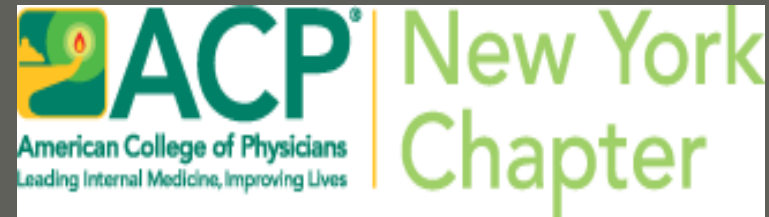


New York Chapter



Effective Tobacco Dependence Treatment: Medications For Cessation

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7 FDA – approved medications for smoking cessation in the United States

Nicotine Replacement Therapy

- Patch 1991-1992
- Gum 1984
- Lozenge 2002
- Oral inhaler 1997
- Nasal spray 1996

Bupropion SR: Zyban 1997

Varenicline: Chantix 2006

68% of smokers wanted to quit
55% made a quit attempt in
the past year

**31% of smokers trying to quit
used medications and/or
counseling**

National Health Interview Survey of
noninstitutionalized US civilian population

MMWR 2017

Goal: Advise and prescribe medications for nicotine-dependent adult smokers who want to quit

Learning Objectives

1. **Evaluate the smoker** for factors relevant to successful quitting, including nicotine dependence, as well as other aspects of the smoker's history which could affect choice of medication
2. Compare the basic **mechanism of action** of nicotine replacement therapy, bupropion, and varenicline and contrast with the action of nicotine from cigarette smoking on the brain
3. Compare the **three classes of medications** in terms of efficacy, major side effects, contraindications and cautions
4. Discuss ways to **increase the effectiveness of medications**, including preloading, extending duration, and combining therapies.
5. Apply what you learn to **three clinical scenarios**

Outline

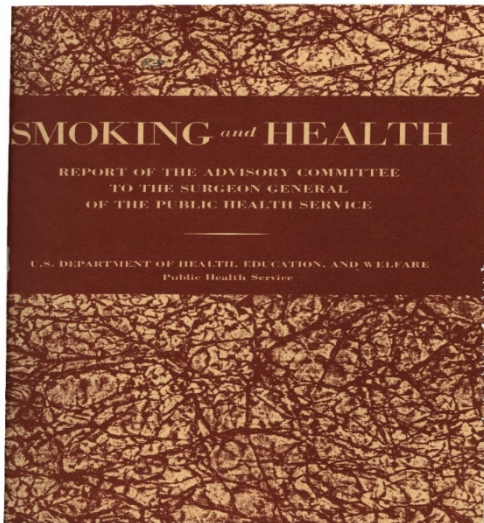
- Background
- Choosing and prescribing medication: three case examples
- Increasing quit rates with preloading, extended duration, and combination therapy
- Summary

Outline

- **Background**
- Choosing and prescribing medication: three case examples
- Increasing quit rates with preloading, extended duration, and combination therapy
- Summary

Smoking is still the most common cause of preventable death in the United States

1964

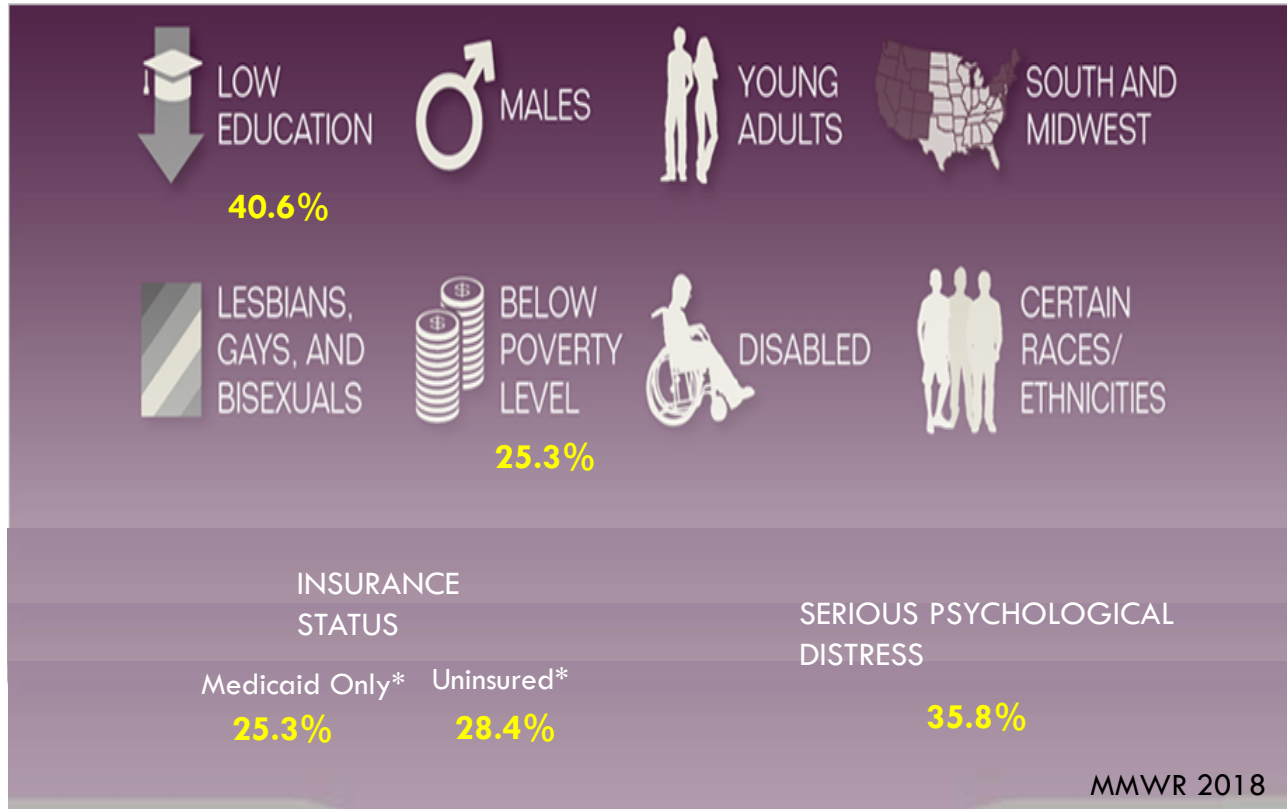


Prevalence ~ 42%

2018

- Prevalence 13.7% in U.S. adults 18 and older
- 34.2 million people
MMWR Nov 15, 2019
- Impact of e-cigarette epidemic not fully known yet
- Disparities in prevalence and subsequent morbidity, mortality

Higher prevalence in some populations



High prevalence in people with psychiatric disease, alcohol and other substance abuse disorders, the homeless, incarcerated.

Why do people smoke? Why do they have difficulty quitting?

