Opioid Agonist Therapy: The Duration Dilemma

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Presenter Disclosures

- Edwin A. Salsitz, M.D. has no financial relationships with an ACCME defined commercial interest.

The contents of this activity may include discussion of off label or investigative drug uses. The faculty is aware that it is their responsibility to disclose this information.
OUTLINE

- History and Evolution of Opioid Agonist Therapy (OAT)
- Evidence of Effectiveness of Maintenance
- Safety Issues
- Methadone Medical Maintenance (OBOT)
- Stigma Issues
- Barriers to Long Term Maintenance
- Conclusions
- Discussion

Treatment of Opioid Addiction

- Medication Assisted: Therapy, Treatment, Recovery
- Opioid Full/Partial Agonist Therapy (OAT): Methadone, Buprenorphine,
- Opioid Antagonist Therapy: Naltrexone (po) and IM
- Medication Plus Psychosocial—±Optimal Outcomes
- Drug Free Recovery—“Abstinence Based”
- Mutual Help, CBT, DBT, MI, etc.
## Addiction Treatment: MAT

<table>
<thead>
<tr>
<th>Psychosocial</th>
<th>Medication</th>
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</tbody>
</table>

Courtesy A.W.

## MEDICATION ASSISTED ADDICTION TREATMENT

“**All** Treatments Work For **Some** People/Patients”

“**No One** Treatment Works for **All** People/Patients”

*Alan I. Leshner, Ph.D*

Former Director NIDA
MEDICATION ASSISTED ADDICTION TREATMENT

For Emphasis and Clarity,

Please Allow Me to Repeat:

“**All** Treatments Work For **Some** People/Patients”
“**No One** Treatment Works for **All** People/Patients”

Alan I. Leshner, Ph.D
Former Director NIDA
My Treatment “Bias”

AGONIST  ANTAGONIST

George Santayana 1863-1952

“Those who do not remember the past are condemned to repeat it.”
Poppy Seeds UDS

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<td>POS</td>
<td>&lt;300 N/G/ML</td>
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BAYER PHARMACEUTICAL PRODUCTS

Send for samples and Literature to

FARBENFABRIKEN OF ELBERFELD CO.
40 STONE STREET, NEW YORK.
Morphine Clinics

- 1919—1923: Government Regulated
- Attempt to treat opium/morphine/heroin addicted patients
- Closed because abstinence from morphine was not achieved
- Physicians unable to treat opioid addiction
The Lexington Narcotic Farm

The first facility opened on May 25, 1935, outside Lexington, Ky. The 1,050-acre site included a farm and dairy, working on which was considered therapeutic for patients. Morphine and methadone for w/d Rx. With the increased availability of state and local drug abuse treatment programs, The hospital was closed in February 1974.

Drs. Kolb, Himmelsbach, Wikler, Jaffe, Kleber, Vaillant

ONE PROBLEM:

RELAPSE
UPON RETURN
HOME

Drs. Dole, Nyswander, and Kreek

Dr. Vincent Dole and Dr. Marie Nyswander
Methodone Pioneers

Dr. Mary Jeanne Kreek, Addiction Laboratory
Rockefeller University
Initial Publication

A Medical Treatment for Diacetylmorphine (Heroin) Addiction

A Clinical Trial With Methadone Hydrochloride

Vincent P. Doie, MD, and Marie Neumann, MD

A group of 22 patients, previously addicted to diacetylmorphine (heroin), have been maintained on oral methadone hydrochloride. This medication appears to have two useful effects: (1) relief of narcotic hunger, and (2) induction of sufficient tolerance to block the euphoric effect of an average illegal dose of diacetylmorphine.

Commentary by Herbert D. Kleber, MD

JAMA. 1965;193(8):646-650

Exclusion: non-opioid addiction/misuse, severe psychiatric problems

TREATMENT FOR DIACETYLMORPHINE--DOLE & NYSWANDER

Maintenance Therapy of Ex-Addicts With Methadone Hydrochloride, Summary of First 15 Months (February 1964 to May 1965)

Status Before Addition to Program Status When Added

Exclusion: non-opioid addiction/misuse, severe psychiatric problems

Narcotic Hunger
Distribution of Opioid Treatment Programs (OTPs) 2002

[Map showing distribution of OTPs in urban and non-urban areas]

SAMHSA/CSAT

SAMHSA Center for Substance Abuse Treatment
Distribution of Opioid Treatment Programs in the United States

[Map showing distribution of OTPs in the United States]

Number of OTPs:
- 44 or More
- 17 to 43
- 12 to 16
- 7 to 11
- 1 to 6

Puerto Rico & US Virgin Islands
Missouri OTPs (MMTPs)

Brockhollow Hills
St. Louis Metro Treatment Center
9725 St. Charles Rock Road
Suite 108
Brockhollow Hills, MO 63124
(314) 439-7820

Cape Girardeau
Cape Girardeau Treatment Center
768 S. Kings Highway
Suite F
Cape Girardeau, MO 63703
(573) 335-4393

Columbia
Behavioral Health Group - Columbia Medical Clinic
1901 Vandiver Square
Suite F
Columbia, MO 65202
(573) 449-8380

Hazelwood
Center for Life Solutions
637 Dale Road
Suite 108
 Hazelwood, MO 63042
(314) 731-0100

Joplin
Behavioral Health Group - Joplin Treatment Clinic
2919 East 4th Street
Joplin, MO 64801
(417) 762-7666

Kansas City
Behavioral Health Group - Kansas City Medical Clinic
722 East 28th Street
Kansas City, MO 64108
(816) 293-3277

Paseo Comprehensive Rehabilitation Clinic
1060 E 24th Street
Kansas City, MO 64108
(913) 512-7443

Samuel U. Rodgers South Health Center
2708 East 31st Street
Kansas City, MO 64104
(816) 861-7070

Springfield
Behavioral Health Group - Springfield Medical Clinic
454 East Battlefield Road
Springfield, MO 65807
(417) 882-6005

St. Joseph
St. Joseph Metro Treatment Center
3915 Sherrill Avenue
St. Joseph, MO 64506
(816) 239-7500

St. Louis
St. Louis VA Health Care System Opiate Addiction Treatment Program
915 North Lind Boulevard
St. Louis, MO 63106
(314) 290-6418

Find a Doctor Near You

goldenrule.WESTERN.com

Get doctor's permission in the privacy of a doctor's office

WestEnd Clinic, Inc
5736 West Florissant Avenue
St. Louis, MO 63120
(314) 381-0560

Call 1-800-755-9603 to find the nearest clinic or to speak with a drug abuse counselor.
“The Effectiveness Of Methadone Maintenance Treatment,” Ball and Ross, 1991

Comprehensive Study of 6 Methadone Clinics in NYC, Philadelphia, and Baltimore
Objective: “Open the Black Box of Methadone Maintenance Treatment”
N=617 patients over 7 Years
Recent Heroin Use by Current Methadone Dose

Retention in Treatment Relative to Dose

Relative Risk of Leaving Treatment

Adapted from Caplehorn & Bell

"Because methadone maintenance involves the giving of drugs to a drug-seeking, suggestible population, the placebo effect is very important and must be examined"
Vaillant, GE. 1974
Conclusions:
"...informs the public that dependence is a medical disorder that can be effectively treated with significant benefits for the patient and society."

