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## A Practical Approach to Treating Smoking

Hilary A. Tindle, MD, MPH Associate Professor of Medicine William Anderson Spickard, Jr., MD, Chair in Medicine Director of ViTAL: Vanderbilt Center for Tobacco, Addiction and Lifestyle Vanderbilt University Medical Center Nashville, TN

## Disclosures

- Principal Investigator for NIH-supported smoking cessation trials that used smoking cessation medication donated by manufacturer
- Consultant to NCI for Tobacco Control Monograph Series, to CDC for U.S. Surgeon General's Reports on Smoking and Tobacco Use
- Volunteered (unpaid) scientific input to design of a Phase 3 trial for an emerging smoking cessation medication proposed for FDA approval
- Currently volunteer as panel member for:
  - National Comprehensive Cancer Center (NCCN) Smoking Cessation Guidelines
  - Cochrane Review Guidelines for Treating Hospitalized Smokers (2022 Update)

## **Overview**

- Epidemiology: Smoking rates are declining but still threaten cardiometabolic health
- Smoking cessation decreases cardiometabolic risk (and other health risks, too!)
- Screen and Intervene
- Future directions in treatment of smoking and tobacco use

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## Smoking: Epidemiology and Connection to Cardiometabolic Risk

Hilary A. Tindle, MD, MPH Associate Professor of Medicine William Anderson Spickard, Jr., MD, Chair in Medicine Director of ViTAL: Vanderbilt Center for Tobacco, Addiction and Lifestyle Vanderbilt University Medical Center Nashville, TN

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## **FALLING RATES**

By AMERICAN HEART ASSOCIATION NEWS

The cigarette smoking rate among U.S. adults has hit an all-time low, federal data show.

In the U.S., smoking cessation is a public health success story...



#### Annual Adult per Capita Cigarette Consumption and Major Smoking and Health Events- the United States, 1900-1998



# **SMOKING CESSATION**

#### A REPORT OF THE SURGEON GENERAL

#### **HIGHLIGHTS FOR CMHC CCHP 2022**









#### **10 Major Conclusions**



 Smoking cessation is beneficial at any age. Smoking cessation improves health status and enhances quality of life.

 Smoking cessation reduces the risk of premature death and can add as much as a decade to life expectancy.

**3.** Smoking places a substantial financial burden on smokers, healthcare systems, and society. Smoking cessation reduces this burden, including smoking-attributable healthcare expenditures.

4. Smoking cessation reduces risk for many adverse health effects, including reproductive health outcomes, cardiovascular diseases, chronic obstructive pulmonary disease, and cancer. Quitting smoking is also beneficial to those who have been diagnosed with heart disease and chronic obstructive pulmonary disease.

#### **10 Major Conclusions**

and chronic obstructive pulmonary disease.

Smoking Cessation Age	Years of Life Gained	<ol> <li>Smoking cessation is beneficial at any age. Smoking cessation improves health status and enhances quality of life.</li> </ol>
25-34	10	<ul> <li>2. Smoking cessation reduces the risk of premature death and can add as much as a decade to life expectancy.</li> <li>3. Smoking places a substantial financial burden on smokers, healthcare systems, and society. Smoking cessation reduces this burden, including smoking-attributable healthcare expenditures.</li> </ul>
35-44	9	
45-54	6	
55-64	4	
Before age 40: reduces		
risk of death associated		4. Smoking cessation reduces risk for many adverse
with continued smoking		health effects, including reproductive health outcomes,
by 90%, but is <u>effective at</u>		cardiovascular diseases, chronic obstructive pulmonary
any age, including > 65		disease, and cancer. Quitting smoking is also beneficial
	and the second	to those who have been diagnosed with heart disease

#### **10 Major Conclusions**



**1.** Smoking cessation is beneficial at any age. Smoking cessation improves health status and enhances quality of life.

