

Update on Medications for Tobacco Cessation

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MDQuit
Best Practices
Conference
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Nicotine Addiction – the bad news

- “Smoking is the leading preventable cause of disease and death in the US”

Report of Surgeon General on the Health Effects of Smoking, 2004

- 23% of the US population, 58M people
- 440,000 premature deaths per year
- Avg 10 yr decrease life span
- 50% will die of smoking related illness

Nicotine Addiction – the good news (quitting)

- Substantial recovery of pulmonary symptoms and infections after 9 months
- Risk of MI decreased 50% after 1 yr
- 2 years after MI, mortality decreased 36%
- Risk of most cancers decreased 50% after 5 yrs
- Risk of lung CA decreased 50% after 10 yrs
- Almost all disease risk back to background after 15 yrs

Nicotine Addiction – the bad news (quitting)

- <6% quit attempts successful
- 50% quit attempts fail in the 1st week
- Only 1/3 quit attempters have ever sought assistance

Conceptual Issues

- Should medications be used in the treatment of addiction?
 - Is this a philosophical question?
 - Is this a scientific question?
 - Is this a practical question?

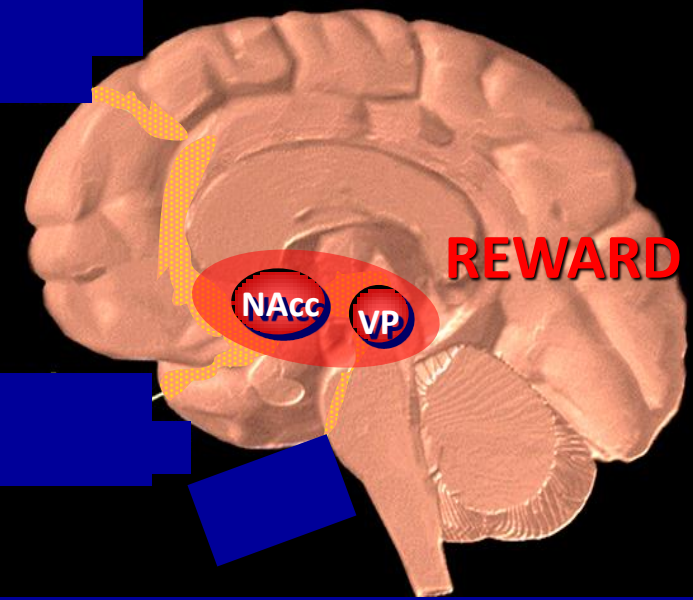
Rationale for medication

- Reduce craving
- Impact the physiology of dependence
- Protect against lapses, which should be expected
- Reduce high rates of relapse
- Improve treatment retention
- Improve outcomes of current psychosocial treatments

Anti-addiction medications - potential effects

- Block the effects of action
- Reduce reward
- Prevent withdrawal
- Act as non-impairing substitute
- Enhance negative consequences
- Prevent relapse after abstinence

Reward Circuits

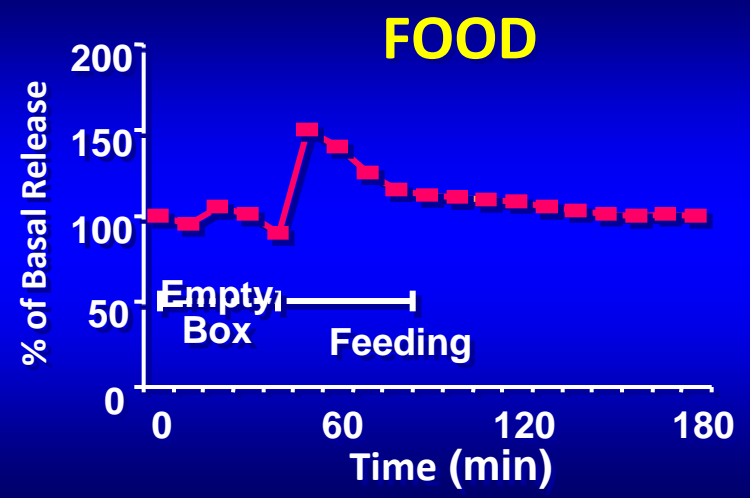
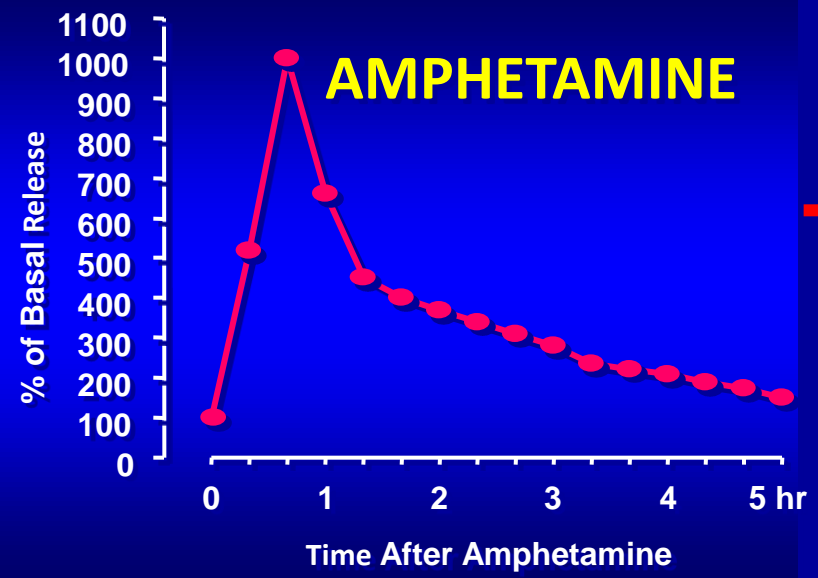
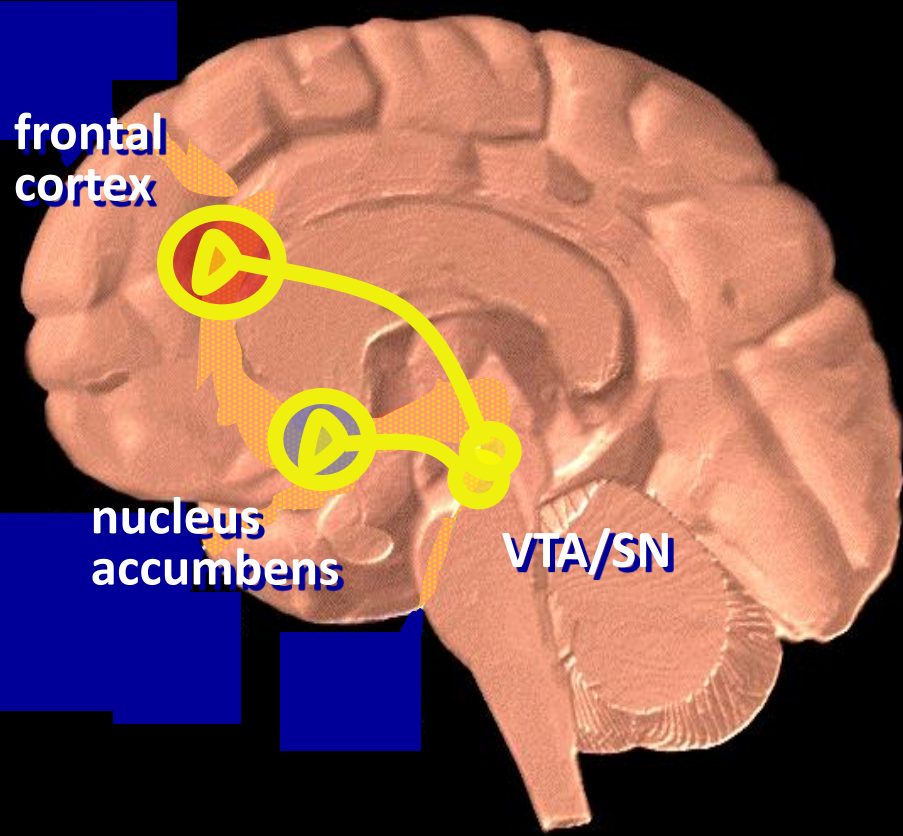


