

Treatment of Tobacco Use Disorders

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**I have no relevant financial relationship
with a commercial interest to disclose.**

Public Health Burden of Tobacco Dependence

- 34.1 million smokers in the US. Number of smokers is INCREASING
- 480,000 tobacco-related deaths annually in the USA, >8 million worldwide
- 100 million people died in the last century from smoking related causes
- 1 billion smokers worldwide anticipated to die from smoking related causes this century
- People with SMI are >4-fold more likely to smoke than people without a mental health disorder

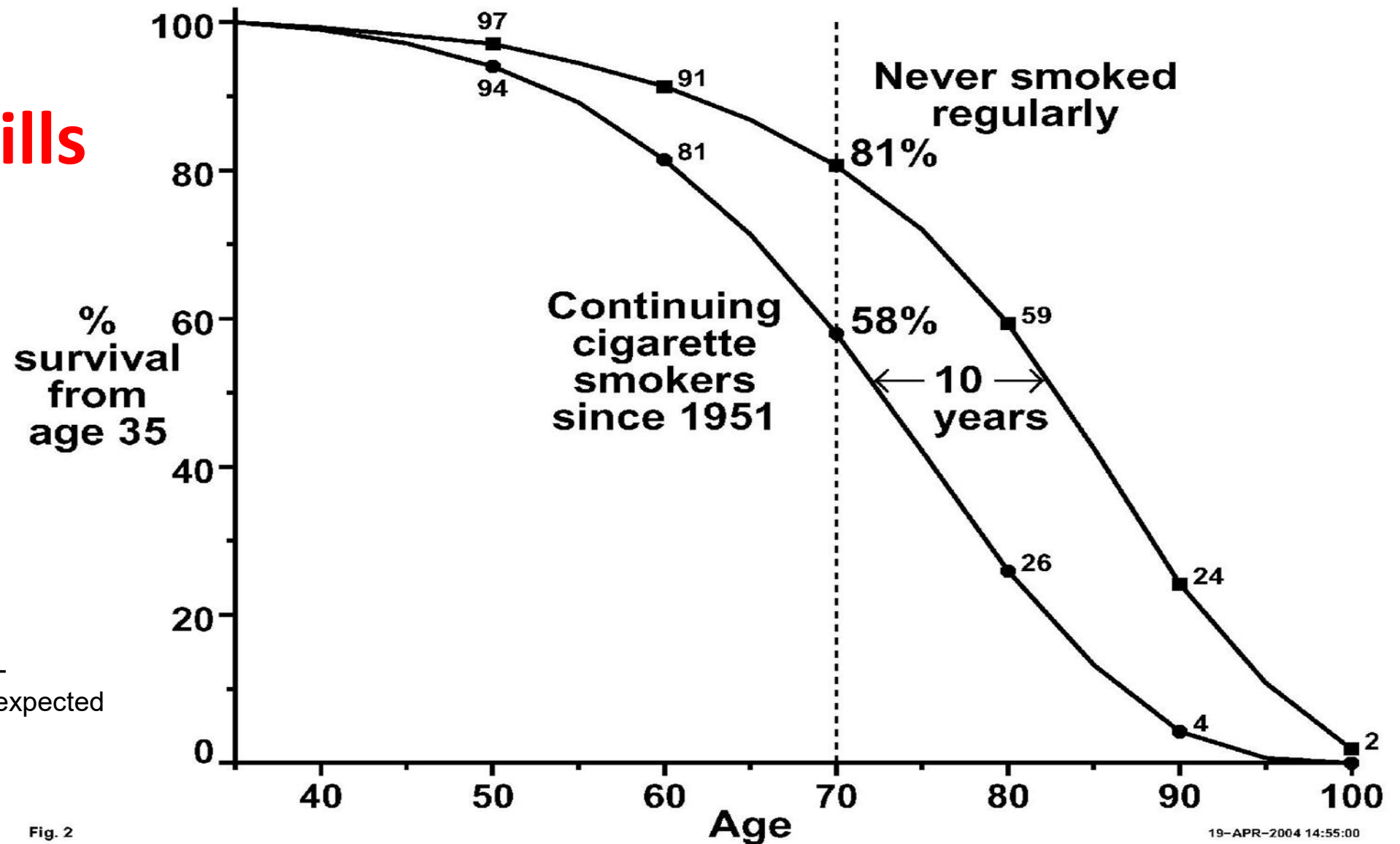


Drug Related Deaths in the US

- **Opioid overdoses** killed approximately 45,000 people in 2025.
- Over 95,000 **alcohol** related deaths per year and increasing.
- Over 480,000 **tobacco** related deaths per year and increasing

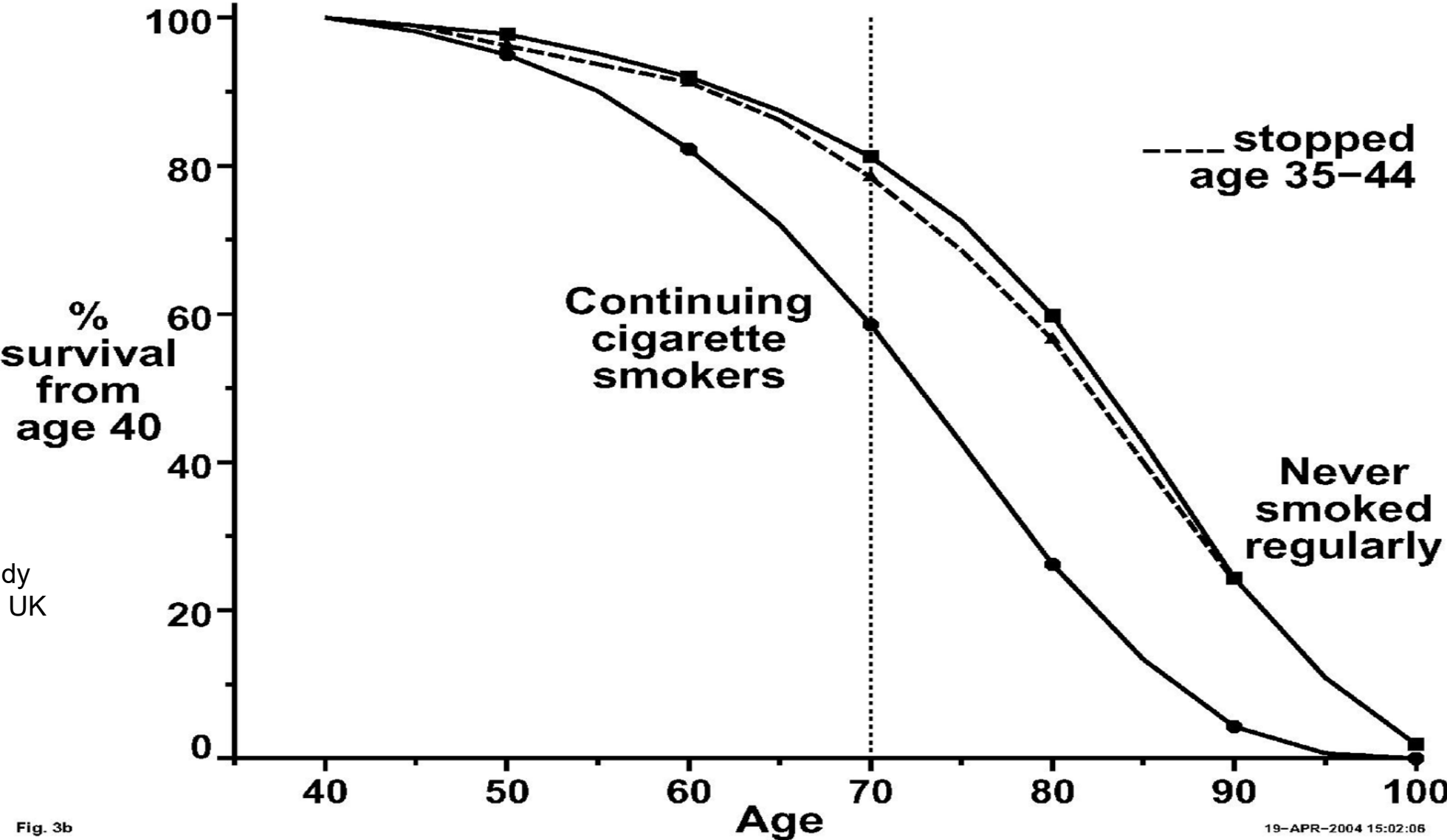
UK male doctors born 1900–1930: continuing cigarette vs never smokers. 50-year follow-up of mortality, 1951–2001