**2.** Smoking cessation reduces the risk of premature death and can add as much as a decade to life expectancy.

**3.** Smoking places a substantial financial burden on smokers, healthcare systems, and society. Smoking cessation reduces this burden, including smoking-attributable healthcare expenditures.

Smoking cessation reduces risk for many adverse health effects, including reproductive health outcomes, cardiovascular diseases, chronic obstructive pulmonary disease, and cancer. Quitting smoking is also beneficial to those who have been diagnosed with heart disease and chronic obstructive pulmonary disease.

#### Where Does Treatment of Smoking Fit In to Prevention?

Intervention	Outcome	NNT
Statins	Prevent 1 death over 5 years	107
Aspirin	Prevent 1 MI over 5 years	118
Antihypertensive therapy	Prevent 1 stroke, MI, death over 1 year	700
Cervical cancer screening	Prevent 1 death over 10 years	1140
MD 5 min advice to stop smoking	Prevent 1 premature death	80
+ cessation medication	Prevent 1 premature death	38-56
+ behavioral support	Prevent 1 premature death	16-40

**NNT = Number Needed to Treat** 

Anthorison, 2006, Ann Intern Med; McQuay & Moore, 2006, Bandolier; Gates 2001, Am Fam Phys; Cochrane Reviews by Stead, Bergeson, et al., 2008; Stead, Perera, et al. 2012; Stead & Lancaster, 2012; Cahill et al., 2010; and USPSTF, 2009

#### **Quitting Smoking Reduces Risk of CVD**

- In the Framingham Heart Study, heavy former vs. current smokers have 39% lower CVD risk in 5 years but remain at higher risk of CVD for 16+ years vs. never smokers.
- Adding pack years, years since quitting, and smoking status (former vs. never) to the ASCVD risk calculator improves risk prediction.



#### **Quitting Smoking Reduces Risk of Lung Cancer**

- Heavy former vs. current smokers have 39% lower risk of lung cancer with in 5 yrs
- Former remain at 3 fold higher risk for up to 25+ years vs. never smokers.
- 41% of lung cancers occurred in former smokers who quit > 15 years ago



#### **10 Major Conclusions - highlights**



5. More than three out of five U.S. adults who have ever smoked cigarettes have quit. Although a majority of cigarette smokers make a quit attempt each year, less than one-third use cessation medications approved by the U.S. Food and Drug Administration (FDA) or behavioral counseling to support quit attempts.

**6.** Considerable disparities exist in the prevalence of smoking across the U.S. population, with higher prevalence in some subgroups. Similarly, the prevalence of key indicators of smoking cessation—quit attempts, receiving advice to quit from a health professional, and using cessation therapies—also varies across the population, with lower prevalence in some subgroups.

**7.** Smoking cessation medications approved by the U.S. Food and Drug Administration (FDA) and behavioral counseling are cost-effective cessation strategies. Cessation medications approved by the FDA and behavioral counseling increase the likelihood of successfully quitting smoking, particularly when used in combination. Using combinations of nicotine replacement therapies can further increase the likelihood of quitting.

#### **10 Major Conclusions - highlights**



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#### **Current Smoking Among Adults**



#### **Current Smoking Among Adults**



#### Cigarette smoking is down, but almost 34 MILLION American adults still smoke

#### Cigarette smoking remains high among certain groups







Lower education



Below poverty level





Uninsured or Medicaid

Disabled



Serious psychological distress





Lesbians, gays, and bisexuals

https://www.cdc.gov/media/releases/2018/p0118-smoking-rates-declining.html

#### **10 Major Conclusions - highlights**



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## Smoking Cessation: Screen and Intervene

#### Hilary A. Tindle, MD, MPH Associate Professor of Medicine William Anderson Spickard, Jr., MD, Chair in Medicine Director of ViTAL: Vanderbilt Center for Tobacco, Addiction and Lifestyle Vanderbilt University Medical Center Nashville, TN

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# NEUROCHEMICAL and RELATED EFFECTS of NICOTINE