Makes You Feel Better

- Pleasurable
- Increases mental and physical functioning
- Decreases stress and anxiety

Habit

- People smoke in response to triggers:
 - After eating
 - When having coffee or alcohol
 - When sad or stressed
 - When around other smokers

Dependence

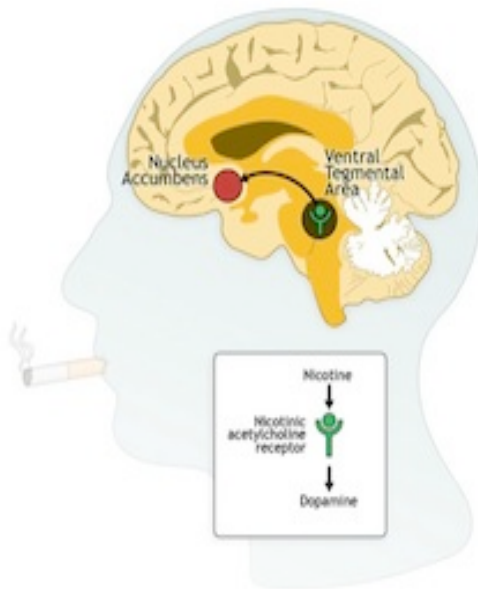
- **Approximately three quarters of smokers are dependent on nicotine**
- **People smoke to relieve their withdrawal symptoms**

Genetics

- Genetic Predisposition
 - fast or slow metabolizers of nicotine to cotinine
 - fast metabolizers - more difficulty quitting

Nicotine from cigarettes can lead to dependence

Nicotine leads to dopamine release in the brain.



- Nicotine binds to nicotinic cholinergic receptors in the midbrain within 10-20 seconds after a puff
- Release of dopamine and other neurotransmitters
- Dopamine is primarily responsible for development of nicotine dependence

Nicotine dependence → withdrawal symptoms and cravings

ICD 10 criteria for dependence

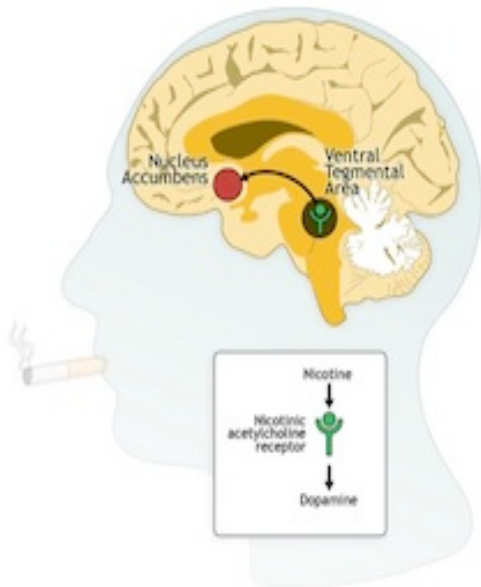
- Compulsion to use
- Difficulty controlling use
- Progressive neglect of other activities/interests
- Persistent use despite harmful effects
- Development of tolerance
- **Withdrawal symptoms**

Withdrawal symptoms

- Restlessness
- Irritability
- Difficulty concentrating
- Depressed mood
- Insomnia
- Anxiety
- Increased appetite

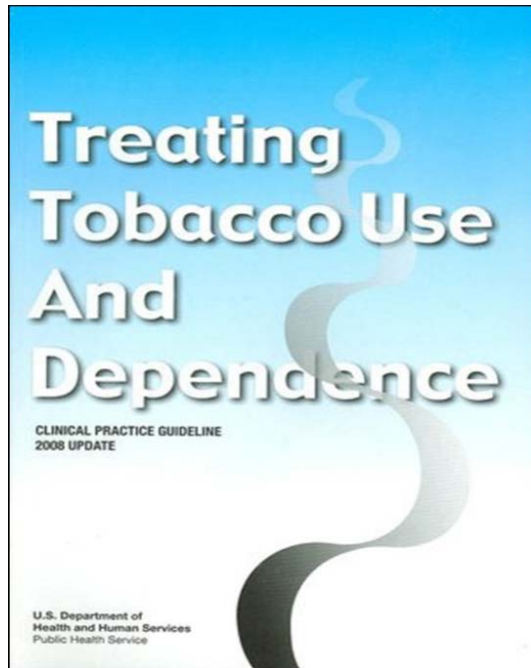
Medications act on the dopamine pathway, decrease withdrawal symptoms and cravings

Nicotine leads to dopamine release in the brain.



- Nicotine Replacement Therapy
 - supplies nicotine which binds to and stimulates the nicotinic receptor
- Bupropion
 - inhibits the reuptake of dopamine and norepinephrine
 - also acts as an antagonist
- Varenicline
 - partial agonist at the **a4b2** nicotinic receptor subtype
 - also acts as an antagonist

Strong evidence base for the effectiveness of medication and counseling in smoking cessation



- Concentrated on adult smokers who wanted to quit
- Brief interventions: the 5 A's Ask, Advise, Assess, **Assist**, Arrange follow up
- Medications and behavioral counseling for smokers who want to quit
- Both are more effective than either one alone

Treating Tobacco Use and Dependence
Clinical Practice Guideline 2008 update
United States Public Health Service

Medication and counseling 6-month quit rates

Single NRT vs placebo

17.6% vs 10.6%

Combination NRT vs placebo

31.5% vs 10.6%

Bupropion SR vs placebo

19.1% vs 10.6%

Varenicline vs placebo

27.6% vs 10.9%

Cochrane Rev 2013 – Absolute cessation rates at 6 months from quit date

Long-term unassisted quit rates less than 5%

Nicotine Replacement Therapy (NRT)

- 5 types of NRT
 - long acting: patch (“passive”)
 - short-acting: gum, lozenge, inhaler, nasal spray (“active”)
- Efficacy RR = 1.55 (Cochrane Rev 2018)
 - 5 types of single NRT are similarly effective
 - combination NRT (patch plus short-acting form) more effective than single NRT RR = 1.25 (Cochrane 2019)
- Few precautions
 - MI in the prior 2 weeks, severe angina, life-threatening arrhythmias

Bupropion sustained-release (Zyban)

- Atypical antidepressant initially used in major depression (Wellbutin)
- Similar efficacy as single NRT RR = 1.62 (Cochrane Review 2014)
- Seizure risk ~ 1:1000
- Precautions
 - medical conditions/medications/substances which lower seizure threshold
 - can increase blood pressure especially when used with NRT
- Contraindications
 - seizure disorder
 - abruptly stopping benzodiazepines, barbiturates, anti-epileptics, heavy alcohol use
 - h/o or current eating disorders (anorexia, bulimia)
 - use of monoamine-oxidase inhibitors within prior 2 weeks

Varenicline (Chantix)

- Most effective single agent RR = 2.24 (Cochrane Review 2016)
- Safe for use in smokers with psychiatric disease
 - black box warning about increased neuropsychiatric effects removed December 2016
- Precautions
 - may need to decrease dose if severely decreased renal function
 - can decrease ability to drive or operate machinery (accidental injury)
 - somnambulism (occ associated with harmful behavior to self or others)
 - seizures (new or worsening)
 - interaction with alcohol (can increase effects of alcohol)

Behavioral counseling

Pre-Quit (STAR and medication)

- Set a quit date
- Tell others (if you want to)
- Anticipate challenges (especially withdrawal symptoms, triggers)
- Remove cigarettes from environment
- Medications: how they help/work, deciding what to use, how to use
- Behavioral counseling: how it helps, resources

Post-Quit (ARRANGE FOLLOW UP)

- Currently smoking?
 - Quit? Any lapses?
- Start/taking medication?
 - Side effects?
- Withdrawal symptoms, cravings?
- How dealing with triggers?
- Concerns?
- Using outside counseling/support?

Outline

- Background
- **Choosing and prescribing medication: three cases**

Charles: 35 year old, smokes 1 ppd, h/o alcohol use disorder

Rachel: 21 year old, smokes 11 cigs per day, obesity and h/o depression

Richard: 48 year old, smokes 2 ppd, schizophrenia and CAD

Is there a medication that you would or would not prescribe for each smoker?

