



**National Behavioral
Health Network**

for Tobacco & Cancer Control

from NATIONAL COUNCIL FOR
MENTAL WELLBEING

Varenicline as a Smoking Cessation Tool for Long-Term Recovery

February 24, 2022 | 2:30 – 3:30 pm ET

Welcome!



Tamanna Patel, MPH
Director,
Practice Improvement



Samara Tahmid
Project Manager,
Practice Improvement



Hope Rothenberg
Project Coordinator,
Practice Improvement



Housekeeping



This workshop is being recorded. All participants are placed in “listen-only” mode.



For audio access, participants can either dial into the conference line or listen through your computer speakers.



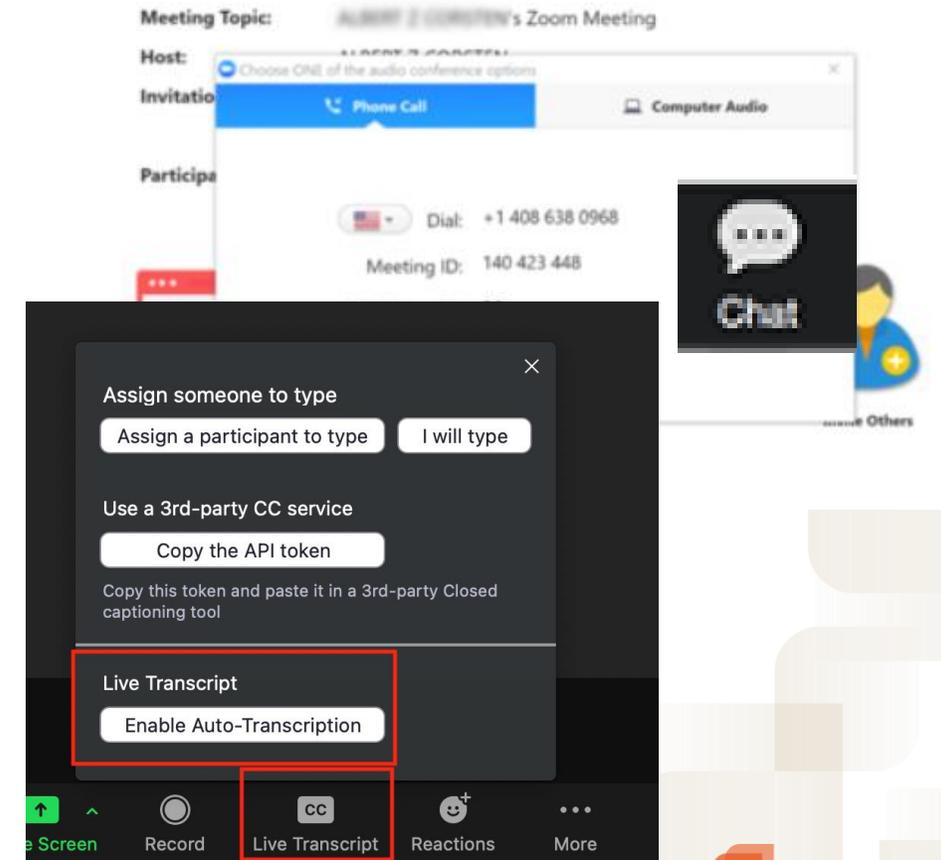
Submit questions by typing them into the chat box or using the Q&A panel.



Access closed captioning by enabling live transcript.



Slide handouts and recording will be posted here: <https://www.bhthechange.org/resources/improving-lung-health-and-mental-wellbeing-during-covid-19/>



**National Behavioral
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MENTAL WELLBEING



National Behavioral Health Network for Tobacco & Cancer Control

- Jointly funded by CDC's *Office on Smoking & Health & Division of Cancer Prevention & Control*
- Provides resources and tools to help organizations reduce tobacco use and cancer among individuals experiencing mental health and substance use challenged
- 1 of 8 CDC National Networks to eliminate cancer and tobacco disparities in priority populations

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National Behavioral Health Network

for Tobacco & Cancer Control

from NATIONAL COUNCIL FOR MENTAL WELLBEING

Today's Featured Speaker



Chad Morris, Ph.D.
Professor of Psychiatry
Director, Behavioral Health & Wellness Program
University of Colorado, Anschutz Medical Campus



Disclosure

Site Principal Investigator for Pfizer Varenicline Clinical Trials:

- Smokers with and without Psychiatric Disorders (EAGLES A3051123-A3051148) - 2011-2014
- Smokers with Depression (A3051122) - 2010-2012
- Persons with Psychotic Disorders (A3051072) - 2008-2009

Explore

the role of FDA-approved pharmacological treatments for cessation

Learn

about the benefits of varenicline as a first-line cessation medication

Examine

the evidence base regarding using varenicline in combination with other cessation medications and behavioral strategies.