Smoking Kills



Effect of stopping smoking at age ~40 on survival from age 40

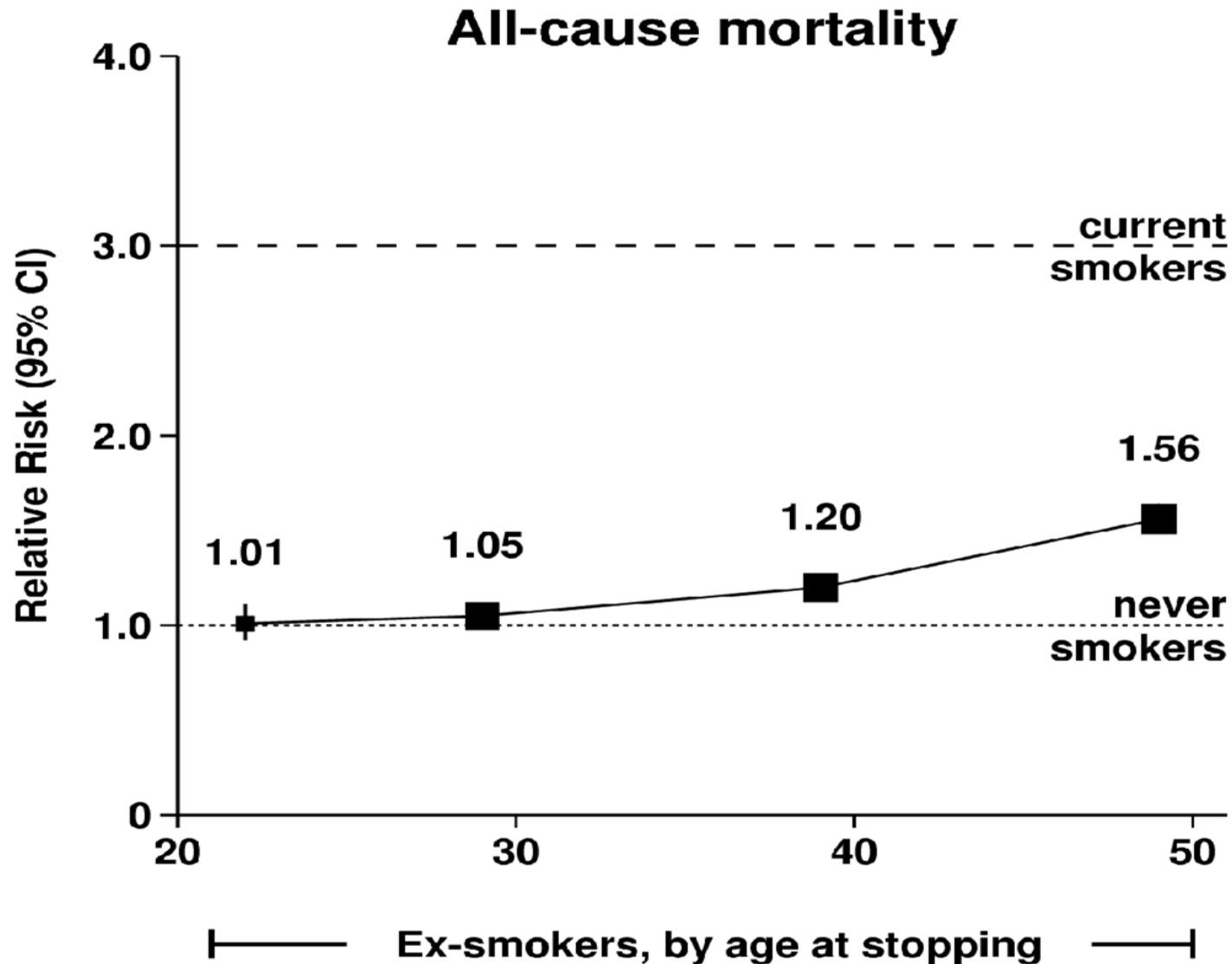
Quitting
Helps



British Physician's Study
Male physicians in the UK
Born 1900 - 1930
followed 50 years

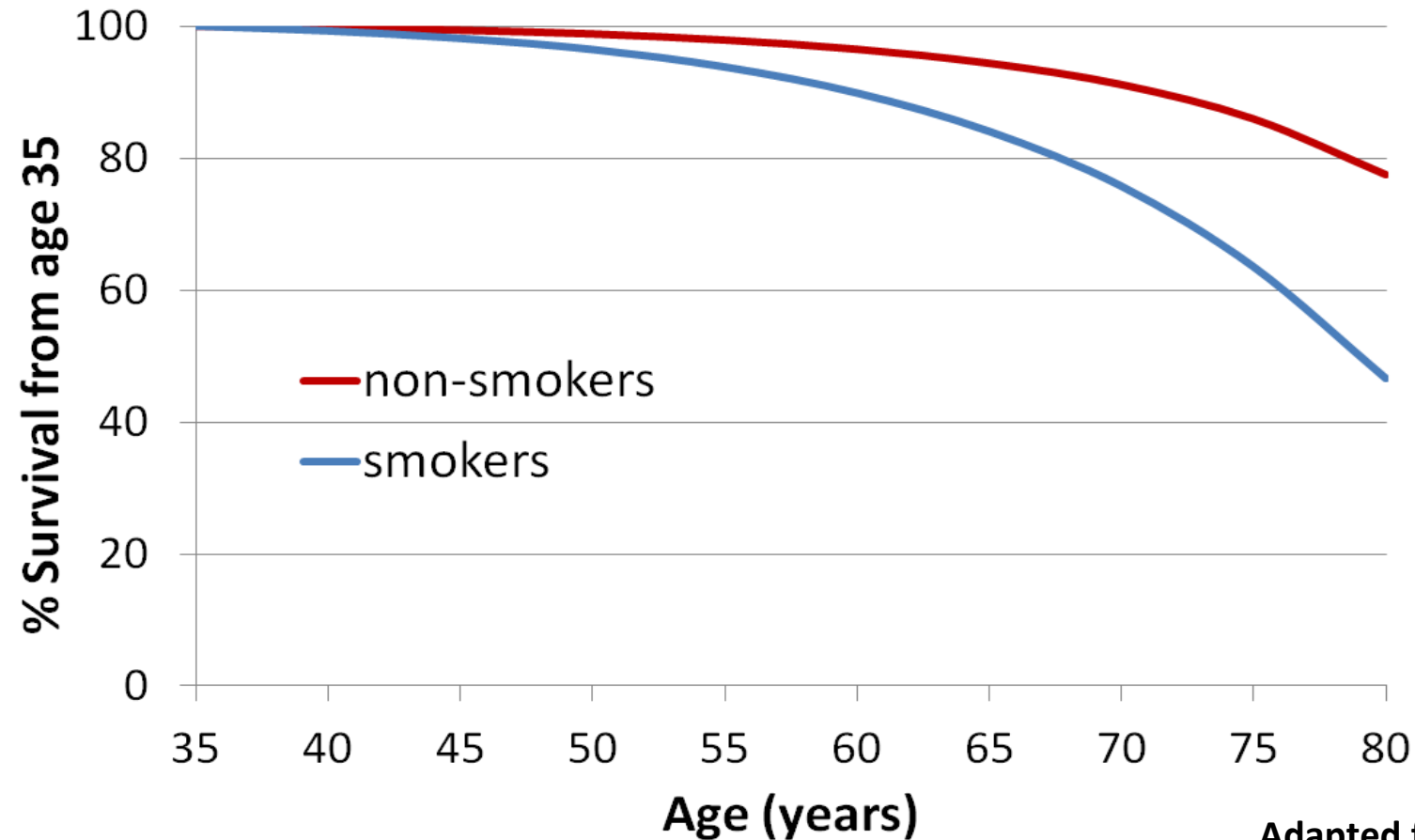
Fig. 3b

THE MILLION WOMEN STUDY



**Quitting by age 50
halves mortality**

One Million Women Study: Effect of 3-fold Difference in Annual Deaths on Survival at Ages 35-79



Adapted from the One Million Women Study.
Pirie, Peto, et al., Lancet 2013

JAMA

Journal of the
American Medical Association



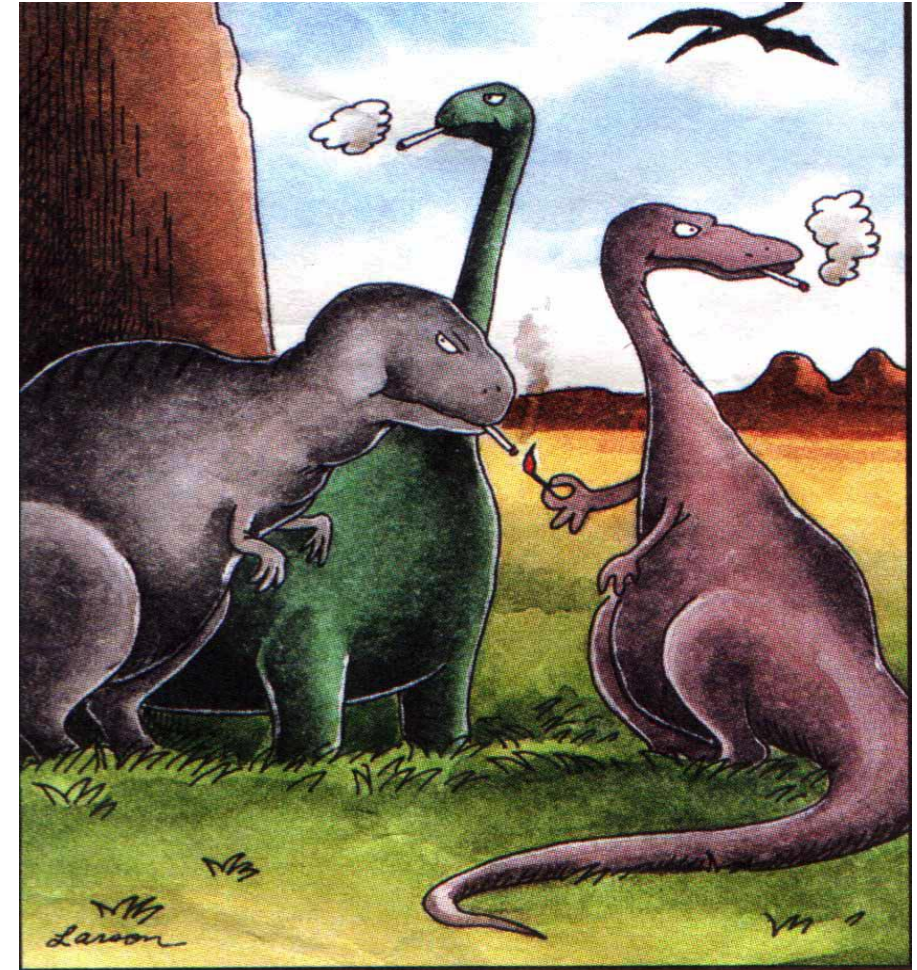
50 Years after the first Surgeon General's report of an association between smoking and cancer, adult smoking has declined 55% in the general US population.

Smoking prevalence among adults with schizophrenia in the US today is >50%.

This is higher than in the US general population in 1964.