How do we decide?

- Increasing quit rates with preloading, extended duration, combination therapy
- Summary

Charles: Evaluation

Charles 35 y.o.
1 pack per day
TTFC = 30 mins
(HSI = 3)

- Estimate nicotine dependence → smokes 1 ppd, TTFC = 30 minutes
- Quit once a few years ago using patch but relapsed. Would like to use patch again
- h/o alcohol dependence, underwent detox, going to AA, last drink 4 weeks ago
- No other medical or psychiatric problems
- Not taking any medications currently

Heaviness of Smoking Index (HSI)

Charles smokes 1 ppd, TTFC = 30 minutes HSI = 3

# cigs smoked per day	score	time to first cig of the day	score
31 or more	3	0 - 5 minutes	3
21 - 30	2	6 - 30 minutes	2
11 - 20	1	31 - 60 minutes	1
1 - 10	0	61 + minutes	0

Score 5-6 = high dependence **Score 3-4 = medium dependence** Score 0-2 = low dependence

Which medication(s) to recommend - Charles

- Nicotine dependence (**HSI = 3**, prior withdrawal sx, time to relapse)
- Psychiatric and substance abuse history (**alcohol use disorder**)
- Patient preference (**patch**)
- What worked before (**patch**)
- Medication cost and availability

Decision: You and Charles prefer NRT over varenicline or bupropion

Consider contraindications, cautions, patient preference

- Patient preference - Charles prefers NRT
- Consider the following if Charles relapsed to heavy drinking:
 - varenicline can interact with alcohol and increase its effects
 - bupropion could lead to seizures in people who suddenly stop heavy alcohol use
- You decide to prescribe combination patch plus short-acting form of NRT

Nicotine transdermal patch OTC



Dosing 21 mg, 14 mg, 7 mg

If > 10 cigs per day,
21 mg patch x 4-6 weeks
14 mg x 2 weeks
7 mg x 2 weeks

If 10 or fewer cigs per day,
14 mg patch x 6 weeks
7 mg patch x 2 weeks

Start on quit date
- can start prior to quit date (later)

Duration
- taper over 2 to 3 months
- can use longer (later)

Most common side effects
- skin irritation ~ 50% - rotate sites
- insomnia – can remove at night

Precautions: skin disorders, allergy to adhesive

Nicotine gum OTC



2 mg and 4 mg doses
- 4 mg if TTFC \leq 30 mins
Start 1 piece q 1-2 hrs/prn

Can use up to 24 pieces
in one day

Start on quit date

“Chew and park”– avoid over-chewing
and swallowing nicotine

No food or drink 15 minutes before & during
use. Acidity interferes with absorption

Main side effects: mouth irritation, jaw soreness
- hiccups, nausea, dyspepsia, heartburn
(usually from over-chewing)

Precaution: Do not use if dentures,
extensive dental work, or TMJ

Nicotine lozenge OTC



Start on quit date

Dissolve in mouth – regular lozenge for about 20-30 minutes. Do not chew.

Mini-lozenge: dissolved and absorbed more quickly

2 mg and 4 mg doses
4 mg if TTFC \leq 30 mins
Start 1 lozenge q 1-2 hr/prn

9-15 lozenges per day x 6 weeks
and taper over next 6 weeks
- can use up to 20 lozenges
in one day

No food or drink 15 minutes before and during use.

Main side effect: mouth soreness.
- can get hiccups, heartburn, or
nausea

Nicotine oral inhaler (“puffer”) Rx

- Absorbed through oral mucosa (oral form like lozenge and gum)
- Puff on the cartridge for up to 20 minutes (~ 80 inhalations)
 - do not inhale (not really an “inhaler”)
 - each cartridge lasts for 3-4 puffing sessions
- Dosing: 6 - 16 cartridges a day
 - start with 1 cartridge every 1-2 hours
- Side Effects: mouth and throat irritation; rhinitis; cough
- Precaution: reactive airway disease



Nicotine nasal spray Rx

- Absorbed through nasal mucosa
- Faster-acting than other NRT forms, so better in more dependent smokers
- Tilt head back, spray, breathe through mouth not nose
 - Don't sniff through nose
 - Don't blow nose for 2-3 mins after spraying
- Dosing 1-2 sprays each nostril; one dose = 1 spray each nostril
 - use 8 to 40 doses/day (max 5/hr)
- Side Effects: **rhinitis, sneezing**; throat irritation, cough, tearing
- Precautions: chronic nasal disorders (sinusitis, rhinitis), reactive airway disease



Discussing and prescribing combination NRT for Charles

- Short-acting NRT is “active” and can be taken prn for withdrawal symptoms.
- Patch is “passive” and provides continuous nicotine regardless of symptoms.
- How to decide which short-acting form to recommend?
 - precautions (gum-dental work, nasal spray-sinusitis)
 - patient preference (previous success?)
 - access
 - gum and lozenge are OTC (might need Rx for insurance coverage)
 - inhaler and nasal spray require a prescription
- For Charles - you prescribe patch 21 mg and lozenge 4 mg as needed, both starting on the quit date

Charles starts patch plus lozenge.

You follow up a few days after his quit date.

- You speak with Charles a few days after his quit date. He tells you a friend offered him a cigarette which he smoked while wearing the patch. **He was worried he might have a heart attack and so he stopped the patch.** After that, he returned to his usual smoking.
- Points to emphasize to Charles
 - it is not dangerous to smoke while using the patch or other NRT
 - if you smoke while using the patch, do not stop the medication
- Important for smoker to have a plan for dealing with lapses
- Early and close follow up is important

NRT FDA labelling change 2013

No significant safety concerns when...

- Combining NRT products
- Smoking while using NRT products
- Using NRT longer than 8-12 weeks

Charles: Questions for follow-up after the quit date

Questions

- Currently smoking
 - If quit, lapses (slips)
- Start/taking medication or not
 - Side effects
- Withdrawal symptoms, cravings
- Triggers
- Concerns
- Using outside counseling/support

Counseling/Medication

- How to deal with lapses
- Counsel about medication usage, withdrawal sx, and triggers.
- Consider adjusting or changing the medication if indicated
- Consider re-referring for counseling/support

Rachel: Evaluation

Rachel 21 y.o.
11 cigs a day
TTFC = 3 + hours
(HSI = 1)

- Tried quitting once before but never used any medications or counseling
- Concerned about gaining weight when she quits
- h/o depression in the past, not currently depressed
- Obesity, BMI = 30
- No other medical problems
- Not taking any medications

Which medication(s) to recommend- Rachel

- Nicotine dependence (**HSI = 1**, prior withdrawal sx, time to relapse)
- Psychiatric and substance abuse history (**h/o depression**)
- Consider other medical comorbidities (**obesity**)
- Patient preference and **concerns (weight gain)**
- What worked before (**never tried medication before**)
- Medication cost and availability

Many, but not all smokers, gain weight when quitting

- Aubin 2012 meta-analysis of randomized controlled trials
 - 84% of smokers gained weight at 12 months
 - mean weight gain 2.9 kg in first 3 months, 4.7 kg at 12 months
- Jeremias-Martins 2019 prospective cohort studies
 - 78.9% gained weight at 12 months
- Women tend to gain more than men, nonwhites more than whites, and heavier smokers more than light smokers
- Weight gain can be a deterrent to quitting and a risk factor for relapse

