

# Medication Assisted Treatment Myths, Facts, and Successful Incorporation into Practice

A. Benjamin Srivastava, M.D.

Department of Psychiatry

Washington University School of Medicine



Washington University School of Medicine in St. Louis

# Financial Disclosures

- None

# Addiction: A Public Health Crisis

- In 2015 67 million people reported a past month history of binge drinking and 27 million were current users of other illicit and/or prescription drugs
- Approximately 21 million (10%) of Americans suffer from a substance use disorder
- Significant morbidity and mortality
  - Alcohol contributes to 88,000 deaths yearly
  - 47,000 deaths via drug overdose, 28,000 due to opioids
- Estimated costs of \$400 billion per year (crime, health and hospitalization, lost productivity)

Office of the Surgeon General. Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health. Washington DC: US Dept of Health and Human Services, 2016 November 2016.

# A call to action

- In 2016 the United States Office of the Surgeon General issued a report on the current state of addiction in America
- Large treatment gap: approximately 10% of individuals with SUDs receive treatment
- Many reasons for disparities in treatment, but lack of access is common
- Surgeon General's report called for greater dissemination and implementation of all evidence based treatments

# Definitions

- MAT: Medication assisted treatment (medications in addition to counseling and behavioral therapies)
- OMT: Opioid maintenance therapy (Buprenorphine, Methadone)

*From: SAMHSA*

# Evidenced Based Pharmacotherapy

- Alcohol use disorder
  - Disulfiram
  - Naltrexone
  - Acamprosate
- Opioid use disorder
  - Naltrexone
  - Buprenorphine
  - Methadone
- Tobacco use disorder
  - Nicotine Replacement Therapy
  - Bupropion
  - Varenicline

# Pharmacotherapy for smoking cessation

- Nicotine replacement therapy
  - Delivers nicotine during times of abstinence
  - Mitigates physical and psychological withdrawal
- Bupropion (NDRI)
  - Repletion of mesolimbic dopamine that is depleted during nicotine withdrawal
- Varenicline ( $\alpha 4\beta$  nicotinic cholinergic receptor partial agonist)
  - $\alpha 4$  and beta  $2\beta$  nicotinic cholinergic receptors in the VTA are indispensable for rewarding effects of Nicotine
  - Partial agonism with varenicline satiates cravings and mitigates withdrawal symptoms

**Srivastava, A.B.** and Gold, M.S. Translating Neurobiology into Practice in Tobacco, Alcohol, Drug, and Behavioral Addictions. In: *Translational Medicine in CNS Drug Development*. Elsevier, Inc. 2017 (SUBMITTED, TO BE PUBLISHED)

# Smoking and AA





# Smoking and AA

From: "The Family Afterward" *Alcoholics Anonymous* pp 133, 135

THE FAMILY AFTERWARD

133

each family play together or separately, as much as their circumstances warrant. We are sure God wants us to be happy, joyous, and free. We cannot subscribe to the belief that this life is a vale of tears, though it once was just that for many of us. But it is clear that

unity to demonstrate His omnipotence.

Now about health: A body badly burned by alcohol does not often recover overnight nor do twisted thinking and depression vanish in a twinkling. We are convinced that a spiritual mode of living is a most powerful health restorative. We, who have recovered from serious drinking, are miracles of mental health. But we have seen remarkable transformations in our bodies. Hardly one of our crowd now shows any mark of dissipation.

But this does not mean that we disregard human health measures. God has abundantly supplied this world with fine doctors, psychologists, and practitioners of various kinds. Do not hesitate to take your health problems to such persons. Most of them give freely of themselves, that their fellows may enjoy sound minds and bodies. Try to remember that though God has wrought miracles among us, we should never belittle a good doctor or psychiatrist. Their services are often indispensable in treating a newcomer and in following his case afterward.

ing upon a doctor's advice. He thought all alcoholics

THE FAMILY AFTERWARD

135

Whether the family goes on a spiritual basis or not, the alcoholic member has to if he would recover. The

Here is a case in point: One of our friends is a heavy smoker and coffee drinker. There was no doubt he over-indulged. Seeing this, and meaning to be helpful, his wife commenced to admonish him about it. He admitted he was overdoing these things, but frankly said that he was not ready to stop. His wife is one of those persons who really feels there is something rather sinful about these commodities, so she nagged, and her intolerance finally threw him into a fit of anger. He got drunk.

Of course our friend was wrong—dead wrong. He had to painfully admit that and mend his spiritual fences. Though he is now a most effective member of Alcoholics Anonymous, he still smokes and drinks coffee, but neither his wife nor anyone else stands in judgment. She sees she was wrong to make a burning issue out of such a matter when his more serious ailments were being rapidly cured.

We have three little mottoes which are apropos.

LOVE AND LET LOVE

*Easy Does It.*

## Coffee and Cigarette Consumption and Perceived Effects in Recovering Alcoholics Participating in Alcoholics Anonymous in Nashville, Tennessee

Michael S. Reich, Mary S. Dietrich, Alistair James Reid Finlayson, Edward F. Fischer, and Peter R. Martin

- 289 AA members surveyed for alcohol, tobacco, and caffeine use
- 56.9% smoked cigarettes
  - Lower than previous estimates (80-95%)
  - 78.7% smoked at least 1/2 PPD
  - Over 60% considered “highly dependent” or “very highly dependent”

Reich MS, Dietrich MS, Finlayson AJR, Fischer EF, Martin PR. Coffee and cigarette consumption and perceived effects in recovering alcoholics participating in alcoholics anonymous in Nashville, TN. *Alcohol Clin Exp Res* 2008;32:1799–1806

# Smoking and Addiction Treatment

- Over 65% of individuals seeking substance treatment smoke cigarettes
- Only ~40% of addiction treatment centers integrate smoking cessation into treatment
  - Related to institutional, state level, and financial factors
- Approximately 50% of deaths following substance treatment are tobacco related
- Integrating smoking cessation into treatment can improve cessation rates without negatively impacting treatment course

Shi Y, Cummins SE. Smoking cessation services and smoke-free policies at substance abuse treatment facilities: national survey results. *Psychiat Serv.* 2015;66(6):610–16.

