Approaches to Treating Addiction in General Medical Settings

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Financial Disclosure Statement

- Funding: National Institute of Drug Abuse (1K23DA023558); No commercial conflicts

Outline

- Identification and assessment of drug/alcohol problems in primary care
- Treatment of ADDICTION using anti-addiction medications in primary care

Identification and Assessment of Drug/Alcohol Problems in Primary Care Settings

SBIRT: Screening, Brief Intervention, Referral to Treatment (Madras, 2009)

- Screened 459,599 patients at primary care clinics, hospitals, and emergency/trauma centers in 6 states
  - 22.7% (104,505) had positive screen (risky use, abuse, or dependence)
  - 15.9% met criteria for brief intervention
  - 3.2% met criteria for brief treatment
  - 3.7% met criteria for referral to specialty treatment
- Among positive screens: 70% needed brief intervention, 14% brief treatment, and only 16% referral for specialty treatment

SAMHSA SBIRT Program: Outcomes (Madras, 2009)

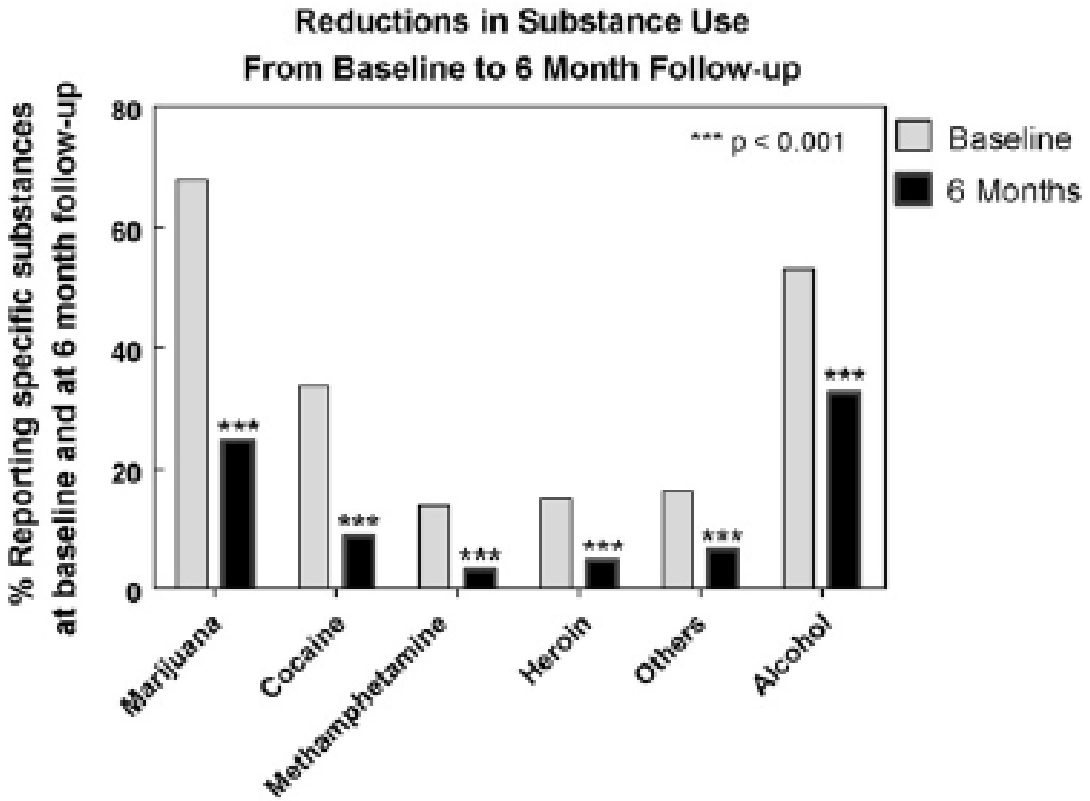


Fig. 1. Among persons reporting illicit drug use at baseline, percent people reporting specific drugs and heavy alcohol at baseline and 6 months after intervention (all $p < 0.001$). Data are based on the sites with higher follow-up rates (Table 3, bottom row).

SBIRT: Coding and Reimbursement

Payor	Code	Description	Fee
Commercial Insurance	99408	15-30 minutes	$33.41
	99409	> 30 minutes	$65.51
Medicare	G0396	15-30 minutes	$29.42
	G0397	> 30 minutes	$57.69
Medicaid	H0049	Brief	$24.00
	H0050	> 15 minutes	$48.00

From: http://sbirt.samhsa.gov/coding.htm

Treatment of Addiction in Primary Care Settings

Audience Participation

- Raise your hand if you think there are any FDA approved medications for treating addiction that are currently available for use in primary care.

