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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 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

Psychosocial Medication

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:

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

My Treatment "Bias"

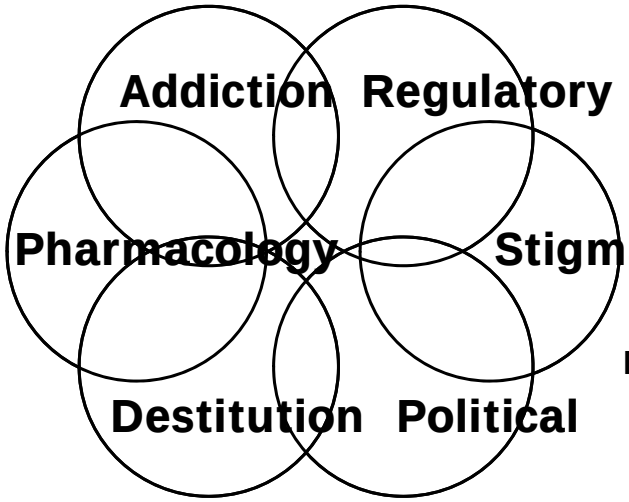
AGONIST ANTAGONIST

Courtesy A.W.

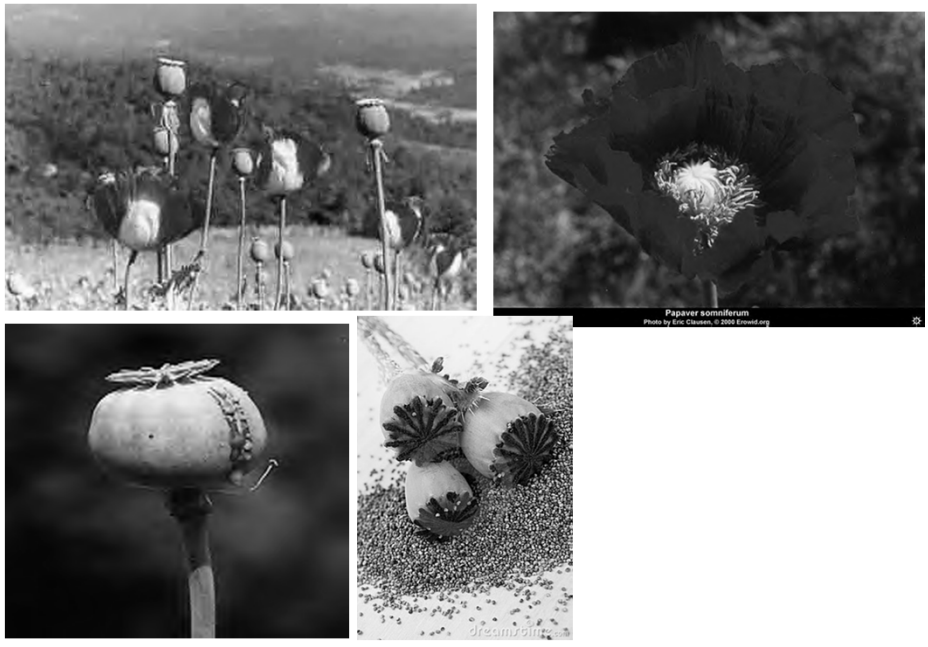
George Santayana 1863-1952

- "Those who do not remember the past are condemned to repeat it."

OPIOID AGONIST THERAPY (OAT)



M>>>>B

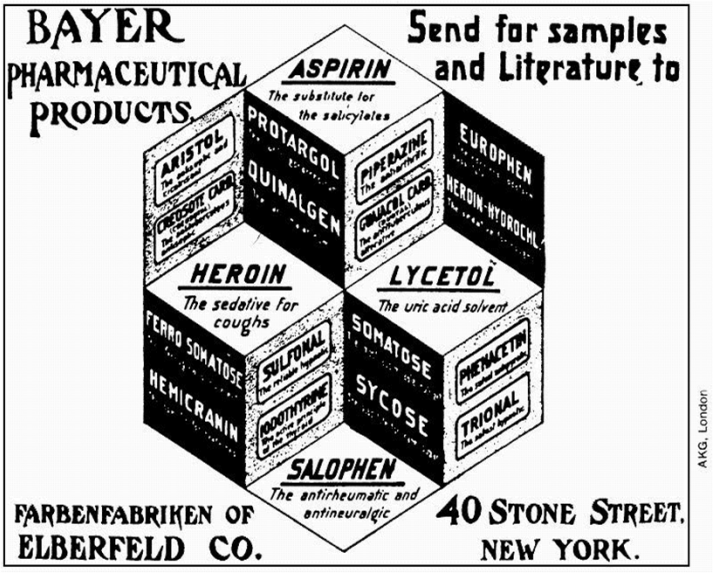


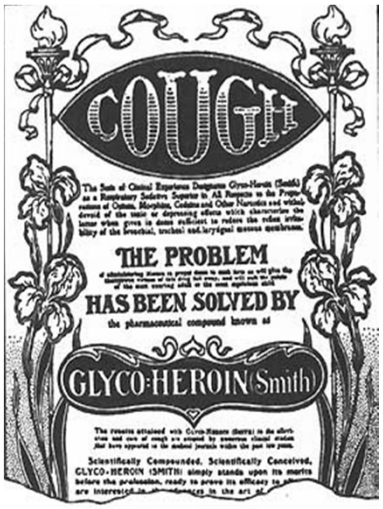
Poppy Seeds UDS

ACC #: 94.100433 PAT #: 55134 PAGE 1

XEAS, PHYSICIAN: SALSITZ, EDWIN M.D. REPORT DATE 08/19/11
1ST AVE at 16TH STREET NEW YORK, NY DATE DRAWN 07/27/11
NEW YORK, NY 10003 TIME DRAWN
SEX: DOB: PHONE (212)-420-4400

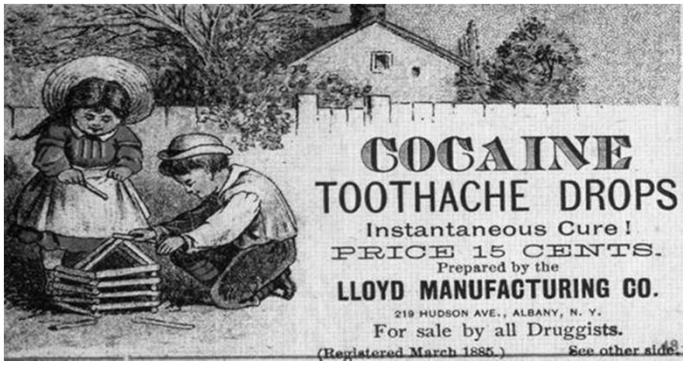
DATE	FLAG	PROCEDURE	RESULT	REFERENCE - RANGE
BI PANEL				
08/05/11		METHADONE- EIA	NEG	CASE DEPEN
08/05/11		COCAINE BY EIA	NEG	<300 NG/ML
08/05/11		OPIATES BY EIA	POS	<300 NG/ML
08/05/11		BARBITURAT EIA	NEG	<300 NG/ML
08/05/11		BENZODIAZE-EIA	NEG NG/ML	<300 NG/ML
08/12/11		MORPHINE TLC	POS	<300 NG/ML





1887

Morphine Syrup 10mg/teaspoon



1885

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

ONE PROBLEM:

RELAPSE UPON RETURN HOME

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

Drs. Dole, Nyswander, and Kreek

Courtesy Dr. Vincent Dole

Dr. Vincent Dole and Dr. Marie Nyswander
Methadone 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. Dole, MD, and Marie Nyswander, MD

A group of 22 patients, previously addicted to diacetylmorphine (heroin), have been stabilized with 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.

ough review of evidence available in 1957,[1] concluded that "The advisability of establishing clinics or some equivalent system to dispense opiates to addicts cannot be settled on the basis of objective facts. Any position taken is necessarily based in part on opinion, and on this question opinions are

JAMA Classics: Celebrating 125 Years
Methadone Maintenance 4 Decades Later
Thousands of Lives Saved But Still Controversial[1]
Commentary by Herbert D. Kleber, MD
JAMA. 2008;300(19):2303-2305

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

From the Rockefeller Institute, and Manhattan General Division of Beth Israel Hospital, New York.

Reprint requests to Rockefeller Institute, New York 10021 (Dr. Dole).

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

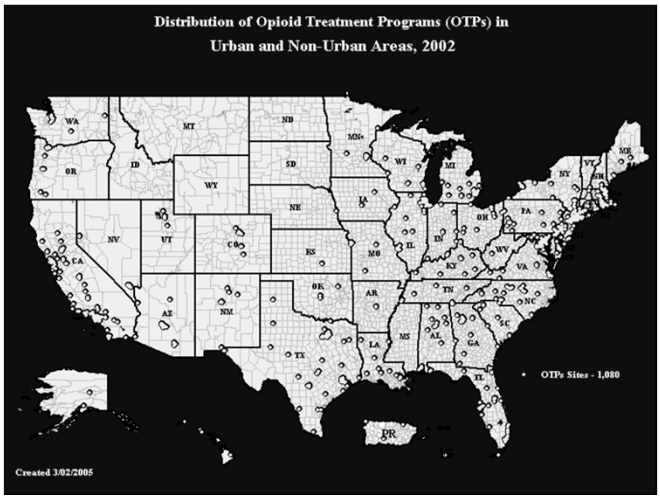
			Status Before Admission to Program								Status Since Admission				
	Age,† Years		Previous Treatments‡												
Ethnic Group*	FD	A	F	S	M	P	Arrests	Education	Best Job§	Military Service‖ Years	Time on Program, Months	D¶	P#	HS**	Present Activity
E	16	22	....	3	3	....	6	8th grade	Truck driver	....	15	150	1a	Cert	Preparing for college (Sept 1965)
E	18	31	3	3	2	....	8	1 year high school	Odd jobs (few months each)	....	15	180	1a	Cert	Horticulture school
P	21	33	2	....	4	....	14	2 years high school	Office clerk	....	10	100	1a	Cert	Employed (rehabilitation work)
E	20	30	1	2	3	1	1	Graduated high school	Store manager	A 3	10	180	1a	....	Employed (usher cashier in theater)
E	17	22	....	....	6	....	4	2 years high school	Shipping clerk	....	11	100	3	....	Employed (parking lot foreman)
E	21	25	....	....	....	12	1	2 years college	Musician	....	10	100	3	....	Employed intermittently (musician)
E	18	25	....	....	2	....	6	Graduated high school	Radio operator in military service	N 4	3	100	2	....	Employed (office work)
N	17	32	1	....	2	....	9	2 years high school	Clothes presser	....	1½	100	1	NS	Seeking employment
N	22	37	....	1	1	....	3	2 years high school	Truck driver	A 4	1½	80	1	NS	Seeking employment
P	15	23	....	....	....	....	1	2 years high school	Head usher	A 3	1½	90	2	Cert Army	Working as waiter
N	16	27	1	....	4	....	1	3 years high school	Stock clerk	A 5	1½	130	1	NS	
E	18	22	3	....	3	2	4	1 year college	Mason	....	1	100	1	....	Seeking employment
P	25	35	1	....	2	....	3	1 year high school	Paint sprayer	....	½	110	1	....	Employed
P	20	32	1	....	4	....	9	2 years high school	Supervisor of shipping department	....	1	100	1	NS	Employed
N	18	30	2	....	....	....	6	3 years high school	Shipping clerk	AF 4	¼	70	1	NS	Seeking employment
E	18	24	....	....	10	....	0	8th grade	Installing window screens	....	3	115	2	NS	Employed
P	14	30	....	....	....	....	2	2 years high school	Office clerk	M 3	3	70	2	NS	Welfare (seeking employment)
P	19	25	....	....	16	....	10	2 years high school	Office clerk	AF 2½	3	110	2	NS	Employed (hospital record room)
E	17	19	....	....	1	1	0	Graduated high school	None	....	3	120	2	....	Vocational school (barber)
P	13	20	....	....	....	1	2	3 years high school	Stock boy	....	3	50	2	NS	Employed (hospital laundry)
E	19	26	....	....	2	....	8	2 years high school	Construction laborer	....	1½	100	2	NS	Seeking employment
N	14	30	....	....	....	....	2	8th grade	Shipping clerk	AF 4	1½	10	2	Cert	Leather goods company interpreter