Hurt RD, Offord KP, Croghan IT, et al. Mortality following inpatient addictions treatment. Role of tobacco use in a community-based cohort. *JAMA.* 1996;275:1097-1103



Regular article

## The implementation of tobacco-related brief interventions in substance abuse treatment: A national study of counselors

Hannah K. Knudsen, (Ph.D.)<sup>a,\*</sup>, Jamie L. Studts, (Ph.D.)<sup>b</sup>

<sup>a</sup>Department of Behavioral Science and Center on Drug and Alcohol Research, University of Kentucky, 109 Medical Behavioral Science Building, Lexington, KY 40536-0086, USA

<sup>b</sup>Department of Behavioral Science, University of Kentucky, 127 Medical Behavioral Science Building, Lexington, KY 40536-0086, USA

Received 17 July 2009; received in revised form 14 December 2009; accepted 31 December 2009

- Over 2000 addiction counselors surveyed
- Counselors who encountered organizational barriers engaged in less routine implementation brief interventions
- Counselors aware of Public Health Services guidelines reported greater implementation
- Lower implementation among counselors who smoked

Knudsen HK, Studts JL (2010) The implementation of tobacco-related brief interventions in substance abuse treatment: a national study of counselors. *J Subst Abuse Treat* 38:212–219.



ELSEVIER

## Drug and Alcohol Dependence

journal homepage: [www.elsevier.com/locate/drugalcdep](http://www.elsevier.com/locate/drugalcdep)



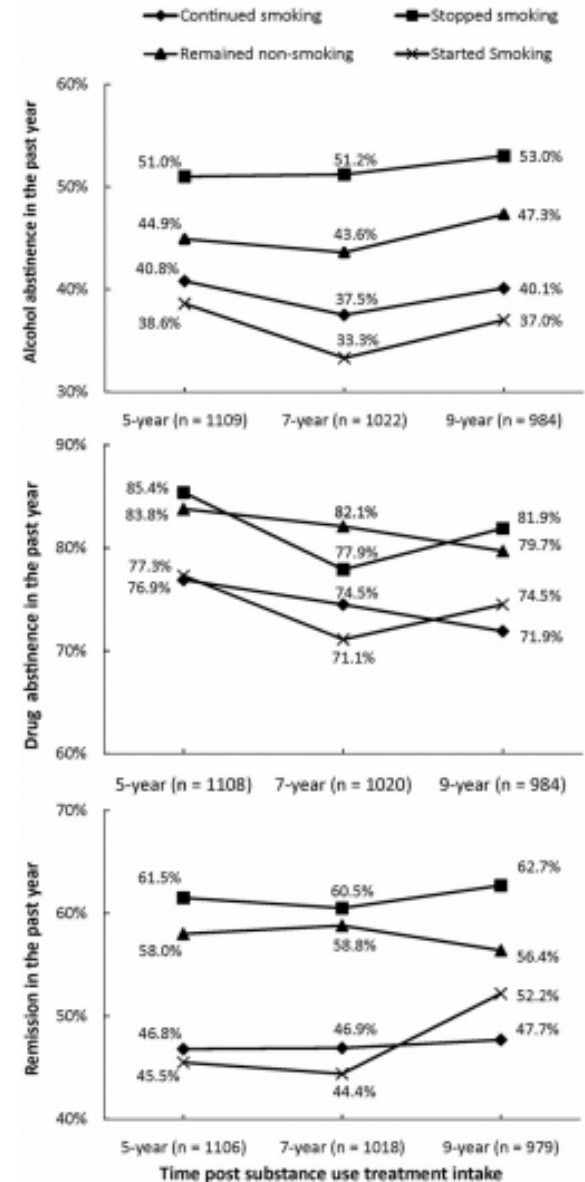
### Stopping smoking during first year of substance use treatment predicted 9-year alcohol and drug treatment outcomes

Janice Y. Tsoh<sup>a,\*</sup>, Felicia W. Chi<sup>b</sup>, Jennifer R. Mertens<sup>b</sup>, Constance M. Weisner<sup>a,b</sup>

<sup>a</sup> Department of Psychiatry, University of California, San Francisco, 401 Parnassus Ave (0984-TRC), San Francisco, CA 94143-0984, United States

<sup>b</sup> Division of Research, Kaiser Permanente Northern California, 2000 Broadway, 3rd Floor, Oakland, CA 94612-2403, United States

- Quitting smoking at 1 year predicted past year abstinence of drugs or drugs+EtOH
- Quitting smoking during the first year predicted 9 year abstinence from drugs and remission from drugs+alcohol
- Quitting smoking during the first year predicted long term alcohol abstinence for drug dependent subjects



---

**Neuropsychiatric safety and efficacy of varenicline, bupropion, and nicotine patch in smokers with and without psychiatric disorders (EAGLES): a double-blind, randomised, placebo-controlled clinical trial**



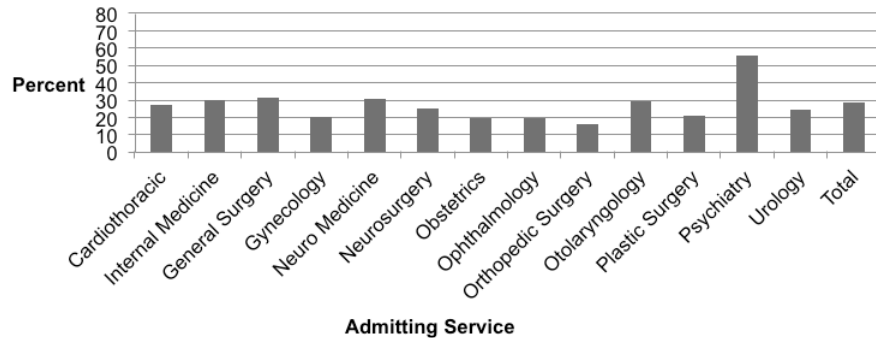
Robert M Anthenelli, Neal L Benowitz, Robert West, Lisa St Aubin, Thomas McRae, David Lawrence, John Ascher, Cristina Russ, Alok Krishen, A Eden Evins