FDA Approved Anti-Addiction Medications Available to Primary Care

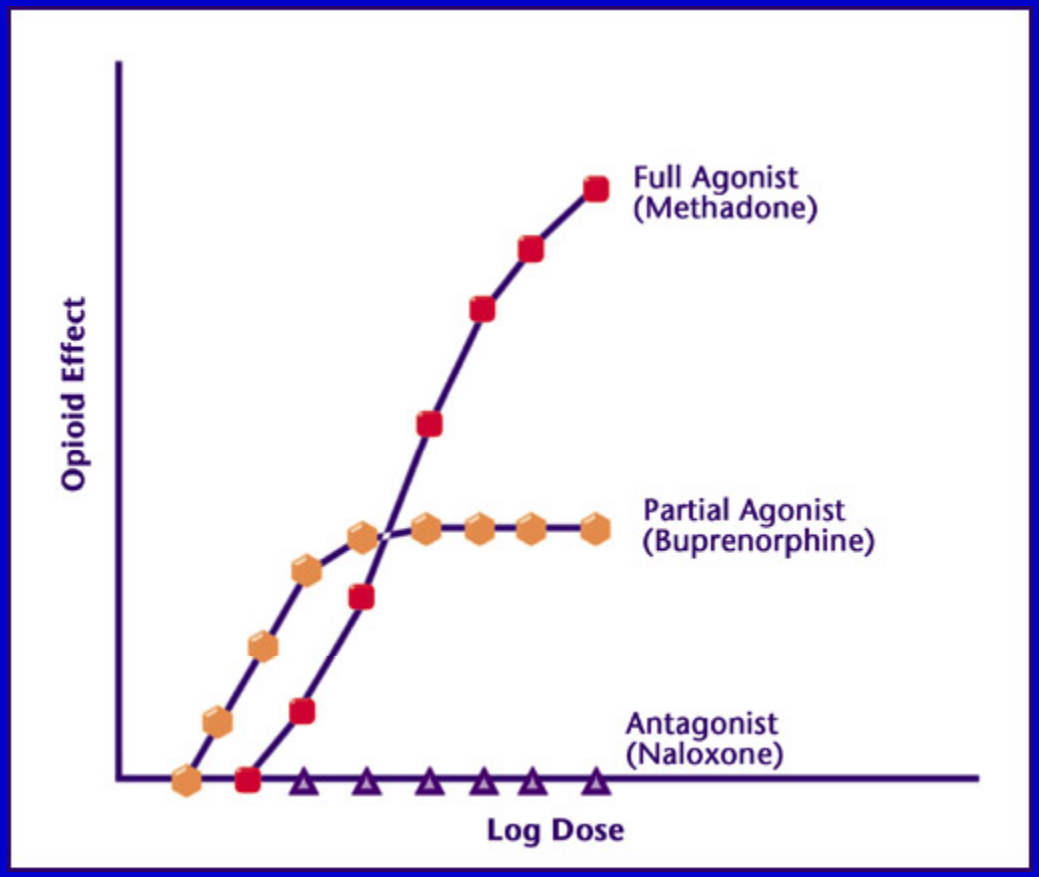
- Alcohol Dependence
  - Naltrexone (Revia® and Vivitrol®)
  - Acamprosate (Campral®)
  - Disulfiram (Antabuse®)
- Opioid Dependence (heroin, Rx opioids)
  - Buprenorphine (Suboxone® and Subutex®)
  - Naltrexone (Vivitrol®)
- No approved medications for cocaine, methamphetamine, marijuana, ecstasy, etc. (refer patients to clinical trials!)

Primary Care/Office-based Treatment of Addiction

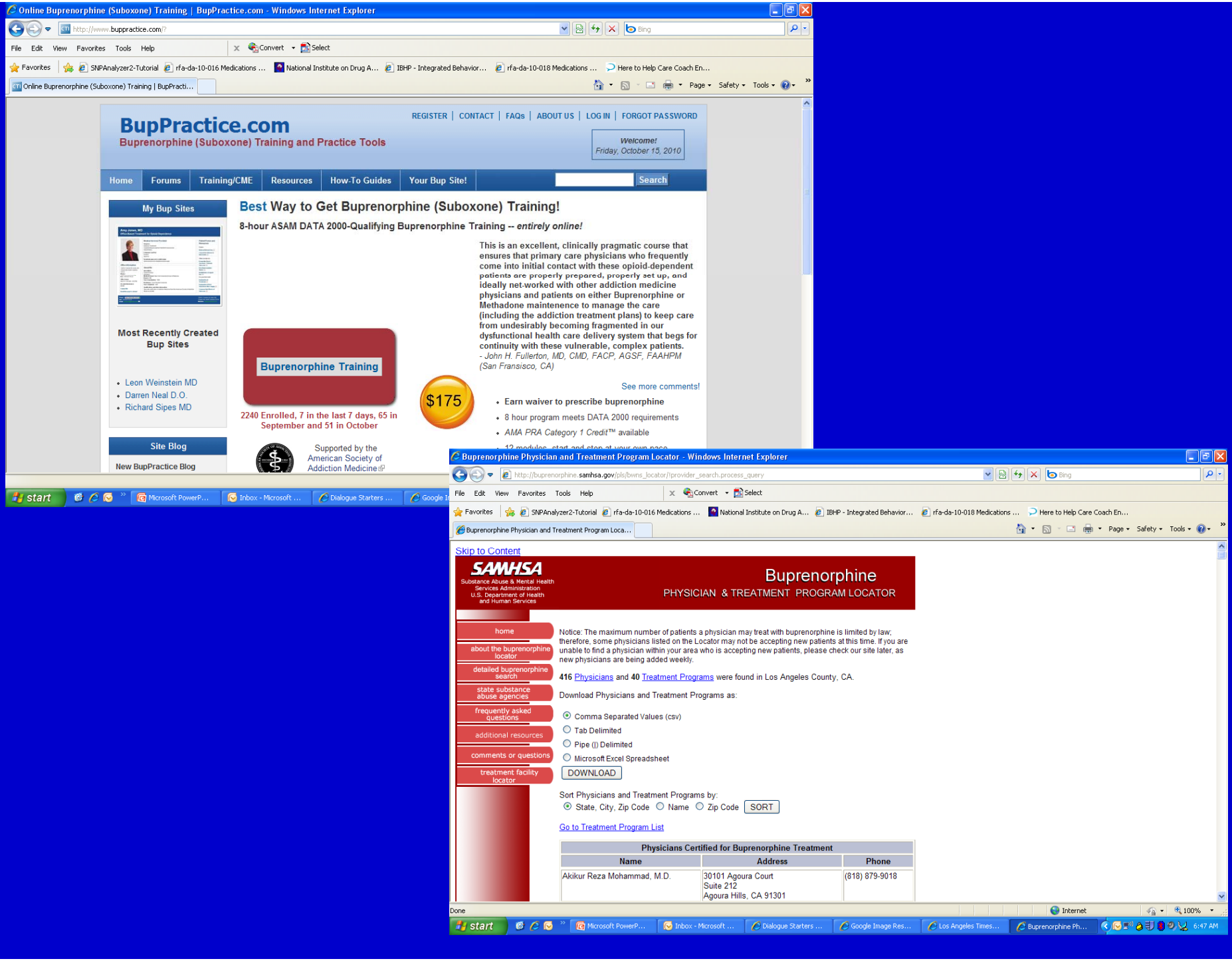
- A combination of three components, depending on patient's specific needs:
  - Medication: medically-assisted withdrawal, abstinence initiation, relapse prevention, reduction of co-morbid symptoms
  - Counseling: cognitive behavioral therapy, behavioral approaches, on-site or referral
  - Support: self-help including AA, family/friends, supportive environment, case management