N=22

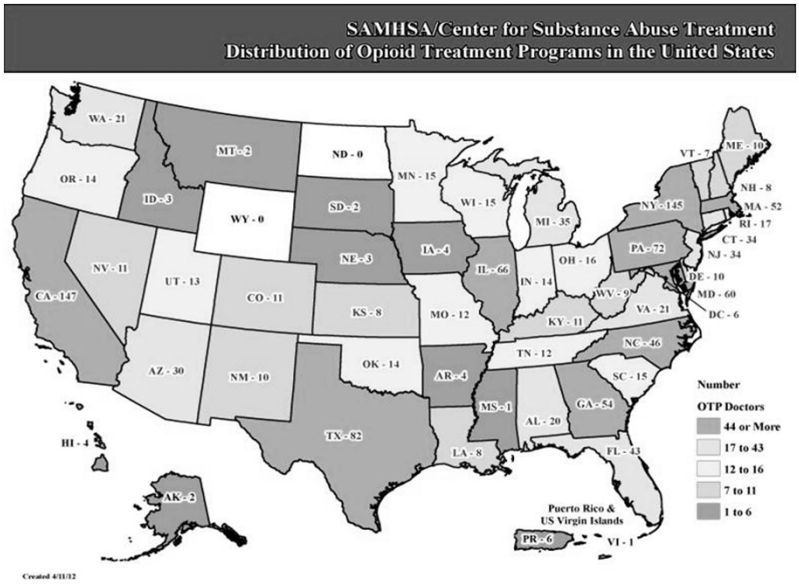
"Narcotic Hunger"

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

Distribution of Opioid Treatment Programs (OTPs) 2002



SAMHSA / CSAT



Missouri OTPs (MMTPs)

Breckinridge Hills

St. Louis Metro Treatment Center
9733 St. Charles Rock Road
Suite 108
Breckinridge Hills, MO 63114
(314) 423-7030

Cape Girardeau

Cape Girardeau Treatment Center
760 S. Kings Highway
Suite F
Cape Girardeau, MO 63703
(573) 335-4333

Columbia

Behavioral Health Group - Columbia Medical Clinic
1301 Vandiver Square
Suite Y
Columbia, MO 65202
(573) 449-8338

Hazelwood

Center for Life Solutions
637 Dunn Road
Suite 180
Hazelwood, MO 63042
(314) 731-0100

Joplin

Behavioral Health Group - Joplin Treatment Clinic
2919 East 4th Street
Joplin, MO 64801
(417) 782-7966

Kansas City

Behavioral Health Group - Kansas City Medical Clinic
723 East 18th Street
Kansas City, MO 64108
(816) 283-3877

Paseo Comprehensive Rehabilitation Clinic
1000 East 24th Street
Kansas City, MO 64108
(816) 512-7143

Samuel U. Rodgers South
2701 East 31st Street
Kansas City, MO 64128
(816) 861-7070

Springfield

Behavioral Health Group - Springfield Medical Clinic
404 East Battlefield Road
Springfield, MO 65807
(417) 865-8045

St. Joseph

St. Joseph Metro Treatment Center
3935 Sherman Avenue
St. Joseph, MO 64506
(816) 233-7300

St. Louis

St. Louis VA Health Care System Opiate Addiction Treatment Program
915 North Grand Boulevard
St. Louis, MO 63106
(314) 289-6418

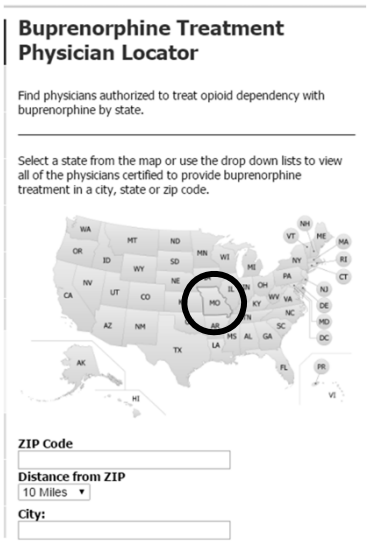
Westend Clinic Inc
5736 West Florissant Avenue
St. Louis, MO 63120
(314) 381-0560

Updated October 13, 2013

Missouri OTPs (MMTPs)

Call 1-800-755-9603 to find the nearest clinic or to speak with a drug abuse counselor.

SAMHSA.gov



? ~ 200 Waivered

"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

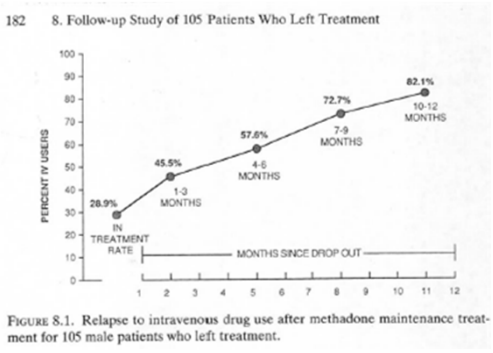
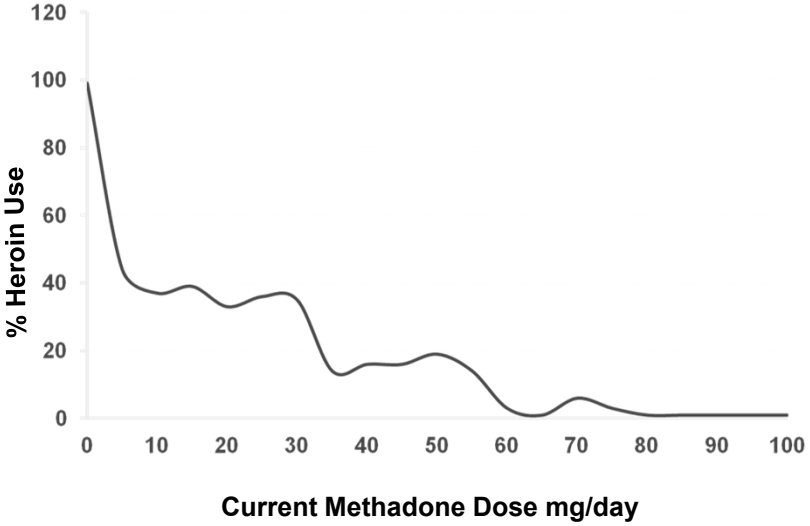


FIGURE 8.1. Relapse to intravenous drug use after methadone maintenance treatment for 105 male patients who left treatment.

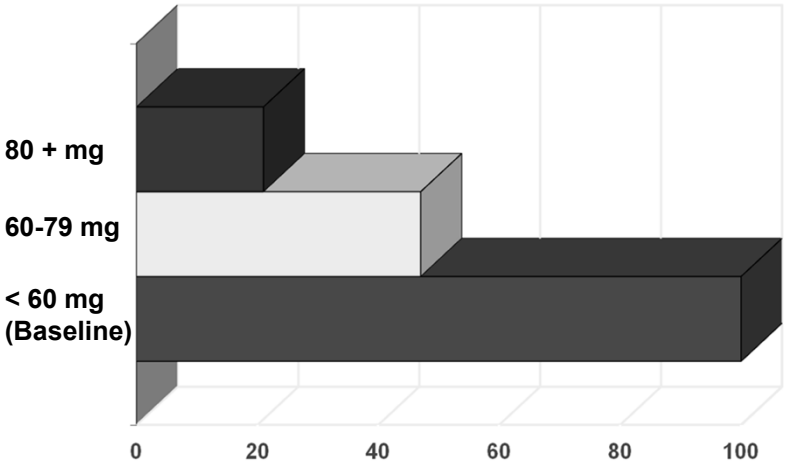
Recent Heroin Use by Current Methadone Dose



J. C. Ball, November 18, 1988

Retention in Treatment Relative to Dose

Relative Risk of Leaving Treatment



Adapted from Caplehorn & Bell

Med J Aust. 1991 Feb 4;154(3):195-9

"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

The Lancet · Saturday 8 September 1979

DOUBLE-BLIND COMPARISON OF METHADONE AND PLACEBO MAINTENANCE TREATMENTS OF NARCOTIC ADDICTS IN HONG KONG

ROBERT G. NEWMAN*

Beth Israel Medical Center, Mount Sinai School of Medicine, New York, U.S.A.

WALDEN B. WHITEHILL†

Medical Service Division, U.S. Penitentiary, Atlanta, Georgia, U.S.A.

Summary In a double-blind study carried out between 1972 and 1975 in Hong Kong 100 heroin addict volunteers were initially admitted to hospital for two weeks for stabilisation on 60 mg of methadone before being assigned at random to two groups: one group received methadone (range 30–130 mg, average 97 mg/day); those in the other group had their dose of methadone reduced at the rate of 1 mg/day and were then maintained on placebo. All subjects were provided with a broad range of supportive services. After thirty-two weeks 10% of the controls were still on treatment, compared with 76% of those receiving methadone. At the end of the three-year project, only 1 of the original 50 placebo subjects still turned up for treatment (2%), whereas the retention-rate (proportion still on treatment) for methadone subjects was 56%. Subjects who had dropped out of the study and were readmitted for methadone treatment under known conditions had the same retention-rate as the original treatment group.

"Because methadone maintenance involves the giving of drugs to a drug-seeking, suggestible population, the placebo effect is very important and must be examined."