Gain

practical tools to initiate conversations about varenicline

61-90% Schizophrenia

51-70% Bipolar Disorder

49-80% Other Drug Abuse

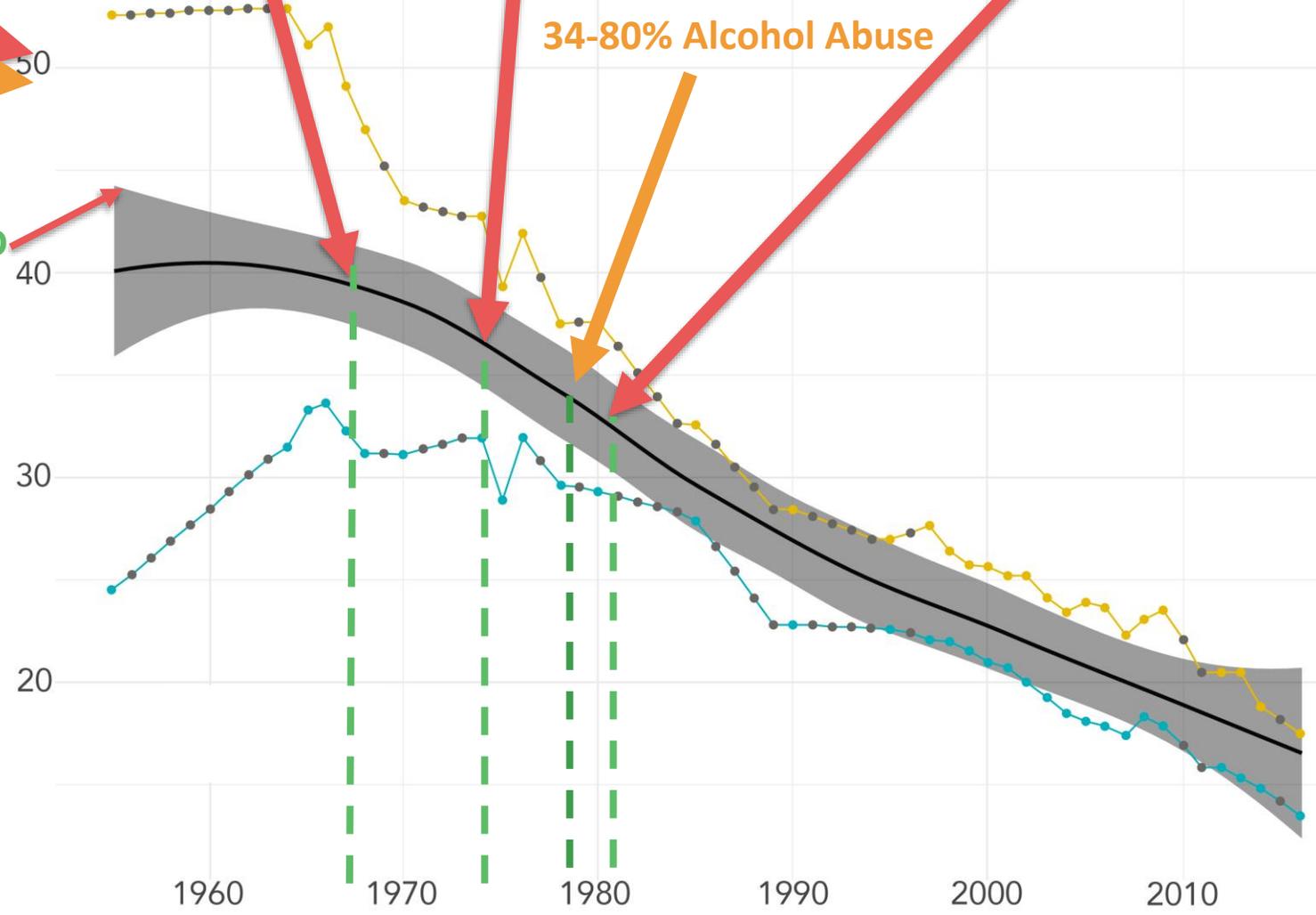
38-42% ADHD

36-80% Major Depression

34-80% Alcohol Abuse

32-60% Anxiety

45-60% PTSD



13.7% of adults are current smokers

Medication Assisted Treatment

- Combination of behavioral interventions and medications
- Highly effective treatment option for alcohol, opioid, or tobacco dependence
- Reduces illicit drug use and overdose deaths



Treatment Effectiveness

Treatment Format	Abstinence Rate
Unaided	4-7%
Self-help	11-14%
Quitline	11-15%
Individual counseling	15-19%
Group counseling	12-16%
Medication alone	22%
Medication + counseling	25-30%