- Pleasure, appetite suppression
- ➔ Arousal, appetite suppression
- ➔ Arousal, cognitive enhancement
- ➔ Learning, memory enhancement
- ➔ Mood modulation, appetite suppression
- Reduction of anxiety and tension
- Reduction of anxiety and tension

#### **Nicotinic Acetylcholine Receptors**



Ventral Tegmental Area (VTA)

https://basicmedicalkey.com/acetylcholine-receptor-agonists/

http://www.treatobacco.net/en/uploads/image/nach\_receptors.jpg



# Pagemener of Phaloh and Phaneer Services

**Smoking Cessation** 

A Report of the Surgeon General

#### Source: Changeux (2010, p. 391)

#### Figure 3.3 Neuronal mechanisms involved in nicotine addiction: A model

#### **Cellular Basis of Memory for Addiction**

Eric J. Nestler, MD, PhD

"Despite the importance of numerous psychological factors, at is core, drug addiction involves a biological process: the ability of repeated exposure to a drug of abuse to induce changes in a vulnerable brain that drive the compulsive seeking and taking of drugs, and loss of control over drug use, that define a state of addiction.... the types of molecular and cellular adaptations that occur in specific brain regions to mediate addictionassociated behavioral abnormalities... include alterations in gene expression achieved in part via epigenetic mechanisms, plasticity in the neurophysiologic functioning of neurons and synapses, and associated plasticity in neuronal and synaptic morphology, mediated in part by altered neurotrophic factor signaling. . . drug induced modifications can be viewed as a form of 'cellular or molecular memory."



# **Smoking Cessation Treatment Guidelines**

2008 US Public Health Service, 2015 US Preventive Services Task Force, 2020 SGR

- Effective treatments exist
- Pharmacotherapy *targets nicotine addiction*
- Behavioral support targets behavioral components

- delivery: in-person, by phone, web, apps

- **Combination** is superior to either alone
- More intensive treatment is better, but brief intervention is effective

#### **Screening and Intervening: The 5 A's**



#### **EVERY PATIENT, EVERY TIME!**

Source: US Department of Health and Human Services. Treating Tobacco Use and Dependence: 2008 Update. Graphics: Adapted from Rx for Change

#### Screening and Intervening - The 5 A's: Modified





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Fig

Smoking Cessation Pharmacotherapy: Guidelines and Evidence

Hilary A. Tindle, MD, MPH Associate Professor of Medicine William Anderson Spickard, Jr., MD, Chair in Medicine Director of ViTAL: Vanderbilt Center for Tobacco, Addiction and Lifestyle Vanderbilt University Medical Center Nashville, TN

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** 



#### **Pharmacotherapy**

2008 US Public Health Service, 2015 USPSTF, 2020 Surgeon General's Report

• Nicotine replacement

Skin patch(OTC)Gum(OTC)Lozenge(OTC)Oral inhaler(Rx)Nasal spray(Rx)

FDA approved for cessation, 2X quit rate vs. placebo

- Bupropion SR
- Varenicline (Since the global recall in 2021, other generic forms have become relevant)

#### Long-term (≥6 month) Quit Rates for Available Cessation Medications



#### **Current Pharmacotherapy Options** Cochrane meta-analysis



## National Guidelines: Pharmacotherapy

- 2018 American College of Cardiology (ACC)
- 2020 National Comprehensive Cancer Network (NCCN)
- 2020 SPAQI (Perioperative)
- 2020 American Thoracic Society (ATS)

<u>Begin with:</u> Varenicline or Combination NRT

## **Nicotine Replacement Options**

#### Long-acting, slow onset nicotine delivery $\rightarrow$ *patch*

- + Constant nicotine level to avoid withdrawal
- + Simplest to use
- User has no control of dose

#### Short-acting, faster onset → *gum*, *lozenge*, *inhaler*, *spray*

- + User controls dose
- Nicotine blood levels fluctuate more
- Many smokers do not use enough
# Plasma Nicotine Levels Cigarettes vs. Nicotine Replacement Products



