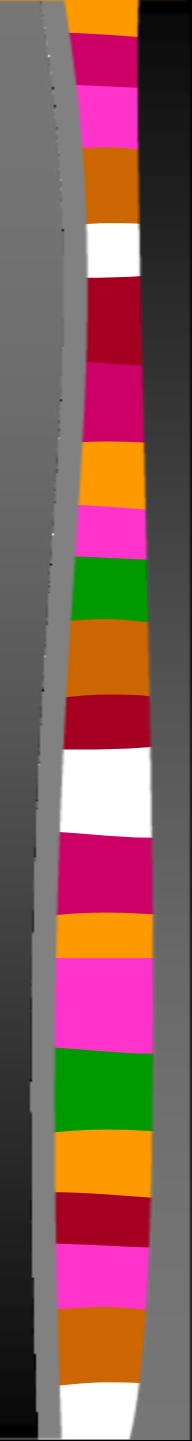


Pharmacological Options for Smoking Cessation

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Cigarette smoking is
the single most
important cause of
disease and
premature death in
the United States



Pharmacological treatment

- NRT - “methadone for the smoker”
 - Gum
 - Patch
 - nasal spray
 - Inhaler
 - lozenge
- bupropion
- varenicline
- all decrease cravings, withdrawal
- 20-25% quit rates at 1 year



Nicotine replacement - gum

- available since 1984
- 2 mg. and 4 mg. strength
- “chew, park, chew, park”
- 2 mg. - 30 pieces/day maximum
- 4 mg. - 20 pieces/day maximum
- wean after 3 months, 6 months maximum
- use in conjunction with patches, bupropion



Nicotine replacement - patches

- 7, 14, 21 mg patches - OTC
- 21 mg X 6 wk, 14 mg X 2 wk, 7 mg X 2 wk
- wean vs. single dose
- first patch - night before quit day
- rashes, abnormal dreams
- no euphoria - no stimulant effect
- no increased risk of MI



Nicotine nasal spray

- one dose: 2 sprays (1 mg)
- minimum: 8 doses/day
- maximum: 40 doses/day (1/2 bottle)
- if not abstinent by week 4 - stop
- use for 8 weeks
- Taper over 4-6 weeks
- nasal irritation limits use
- Cost: at least \$ 3/d



Nicotine inhaler

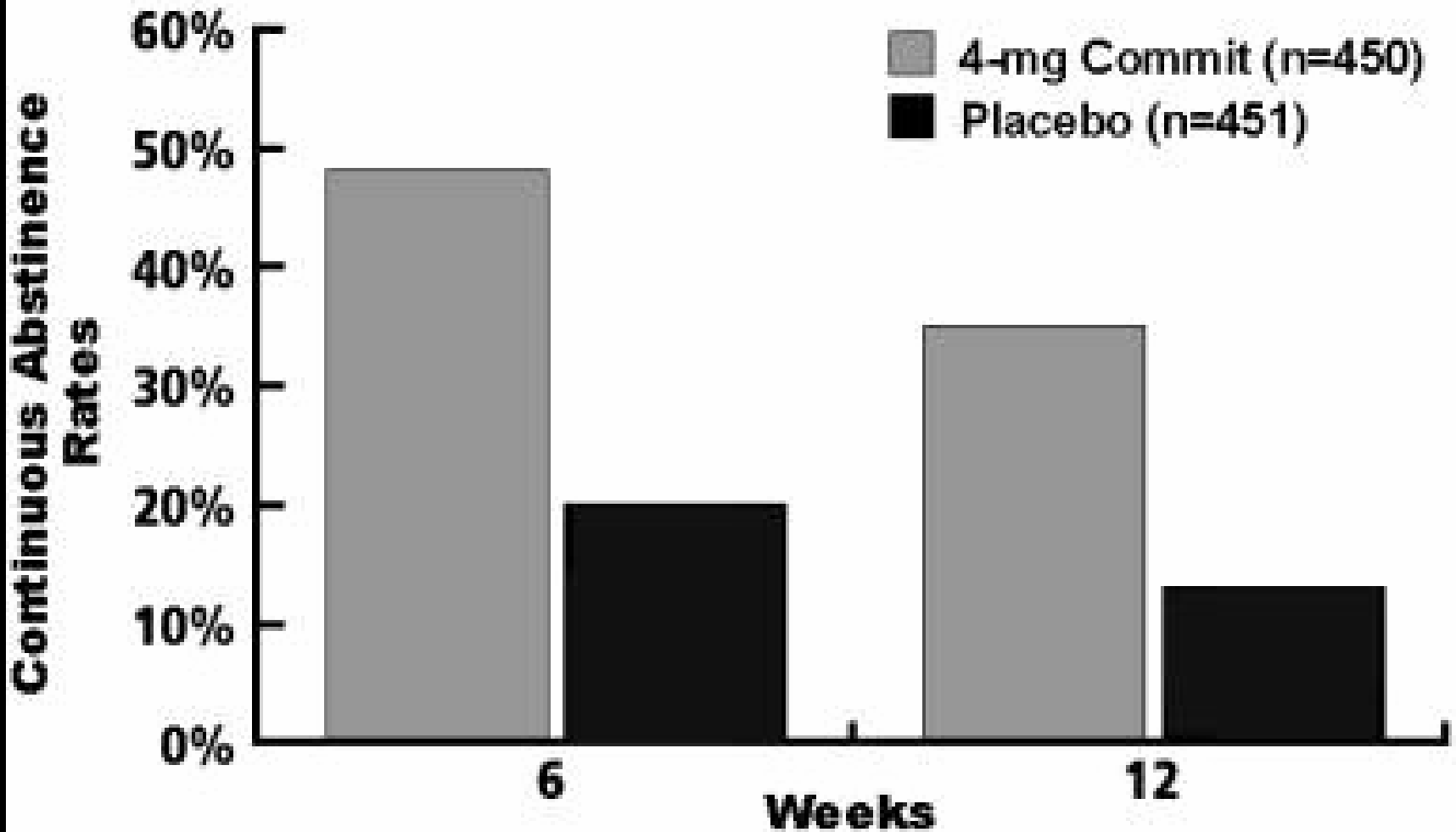
- nicotine deposited in mouth
- 4 mg per insert, 50% absorbed
- 80 puffs in 20 minutes
- 6 - 16 cartridges/day
- 3 months then wean over 3 months
- 40% throat irritation
- \$ 1 per cartridge