Bupropion limits weight gain while taken

- Bupropion, NRT, and varenicline limit post-cessation weight gain while taken
- Bupropion limits weight gain more than NRT or varenicline
 - bupropion - 1.12 kg
 - NRT - 0.69 kg (esp gum, lozenge)
 - varenicline - 0.41 kg
- No significant effect at 1 year post-cessation (off medications)

Cochrane Rev 2012

Bupropion may increase cessation in smokers with h/o depression

- Depressed mood, like increased appetite, is one of the withdrawal symptoms
- More common in those with a history of depression
- Risk factor for relapse
- Important to monitor all smokers who are quitting for changes in mood
- Bupropion increased cessation in smokers with h/o depression RR = 2.04
(Cochrane Rev 2013)

Decision: You and Rachel decide on bupropion

- Rachel has a low level of dependence (HSI = 1)
- Obesity, concerned about weight gain
 - bupropion can blunt weight gain
- h/o depression
 - bupropion good choice for smokers with h/o depression

Bupropion sustained-release (Zyban, Wellbutrin SR)



Metabolized by liver and kidneys.
Decrease dose in patients with
renal or hepatic disease

Increased seizure risk (~0.1%)

Full dosing bupropion sustained-release
-150 mg po daily x 3 days, then 150 mg po bid

Can also use bupropion 24-hour extended –
release form (bupropion XL)
- 150 mg daily, then 300 mg daily

Start 1 week prior to quit date
Duration: 7-12 weeks. Safe to give longer.

Most common side effects
- insomnia – take 2nd dose earlier in the
day but must be 8 hours after 1st dose
- dry mouth

Rachel: Questions for follow-up after the quit date

Questions

- Currently smoking
 - If quit, lapses (slips)
- Start/taking medication or not
 - Side effects
- Withdrawal symptoms, cravings
- Triggers
- Concerns: weight gain
- Check for depressed feelings (h/o depression)
- Using outside counseling/support

Counseling/Medication

- How to deal with lapses
- Counsel about medication usage, withdrawal sx, and triggers.
- Consider adjusting or changing the medication if indicated
- Consider re-referring for counseling/support if needed

Richard

Richard 48 y.o.

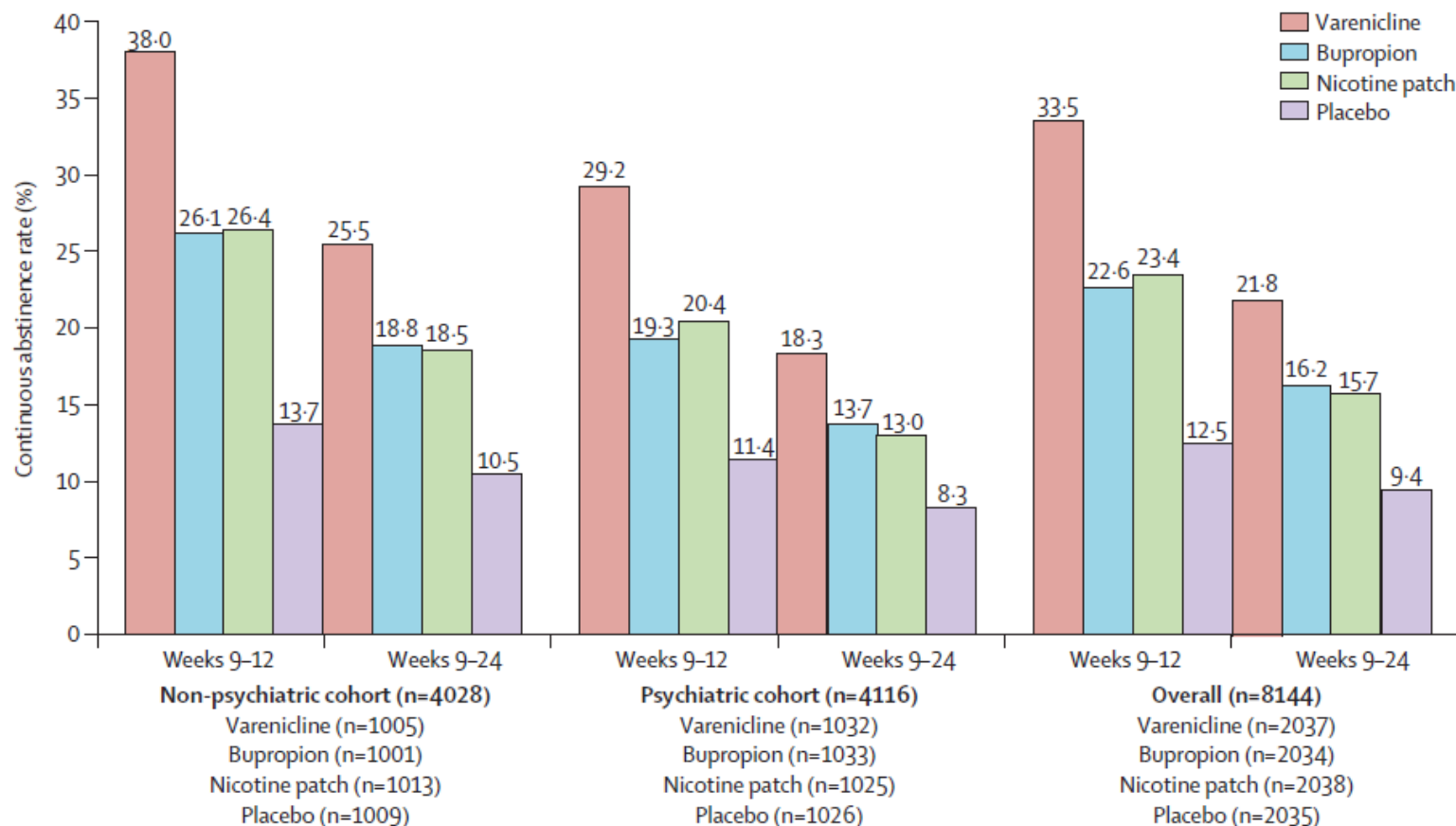
2 ppd

TTFC = 20
minutes

(HSI = 5)

- Tried to quit many times in the past, but always relapsed
- States that NRT “did not work”
- h/o schizophrenia controlled on medication, HTN, DM, hyperlipidemia, CAD, s/p MI 5 years ago
- Meds: olanzapine, lisinopril, HCTZ, metformin, ASA, atorvastatin