(D.P.A.S.), and was designed as a small, double-blind, control study of methadone versus placebo. This report describes the experience of the three-year D.P.A.S. programme.

Patients and Methods

Selection Criteria

100 subjects were selected on a first-come, first-served basis, according to the following criteria:
1. Male, aged 22 to 38 years.
2. Documented history of heroin addiction for at least four years and at least one previous course of treatment.
3. Evidence of current addiction to heroin as determined by three consecutive positive urine tests for morphine.
4. Voluntary application for admission (referrals by the criminal justice system were excluded).
5. A resident with proven fixed address in Kowloon in a district near the treatment clinic.
6. Absence of past or present major psychiatric or medical illness (for example, tuberculosis, peptic ulcer, psychosis).

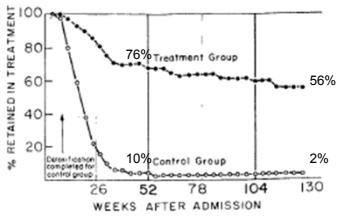
Protocol

Informed consent for participation in the study was given by all subjects.

Those accepted for the trial were admitted to hospital for two weeks for stabilisation on 60 mg of methadone/day, given orally. Because of shortage of beds, only 8 patients could be admitted at a time, so the admission of the 100 subjects extended over seven months.

Outpatient treatment was provided in a clinic specially established for this purpose in the Tung Tau district of Kowloon. The clinic was manned by a physician, two social workers, a medical assistant in charge of pharmacy, and a medical research director, none of whom had had any previous experience with methadone treatment.

On discharge from hospital, subjects were randomly



ig. 1—Proportion of subjects retained in study.
Admission to the study occurred over 7 months; at least 128 weeks apsed between admission of last subject and conclusion of the study.

Mortality in heroin addiction: impact of methadone treatment

Grönbladh L, Öhlund LS, Gunne LM. Mortality in heroin addiction: impact of methadone treatment.
Acta Psychiatr Scand 1990: 82: 223–227.

L. Grönbladh, L. S. Öhlund,
L. M. Gunne
Department of Psychiatry, Ulleråker, Uppsala,

1979-1984; N0 Admit to MMTP

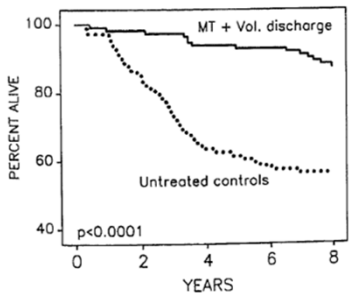


Fig. 2. Survivors in cohorts 1 + 2 (solid line) compared with controls (dotted).

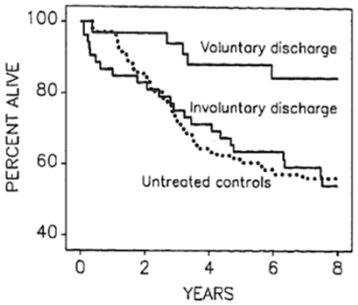


Fig. 3. Cohort 2 (voluntary discharge; upper solid line) contrasted to cohort 3 (involuntary discharge; lower solid line) and controls (dotted line).

Yearly Death Rates: IV ODs
MT=1.4, VD=1.7,
ID=6.91, UC=7.2

U.S. Department of Health & Human Services • National Institutes of Health

NIH Consensus Development Program

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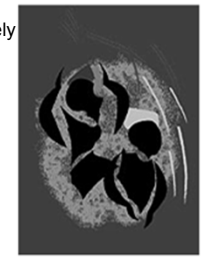
Effective Medical Treatment of Opiate Addiction

National Institutes of Health
Consensus Development Conference Statement
November 17-19, 1997

Conclusions:
"…inform 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

Karen L. Sees, DO
Kevin L. Delucchi, PhD
Carmen Masson, PhD
Amy Rosen, PsyD
H. Westley Clark, MD
Helen Robillard, RN, MSN, MA
Peter Banys, MD
Sharon M. Hall, PhD

Context Despite evidence that methadone maintenance treatment (MMT) is effective for opioid dependence, it remains a controversial therapy because of its indefinite provision of a dependence-producing medication.

Objective To compare outcomes of patients with opioid dependence treated with MMT vs an alternative treatment, psychosocially enriched 180-day methadone-assisted detoxification.

Design Randomized controlled trial conducted from May 1995 to April 1999.

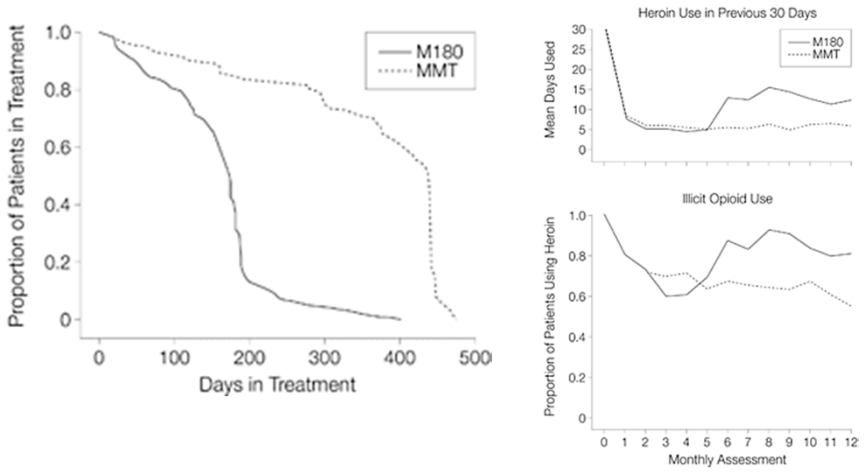
Setting Research clinic in an established drug treatment service.

Patients Of 858 volunteers screened, 179 adults with diagnosed opioid depen-

JAMA 2000:283:1303-1310

Methadone Maintenance vs. 180 Day Detoxification

Sees, K. L. et al. JAMA 2000;283:1303-1310

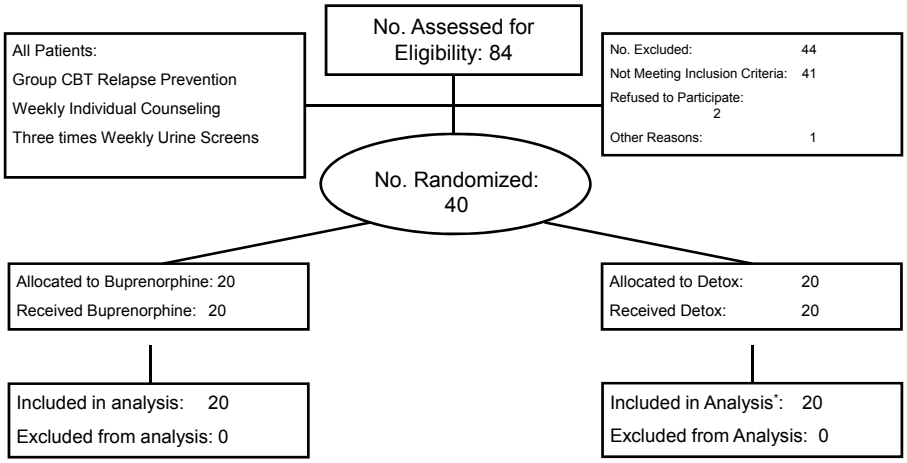


DATA 2000: Buprenorphine

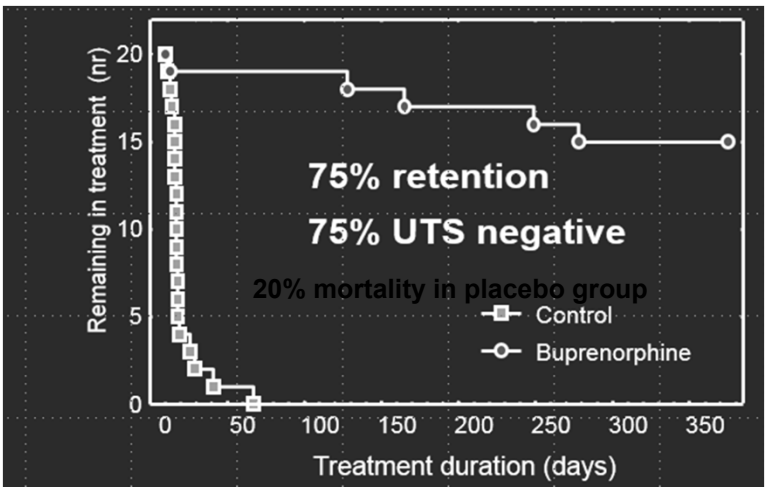
- Major Paradigm Shift: OBOT vs MMTP/OTP
- Mechanism of Action: Similar to methadone
- Partial Agonist: Safety Implications
- 13 years of use in USA
- Now, more patients treated with Bupe than methadone
- Some of the same issues developing:
- 1. **Diversion, Misuse, Abuse**
- 2. Dosage
- 3. Duration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

Detoxification vs. Maintenance

Kakko, Lancet 2003 IV Heroin



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



Prescription Opioid Addiction Treatment Study "POATS"

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

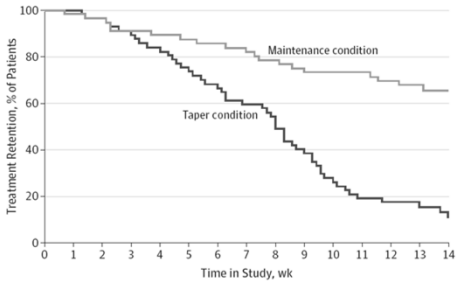
	Observed, No./Total No. (%) [95% CI]		GEE Model–Based Results	
Time Point	SMM	SMM+ODC	OR (95% CI)[a]	*P* Value
End of phase 1	24/323 (7.4) [4.8-10.8]	19/329 (5.8) [3.5-8.9]	1.3 (0.7-2.4)[b]	.36
Phase 2, end of treatment	84/180 (46.7) [39.2-54.2]	93/180 (51.7) [44.1-59.2]	0.8 (0.5-1.2)[c]	.27
Phase 2, 8-wk posttreatment follow-up	13/180 (7.2) [3.9-12.0]	18/180 (10.0) [6.0-15.3]	0.7 (0.3-1.3)[c]	.22

Abbreviations: GEE, generalized estimating equation; ODC, opioid dependence counseling; OR, odds ratio; SMM, standard medical management.
[a]The reference category is SMM+ODC.
[b]Adjusted for chronic pain at baseline and lifetime history of heroin use.
[c]Adjusted 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

Figure 2. Treatment Retention and Mean Buprenorphine Dosage for Patients With Prescription Opioid Dependence



Mean buprenorphine dosage, mg/d

Maintenance condition	14.9	15.1	15.2	15.3	15.3	16.0	15.9	16.2	16.2	16.6	16.8	16.2	16.1	15.8	14.6
Taper condition	15.6	15.6	15.4	15.3	14.2	9.7	5.7	3.1	0.6	0.2	0	0	0	0	0

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.