# Varenicline

- Partial agonist at α4β2 nicotinic receptor
- Dual mechanism of action
  - Partial agonist

Stimulates receptor to treat craving, withdrawal

• Antagonist

Prevents nicotine from binding to the receptor  $\rightarrow$  Blocks reward, reinforcement of smoking

- Most common side effects: nausea/GI, vivid dreams
- Avoid in pregnancy, unstable mental illness; dose reduce in severe renal impairment



# Varenicline



#### Varenicline: Safety Concerns

#### FDA Public Health Advisory - July 2009

• "[*Varenicline*] or [*bupropion*] has been associated with reports of changes in behavior such as hostility, agitation, depressed mood, and suicidal thoughts or actions."

 "FDA is requiring the manufacturers of <u>both</u> products to add a new *Boxed Warning*"

# **EAGLES Trial – Methods**

- Double blind, placebo-controlled trial of motivated smokers (≥ 10 CPD) +/- psychiatric disorders randomized 1:1:1:1 (V:B:NRT:P)
  - 3984 without psychiatric disorders
  - 4074 with psychiatric disorders: 70% affective, 19% anxiety, 9.5% psychotic, 0.6% personality; 1/3 stable psychotropic meds
  - Safety: Composite endpoint of 16 NPS AEs including
    - anxiety, depression, feeling abnormal, and hostility (all rated as severe), and agitation, aggression, delusions, hallucinations, homicidal ideation, mania, panic, paranoia, psychosis, suicidal ideation, suicidal behavior, and completed suicide (all rated as moderate or severe)
- Efficacy: abstinence wks 9-24, CO-confirmed

# **EAGLES Trial – Safety**

#### Composite neuropsychiatric event endpoint

Non-psychiatric	Non-psychiatric cohort* (n=3984)			
cohort	Varenicline (n=990)	Bupropion (n=989)	Nicotine patch (n=1006)	Placebo (n=999)
Primary composite neuropsychiatric endpoint	13 (1.3%)	22 (2·2%)	25 (2.5%)	24 (2·4%)
Estimated primary composite neuropsychiatric adverse events (% [95% CI])	1·25% (0·60 to 1·90)	2·44% (1·52 to 3·36)	2·31% (1·37 to 3·25)	2·52% (1·58 to 3·46)
Difference in risk of composite primary endpoint (	RD% [95% CI])			
Versus placebo	-1·28 (-2·40 to -0·15)	-0·08 (-1·37 to 1·21)	-0·21 (-1·54 to 1·12)	
Versus nicotine patch	-1·07 (-2·21 to 0·08)	0·13 (–1·19 to 1·45)		
Versus bupropion	-1·19 (-2·30 to -0·09)		<sup>"</sup> Psy	/cħiatr

No difference among drugs in rates of psychiatric adverse events in either stratum

As a consequence of EAGLES, the FDA removed Black Box warnings December 2016

Psychiatric cohort	Psychiatric cohort* (n=40/4)					
i sychiatric conort	Varenicline (n=1026)	Bupropion (n=1017)	Nicotine patch (n=1016)	Placebo (n=1015)		
Primary composite neuropsychiatric endpoint	67 (6.5%)	68 (6.7%)	53 (5·2%)†	50 (4·9%)		
Estimated primary composite neuropsychiatric adverse events (% [95% CI])	6·42% (4·91 to 7·93)	6.62% (5.09 to 8.15)	5·20% (3·84 to 6·56)	4·83% (3·51 to 6·16)		
Difference in risk of composite primary endpoint (RD% [95% CI])						
Versus placebo	1.59 (-0.42 to 3.59)	1·78 (-0·24 to 3·81)	0·37 (-1·53 to 2·26)			
Versus nicotine patch	1·22 (-0·81 to 3·25)	1·42 (-0·63 to 3·46)				
Versus bupropion	-0·20 (-2·34 to 1·95)					

### **EAGLES - Efficacy Results**



Figure 3: Continuous abstinence rates for weeks 9–12 and 9–24 Analyses based on the all-randomised population. OR=odds ratio.