Smoking-Related Mortality in Those with Psychiatric Disorders

- In those with one or more lifetime hospitalizations for schizophrenia, bipolar disorder, or MDD:
- HALF died from 1 of 19 diseases identified by CDC as causally linked to tobacco use



The real reason dinosaurs became extinct

Quitting Tobacco Smoking Reduces

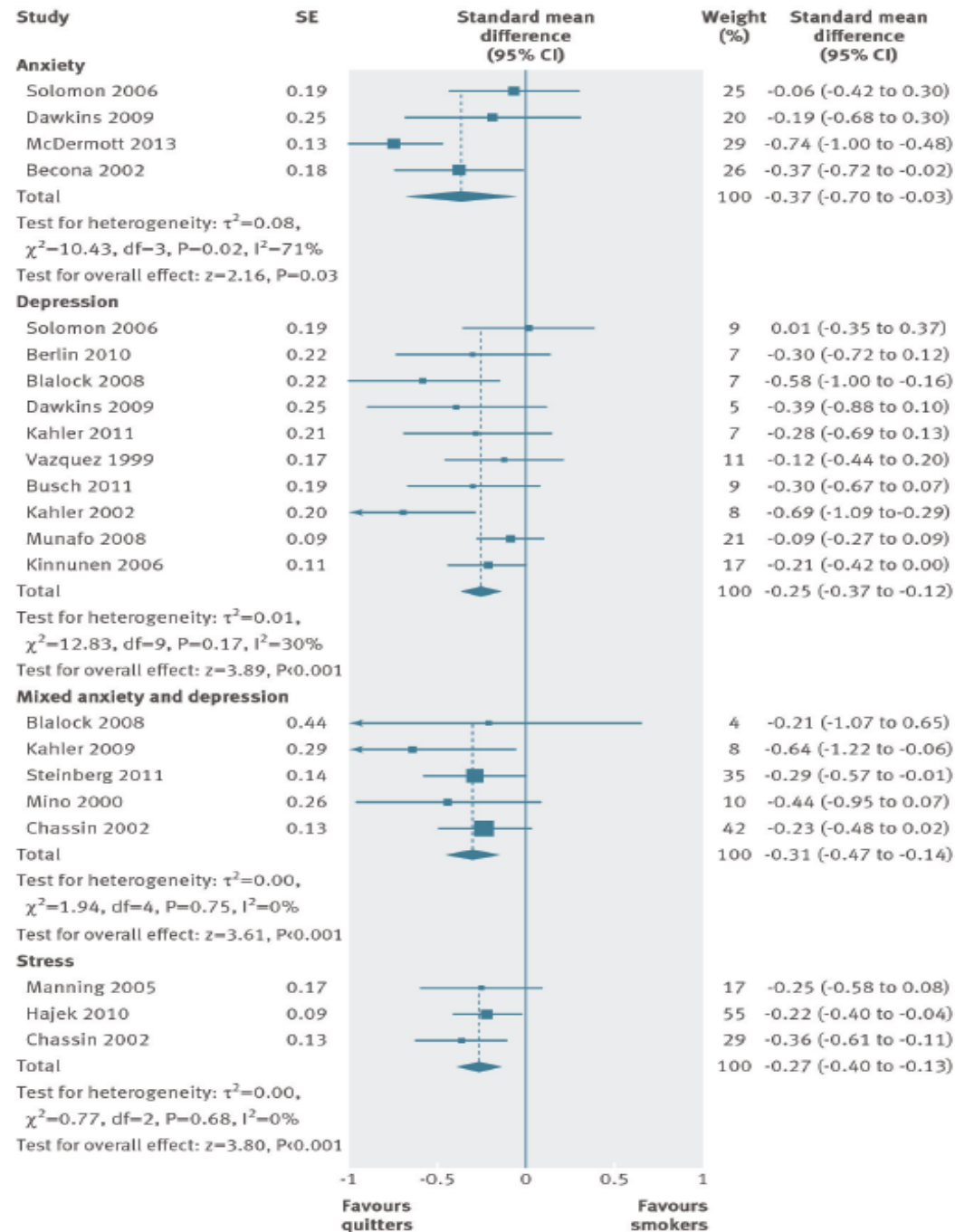
- **Death**
- **MI**
- **Stroke**
- **Cancer Risk**
- **Diabetes morbidity**
- **Atherosclerosis and COPD progression**
- **Bronchitis**

META-ANALYSIS: SMOKING CESSATION IMPROVES PSYCHIATRIC SYMPTOMS, QUALITY OF LIFE

- 26 studies
- Change in psychiatric symptoms was compared between continuing smokers and successful quitters
- **Depression, anxiety, stress and quality of life** improved among those who quit smoking significantly compared to those who continued smoking.
- It did not matter whether one had a pre-existing psychiatric diagnosis or not!!!
- Effect sizes comparable to those observed for antidepressant medications!!!

META-ANALYSIS: Smoking Cessation Is Associated with Improved Psychiatric Symptoms

Taylor et al., BMJ, 2014



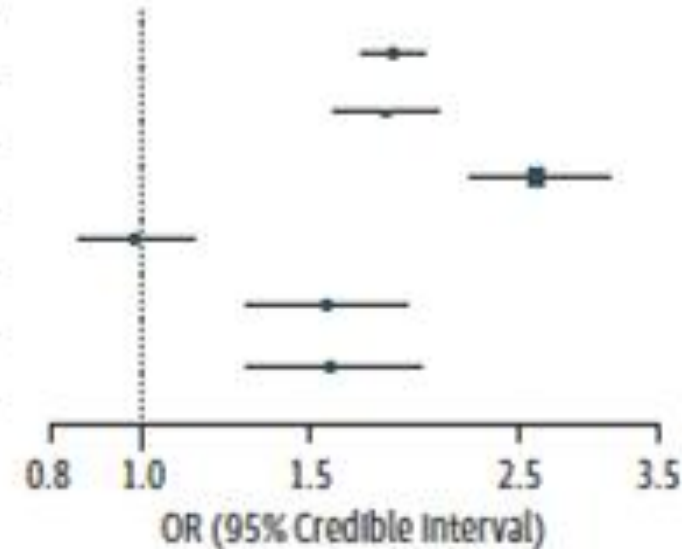
Addiction to Nicotine: Mechanism and Therapeutic Targets

- Nicotine binds to nicotinic cholinergic receptors ($\alpha 4\beta 2$, $\alpha 3\beta 4$, $\alpha 7$) -> neurotransmitter release
 - dopamine, glutamate, GABA important in develop of nicotine dependence
 - Corticotropin-releasing factor contributes to nicotine withdrawal
- Agonist therapies target nicotinic receptors: NRT, Varenicline
- Bupropion – increases levels of dopamine and norepinephrine, some nicotinic receptor-blocking activity

Pharmacotherapy with Behavioral Therapy Doubles to Triples Abstinence Rates

Figure. Odds Ratios for Smoking Abstinence of 6 Months or More

Comparison (Intervention vs Control)	No. of Studies	Total No. of Individuals	Absolute Quit Rates		Odds Ratio (95% Credible Interval)
			Intervention n/N (%)	Control n/N (%)	
NRT vs placebo	119	51 225	4704/27 258 (17.3)	2464/23 967 (10.3)	1.84 (1.71-1.99)
Bupropion vs placebo	36	11 440	1214/6409 (18.9)	535/5031 (10.6)	1.82 (1.60-2.06)
Varenicline vs placebo	15	6293	964/3496 (27.6)	332/2797 (11.9)	2.88 (2.40-3.47)
Bupropion vs NRT	8	2581	191/954 (20.0)	375/1627 (23.0)	0.99 (0.86-1.13)
Varenicline vs NRT	0	0	NA	NA	1.57 (1.29-1.91)
Varenicline vs bupropion	3	1622	174/823 (21.1)	111/799 (13.9)	1.59 (1.29-1.96)



Expect and Treat Relapses

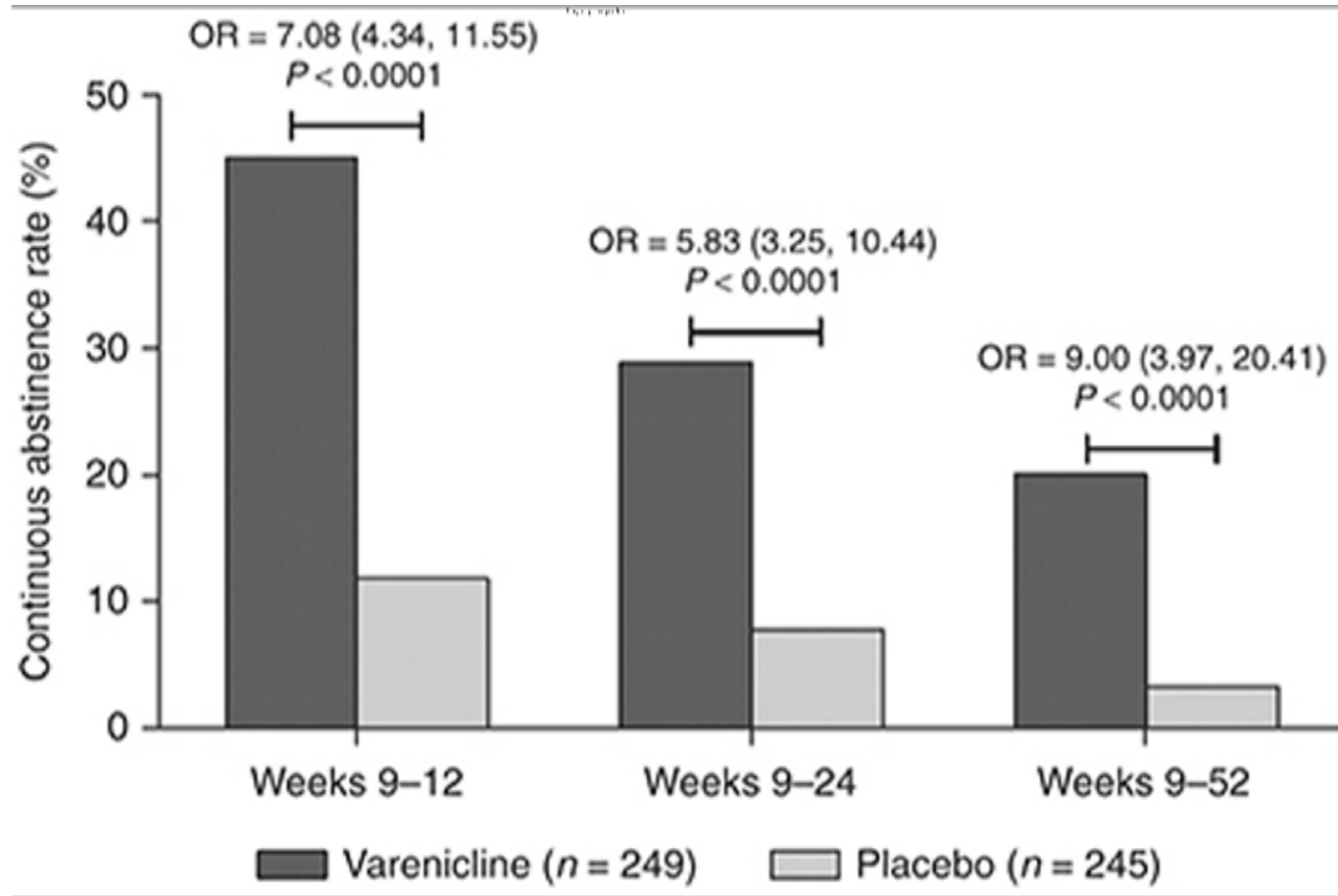
For tobacco dependence: average of 5 attempts at tobacco abstinence before long-term abstinence achieved

Treatments double to triple abstinence rates and are Underutilized!