Buprenorphine: Sublingual Tabs/Film

Buprenorphine: Partial Agonist and Ceiling Effect



From: SAMHSA TIP #40: Buprenorphine Practice Guidelines


Online Buprenorphine (Suboxone) Training | BupPractice.com - Windows Internet Explorer
BupPractice.com
Buprenorphine (Suboxone) Training and Practice Tools
REGISTER | CONTACT | FAQs | ABOUT US | LOG IN | FORGOT PASSWORD
Welcome!
Friday, October 15, 2010
Home
Forums
Training/CME
Resources
How-To Guides
Your Bup Site!
Search
My Bup Sites
Most Recently Created Bup Sites
Leon Weinstein MD
Darren Neal D.O.
Richard Sipes MD
Site Blog
New BupPractice Blog
Best Way to Get Buprenorphine (Suboxone) Training!
8-hour ASAM DATA 2000-Qualifying Buprenorphine Training -- entirely online!
This is an excellent, clinically pragmatic course that ensures that primary care physicians who frequently come into initial contact with these opioid-dependent patients are properly prepared, properly set up, and ideally net-worked with other addiction medicine physicians and patients on either Buprenorphine or Methadone maintenence to manage the care (including the addiction treatment plans) to keep care from undesirably becoming fragmented in our dysfunctional health care delivery system that begs for continuity with these vulnerable, complex patients.
- John H. Fullerton, MD, CMD, FACP, AGSF, FAAHPM (San Fransisco, CA)
See more comments!
Buprenorphine Training
2240 Enrolled, 7 in the last 7 days, 65 in September and 51 in October
$175
Earn waiver to prescribe buprenorphine
8 hour program meets DATA 2000 requirements
AMA PRA Category 1 Credit™ available
Supported by the American Society of Addiction Medicine
Buprenorphine Physician and Treatment Program Locator - Windows Internet Explorer
Skip to Content
SAMHSA
Substance Abuse & Mental Health Services Administration
U.S. Department of Health and Human Services
Buprenorphine
PHYSICIAN & TREATMENT PROGRAM LOCATOR
home
about the buprenorphine locator
detailed buprenorphine search
state substance abuse agencies
frequently asked questions
additional resources
comments or questions
treatment facility locator
Notice: The maximum number of patients a physician may treat with buprenorphine is limited by law; therefore, some physicians listed on the Locator may not be accepting new patients at this time. If you are unable to find a physician within your area who is accepting new patients, please check our site later, as new physicians are being added weekly.
416 Physicians and 40 Treatment Programs were found in Los Angeles County, CA.
Download Physicians and Treatment Programs as:
Comma Separated Values (csv)
Tab Delimited
Pipe (|) Delimited
Microsoft Excel Spreadsheet
DOWNLOAD
Sort Physicians and Treatment Programs by:
State, City, Zip Code
Name
Zip Code
SORT
Go to Treatment Program List
Physicians Certified for Buprenorphine Treatment
Name
Address
Phone
Akikur Reza Mohammad, M.D.
30101 Agoura Court
Suite 212
Agoura Hills, CA 91301
(818) 879-9018

ARTICLE | Annals of Internal Medicine

Clinic-Based Treatment of Opioid-Dependent HIV-Infected Patients Versus Referral to an Opioid Treatment Program

A Randomized Trial

Gregory M. Lucas, MD, PhD; Amina Chaudhry, MD, MPH; Jeffrey Hsu, MD; Tanita Woodson, CRNP; Bryan Lau, PhD; Yngvild Olsen, MD; Jeanne C. Keruly, CRNP; David A. Fiellin, MD; Ruth Finkelstein, ScD; Patricia Barditch-Crovo, MD; Katie Cook, BA; and Richard D. Moore, MD

Background: Opioid dependence is common in HIV clinics. Buprenorphine–naloxone (BUP) is an effective treatment of opioid dependence that may be used in routine medical settings.

Objective: To compare clinic-based treatment with BUP (clinic-based BUP) with case management and referral to an opioid treatment program (referred treatment).