### Quitting Stats: Every Year in the US . . .

- 8/10 smokers see a health care provider
- 7/10 smokers want to quit, over ½ attempt
- Only **5%** receive recommended care: medication <u>and</u> counseling
- 95% of unaided quit attempts "fail", so quit rates remain low.
- Why the disconnect between evidence and treatment?

### **Misconceptions: Health Care Providers**

- I don't have enough time
- The patient:
  - Is not going to quit
  - has too much going on right now
  - is too high risk for smoking cessation meds/meds dangerous (varenicline)
- I might alienate my patients if I bring it up
- We don't have a smoking program at my hospital/clinic

### **Misconceptions: Patients**

- I can't quit
- Quitting doesn't matter- damage is done/I'm too old
- I have too much going on right now
- Quit smoking medicines don't work
- Quit smoking medicines are dangerous
- Using medicines is just trading one addiction for another
- Using medicines is a crutch

# The 5 A's



#### **EVERY PATIENT, EVERY TIME!**

Source: US Department of Health and Human Services. Treating Tobacco Use and Dependence: 2008 Update. Graphics: Adapted from Rx for Change

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# Smoking Cessation: Patient Case

#### Hilary A. Tindle, MD, MPH

Associate Professor of Medicine William Anderson Spickard, Jr., MD, Chair in Medicine Director of ViTAL: Vanderbilt Center for Tobacco, Addiction and Lifestyle Vanderbilt University Medical Center Nashville, TN

#### Case

- 58 yo man w/HTN, HIV+, stable depression on SSRI, + AUDIT-C, presents with pneumonia
- Smokes 20 cigarettes/d since age 18
- Drinks 3 beers/d, more on weekends
- Wants to smoke now but feels too weak
- In the past tried "everything" to quit, including ecigs

#### Case

- 58 yo man w/HTN, HIV+, stable depression on SSRI, + AUDIT-C, presents with pneumonia
- Your initial assessment and thoughts:
  - High risk for smoking related disease (age, male, HIV status, depression, alcohol use)
  - High risk for other diseases, including lung cancer.
    Smoked 40 years x 1 ppd = 40 pack years (eligible for LCS > 55, > 30 pk yrs)

**Case: Advise** 

58 yo man w/HTN, HIV+, stable depression on SSRI, + AUDIT-C, presents with pneumonia

 Advise: "Quitting smoking is the best thing you can do for your health right now, and is especially important as you heal from pneumonia"

#### **Case: Assess**

# 58 yo man w/HTN, HIV+, stable depression on SSRI, + AUDIT-C, presents with pneumonia

 Assess: Says he knows he needs to quit, has tried "everything." (What does this mean?)

• How much is he smoking now?

#### **Case: Assess, continued**

 58 yo man w/HTN, HIV+, stable depression on SSRI, + AUDIT-C, presents with pneumonia, smoking <u>1 pack</u> per day

- nicotine patch used 1 week, craved, relapsed
- bupropion cut down, did not quit
- electronic cigarette used for 3 months but kept smoked. Eventually didn't like it and resumed smoking.
- Varenicline quit 3 years ago but relapsed after divorce. He adds that his neighbor told him, "this is the worst drug" but his friend said is was the best drug to quit smoking." He asks what you think.

#### **Case: Next Steps**

- 58 yo man w/HTN, HIV+, stable depression on SSRI, + AUDIT-C, admitted with pneumonia
- Your updated assessment motivated to quit now and seems willing to consider medication
- What should you do next?

#### **Case: Assist**

- 58 yo man w/HTN, HIV+, stable depression on SSRI, + AUDIT-C, admitted with pneumonia, smokes 1 ppd
- Assist:
  - -Set a Target Quit Date ideally within 2 weeks
  - -Combine pharmacologic & behavioral support
    - Most national guidelines recommend beginning with varenicline or two forms of NRT
    - What about for this patient?