				End	Start		
	MICHAEL	12/22/79	Suboxone 8mg qd	7/23/10	6/19/09	XXX drop out 1	oxycodone, oxycontin
	MICHAEL 2	12/22/79	Suboxone 8mg qd Film	10/16/11	4/12/11	XXX drop out 2	Relapse oxycodone IR ER
	MICHAEL 3	12/22/79	Suboxone 12 mg Film	2/21/12	12/21/11	XXX drop out 3	Relapse oxycodone IR ER
	MICHAEL 4	12/22/1979	Suboxone 12mg Film	5/13/2012	4/13/2012	XXX drop out 4	Relapse oxycodone IR ER

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

Buprenorphine: Dosage Issue

Addiction

RESEARCH REPORT

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

Yih-Ing Hser[1], Andrew J. Saxon[2], David Huang[1], Al Hasson[1], Christie Thomas[1], Maureen Hillhouse[1], Petra Jacobs[3], Cheryl Teruya[1], Paul McLaughlin[4], Katharina Wiest[1], Allan Cohen[4] & Walter Ling[5]

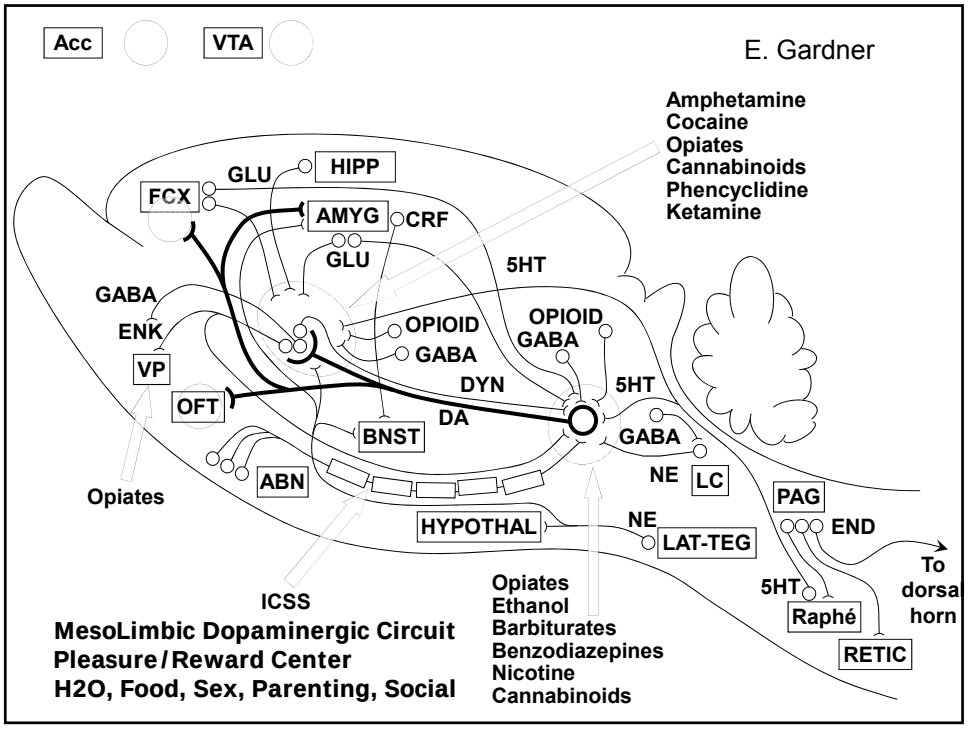
2013

Review

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

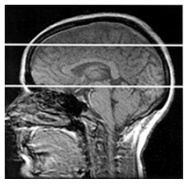
Mark K. Greenwald[a,*], Sandra D. Comer[b], David A. Fiellin[c]

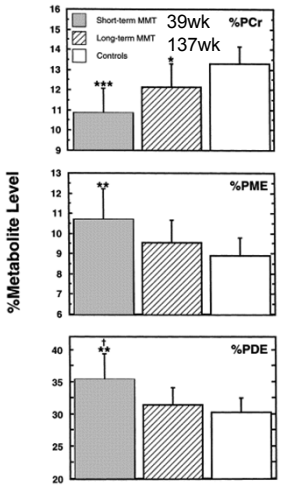
Drug and Alcohol Dependence, 144, 2014



Methadone: Effectiveness/MOA

Cerebral phosphorus metabolite abnormalities in opiate-dependent polydrug abusers in **methadone maintenance**





Psychiatry Research: Neuroimaging
Volume 90, Issue 3 , 30 June 1999, Pages 143-152
Kaufman,M

Phosphorous 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

Article

Acute Effect of Methadone Maintenance Dose on Brain fMRI Response to Heroin-Related Cues

Daniel D. Langleben, M.D.
Kosha Ruparel, M.S.E.
Igor Elman, M.D.
Samantha Busch-Winokur, B.A.
Ramapriyan Pratiwadi, B.S.E.
James Loughead, Ph.D.
Charles P. O'Brien, M.D., Ph.D.
Anna R. Childress, Ph.D.

Objective: Environmental drug-related cues have been implicated as a cause of illicit heroin use during methadone maintenance treatment of heroin dependence. The authors sought to identify the functional neuroanatomy of the brain response to visual heroin-related stimuli in methadone maintenance patients.

Method: Event-related functional magnetic resonance imaging was used to compare brain responses to heroin-related stimuli and matched neutral stimuli in 25 patients in methadone maintenance treatment. Patients were studied before and after administration of their regular daily methadone dose.

Results: The heightened responses to heroin-related stimuli in the insula, amygdala, and hippocampal complex, but not the orbitofrontal and ventral anterior cingulate cortices, were acutely reduced after administration of the daily methadone dose.

Conclusions: The medial prefrontal cortex and the extended limbic system in methadone maintenance patients with a history of heroin dependence remains responsive to salient drug cues, which suggests a continued vulnerability to relapse. Vulnerability may be highest at the end of the 24-hour interdose interval.

(Am J Psychiatry 2008; 165:390–394)

Methadone: Effectiveness/MOA

N=25
Mean=54mos MMTP

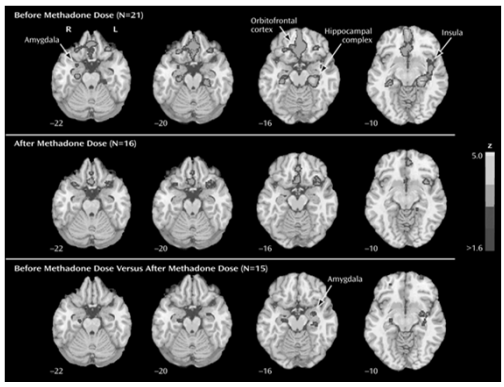


Figure 1. Activation Maps of Brain fMRI Response to Heroin-Related Stimuli in Methadone Maintenance Patients Before and After Daily Methadone Dose.

Am J Psychiatry 2008; 165:390-394

Duration: Potential "Pleiotropic" Benefits

HPA AXIS

TABLE 3. Stress Response Hormones

	Adrenocorticotropic hormone	Cortisol
Short-acting opiates	↓	↓
Opiate withdrawal	↑	↑
Methadone	↔	↔
Buprenorphine	↔	↔
Naltrexone (oral)	↑	↑
Naltrexone (extended release)	?	?

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

Gavin Bart MD, FACP, FASAM
(2012) Maintenance Medication for Opiate Addiction: The Foundation of Recovery, Journal of Addictive Diseases, 31:3, 207-225,

Psychotherapeutic Benefits of Opioid Agonist Therapy

Peter L. Tenore, MD, FASAM

TABLE 3. Mechanism of Opioid Psychiatric Effects

Effect	Neurotransmitter	Mechanism	Function/Model
a) Antidepressant	Serotonin	Block serotonin re-uptake	SSRI[30]
b) Antidepressant	Glutamate	Serotonin-mediated Glutamate Inhib	SSRI[60]
c) Antidepressant	Serotonin	Inhibit Monoamine Oxidase	MAO Inhibitor[38]
d) Antidepressant	Norepinephrine	Inhibit NE Re-uptake	Tricyclic AD[25]
e) Antidepressant	Epinephrine	Inhibit EPI Re-uptake	Tricyclic AD[25]
f) Antidepressant	Epinephrine/Norepinephrine	Inhibit Monoamine Oxidase	MAO Inhibitors[38]
g) Antidepressant	Serotonin/Dopamine	Inhibit Monoamine Oxidase	MAO Inhibitors[38]
h) Antidepressant	Glutamate	NMDA Antagonism	Ketamine[47]
i) Antidepressant	Glutamate	Mu-mediated Glut Release Inhib	Endorphin[66]
j) Antidepressant Restores Hedonic Tone	Dopamine	Mu-opiate Receptor Stimulation	Endorphin[8]
k) Antidepressant Pleasure/Reward Sense	Dopamine	Mu-stimulation	Endorphin[14]
l) Antidepressant	Cortisol	Cortisol Suppression	Endorphin[41]
m) Antianxiety	Serotonin	Block Serotonin Re-uptake	SSRI[58]
n) Antianxiety	Glutamate	Serotonin-Mediated Glutamate Inhib	SSRI[60]
o) Antianxiety	Glutamate	Mu-mediated Glut Inhib	Endorphin[66]
p) Antianxiety	Glutamate	NMDA Antagonism	Lamictal[47]
q) Antianxiety	Serotonin/Dopamine	Inhibit Monoamine Oxidase	MAO Inhibitors[38]
r) Antianxiety	Cortisol	Cortisol Suppression	Endorphin[42]

NMDA = N-Methyl d-Aspartate.

Journal of Addictive Diseases, Vol.27(3) 2008

Prevalence of HIV-1 (AIDS Virus) Infection in Intravenous Drug Users New York City: 1983 - 1984 Study: Protective Effect of Methadone Maintenance Treatment

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

Kreek , 1984; Des Jarlais et al., 1984; 1989

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

Drug Enforcement vs. AIDS Treatment Issue Hits U.N.

OCT. 26, 2015

Is the war on drugs crippling the war on AIDS? And might the AIDS epidemic make governments more willing to treat drug abusers as suffering patients rather than as hardened criminals?

Those questions came to the fore last week because of a fumbled news story. It was announced — incorrectly, it turned out — that the United Nations Office on Drugs and Crime, which oversees the fight against cross-border drug trafficking, was about to do a startling about-face and advocate ending penalties for personal use of all drugs.

The schisms revealed by the news — U.N. agencies, not to mention nations and political parties, are sharply divided over the issue — showed how the debate is shifting, in part because of H.I.V.