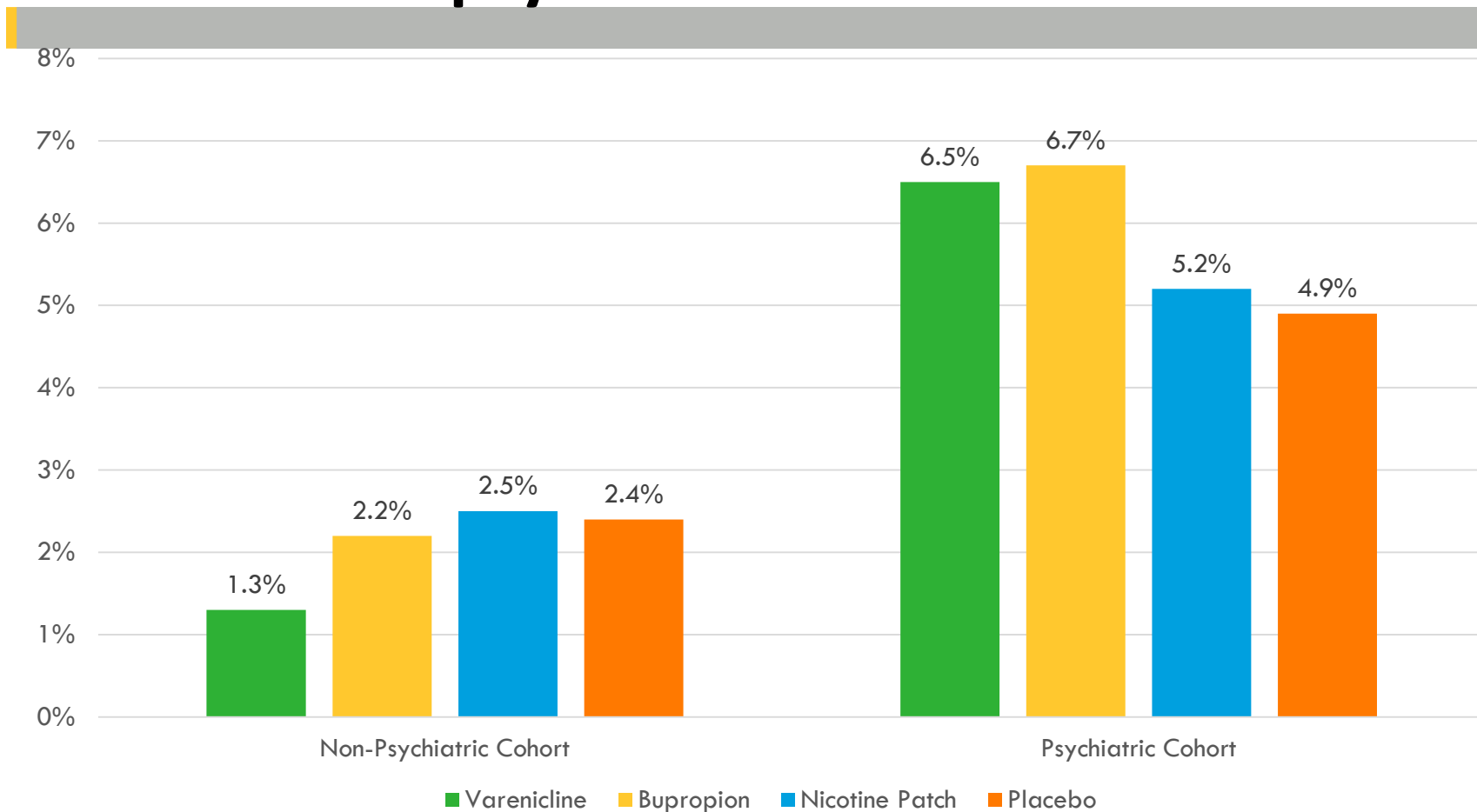
Quit rates in patients without and with psychiatric disease: EAGLES trial 2016



Which medication(s) to recommend?

- **Medication efficacy**, contraindications, cautions
- **Nicotine dependence** (**HSI = 5**, prior withdrawal sx, time to relapse)
- **Psychiatric** and substance abuse history (**schizophrenia**)
- Consider other medical comorbidities (**CAD**)
- Patient preference (**states NRT did not work**)
- What worked before (**NRT did not work according to patient**)
- Medication cost and availability

EAGLES Trial: Varenicline Neuropsychiatric Adverse Events



Anthenelli RM, et al. Lancet. 2016.

No evidence for increased neuropsychiatric effects with varenicline vs NRT or bupropion

- 2009 – black box warning added – can develop serious neuropsychiatric symptoms and events
 - changes in behavior
 - hostility
 - depressed mood
 - suicidal ideation
 - suicide
- Dec 2016 – FDA removed black box warning
 - based on EAGLES trial
 - RECOMMEND MONITOR for symptoms

Richard has stable CAD, h/o MI 5 years ago

Can he take varenicline?

- Rigotti 2010
 - increased rate of nonfatal MI, need for coronary revascularization, and new dx of PVD - But not stat significant
 - cardiovascular mortality was lower (also not statistically significant)
- Benowitz 2018 EAGLES extension trial
 - no significant difference in time to onset of MACE or MACE + for varenicline, bupropion, or NRT
 - no difference in incidence of cv events across treatment groups

Varenicline, as well as NRT and bupropion, is generally safe in smokers with stable cardiovascular disease.

Decision: You prescribe varenicline for Richard



Fixed quit date: quit 1 week after starting varenicline

Flexible quit date: quit anytime 8 to 35 days after starting varenicline (later)

Reduce to quit: If unwilling or unable to quit abruptly but willing to cut down and make quit attempt by 3 months (Ebbert JAMA 2015)

Full dosing

- 0.5 mg po daily x 3 days,
- 0.5 mg po bid x 4 days,
- 1 mg po bid

Decrease dose if creatinine clearance < 30 ml/min

Duration: 3 - 6 months

Most common side effects

- nausea – titrate up, take after eating with full glass of water
- insomnia, abnormal dreams

Richard: Questions for follow-up after the quit date

Questions

- Currently smoking
 - If quit, lapses (slips)
- Start/taking medication or not
 - Side effects - neuropsychiatric
(consult with psych?)
- Withdrawal symptoms, cravings
- Triggers
- Concerns
- Using outside counseling/support

Counseling/Medication

- How to deal with lapses
- Counsel about medication usage, withdrawal sx, and triggers.
- Consider adjusting or changing the medication if indicated
- Consider re-referring for counseling/support

Outline

- Background
- Choosing and prescribing medication: three case examples
- **Can we increase quit rates with preloading, extended duration, and combination therapy?**
Revisiting Richard, Charles, and Rachel
- Summary

Can we increase quit rates with varenicline, NRT, or bupropion SR further?

- Charles (alcohol use disorder) took combination patch plus lozenge
 - Rachel (h/o depression) took bupropion SR
 - Richard (schizophrenia) took varenicline
-

- Quit rates with optimal treatment are less than 40% at 6 months
- Relapse is common
 - Risk factors include high level of nicotine dependence, psychiatric disease, substance use disorders, and living with a smoker
- Possible ways to increase the effectiveness of medication include preloading, extended duration, and combination therapy

Preloading or extended duration: definitions

- Preloading = prequit = precessation
 - using medication prior to quit date while still smoking
 - can decrease urges to smoke prior to and after quit date
- Extended duration
 - continuing medication longer

Varenicline preloading and extended duration significantly increase quit rates

- Preloading
 - Hajek 2011: 4 week prequit varenicline vs placebo + 1 week varenicline prior to quit date.
Both prequit and standard groups treated with varenicline x 12 weeks.
Increased abstinence at 12 weeks (EOT), prequit group: **47.2% vs 20.8%**
- Extended duration
 - Tonstad 2006: all smokers treated with varenicline x 12 weeks
those abstinent at 12 weeks → additional 12 weeks varenicline vs placebo.
Increased abstinence weeks 13-24 (EOT): **70.5% vs 49.6%** and weeks 13-52: **43.6% vs 36.9%**
 - Evins 2014: schizophrenia/bipolar. Rx 12 weeks. If abstinent → 40 weeks varenicline vs placebo
Increased abstinence weeks 12-52 (EOT), weeks 12-64, and weeks 12-76: **30.0% vs 11.0%**

In 2011, FDA approved flexible quit date (quit 8 - 35 days after starting varenicline) and 6 month duration.