Drugs of Abuse
Engage
Systems in the
*Motivation
Pathways*
of the Brain

Vocabulary

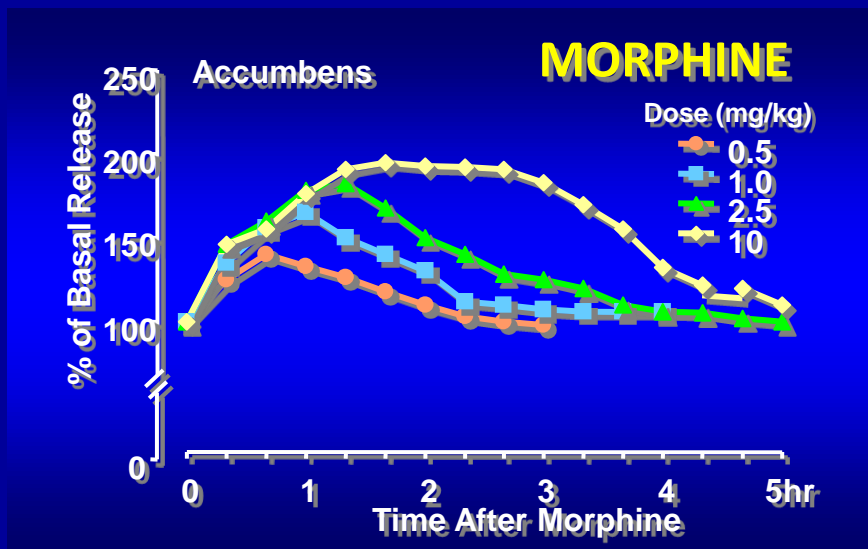
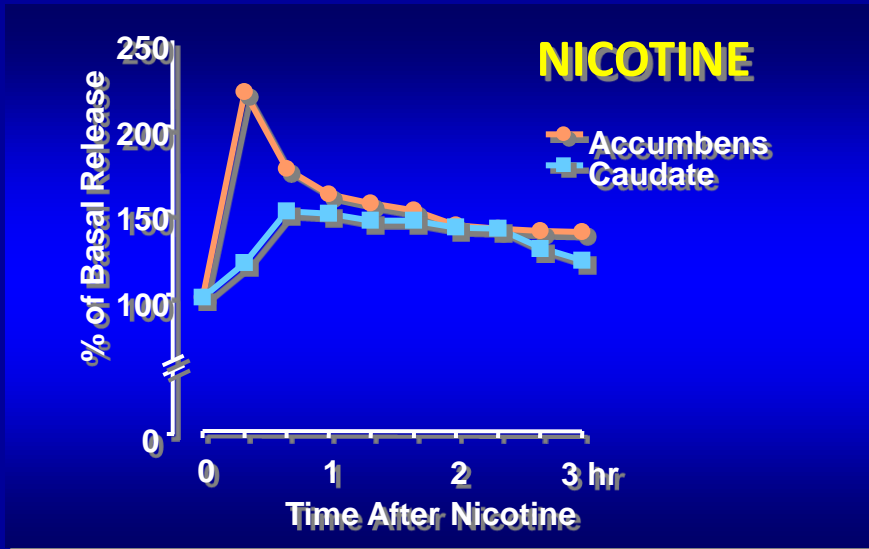
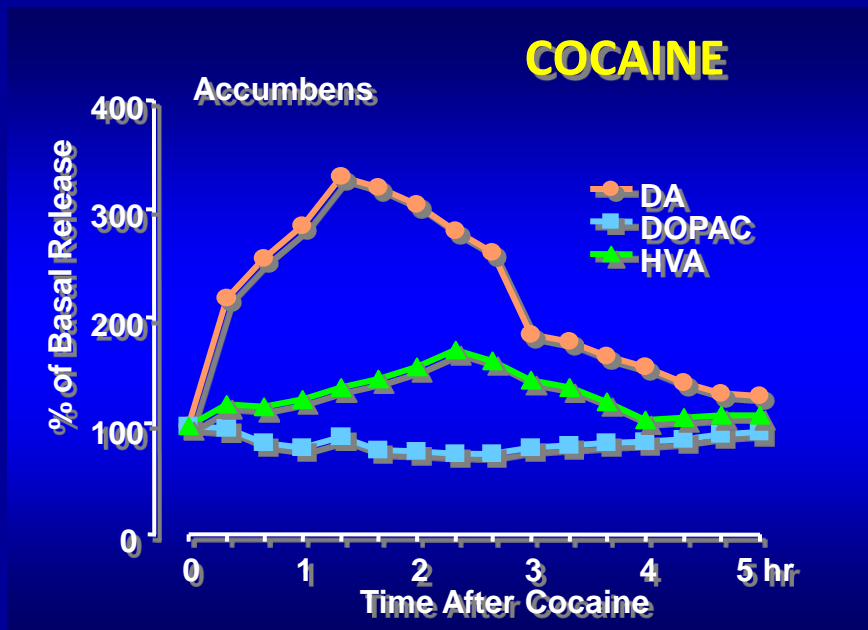
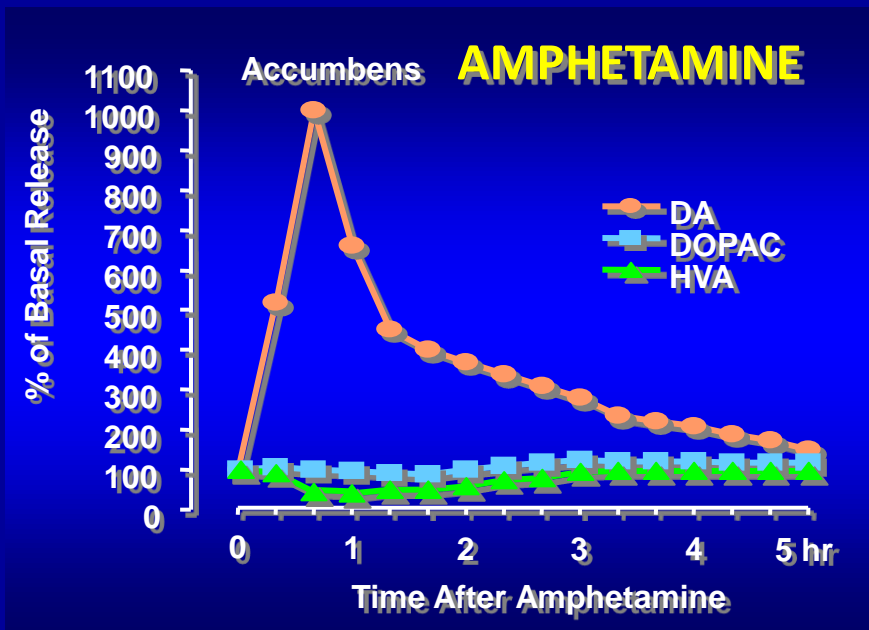
- Agonist - drug that activates a receptor
- Antagonist - drug that blocks a receptor
- Partial agonist/antagonist - drug that does some of both