Clinical Practice Guideline Treating Tobacco Use and Dependence 2008



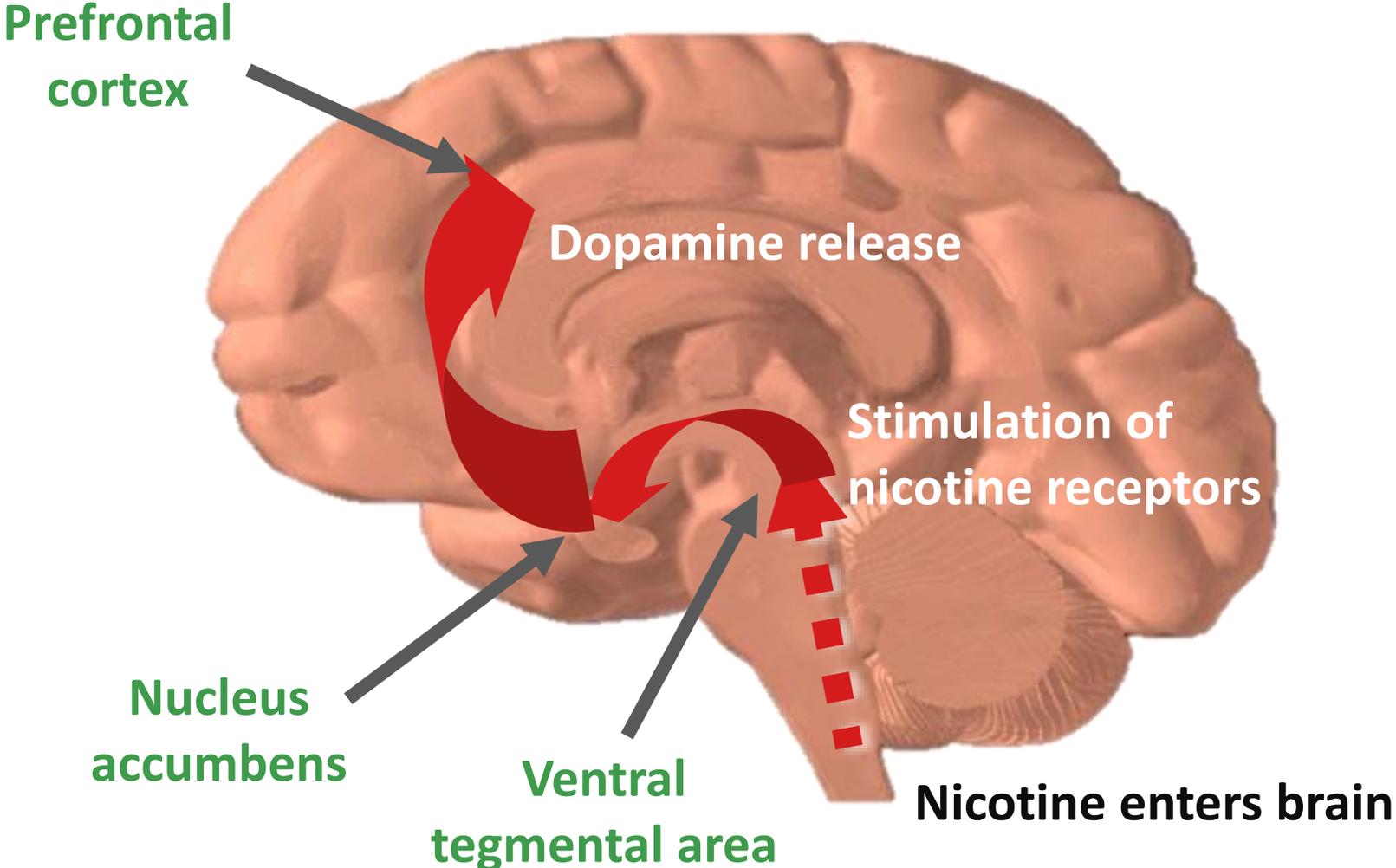
Tobacco Cessation Medications

The only medications approved by the Food and Drug Administration (FDA) for tobacco cessation are:

- Nicotine patch
- Nicotine gum
- Nicotine lozenge
- Nicotine nasal spray
- Nicotine inhaler
- Bupropion SR tablets
- Varenicline tablets



Dopamine Reward Pathway



Varenicline Tartrate

- Selective $\alpha 4\beta 2$ nicotinic acetylcholine receptor (nAChR) receptor partial agonist. It works in two ways:
 - It acts like nicotine in the brain but does not have as strong of an effect.
 - It blocks the places in the brain where nicotine would normally work.
- Initial dosing is 0.5 mg/day for 3 days and then twice daily for 4 days. For next 11 weeks, dosing is 1 mg twice daily



Varenicline:

Side Effects & Precautions

- Side effects include:
 - Nausea
 - Headache
 - Insomnia and abnormal dreams
 - Constipation and flatulence
- Precautions for individuals:
 - Operating heavy machinery
 - With kidney or cardiac problems
 - Taking insulin, asthma medications, or blood thinners

New Bohemians member shot to death

Jeffrey Carter Albrecht, a keyboard player for the band Edie Brickell & New Bohemians, was shot to death early Monday while trying to kick in the door of his girlfriend's neighbor, police said.