NRT preloading may lead to higher quit rates than when started on quit date

- Aveyard BMJ 2018
 - 6 month increased abstinence preloading patch x 4 weeks vs patch on quit date (adjusted for varenicline use post quit): **17.5% vs 14.4%** OR = 1.34
 - 12 month increased abstinence (adjusted): **14.3% vs 11.1%** OR = 1.80
- Cochrane Rev 2019
 - RR = 1.25 9 studies including patch, gum only, patch plus gum studies. Most studies used patch, 4395 participants
 - BUT If remove 5 studies thought to be at high risk of bias, not statistically significant

Extended duration of NRT: benefit while on treatment up to 24 weeks

- Schnoll 2010
 - randomized to 8 weeks (“standard”) vs. 24 weeks (extended)
 - 24 weeks abstinence (EOT): **31.6% vs 20.3%** OR = 1.81
 - 52 weeks - no longer stat significant difference between the two groups
- Schnoll 2015
 - randomized to 8 weeks (“standard”), 24 weeks (extended), 52 weeks (maintenance)
 - 24 weeks abstinence: **27.2% vs 21.75** OR = 1.70
 - 52 weeks (EOT): no significantly increased abstinence BUT decreased compliance
- Cochrane Review NRT 2019 (insufficient evidence)

Bupropion: preloading or extended duration

- Prequit bupropion Hawk 2015
 - 4 week run-in versus 3 week placebo followed by bupropion x 1 week
 - prequit group - decreased smoking (CPD) at 4 weeks after quit date
 - prequit group - increased abstinence at 4 weeks (EOT) **53% vs 31%**

- Extended bupropion Hays 2001
 - abstainers at end of 7 weeks, randomized to bupropion vs placebo x 45 weeks
 - 52 weeks (EOT), extended group - increased abstinence **55.1% vs 42.3%**
 - 78 weeks, **47.7% vs 37.7%**
 - 104 weeks, no statistically sig difference

FDA-approved combination therapies: nicotine patch and short-acting NRT, NRT and bupropion

- Combination NRT (patch plus short-acting) more effective than single NRT
- RR = 1.25 (Cochrane Rev 2018)
- Combination bupropion with NRT vs bupropion alone is more effective
- RR = 1.24 (ci=1.06-1.45) NRT plus bupropion vs bupropion alone
Cochrane Rev 2012
- Combination bupropion with NRT vs NRT alone – mixed results
- Cochrane Rev 2014 RR = 1.19 not significant

Combination varenicline and nicotine patch vs varenicline and placebo: Koegelenberg 2014

446 healthy adults (435 included in analysis), smoked 10 or more cigarettes per day

Varenicline + nicotine patch vs varenicline + placebo patch x 14 weeks

- patch started 2 weeks prior to quit date, continued 12 weeks after quit date
- varenicline started 1 week prior to quit date and tapered off during wk 13

Time Since TQD	Time Period	Per-Protocol Analysis				Multiple Imputation Analysis of Main Outcomes			
		No. (%)		OR (95% CI)	P Value	No. (%) ^a		OR (95% CI)	P Value
		Varenicline and Active Nicotine Patch (n = 216)	Varenicline and Placebo Patch (n = 219)			Varenicline and Active Nicotine Patch (n = 216)	Varenicline and Placebo Patch ^b		
Continuous Abstinence									
8 wk	Weeks 5-8	96 (44.4)	76 (34.7)	1.50 (1.02-2.22)	.04				
12 wk	Weeks 9-12	99 (45.8)	70 (32.0)	1.80 (1.22-2.66)	.003	120 (55.4)	90 (40.9)	1.85 (1.19-2.89)	.007
16 wk	Weeks 9-16	84 (38.9)	56 (25.6)	1.85 (1.23-2.79)	.003				
24 wk	Weeks 9-24	71 (32.9)	42 (19.2)	2.06 (1.33-3.21)	.001	106 (49.0)	71 (32.6)	1.98 (1.25-3.14)	.004

Varenicline and bupropion vs varenicline plus placebo: Ebbert 2014

506 adults age 18 and older, smoked 19 or more cigs per day

Varenicline + bupropion SR vs varenicline + placebo x 12 wks; followed 52 weeks

Table 2. Smoking Abstinence Outcomes

		7-Day Point-Prevalence Smoking Abstinence ^a			Prolonged Smoking Abstinence ^{a,b}		
Overall	No. of Participants ^c	No. (%)	OR (95% CI)	P Value	No. (%)	OR (95% CI)	P Value
Week 12							
Varenicline + bupropion SR	249	140 (56.2)	1.36 (0.95-1.93)	.09	132 (53.0)	1.49 (1.05-2.12)	.03
Varenicline + placebo	257	125 (48.6)			111 (43.2)		
Week 26							
Varenicline + bupropion SR	249	95 (38.2)	1.32 (0.91-1.91)	.14	91 (36.6)	1.52 (1.04-2.22)	.03
Varenicline + placebo	257	82 (31.9)			71 (27.6)		
Week 52							
Varenicline + bupropion SR	249	91 (36.6)	1.40 (0.96-2.05)	.08	77 (30.9)	1.39 (0.93-2.07)	.11
Varenicline + placebo	257	75 (29.2)			63 (24.5)		

