

Tailoring Tobacco Cessation Treatment

Nancy Rigotti, MD

Professor of Medicine, Harvard Medical School
Director, Tobacco Research & Treatment Center,
Massachusetts General Hospital, Boston, MA USA

Disclosures

Nancy Rigotti, MD

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Overview

- The core of evidence-based guidance
- Treatment choices for which evidence exists
- Clinical situations where evidence is limited or absent
 - I will present my interpretation of evidence
- Treatment choices should be made jointly by the smoker and the clinician

Tailoring Treatment

- A core of evidence-based guidance exists and applies to most smokers

Core Evidence-based Guidance

*2008 US Public Health Service Guideline
2015 US Preventive Services Task Force*

- Effective tobacco cessation treatments exist
 - **Counseling** (*in-person, group, telephone*)
 - **Pharmacotherapy** (*NRT, bupropion, varenicline*)
 - **Combination** is better than either one alone
- More intensive treatment has better outcomes but even brief intervention works

Tailoring Treatment

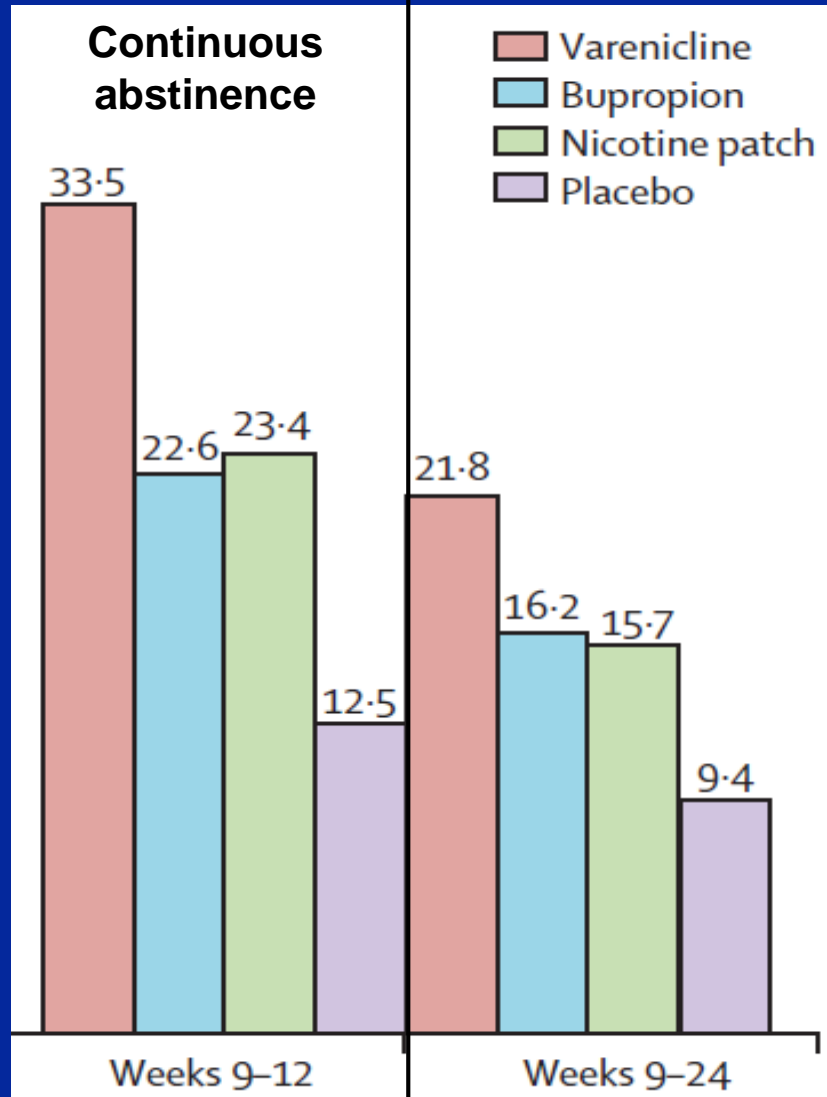
- A core of evidence-based guidance exists and applies to most smokers
- Within this core guidance, choices exist
 - **Medication:** choice, dose, and duration

EAGLES Randomized Controlled Trial

Nicotine patch vs. bupropion vs. varenicline vs. placebo

8000 smokers (4000 with + 4000 without psychiatric diagnosis)