Recommendations:
Expand Access to MMT
CJS ↑ Access
Education of Providers
↓ Regulations
↑ Funding
Parity with all medical/psych disorders
Pregnancy ↑ Access

Methadone Maintenance vs 180-Day Psychosocially Enriched Detoxification for Treatment of Opioid Dependence
A Randomized Controlled Trial

JAMA 2000:283:1303-1310
Methadone Maintenance vs. 180 Day Detoxification


DATA 2000: Buprenorphine

- Major Paradigm Shift: OBOT vs MMTP/OTP
- Mechanism of Action: Similar to methadone
- Partial Agonist: Safety Implications
- 13 years of use in USA
- Now, more patients treated with Bupe than methadone
- Some of the same issues developing:
  - 1. Diversion, Misuse, Abuse
  - 2. Dosage
  - 3. Duration
  - 4. Other Drug Use Disorders
  - 5. Access
  - 6. Insurance Coverage, Prior Authorizations
Detoxification vs. Maintenance
Kakko, Lancet 2003  IV Heroin

No. Assessed for Eligibility: 84
No. Excluded: 44
Not Meeting Inclusion Criteria: 41
Refused to Participate: 2
Other Reasons: 1

No. Randomized: 40
Allocated to Buprenorphine: 20
Allocated to Detox: 20
Received Buprenorphine: 20
Received Detox: 20

Included in analysis: 20
Included in Analysis*: 20
Excluded from analysis: 0
Excluded from Analysis: 0

All Patients:
- Group CBT Relapse Prevention
- Weekly Individual Counseling
- Three times Weekly Urine Screens

Kakko et al, Lancet Feb 22, 2003
Buprenorphine Maintenance/Withdrawal: Mortality

20% mortality in placebo group
Prescription Opioid Addiction Treatment Study “POATS”

Table 2. Successful Opioid Use Outcome by Counseling Condition (SMM vs SMM + ODC) at 3 Time Points

<table>
<thead>
<tr>
<th>Time Point</th>
<th>SMM</th>
<th>SMM + ODC</th>
<th>OR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>End of phase 1</td>
<td>24/30 (80%)</td>
<td>10/10 (100%)</td>
<td>1.3 (0.7-2.6)</td>
<td>.26</td>
</tr>
<tr>
<td>Phase 2, end of treatment</td>
<td>64/100 (64%)</td>
<td>90/100 (90%)</td>
<td>0.8 (0.5-1.2)</td>
<td>.27</td>
</tr>
<tr>
<td>Phase 2, 8-week posttreatment follow-up</td>
<td>13/18 (72%)</td>
<td>10/18 (56%)</td>
<td>0.7 (0.3-1.3)</td>
<td>.22</td>
</tr>
</tbody>
</table>

Abbreviations: GEE = generalized estimating equation; ODC = opioid dependence counseling; OR = odds ratio; SMM = standard medical management.

*aThe reference category is SMM + ODC.
*bAdjusted for chronic pain at baseline and lifetime history of heroin use.
*cAdjusted for chronic pain at baseline, lifetime history of heroin use, and phase 1 randomization.

Primary Care-Based Buprenorphine Taper vs Maintenance Prescription Opioid Use Disorder

Results: Completion of 14 week trial: taper 11% vs maintenance 66%
Mean percentage of urine negative for opioids: taper 35% vs maintenance 53%
Fiellin DA et al. JAMA Intern Med 2014
Buprenorphine: Recurrent Relapse

30 yo male. Buprenorphine was effective. Significant psychosocial problems, including high stress job, and many co-workers misusing prescription oxycodone. Unable or unwilling to access counseling, and dispute with wife over maintenance paradigm. Advised to return for treatment. Lost to F/U.

<table>
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<th>End</th>
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<td>7/23/10</td>
</tr>
<tr>
<td>3/22/11</td>
<td>7/18/11</td>
</tr>
<tr>
<td>3/12/12</td>
<td>12/21/11</td>
</tr>
<tr>
<td>3/13/12</td>
<td>4/13/12</td>
</tr>
</tbody>
</table>

1st: 13 mos.
2nd: 6 mos.
3rd: 3 mos.
4th: 1 mos.

Buprenorphine: Dosage Issue

Treatment retention among patients randomized to buprenorphine/naloxone compared to methadone in a multi-site trial

Review
Buprenorphine maintenance and mu-opioid receptor availability in the treatment of opioid use disorder: Implications for clinical use and policy

Drug and Alcohol Dependence, 144, 2014
Cerebral phosphorus metabolite abnormalities in opiate-dependent polydrug abusers in methadone maintenance.

Methadone: Effectiveness/MOA

Phosphorus MR Spectroscopy

Fig. 3. Metabolite levels in control subjects (n=16) and in short- (n=7) and long-term (n=8) methadone maintenance treatment (MMT) subgroups. Shown are means±S.D. of percent metabolite measures.
Methadone: Effectiveness/MOA

From these data, we conclude that polydrug abusers in MMT have 31P-MRS results consistent with abnormal brain metabolism and phospholipid balance. The nearly normal metabolite profile in long-term MMT subjects suggests that prolonged MMT may be associated with improved neurochemistry.

Psychiatry Research: Neuroimaging
Volume 90, Issue 3, 30 June 1999,
Pages 143-152
**Methadone: Effectiveness/MOA**

Figure 1. Activation Maps of Brain fMRI Response to Heroin-Related Stimuli in Methadone Maintenance Patients Before and After Daily Methadone Dose. Am J Psychiatry 2008; 165:390-394

**Duration: Potential “Pleiotropic” Benefits**

<table>
<thead>
<tr>
<th>TABLE 3. Stress Response Hormones</th>
<th>Adrenocorticotropic hormone</th>
<th>Cortical</th>
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<tr>
<td>Short-acting opioids</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Opiate withdrawal</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Methadone</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Morphine</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Naltrexone (oral)</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Naltrexone (extended release)</td>
<td>↑</td>
<td>↑</td>
</tr>
</tbody>
</table>

↑ = stimulate; ↓ = suppress; ↔ = no change.

Prevalence of HIV-1 (AIDS Virus) Infection in Intravenous Drug Users

50 – 60%
Untreated, street heroin addicts:
Positive for HIV-1 antibody

9%
Methadone maintained since <1978
(beginning of AIDS epidemic):
less than 10% positive for HIV-1 antibody

Kreek, 1984; Des Jarlais et al., 1984; 1989
“Those who do not remember the past are condemned to repeat it.”

China, for example, dropped a zero-tolerance policy on heroin in favor of clean syringes and methadone. It now has 700 clinics treating 200,000 patients, and new H.I.V. cases among those patients have dropped by 90 percent, Mr. Sidibé said.

Russia has 85,000 new H.I.V. infections a year, and the head of Moscow’s Federal AIDS Center said that 57 percent were from drug injection. No OAT. No Syringe Exch.