Combination varenicline and bupropion meta-analysis Zhong 2019

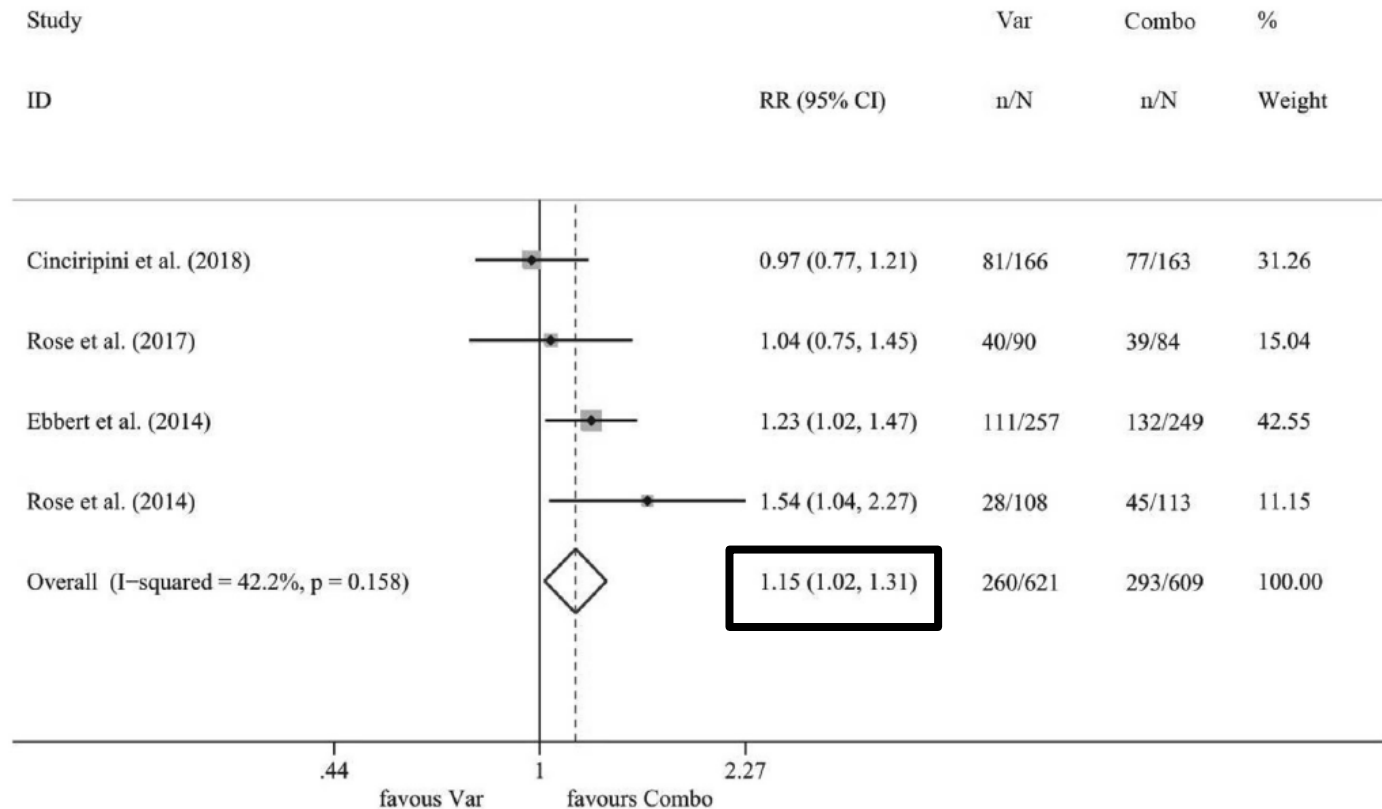


Fig. 3. Forest plot for the abstinence rate at the end of treatment. Compared with Var group, Combo therapy significantly improves the abstinence rate at the end of treatment. Combo= varenicline plus bupropion; Var= varenicline plus placebo; RR= relative risk; n = number of subjects with events; N = number of total subjects.

Combination varenicline and bupropion meta-analysis in highly dependent smokers Zhong 2019

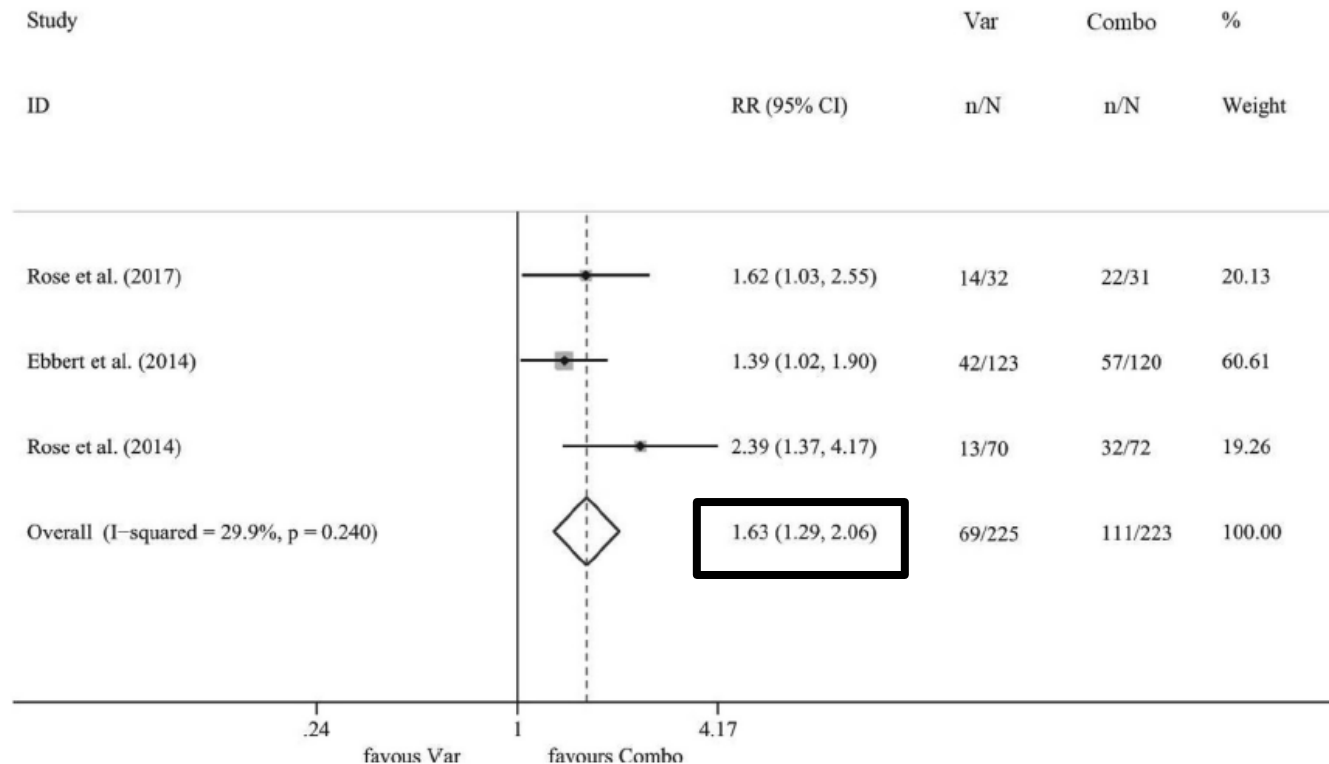


Fig. 4. Forest plot for the abstinence rate at the end of treatment in highly dependent smokers. Compared with Var group, Combo therapy significantly increased the abstinence rate at the end of treatment in highly dependent smokers. Combo = varenicline plus bupropion; Var = varenicline plus placebo; RR = relative risk; n = number of subjects with events; N = number of total subjects.

Charles, Rachel, Richard: increasing effectiveness of the medication

- Charles (alcohol use disorder): combination patch plus lozenge
 - Rachel (h/o depression): bupropion SR
 - Richard (schizophrenia): varenicline
-
- Charles – could start patch 2- 4 weeks prior to quit date and could continue longer than 3 months
 - Rachel – could add combination NRT to bupropion and could continue longer than 3 months
 - Richard – could start varenicline 35 days prior to quit date and could take it for 6 months

Summary

- For many, smoking is a chronic disease of nicotine dependence
- Comprehensive treatment includes both medication and behavioral counseling
- Evaluation for cessation medication includes assessing the smoker's nicotine dependence, co-morbidities, current medications, preference, and medication contraindications and cautions.
- Nicotine replacement therapy (NRT), bupropion, and varenicline are all effective
- Varenicline is more effective than a single form of NRT or bupropion and similarly effective as combination NRT (patch plus short-acting form)
- Varenicline, as well as NRT and bupropion, is safe in people with psychiatric disease
- Varenicline or combination NRT (patch plus short-acting form) may be best first-line treatments as of February, 2020

Summary: Increasing effectiveness of medication with combination, preloading, and extended duration

- Combination NRT (patch plus short-acting form) and combination bupropion with NRT are FDA-approved.
- Combination varenicline with NRT and combination varenicline with bupropion are safe and potentially effective. Neither combination is FDA-approved as of Feb, 2020
- Preloading
 - varenicline can be more effective with preloading (flexible quit date: quit 8-35 days after starting varenicline)
 - NRT possibly more effective with preloading
- Extended duration
 - varenicline can be more effective with 6 month duration than 3 month duration
 - NRT and bupropion can be given longer than 3 months

Summary: Increasing reach by including more smokers

- We have discussed medications for adult smokers who want to quit
5 A's model: **A**sk, **A**dvice, **A**ssess if ready to quit, **A**ssist, **A**rrange follow up
- Opt-out model: offer treatment to all smokers, including those not ready to quit
-varenicline and NRT can be effective (Ali Am J Prev Med 2018)
- Focus effort on smokers being screened for lung cancer with low dose CT, as well as those undergoing surgery or being hospitalized

Thank you!