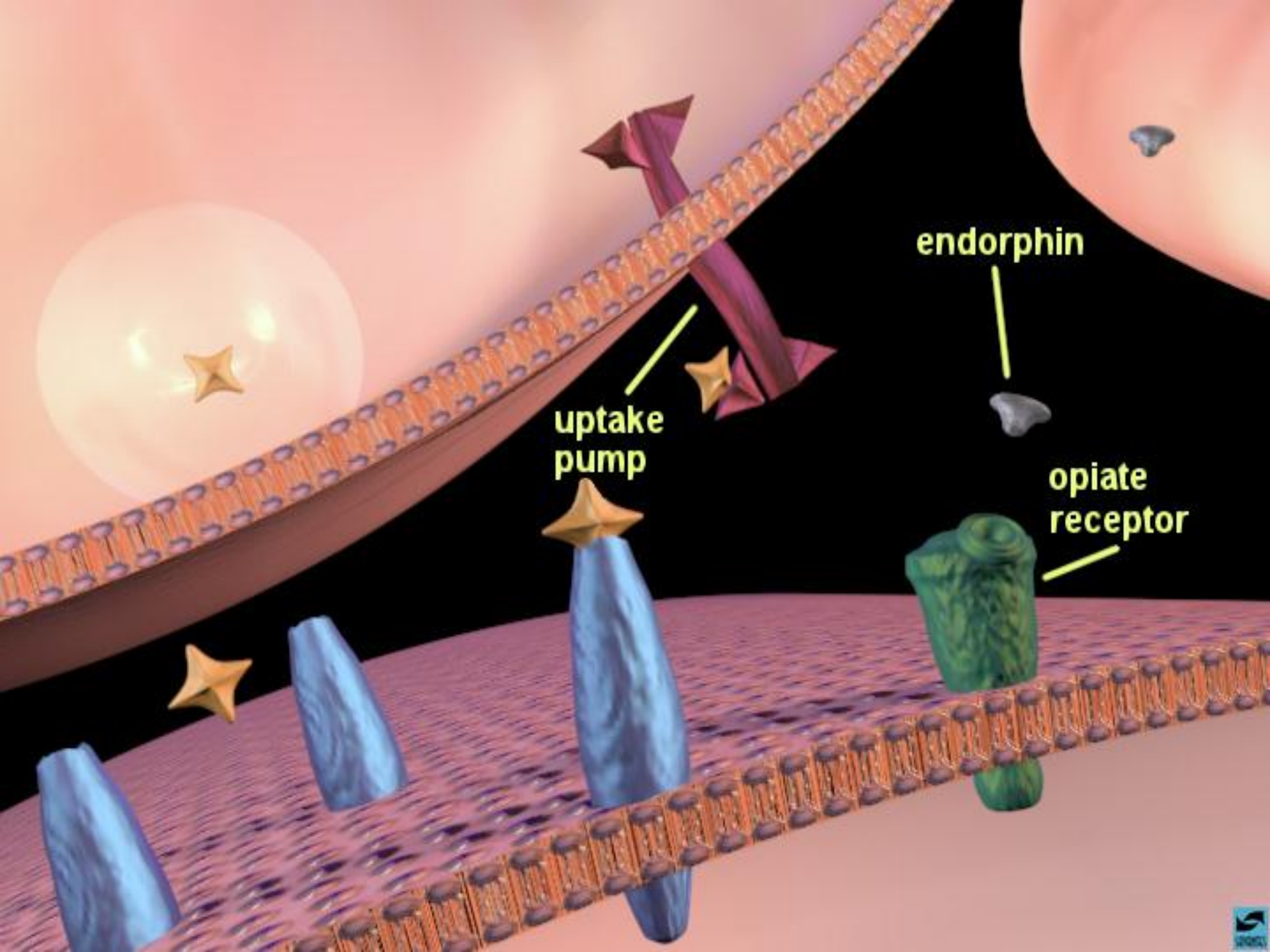
Drugs of Abuse Cause a Release of Dopamine