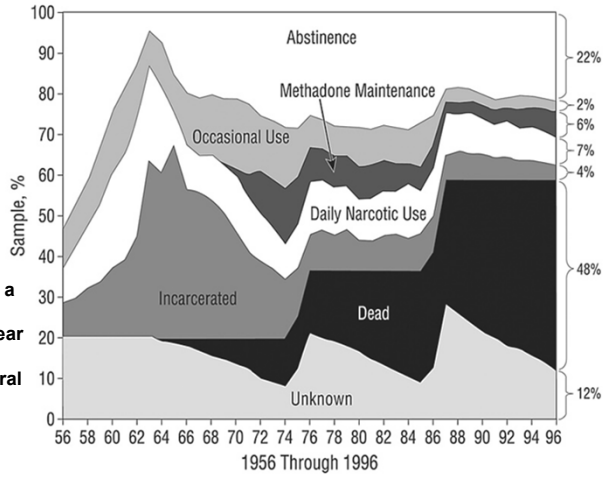
A man in Myanmar's Kachin State injecting heroin. The debate over criminal penalties for drug use has shifted in part as a result of the spread of H.I.V. Adam Dean for The New York Times

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



The natural history of narcotics addiction among a male sample (N = 581). Hser Y, et. al., 2001. A 33-Year Follow-up of Narcotics Addicts. Archives of General Psychiatry, 58:503-508)

Hser Y, et. al., 2001. A 33-Year Follow-up of Narcotics Addicts. Archives of General Psychiatry, 58:503-508

- 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.

Maintenance Taper/Abstinence

RELAPSE DANGER

March 18, 2015
Contact: DEA Public Affairs
(202) 307-7977

DEA Issues Nationwide Alert on Fentanyl as Threat to Health and Public Safety

MAR 18 (WASHINGTON) - The United States Drug Enforcement Administration (DEA) today issued a nationwide alert about the dangers of fentanyl and fentanyl analogues/compounds. Fentanyl is commonly laced in heroin, causing significant problems across the country, particularly as heroin abuse has increased. This alert was issued through the multi-agency El Paso Intelligence Center (EPIC) to all U.S. law enforcement.

•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

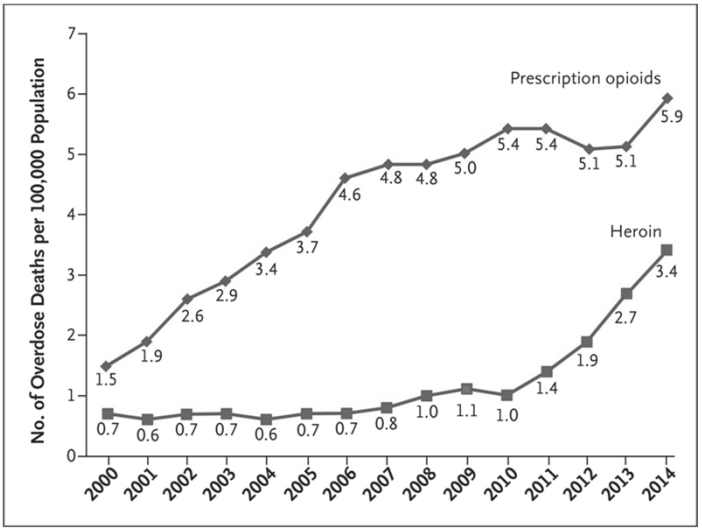
- Low rates of retention in treatment
- High rates of relapse post-treatment
  - < 50% abstinent at 6 months
  - < 15% abstinent at 12 months
  - Increased rates of overdose due to decreased tolerance
  - Walter Ling “Quote”

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

Age-Adjusted Rates of Death Related to Prescription Opioids and Heroin Drug Poisoning in the United States, 2000–2014.



Compton WM et al. N Engl J Med 2016;374:154-163

Compton WM et al. N Engl J Med 2016;374:154-163

Duration:Safety

Drug and Alcohol Dependence, 33 (1993) 235 - 245
Elsevier Scientific Publishers Ireland Ltd.

The medical status of methadone maintenance patients in treatment for 11 – 18 years

N=111

David M. Novick[a,b], Beverly L. Richman[c], Jeffrey M. Friedman[a], Jacqueline E. Friedman[a], Christine Fried[b], Janifer P. Wilson[b], Anita Townley[c] and Mary Jeanne Kreek[a]

[a]The Rockefeller University, New York, NY 10021 and [b]Department of Medicine and [c]Methadone Maintenance Treatment Program, Beth Israel Medical Center, New York, NY 10003 (USA)

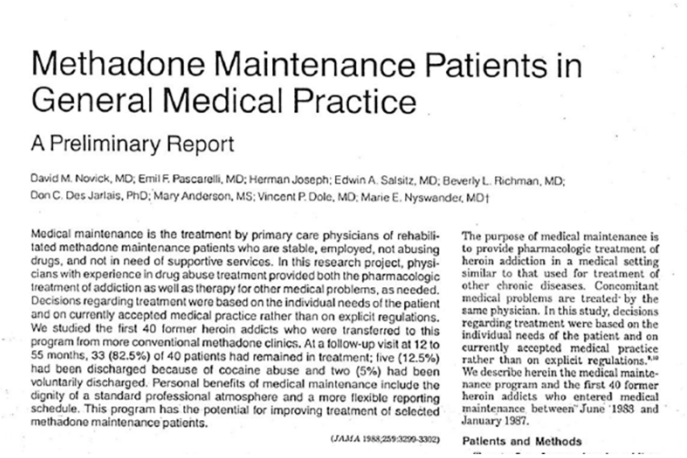
(Accepted April 7, 1993)

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

David M. Novick, MD; Emil F. Pascarelli, MD; Herman Joseph; Edwin A. Salsitz, MD; Beverly L. Richman, MD; Don C. Des Jarlais, PhD; Mary Anderson, MS; Vincent P. Dole, MD; Marie E. Nyswander, MD†

Medical maintenance is the treatment by primary care physicians of rehabilitated methadone maintenance patients who are stable, employed, not abusing drugs, and not in need of supportive services. In this research project, physicians with experience in drug abuse treatment provided both the pharmacologic treatment of addiction as well as therapy for other medical problems, as needed. Decisions regarding treatment were based on the individual needs of the patient and on currently accepted medical practice rather than on explicit regulations. We studied the first 40 former heroin addicts who were transferred to this program from more conventional methadone clinics. At a follow-up visit at 12 to 55 months, 33 (82.5%) 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 selected methadone maintenance patients.

(JAMA 1988;259:3299-3302)

The purpose of medical maintenance is to provide pharmacologic treatment of heroin addiction in a medical setting similar to that used for treatment of other chronic diseases. Concomitant medical problems are treated by the same physician. In this study, decisions regarding treatment were based on the individual needs of the patient and on currently accepted medical practice rather than on explicit regulations.[1,2] We describe herein the medical maintenance program and the first 40 former heroin addicts who entered medical maintenance between June 1983 and January 1987.

Patients and Methods

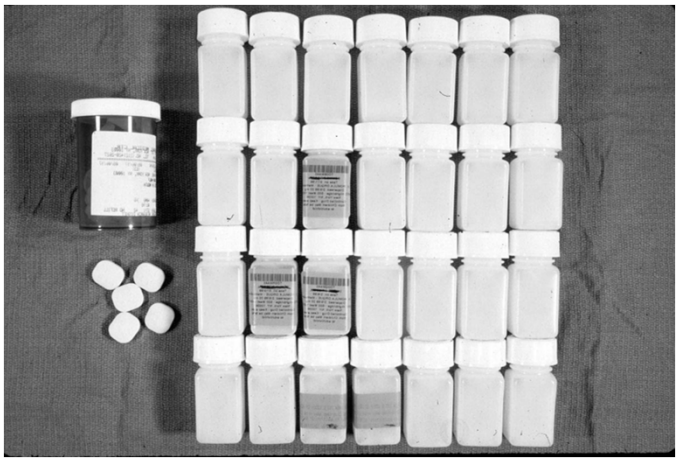
Medical Maintenance Admission Criteria

- 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

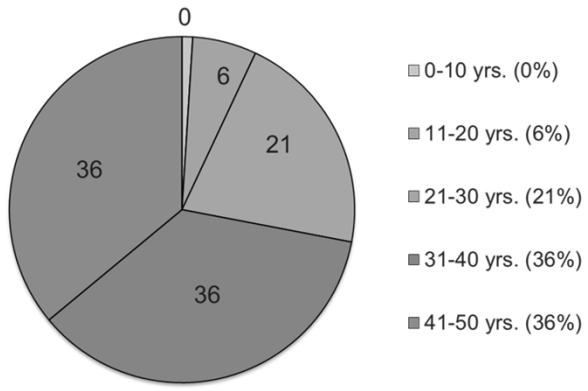
- Patient given 28 day supply of methadone, by MD,in disket/tablet form, every 4 weeks.
- Medication prepared by hospital pharmacy in usual Rx type bottle and label
- Routine urine toxicology
- Patient returns before “run out” date
- Primary care provided

Medical Maintenance




EXIT
3F
Allergy &
Medical Specialties

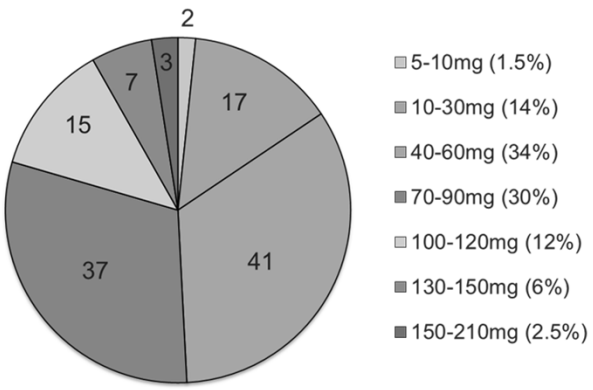
Total Years on Methadone



Courtesy A.W.

Medical Maintenance: Dose N=122

AVERAGE DOSE = 68mg.
RANGE: 5mg–210mg



Courtesy A. W.