- RCT involving over 8000 subjects evaluating efficacy and side effect profiles of varenicline, NRT, and Bupropion
- Greatest 12 abstinence rates from varenicline; both bupropion and NRT were superior to placebo
- No increase in adverse, neuropsychiatric with any medication vs placebo
- Significant side effects GI upset (varenicline), insomnia (bupropion), abnormal dreams (NRT), and headache (placebo)

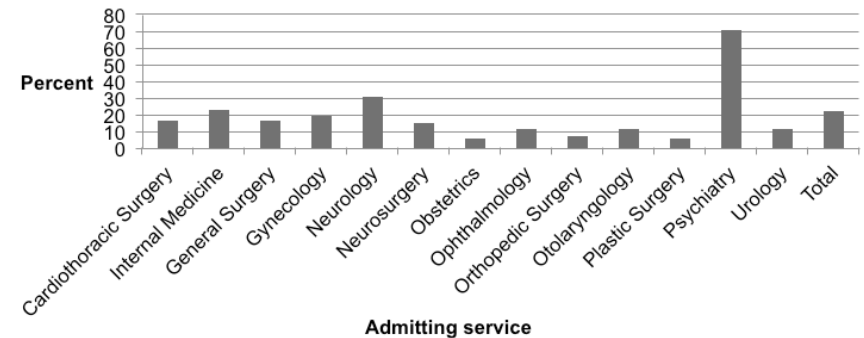
Anthenelli RM Benowitz NL West R et al . Neuropsychiatric safety and efficacy of varenicline, bupropion, and nicotine patch in smokers with and without psychiatric disorders (EAGLES): a double-blind, randomised, placebo-controlled clinical trial. *Lancet* . 2016;387(10037):2507–2520.

# Hospital Smoking: an example?

Smoking by Service 2010-2015



Prescriptions by Service 2010-2015



- Differential patterns of both smoking and prescriptions among patients
- Cancer patients prescribed pharmacotherapy less than non-cancer patients
- Differences among age, gender, race
- Avenues for implementation: EMR/protocolization

Srivastava, et al 2017. IN PREPARATION

# ...But in the long term?

Research

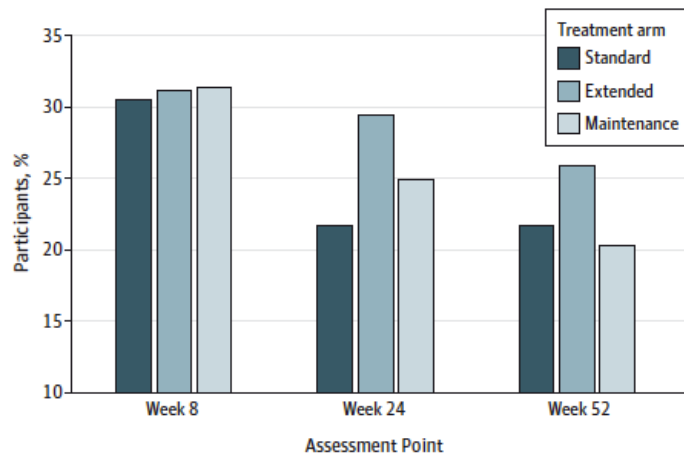
Original Investigation

## Long-term Nicotine Replacement Therapy A Randomized Clinical Trial

Robert A. Schnoll, PhD; Patricia M. Goelz, MPH; Anna Veluz-Wilkins, MA; Sonja Blazekovic, BA;  
Lindsay Powers, MA; Frank T. Leone, MD; Peter Gariti, PhD; E. Paul Wileyto, PhD; Brian Hitsman, PhD

- 525 patients randomized to 8, 24, or 52 weeks of NRT
- At 24 weeks continued NRT was more efficacious
- Treatment effect not present at 52 weeks

Figure 2. Seven-Day Point Prevalence Abstinence Rates by Treatment Arm and Assessment Point



R.A. Schnoll, P.M. Goelz, A. Veluz-Wilkins, S. Blazekovic, L. Powers, F.T. Leone, P. Gariti, E.P. Wileyto, B. Hitsman. A randomized clinical trial of long-term nicotine replacement therapy in a community-based sample of smokers  
JAMA Intern. Med., 175 (2015), pp. 504–511



# Sustained-Release Bupropion for Pharmacologic Relapse Prevention after Smoking Cessation

## A Randomized, Controlled Trial

J. Taylor Hays, MD; Richard D. Hurt, MD; Nancy A. Rigotti, MD; Raymond Niaura, PhD; David Gonzales, PhD; Michael J. Durcan, PhD; David P.L. Sachs, MD; Troy D. Wolter, MS; A. Sonia Buist, MD; J. Andrew Johnston, PhD; and Jonathan D. White, MS

- RCT of 429 patients comparing bupropion vs placebo regarding long term abstinence
- Significantly higher abstinence rates in bupropion group at 52 weeks (55.1% vs 42.3%;  $p=.008$ )
- Difference disappears at 104 weeks (41.6% vs 40.0 weeks)

Hays JT, Hurt RD, Rigotti NA, et al. 2001. Sustained-release bupropion for pharmacologic relapse prevention after smoking cessation: a randomized, controlled trial. *Ann. Intern. Med.* 135:423–33

## Effect of Maintenance Therapy With Varenicline on Smoking Cessation

A Randomized Controlled Trial

- 52 week RCT demonstrating improved abstinence with varenicline compared to placebo (43.6% vs 36.9%; OR, 1.34; 95%)

Tonstad S, Tønnesen P, Hajek P, Williams KE, Billing CB, Reeves KR; Varenicline Phase 3 Study Group. Effect of maintenance therapy with varenicline on smoking cessation: a randomized controlled trial. *JAMA*. 2006;296(1):64-71.