581 Male Heroin Addicted Followed for 33yrs

? A Medical Tragedy


- California cohort of heroin addicted males-CJS
- After 15 years of abstinence, 25% relapsed to heroin
- Participation rates in methadone maintenance were <10% in any given year

Relapses

- May be delayed and gradual
- ODs and OD death, e.g., fentanyl contamination
- Relationships
- Employment
- Child Custody
- Criminal Justice System
- New Infectious Agent
- Shame and guilt
- Etc.
RELAPSE DANGER

New Hampshire State Laboratory recently reported four fentanyl overdose deaths within a two-month period.

New Jersey saw a huge spike in fentanyl deaths in 2014, reporting as many as 80 in the first six months of the fiscal year.

Rhode Island and Pennsylvania have also seen huge increases since 2013. In a 15-month period, about 200 deaths were reported in Pennsylvania related to fentanyl.

In the St. Louis area, based on information provided by medical examiners over a 10-year period, fentanyl was the only drug attributed as a primary death factor in 44 percent of fentanyl-related overdose cases. The other 56 percent involved fentanyl and other substances such as alcohol, pharmaceuticals, cocaine or heroin.

In June 2014, DEA New York dismantled a heroin and fentanyl network and arrested the two heads of the organization. These individuals were linked to at least three overdose deaths from heroin and fentanyl they sold.

Opioid Detoxification Outcomes

- Low rates of retention in treatment
- High rates of relapse post-treatment
  - < 50% abstinent at 6 months
  - < 15% abstinent at 12 months
- Increased rates of overdose due to decreased tolerance
- Walter Ling “Quote”

O’Connor PG JAMA 2005
Mattick RP, Hall WD. Lancet 1996
Stimmel B et al. JAMA 1977
Opioid Overdose

- Increasing cause of morbidity and mortality in the US

- Tapered patients are at increased risk due to decreased tolerance
  - Risk should be part of conversation (informed consent) about taper
  - Naloxone OD Prevention


As compared to active IV heroin users the methadone patients gained weight, and had less sexual dysfunction. Chronic liver disease was common, and antedated methadone treatment. “No clusters of unusual medical complications were observed.” *(EKGs not done)*

OAT Duration: Safety

- Avoid OD: Induction → Methadone Deaths → Pain Rx
- Drug/Drug Interactions: M>B
- Constipation
- Sweating
- Secondary Hypogonadism; ?M>B
- QTc Prolongation: M
- Other: Nausea, arousal, sedation, etc.
- No Organ Damage: Compare to Alcohol, Cocaine and Tobacco
- “Rots Teeth and Bones:” An enduring myth
Medical Maintenance: 1983--Present

Methadone Maintenance Patients in General Medical Practice
A Preliminary Report

Medical maintenance is the treatment by primary care physicians of rehabilitated methadone maintenance patients who are stable, employed, and abusing drugs, and not in need of supportive services. In this research project, physicians with experience in drug abuse treatment administered methadone maintenance in addition to treatment of addiction as well as therapy or other medical problems, as needed. Decisions regarding treatment were based on the individual needs of the patient and on generally accepted medical practice rather than on explicit regulations. We studied the first 40 former heroin addicts who were transferred to this program from several conventional methadone clinics. At a follow-up visit 12 to 16 months, 39 (92.5%) of 40 patients had remained in treatment; five (12.5%) had been discharged because of cocaine abuse and two (5%) had been voluntarily discharged. Personal benefits of medical maintenance include the dignity of a standard professional atmosphere and a more flexible reporting schedule. This program has the potential for improving treatment of addicted methadone maintenance patients.

Patients and Methods

Medical Maintenance
Admission Criteria

- At least 4 years in MMTP
- Negative urines for last 3 years
- Working/School etc.
- Adequate income for fees
- Recommendation from clinic
- Not in military reserves
- Stable and safe storage environment
Medical Maintenance Procedures

- Patient given 28 day supply of methadone, by MD, in disket/tablet form, every 4 weeks.
- Medication prepared by hospital pharmacy in usual Rx type bottle and label
- Routine urine toxicology
- Patient returns before “run out” date
- Primary care provided
Total Years on Methadone

- 0-10 yrs. (0%)
- 11-20 yrs. (6%)
- 21-30 yrs. (21%)
- 31-40 yrs. (36%)
- 41-50 yrs. (36%)

Courtesy A.W.
Medical Maintenance: Dose N=122

AVERAGE DOSE = 68mg.
RANGE: 5mg–210mg

- 5-10mg (1.5%)
- 10-30mg (14%)
- 40-60mg (34%)
- 70-90mg (30%)
- 100-120mg (12%)
- 130-150mg (6%)
- 150-210mg (2.5%)

Medical Maintenance
1983 - Present

347 = Total Enrolled

Withdrew
25 (7.5%)
- Transfer MMTP
  14
- Pain
  10

MMTP/DISCH
44 (13%)
- Cocaine
  19
- Cause
  25

Deaths
79 (22%)
- Tobacco
  31
- Hepatitis C
  19
- Lymphoma
  5
- Medical
  13
- HIV
  4
- Old Age
  1
- Homi/Suicide
  2
- Prostate Ca
  1
- Leukemia
  1
- Diabetes
  1
- Ovarian CA
  1

Active
122 (35%)
- Buprenorphine
  53
  Deaths: 1 Tob 1 Hep C
  9 liver transplants
  8 patients
  4 alive

Revised - 2/1/15

Courtesy A. W.
## Deaths

82 (22%)

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<th># of Patients</th>
<th>Cause</th>
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<tr>
<td>31</td>
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<td>19</td>
<td>Hepatitis C</td>
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<td>5</td>
<td>Lymphoma</td>
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<tr>
<td>13</td>
<td>Medical</td>
</tr>
<tr>
<td>4</td>
<td>HIV</td>
</tr>
<tr>
<td>1</td>
<td>Old Age</td>
</tr>
<tr>
<td>2</td>
<td>Homicide/Suicide</td>
</tr>
<tr>
<td>1</td>
<td>Prostate Cancer</td>
</tr>
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<tr>
<td>1</td>
<td>Diabetes</td>
</tr>
<tr>
<td>1</td>
<td>Ovarian Cancer</td>
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### Methadone Medical Maintenance

**Abstract**

- Human immunodeficiency virus (HIV) infection has become widespread among parenteral drug abusers. We measured antibody to HIV and hepatitis B virus markers in 58 long-term, socially rehabilitated methadone-maintained former heroin addicts. None of the 58 had antibody to HIV, but one or more markers of hepatitis B virus infection were seen in 32 (55%). The duration of methadone maintenance was 26.7 years, and the median dose of methadone was 80 mg (range, 5 to 100 mg). Before methadone treatment, the patients had abused heroin parenterally for 10.3 years, and they had engaged in additional high-risk practices for HIV infection. We conclude that successful outcomes during methadone maintenance treatment are associated with sparing of parenteral drug abusers from HIV infection.