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%)

- **31 Tobacco**
- **19 Hepatitis C**
- **5 Lymphoma**
- **13 Medical**
- **4 HIV**
- **1 Old Age**
- **2 Homi/Suicide**
- **1 Prostate Ca**
- **1 Leukemia**
- **1 Diabetes**
- **1 Ovarian CA**

Active
122 (35%)

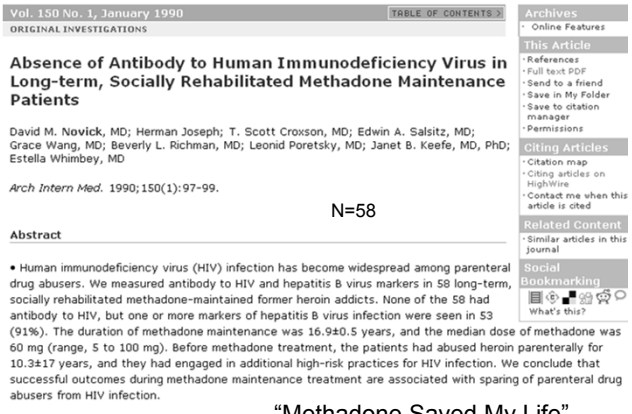
- **Buprenorphine 53**
  Deaths: 1 Tob 1 Hep C
- **9 liver transplants**
  8 patients
  4 alive

Revised - 2/1/15

Deaths
82 (22%)

# of Patients	Cause
31	Tobacco
19	Hepatitis C
5	Lymphoma
13	Medical
4	HIV
1	Old Age
2	Homicide/Suicide
1	Prostate Cancer
1	Leukemia
1	Diabetes
1	Ovarian Cancer

Methadone Medical Maintenance



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ORIGINAL INVESTIGATIONS

Absence of Antibody to Human Immunodeficiency Virus in Long-term, Socially Rehabilitated Methadone Maintenance Patients

David M. **Novick**, MD; Herman Joseph; T. Scott Croxson, MD; Edwin A. Salsitz, MD; Grace Wang, MD; Beverly L. Richman, MD; Leonid Poretsky, MD; Janet B. Keefe, MD, PhD; Estella Whimbey, MD

Arch Intern Med. 1990;150(1):97-99.

N=58

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 53 (91%). The duration of methadone maintenance was 16.9±0.5 years, and the median dose of methadone was 60 mg (range, 5 to 100 mg). Before methadone treatment, the patients had abused heroin parenterally for 10.3±17 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.

(*Arch Intern Med.* 1990;150:97-99)

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What's this?

"

"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 Couselor
- 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
- Entrepeuner
- Musician
- Nurse

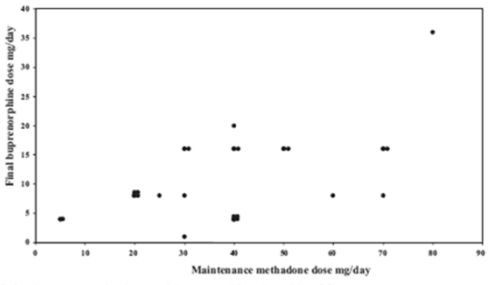
*** Safety Sensitive—Employer's OK**

Methadone→Buprenorphine

ORIGINAL ARTICLE

Transitioning Stable Methadone Maintenance Patients to Buprenorphine Maintenance

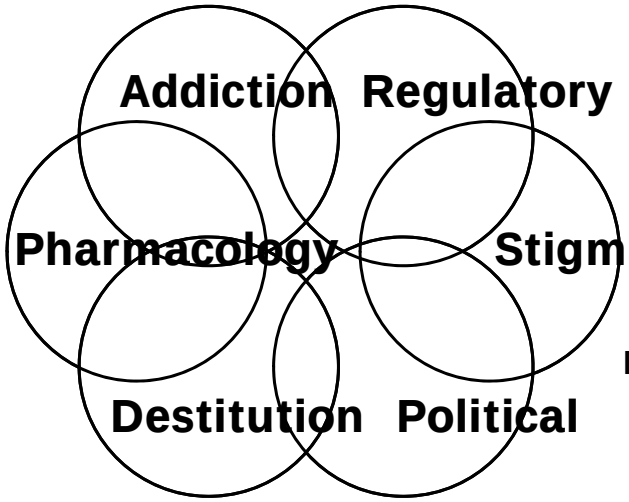
Edwin A. Salsitz, MD, Christopher C. Holden, MD, Susan Tross, PhD, and Ann Nugent, BA



Association between methadone and buprenorphine dose (N = 25).

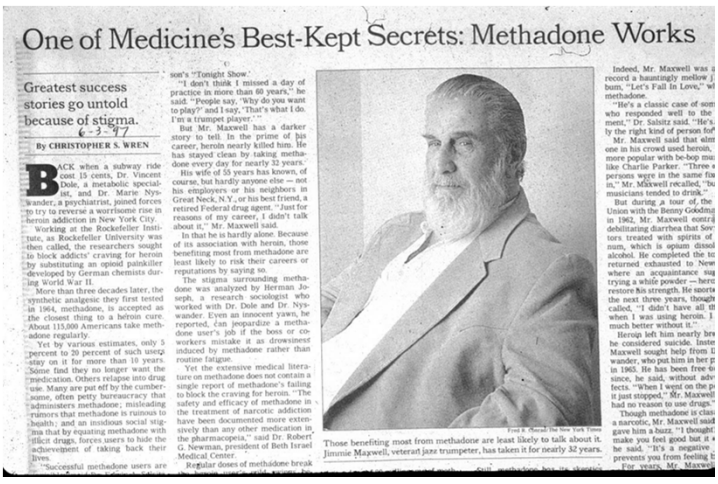
JAM, 2010 (4) 88-92

OPIOID AGONIST THERAPY (OAT)



M>>>>B

OAT: Stigma



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

Greatest success stories go untold because of stigma.

6-3-97

By CHRISTOPHER S. WREN

BACK when a subway ride cost 15 cents, Dr. Vincent Dole, a metabolic specialist, and Dr. Marie Nyswander, a psychiatrist, joined forces to try to reverse a worrisome rise in heroin addiction in New York City.

Working at the Rockefeller Institute, as Rockefeller University was then called, the researchers sought to block addicts' craving for heroin by substituting an opioid painkiller developed by German chemists during World War II.

More than three decades later, the synthetic analgesic they first tested in 1964, methadone, is accepted as the closest thing to a heroin cure. About 115,000 Americans take methadone regularly.

Yet by various estimates, only 5 percent to 20 percent of such users stay on it for more than 10 years. Some find they no longer want the medication. Others relapse into drug use. Many are put off by the cumbersome, often petty bureaucracy that administers methadone; misleading rumors that methadone is ruinous to health; and an insidious social stigma that by equating methadone with illicit drugs, forces users to hide the achievement of taking back their lives.

"Successful methadone users are

son's "Tonight Show."

"I don't think I missed a day of practice in more than 60 years," he said. "People say, 'Why do you want to play?' and I say, 'That's what I do. I'm a trumpet player.'"

But Mr. Maxwell has a darker story to tell. In the prime of his career, heroin nearly killed him. He has stayed clean by taking methadone every day for nearly 32 years.

His wife of 55 years has known, of course, but hardly anyone else — not his employers or his neighbors in Great Neck, N.Y., or his best friend, a retired Federal drug agent. "Just for reasons of my career, I didn't talk about it," Mr. Maxwell said.

In that he is hardly alone. Because of its association with heroin, those benefiting most from methadone are least likely to risk their careers or reputations by saying so.

The stigma surrounding methadone was analyzed by Herman Joseph, a research sociologist who worked with Dr. Dole and Dr. Nyswander. Even an innocent yawn, he reported, can jeopardize a methadone user's job if the boss or coworkers mistake it as drowsiness induced by methadone rather than routine fatigue.

Yet the extensive medical literature on methadone does not contain a single report of methadone's failing to block the craving for heroin. "The safety and efficacy of methadone in the treatment of narcotic addiction have been documented more extensively than any other medication in the pharmacopeia," said Dr. Robert G. Newman, president of Beth Israel Medical Center.

Regular doses of methadone break

Fred R. Conrad/The New York Times

Those benefiting most from methadone are least likely to talk about it. Jimmie Maxwell, veteran jazz trumpeter, has taken it for nearly 32 years.

Indeed, Mr. Maxwell was a record a hauntingly mellow bum, "Let's Fall In Love," w methadone.

"He's a classic case of som who responded well to the ment," Dr. Salsitz said. "He's by the right kind of person fro

Mr. Maxwell said that alm one in his crowd used heroin, more popular with be-bop mu like Charlie Parker. "Three persons were in the same fla in," Mr. Maxwell recalled. "Bu musicians tended to drink."

But during a tour of the Union with the Benny Goodma in 1962, Mr. Maxwell contra debilitating diarrhea that Sev tors treated with spirits of num, which is opium dissol alcohol. He completed the tu returned exhausted to New where an acquaintance sug trying a white powder — herc restore his strength. He snorte the next three years, though called, "I didn't have all th when I was using heroin. I much better without it."

Heroin left him nearly bro he considered suicide. Inste Maxwell sought help from D wander, who put him in her p in 1965. He has been free d since, he said, without adv fects. "When I went on the p it just stopped," Mr. Maxwell had no reason to use drugs."

Though methadone is clas a narcotic, Mr. Maxwell said gave him a buzz. "I thought make you feel good but it a he said. "It's a negative prevents you from feeling h

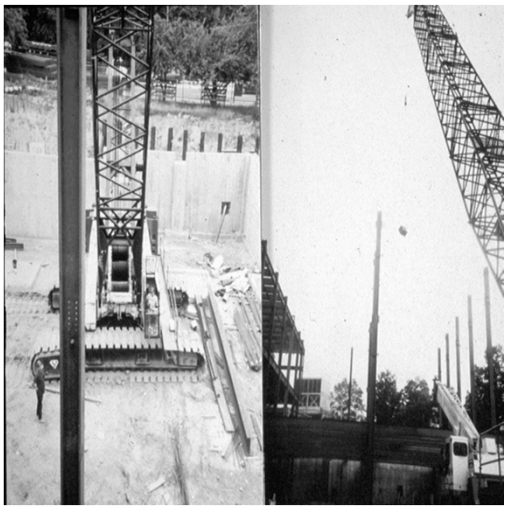
For years, Mr. Maxwell

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 B1

The New York Times SATURDAY, SEPTEMBER 18, 1999

Crane Secured for Storm Falls, Killing a Worker in Chelsea

By JODI WILGOREN with KEVIN FLYNN 9/99

A huge crane collapsed at a Chelsea construction site yesterday morning, killing one worker and injuring three others after the crane operator tried to hoist the boom without releasing special restraints intended to prevent an accident once Hurricane Floyd reached the city, officials said.

The 30-ton red steel crane, which had become a fixture in the bustling neighborhood, buckled under the restraints, tumbled backward and crashed at the corner of 24th Street and the Avenue of the Americas just after 7 A.M., crushing a carpenter who was having breakfast on the sidewalk before heading to work at the site.

The man, Kenneth Freiman, 43, suffered severe head injuries and was pronounced dead at the scene, where the crane knocked over a traffic light and a lamppost and left a hole 4 feet deep in the sidewalk.

The other three workers were hit by debris and had only minor injuries. The crane operator, Paul Bettinger, spent most of yesterday being questioned by the police, as well as investigators from the city's Buildings Department and the Federal Occupational Safety and Health Administration.

The fatal accident came 14 months after the collapse of a temporary elevator tower at a problem-plagued construction site in Times Square killed an 85-year-old woman, and is the latest in a spate of high-profile construction debacles in Manhattan. Several blocks of the Avenue of the Americas, a busy commercial artery, were shut down for more than two hours during the morning rush, as workers in hard hats stood a stoic vigil on a street corner, staring toward the shrouded body of their fallen colleague.