Design: Single-center, 12-month randomized trial. Participants and investigators were aware of treatment assignments. (ClinicalTrials.gov registration number: NCT00130819)

Setting: HIV clinic in Baltimore, Maryland.

Patients: 93 HIV-infected, opioid-dependent participants who were not receiving opioid agonist therapy and were not dependent on alcohol or benzodiazepines.

Intervention: Clinic-based BUP included BUP induction and dose titration, urine drug testing, and individual counseling. Referred treatment included case management and referral to an opioid-treatment program.

Measurements: Initiation and long-term receipt of opioid agonist therapy, urine drug test results, visit attendance with primary HIV care providers, use of antiretroviral therapy, and changes in HIV RNA levels and CD4 cell counts.

Results: The average estimated participation in opioid agonist therapy was 74% (95% CI, 61% to 84%) for clinic-based BUP and 41% (CI, 29% to 53%) for referred treatment ($P < 0.001$). Positive test results for opioids and cocaine were significantly less frequent in clinic-based BUP than in referred treatment, and study participants receiving clinic-based BUP attended significantly more HIV primary care visits than those receiving referred treatment. Use of antiretroviral therapy and changes in HIV RNA levels and CD4 cell counts did not differ between the 2 groups.

Limitation: This was a small single-center study, follow-up was only moderate, and the study groups were unbalanced in terms of recent drug injections at baseline.

Conclusion: Management of HIV-infected, opioid-dependent patients with a clinic-based BUP strategy facilitates access to opioid agonist therapy and improves outcomes of substance abuse treatment.

Primary Funding Source: Health Resources and Services Administration Special Projects of National Significance program.

Ann Intern Med. 2010;152:704-711. www.annals.org

For author affiliations, see end of text.

Buprenorphine: Effectiveness in Primary Care Settings

- A 24-week randomized, controlled clinical trial (N=166) compared primary care-based buprenorphine with standard medical management and: (1) once-weekly visits, (2) thrice-weekly visits, or (3) thrice-weekly visits and enhanced medical management.
- Standard medical management was brief, manual-guided, medically focused counseling; enhanced medical management was similar, but each session was extended.

- Source: Fiellin DA, Pantalon MV, Chawarski MC, Moore BA, Sullivan LE, O'Connor PG, Schottenfeld RS. Counseling plus buprenorphine-naloxone maintenance therapy for opioid dependence. N Engl J Med. 2006 Jul 27;355(4):365-74.

Buprenorphine: Effectiveness in Primary Care Settings

	Once-weekly	Thrice-weekly	Thrice-weekly + Enhanced MM
% opioid-free urines	44%	40%	40%
Longest Abstinence	6.7 wks	5.7 wks	5.5 wks
Completed treatment	48%	43%	39%

Buprenorphine vs. Methadone Maintenance: Cochrane Review

- Buprenorphine (>=8mg/day) superior to placebo for suppressing heroin use and increasing treatment retention
- Methadone superior to buprenorphine for retention with flexible dosing (RR= 0.80; 95% CI: 0.68 - 0.95), but similar in suppression of heroin use
- Limitations: only heroin users (? Rx opioids), low dose methadone less clearly superior, access to methadone limited

Primary Care (PC) Buprenorphine versus Opiate Treatment Program (OTP)

- PC patients more likely than OTP patients to:
  - Be full-time employed (46% versus 15%, $p < 0.001$)
  - Have no history of methadone treatment (46% versus 61%, $p < 0.05$)
  - Have fewer years of opioid dependence (10 versus 15, $p < 0.001$)
  - Have lower rates of injection drug use (IDU) (44% versus 60%, $p = 0.03$).
- New to treatment PC patients had lower rates of hepatitis C (25% versus 61%, $p = 0.002$) than subjects with prior methadone treatment.

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Naltrexone for Alcohol Dependence

- Ethanol releases endogenous opioids (e.g. β-endorphin)
  - Opioid release mediates ethanol-induced euphoria and reward
- Naltrexone = μ-opioid receptor antagonist
  - Reduced ethanol-induced stimulation, positive mood, craving, and enjoyment in human lab studies (Ray and Hutchison, 2007)

COMBINE Study (Anton, JAMA, 2006)

- Randomized, double-blind, placebo-controlled 16 week clinical trial
- 1,383 recently abstinent participants with alcohol dependence (DMS-IV)
- Medications: Naltrexone, acamprosate, both, placebo, or no pills (CBI alone)
- Counseling: Medical Management, Combined Behavioral Intervention, or both