“Methadone Saved My Life”

“I Never Thought I’d Get To Be __Yrs Old”

---

“N=58”

“Methadone Saved My Life”

“I Never Thought I’d Get To Be __Yrs Old”
Occupations of OBOT OAT Patients

- Teacher
- Electrician
- Plumber
- Social Worker
- Psychologist
- Chauffer
- Computer/IT
- Drug Counselor
- Accountant
- Retail Manager
- Home Security Systems
- Restauranteur
- Fish Dept. Manager
- Movie Editing
- Student(Ph.D)
- HVAC Tech.
- Stamps
- School Principal
- Artist
- Advertising VP

- Bus Driver—MTA*
- Sanitation Driver*
- Con Ed Utility*
- Subway Signal—MTA*
- Sales
- Secretarial
- Administrator
- Piano Teacher
- Elevator Repair
- Lawyer
- Physician
- Landscape
- Car Salesman/Repair
- Videographer
- Heavy Equipment
- Contractor
- Entrepreneur
- Musician
- Nurse

* Safety Sensitive—Employer’s OK

Methadone→Buprenorphine

Transitioning Stable Methadone Maintenance Patients to Buprenorphine Maintenance

Edwin A. Sobbs, MD; Christopher C. Holden, MD; Susan Trow, PhD, and Ann Ngapen, BA

JAM, 2010 (4) 88-92
OPIOID AGONIST THERAPY (OAT)

Addiction
Regulatory
Pharmacology
Stigma
Destitution
Political

OAT: Stigma

One of Medicine's Best-Kept Secrets: Methadone Works
STIGMA--METHADONE

• “My Wife’s Opinion Is that Methadone Maintenance Treatment Is As Close To Evil As You Can Get, Without Killing Someone.”

A “successful” methadone patient quoting his wife’s attitude toward methadone maintenance treatment.

OAT: Stigma
OAT: Stigma

The Metro Section

Crane Secured for Storm Falls, Killing a Worker in Chelsea

9/29/2016
Mike confesses to Dr. Drew that he has been using methadone for 6 to 7 years at a dose of 100 mg per day. Dr. Drew pursed his lips at this and cocked his head in a thinly veiled mask of empathy and remarked, “Methadone takes your soul away.....it’s no way to live”. Mike admits to having been in many rehabs before, with no success. NO MEDICAL PROTOCOL IS DISCUSSED FOR MIKE’S SOON-TO-BE SUBSTANTIAL WITHDRAWAL FROM A 6 TO 7 YEAR, 100 MG PER DAY METHADONE HABIT. As the camera follows Mike pacing anxiously back and forth outside in the patient outdoor/garden/smoking area, Dr. Drew opines in a voice-over: "Mike is a hard core polydrug addict, which means he is addicted to multiple drugs. But my main concern at this point is the methadone. Methadone is a government-approved drug that helps patients wean off of heroin. Because you have to take enough methadone to suppress your addictive drive, addicts that are hard-core like Mike can develop a methadone addiction. Withdrawal from methadone can be severe - in fact it often leads to medical and psychiatric complications that require hospitalizations, and I’m concerned that that is exactly where Mike is going to end up."

As Dr. Drew proceeds with his examination of this poor suffering patient, his voice-over continues......"Mike is in for a painful and even dangerous journey...withdrawal from methadone is bone-crushing pain....imagine the worse flu of your life with somebody putting your limbs in a vise and squeezing them...and vomiting...and desperation...and dysphoria...it's almost intolerable. It's almost inhuman." Dr. Drew then, to my great shock and disgust, cheerily pats Mike on the shoulder and proclaims proudly - - "You're in it, you're in it Baby - -  Hope it'll be fast."

Day 18—To Mike who c/o not feeling right: “It’s the G-DDAMN Methadone coming out of your system!
OAT: Stigma

Messages About Methadone and Buprenorphine in Reality Television: A Content Analysis of Celebrity Rehab With Dr. Drew

Robert Rosse, Liza Fuentes, and Mandep Cheema

1 Albert Einstein College of Medicine, Division of Substance Abuse, Bronx, New York, USA; 2 University of New York School of Public Health, New York, USA; 3 University of Toronto, Toronto, Ontario, Canada

<table>
<thead>
<tr>
<th>Medication</th>
<th>Total # of references</th>
<th>Message of reference</th>
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<tr>
<td>Methadone</td>
<td>20</td>
<td>Endorsed as treatment option</td>
</tr>
<tr>
<td>Buprenorphine</td>
<td>8</td>
<td>Rejected as treatment option</td>
</tr>
</tbody>
</table>

OAT: Stigma

R.I.P.

'Celeb Rehab' Rocker Mike Starr Dead

Former Alice In Chains bassist Mike Starr died in Utah... TMZ has learned.

Star appeared on the third season of "Celebrity Rehab" back in 2009 — and was arrested last month for felony possession of a controlled substance. TMZ's Cops say he had 9 Opana pills and 6 Opana (pamela) pills when he was busted.
OAT: Stigma

SM: You must be excited to see him when he comes back?
Mrs. Claus: By the time he stumbles in at 6AM, Chris has eaten roughly 2 Billion cookies, so he pukes for a solid day! She continues-
THEN HE SPENDS A WEEK IN A METHADONE CLINIC TO COME DOWN FROM THE SUGAR HIGH.

Aidy Bryant, Seth Meyers. SNL, 12/8/12

Duration Barriers: Stigma
OAT: Stigma

FEBRUARY 2, 1997

QUOTATION OF THE DAY

"A methadone patient is monitored more closely than a paroled murderer."

DR. EDWIN A. SALSITZ, of Beth Israel Hospital in New York City.

OAT Barriers: Terminology

TIME

SEX, STRESS, SLEEP, SMOKING
Scientists are discovering the chemical secret to HOW WE GET ADDICTED... and how we might get cured

THE DOPAMINE CYCLE

05/1997
OAT Barriers: Terminology

Clean vs Dirty Urine
National Briefing | Midwest: Minnesota: Prize Steer Fails Drug Test

By Elizabeth Stanton (NYT)
Published: October 25, 2001

A contestant in the state fair steer competition was stripped of his award and about $5,000 because his steer failed a drug test. It is the first time a contestant has been expelled since the fair began testing for illegal drugs 10 years ago. Tests on Brandon Lusk’s steer found a diuretic. Steve Pouch, assistant fair manager, said the drug could help a steer qualify for a lighter weight class, then it could be rehydrated to gain weight. Mr. Lusk, 19, denied giving the steer the drugs. Elizabeth Stanton (NYT)
Cow Dung

<table>
<thead>
<tr>
<th>Slang</th>
<th>Medical</th>
</tr>
</thead>
<tbody>
<tr>
<td>Addict</td>
<td>Addicted patient, patient with the disease of addiction</td>
</tr>
<tr>
<td>Junkie, dope fiend</td>
<td>Opiate addicted patient, cocaine addicted patient</td>
</tr>
<tr>
<td>Clean urine</td>
<td>Urine negative for illicit or non-prescribed drugs</td>
</tr>
<tr>
<td>Dirty urine</td>
<td>Urine positive for yore</td>
</tr>
<tr>
<td>Drunk, smashed, bombed</td>
<td>Alcohol addicted, intoxicated</td>
</tr>
<tr>
<td>Crackhead, pothead</td>
<td>Cocaine addicted, THC abuse</td>
</tr>
<tr>
<td>La La Land</td>
<td>Intoxicated</td>
</tr>
<tr>
<td>Street addict, hard core addict</td>
<td>Patient with the disease of addiction</td>
</tr>
<tr>
<td>Speed-balling</td>
<td>Using heroin and cocaine together</td>
</tr>
<tr>
<td>Meth</td>
<td>Methadone, or methamphetamine</td>
</tr>
<tr>
<td>Tinfoil</td>
<td>Diluted, intoxicated</td>
</tr>
<tr>
<td>Cop/Hit</td>
<td>Obtain, purchase/Dosed, took</td>
</tr>
<tr>
<td>Hooked</td>
<td>Addicted</td>
</tr>
<tr>
<td>Sniffling</td>
<td>Withdrawal Syndrome</td>
</tr>
</tbody>
</table>
Duration Barriers: Terminology

• “Substitution Treatment” “OST”
• Standard terminology in Europe and Australia
• ?? Accurate ?? Helpful ?? Harmful
• “Aren’t you just substituting one drug or addiction for another??”
• Why not just call it “Treatment for Opioid Use Disorder?”