"I sit there every morning," said William Hirrell, 33, a steel laborer at the site whose 53-mile commute from Greenwood Lake, N.Y., was delayed yesterday because of the storm. "That's where I would have been if I was on time."

A field supervisor for Laquila/Pinnacle said both the crane operator and the victim worked for the company, which is based in Mamaroneck, N.Y. Laquila/Pinnacle has been subcontracted to create the concrete superstructure for the 28-story, $75 million apartment building, which is scheduled to open in the spring. The crane belonged to New York Crane, a subsidiary of Lomma Construction.

Officials at the city's Buildings Department said the project had all its permits in order, and that inspectors had been careful to visit construction sites throughout New York on Wednesday and Thursday to insure that large cranes were tied down so the wind could not knock them around. But the extra safety measures backfired at the Avenue of the Americas site, investigators said, when yesterday morning a crane operator either was unaware or forgot that the equipment was tied, and tried to hoist it up without releasing the restraints.

Richard C. Visconti, the Acting Buildings Commissioner, said that in preparation for the storm, the boom, or swinging arm of the crane, had been lowered and secured to the mast, or tower, with wire ropes, to avoid a

Continued on Page B6

A crane fell at 24th Street and the Avenue of the Americas yesterday, killing a worker.

Associated Press

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 <u>severe</u> - 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

Substance Use & Misuse, 47:1117–1124, 2012
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DOI: 10.3109/10826084.2012.680172

informa
healthcare

ORIGINAL ARTICLE

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

Robert Roose[1], Liza Fuentes[2] and Mandeep Cheema[3]

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

TABLE 2 Frequency of references to methadone and buprenorphine based on message

		Message of reference		
Medication	Total # of references	Endorsed as treatment option	Rejected as treatment option	Drug of abuse
Methadone	20	0	3	17
Buprenorphine	8	0	1	7

OAT: Stigma

R.I.P.

'Celeb Rehab' Rocker Mike Starr Dead

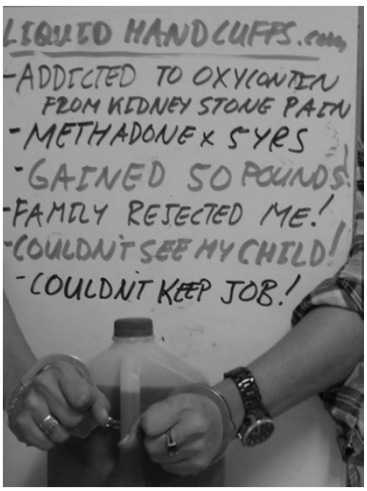
3/8/2011 2:58 PM PST by TMZ Staff Like 38K

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

Getty

Starr appeared on the third season of "**Celebrity** Rehab" back in 2009 -- and was arrested last month for felony possession of a controlled substance. Salt Lake City cops say he had 6 Xanax pills and 6 Opana (painkiller) pills when he was busted.

OAT: Stigma



Duration Barriers: Stigma

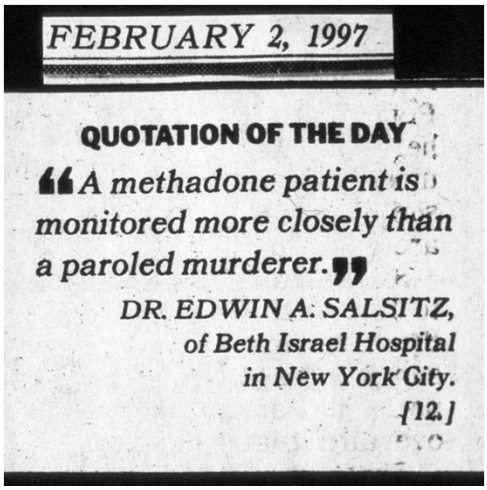
SM: You must be excited to see him when he comes back?

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

OAT: Stigma



FEBRUARY 2, 1997

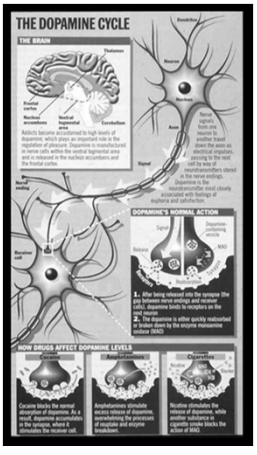
QUOTATION OF THE DAY

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

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

[12.]

OAT Barriers: Terminology



05/1997

OAT Barriers: Terminology

A Way Out for Junkies?

In trials going on nationwide, buprenorphine seems to block the cravings of heroin withdrawal

By JOHN CLOUD

WHEN TED C., A HEROIN JUNKIE AND former baseball umpire, heard about an experimental new drug that might be for his addiction, he was skeptical. Doctors told him that a single pill called buprenorphine could eradicate his enormous craving for the narcotic, which he had been snorting daily for several years. It sounded too good to be true—junkies live in fear of the agony that arrives when a hit wears off—so Ted bought an extra bag of heroin the night before he took buprenorphine for the first time. Just in case.

But this time there was no pain. "I went to the clinic, took the pill and went home. I used the last of the bag and haven't touched heroin since," he says. That was April, and today he still takes the tablets—one a day keeps the craving away—but he expects to stop using the drug in a few months. "There was no struggle," he says. "There is no downside to the drug."

Testimonials such as Ted's have researchers across the U.S. claiming a breakthrough in the treatment of heroin addiction. Today most addicts who want to kick the drug are sent to clinics that administer methadone. But that cure is nearly as troublesome as the disease it treats. Methadone produces its own high and is so addictive that it has its own black market. To receive it legally, addicts must report every day to authorized clinics, something many are loath to do. Before buprenorphine, Ted tried methadone and found the experience a lot like taking heroin—only he had to get his fix in front of a mangy group of drug pushers and criminals. The scene made him feel closer to drugs, not free of them.

Buprenorphine is an opiate too, but it creates only a passing flicker of a high, if that—and it is not addictive. Consequently, the FDA is expected to approve the drug by spring, which would allow physicians to dispense it from the privacy of their offices. For many, that will be not a moment too soon. During the 1990s, heroin addiction has spread to groups ill-served by existing treatment networks: professionals like Ted and middle-class, often suburban, teens. The majority of addicts are still poor, city-dwelling adults, but teens account for more than a fifth of those who say they have taken heroin in the past year, double the proportion in the early '90s. Researchers believe more kids are using it because it is now sold in purer form—pure enough to snort or smoke. Like Ted, most teens will not inject, but they don't mind taking a puff or a sniff. (Injecting heroin is the quickest way to experience its rush, but the drug still packs a punch when snorted or smoked.)

For suburban kids, treatment options are sparse. Federally funded methadone clinics are off limits to those younger than 21. Even at private clinics, doctors are reluctant to prescribe methadone for all but the most hard-core addicts. "Methadone itself is a terribly shackling drug, and getting young or short-time users ... on methadone is criminal," says Paul Earley, an addiction specialist at the Ridgeview Institute, outside Atlanta.

In the fight against addiction, breakthrough promises have been made and broken many times; methadone was once considered a miracle drug, and heroin itself was developed to cure addictions. But researchers say buprenorphine could be the answer. Like heroin and methadone, it bonds to certain receptors in the brain, blocking the pain they transmit and convincing the brain that the cravings have been satisfied. Yet somehow it does that without creating cravings for itself. Even long-term junkies who try buprenorphine simply do not want heroin anymore.

So why has buprenorphine not replaced methadone? Although the drug has been rumored since the 1970s to work well for addicts—and has been used in France for more than a year—scientists only recently began the costly clinical trials needed for government approval. Conducted at 12 hospitals around the U.S. and coordinated jointly by the government and drugmaker Reckitt & Colman, the trials have gone extremely well—so well that clinicians stopped giving placebos to control groups. "We could not morally go on giving placebos to people who needed the drug," says Dr. John Rotrosen, one of the study's administrators.

THE PROBLEM

THE SOLUTION

GETTING WELL: An addict shoots up in a New York City park; another receives his weekly dosage of buprenorphine, an experimental antidote that erases cravings for the opiate

The inevitable catch? No one is sure how long patients will have to take buprenorphine before they can be free of it. Doctors say most heroin addicts are addicted for life, even if they stop using it—a warning Ted C. might well heed. What's more, buprenorphine will probably cost more than methadone, ruling it out for poor junkies without government aid. Still, it could be a lifeline for many of the estimated half-million American addicts. Predicts Rotrosen: "It will fundamentally change the way heroin is treated in the U.S." —*Reported by Edward Barnes/New York, Greg Fallon/Atlanta and Chandrani Ghosh/Washington*

TIME, JANUARY 19, 1998

1998

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 Pooch, 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

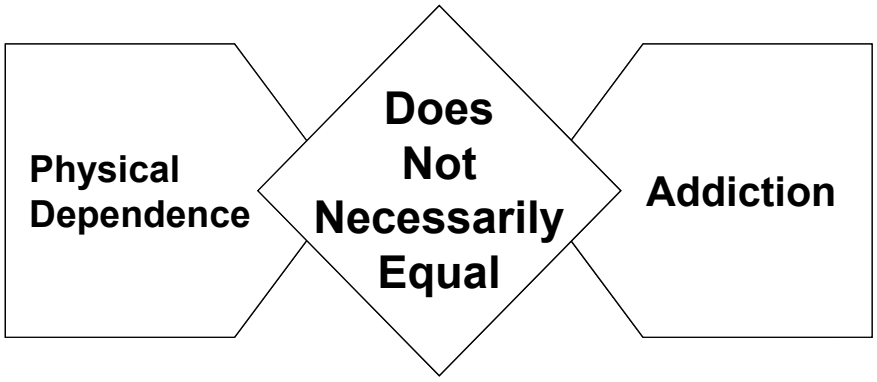
ADDICTION VOCABULARY

Slang	Medical
Addict	Addicted patient, patient with the disease of addiction
Junkie, dope fiend	Opiate addicted patient, cocaine addicted patient
Clean urine	Urine negative for illicit or non-prescribed drugs
Dirty urine	Urine positive for x,y,or z
Drunk, smashed, bombed	Alcohol addicted, intoxicated
Crack head, pot head	Cocaine addicted, THC abuse
La La Land	Intoxicated
Street addict, hard-core addict	Patient with the disease of addiction
Speed-balling	Using heroin and cocaine together
Meth	Methadone or Methamphetamine
Strung out	Debilitated, intoxicated
Cop/Fix	Obtain, purchase/Dosed, took
Hooked	Addicted
Kicking	Withdrawal Syndrome

Duration Barriers: Terminology

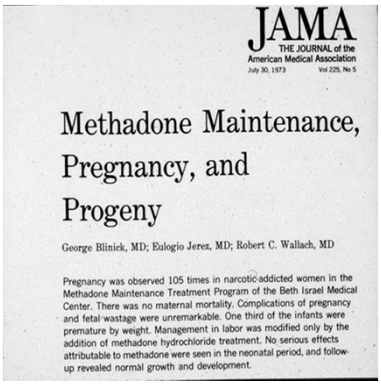
- "Substitution Treatment" "OST"
- Standard terminology in Europe and Australia
- ?? Accurate ?? Helpful ?? Harmful
- "Aren't you just substituting one drug or addiction for another??"
- Why not just call it "Treatment for Opioid Use Disorder?"