Anthenelli R et al. Lancet 2016



Provides a rationale for this hierarchy of medication:

1. Varenicline
2. Bupropion or Nicotine Patch

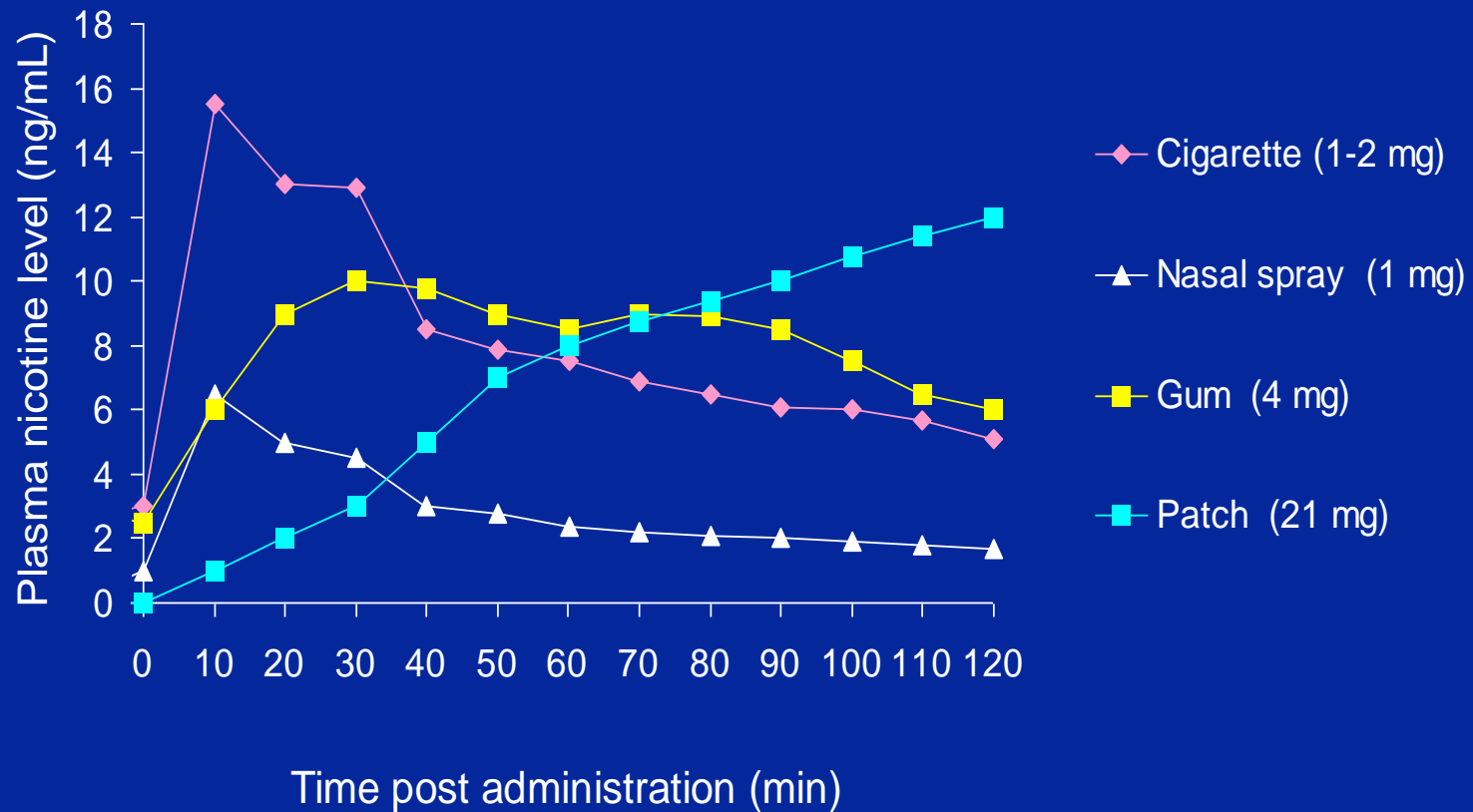
Further inference:

All nicotine medications used individually have comparable efficacy to nicotine patch

