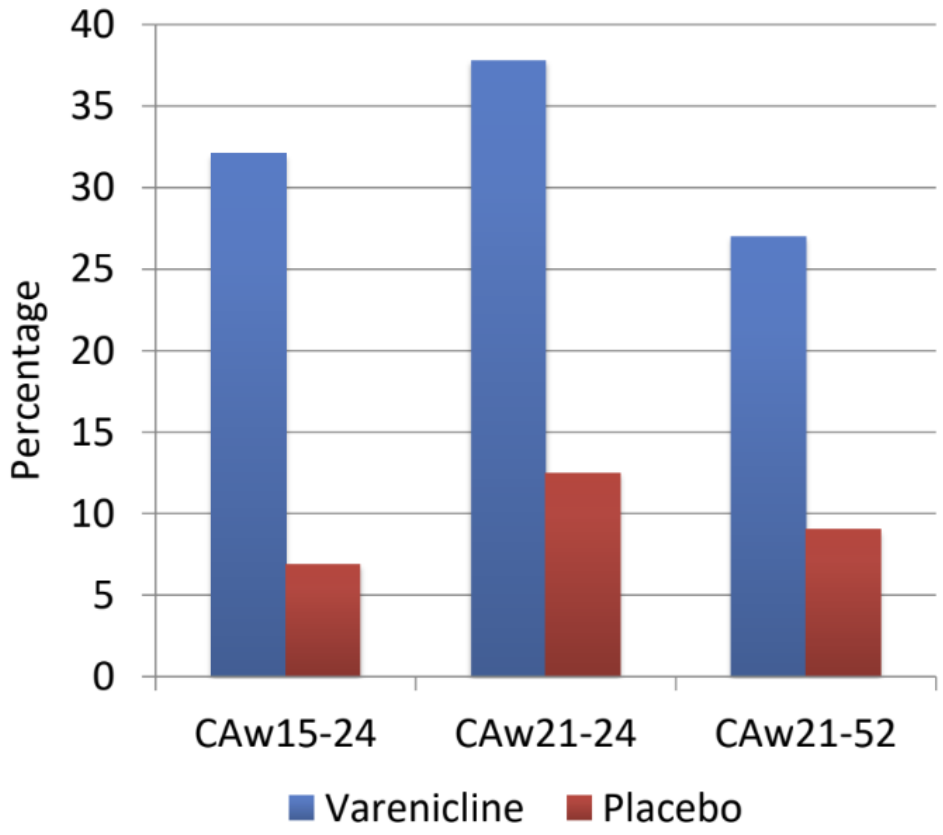




Smoking reduction with Varenicline

- 52-week double blind placebo controlled study of 1,510 subjects who were not able/willing to quit smoking within four weeks, but were willing to gradually reduce their smoking over 12 weeks
- Varenicline 1 mg BID (N=760) or placebo (N=750) for 24 weeks
- Subjects instructed to reduce cigarettes per day by 50% end of first four weeks of treatment, followed by further 50% reduction from week 4-8, with the goal of reaching complete abstinence by 12 weeks.

Reduction with Varenicline had a significant increase in quit rates



Chantix Package Insert
(on label)

Consider a gradual approach to quitting smoking for patients who are sure that they are not able or willing to quit abruptly

CA= continuous abstinence

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Conclusions

- It's the smoke that kills
- Approach tobacco use as a co-occurring disorder
- Ask, Advise, Refer
- Medications + counseling
- Think about medications for anyone TTFC < 30 mins
- Varenicline OR combination NRT two very good medication options

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THANK YOU
for your
ATTENTION!

Which of the following statements is FALSE regarding the tobacco withdrawal syndrome?

A. Increase appetite is a tobacco withdrawal symptom because nicotine is an appetite suppressant

B. Some smokers wake up every morning in tobacco withdrawal

C. Non-nicotine treatments (varenicline and bupropion) are ineffective for treating tobacco withdrawal symptoms

D. Tobacco withdrawal symptoms can include insomnia

E. Withdrawal symptoms can emerge hours after the last use of tobacco

Which of the following statements is TRUE regarding nicotine replacement therapies (NRT)?

A. Most people who use NRT become long term users of it

B. Nicotine has good gastrointestinal absorption and produces serum nicotine levels which are higher than that of a smoked cigarette

C. Most people use NRT incorrectly or at too low a dose

D. Few people discontinue nicotine nasal spray due to side effects

E. Nicotine cannot be used in individuals with cardiovascular disease

Reasonable approaches to tobacco use disorder include:

A. Waiting until the patient brings it up

B. Brief interventions such as Ask, Advise and Refer

C. Avoiding medication combinations due to high risk of toxicity and overdose

D. Referrals for hypnosis

E. Telling patients to switch to chewing tobacco

Which of the following statements is TRUE regarding tobacco use disorder treatment?

A. Bupropion is more effective in smokers with a past or family history of major depression

B. Varenicline causes clinically important medication interactions via the cytochrome P450 system

C. Smokers with a history of substance use disorder cannot be treated with bupropion due to the risk of seizures

D. Varenicline works primarily as a nicotinic partial agonist

E. Varenicline causes neuropsychiatric side effects in half of the smokers who use it

A brief individualized approach to treating tobacco addiction may include:

A. A discussion of how tobacco use impacts finances, health and quality of life

B. Advice to quit in clear and personalized terms

C. An assessment of the individual's willingness to quit

D. Referring to a specialized counseling service like telephone quitline

E. All of the above