SOURCE: Di Chiara et al

Drugs of Abuse Cause a Release of Dopamine



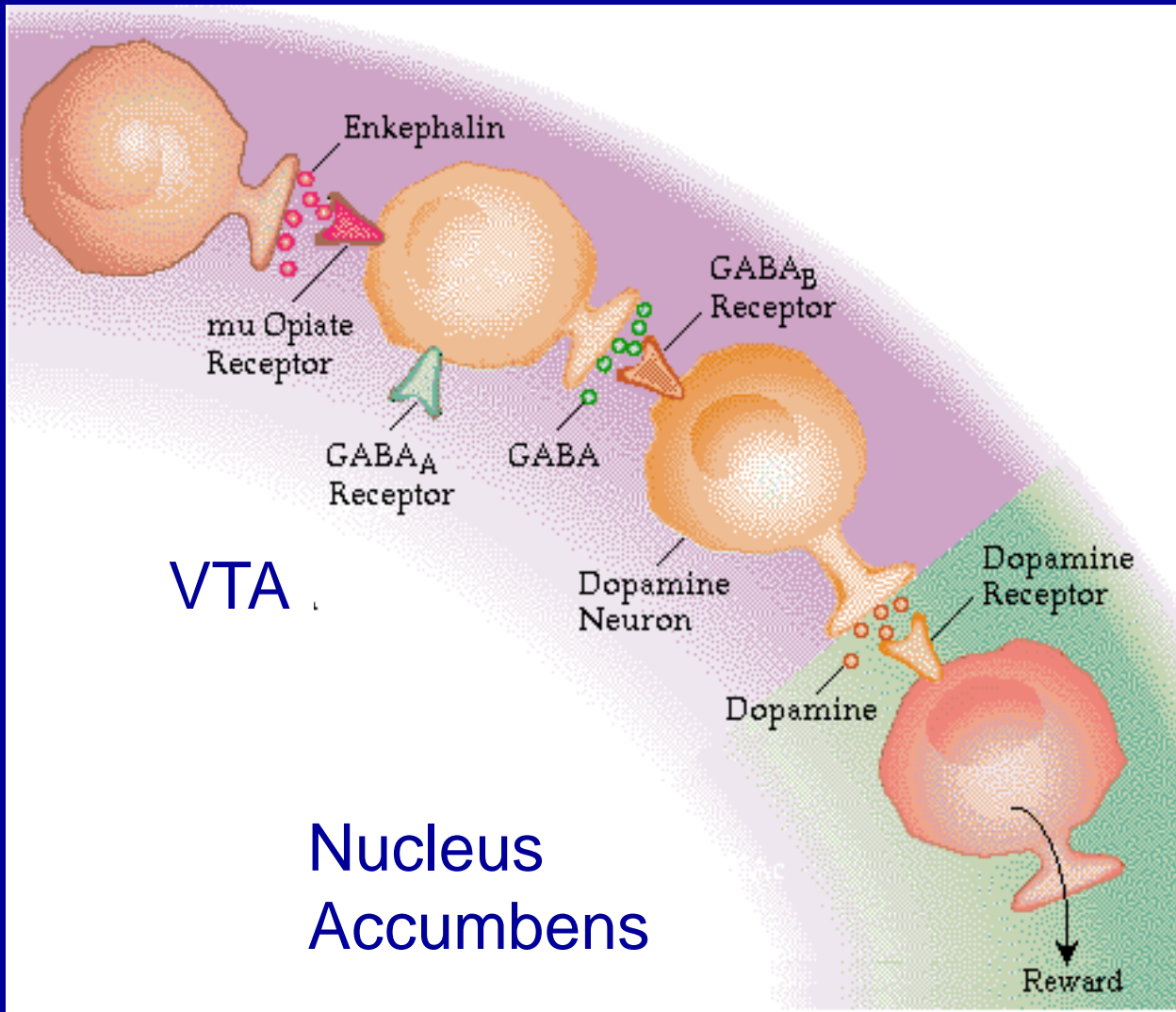


endorphin

uptake pump

opiate receptor





Vocabulary

- Craving - subjective sense of hunger for substance
- Triggers – salience of environmental cues, associated with behaviors (conscious or unconscious)
- Reinforcement - response that increases likelihood of behavior
- Positive reinforcement - positive stimulus (reward craving) that increases likelihood of behavior
- Negative reinforcement - removal of noxious stimulus (relief craving) that increases likelihood of behavior
- Punishment - noxious stimulus that decreases likelihood of behavior

Multiple Mechanisms of Action

- Agonists
- Antagonists
- Modulators of reinforcement pathways
- Aversive agents
- Modulators of metabolism
- Immunization
- Modulators of sustaining or re-instatement pathways
- Others?