Optimizing Pharmacotherapy

Combine drugs

Short- and long-acting NRT



Nicotine Replacement

Long-acting, slow onset → *skin patch*

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

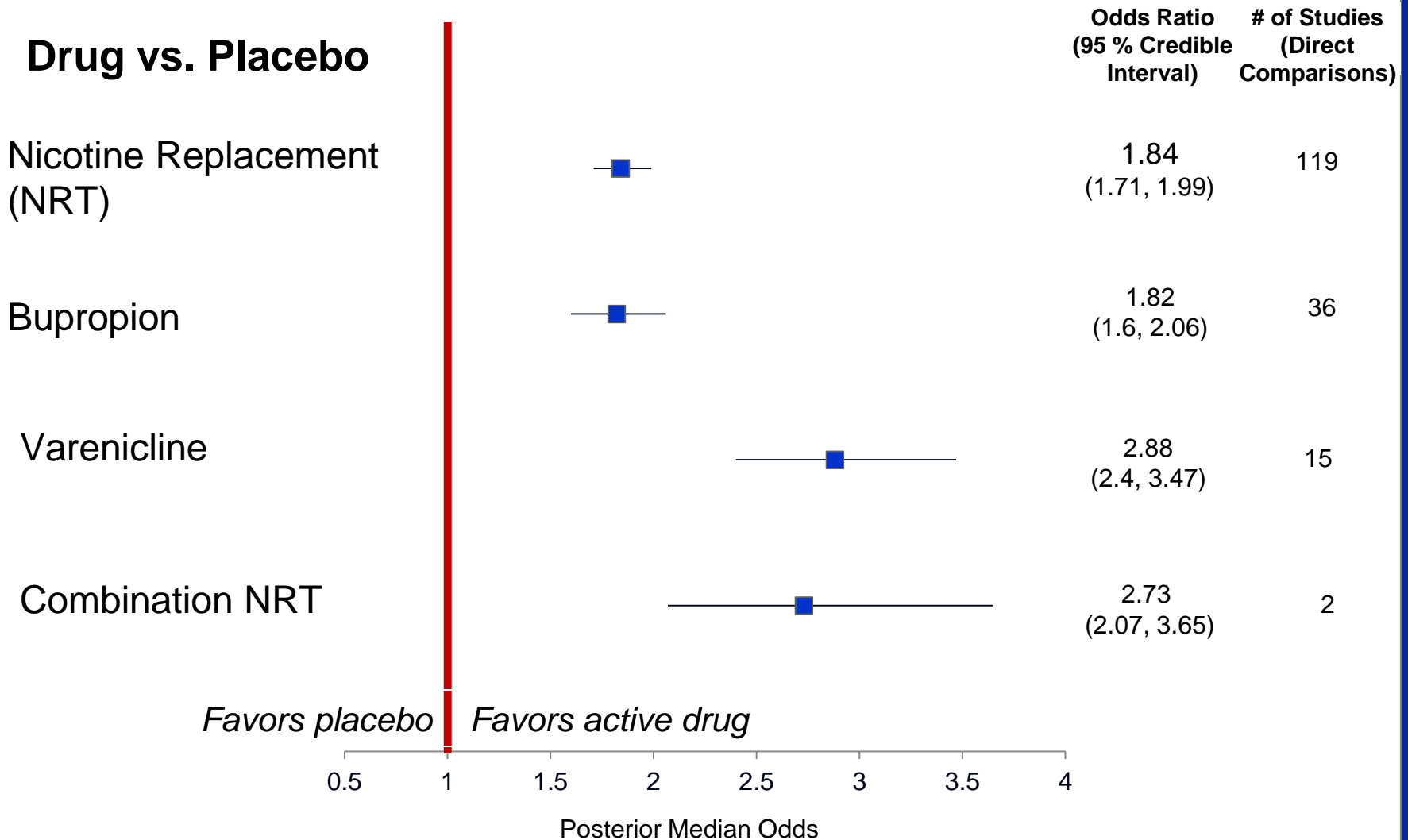
Short-acting, faster onset

→ *gum, lozenge, inhaler, spray*

- + User controls dose
- - Nicotine blood levels fluctuate more
- - Many smokers do not use enough

Current Pharmacotherapy Options

Cochrane meta-analysis, 2013 (JAMA. 2014;311:193-194)