OAT: Terminology

Does Not Necessarily Equal

Physical Dependence  Addiction

Courtesy A.W.
Duration Barriers: Pregnancy

Methadone Maintenance, Pregnancy, and Progeny

George Wilklls, MD; Judith Jones, MD; Robert C. Wallack, MD

Pregnancy was observed 120 times in unselected women in the Methadone Maintenance Treatment Program of the Boston Medical Center. There was no significant difference in the proportion of spontaneous abortions or preterm births in infants born to women who did or did not receive methadone. The only difference in the medication was noted only after one added methadone hydrochloride and the third trimester and follow up revealed normal growth and development.

Neonatal Abstinence Syndrome after Methadone or Buprenorphine Exposure

Hendrie E. Jones, Ph.D., Karol Kaltenbach, Ph.D., Sarah H. Heil, Ph.D., Susan M. Stone, M.D., Ph.D., Mara G. Coyne, M.D., Amelia M. Arrua, Ph.D., Kevin E. O’Grady, Ph.D., Peter Selby, M.B., B.S., Peter R. Martin, M.D., and Gabriele Fischer, M.D.

MOTHER Study, NEJM. 2010

Duration Barriers: Policy

Mayor Steps Up His Criticism Of Methadone

By RACHEL L. SWAIN

Published: August 15, 1988

One day after detailing his plan to wean 2,000 heroin addicts off methadone at city hospitals, Mayor Rudolph W. Giuliani stepped up his attack on methadone treatment providers yesterday, accusing them of enlisting former drug users instead of pushing them toward abstinence.

TURNAROUND RUDY PUTS $5M IN METHADONE CLINICS

By Susan Rubenstein

October 4, 1999 | Article

Mayor Giuliani has backed off further from his vow to end methadone treatment for heroin addicts — funding a $5 million expansion of the city’s clinics.

The money is going to methadone centers at all 11 public hospitals in 11 clinic hours and add job training and psychological evaluations, said City Health and Hospitals Corporation spokeswoman Jane Timmerman.

The move comes a year after Giuliani called Clinton administration drug czar Barry McCaffrey “a disaster” for backing methadone treatment over abstinence.

Jan, 2015, Alcoholism Drug Abuse Weekly

Maine governor proposes to eliminate Medicaid funding for OTPs

Gov. Paul LePage, who has been trying to limit treatment with methadone and buprenorphine in Maine for several years, this month proposed to eliminate all Medicaid funding for opioid treatment programs (OTP) and methadone, and to transfer patients to office-based buprenorphine treatment. More Methadone

in the Bangor Daily News (BDN). Under his proposal, LePage would cut $27,000 in funding for MainCare in fiscal year 2016 and $66,000 in fiscal year 2017. This would also mean the state would not receive Medicaid matching funds from the federal government for those users, which would be $41 million...
CJS Barriers: Good News

SAMHSA Bans Drug Court Grantees from Ordering Participants off MAT

February 24, 2015 by kTIman

“A grant announcement issued by the Substance Abuse and Mental Health Services Administration (SAMHSA) last month to fund drug courts contains an important new condition: drug courts funded by the grants would no longer be allowed to tell offenders to stop taking medications to treat opioid use disorders. Many drug court judges have opposed methadone or buprenorphine and required participants to stop taking them. Drug courts prefer either abstinence or Vivitrol.

From the SAMHSA Request for Applications (RFAs): “Under no circumstances may a drug court judge, other judicial official, correctional supervision officer, or any other staff connected to the identified drug court deny the use of those medications when made available to the client under the care of a properly authorized physician and pursuant to a valid prescription and under the conditions described above.”

The grant language refers to medication-assisted treatment (MAT) and includes methadone, buprenorphine, oral naltrexone, Vivitrol (injectable 30-day naltrexone) and other medications.”


Sources: AlcoholismDrugAbuseWeekly.com – February 16, 2015
“Makes No Sense” Paradigm

- The patients who have responded well to OAT, are the patients who are urged to “get off” their medication. They are often not rewarded with the Federal and State regulations for which they are entitled.
- The patients doing well, feel the most stigmatized.
- No other chronic medical disease is viewed this way by providers—asthma, hypertension, diabetes, depression
- No acceptance by insurers of long term maintenance, no longer requiring weekly UDTs or documented counseling
APA Guideline: MDD 2010
Antidepressant Pharmacotherapy

- For many patients, particularly for those with chronic and recurrent major depressive disorder or co-occurring medical and/or psychiatric disorders, some form of maintenance treatment will be required indefinitely [I].
- Maintenance therapy should also be considered for patients with additional risk factors for recurrence, such as the presence of residual symptoms, ongoing psychosocial stressors, early age at onset, and family history of mood disorders [II].

What If There Were a Methadone or Buprenorphine for:

- Methamphetamine and Cocaine Addiction?
- Alcohol Addiction?
- Tobacco Addiction?
- Benzodiazepine Addiction?
- Food Addiction?
- Pathological Gambling?
Methadone Maintenance 4 Decades Later
Commentary, Herbert Kleber, M.D. JAMA, 2008

• Ironically, even though 12-step programs have often been hostile to MMT, Dole, a friend of the cofounder of Alcoholics Anonymous recounted, “He [Bill W.] suggested that in my future research, I should look for an analogue of , a medication that would relieve the alcoholic's sometimes irresistible craving and enable him to progress in AA toward social and emotional recovery.”