BY ASSOCIATED PRESS, AP SEPTEMBER 5, 2007 5:00AM



Exacerbation of Schizophrenia by Varenicline

Am J Psychiatry 164:8, August 2007

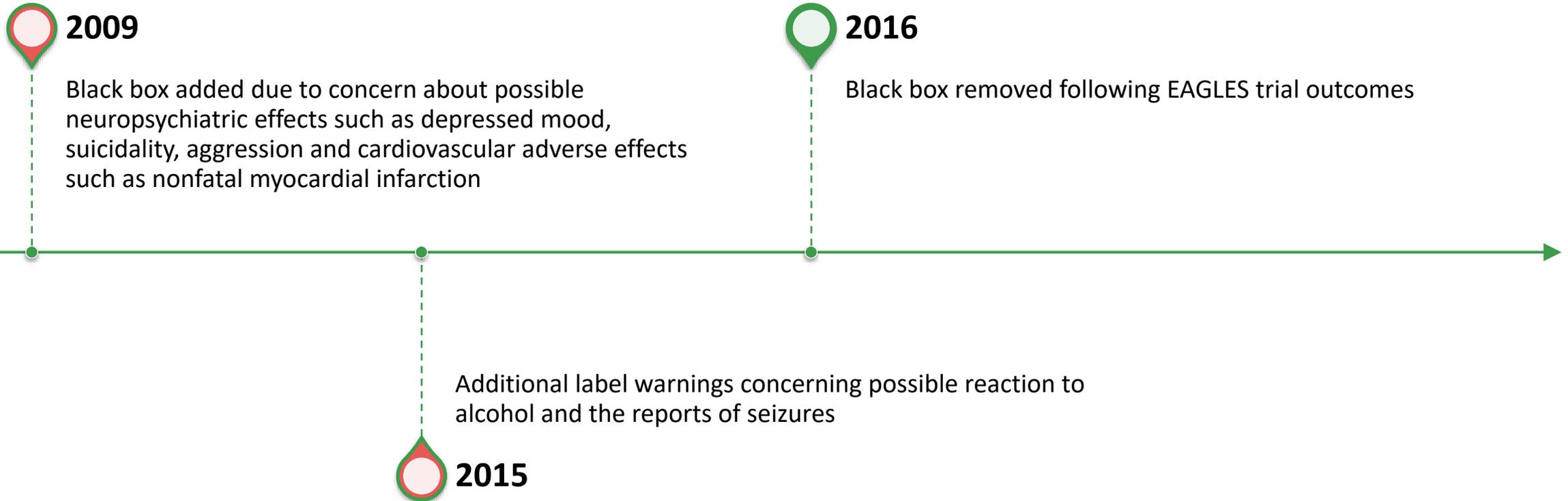
Journal of Analytical Toxicology, Vol. 33, March 2009

Smoking Cessation with Varenicline: A Fatal Suicide

Pascal Kintz^{1,*}, M Villain¹, Julie Evans², Marion Villain¹, and Vincent Cirimele¹

¹Laboratoire ChemTox, 3 rue Gruninger, 67400 Illkirch, France; ²Eurofins Genetic Services, Chorley, UK

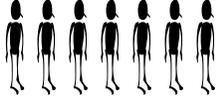
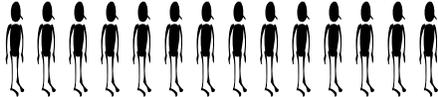
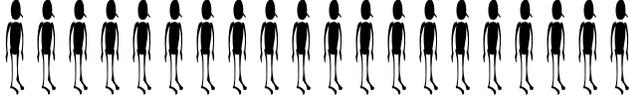
Black Box Warning





Effectiveness of Varenicline

Numbers Needed to Treat Cochrane Review

Intervention	NNT	Impact on Patient
CHANTIX™ vs placebo	8	
Bupropion SR vs placebo	15	
NRT vs placebo	20	

- **Interpretation of NNT: CHANTIX™ therapy accounts for 1 additional quitter for every 8 patients treated; having the lowest # of patients needed to treat in order to gain 1 quitter.**