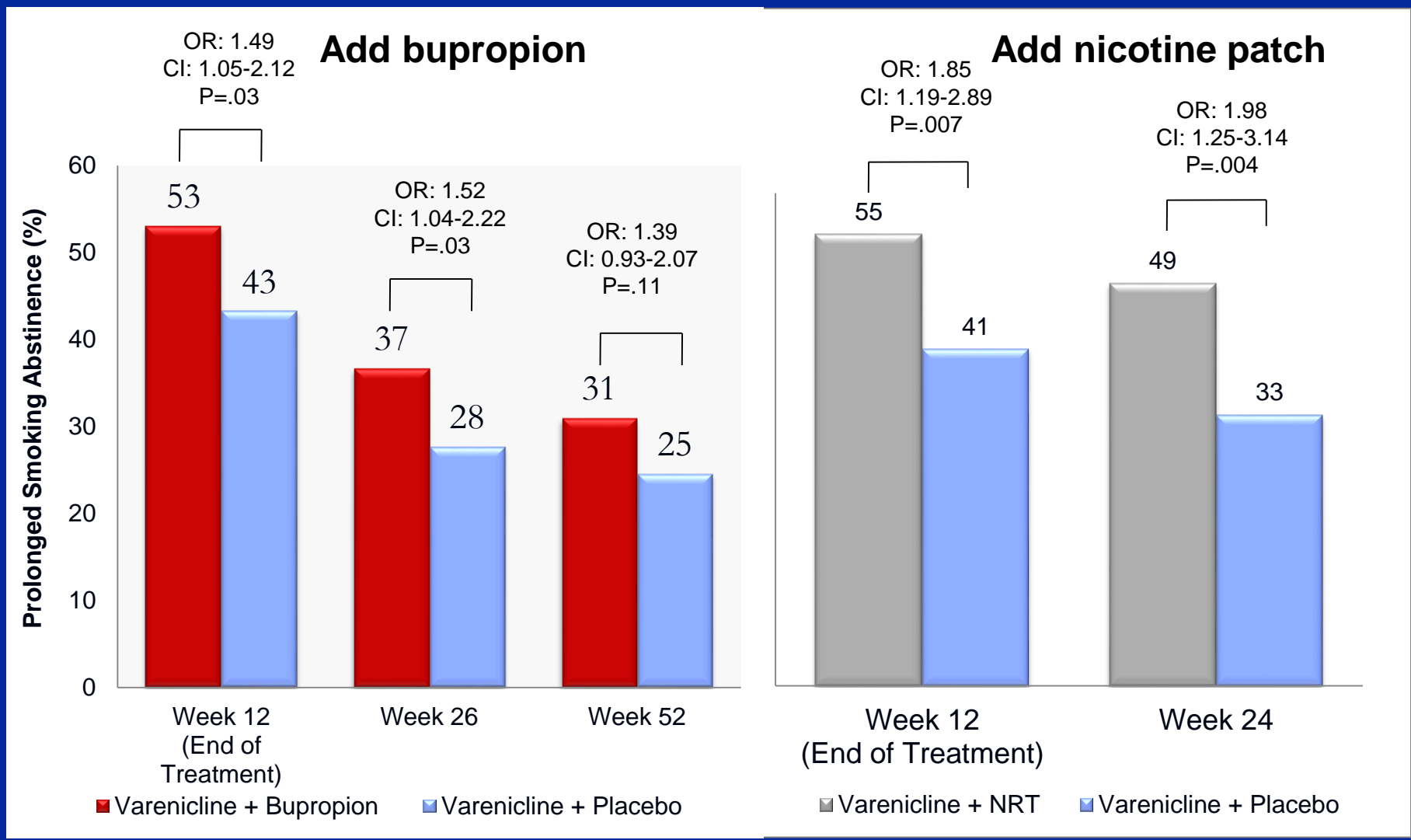
Optimizing Pharmacotherapy

- Combine drugs
 - Short- and long-acting NRT
 - Drugs from different classes

Combining Drugs Across Classes

- 2 placebo controlled randomized trials
 - Each started with varenicline
 - 1 added bupropion (vs. placebo)
 - 1 added nicotine patch (vs. placebo)

Add Bupropion or NRT to Varenicline?