COMBINE Study: Results

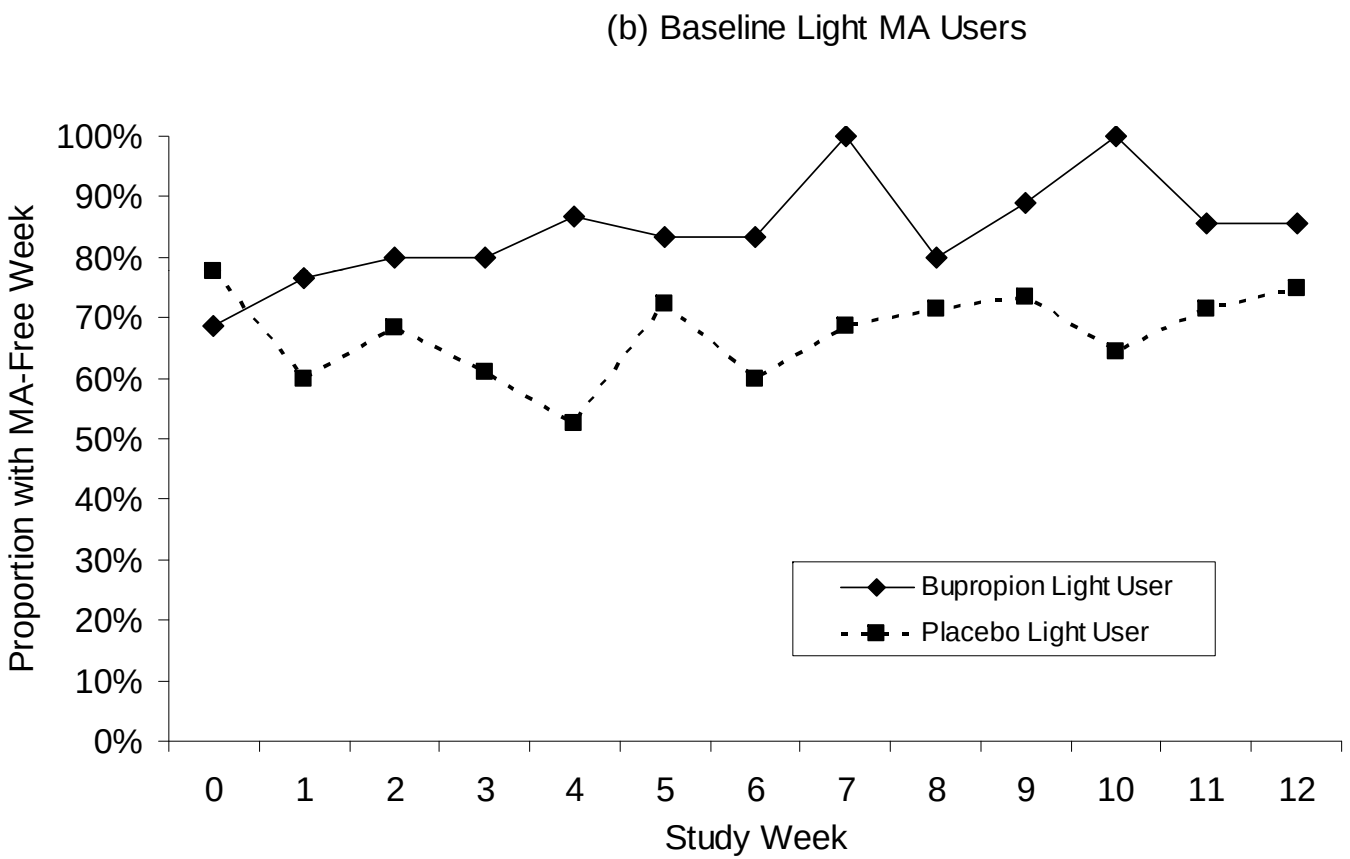
At end of 16 week tx:	Mean % days abstinent [1]	% with heavy drinking day [2]
CBI alone (no pills)	67%	79%
Placebo + MM	75%	73%
Naltrexone + MM	**81%**	**66%**
Placebo + MM + CBI	**79%**	**70%**
Naltrexone + MM + CBI	77%	70%
Acamprosate no different than placebo		

[1] Pre-treatment mean = 25%. [2] Heavy drinking day = 5 or more drinks per day for men; 4 or more drinks per day for women.

Naltrexone for Alcohol Dependence: Cochrane Review

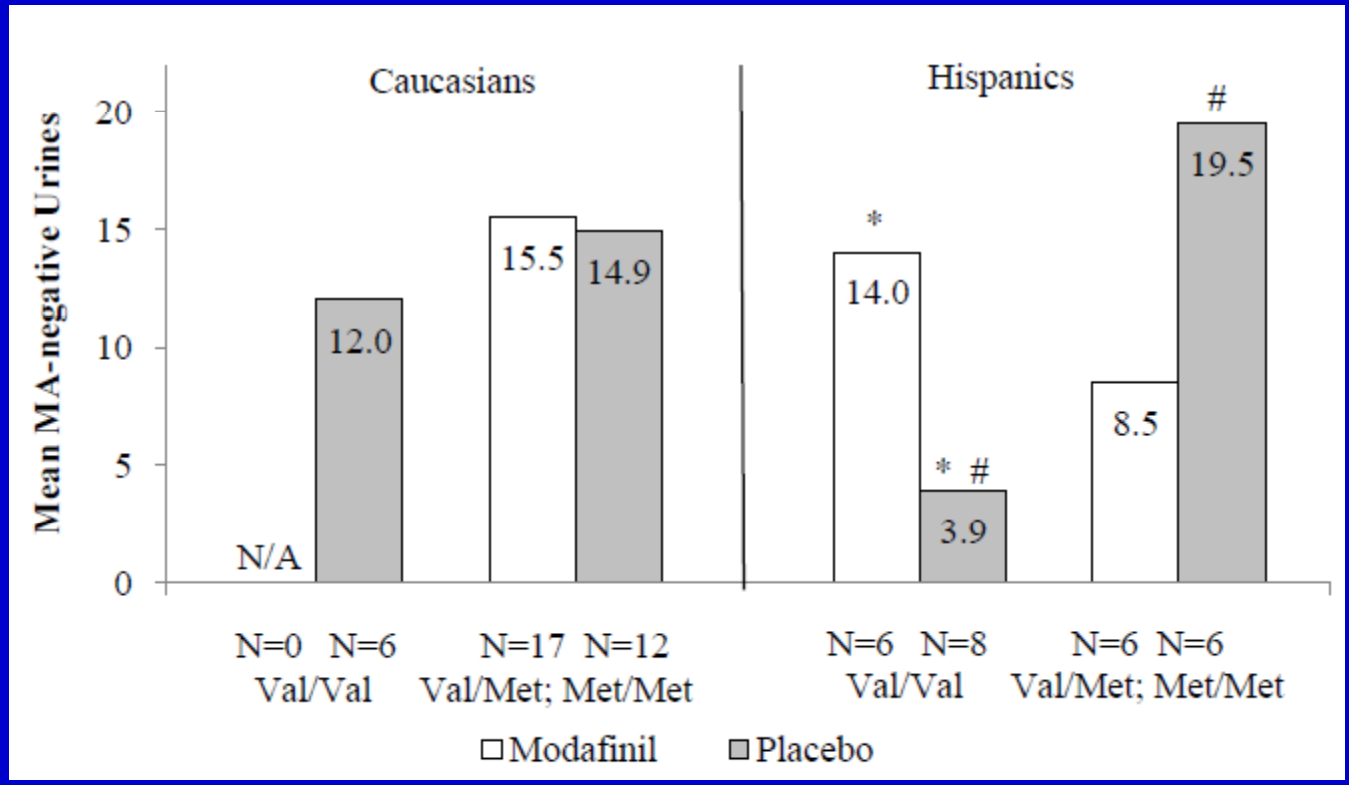
- Included 29 randomized controlled trials
- Naltrexone for 12 weeks (c/w placebo)
  - 36% reduction in relapse to heavy drinking (NNT=7; RR (95% CI) = 0.64 (0.51 to 0.82))
  - 13% reduction in relapse to any drinking (NNT=12; RR (95% CI) = 0.87 (0.76 to 1.00))
  - 18% reduction in treatment drop-out (NNT=13; RR (95% CI) = 0.82 (0.70 to 0.97))
  - But 37% of participants **discontinued NTX** (Vivitrol?)