Original Investigation

**Combination Varenicline and Bupropion SR for Tobacco-Dependence Treatment in Cigarette Smokers  
A Randomized Trial**

Jon O. Ebbert, MD, MSc; Dorothy K. Hatsukami, PhD; Ivana T. Croghan, PhD; Darrell R. Schroeder, MS; Sharon S. Allen, MD; J. Taylor Hays, MD; Richard D. Hurt, MD

Ebbert JO, Hatsukami DK, Croghan IT, et al. 2014. Combination varenicline and bupropion SR for tobacco-dependence treatment in cigarette smokers: a randomized trial. JAMA 311:155–63

- RCT comparing varenicline with bupropion vs varenicline +placebo
- No difference in abstinence rates at 52 weeks (varenicline+bupropion 30.9%; varenicline +placebo 24.5%)

Original Investigation

**Effects of Nicotine Patch vs Varenicline vs Combination Nicotine Replacement Therapy on Smoking Cessation at 26 Weeks  
A Randomized Clinical Trial**

Timothy B. Baker, PhD; Megan E. Piper, PhD; James H. Stein, MD; Stevens S. Smith, PhD; Daniel M. Bolt, PhD; David L. Fraser, MS; Michael C. Fiore, MD, MPH, MBA

Baker TB, Piper ME, Stein JH, Smith SS, Bolt DM, Fraser DL, et al. Effects of Nicotine Patch vs Varenicline vs Combination Nicotine Replacement Therapy on Smoking Cessation at 26 Weeks: A Randomized Clinical Trial. JAMA. 2016;315(4):371–9

- RCT comparing combined NRT with NRT patch with Varenicline
- No difference in quit rates at 52 weeks (patch 20.8%, Varenicline 19.1%, C-NRT 20.2%)

# The Past, Present, and Future of Nicotine Addiction Therapy

Judith J. Prochaska<sup>1</sup> and Neal L. Benowitz<sup>2</sup>

<sup>1</sup>Stanford Prevention Research Center, Department of Medicine, Stanford University, Stanford, California 94305; email: JPro@Stanford.edu

<sup>2</sup>Departments of Medicine and Bioengineering & Therapeutic Sciences, Division of Clinical Pharmacology and Experimental Therapeutics, University of California, San Francisco, California 94143; email: Neal.Benowitz@ucsf.edu

Prochaska JJ, Benowitz NL. The past, present, and future of nicotine addiction therapy. *Annu Rev Med* 2016;67:467–86.

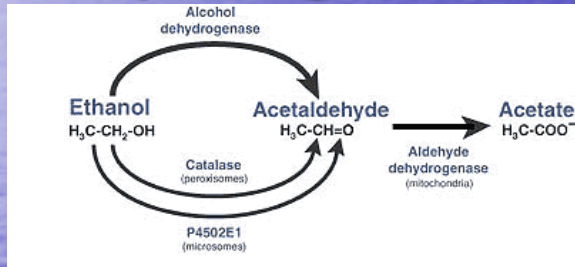
“Nicotine addiction is a chronic, relapsing disorder for many smokers, necessitating ongoing care. Increasing quit rates will likely require a combination of counseling and personalized medications, with a chronic disease management approach, supported by healthcare policies that make tobacco use costly and inconvenient and nonsmoking the norm.”

# Reductions in Smoking: A Public Health Success

- Cigarette smoking in the US has declined dramatically, from 20.9% in 2005 to 15.1% in 2015
  - Tobacco tax increases
  - Smoke-free air policies (workplace, restaurants)
1. CDC.gov
  2. Hahn EJ. Smokefree legislation: a review of health and economic outcomes research. Am J Prev Med 2010;39:S66–76

# Disulfram

- Competitive inhibitor of acetaldehyde dehydrogenase



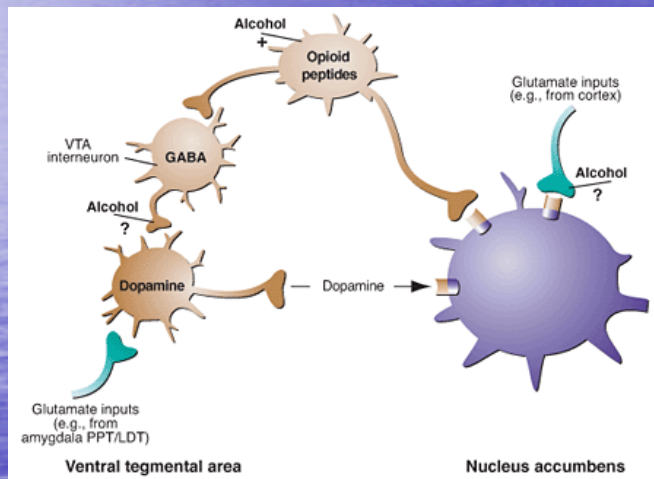
*From: NIAAA*

- Compared to placebo improves short term abstinence
- Prolongs time to relapse
- Reduces number of drinking days

Jorgensen CH, Pedersen B, Tonnesen H. The efficacy of disulfiram for the treatment of alcohol use disorder. *Alcoholism, clinical and experimental research*. 2011;35(10):1749-58

# Naltrexone

- Mu opioid receptor antagonist



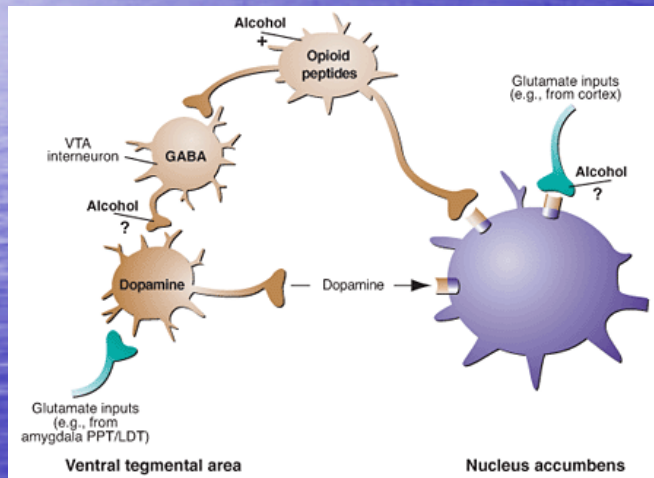
*Courtesy: NIAAA*

- Variable effects in different studies
- Consistent findings of delays in returning to drinking after abstinence
- Reduction in heavy drinking days
- Available in IM formulation to improve compliance

Jonas DE, Amick HR, Feltner C, et al. Pharmacotherapy for adults with alcohol use disorders in outpatient settings: A systematic review and meta-analysis. *Jama*. 2014;311(18):1889-900.