#### **Question 1: True or False**

- This patient's history of depression makes him <u>ineligible</u> for smoking cessation medication.
  - a. True
  - b. False

#### **Question 1: True or False**

• This patient's history of depression makes him <u>ineligible</u> for smoking cessation medication.

False - This patient CAN use FDA-approved smoking cessation medications: nicotine replacement therapy, varenicline, and bupropion. He has stable depression. In the EAGLES trial, 70% of the 4074 participants in the cohort with pre-existing psychiatric diagnoses had mood disorders, including major depression and bipolar depression. Individuals were considered stable if they had not had any recent worsening of symptoms prompting medication or dosage changes, ED visits, hospitalizations, etc. Today in clinical practice, a period of about 3 months is reasonable, but this varies case-by-case.

Varenicline has also been studied in several RCTs in patients with HIV and can be safely and effectively used in this population. Varenicline has also been studied in people with SUD (alcohol and opioid use disorder).

#### **Case: Assist**

- 58 yo man w/HTN, HIV+, stable depression on SSRI, + AUDIT-C, admitted with pneumonia, smokes 1 ppd
- Assist:
  - -Set a Target Quit Date ideally within 2 weeks
  - Combine pharmacologic & behavioral support
    - What smoking cessation prescription should you write?

# **Question 2:**

- What is an appropriate first step for medication? (What prescription should you write?)
  - A. Nicotine replacement therapy (NRT) monotherapy (e.g., patch)
  - B. Nicotine replacement therapy (NRT) combination therapy ("patch plus")
  - C. Varenicline
  - D. A only
  - E. Bonly
  - F. Conly
  - G. B or C

# **Question 2:**

- What is an appropriate first step for medication? (What prescription should you write?)
  - A. Nicotine replacement therapy (NRT) monotherapy (such as patch)
  - B. Nicotine replacement therapy (NRT) combination therapy (such as patch plus oral lozenges)
  - C. Varenicline
  - D. A only
  - E. Bonly
  - F. Conly

G. B or C – Correct Answer. Most treatment guidelines recommend starting with <u>either</u> <u>combination NRT or varenicline as an initial choice</u> for pharmacotherapy. Varenicline is the most effective monotherapy, and combination (2 forms) NRT is generally considered to be more effective (and more comfortable for patients) than 1 form of NRT alone. Recall the pharmacokinetics of different NRT products: patch yields a slow rise in blood concentration (4-6+ hours), while oral/inhaled NRT has faster increase in blood levels (15-30 minutes). Note: NRT product approaches the fast delivery of cigarettes (seconds).

#### **Case: Assist**

- 58 yo man w/HTN, HIV+, stable depression on SSRI, + AUDIT-C, admitted with pneumonia, smokes 1 ppd
- Assist:
  - Set a Target Quit Date ideally within 2 weeks
  - Combine pharmacologic & behavioral support
    - Varenicline or two forms of NRT
    - Brief counseling triggers, what has worked before, anticipating rough spots (temptations), etc
    - Referral

# **Case: Assist - Selecting Pharmacotherapy**

- 58 yo man w/HTN, HIV+, stable depression on SSRI, + AUDIT-C, admitted with pneumonia. Smokes 1 ppd
- Any advantage to varenicline or combination NRT?
  - Medically eligible to take either
  - Both are effective but varenicline is most effective monotherapy
  - Patient preference, coverage, out-of-pocket cost
  - What about the alcohol?