Nicotine lozenges (Commit[®])

- 2 and 4 mg strengths
- 4 mg if smoke w/in 30 minutes of waking
- 12 week program:
 - Weeks 1-6: 1 lozenge every 1 to 2 hours
 - Weeks 7-9: 1 lozenge every 2 to 4 hours
 - Weeks 10-12: 1 lozenge every 4 to 8 hours
- at least 9 per day for the first 6 weeks
- hiccups, heartburn, nausea
- no more than 5 in 6 hours, 20 per day
- \$ 0.30 – 0.50 per lozenge
- Can work when patch, gum failed

COMMIT 4-mg Lozenge Doubles Quit Rates vs Placebo



Shiffman S, Dresler CM, et al. *Arch Intern Med.* 2002;162:1267-1276.



Bupropion (Zyban[®])

- Probably works by increasing dopamine in nucleus accumbens
- 150 mg qd X 3 days, 150 mg b.i.d. X 4 days, then QUIT
- continue for 7 - 12 weeks
- if not stopped by 8 weeks, discontinue
- Can use with nicotine replacement



Bupropion - contraindications

- seizure disorder
- prior or current eating disorder
- MAO inhibitors
- concurrent use of Wellbutrin[®]

Rates of Continuous Abstinence



Jorenby NEJM 1999

- Bupropion and nicotine patch
- Bupropion
- Nicotine patch
- Placebo

Meta-Analysis Smoking Cessation Medications (placebo controlled trials, 6 month quit rates)

Therapy	# studies	Abstinence Rate	Odds ratio (vs. placebo)
Gum	13	23.7	1.5
Patch	27	17.7	1.9
Inhaler	4	22.8	2.5
Nasal spray	3	30.5	2.7
Bupropion SR	2	30.5	2.1