# Acamprosate

- Mechanism not completely elucidated; possibly up-regulates GABA and down regulates glutamate



- Variable clinical effects
- Prolongs time to relapse
- Hypothesized to reduce post acute withdrawal anxiety based on animal models

Jonas DE, Amick HR, Feltner C, et al. Pharmacotherapy for adults with alcohol use disorders in outpatient settings: A systematic review and meta-analysis. *Jama*. 2014;311(18):1889-900.



# Current Trends and Practices

- NIDA recommends that pharmacotherapy should be considered for every patient
- Even so, only ~15% of treatment facilities use evidence based pharmacotherapy
  - Philosophy of treatment program
  - Personal biases
  - Lack of training
  - Specialty of physician prescribing



## Pharmacotherapy for Alcohol Use Disorders: Physicians' Perceptions and Practices

Caridad Ponce Martinez<sup>1</sup>, Priyanka Vakkalanka<sup>2</sup> and Nassima Ait-Daoud<sup>3\*</sup>

<sup>1</sup>Department of Psychiatry, Yale School of Medicine, New Haven, CT, USA, <sup>2</sup>Department of Emergency Medicine, University of Virginia, Charlottesville, VA, USA, <sup>3</sup>Department of Psychiatry and Neurobehavioral Sciences, University of Virginia, Charlottesville, VA, USA

- Anonymous, nationwide survey sent to family medicine physicians and psychiatrists
- Psychiatrists were more likely to use pharmacotherapy
- Physicians with more experience were more likely to use pharmacotherapy
- Family medicine physicians had more concerns with efficacy and costs
- Family medicine physicians were more likely to refer patients to AA/other 12 Step programs
- All physicians would increase use with increased training

Ponce Martinez C, Vakkalanka P and Ait-Daoud N (2016) Pharmacotherapy for Alcohol Use Disorders: Physicians' Perceptions and Practices. *Front. Psychiatry* 7:182. doi: 10.3389/fpsy.2016.00182

# Combined Pharmacotherapies and Behavioral Interventions for Alcohol Dependence

The COMBINE Study: A Randomized Controlled Trial

- RCT involving >1000 subjects examining time to relapse and % days abstinent from alcohol comparing NTX, acamprosate, combination, with or without CBI
- Overall Naltrexone, CBI, or Naltrexone +CBI resulted in improved drinking outcomes (no added benefit with acamprosate)

Anton RF, O'Malley SS, Ciraulo DA, Cisler RA, Couper D, Donovan DM, Gastfriend DR, Hosking JD, Johnson BA, LoCastro JS, Longabaugh R, Mason BJ, Mattson ME, Miller WR, Pettinati HM, Randall CL, Swift R, Weiss RD, Williams LD, Zweben A. Combined pharmacotherapies and behavioral interventions for alcohol dependence: the COMBINE study: a randomized controlled trial. *JAMA*. 2006;295:2003-17.

## What happens when people discontinue taking medications? Lessons from COMBINE

**Robert L. Stout<sup>1</sup>, Jordan M. Braciszewski<sup>1</sup>, Meenakshi Sabina Subbaraman<sup>2</sup>, Henry R. Kranzler<sup>3</sup>, Stephanie S. O'Malley<sup>4</sup>, Daniel Falk<sup>5</sup> in collaboration with the ACTIVE group**

Decision Sciences Institute, Pacific Institute for Research and Evaluation, Pawtucket, RI, USA,<sup>1</sup> Alcohol Research Group, University of California at Berkeley School of Public Health, Berkeley, CA, USA,<sup>2</sup> University of Pennsylvania, Philadelphia, PA, USA,<sup>3</sup> Yale University, New Haven, CT, USA<sup>4</sup> and Division of Treatment and Recovery Research, National Institute on Alcohol Abuse and Alcoholism, Rockville, MD, USA<sup>5</sup>

“A patient’s decision to stop taking medications during alcohol treatment appears to take place during a weeks-long process of disengagement from treatment. Patients who discontinue medications early in treatment or without medical consultation appear to drink more frequently and more heavily.”

Stout RL, Braciszewski JM, Subbaraman MS, Kranzler HR, O'Malley SS, Falk D. What happens when people discontinue taking medications? Lessons from COMBINE. *Addiction* 2014;109:2044–52.

# Lessons Learned from Translational Research

- Detoxification: Crucial for preventing most severe forms of withdrawal (seizures, DTs) but is insufficient for long term abstinence
- Inpatient rehabilitation can be beneficial; however given heterogeneity in treatment culture and lack of systematic long term follow up can limit conclusions drawn from reported success rates

# Methadone

- Full MOR agonist
- Long half life (8-150 hours) and variable blood levels
- Must be dispensed at a licensed clinic
- Concerns for respiratory depression when combined with CNS sedating agents

# Buprenorphine (and Subutex and Suboxone)

NDC 12496-1208-1  
1 sublingual film

8 mg/2 mg 

***Suboxone***<sup>®</sup>  
(buprenorphine and naloxone) sublingual film  
8 mg/2 mg

**Rx only**

Children who accidentally take SUBOXONE will need emergency medical care. Keep SUBOXONE out of the reach of children.