# Varenicline for smoking – and alcohol?

- Smoking and heavy drinking co-occur, and each independently increase health risk.
   Polypharmacy: mitigate with 1 drug for 2 diseases
- Meta-analysis of varenicline vs. placebo (5-9 studies)
  - Moderate effect size for drinks/unit time
  - No difference for heavy drinking, drinking days, dropouts



# Varenicline for smoking – and alcohol?

- Effects of varenicline for alcohol consumption may be more pronounced among men and among depressed individuals
- Meta-analysis of 10 studies in alcohol use disorder: varenicline reduces craving, but not consumption

# **Case: Begin with Combo NRT or Varenicline**

- NRT: combine long acting 21 mg patch + short-acting oral titrate to comfort
  - Most common dosing is "Step down" 21 mg x 1 month, 14 mg x 1 month, then 7 mg x 1 month, but dosing is flexible and should be guided by patient's symptoms
- Varenicline 12 weeks
  - "starter pack" 1 month, then "maintenance pack" 2 months
  - Note: prolonged global shortage of may require alternative manufacturers other than Pfizer: "Par" and "Apotex" brand varenicline are available in some regions of the US and providers may need to work with pharmacists to obtain varenicline

# Nicotinic Receptors are Upregulated in Smokers, Take Weeks to Normalize



#### Figure 2.

Mean parametric images illustrating  $\beta_2^*$ -nAChR availability in nonsmokers and tobacco smokers at 1 day, 1 week, 2 weeks, 4 weeks, and 6-12 weeks of abstinence at similar transaxial levels of brain. The color scale is shown with red, yellow, green and blue corresponding to  $V_T/f_P$  values.



Cochrane Database of Systematic Reviews

# Do Electronic Cigarettes Have a Role in Smoking Cessation?

Electronic cigarettes for smoking cessation (Review)

Hartmann-Boyce J, McRobbie H, Lindson N, Bullen C, Begh R, Theodoulou A, Notley C, Rigotti NA, Turner T, Butler AR, Fanshawe TR, Hajek P

- 2020 Cochrane review: 50 studies, 26 RCTs in over 12,000 people
- Limited by imprecision due to few large trials
  - e-cigs with nicotine increases quit rates at 6+ months compared to e-cigs without nicotine and compared to NRT (Moderate certainty)
  - e-cigs with nicotine increased quit rates compared to behavior support alone/no support (Low certainty)
- Controversial conclusions in the Hajek et al RCT (NEJM, 2019) 80% of those assigned to e-cigs were still using them at 1 year, and some of those who did not quit smoking became dual users
- Important context: in the US, e-cigs are not approved by FDA for treatment

#### **Case: Arrange**

# **Refer/Connect for ongoing support**

Internal program

–inpatient/outpatient tobacco treatment service

# • External program

- -State quitline 1-800-QUIT NOW
- -Web: Smokefree.gov, BecomeanEx.org

-Local community programs

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# **Smoking Cessation: Tips and Resources**

Hilary A. Tindle, MD, MPH Associate Professor of Medicine William Anderson Spickard, Jr., MD, Chair in Medicine Director of ViTAL: Vanderbilt Center for Tobacco, Addiction and Lifestyle Vanderbilt University Medical Center Nashville, TN

#### Screening and Intervening - The 5 A's: Modified





# www.Smokefree.gov



#### **Becomeanex.org - Truth Initiative + Mayo Clinic**



#### **Decide to Quit**

Quitting can seem overwhelming. Tobacco is part of your life and change is hard. We know.

We also know amazing change can happen when you have the right support and tools to guide you.

BecomeAnEX works because it was built for you—with expert knowledge from Mayo Clinic and real tobacco users who understand the struggle and how tps://www.becomeanex.org/recently-quit/
## An Important Discussion Point When Talking With Patients: People who quit smoking often *feel better*

- There is a growing body of research on the impact of smoking and quitting smoking on mood and health related quality of life
- Levy et al conducted a longitudinal assessment of health-related quality of life (HRQoL) changes among recently-hospitalized patients who smoke
- Compared change in HRQoL between those who did or did not quit smoking 6 months after hospital discharge
  - Single-item global health measure (SF-1)
  - Patient Health Questionnaire for Depression and Anxiety (PHQ-4)
  - EQ-5D-5L health utilities measure

## Quitting Smoking After Hospitalization Associated With Better HRQoL

Abstinent patients at 6 months: 30% more likely to report at least good health on SF1 (aRR 95% CI 1.14–1.45)