Pharmacotherapy Efficacy

Abstinence rates compared to placebo
at 6-months or greater post-quit

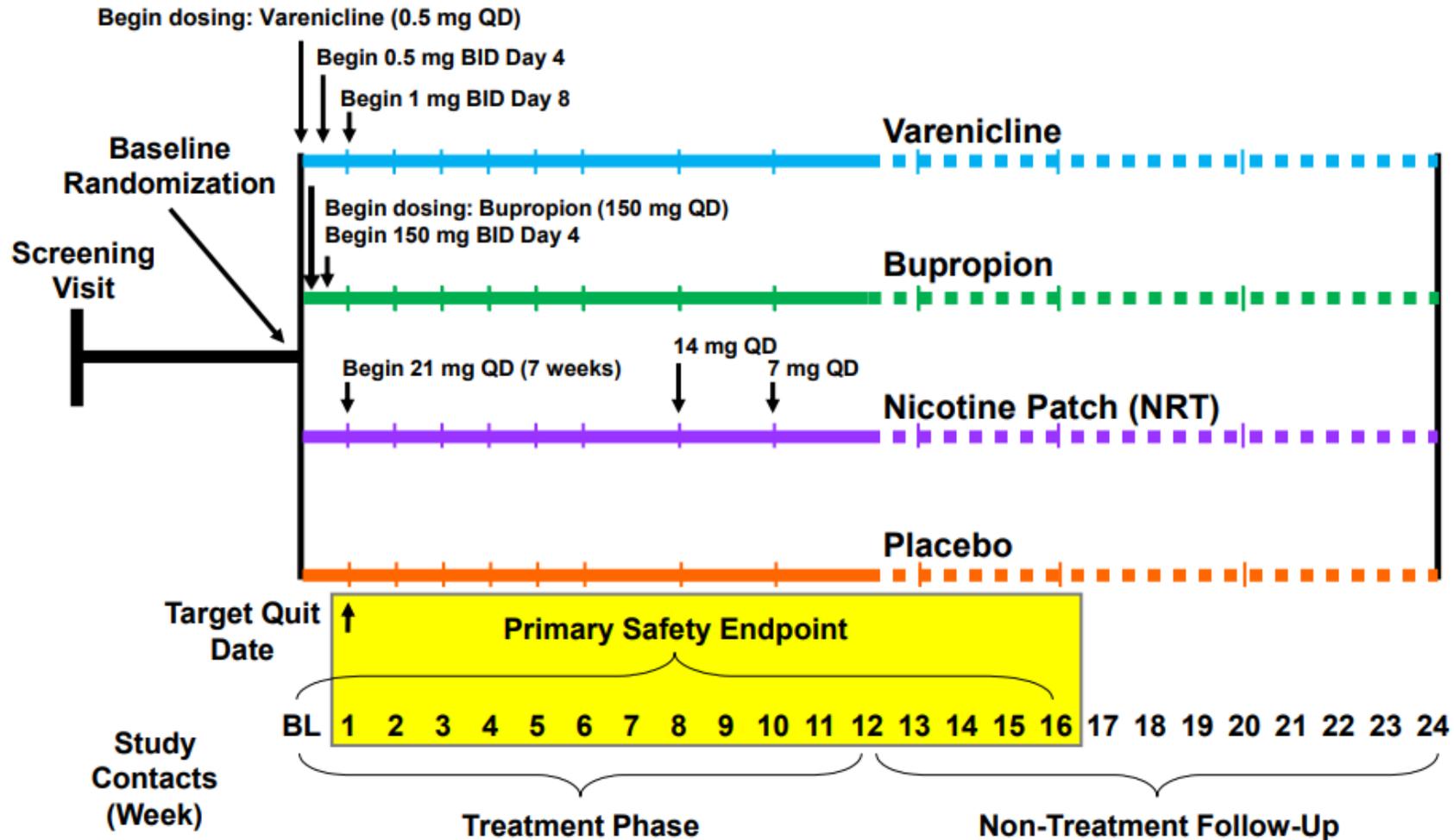
Medication	Number of Trials (People)	Estimated Risk Ratio
NRT	133 (64,640)	1.6 (1.5-1.6)
Bupropion	46 (17,866)	1.6 (1.5-1.8)
Varenicline	27 (12,625)	2.2 (2.1-2.4)

(Cahill et al., 2016; Hartmann-Boyce et al., 2018; Howes et al., 2020)

EAGLES Study Design

- ❖ **Design:** Prospective, randomized, double-blind, 24-week trial
- ❖ **Treatments:** Varenicline, bupropion, NRT patch, placebo
- ❖ **Duration:** 12 weeks treatment: 12 weeks non-treatment follow-up
- ❖ **Sample Size:** 8,144 randomized participants (4,116 to the psychiatric cohort and 4,028) without psychiatric disorder

EAGLES Study Design



Vertical ticks represent subject clinic visits
 BID=Twice Daily; BL=Baseline; QD=once Daily

Effectiveness: EAGLES

- **Efficacy-** Evaluate CO-confirmed continuous abstinence rate for weeks 9-12 and 9-24 as a function of treatment, psychiatric disorder and the interaction of treatment and psychiatric disorder.
- **Interpretation-** Varenicline was more effective than placebo, nicotine patch, and bupropion in helping smokers achieve abstinence, whereas bupropion and nicotine patch were more effective than placebo.

Anthenelli et al., 2016

Effectiveness: Prospective Cohort Study

- **Design-** Electronic Medical Records from 654 practices
- **Sample-** 235,314 (159,736 NRT; 75,578 varenicline)
- **Interpretation-** Triangulating evidence across three analytical approaches, varenicline was more effective than NRT for smoking cessation in patients with mental disorders.

(Taylor et al., 2020)



Effectiveness: Systemic Reviews and Meta-Analyses

- **Design-** Systematic reviews and Bayesian network meta-analyses of RCTs, in any setting, of varenicline, bupropion, NRT and e-cigarettes
- **Sample-** 363 trials for effectiveness and 355 for safety
- **Interpretation-** monotherapy with varenicline increased cessation compared to bupropion and to NRT, while finding inconclusive evidence of a difference in quitting between bupropion and NRT

Thomas et al., 2021

Effectiveness: Combined Pharmacotherapy

- **Thomas et al., 2021**- Findings were consistent for combined varenicline + NRT, which showed improved probability of quitting compared to bupropion and NRT monotherapies
- **Leone et al., 2020** - Conditional recommendation for combining a nicotine patch with varenicline rather than using varenicline alone





Safety of Varenicline

Types of Adverse Events

- Major adverse cardiovascular events (MACEs)
- Serious adverse events(SAEs)
 - death, life-threatening, required hospitalization or resulted in significant disability
- Major adverse neuropsychiatric events (MANEs)
 - suicide, attempted suicide, suicidal ideation, depression, seizures