Conceptual underpinnings

- Use as many effective tools as are available
- One size does not fit all: as many doors as possible
- A full continuum of care: multiple services with flexible responses
- Institutional affiliation promotes engagement
- Expectation of relapsing/remitting course
- Expectation of variable and shifting treatment readiness
- Recovery as a gradual process, not an overnight event -- expectation of incremental progress

Medications for Nicotine Dependence

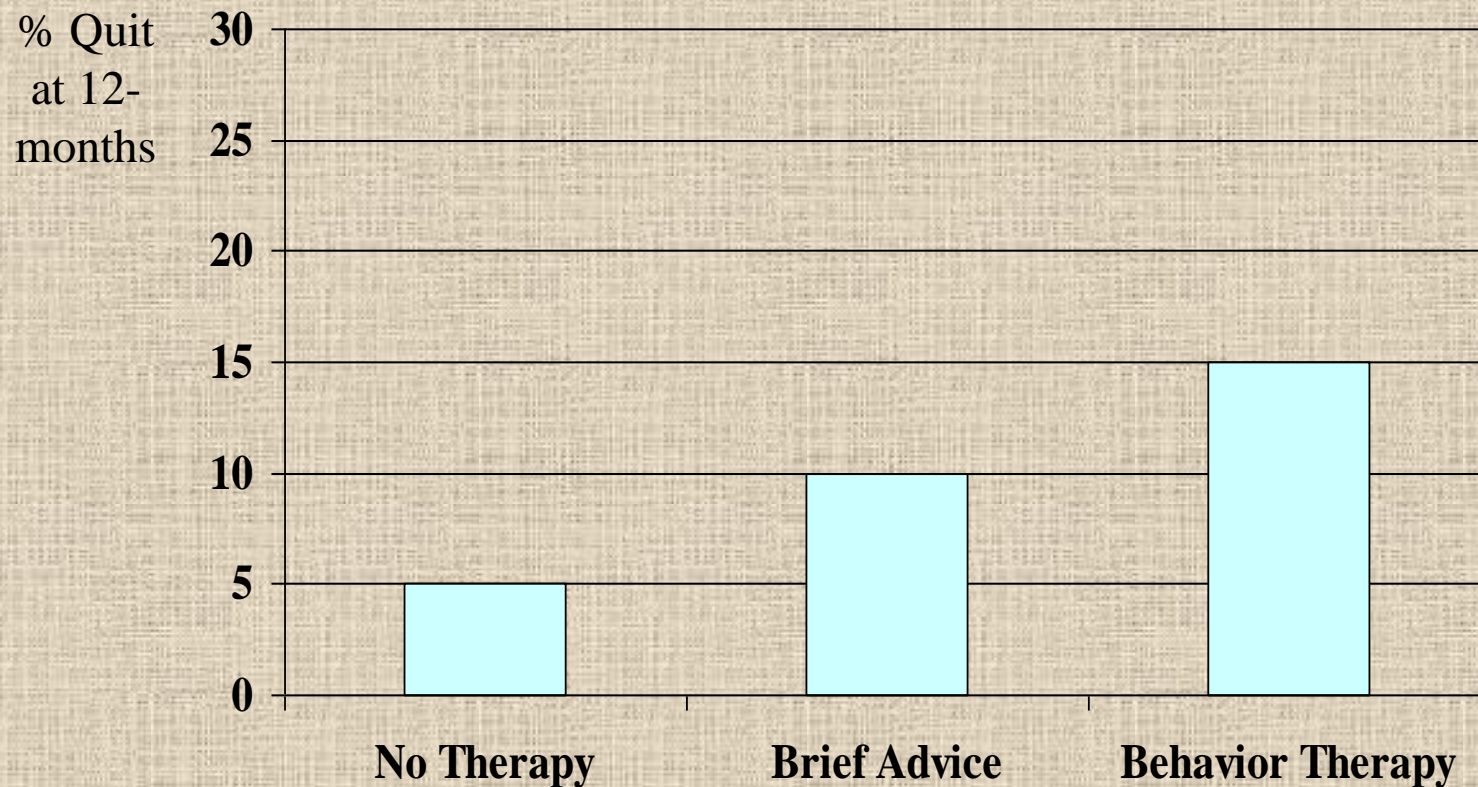
Nicotine replacement therapy

Bupropion

Varenacline

Current treatments

Effectiveness of Non-Pharmacologic Treatments



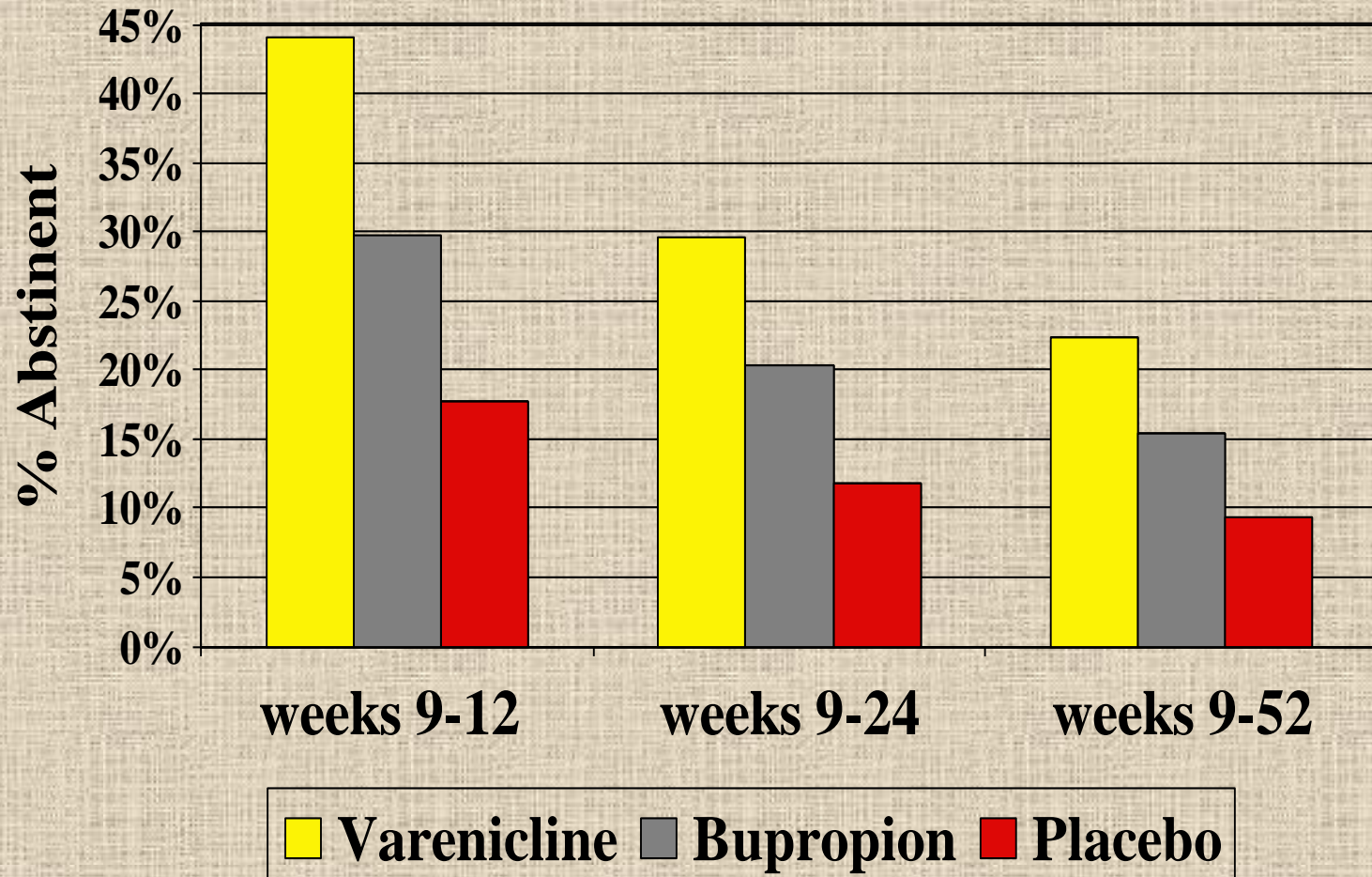
Lerman, Patterson, & Berrittini, 2005.