Final Comments: OAT Duration

• The scientific evidence base, and 50 years of clinical experience overwhelmingly support maintenance in the OAT treatment paradigm.
• The goal of OAT maintenance is not to see how fast a patient can “get off” medication.
• The goal is normalization and stabilization of the brain, establishing durable and safe hedonic tone, and functioning at maximal potential at home and at work.
• Like most chronic medical therapies, the medication only works, when it is taken.
• “If It Ain’t Broke, Why Fix It?”
## Opioid Agonist Therapy Stage

<table>
<thead>
<tr>
<th>OAT-M/B</th>
<th>YES</th>
<th>NO</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Opioids</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Less Opioids</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other Drugs</td>
<td></td>
<td>✓</td>
</tr>
<tr>
<td>IV vs. IN vs. PO</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Productive Use of Time</td>
<td>✓</td>
<td></td>
</tr>
<tr>
<td>Counseling</td>
<td>✓</td>
<td></td>
</tr>
</tbody>
</table>

### MEDICATION ASSISTED ADDICTION TREATMENT

“**All Treatments Work For Some People/Patients**”

“**No One Treatment Works for All People/Patients**”

If your treatment is working, keep doing the treatment

If your treatment is not working, change your treatment!!
Injectable extended-release naltrexone for opioid dependence: a double-blind, placebo-controlled, multicentre randomised trial

Summary

Background Opioid dependence is associated with low rates of treatment-seeking, poor adherence to treatment, frequent relapse, and major societal consequences. We aimed to assess the efficacy, safety, and patient-reported outcomes of an injectable, once-monthly extended-release formulation of the opioid antagonist naltrexone (XR-NTX) for treatment of patients with opioid dependence after detoxification.

Methods We did a double-blind, placebo-controlled, randomised, 24-week trial of patients with opioid dependence disorder. Patients aged 18 years or over who had 10 days or less of inpatient detoxification and 7 days or more of all opioids were enrolled at 13 clinical sites in Russia. We randomly assigned patients (1:1) to either 300 mg XR-NTX or placebo by an interactive voice response system, stratified by site and gender in a controlled, permuted-block method. Participants also received 12 bi-weekly counselling sessions. Participants, investigators, staff, and the sponsor were masked to treatment allocation. The primary endpoint was the proportion of patients in each treatment group with 90% of self-reported opioid-free days, assessed by urine drug tests and self-report of non-use. Secondary endpoints were self-reported opioid-free days, opioid craving scores, number of days of retention, and relapse to physiological opioid dependence. Analyses were by intention to treat. This trial is registered at ClinicalTrials.gov (NCT00274345).

Findings Between July 3, 2008, and Oct 5, 2009, 250 patients were randomly assigned to XR-NTX (n=126) or placebo (n=124). The median proportion of weeks of confirmed abstinence was 90.0% (95% CI 69.6-92.4) in the XR-NTX group compared with 11.0% (9.4-12.6) in the placebo group (p<0.0001). Patients in the XR-NTX group self-reported a median of 99.5% (range 89.3-100.0) opioid-free days compared with 65.4% (46.2-73.9) for the placebo group (p<0.0001). The mean change in craving was –18.1 (95% CI –12.3 to –23.9) in the XR-NTX group compared with 6.7 (1.3-12.1) in the placebo group (p<0.0001). Median retention was 124 days in the XR-NTX group compared with 54 days (95% CI 53-158) for patients in the placebo group (p<0.0001). Naloxone challenge confirmed relapse to physiological opioid dependence in 57 patients in the placebo group compared with none in the XR-NTX group (p<0.0001). XR-NTX was well tolerated. Two patients in each group discontinued owing to adverse events. No XR-NTX-treated patients died, overdosed, or discontinued owing to severe adverse events.

HEROIN MAINTENANCE

• Harm Reduction
• Positive outcome studies from Switzerland and Canada (Montreal and Vancouver)

I.M. Naltrexone

THE AMERICAN JOURNAL ON ADDICTIONS

Long-Term Opioid Blockade and Hedonic Response: Preliminary Data from Two Open-Label Extension Studies with Extended-Release Naltrexone

Charles P. O’Brien, MD, PhD,1 David R. Gastfriend, MD,2 Robert F. Forman, PhD,2 Edward Schweitzer, MD,2 Helen M. Pettinati, PhD1

1Department of Psychiatry, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania
2Alkermes, Waltham, Massachusetts
3Paladin Consulting Group, Hoboken, New Jersey
It is postulated that the high rate of relapse of addicts after detoxification from heroin use is due to persistent derangement of the endogenous ligand-narcotic receptor system and that methadone in an adequate daily dose compensates for this defect. **Some patients with long histories of heroin use and subsequent rehabilitation on a maintenance program do well when the treatment is terminated. The majority, unfortunately, experience a return of symptoms after maintenance is stopped. The treatment, therefore, is corrective but not curative for severely addicted persons.** A major challenge for future research is to identify the specific defect in receptor function and to repair it. **Meanwhile, methadone maintenance provides a safe and effective way to normalize the function of otherwise intractable narcotic addicted patients.**
Why Is This So Important?

Actor Philip Seymour Hoffman, who was found dead February 2, 2014 on the bathroom floor of his New York apartment with a syringe in his left arm, died of acute mixed drug intoxication, including heroin, cocaine, benzodiazepines and amphetamine, the New York medical examiner’s office said Friday.

I’m Ed Salsitz, and I Approved this Lecture
Addiction Pharmacotherapy: Medication Assisted Recovery

Edwin A. Salsitz, M.D., FASAM
Mount Sinai Beth Israel
New York City

ADDICTION TREATMENT

“All Treatments Work For Some People/Patients”
“No One Treatment Works for All People/Patients”

Alan I. Leshner, Ph.D
Former Director NIDA
MEDITATION/ PSYCHOSOCIAL

“I medicate first and ask questions later.”

MEDITATION/ PSYCHOSOCIAL

“Sorry, no water. We’re just a support group.”
Texting While In Therapy

Comprehensive Addiction Treatment

Cortex
Role: Decision Making
Intervention: Counseling

Limbic Region
Role: Drive Generation
Intervention: Pharmacotherapy
ADDICTION PHARMACOTHERAPY

- Treatment of Withdrawal vs. Maintenance Treatment/Relapse Prevention
- Tobacco---Nicotine Replacement
- Opioids---Methadone, Bupe, Clonidine
- Alcohol---Benzodiazepines, Phenobarbital, anti-convulsants
- Benzodiazepines---B/Z, Phenobarb.
- Cocaine/Amphetamine---Symptomatic
- Marijuana---?Marinol

TOBACCO ADDICTION

- Tobacco vs. Nicotine   (Coffee vs. Caffeine)
- Nicotine Replacement Therapy (NRT)  
  patches, gum, lozenges, inhaler, nasal spray
- Bupropion (Zyban, Wellbutrin)
- Varenicline (Chantix)
- Electronic Cigarette
- (Rimonabant—cannabinoid antagonist)
Comparable data on smoking prevalence were not collected before 1965.
Smoking Your Wife to Death

Those personal marriage-solicitation ads listing all the qualities sought in an ideal mate — good looks, brains, tenderness, energy, wealth — sometimes add “nonsmokers only.” The smell of stale tobacco can turn off even the most ardent suitor. But now it turns out that there may also be sound medical reasons for shunning the smokers.

A major study in Japan has found that nonsmoking wives of heavy smokers developed lung cancer at a surprisingly high rate. They had become “passive smokers” who regularly breathed smoke in the air. This study is the best evidence yet that smokers are a menace not just to themselves but to the rest of us as well. The study, spanning 14 years and 200,000 people, found that nonsmoking women married to heavy smokers were twice as likely to die of lung cancer as women married to nonsmokers. In farm areas, where there were few other pollutants to complicate the results, the risk more than quadrupled.