****Clinical Practice Guidelines: Treat All Smokers****

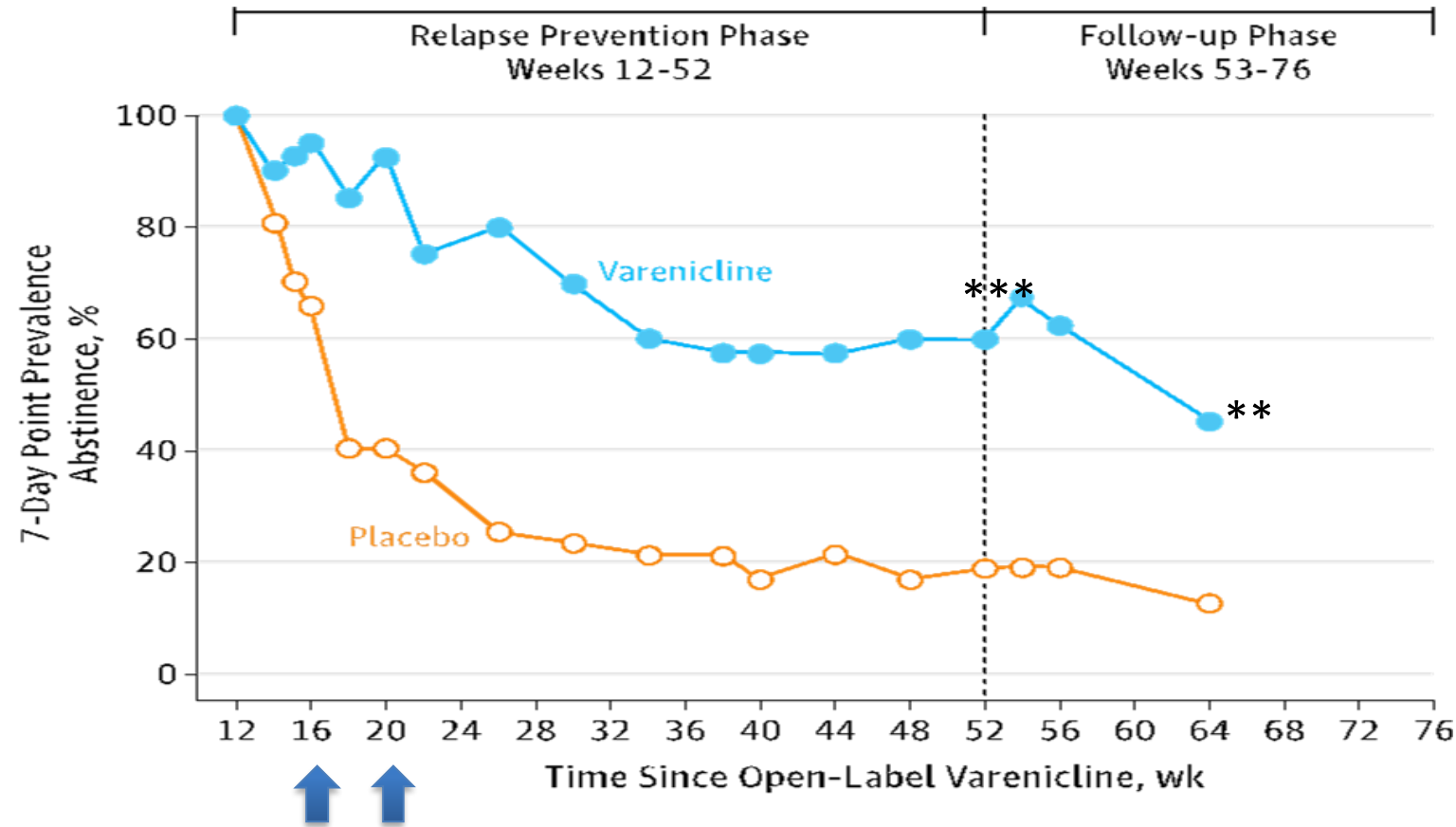
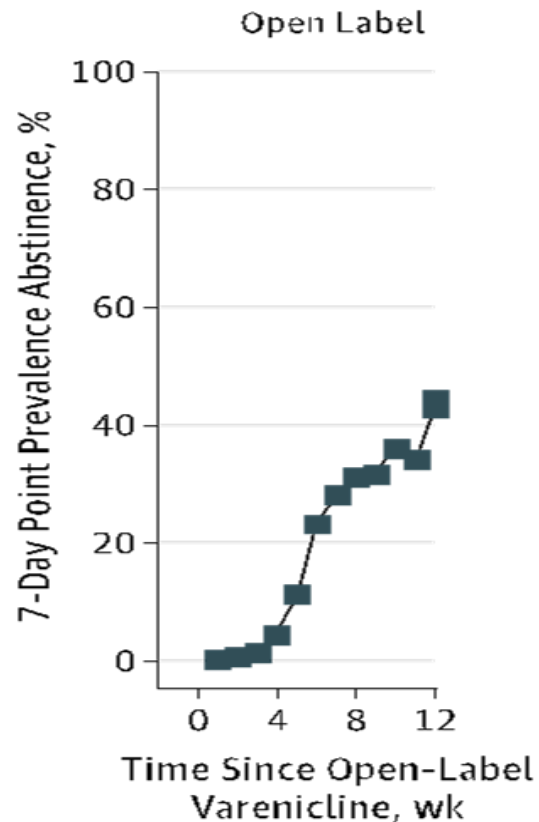
Encourage a trial of smoking cessation pharmacotherapy and behavioral support for all people with nicotine dependence who willing to accept such treatment, not just those who ask for it or who report being 'ready to quit'

Repeat Cessation Attempts Are Effective



12 weeks varenicline superior to placebo in those who had failed ≥ 1 prior varenicline trials.

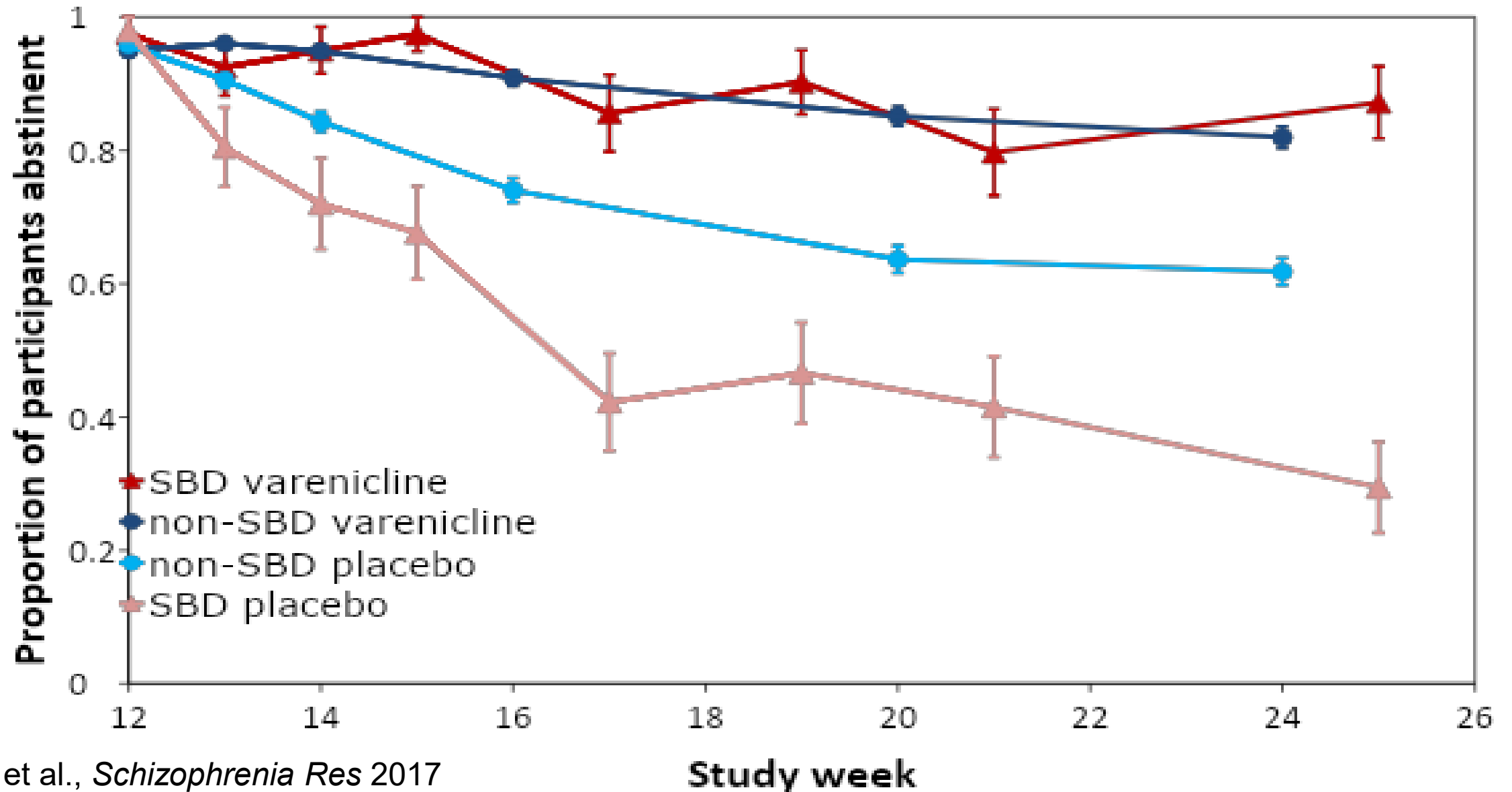
How Long to Treat? Varenicline Maintenance Triples Abstinence Rates at One Year in Smokers with Schizophrenia