[suboxone.com](http://suboxone.com)





# Getting a Buprenorphine Waiver

- Board certification in addiction psychiatry
- Addiction certification from ASAM
- Addiction medicine board certification from AOA
- At least eight hours of training in management of opioid use disorders
- Participate as investigator in a clinical trial for a Schedule III, IV, or V narcotic used for detox or OMT
- Other training that state medical board deems appropriate for managing patients with OUD
- Other training that HHS deems appropriate for managing patients with OUD

# Buprenorphine (and Methadone)

- Both improve abstinence and treatment retention (MTD>Bup)
- Both reduce transmission of Hepatitis C and HIV
- Both are safe in pregnancy
  - Methadone has better treatment retention rates
  - Buprenorphine has a less protracted Neonatal Abstinence Syndrome
- When either is stopped, relapse rates dramatically increase

Connery HS. Medication-assisted treatment of opioid use disorder: review of the evidence and future directions. *Harvard review of psychiatry*. 2015;23(2): 63-75

# Probuphine

- 6 month implantable formulation of Buprenorphine
- Possibly comparable abstinence rates (non inferiority) to sublingual buprenorphine
- Cost \$4950/6 months

Buprenorphine implants (probuphine) for opioid dependence. *Jama*. 2016;316(17): 1820-1.

Rosenthal R. (2017). Sensitivity analysis of a comparative trial of 6 month buprenorphine implants (probuphine) and sublingual buprenorphine in stable opioid-dependent patients. *Drug and Alcohol Dependence*. 171. p.e179.

# Naltrexone (again)

- Oral formulation has poor compliance rates, increased severity of relapse
- Weak evidence for IM formulation (one RCT with open label extension)
- No abuse potential; does not decrease respiratory drive

# Common beliefs about OMT

- “It substitutes one drug for another”
  - Essentially true
- “Using Buprenorphine is not real Recovery”
  - False, if used in the context of a recovery program
- “Patients will sell their Suboxone”
  - True, but rare
- “Naltrexone is more appropriate than buprenorphine”
  - True for MDs
- “Medications are not effective”
  - False; insofar as medication compliance is maintained

# Common reasons for not prescribing OMT

- OMT is underutilized in substance treatment settings (30%)
  - State regulations (10-78%)
  - Lack of funding (financing, reimbursing) (60-71%)
  - Lack of adequately trained physicians/staff (30-60%)
  - Inconsistent philosophically (30-40%)
  - Belief that treatment won't work (20-40%)

Knudsen HK, Abraham AJ, Oser CB. Barriers to the implementation of medication-assisted treatment for substance use disorders: the importance of funding policies and medical infrastructure. *Evaluation and Program Planning*. 2011;34(4):375–381.



### Buprenorphine Treatment and 12-step Meeting Attendance: Conflicts, Compatibilities, and Patient Outcomes



Laura B. Monico, M.A. <sup>a,\*</sup>, Jan Gryczynski, Ph.D. <sup>a</sup>, Shannon Gwin Mitchell, Ph.D. <sup>a</sup>, Robert P. Schwartz, M.D. <sup>a</sup>, Kevin E. O'Grady, Ph.D. <sup>b</sup>, Jerome H. Jaffe, M.D. <sup>a,c</sup>

<sup>a</sup> Friends Research Institute, 1040 Park Ave., Suite 103, Baltimore, MD, 21201, USA

<sup>b</sup> Department of Psychology, University of Maryland, Biology/Psychology Building, College Park, MD, 20742, USA

<sup>c</sup> University of Maryland School of Medicine, Department of Psychiatry, 110 South Poca St. 4th floor, Baltimore, MD, USA

Monico LB, et al. Buprenorphine treatment and 12-step meeting attendance: conflicts, compatibilities, and patient outcomes. J Subst Abuse Treat. 2015;57:89–95.

- Prospective, randomized examination of outcomes related to 12 Step attendance in OMT program
- Number of meetings attended correlated with greater retention in treatment/abstinence at 6 month follow up
- Required meeting attendance did not have effects on outcomes
- Many participants felt stigma from being on OMT in 12 Step meetings
  - Buprenorphine is a “crutch”
  - Using OMT equates to not being “clean”
  - Participants chose meetings based on relative acceptance of Bup
  - Bup was considered generally more acceptable than MTD in 12 Step meetings

## A Randomized Trial of Cognitive Behavioral Therapy in Primary Care-based Buprenorphine

David A. Fiellin, MD,<sup>a</sup> Declan T. Barry, PhD,<sup>b</sup> Lynn E. Sullivan, MD,<sup>a</sup> Christopher J. Cutter, PhD,<sup>a</sup>  
Brent A. Moore, PhD,<sup>b</sup> Patrick G. O'Connor, MD, MPH,<sup>a</sup> Richard S. Schottenfeld, MD<sup>b</sup>

<sup>a</sup>Department of Internal Medicine and <sup>b</sup>Department of Psychiatry, Yale University School of Medicine, New Haven, Conn.

- Prospective, RCT looking at effects of CBT and Bup treatment
- Patients randomized to either Bup or CBT +Bup
- No group differences in frequency of opioid use reduction (5.3 to.4 days/week), abstinence, or study completion

Fiellin DA, et al. A randomized trial of cognitive behavioral therapy in primary care-based buprenorphine. *Am J Med.* 2013;126(1):74 e11–74 e17.





### Buprenorphine Treatment and 12-step Meeting Attendance: Conflicts, Compatibilities, and Patient Outcomes



Laura B. Monico, M.A.<sup>a,\*</sup>, Jan Gryczynski, Ph.D.<sup>a</sup>, Shannon Gwin Mitchell, Ph.D.<sup>a</sup>, Robert P. Schwartz, M.D.<sup>a</sup>, Kevin E. O'Grady, Ph.D.<sup>b</sup>, Jerome H. Jaffe, M.D.<sup>a,c</sup>

<sup>a</sup> Friends Research Institute, 1040 Park Ave., Suite 103, Baltimore, MD, 21201, USA

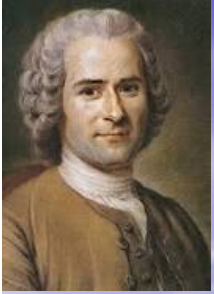
<sup>b</sup> Department of Psychology, University of Maryland, Biology/Psychology Building, College Park, MD, 20742, USA

<sup>c</sup> University of Maryland School of Medicine, Department of Psychiatry, 110 South Poca St. 4th floor, Baltimore, MD, USA

Cicero TJ, Ellis MS, Surratt HL, Kurtz SP. Factors contributing to the rise of buprenorphine misuse: 2008-2013. *Drug Alcohol Depen.* 2014;142:98–104.