Adapted from Fiore MC U.S. Public Health Service, 2000

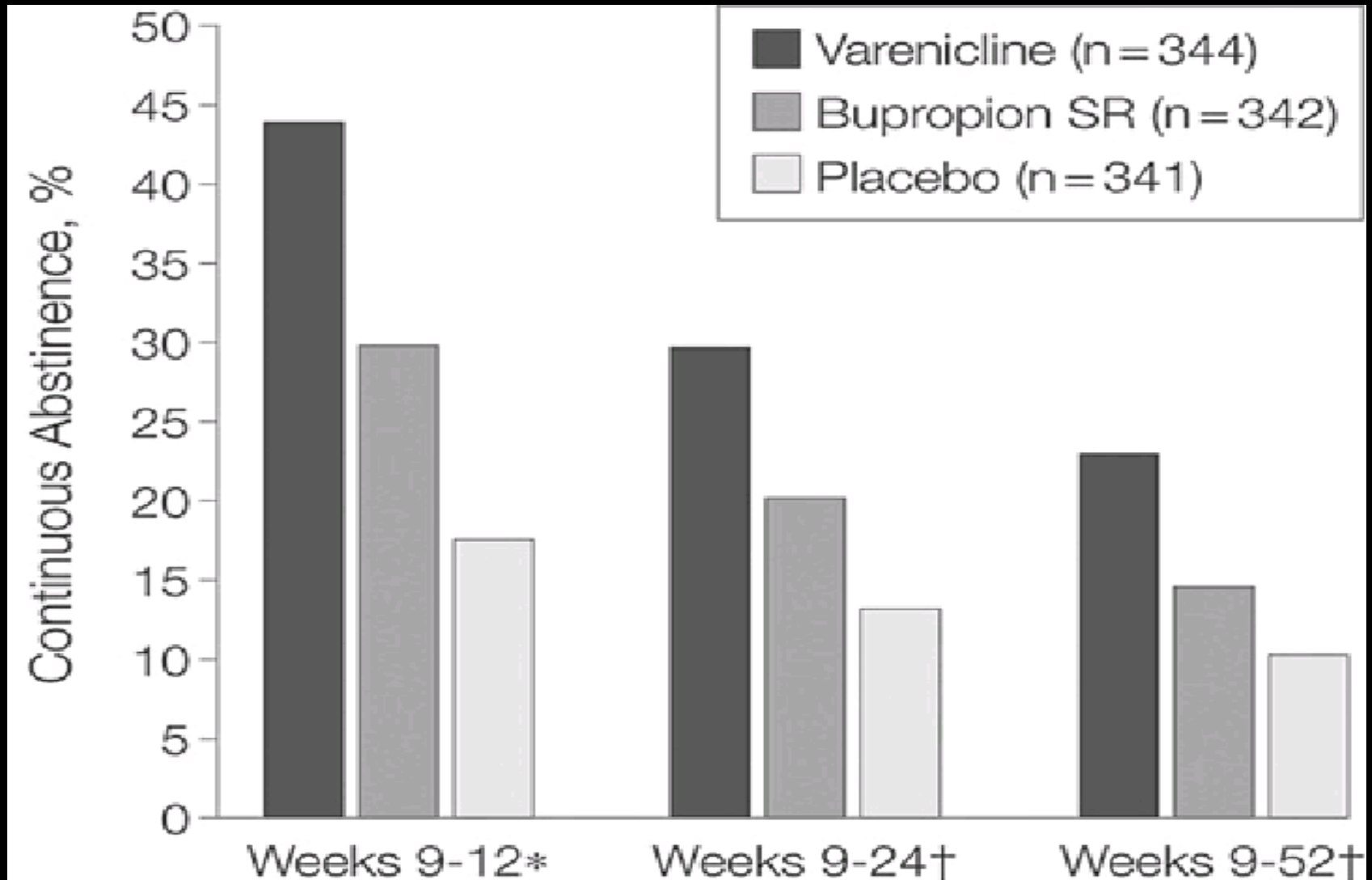


Varenicline (Chantix[®])

- [alpha]4[beta]2 nicotinic acetylcholine receptors reinforce effects of nicotine, maintain smoking
- partial agonist, antagonist (blocks binding)
- 0.5 mg X 3 d, 0.5 mg b.i.d. X 4 d, 1 mg b.i.d.
- Stop smoking after 7 days on medicine
- Can use for up to 6 months – preferable
- Probably higher rates of quitting
- Nausea, constipation, abnormal dreams
- Reports of suicidal ideation, depression
 - No evidence of causal relationship
 - Probably due to cessation of addiction
- Costs about \$ 3-4/day

Continuous Smoking Abstinence Rates

©



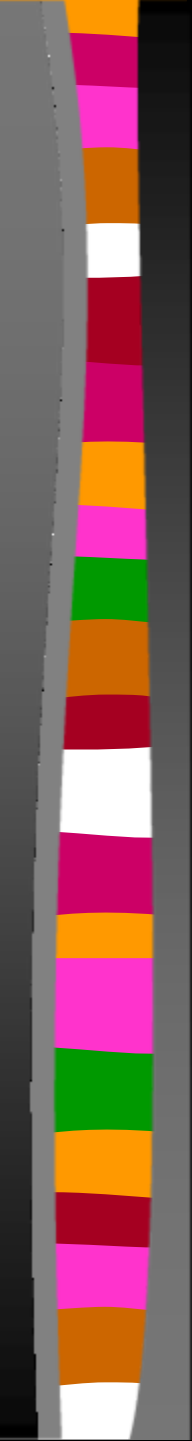
* weeks 9–52: varenicline vs placebo, $P < .001$; varenicline vs bupropion, $P = .004$; bupropion vs placebo, $P = .08$.

Jorenby DE, et al *JAMA*. 296(1):56-63, 2006 Jul 5.



Second-line medications

- Clonidine: 0.15 – 0.75 mg/d for 3 – 10 weeks
- Nortriptyline: 75 – 100 mg/d for 12 weeks



All pharmacotherapy should
always be used in
conjunction with behavior
modification

How are we doing with our patients?

- 1991:
 - < 50% of patients reported ever being told to stop¹
- 1998:
 - 67% Ask, 74% Advise, 35% Assist, 8% Follow-up²
- 2003: (patients that got prescription)³
 - 36% told to set quit date, 25% counseled, 13% advised to follow up

Many smokers do not get the advice and help they need!!!

¹Frank, E., Winkleby, M.A., Altman, D.G., et al. *JAMA* 1991;266:3139-3134.

²Goldstein MG, et al. *Preventive Medicine*. 27(5 Pt 1):720-9, 1998 Sep-Oct.

³Solberg LI, et al. *Archives of internal medicine*, 2005;165:656



The future

- Nicotine vaccine (NicVAX)
 - Phase two trials are promising
 - five shots in six months
 - antibodies attach to nicotine in bloodstream, prevent crossing blood-brain barrier
 - six months after last shot —
 - 14-16% quit rate, 6% w/ placebo
- Different forms of nicotine replacement
- Rimonabant
 - cannabinoid receptor antagonist
 - Also treats obesity
 - Won't be released in US