Perhaps the most striking finding is just how bad passive smoking turns out to be, causing from a third to a half the harm caused by direct smoking. In Japan, where relatively few women smoke, such passive smoking almost certainly causes more lung cancer in women than the cigarette habit itself.

So much for the notion that second-hand smoke is merely a nuisance. The Japanese study, published in the authoritative British Medical Journal, adds to the growing evidence that second-hand smoke kills. The results strengthen the case for banning smoking in public places, especially where abstainers are exposed to smoke for long periods.

NYT, January, 1981
Tobacco Use Disorder Terminology

- Tobacco Addiction is the Problem
- Not Nicotine Addiction
- Nicotine dependence ≠ Tobacco Addiction
- Consider NRT Treatment
- ? Harm from Nicotine Alone
  Pregnancy and Apoptosis
Tobacco Addiction Cycle

Smoking is a Risk Factor Across an Array of Diseases

Cardiovascular
1. Ischemic heart disease (#2)*
2. Stroke – Vascular dementia
3. Peripheral vascular disease
4. Abdominal aortic aneurysm

Respiratory
1. COPD (#3)*
2. Community-acquired pneumonia
3. Poor asthma control

Reproductive
1. Erectile dysfunction
2. Reduced fertility
3. Pregnancy complications
4. Low birthweight
5. SIDS

Other
1. Adverse surgical outcomes/
wound healing
2. Hip fractures
3. Low bone density
4. Cataract
5. Peptic ulcer disease
6. Metabolic syndrome

Active Smoking


Prevalence of Smoking Among Patients With Mental Illness and Substance Abuse

<table>
<thead>
<tr>
<th>Condition</th>
<th>Smoking Prevalence, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Schizophrenia†,6</td>
<td>45-88</td>
</tr>
<tr>
<td>Major depression†</td>
<td>40-60</td>
</tr>
<tr>
<td>Bipolar disorder†</td>
<td>55-70</td>
</tr>
<tr>
<td>Anxiety disorder†</td>
<td>19.2-56</td>
</tr>
<tr>
<td>Panic attacks†,5,6</td>
<td>38-46</td>
</tr>
<tr>
<td>Attention-deficit/hyperactivity disorder†</td>
<td>41-42</td>
</tr>
<tr>
<td>Posttraumatic stress disorder†,4,6,9</td>
<td>45-66</td>
</tr>
<tr>
<td>Alcohol abuse†,7-10</td>
<td>43-80</td>
</tr>
<tr>
<td>Drug abuse†,7,10</td>
<td>49-96</td>
</tr>
<tr>
<td>General population†,11</td>
<td>19.8</td>
</tr>
</tbody>
</table>

*General population includes all the above categories of mental illness.

Schroeder, S. A. JAMA 2009;301:522-531.
Important!

3 packs of Cigarettes
Per person, per day.
Tobacco and HIV

- Smokers with HIV, with access to care, are more likely to die from smoking related causes than HIV related causes
- HIV smokers ↓ adherence to meds, ↓ QOL
- ~ 40% of HIV patients smoke---up to 80% in indigent
- Smoking ↑ pneumonia, COPD and CVD
- Tobacco Related Cancers: 5X ↑ over non HIV smokers
- No ↑ in virological cancers: lymphoma, anal, cervical
- ↑ oral and esophageal candidiasis
- Mortality rate ratio: ~ 2x ↑ HIV smoker vs. non smoker
- 35 yo HIV smoker: Life Expect: 62, Non smoker: 78
Why Quit?
Potential Lifetime Health Benefits of Smoking Cessation

- CHD risk is similar to that of persons who have never smoked
- Lung cancer risk is 30-50% that of continuing smokers
- Stroke risk returns to the level of people who have never smoked at 5-15 years post-cessation
- CHD: excess risk is reduced by 50% among ex-smokers
- Lung function starts to improve with decreased cough, sinus congestion, fatigue, and shortness of breath
- Cosmetic benefits

Cessation

2 weeks 3 months 6 months 1 year 5 years 10 years 15 years

Other Potential Benefits:
- COPD: rate of lung function decline among former smokers returns to that of never smokers
- Decreased risk of developing gastric and duodenal ulcers
- Smoking cessation is also known to reduce the risk of cancers of the larynx, oral cavity, esophagus, pancreas, and urinary bladder

"Reach for a Lucky instead"

"It's toasted"

Your system has been compromised. The magazine images can be found in the next page.
Mortality Following Inpatient Addictions Treatment

Conclusions

• High risk for premature mortality
• Tobacco-related diseases leading cause of death
• Treating tobacco dependence is imperative in this high risk group

### Effectiveness of First Line Medications

Results from meta-analyses comparing to placebo (6 month F/U)

<table>
<thead>
<tr>
<th>Medication</th>
<th>No. Studies</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nic. Patch (6-14 wks)</td>
<td>32</td>
<td>1.9</td>
<td>1.7-2.2</td>
</tr>
<tr>
<td>Nic. Gum (6-14 wks)</td>
<td>15</td>
<td>1.5</td>
<td>1.2-1.7</td>
</tr>
<tr>
<td>Nic. Inhaler</td>
<td>6</td>
<td>2.1</td>
<td>1.5-2.9</td>
</tr>
<tr>
<td>Nic. Spray</td>
<td>4</td>
<td>2.3</td>
<td>1.7-3.0</td>
</tr>
<tr>
<td>Buproprion</td>
<td>26</td>
<td>2.0</td>
<td>1.8-2.2</td>
</tr>
<tr>
<td>Varenicline (2mg/day)</td>
<td>5</td>
<td>3.1</td>
<td>2.5-3.8</td>
</tr>
</tbody>
</table>

*PHS Clinical Practice Guideline 2005 Update*
### Bupropion Summary

- Dose response efficacy in treating smokers
- Attenuates weight gain
- May be more effective than nicotine patch therapy
- Delays relapse to smoking
- Can be prescribed to diverse populations of smokers with expected comparable results

Varenicline
Mode of Action

• Partial agonist with specificity for the α4β2 nicotine acetylcholine receptor
• Agonist action: stimulates the nAChr to ↓ nicotine withdrawal
• Antagonist action: blocks the nAChr to ↓ the reinforcing effect of smoking

Varenicline and Neuropsychiatric Side Effects
• Meta analysis 39 RCT (10,761 participants)
• Study not sponsored by Pfizer
• Industry and non-industry funded studies
• No increased risk of suicide
• No increased risk of suicidal ideation
• No increased risk of depression
• No increased risk of irritability
• No increased risk of aggression
• Increased risk of sleep disorders
• Increased risk of insomnia
• Increased risk of abnormal dreams
• Reduced risk of anxiety  
  Thomas et al., 2015; BMJ
Acupuncture and Related Interventions for Smoking Cessation

- Plain language summary
  Acupuncture and related therapies do not appear to help smokers who are trying to quit.

  Acupuncture is a traditional Chinese therapy, generally using needles to stimulate particular points in the body. Acupuncture is used with the aim of reducing the withdrawal symptoms people experience when they try to quit smoking. Related therapies include acupressure, laser therapy and electrical stimulation. The review looked at trials comparing active acupuncture with sham acupuncture (using needles at other places in the body not thought to be useful) or other control conditions. The review did not find consistent evidence that active acupuncture or related techniques increased the number of people who could successfully quit smoking. However, acupuncture may be better than doing nothing, at least in the short term; and there is not enough evidence to dismiss the possibility that acupuncture might have an effect greater than placebo.