- Buprenorphine is the 4<sup>th</sup> most commonly diverted opioid (33%)
- Reasons for diversion
  - Maintain abstinence from DOCs (63%)
  - DOC not available (60%)
  - Known lack of access to other drugs (60%)
- Is naloxone a deterrent?
  - 61.8% injected buprenorphine tablets
  - 43.6% injected combination tablets
  - 32.1% injected oral films

“Participants reported a number of simple and easy methods, unethical to specify in this paper, which they believed separated buprenorphine from naloxone, resulting in what they termed “pure buprenorphine” for injection.”



# France: A Model or Warning?

*“I warn the reader that this chapter requires careful reading; and that I am unable to make myself clear to those who refuse to be attentive” –Jean-Jacques Rousseau, *The Social Contract*; Book III, Chapter I*

- In 1996 France allowed all physicians to prescribe buprenorphine (single formulation) without restriction
- Heroin overdose were reduced by 80% over 12 years
- HIV among IV drug users fell from 25% to 6% from the mid 1990s to 2010

...HOWEVER....

- Increase in overall drug-induced deaths 2003-2010; decreased from 2012-2013.
  - Mainly heroin and MTD overdoses
  - OPIOID SUBSTITUTION MEDICATIONS INVOLVED IN 54% OF DEATHS IN 2013
- In 2004 prevalence of Hep C was 73.8% among IVD users; in 2012 self reported Hep C was down to 7.6%

1. Polomeni P, Schwan R: Management of opioid addiction with buprenorphine: French history and current management. *Int J Gen Med.* 2014;7:143–8.
2. Lofwall MR, Walsh SL. A review of buprenorphine diversion and misuse: the current evidence base and experiences from around the world. *J Addict Med.* 2014;8(5):315–326.
3. European Monitoring Centre for Drugs and Addiction <http://www.emcdda.europa.eu/countries/france>

Special article

Setting the standard for recovery: Physicians' Health Programs

Robert L. DuPont, (M.D.)<sup>a</sup>, A. Thomas McLellan, (Ph.D.)<sup>b,\*</sup>, William L. White, (M.A.)<sup>c</sup>,  
Lisa J. Merlo, (Ph.D.)<sup>d</sup>, Mark S. Gold, (M.D.)<sup>d</sup>

<sup>a</sup>Institute for Behavior and Health, Rockville, MD, USA

<sup>b</sup>Treatment Research Institute, Philadelphia PA, USA

<sup>c</sup>Chestnut Health Systems, Bloomington IL, USA

<sup>d</sup>Department of Psychiatry, University of Florida, Gainesville, FL, USA

Received 22 October 2007; received in revised form 4 January 2008; accepted 8 January 2008

DuPont R. L., McLellan A. T., White W. L., Merlo L., Gold M. S. Setting the standard for recovery: Physicians Health Programs evaluation review. *J Subst Abuse Treat* 2009; 36:159–71.

- Survey of over 900 physicians admitted to state PHPs for 5 year monitoring for SUDs
- Integrative care with intensive monitoring and support
- 78% 5 year UDS confirmed abstinence rate
- 72% return to work rate
- Physicians with OUDs were just as likely as other physicians to be successful in 5 year PHP enrollment (Merlo et al 2016)

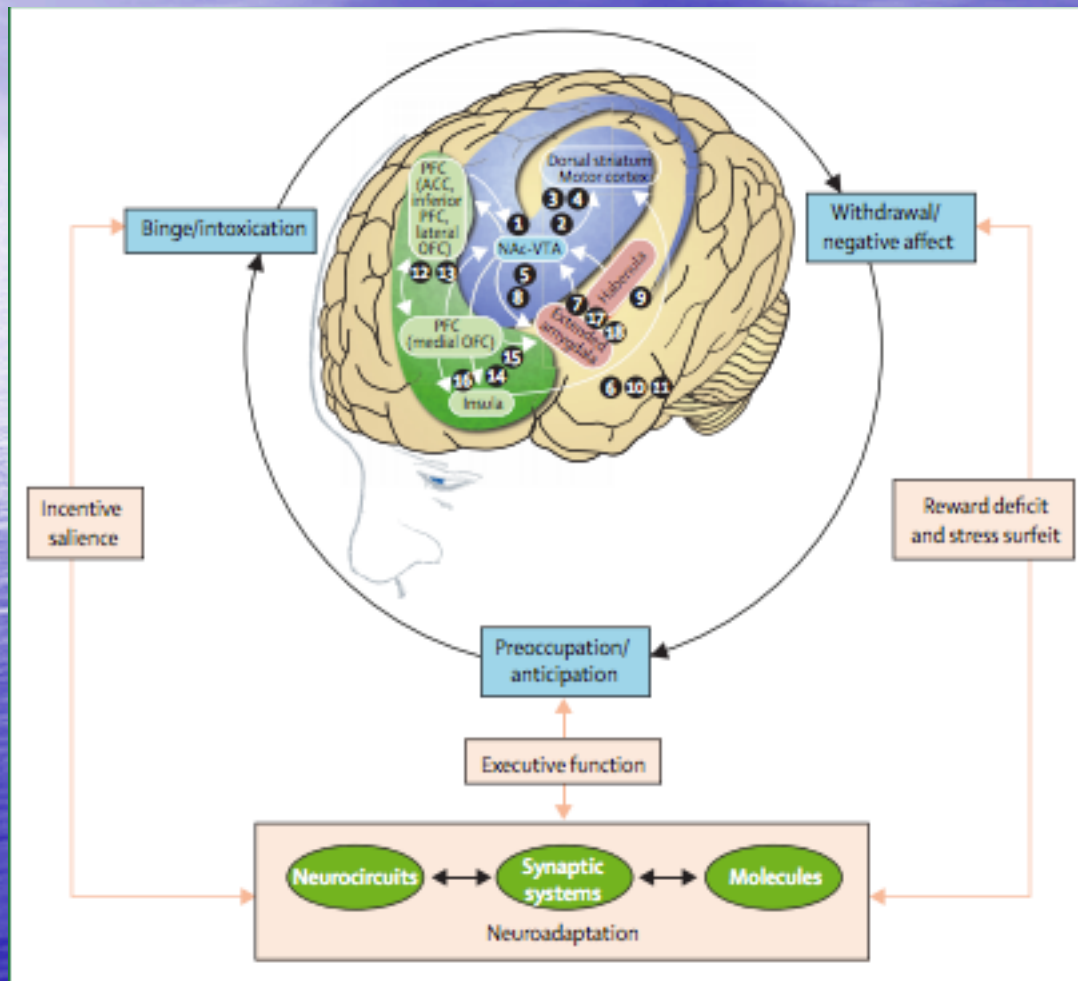
# Individualized “real world” Recovery programs