Methamphetamine: Bupropion > Placebo In Baseline Light MA Users?



Light MA Users: 0 to 2 of 6 baseline urine drug screens positive for MA

COMT Val158Met Polymorphism and Modafinil for Meth Dependence



Val/Val = (1) poor outcomes with behavioral therapy alone (placebo), and (2) response to modafinil with improved outcomes

THANK YOU!

- Questions or comments:
  - Email me: heinzk@ucla.edu
  - Page me: 310-825-6301, ext. 21764
  - On the web: www.uclasarx.org

- To refer a patient for medical treatment of addiction or to participate in a clinical trial:

866-449-UCLA

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Naltrexone for Alcohol Dependence

- Tablets for oral dosing (50 mg daily)
  - Non-adherence is common problem
- Long-acting injectable form (Vivitrol®)
  - Monthly intra-muscular gluteal injection (380mg): **Improved adherence!**
  - Injection site infections/abscess
- Side effects: nausea (33%), headache (25%), depression (8%), elevated liver enzymes (2%)

Acamprosate for Alcohol Dependence

- Ethanol inhibits NMDA and mGluR5 glutamate receptors
  - Response: Up-regulation of glutamate receptors resulting in hyper-glutamatergic (excitatory) state
- Acamprosate: thought to be NMDA and mGluR5 receptor antagonist
  - Restores balance between excitatory (GLU) and inhibitory (GABA) systems

Acamprosate for Alcohol Dependence

- Oral dosing: 666 mg three times daily
  - Reduce dose for renal disease and low body weight (< 60 kg)
- Side effects: diarrhea (17%), nausea (4%)
- Recommended to start medication immediately after initiation of abstinence (finished with detoxification)

COMBINE Study (Anton, JAMA, 2006)

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Naltrexone for Alcohol Dependence: Genetics

- A118G single nucleotide polymorphism in OPRM1 (μ-opioid receptor gene)
  - asparagine-to-aspartate amino acid substitution at position 40 (Asn40Asp)
  - G allele (Asp40) in 15% of Caucasian and 4% of African Americans
  - Asp40 may have increased affinity for β-endorphin or reduced receptor levels