43% attained abstinence with 12 weeks open label varenicline and were randomized to 40 weeks varenicline or placebo + Group CBT

Evins, Cather, et al., *JAMA*. 2014

Maintenance Tx Normalizes Relapse Rates for Smokers with SMI



Most Effective Smoking Cessation Pharmacotherapy Underutilized, Particularly in Psychosis

- 2010 PORT guidelines for tx of schizophrenia recommend pharmacotherapy and physician advice to quit for all smokers with schizophrenia.
- Psychiatrists rarely offer counseling to quit smoking. In one study, only 12.4% of smoking patients were advised to quit.
- Smokers with SMI are even less likely to receive a medication to help them to quit.
- Varenicline especially underutilized in smokers with psychosis

[Treatment is effective and under-prescribed](#)

Buchanan et al., 2010; Himloch and Daumit, 2003; Thorndike et al., 2001; Huang et al., 2014; Cook 2014

EAGLES Trial

- Compare risk of clinically significant neuropsychiatric AEs & efficacy of varenicline, bupropion, NRT patch, placebo
- >8000 Smokers aged 18 to 75 years; ≥ 10 cigs/day
- > 4000 smokers, no lifetime psychiatric diagnosis
- > 4000 smokers, 1+ clinically stable, lifetime diagnoses

Mood Disorders	Major depressive disorder (MDD), bipolar I, bipolar II
Anxiety Disorders	Panic disorder with or without agoraphobia, post-traumatic stress disorder, obsessive-compulsive disorder, social phobia, generalized anxiety disorder
Psychotic Disorders	Schizophrenia, schizoaffective disorder

Anthenelli RM, Benowitz NL, West R, St. Aubin L, McRae T, Lawrence D, Ascher J, Russ C, Krishen A, Evins AE. *Lancet*. 2016

Clinical Characteristics of the EAGLES Psychiatric Cohort

- Included:
 - Stable but symptomatic
 - 1/2 on psychotropic medication at baseline (>95% with psychotic disorder)
 - 1/2 with MDD had recurrent depression
 - 1/3 had a second psychiatric diagnosis / comorbidity
 - 1/4 had a lifetime substance use disorder
 - 1/8 had made a prior suicide attempt
- Excluded: those with active self-injurious behaviors, imminent suicide risk, active SUD

EAGLES 1⁰ Endpoint: Composite Neuropsychiatric Adverse Event

Percent of subjects reporting worsening or new onset of any of the following during treatment + 30 days

≥1 "severe" AE of:			
Anxiety	Depression	Feeling abnormal	Hostility
And/or ≥1 "moderate" or "severe" AE of:			
Agitation	Aggression	Delusions	Hallucinations
Homicidal ideation	Mania	Panic	Paranoia
Psychosis	Suicidal ideation	Suicidal behavior	Completed suicide
AE, adverse event; NPS, neuropsychiatric			

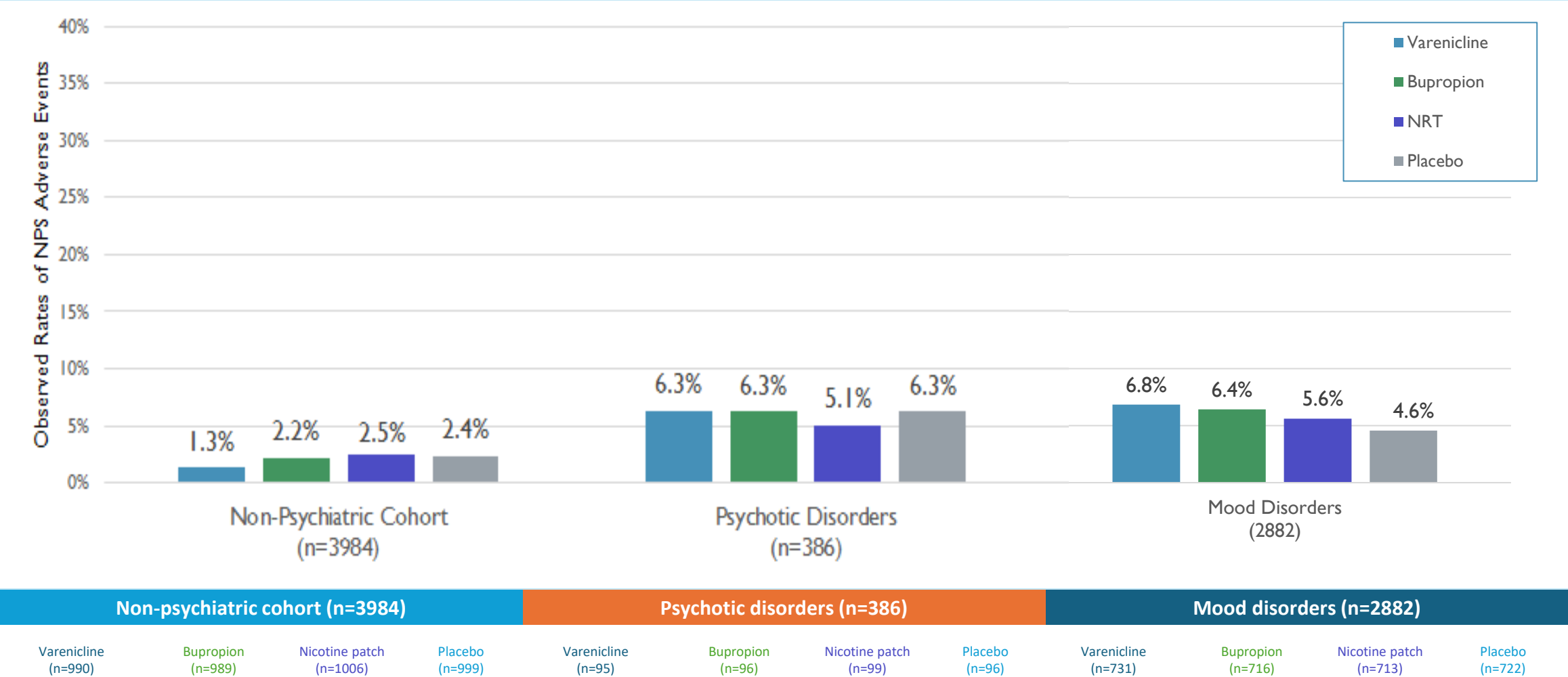
Designed in collaboration with FDA and EMA to be broad and capture an array of events.

Severity: Moderate = interferes to some extent with usual function

Severe = interferes significantly with subject's usual function

SAFETY: Varenicline, Bupropion Do NOT Increase NPSAEs

NPSAEs During Weeks 1 - 12 +30d in Adult Smokers Without or With a History of Psychiatric Disorder



Evins et al., *J Clin Psychopharm* 2019; Anthenellii et al., *Lancet* 2016. Neuropsychiatric (NPS) safety data based on EAGLES, an FDA required trial to evaluate NPS safety in over 8000 smokers with and without a psychotic, anxiety or mood disorder†

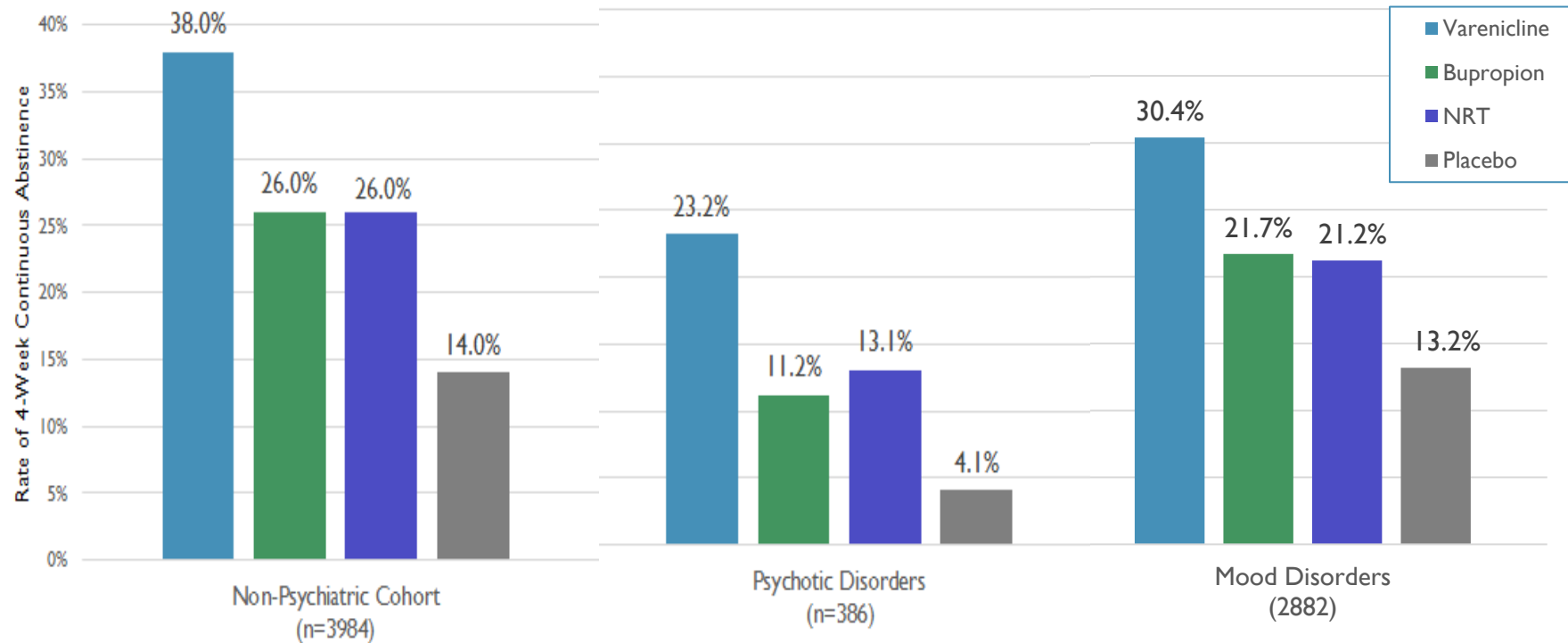
SAFETY

EAGLES provides data that can be used to counsel smokers on the likelihood of experiencing a moderate to severe NPS adverse event during a smoking cessation attempt.