- MD, RN, Therapists, Recovery advisor
- Tailored to meet patients needs
- UDS, GPS trackers
- Access to pharmacotherapy
- \$38,000/year (about one month of residential treatment)



# Neurobiology of addiction: a neurocircuitry analysis

George F Koob, Nora D Volkow



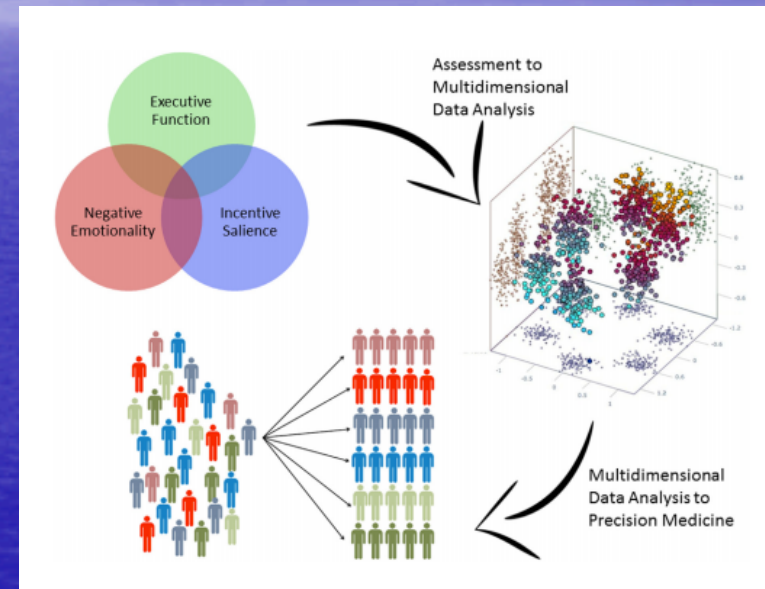
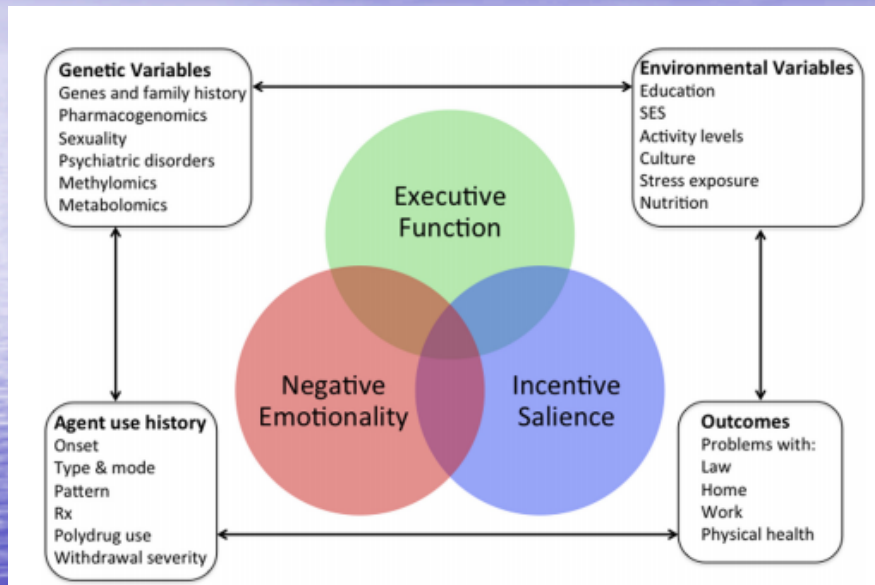
Koob GF, Volkow ND. Neurobiology of addiction: a neurocircuitry analysis. *Lancet Psychiatry*. 2016;3(8):760–773. doi: 10.1016/S2215-0366(16)00104-8.

## Review

Biological  
Psychiatry

### Addictions Neuroclinical Assessment: A Neuroscience-Based Framework for Addictive Disorders

Laura E. Kwako, Reza Momenan, Raye Z. Litten, George F. Koob, and David Goldman



Kwako LE, Momenan R, Litten RZ, Koob GF, Goldman D. Addictions neuroclinical assessment: a neuroscience-based framework for addictive disorders. *Biol Psychiatry* (2016) 80:179–89. [10.1016/j.biopsych.2015.10.024](https://doi.org/10.1016/j.biopsych.2015.10.024)

# Conclusions

- Addiction is America's number one public health problem accounting for significant morbidity and mortality
- Addiction is also a chronic, complex brain disorder affecting multiple networks and processes
- Pharmacotherapy can be a useful part of addiction treatment and is indeed under-utilized but should be included as part of a comprehensive, long term treatment program
- All addiction providers and treatment programs should treat smoking as an addiction in itself with comprehensive, evidence based treatments (including pharmacotherapy)
- Comprehensive, personalized longitudinal care programs based on PHPs are effective and evidenced-based treatments for maintaining Recovery

# Acknowledgements

- University of Florida  
College of Medicine
  - Scott Teitelbaum, M.D.
  - William Greene, M.D.
  - Lisa Merlo, Ph.D.
- Washington University  
School of Medicine
  - Laura Bierut, M.D.
  - Li-Shiun Chen, M.D., MPH, Sc.D.



# The Ultimate Acknowledgement: Mark S. Gold, M.D.