OPRM1 genotype is associated with response to naltrexone

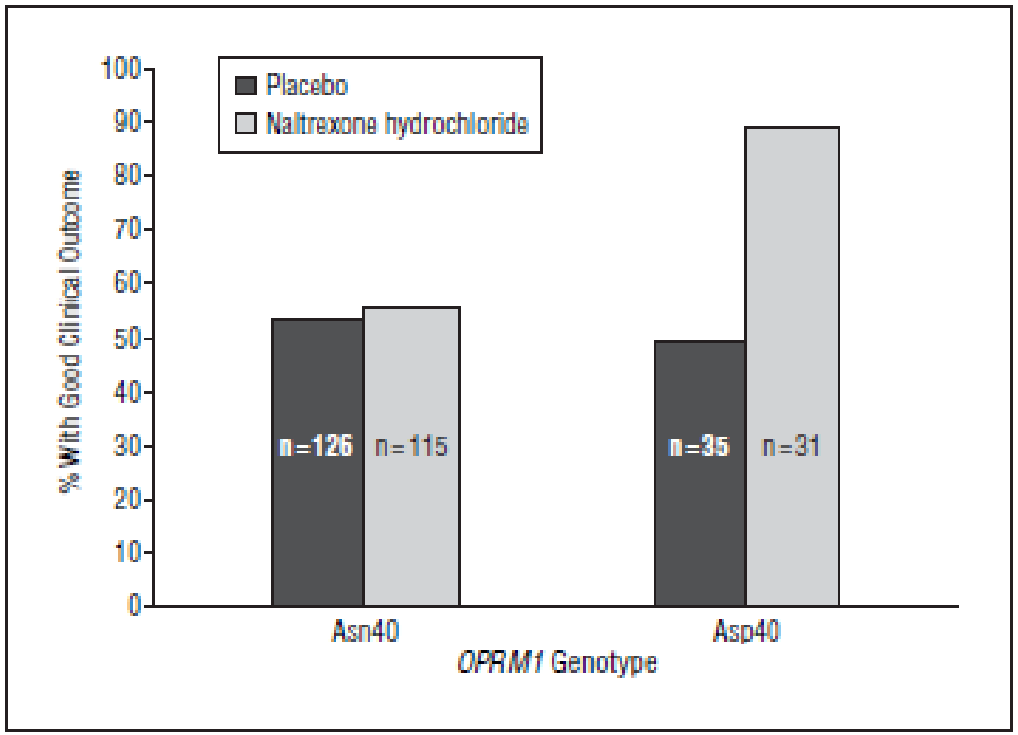

Figure 4. Good clinical outcome based on *OPRM1* and medication group in those receiving medical management alone (no combined behavioral intervention) (test of genotype × medication interaction, $P=.005$). All subjects with missing values were considered not to have a good response. Asn40 includes subjects who were Asn40/Asn40 homozygotes. Asp40 includes those with either Asn40/Asp40 or Asp40/Asp40 genotypes.

From: Anton RF, Arch Gen Psych, 2008

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  - 18% reduction in treatment drop-out (NNT=13; RR (95% CI) = 0.82 (0.70 to 0.97))
  - But 37% of participants discontinued NTX

Acamprosate for Alcohol Dependence: Meta-analysis

- Included 11 European randomized controlled trials (Bouza, 2004)
- Acamprosate (c/w placebo)
  - Increased odds of abstinence (OR (95% CI) = 1.88 (1.57-2.25))
  - Increased duration of abstinence (mean (95% CI) = 26.55 (17.56-35.54) days over placebo)
- Results of US studies mixed- but some show increased odds of complete abstinence (Kranzler and Gage, 2008)

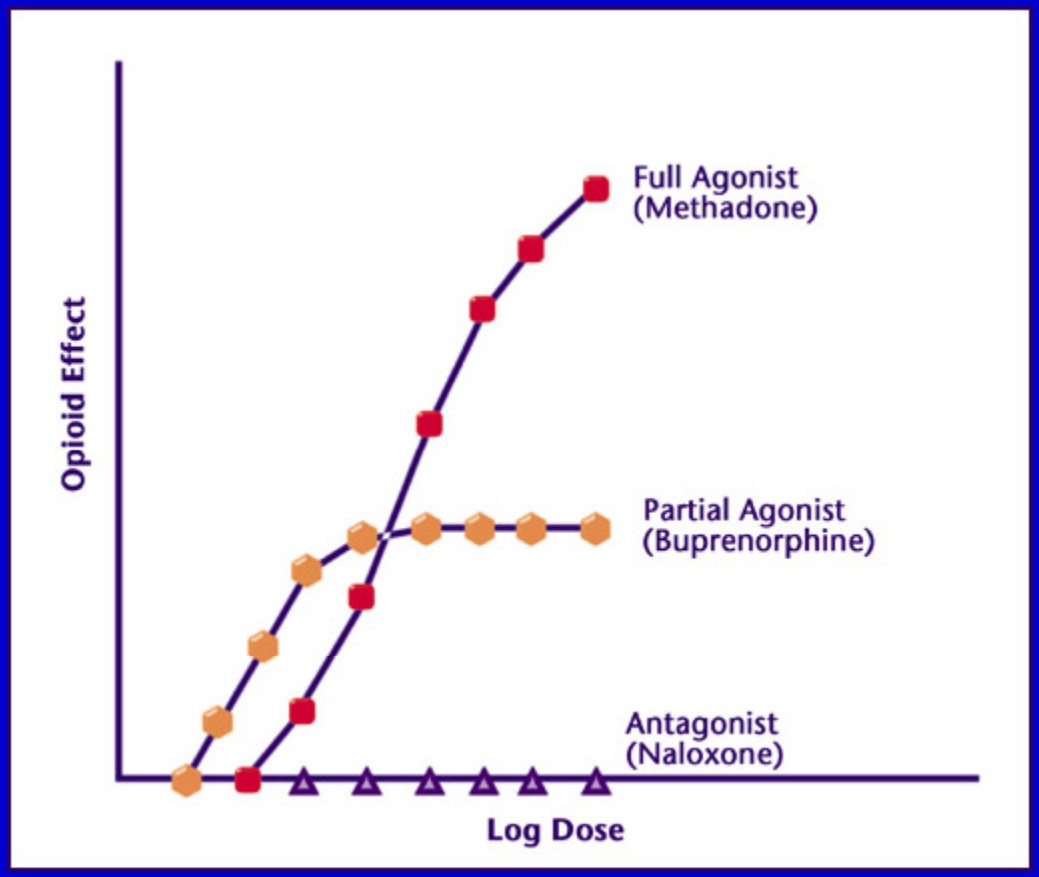
Summary: Approved Medications for Alcohol Dependence