- Risk of NPS AE is independent of treatment
 - ~2% NPS AE rate in smokers without mental illness
 - ~6% NPS AE rate in smokers with mental illness
- NPS AE rates during a cessation attempt are not different across 3 active treatments or placebo
- No pattern for the most worrisome NPS AEs
- No psychiatric subgroup appears to be at particularly increased risk

COMPARATIVE EFFICACY

Biochemically Confirmed Continuous Abstinence for Weeks 9 - 12 in Adult Smokers Without or With a Psychiatric Disorder



Varenicline was superior to bupropion, NRT & placebo

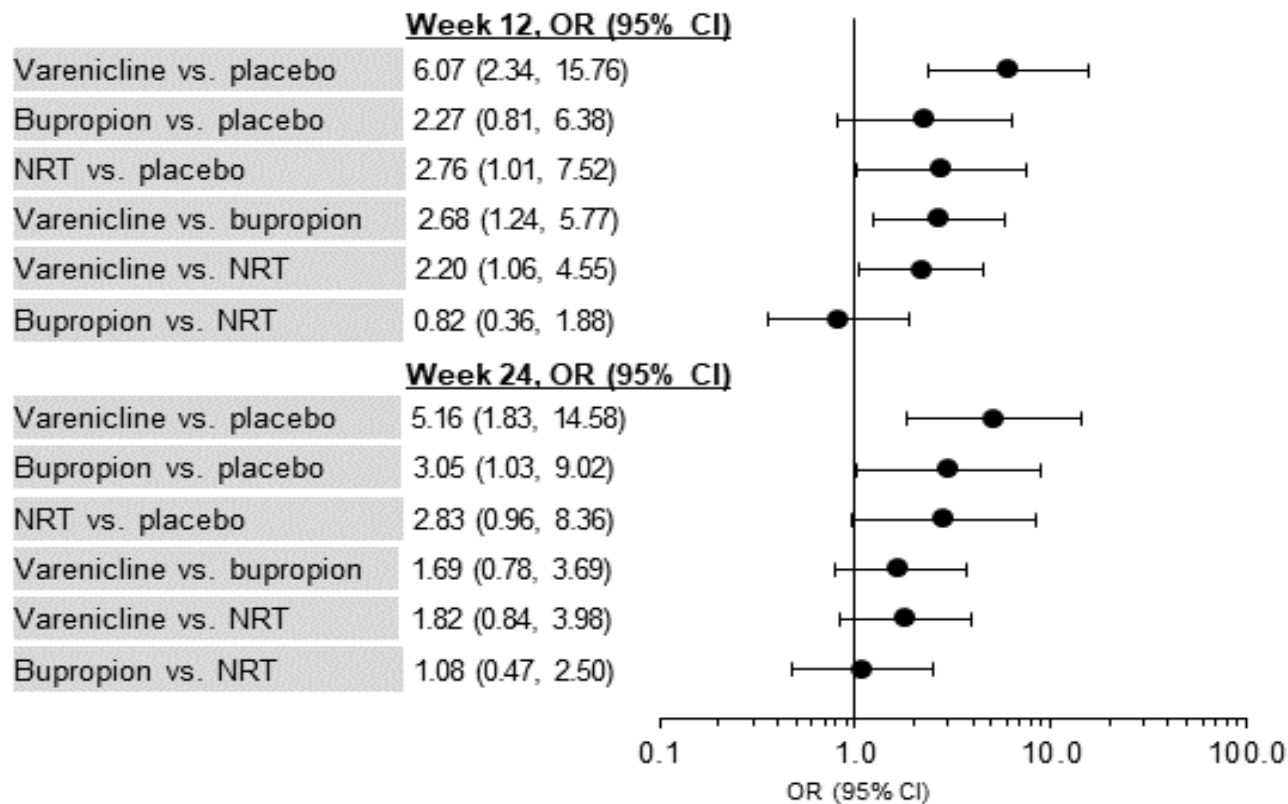
Bupropion and NRT superior to placebo

Antheneli et al., *The Lancet* (2016) and Evins et al., *J Clin Psychopharm* 2019