Ebbert JO. JAMA. 2014;311(2):193-194.

Koegelenberg C. JAMA 2014; 312:155.

Evidence-based Protocol for Selecting Smoking a Cessation Medication

1 st line	Varenicline OR combination NRT
2 nd line	Bupropion OR Single NRT product
3 rd line	Nortriptyline
If single agent is insufficient	Combine categories of FDA-approved drugs: Varenicline + NRT Varenicline + bupropion Bupropion + NRT

Tailoring Treatment

- A core of evidence-based guidance exists and applies to most smokers
- Within this core guidance, choices exist
 - **Medication:** choice, dose, and duration
 - **Behavioral support:** delivery mode, intensity, duration

Behavioral Support

- Treatments have a similar content
 - Cognitive-behavioral therapy \pm motivational interviewing
- Treatments differ
 - How content is delivered to the smoker
 - Individual, in person
 - Group, in person
 - Telephone: voice, text message, automated calls
 - Web-based
 - Treatment intensity (minutes of contact)
 - Treatment duration (over how many weeks)

Behavioral Support: Tailoring

- Strongly recommend the use of behavioral treatment
- Let the smoker choose the mode of delivery that he or she prefers
- Make “proactive referrals” to make sure that the smoker connects to the resource.
- Encourage smokers to use longer duration and greater intensity?
 - Appropriate treatment for a chronic disease

Which smokers might need more intensive or longer treatment?

- Smokers with greater difficulty quitting
 - More nicotine dependence
 - Psychiatric comorbidity
 - Other (non-tobacco) substance use
 - Lower income, less education
 - LGBT
 - Less confidence to quit, little social support
 - Failure to stay quit with previous treatment

Which smokers might need more intensive or longer treatment?

- Evidence that more intensive or longer treatment is more effective does not exist for all of these groups
 - Psychiatric comorbidity – some evidence
 - Lower income, less education - ??
 - Living with a smoker – environmental change

Tailoring Treatment: Prior Use of Drug

- What was the problem?
 - Did not fill prescription
 - Address fears of medication, ambivalence about quitting
 - Side effect of medication
 - Was the symptom likely to be due to the drug?
 - If yes, reduce dose or choose another drug
 - Tolerable but little reduction in cigarettes/day
 - Undertreatment (NRT)?
 - Switch to different medication (bupropion, varenicline)
 - Smoker reduced smoking but did not quit or relapsed
 - Reuse medication as a base
 - Add a second medication

Tailoring Treatment: Nicotine Dependence

- Assessment
 - Age started to smoke
 - Heaviness of smoking index
 - Cigarettes/day
 - Time to first morning cigarette
- How is the information used?
 - To determine medication dose
 - Indicate need for more intensive behavioral support and closer follow-up

Tailoring Treatment: Medical Comorbidity

■ Safety

- Is a drug contraindicated?
 - Pregnancy: varenicline
 - Severe renal disease: varenicline
 - Seizure disorder: bupropion, ?varenicline
 - Unstable cardiovascular disease: NRT (outside the hospital)
- Will an interaction with other drugs affect dosing?

■ Efficacy

- Not a major factor in most medical diseases
 - To the extent tested, drugs work in smokers with various chronic diseases

Tailoring Treatment: Psychiatric or Substance Use Disorders

■ Efficacy

- Treatments are effective
- Absolute quit rates are lower
- Some evidence supports longer duration of medications

■ Safety

- Medications are safe to use, even in severe mental illness
- Consider interactions with psychiatric drugs
- Treating tobacco along with other drug dependence does not impair success

■ Action

- Coordinate care with the patient's psychiatrist or counselor

Tailoring Treatment: Concern about Weight Gain

- No simple solution
 - Bupropion, some NRT may help temporarily
 - Limited evidence that exercise program increases cessation but it might help reduce weight gain
- Clear evidence that weight gain does not reduce benefits of quitting smoking

Tailoring Treatment: Genetics

- Nicotine Metabolite Ratio (NMR)
 - Ratio of 3-hydroxy-cotinine / cotinine
 - Reflects rate of nicotine metabolism by liver CYP2A6 enzyme
 - Level of CYP 2A6 is genetically determined
 - Implication for treatment: RCT
 - Normal metabolizers do better with varenicline than NRT
 - Slow metabolizers have equal success with either drug
- Limitations: feasibility and cost
 - No point of care test available yet