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Resources: contents

- Telephone Quit lines (1-800-QUIT NOW)
- Smokefree.gov website
- Smoking Cessation Benefit in NY Medicaid Fee-for-Service and Medicaid Managed Care
- NYS Medicaid coverage
- Lung cancer screening with low dose CT
- Key points: NRT, bupropion SR, varenicline

National quit lines and smokefree.gov website

- Telephone Quit line
 - national quit line 1-800-QUIT-NOW, 1-855-DEJELO-YA (1-855-335-3569)
 - NYS Quit line 1-866-NY-QUITS (1-866-697-8487)
 - counseling and NRT when indicated

- Smokefree.gov website (National Cancer Institute website)
 - can sign up for smokefreeTXT (get 3-5 messages daily, 6-8 weeks)
complete form on line or text QUIT to 47848
 - there is also smokefreeTXT en espanol, smokefreeMOM, smokefreeVET
 - can download smart phone apps (quitSTART)

New York State Smoker's Quitline

- 1-866-NY-QUITS (1-866-697-8487)

<https://www.nysmokefree.com/> Confidential evidence-based services for NYS residents who want to stop smoking or using other forms of tobacco

- Free Quit Coaching
 - Free Nicotine Replacement Therapy (for those who qualify)
 - Free Resources
 - Patient Referral Program - an adjunct to healthcare providers' efforts to help their patients stop smoking. It ensures stop-smoking support is readily available to patients following their healthcare visit
- Locate a Health Systems for a Tobacco Free NY professional near you <http://hstnymed.org/>
 - <https://talktoyourpatients.health.ny.gov/>

NYS Smokers' Quitline

Online resources and tools for patients

- Screening for a two-week starter kit of free quit-smoking medications
- Information about which stop-smoking services are covered by health insurance plans including Medicaid
- Help finding local support programs
- Interactive quit tips and on-demand, customizable messages, including SMS (Short Message Service or text messaging), IVR (Interactive Voice Recording) and email
- Treatment services now available to adults and youth trying to quit vaping products

Update on the Smoking Cessation Benefit in NY Medicaid Fee-for-Service and Medicaid Managed Care

- Effective December 1, 2016, Medicaid FFS and Medicaid Managed Care (MMC) have now aligned criteria to provide the following Smoking Cessation Benefit to all Medicaid members:
 - **Removed** the two-course **annual limit** for smoking cessation agents
 - **Removed Prior Authorization** of smoking cessation agents (exceptions would apply for brand name medications with generic equivalents available)
 - Include formulary **coverage** of **all smoking cessation agents** (exceptions would apply for brand name medications with generic equivalents available)
 - Allow **concomitant utilization of 2 agents**
 - Follow FDA approved/Compendia supported limits for Age Restrictions
 - Follow FDA approved/Compendia supported Quantity Limits

NYS Medicaid covers all seven FDA-approved medications when prescribed

INSURANCE PROVIDER EXAMPLES

Product	Drug Class	CDPHP	EMPIRE BCBS HealthPlus	EXCELLUS	FIDELIS	MVP Healthcare	United Healthcare
Nicotine Gum	OTC	Covered (all strengths generic only)	Covered (all strengths generic only)	Covered (generic 4mg, brand & generic 2mg)	Covered (all strengths generic only)	Covered (all strengths generic only)	Covered (all strengths generic only)
Nicotine Lozenge	OTC	Covered (2mg & 4mg generic only)	Covered (2mg & 4mg generic only)	Covered (2mg & 4mg brand & generic)	Covered (2mg & 4mg generic only)	Covered (2mg & 4mg generic only)	Covered (2mg & 4mg generic only)
Nicotine Patch	OTC	Covered (all strengths generic only)	Covered (all strengths generic only)	Covered (generic 7 & 14 mg, 21 mg brand & generic)	Covered (all strengths generic only)	Covered (all strengths generic only)	Covered (all strengths generic only)
Nicotine Nasal Spray	Rx	Covered	Covered	Covered	Covered	Covered	Covered
Nicotine Oral Inhaler	Rx	Covered	Covered	Covered	Covered	Covered	Covered
Bupropion (Zyban/Wellbutrin)	Rx	Covered (all strengths generic only)	Covered (all strengths generic only)	Covered (all generic wellbutrin & 150mg Zyban)	Covered (all strengths generic only)	Covered (all strengths generic only)	Covered (all strengths generic only)
Varenicline (Chantix)	Rx	Covered	Covered	Covered	Covered	Covered	Covered

- information from <http://mmcdruginformation.nysdoh.suny.edu/search/>

COVERAGES LISTED FOR THE PHARMACY BENEFIT OF THE PLAN

LDCT lung cancer screening in high risk populations decreases lung cancer mortality

- Aberle 2011 NEJM lung cancer screening with low dose CT compared with chest radiography decreased lung cancer mortality by 20% and all-cause mortality by 6.7% in high risk current or past smokers.
- High risk smokers ages 55-74 with a 30 pack-year smoking history or more, who were either still smoking or who had quit within the prior 15 years
- LDCT recommended by US Preventive Services Task Force in 2013 (age 55-80), American Cancer Society in 2013 (age 55-74), American College of Chest Physicians in 2018 (age 55-77), and Centers for Medicare and Medicaid Services in 2015 (age 55-77), and others

Targeting LDCT lung cancer screening participants for smoking cessation interventions

- Unique opportunity to intervene with smokers who are at increased risk for lung cancer
 - SGR 2020 “The evidence is sufficient to infer that certain life events – including hospitalization, surgery, and lung cancer screening – can trigger attempts to quit smoking, uptake of smoking cessation treatment, and smoking cessation.”
- Recommendations for smoking cessation interventions using the 5 A’s outlined by Society for Research on Nicotine and Tobacco (SNRT) and the Association for the Treatment of Tobacco Use and Dependence (ATTUD)
- Current group of studies on smoking cessation interventions in smoker undergoing LDCT screening: SCALE (Smoking Cessation and Lung Cancer Screening collaborative)

Nicotine replacement therapy: key points

- **Combination NRT is a first-line choice for cessation**
- **Gum, lozenge, inhaler, and nasal spray are the only short-acting forms of medication available to decrease acute withdrawal symptoms**
- **Few contraindications, safe in most populations**



- Short-acting forms of NRT are difficult for some people to use correctly, can get decreased compliance
- Most people under-dose. It would take ~ 10 pieces of 4 mg gum or lozenge to get 20 mg of nicotine.

Bupropion: key points

- **Useful in patients with weight concerns and history of depression**



- Less effective than varenicline or combination NRT
- Some contraindications and precautions
- Some interactions with other medications
- Decrease dose with liver or kidney disease

Varenicline: key points

- Most effective single agent for smoking cessation
 - Can increase efficacy by starting 1 month prior to quit date and extending treatment from 3 to 6 months
 - Safe in smokers with psychiatric disease
 - Black box warning about neuropsychiatric effects removed in 2016, but recommend monitor
 - Safe in stable cardiovascular disease
 - Minimal interactions with other medications
-
- Decrease dose if GFR < 30 mL/minute
 - Many cautions