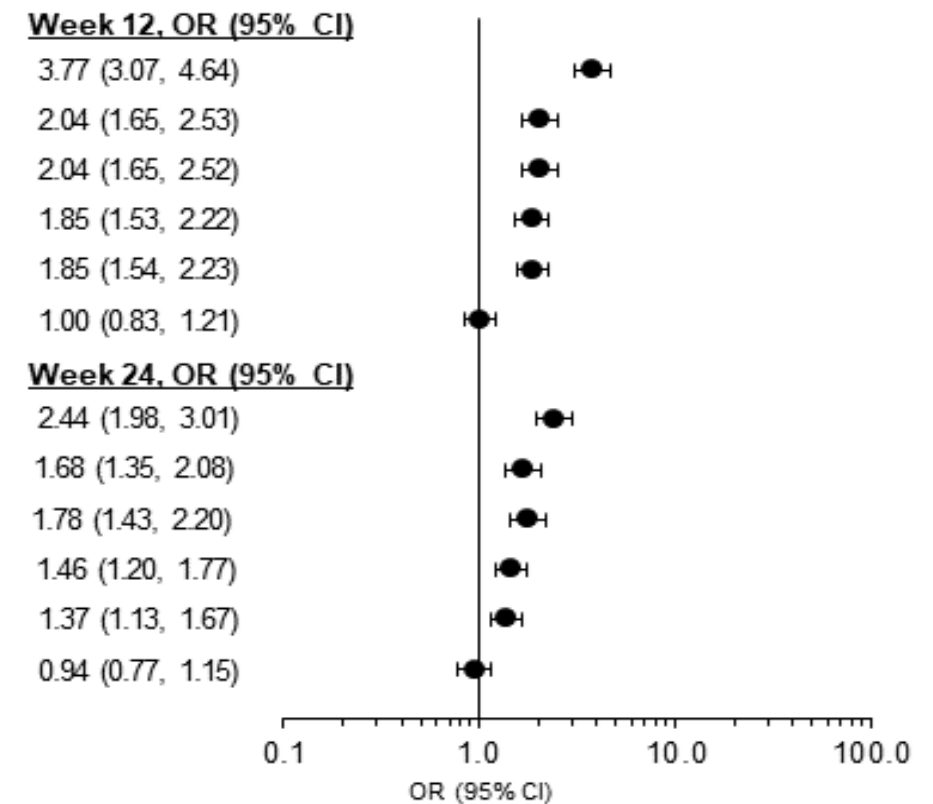
EFFICACY

Comparative efficacy data based on EAGLES²

Schizophrenia spectrum disorders subcohort

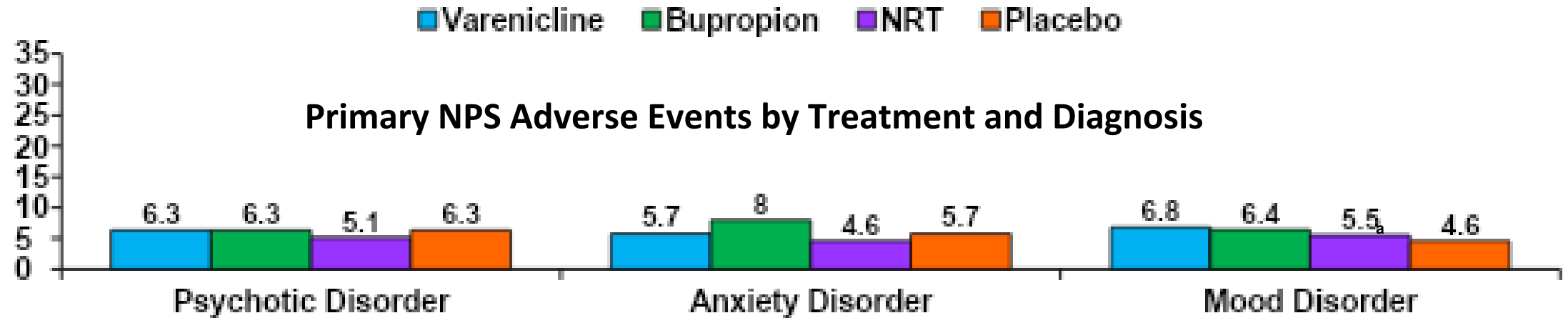


No psychiatric disorders cohort

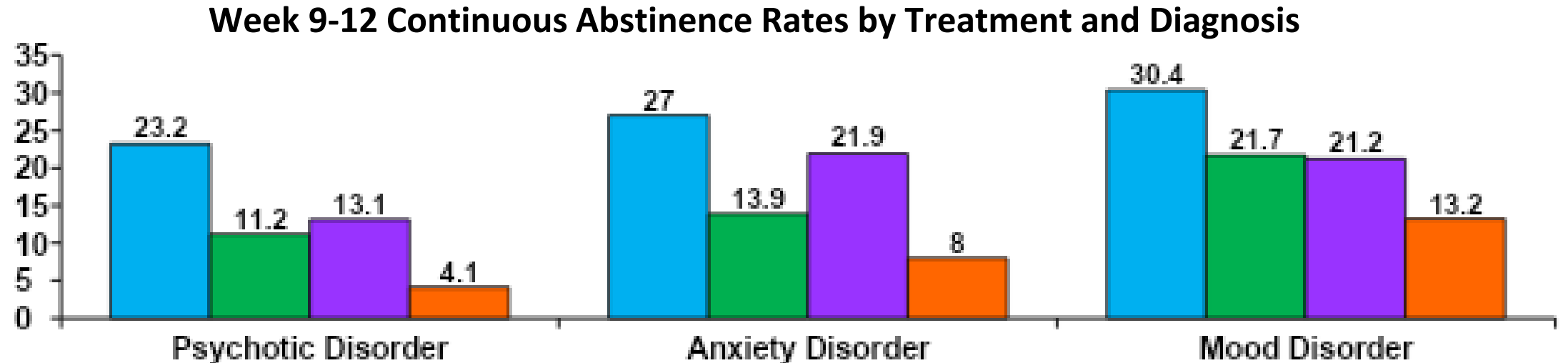


Risk / Benefit: NPS Safety and Efficacy in Those with a Psychiatric Illness

Observed Rate of
NPS Events, %



Observed CARs,
%



Effects of Single Interventions for Smoking Cessation in Adults with SMI

Intervention vs placebo/counseling	Short term abstinence [*]	Long term abstinence [†]	Serious adverse events [‡]	Depression [§]	General psychopathology
Single interventions					
Varenicline	17 more per 100 (95% CI 10 more – 25 more) OR: 3.85 (95% CI 2.63 – 5.67)	11 more per 100 (95% CI 6 more – 17 more) OR: 2.90 (95% CI 1.94 – 4.40)	0 more per 100 (95% CI 0 more – 0 more) OR: 1.11 (95% CI 0.40 – 3.19)	0.27 lower (95% CI 1.03 lower – 0.53 higher)	3.1 higher (95% CI 2.5 lower – 8.7 higher)
Bupropion	7 more per 100 (95% CI 2 more – 13 more) OR: 1.99 (95% 1.28 – 3.05)	6 more per 100 (95% CI 2 more – 11 more) OR: 1.94 (95% CI 1.26 – 3.10)	0 more per 100 (95% CI 0 more – 0 more) OR: 1.10 (95% CI 0.26 – 4.27)	0.34 lower (95% CI 1.25 lower – 0.53 higher)	21.7 lower (95% CI 39.2 lower – 4.3 higher)
NRT	8 more per 100 (95% CI 4 more – 15 more) OR: 2.28 (95% CI 1.52 – 3.53)	4 more per 100 (95% CI 1 more – 9 more) OR: 1.70 (95% CI 1.10 – 2.68)	0 more per 100 (95% CI 0 more – 0 more) OR: 1.26 (95% CI 0.32 – 4.96)	0.15 higher (95% CI 0.8 lower – 1.6 higher)	
Extensive non-pharmacological treatments	19 more per 1000 (95% CI 0 more – 55 more) OR: 4.33 (95% CI 0.98 – 19.8)	5 more per 1000 (95% CI 2 more – 10 more) OR: 1.84 (95% CI 1.22 – 2.88)			

Level of certainty	Category		
	More effective than placebo or minimal care	Worse than placebo or minimal care	No different than placebo or minimal care
High certainty	Definitely more effective than placebo or minimal care	Definitely worse than placebo or minimal care	Definitely no different than placebo or minimal care
Moderate certainty	Probably more effective than placebo or minimal care	Probably worse than placebo or minimal care	Probably no different than placebo or minimal care
Low certainty	Maybe more effective than placebo or minimal care	Maybe worse than placebo or minimal care	Maybe no different than placebo or minimal care
Very low certainty	We are very uncertain		

EFFICACY

Comparative efficacy data based on EAGLES

Varenicline was superior to bupropion, NRT and placebo, while bupropion and NRT were superior to placebo for biochemically-confirmed tobacco abstinence.‡

"FDA removes warnings on smoking cessation medication"

Pharmacy Times, December 16, 2016

FDA and EMA removed boxed warnings for varenicline and bupropion in 2016 based on results of EAGLES, a required, randomized, double-blind, triple dummy, active-and placebo-controlled clinical trial conducted by Pfizer in collaboration with GlaxoSmithKline, designed in consultation with the FDA and the European Medicines Agency (EMA). It is the largest smoking cessation clinical trial ever conducted and the largest samples of smokers with psychotic, anxiety, and mood disorders ever conducted.

EAGLES is a Landmark Study of Clinical and Public Health Importance

- The EAGLES trial is the first:
 - To compare safety and efficacy of all 3 FDA approved smoking cessation therapies in large samples of patients with and without a history of psychiatric disorder
 - To allow for comparison of safety and efficacy of smoking cessation aids in smokers with different mental illnesses

Neuropsychiatric Adverse Events During Smoking Cessation Attempts Are Independent of Treatment

- NPS AEs are seen in trials regardless of treatment
- Clinicians who prescribe a treatment and observe a NPS AE likely attribute this AE to the treatment.
- This happened in our large maintenance treatment trial of varenicline, in trials of bupropion, and in clinical practice.

Anthenelli et al., *Lancet* 2016; Evins, et al., *JAMA* 2014; Evins, et al., *J Clin Psychopharm* 2007

Varenicline Safety in 17 RCTs and 5 Large Observational Studies

Pooled Analysis of ALL Psychiatric AEs in 17 RCT's of Varenicline

Varenicline increased incidence of nausea, not psychiatric AEs

Varenicline increased abstinence rates by 124% vs. placebo and 22% vs. bupropion

Having a psychiatric illness increased the risk for psychiatric AEs equally in those assigned to varenicline and placebo

Observational study in 35,800 outpatients: fewer psychiatric AEs in those prescribed varenicline than those prescribed NRT

Replicated now in DoD, VA, UK NHS

Gibbons and Mann 2013; Tonstad et al., 2010; Kotz et al., 2015

EAGLES is a Confirmatory Trial for Efficacy

- Efficacy conclusions replicate and extend findings from smaller trials and meta-analyses in those with and without mental illness
- The efficacy data are clear:
Varenicline > bupropion and nicotine patch > placebo
- Agreement with large, growing body of evidence raises confidence in the findings

Why Might There be Significant NPS AEs Among Smokers, Independent of Treatment (and Abstinence)?

- Smoking is an addiction; like all drug addictions, there are:
 - Well documented brain changes
 - Increased neuropsychiatric events, e.g. suicide
 - Suicide risk reduced in smokers who quit
- People with psychiatric illness are more likely to smoke
- Attempts to quit smoking are not risk free, with or without pharmacologic support and independent of abstinence
 - Well replicated in smokers with history of depression

Volkow et al., Am. J. Psych, 1999; Fehr et al., Am J Psych 2008; Li, et al., J Psych Res 2012; Berlin et al., NTR 2011; Brown 1996; Tsoh, et al., Am J Psych 2000; Torres, et al., Psychol Med 2010; Evins, et al., JAMA 2014, Evins et al.. Psychol Med 2017

Risk/Benefit Considerations

- Clinicians **overestimate** the risk of NPS AEs with varenicline and bupropion, particularly in those with psychotic illnesses
- And **underestimate** the benefit of varenicline and bupropion on improving quit rates
- It is imperative we find ways to increase use of the most effective smoking cessation treatment for our patients who try time and again to quit smoking

Huang et al., *BMC Public Health* 2014

Standard of Practice: Offer First Line, Evidence Based Smoking Cessation Treatment to ALL Who Smoke Tobacco

- Adults with mental illness:
 - More likely to smoke, to smoke heavily, and be dependent
 - Less likely to quit without a cessation aid
 - More likely to relapse after discontinuation of cessation aids
 - More likely to benefit from maintenance treatment
- Smokers with mental illness are less likely to receive a pharmacotherapeutic cessation aid from a medical provider
 - This contributes to the 25 year mortality gap in those with mental illness from diseases causally related to smoking
 - 28 year mortality gap for those with schizophrenia

Vaping: Safer than smoking, but marketed to youth, most of whom have never smoked



Vaping: The Primary Route to Nicotine Addiction in Youth

- **Addiction to Nicotine**

- In high school students, 70-75% of past daily vapers remain daily nicotine users, similar to smoked tobacco
- Persistence suggests addiction not just experimentation

- **Associated with Other Substance Use**

- High school students who vape have 25-40 times greater odds of using cannabis or alcohol regularly than non-users
 - Same Odds for daily vapers and daily smokers
 - Vaping is now the most popular route of marijuana use in high schools (16-fold increase in 4 years)

Letters

RESEARCH LETTER

ADOLESCENT MENTAL HEALTH

Substance Use, Suicidal Thoughts, and Psychiatric Comorbidities Among High School Students



In our annual school survey in >30,000 students, alcohol, nicotine, and cannabis use frequency were each associated with severity of suicidal thoughts, anxiety, depression, inattention and psychosis. These were significant, dose-related associations

Vaping: Initially promoted to help cigarette smokers, has transformed teen nicotine and cannabis use. Few treatments have been tested.

 **Massachusetts General Hospital**
Founding Member, Mass General Brigham

 **ELF BAR**

 Equivalent to 30 cigarettes





ELF BAR
MAKE IT ELF, ENJOY YOURSELF.



FROM £3.50 - MIX & MATCH

 550 MAH Battery

 Nic Salts

Treatment Trial for Adolescent Vaping Cessation: Eligible Participants...