Hypnotherapy for Smoking Cessation

- Authors’ conclusions
  We have not shown that hypnotherapy has a greater effect on six month quit rates than other interventions or no treatment.

  The effects of hypnotherapy on smoking cessation claimed by uncontrolled studies were not confirmed by analysis of randomized controlled trials.
Obama pledges not to smoke in White House

"There are times where I've fallen off the wagon," president-elect says

WASHINGTON - Barack Obama says you won't catch him lighting up a cigarette in the smoke-free White House.

"There are times where I've fallen off the wagon," the president-elect said when asked in a broadcast interview whether he has kicked the habit.

"I've done a terrific job, under the circumstances, of making myself much healthier," he said. "And I think that you will not see any violations of these rules in the White House," he said on Sunday's "Meet the Press" on NBC.
When To Start Tobacco Cessation Treatment in Patients Addicted and in Treatment for Opioid, Alcohol, Cocaine, Benzodiazepine, etc Addictions?

What About AA and other Mutual Help Meetings?

Please CASAC Counselors: Be Role Models, Not Hypocrites

At a MINIMUM, Do Not SMOKE During Your Work Time
ALCOHOL ADDICTION

- Disulfiram (Antabuse)
- Naltrexone tablets
- Naltrexone injectable (Vivitrol)
- Acamprosate (Campral)
- Topiramate* (Topamax)
- Varenicline* (Chantix)
  *not FDA approved
Undertreatment of Alcohol Use Disorders

SAMHSA, Office of Applied Studies. Substance Dependence, Abuse and Treatment Tables; 2003
IMS - MAT March 2006

DISULFIRAM

- ALDH irreversibly inactivated
- Flushing in 5-10 minutes after EtOH
- Abstain from EtOH for 12 hours prior
- Adverse Effects—Headaches, Dizziness, Tremor, Metallic Taste, Neuropathy, Optic Neuritis, Hepatitis (can be fulminant)
- Drug/Drug Interactions (phenytoin)
- Sensitization may last 14 days until ALDH is regenerated
**ALDH.** Several isozymes of ALDH have been identified, but only the cytosolic ALDH1 and the mitochondrial ALDH2 metabolize acetaldehyde. There is one significant genetic polymorphism of the ALDH2 gene, resulting in allelic variants ALDH2*1 and ALDH2*2, which is virtually inactive. ALDH2*2 is present in about 50 percent of the Taiwanese, Han Chinese, and Japanese populations (Shen et al. 1997) and shows virtually no acetaldehyde metabolizing activity in vitro. People who have one (i.e., heterozygous) or especially two (i.e., homozygous) copies of the ALDH2*2 allele show increased acetaldehyde levels after alcohol consumption (Luu et al. 1995; Wall et al. 1997) and therefore experience negative physiological responses to alcohol.

**Genetic Protection**

Facial flushing in a 22-year-old ALDH2 heterozygote before (left) and after (right) drinking alcohol. The individual pictured in this figure has given written consent for publication of his picture using the PLoS consent form.
Alcohol Effects and Opioid Systems

- Alcohol consumption results in the release of the body’s naturally-occurring opiates, endorphins.
- These opiates bind to receptor sites in the brain and result in the pleasurable effects of alcohol.
- Animals bred to prefer alcohol have reduced opioid peptides in their brains.
- µ-opioid receptor knockout mice do not self-administer alcohol.
- Alcoholics and their family members have reduced plasma levels of β-endorphin (an opioid peptide).

Naltrexone & Abstinence Rates

Efficacy and Tolerability of Long-Acting Injectable Naltrexone for Alcohol Dependence
A Randomized Controlled Trial

Abstract. Alcohol dependence is a chronic disease associated with significant mortality and morbidity. Naltrexone, an opioid antagonist, has been shown by efficacy and tolerability studies to improve outcomes for the treatment of alcohol dependence with the added advantage of being effective for up to 4 weeks with once-daily administration. A randomized, blinded, placebo-controlled, parallel-group study was conducted to evaluate the efficacy and tolerability of long-acting injectable naltrexone (LAN) and a placebo for the treatment of alcohol dependence. LAN was compared with placebo in patients with DSM-IV criteria for alcohol dependence. Assessments were conducted at baseline and at weeks 4 and 12. The primary outcome measure was the percentage of subjects who remained abstinent through 3 months. Differences between the treatment groups were analyzed using a repeated-measures ANOVA. The results showed a significant difference in the percentage of subjects who remained abstinent through 3 months (p=0.048). The percentage of subjects who remained abstinent through 3 months was 33.3% for the LAN group and 11.1% for the placebo group. These results suggest that LAN may be an effective treatment for alcohol dependence.

Percentage of Subjects Abstinent Through 3 Months

* p=0.048
Acamprosate (N-acetylhomotaurine)

- Mechanism: interacts with glutamate and GABA neurotransmitter systems (PI)
- In animal models of alcohol dependence, acamprosate reduced deprivation-induced drinking
- Does not cause dependence or withdrawal
- May reduce protracted withdrawal symptoms

Topiramate

Figure 10. Mean Change (±95% CI) From Baseline in Percent Heavy Drinking Days

Abstinence & AA meeting amount

34 YO Female

60 weeks: Rarely more than 2 drinks per day, rarely more than 3-4 drinking days per week.

- Current Regimen:
  - NTX 50mg daily (declines IM)
  - Gabapentin 600mg tid,
  - Topiramate 50mg bid
  - Venlafaxine XR 150mg daily

- Therapist weekly

Male VA residential patients
n = 2376
Moos et al., J Clin Psychol 2001
Methadone Maintenance 4 Decades Later
Commentary, Herbert Kleber, M.D. JAMA, 2008

- Ironically, even though 12-step programs have often been hostile to MMT, Dole, a friend of the cofounder of Alcoholics Anonymous recounted, “He [Bill W.] suggested that in my future research, I should look for an analogue of a medication that would relieve the alcoholic's sometimes irresistible craving and enable him to progress in AA toward social and emotional recovery.

COCAINEN METHAMPHETAMINE

- No FDA approved Pharmacotherapy
- Modafinil (Provigil)
- Amphetamines
- Baclofen
- Disulfiram (Antabuse)
- “Prometa”
- Vaccine
- Anti-depressants, etc.
MARIJUANA ADDICTION

- No FDA approved Pharmacotherapy
- Dronabinol (Marinol)
- Anti-depressants
- (Rimonabant—antagonist)

Benzodiazepine Addiction

- Other Medications to treat anxiety: SSRIs, SNRIs, Buspirone, others
- Psychotherapy: CBT, others
- Particular Danger with Opioids (Methadone)
- Long-acting vs. Short-acting if used therapeutically
PROCESS ADDICTIONS

- No FDA approved medications
- Food---(Rimonabont)
- Sex
- Gambling---Nalmefene
- Shopping
- Exercise