EAGLES Adverse Events

Primary Safety Endpoint: Percentage of patients reporting at least one of the following NPS AEs during treatment and up to 30 days after last dose

Anxiety
Depression
Feeling Abnormal
Hostility

Classified as
Severe

Agitation
Aggression
Delusions
Hallucinations
Homicidal Ideation
Mania
Panic
Paranoia
Psychosis
Suicidal Ideation
Suicidal Behavior
Suicide (Includes completed
suicide and suicidal
depression)

Classified as
Moderate
or
Severe

Severity Assessment

Moderate = interferes to some extent with subject's usual function

Severe = interferes significantly with subject's usual function

Safety: EAGLES

- **Safety-** Characterize the neuropsychiatric events as a function of treatment, psychiatric disorder and the interaction of treatment and psychiatric disorder.
- **Interpretation-** No significant increase in neuropsychiatric adverse events attributable to varenicline or bupropion relative to nicotine patch or placebo.

Safety:

Prospective Cohort Study

- **Design-** Electronic Medical Records from 654 practices
- **Sample-** 235,314 (159,736 NRT; 75,578 varenicline)
- **Interpretation-** Varenicline was generally associated with decreased or similar odds of depression or anxiety compared to NRT.

(Taylor et al., 2020)

Safety: Systemic Reviews and Meta-Analyses

- **Design-** Systematic reviews and Bayesian network meta-analyses of RCTs
- **Sample-** 363 trials for effectiveness and 355 for safety
- **Interpretation-** (1) No evidence of increasing MACEs compared to placebo or each other. (2) No strong evidence that varenicline increased SAEs. (3) But increased odds of MANEs for varenicline compared to bupropion. (4) Evidence that bupropion increased odds of SAEs compared to placebo.