- Naltrexone effective in most trials
  - Delivery by Primary Care Providers effective
  - Compliance can be issue > Vivitrol®?
  - Effect primarily in reduced heavy drinking days (preventing full relapse)
  - Genetics may explain modest effect size
- Acamprosate less consistent in trials
  - Effect primarily in sustaining abstinence (preventing initial lapse)
  - Must be abstinent prior to starting medication

Buprenorphine for Opioid Dependence

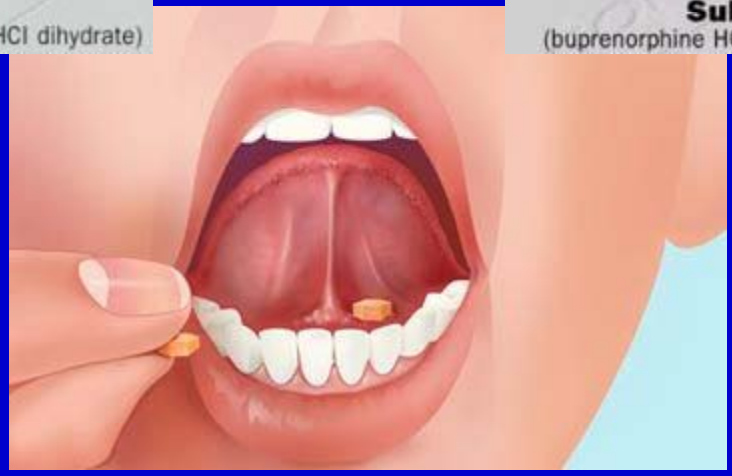
- Buprenorphine: Partial μ-opioid receptor agonist
  - Safety: partial agonist ceiling effect (next slides)
  - Tablets (sublingual): Suboxone® (buprenorphine/naloxone), Subutex® (buprenorphine)
  - Naloxone: Lower diversion risk for Suboxone®
  - High receptor affinity: blocks other opioids, nice taper
- Drug Abuse Treatment Act of 2000
  - DEA Schedule III: qualified MDs can prescribe for office-based treatment of opioid dependence

Buprenorphine: Partial Agonist and Ceiling Effect



From: SAMHSA TIP #40: Buprenorphine Practice Guidelines

Buprenorphine: Sublingual Tablets



Buprenorphine: Treatment Stages

- Induction (Home versus office)
  - Must be in mild-moderate opiate withdrawal (COWS)
  - Short-acting opioids: 12 hours after last dose
  - Methadone: 72 hours after last dose, 40mg or less
- Stabilization
  - Typical dose 16 mg/day (max 32 mg/day)
  - Medication management, counseling, and support
- Maintenance
  - Follow liver function tests
- Taper ("detox")
  - Comfortable compared to other opioids

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Summary: Buprenorphine for Opioid Dependence

- Buprenorphine (>=8mg/day) is effective
- Delivery of treatment in primary care is feasible and effective
- Studies with prescription opioid users needed (expected to exceed heroin use)
- Online certification from ASAM
  - $175 and 8 hours AMA PRA Category 1 CME Credit
  - http://www.asam.org/BuprenorphineCME.html

Methamphetamine- Medication Development

- Bupropion- 2 trials (Shoptaw et al and Elkashef et al) show effect in **intermittent** meth users
- Modafinil- 1 trial with effect in **daily/near daily** meth users (Heinzerling et al) and 1 trial with effect in highly adherent (Shearer et al)
- Current UCLA Trials:
  - Adults: Bupropion and varenicline
  - Adolescents: Bupropion (in East LA)

Audience Participation

- How many medications available for smoking cessation can you name?

Medications Effective for Smoking Cessation

Medication	Quit @ 6 mos
Placebo	14%
Nicotine Patches	23%
Zyban® (bupropion SR)	24%
Nicotine Inhaler	25%
Nicotine Nasal Spray	27%
Patch plus Zyban®	29%
Chantix ® (varenicline)	33%
Patch (>14 weeks) plus *ad lib* gum	37%

Multiple Nicotine Replacement Options Available

Zyban® (bupropion SR)

- Anti-depressant (Wellbutrin)
- Delays (but does not prevent) weight gain
- Side effects:
  - Insomnia
  - Seizure (RARE!)
  - Elevated blood pressure
- Cost: $100/month (generic) and $200/month (brand)

Chantix® (varenicline)

- Side effects:
  - Nausea
  - Insomnia, vivid dreams
- FDA Warning: Reports of depressed mood, agitation, changes in behavior, suicidal ideation, and suicide
- Cost: $130/month

Medications may not be appropriate for certain groups

- Pregnant women
- Light smokers (less than 10 cigarettes per day)
- Adolescent smokers
- Smokeless tobacco users
- Consider seeing a specialist
- Research is underway

Medication alone is NOT effective- counseling/support

- Individual, group, and pro-active telephone counseling are all effective
- Effective counseling incorporates:
  - At least 4 sessions
  - Focus on practical problem solving skills and social support
- Formal (self-help groups) and informal (family/friends) support- STRENGTH IN NUMBERS!

Low Cost Counseling Options

- UCLA Freedom from Smoking Classes: (310) 825-0014
- CA Quitline: 1-800-NO-BUTTS
- American Lung Association Web Site: http://www.ffsonline.org/
- Become An EX: www.BecomeAnEx.org

THANK YOU!

- Questions or comments:
  - Email me: heinzk@ucla.edu
  - Page me: 310-825-6301, ext. 21764
  - On the web: www.uclasarx.org

- To refer a patient for medical treatment of addiction or to participate in a clinical trial:

866-449-UCLA