Nicotine replacement therapy (NRT)

- Patches
- Gum
- Nasal spray
- Inhaler
- Lozenge
- [E-cigarettes??]

Nicotine – current (but under-utilized) treatments

Abstinence Rates Varenicline vs. Bupropion vs. Placebo



Use of medications – the basics

- Step #1: enhance motivation
- Repeat step #1 endlessly until action stage
- When in action stage, establish a plan
- Set a quit date
- Self-directed cutting down until then
- Prescribe craving medication now, with plan to start 1-3 weeks before quit date
- Start NRT on quit date

Use of medications – the advanced course

- The more monitoring the better
- Add-on counseling if available (group, individual, telephone, on-line)
- Establish the *personal* link to health outcomes
- Frequent visits and debriefing
- Encourage successes (even small)
- Encourage multiple quit attempts

Barriers to effectiveness and adoption

- Cost
- Knowledge and training
- Prejudice and misunderstanding
- Lack of medical involvement in treatment
- Lack of delivery system models
- Limited potency of medications
- Side effects
- Problems with adherence and compliance

Role of medical professionals

- Screening
- Assessment
- Brief intervention
- Extended intervention
- Referral

Role of medical professionals

- Problem: doctors have no time
- Solution: the 3 questions approach
 - How much do you smoke?
 - Would you like to try to quit or cut down?
 - Why or why not?

Role of medical professionals

- Problem: even if they say yes I don't know what to do (I'd rather not know)
- Solution: you've already done something (advancing motivation is an effective intervention)

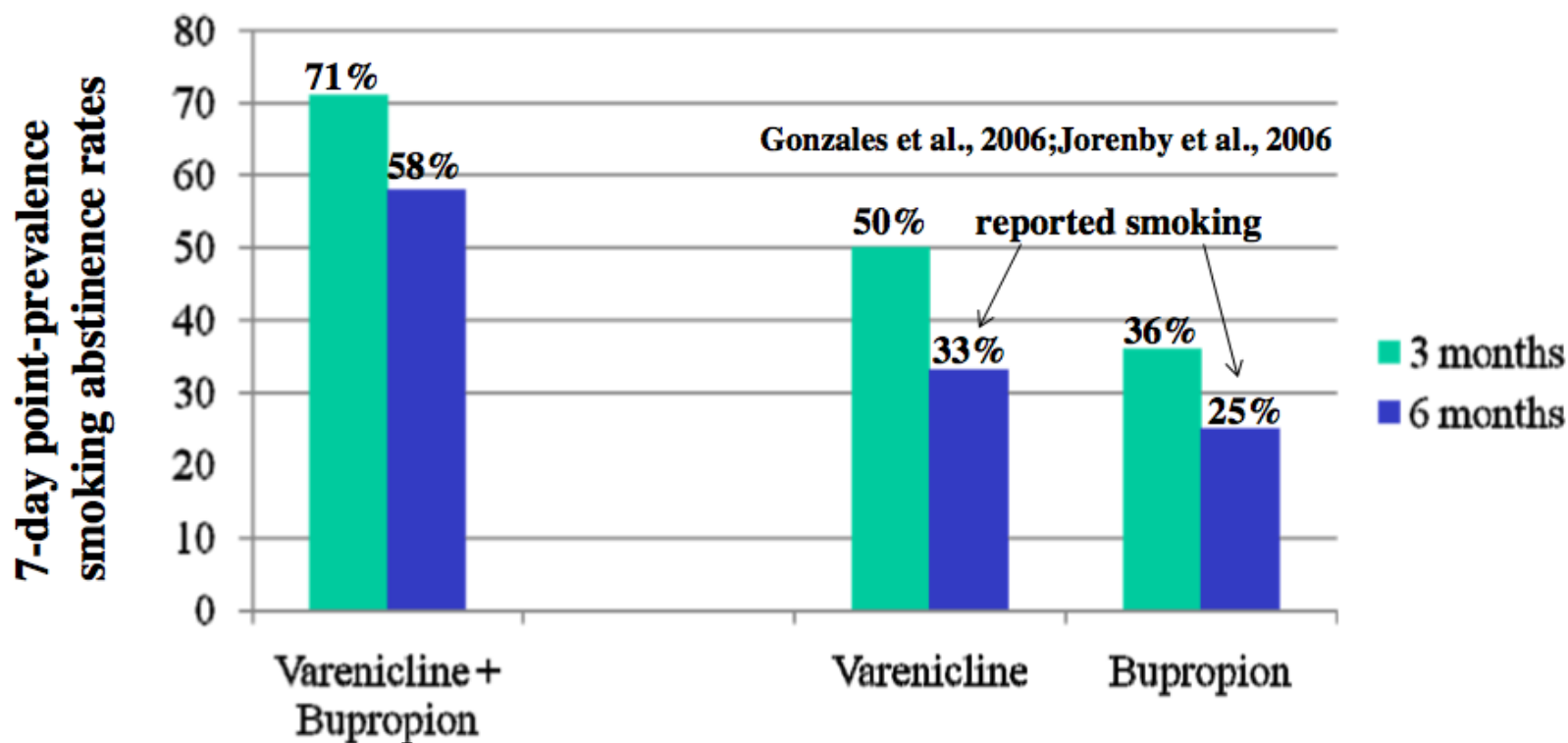
Barriers to greater medical role

- Only half of smokers receive quit advice from physicians – WHY?
- Frustration at low success rates (lower in real world than in research)
- Time pressures in medical settings
- Concerns about medication side effects