Thomas et al., 2021





Clinical Implications

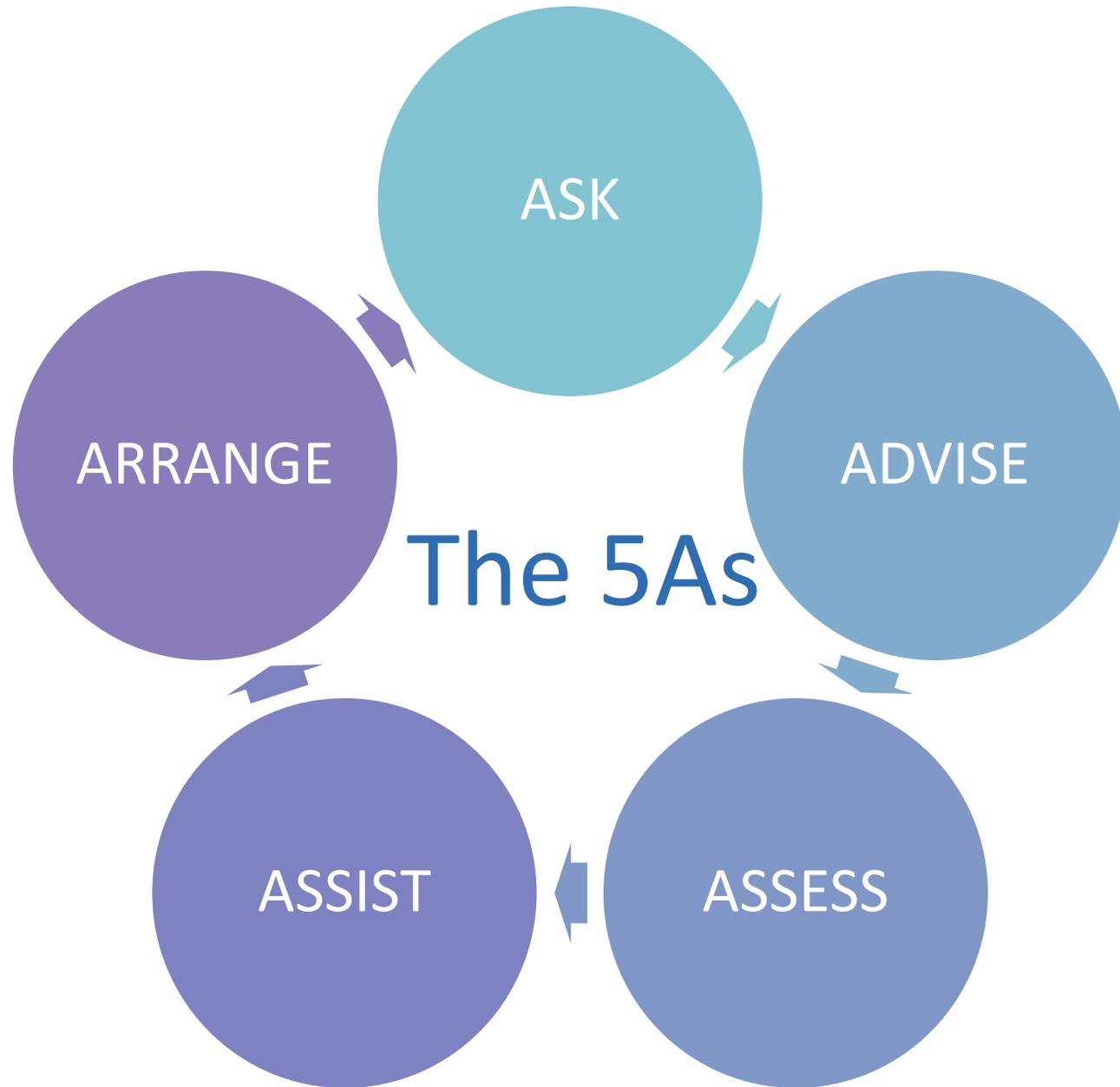
Expert Panel Recommendations

Strong Recommendations Include

- Using varenicline rather than a nicotine patch
- Using varenicline rather than bupropion
- Using varenicline rather than a nicotine patch in adults with a comorbid psychiatric condition
- Initiating varenicline in adults even if they are unready to quit
- Extending treatment duration to greater than 12 weeks.

Conditional Recommendations Include

- Combining a nicotine patch with varenicline rather than using varenicline alone
- Using varenicline rather than electronic cigarettes.



Treatment Intervention Model

(1) Prescribe FDA-approved pharmacotherapy

- **First-line treatment**
 - Varenicline *or*
 - Combination of nicotine replacement products (patch + choice of lozenge, gum, inhaler, or nasal spray as needed to control cravings)



(2) If patient preference or first-line treatment intolerance or contraindication

- **Second-line treatment**
 - Single nicotine replacement product (patch, lozenge, gum, inhaler, or nasal spray) *or*
 - Bupropion



(3) If single agent is not sufficient to achieve abstinence

- **Consider combining categories of FDA-approved drugs**
 - Varenicline + nicotine replacement product
 - Varenicline + bupropion
 - Bupropion + nicotine replacement product

Rigotti et al., 2022

Cross-Cutting Interventions

Motivational
Enhancement

Cognitive
Behavioral Therapy
and Variants

Contingency
Management





Current Considerations

Chantix Recall

- **Chantix is currently unavailable**
- **July- Sept 2021 recall-** to include all lots of Chantix due to the presence of a nitrosamine impurity above the FDA's acceptable daily intake limit.
- **Long-term use of impure product use-** increased cancer risk



Varenicline Availability

- Patent protection for Chantix expired in May 2020
- Par Pharmaceutical's varenicline product was approved by FDA on August 11, 2021
- Apotex is distributing Apo-Varenicline, a Canadian-approved drug product, under FDA's temporary exercise of regulatory flexibility and discretion



Coverage & Billing





Future Possibilities

Cytisine

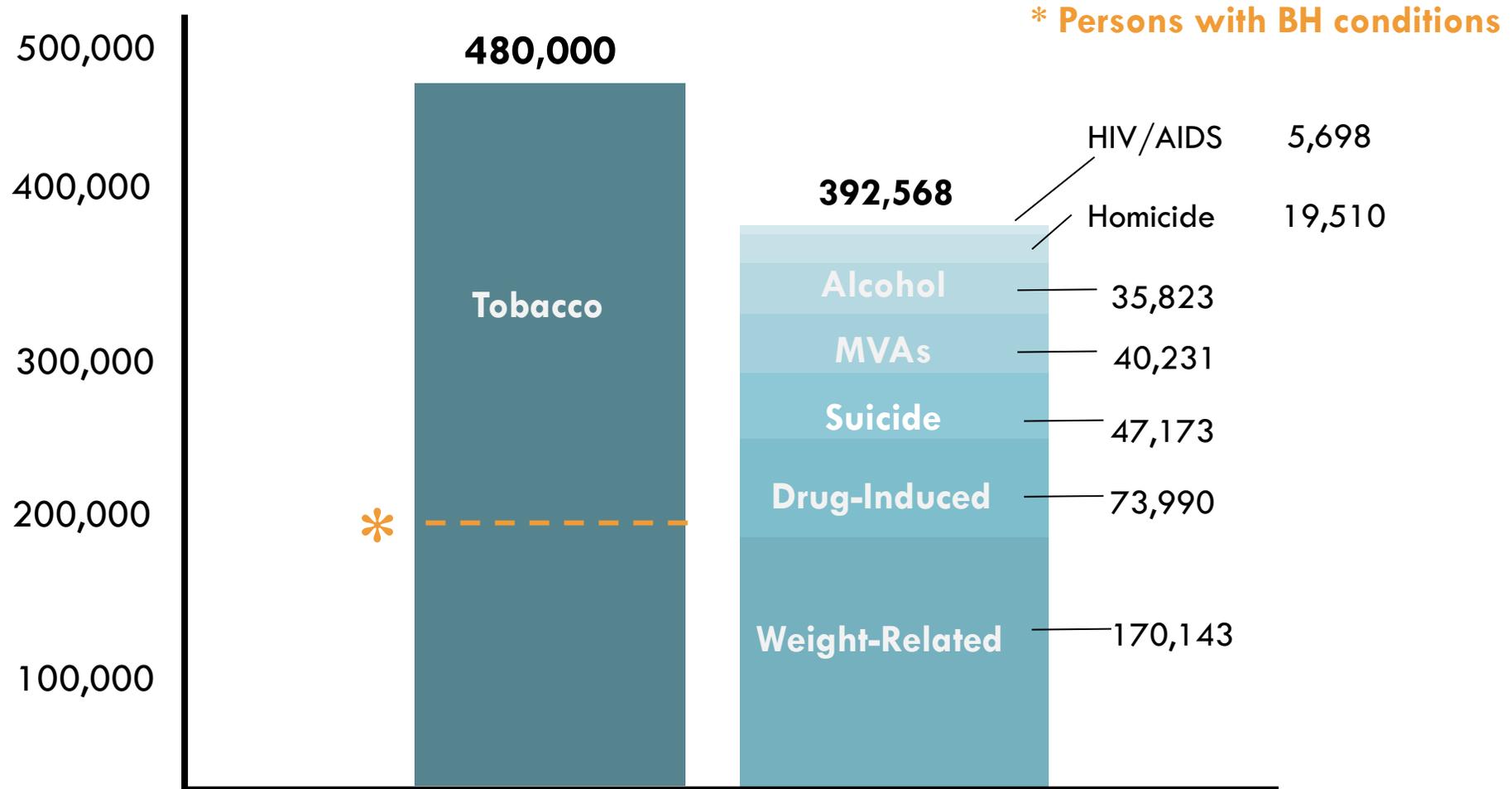
- Similar to varenicline but found to have fewer side effects
- Marketed as Tabex
- Has demonstrated efficacy
- Very low cost
- A US randomized trial began in 2020