- 300 adolescents, aged 16-25, addicted to vaped nicotine, who never smoked tobacco regularly (≥ 5 days per week) and wished to reduce or quit nicotine use, recruited from community settings
- Few other exclusions to maximize generalizability
- Comorbid drug use, drug use disorders, psych dx and tx all allowed

Varenicline for Youth Nicotine Vaping Cessation

A Randomized Clinical Trial

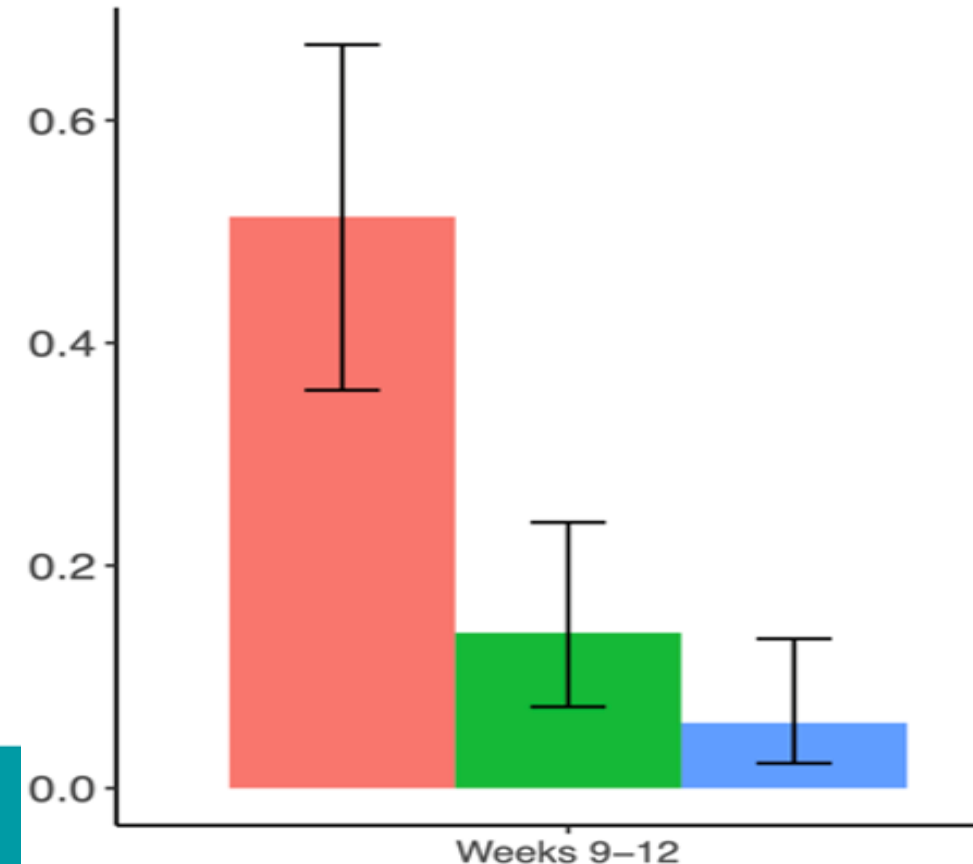
A. Eden Evins, MD; Corinne Cather, PhD; Harrison T. Reeder, PhD; Bryn Evohr, BS; Kevin Potter, PhD; Gladys N. Pachas, MD; Kevin M. Gray, MD; Sharon Levy, MD; Nancy A. Rigotti, MD; Vanessa Iroegbulem, BA; Jason Dufour, BS; Kelly Casottana, BS; Meghan A. Costello, PhD; Jodi M. Gilman, PhD; Randi M. Schuster, PhD

97% study completion rate

**53% abstinence on
Varenicline + Counseling + Texting Support Referral**

**14% abstinence on
Placebo + Counseling + Texting Support Referral**

6% abstinence with Texting Support referral



MYTH

People with SMI
don't want to
quit smoking

Quitting
worsens
psychiatric
symptoms

Medications
don't help
people with SMI
stop smoking

Meds should
only be
prescribed for
smokers ready to
quit completely

FACT

**60-70% of
smokers with
SMI want to quit**

**Stopping smoking
improves
depressive
symptoms (like
anti-depressant
medication)**

**Smokers with SMI
are 3-6x more
likely to quit with
medication**
-Only 4% quit without
a medication

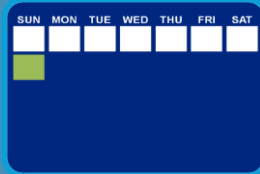
**'Flexible quit' and
'gradual quit' after
starting meds are
validated ways to
quit**

2018 American College of Cardiology Expert Consensus Decision Pathway on Tobacco Cessation Treatment

- Recommend/Prescribe Pharmacotherapeutic Cessation Aid to ALL Smokers, not just those who state they are ready to quit.
- Prescribe to all smokers willing to start a pharmacotherapy
- Follow up in 2-4 weeks for tolerability
- For those who decline, continuous engagement to quit at each clinic visit

Barua et al., JACC 2018

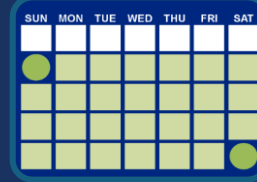
THREE WAYS TO QUIT SMOKING: All Start with Smoking Cessation Medication



FIXED QUIT

For people who want to quit smoking in a week

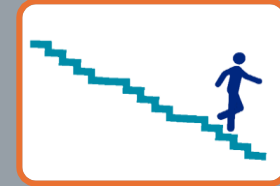
- Set a target quit date 1 week after starting smoking cessation med
- Can keep smoking for the first week while they prepare to quit
- Take smoking cessation medication for 12-24 weeks



FLEXIBLE QUIT

****Recommended****

- Start taking smoking cessation medication and pick a quit date 8 to 35 days after starting treatment
- *Can keep smoking for up to a month on smoking cessation medication while preparing to quit*
- Take smoking cessation meds for 12-24 weeks



GRADUAL QUIT

For people not able/willing to quit abruptly

- Start taking smoking cessation med and reduce smoking by 50% over 4 wks, by another 50% in the next 4 wks, etc. Goal of quitting by 12 weeks.
- Continue smoking cessation med for an additional 12 weeks, for a total of 24 weeks

STEPS TO ADDRESS SMOKING

Assess

At each clinic visit, ask patients if they currently smoke tobacco. (most with SMI smoke)

Engage

Remind patients that quitting is the single best thing they can do for their health. Recommend EVERY smoker start treatment to quit. Med use may increase readiness to quit.

Prescribe

Start medication for all smokers who are willing. Emphasize importance of adherence to treatment. Decide on fixed, flexible, or gradual quit.

Follow Through

Schedule 1-4 week follow-up to assess med tolerability, plan quit. Remind pts that most AEs are mild, transient. Problem solve around missed med doses . Reinforce progress and persistence. Most need repeat quit attempts.

How To:

VARENICLINE

Available as 0.5 and 1.0 mg tabs

- 0.5 mg/d at hs x 3 d
- 0.5 mg bid x 4 d
- 1.0 mg bid x 11 weeks
- Additional 3-9 months Tx recommended in those who achieve abstinence
- 12-month safety data published: well tolerated

Renal excretion, used in chronic renal disease with dose reduction

No significant drug-drug interactions or effect on cytochrome enzymes

Nausea, headache, insomnia, and vivid dreams are common

How To:

DUAL NICOTINE REPLACEMENT THERAPY

NICOTINE PATCH +

Dosing: 21 mg/d x 4-6 weeks then

- 14 mg/d x 4 weeks then
- 7 mg/d x 3-4 weeks

Apply one new patch every 24 hours (preferable am) to dry, clean skin

Move site with each new patch to avoid skin irritation

Remove patch at night if bothered by insomnia or vivid dreams

NICOTINE GUM, LOZENGE

Dosing: up to 20 mg/d x 4-5 weeks then

- Up to 14 mg/d x 4 weeks then
- Up to 10 mg/d x 3-4 weeks

Do not chew, break, crush, or swallow whole

Gum: Chew a few times then 'park it' between cheek and gum

Move around mouth until it melts (lozenge) or loses flavor (gum)

Do not eat or drink for 15 minutes before or during use

How To:

**BUPROPION
SR OR XL**

Dosing:
150mg QD x 3 days, then 150mg BD

Insomnia common

Meta-analysis of 182 studies
with 70,000 smokers:⁹
Varenicline **triples** chances of
quitting vs. placebo
and increases odds of quitting by
50% over NRT and bupropion

NRT and bupropion nearly
double odds of quitting vs.
placebo (80% increase)

Combination Pharmacotherapy for Nicotine Dependence Treatment

May improve abstinence rates

For smokers who have relapsed after treatment with single agent, consider maintenance treatment or combination treatment:

- NRT: **long acting** (patch) + **short acting** (gum, inhaler or nasal spray) + CBT -now standard in clinical practice
- Bupropion 150 mg bid + NRT + CBT
- Varenicline + NRT-2 studies, conflicting findings

Behavioral Interventions

- Current guidelines recommend behavioral tx **+ pharmacotherapy**
 - Motivational enhancement
 - Relapse prevention
 - Partner support
- Guidelines are based on several large meta-analyses of controlled trials
- Telephone counseling provides a modest benefit in quit rates vs minimal intervention, patient follow through can be low
 - www.trytostop.org or **1-800-TRY-TO-STOP**
- Physical exercise can decrease cravings and attenuate weight gain

Nicotine Withdrawal Syndrome

- Peaks in 4 days
- Lasts 2-3 weeks
- Can be severe, not life threatening
 - Anxiety
 - Awakening during sleep
 - Depressed mood
 - Difficulty concentrating
 - Impatience
 - Irritability/anger
 - Restlessness
 - Decreased heart rate
 - Weight gain



Tobacco Abstinence: Effects on Metabolism

- Smoking speeds hepatic metabolism of many medications
- Serum concentrations of medications that are stable in smokers may rise following abstinence, allowing lower doses
- CYP 1A1, 1A2, and 2E1
 - Abstinence associated with 30-42% reduction in 1A2 activity over the first 1-3 days of abstinence
 - Therapeutic drug monitoring and 10% dose reduction has been recommended
- Take care when prescribing bupropion to those on clozapine because of additive seizure risk

Seppala NH, et al.,1999; Desai HD, et al., 2001; Faber & Fuhr, 2004.