Use of medications – the advanced course 2

- Start NRT 1-3 wks before quit date
- Combine long acting NRT (patch) with short acting NRT (gum, lozenge, spray, inhaler)
- Consider *combining* bupropion + varenicline + NRT

Varenicline & Bupropion SR Combination Therapy for Smoking Cessation



Ebbert JO et al. Nic Tobacco Research 2009;11(3):234-239.

Medications and substance use: linear pharmacological model

MEDICATION

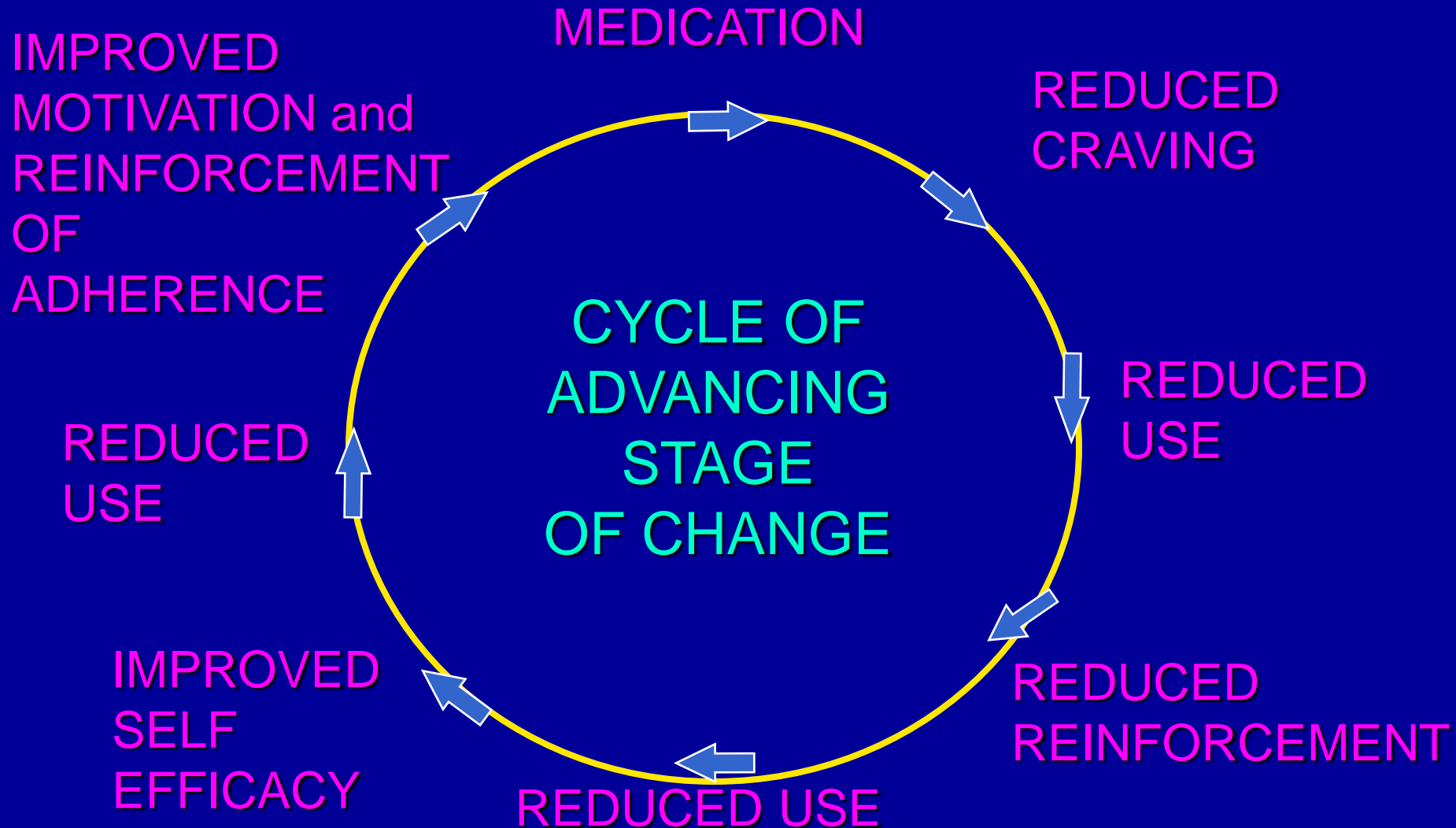


REDUCED CRAVING and REWARD



REDUCED USE

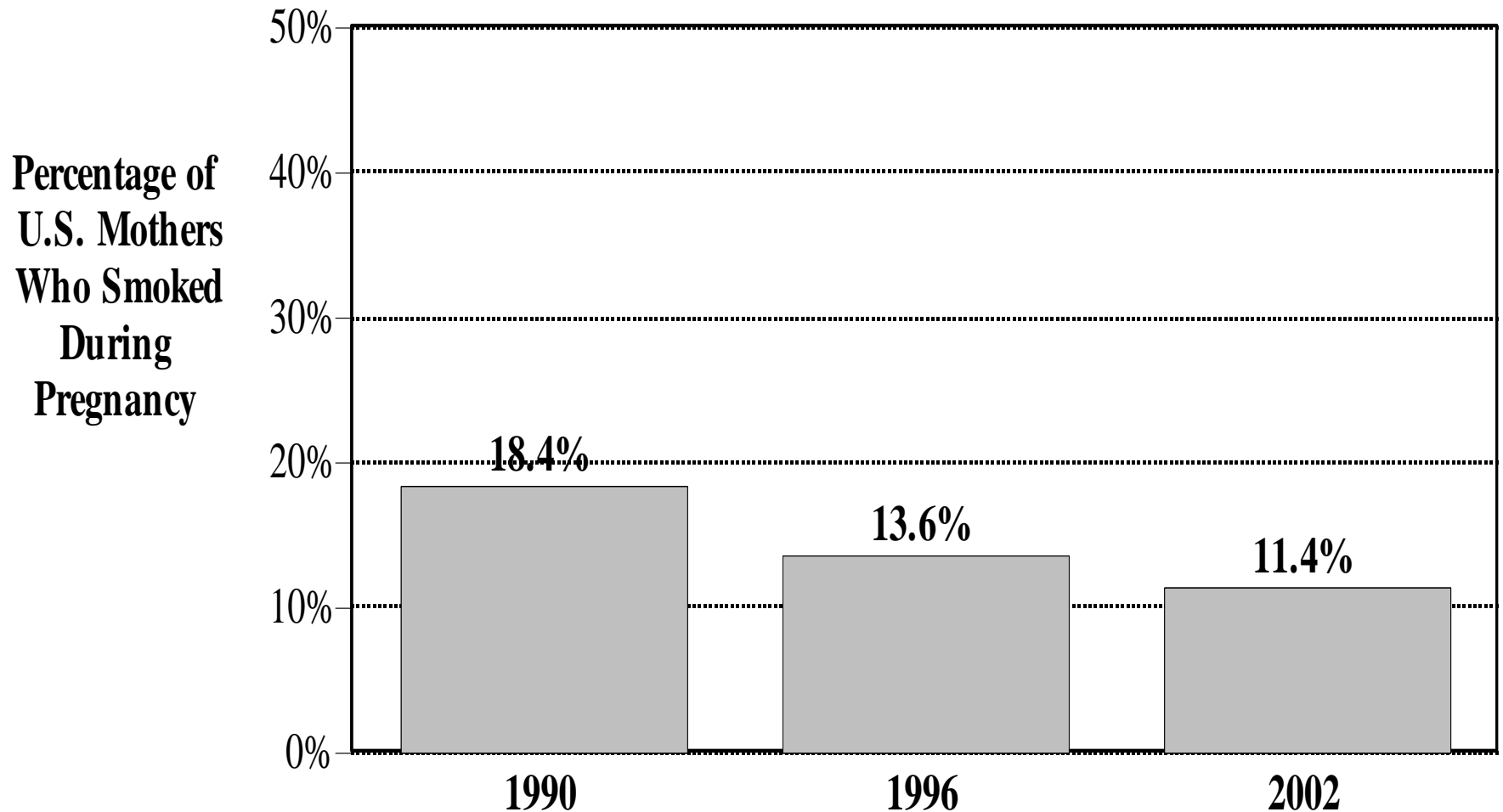
Medications and stages of change: Potential positive feedback loop



Use of medications – Innovative delivery techniques

- Practice Quit Attempts (PQA) – attempting to not smoke for a few hours or days, without pressure to quit for good
- NRT sampling as a possible facilitator
- NRT sampling increases conversion of PQA's into more serious quit attempts and might increase success
- A potential technique for advancing stage of change: contemplation → preparation?

Smoking during pregnancy



Centers for Disease Control and Prevention. "Smoking During Pregnancy—United States, 1990-2002," *Morbidity and Mortality Weekly Report* 53(39):911-915, 2004

Pregnancy

- Unfortunately safety and efficacy not well studied in pregnancy
- Clinical consensus – use bupropion + NRT (safer than smoking)

Co-Morbidity

Scope of the problem

Rates of smoking:

- Background population 25%
- Alcohol addiction 90%
- Drug addiction 90%
- Schizophrenia 85%
- Depression 80%

Co-Morbidity

Treatment approaches

- Target these populations for tobacco cessation
- Treat the co-morbidity!

Is everything
on the
menu?

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searchy/Deepen40
E.J. Pettinger '13

*"And if you like comfort food, I would
recommend the Xanax stuffed pork-loin."*

Psychiatric co-morbidity

Special considerations

- Psychiatric side effects in general population, and higher rates in patients with psychiatric co-morbidity
 - Risk of depression/anxiety with varenicline
 - Risk of irritability or agitation with bupropion
 - Risk of mania with bupropion in bipolar disorder