Tailoring Treatment: Smokers Not Ready to Quit Now

- Motivational interviewing
- Reduce smoking (reduce to quit paradigm)
 - Varenicline, NRT

Original Investigation

Effect of Varenicline on Smoking Cessation Through Smoking Reduction

A Randomized Clinical Trial

JAMA 2015

Jon O. Ebbert, MD, MSc; John R. Hughes, MD; Robert J. West, PhD; Stephen I. Rennard, MD; Cristina Russ, MD; Thomas D. McRae, MD; Joan Treadow, RN, BSN; Ching-Ray Yu, PhD; Michael P. Dutro, PharmD; Peter W. Park, PhD

PARTICIPANTS

Smokers who want to quit in the next 3 months but are not willing to set a quit date within 1 month

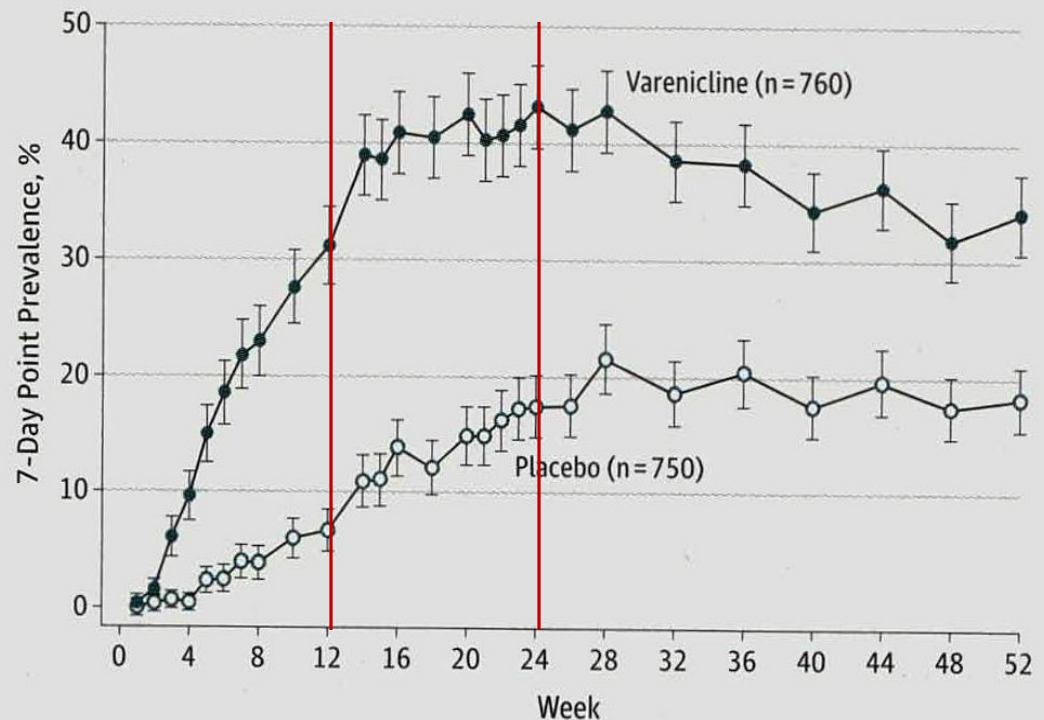
CONDITIONS

Randomized to varenicline vs PCB for 24 weeks

OUTCOMES

Abstinence at 24, 52 weeks

Figure 2. Seven-Day Point Prevalence Smoking Abstinence for Participants Receiving Varenicline vs Placebo



Tailoring Treatment: Smokers Not Ready to Quit Now

- Motivational interviewing
- Reduce smoking (reduce to quit paradigm)
 - Varenicline, NRT
- Brief advice to quit
- Recommend adopting no-smoking policy for home and car
 - To protect family and friends
 - Smoker takes first step toward changing behavior

Summary

- A core of evidence-based guidance applies to most smokers
- Choices exist within this core guidance
 - **Medication:** choice, dose, and duration
 - **Behavioral support:** delivery mode, intensity, duration
- Treating smokers always presents situations where evidence is limited or absent
- Treatment choices should be made jointly by the smoker and the clinician (Shared decision making)