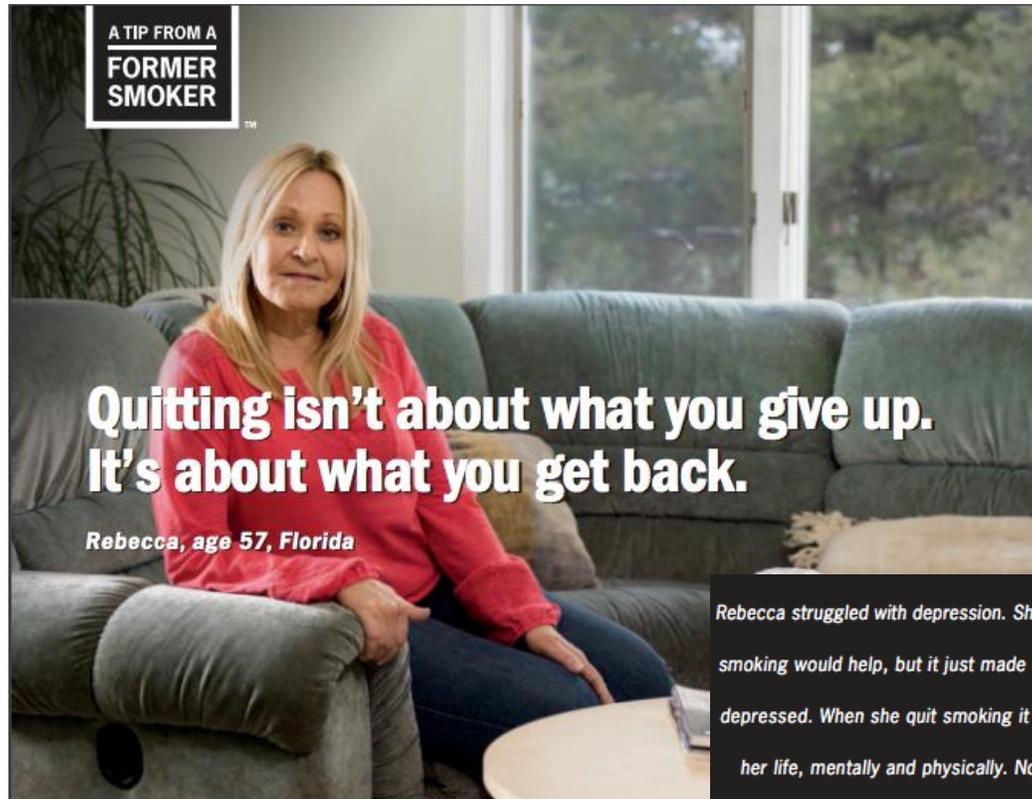


Making the Case

Behavioral Causes of Death in US



Quitting: It Can Be Done



**Quitting isn't about what you give up.
It's about what you get back.**

Rebecca, age 57, Florida

Rebecca struggled with depression. She thought smoking would help, but it just made her more depressed. When she quit smoking it changed her life, mentally and physically. Now she runs 5Ks and hopes to live to be one hundred.

You can quit smoking.

**For free help, call
1-800-QUIT-NOW.**



U.S. Department of
Health and Human Services
Centers for Disease
Control and Prevention
[CDC.gov/tips](https://www.cdc.gov/tips)

#CDCTips

- **Persons with behavioral health conditions:**
- Are able to quit using
- 75% want to quit using
- 65% tried to quit in the last 12-months



Questions?





Behavioral Health & Wellness Program

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www.bhwellness.org



Behavioral Health and
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BHWP_UCD

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