#### Levy et al, Preventive Medicine 2018.

### **Quitting Smoking After Hospitalization is Associated With Better HRQoL on the EQ-5D-5L**

- Overall increase in mean score of 0.05 (0.02, 0.08)
- Higher odds of improvement in:

Subscale interval

- Mobility 12%
- Self-care 69%
- Pain/discomfort 71%
- Anxiety/depression 62%

Adjusted odds ratio & 95% confidence

- 1.12 (0.82, 1.53)
- 1.69 (1.01, 2.83)
- 1.71 (1.28, 2.30)
- 1.62 (1.18, 2.21)

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## Foundations of Cardiometabolic Health Certification Course

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# Future Directions in Treatment of Smoking

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## **Overview**

- Epidemiology: Smoking rates are declining but still threaten cardiometabolic health
- Smoking cessation decreases cardiometabolic risk (and other health risks, too!)
- Screen and Intervene
- Future directions in treatment of smoking

# Cytisine

- Naturally occurring botanic alkaloid; nicotine receptor partial agonist
- Effective for tobacco cessation
- \$\$ lower expense
- Not yet FDA approved







Coe JW, J Med Chem. 2005; Erwin & Slaton. Annals of Pharmacotherapy. 2014; Sajja RK, Rahman S. Alcohol. 2013; Sajja RK, Rahman S. Pharmacol Biochem Behav. 2012;102(1):36-43;Bell RL, et a; Alcohol. 2009.; West R, et al. N Engl J Med. 2011; 7Rigotti NA. N Engl J Med. 2014;371(25):2429-2430.

## **Genetics of Smoking**





#### c) Smoking Cessation (SmkCes)



Association studies of up to 1.2 million individuals yield new insights into the genetic etiology of tobacco and alcohol use

- Many additional genome-wide significant variants exhibiting polygenic risk for smoking
- Translating this information into precision approaches requires synthesis of data and replication in prospective studies → not yet standard of care.

# Pharmacogenomics of smoking cessation

- Genes in multiple pathways associated w/ treatment response and side effects
  - dopamine (ANKK1, DRD2, DRD4, SLC6A3),
  - nAChRs (CHRNA3, CHRNA4, CHRNA5, CHRNA7, CHRNB2, CHRNB4)
  - nicotine metabolism (cytochrome 2A6 (CYP2A6) and nicotine metabolite ratio (NMR)) associated w/treatment response, side effects.
- Goals of precision medicine: who is more/less likely to respond to cessation medications.
- Precision approaches *becoming* actionable, but currently not standard of care

## **Nicotine Metabolism Ratio: NMR**



# Faster Metabolizers exhibit some important features

- Characteristics of higher NMR (higher CYP2A6 activity)
  - Smoke more cigarettes per day; more intensely
  - Exhibit pronounced responses to smoking cues
  - Have greater availability of nicotinic receptors
  - Have difficulty quitting smoking
  - Lower quit rates with nicotine replacement

## CYP2A6 Activity (NMR) Interacts with Treatment Outcomes



Optimize pharmacotherapy based on nicotine metabolism ? or Polygenic risk scores?

### Nicotine Metabolite Ratio (NMR)



# Summary - Smoking is a chronic disease that can be successfully addressed in the healthcare system

- Successful 50+ year public health campaign, but 34 million still smoke
- Most want to quit and try to quit each year, but only 5% receive standard of care.
- FDA approved meds are safe and effective
- Behavioral therapy networks are available
- Residual smoking-related disease risk can persist long after smoking cessation – think screening
- New treatments are coming stay tuned!

## **Resources Available**

To read the full report and access related materials, visit: www.SurgeonGeneral.gov

To learn more about tobacco control and prevention and quitting smoking, visit: www.CDC.gov/tobacco www.CDC.gov/quit www.smokefree.gov

#### **Contact Info:**





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**Smoking Cessation** 

A Report of the Surgeon General



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