- Worsening of depression with quit attempt should be addressed

Addiction co-morbidity

- Conflict in the field:
 - Tobacco use worsens addiction treatment outcomes, vs
 - “I can’t deal with that now... one thing at a time...”

Weight gain

- Avg 4 lbs with smoking cessation
- But 1 in 10 have larger gain of ≥ 25 lbs

Youth

- Unfortunately treatment trials in adolescents disappointing
- Adolescents are complicated and hard to treat (*I know – you're shocked*)

Genetics

- Variations in the genes for nicotine receptors predict severity and treatment response
- One high risk variant (1/3 European descent population) correlate with more smoking, later quit age, lower rates of quitting, poorer response to treatment
- Some evidence that medication eliminates this risk, and this variant accounts for most of medication effect

Practical Treatment Approaches

- 95% is just showing up

Medication Treatment Collaborative Team Approach

- Illness education and role induction
- Family (or other support network) involvement and commitment
- Cross discipline monitoring
 - Presence of symptoms
 - Medication compliance
 - Treatment response
 - Side effects
 - Social influences
- Expectations and arrangements for continuing care

Pharmacological Treatment

- Question:
 - Which is better - medications or counseling?
- Answer:
 - Yes

A sprint or a marathon?

Early: I agree I was huffing and puffing with my smoking out of control, but I've cut down to less than a pack a day.

Later: I've been trying to quit, and the medication my doctor gave me has really been helping. But those last 10 cigarettes are a bear...

Even Later: I've quit a few times...I even got up to 6 months. But something always seems to happen ... sometimes when I get stressed I just can't resist the first cigarette, and then it's off to the races again. Maybe I'll try those meds again?

(sigh)

The future?

- Nicotine vaccine
- Nicotine metabolism enhancers
- Other reinforcement modulators
 - N-Acetyl Cysteine
 - Others
- NK-1 (substance P; neurokinin) antagonists for stress-induced relapse

We've come a long way