OAT: Terminology



Courtesy A.W.

Duration Barriers: Pregnancy



JAMA
THE JOURNAL of the American Medical Association
July 30, 1973 Vol 225, No 5

Methadone Maintenance, Pregnancy, and Progeny

George Blinick, MD; Eulogio Jerez, MD; Robert C. Wallach, MD

Pregnancy was observed 105 times in narcotic-addicted women in the Methadone Maintenance Treatment Program of the Beth Israel Medical Center. There was no maternal mortality. Complications of pregnancy and fetal wastage were unremarkable. One third of the infants were premature by weight. Management in labor was modified only by the addition of methadone hydrochloride treatment. No serious effects attributable to methadone were seen in the neonatal period, and follow-up revealed normal growth and development.

Neonatal Abstinence Syndrome after Methadone or Buprenorphine Exposure

Hendrée E. Jones, Ph.D., Karol Kaltenbach, Ph.D., Sarah H. Heil, Ph.D., Susan M. Stine, M.D., Ph.D., Mara G. Coyle, M.D., Amelia M. Arria, 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. SWARNS
Published: August 16, 1998

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 enslaving former drug users instead of pushing them toward abstinence.

TURNAROUND RUDY PUTS $5M IN METHADONE CLINICS

By Susan Rubinowitz October 6, 1999 | 4:00am

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 to extend clinic hours and add job-training and psychological evaluations, said city Health and Hospitals Corporation spokeswoman Jane Zimmerman.

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 (OTPs) and methadone, and to transfer patients to office-based buprenorphine treatment. Mary Mayhew

in the *Bangor Daily News* (*BDN*).

Under his proposal, LePage would cut $727,000 in funding for MaineCare in fiscal year 2016 and $868,000 in fiscal year 2017; this would also mean the state would not receive Medicaid matching funds from the federal government for those years, which would be $1.2

CJS Barriers: Good News

SAMHSA Bans Drug Court Grantees from Ordering Participants off MAT

February 24, 2015 by ATForum

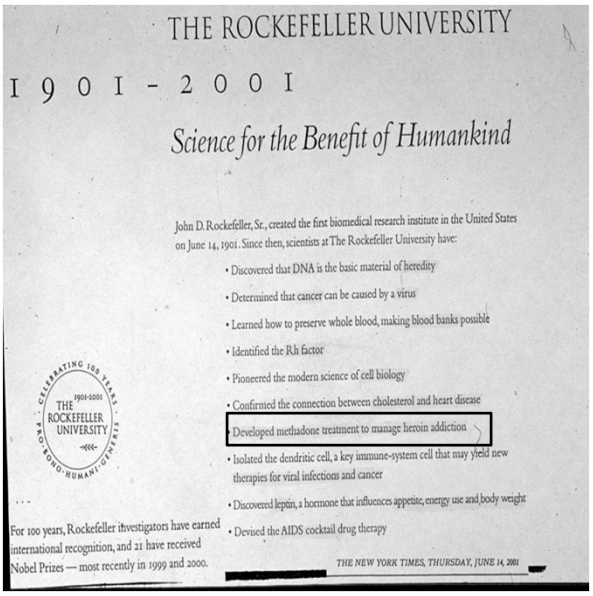
"A grant announcement issued by the Substance Abuse and Mental Health Services Administration (SAMHSA) last month to fund drug courts contains an important new condition: drug courts funded by the grants would no longer be allowed to tell offenders to stop taking medications to treat opioid use disorders. 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 (RFA): "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 these 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."

Read more at: http://www.alcoholismdrugabuseweekly.com/Article-Detail/samhsa-bans-drug-court-grantees-from-ordering-participants-off-mat.aspx

Source: AlcoholismDrugAbuseWeekly.com – February 16, 2015



THE ROCKEFELLER UNIVERSITY

1901-2001

Science for the Benefit of Humankind

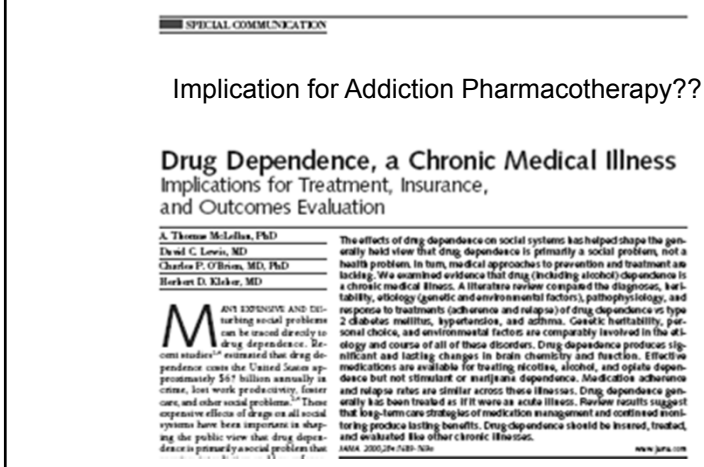
John D. Rockefeller, Sr., created the first biomedical research institute in the United States on June 14, 1901. Since then, scientists at The Rockefeller University have:

- Discovered that DNA is the basic material of heredity
- Determined that cancer can be caused by a virus
- Learned how to preserve whole blood, making blood banks possible
- Identified the Rh factor
- Pioneered the modern science of cell biology
- Confirmed the connection between cholesterol and heart disease
- Developed methadone treatment to manage heroin addiction
- Isolated the dendritic cell, a key immune-system cell that may yield new therapies for viral infections and cancer
- Discovered leptin, a hormone that influences appetite, energy use and body weight
- Devised the AIDS cocktail drug therapy

THE ROCKEFELLER UNIVERSITY 1901-2001 CELEBRATING 100 YEARS PRO BONO HUMANI GENERIS

For 100 years, Rockefeller investigators have earned international recognition, and 21 have received Nobel Prizes — most recently in 1999 and 2000.

THE NEW YORK TIMES, THURSDAY, JUNE 14, 2001



SPECIAL COMMUNICATION

Implication for Addiction Pharmacotherapy??

Drug Dependence, a Chronic Medical Illness
Implications for Treatment, Insurance, and Outcomes Evaluation

A. Thomas McLellan, PhD
David C. Lewis, MD
Charles P. O'Brien, MD, PhD
Herbert D. Kleber, MD

MANY EXPENSIVE AND DISturbing social problems can be traced directly to drug dependence. Recent studies[1-4] estimated that drug dependence costs the United States approximately $67 billion annually in crime, lost work productivity, foster care, and other social problems.[5,6] These expensive effects of drugs on all social systems have been important in shaping the public view that drug dependence is primarily a social problem that

The effects of drug dependence on social systems has helped shape the generally held view that drug dependence is primarily a social problem, not a health problem. In turn, medical approaches to prevention and treatment are lacking. We examined evidence that drug (including alcohol) dependence is a chronic medical illness. A literature review compared the diagnoses, heritability, etiology (genetic and environmental factors), pathophysiology, and response to treatments (adherence and relapse) of drug dependence vs type 2 diabetes mellitus, hypertension, and asthma. Genetic heritability, personal choice, and environmental factors are comparably involved in the etiology and course of all of these disorders. Drug dependence produces significant and lasting changes in brain chemistry and function. Effective medications are available for treating nicotine, alcohol, and opiate dependence but not stimulant or marijuana dependence. Medication adherence and relapse rates are similar across these illnesses. Drug dependence generally has been treated as if it were an acute illness. Review results suggest that long-term care strategies of medication management and continued monitoring produce lasting benefits. Drug dependence should be insured, treated, and evaluated like other chronic illnesses.

JAMA. 2000;284:1689-1695 www.jama.com

"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?

MethadoneMaintenance 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 irrestible 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

OAT-M/B	YES	NO
No Opioids	☑	
Less Opioids		
Other Drugs		☑
IV vs. IN vs. PO		
Productive Use of Time	☑	
Counseling	☑	

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

Evgeny Krupitsky, Edward V Nunes, Walter Ling, Ari Illeperuma, David R Gastfriend, Bernard L Silverman

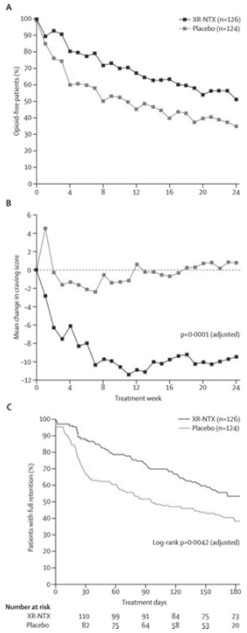
Summary

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 30 days or less of inpatient detoxification and 7 days or more off all opioids were enrolled at 13 clinical sites in Russia. We randomly assigned patients (1:1) to either 380 mg XR-NTX or placebo by an interactive voice response system, stratified by site and gender in a centralised, permuted-block method. Participants also received 12 biweekly counselling sessions. Participants, investigators, staff, and the sponsor were masked to treatment allocation. The primary endpoint was the response profile for confirmed abstinence during weeks 5–24, 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, NCT00678418.

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 69·9–92·4) in the XR-NTX group compared with 35·0% (11·4–63·8) in the placebo group (p=0·0002). Patients in the XR-NTX group self-reported a median of 99·2% (range 89·1–99·4) opioid-free days compared with 60·4% (46·2–94·0) for the placebo group (p=0·0004). The mean change in craving was −10·1 (95% CI −12·3 to −7·8) in the XR-NTX group compared with 0·7 (−3·1 to 4·4) in the placebo group (p<0·0001). Median retention was over 168 days in the XR-NTX group compared with 96 days (95% CI 63–165) in the placebo group (p=0·0042). Naloxone challenge confirmed relapse to physiological opioid dependence in 17 patients in the placebo group compared with one 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.

Lancet. Vol.377 April 30, 2011, 1506-13



HEROIN MAINTENANCE

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

I.M. Naltrexone

THE AMERICAN JOURNAL ON ADDICTIONS

The American Journal on Addictions, 20: 106–112, 2010

ISSN: 1055-0496 print / 1521-0391 online
DOI: 10.1111/j.1521-0391.2010.00107.x

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 Schweizer, MD,[3] Helen M. Pettinati, PhD[1]

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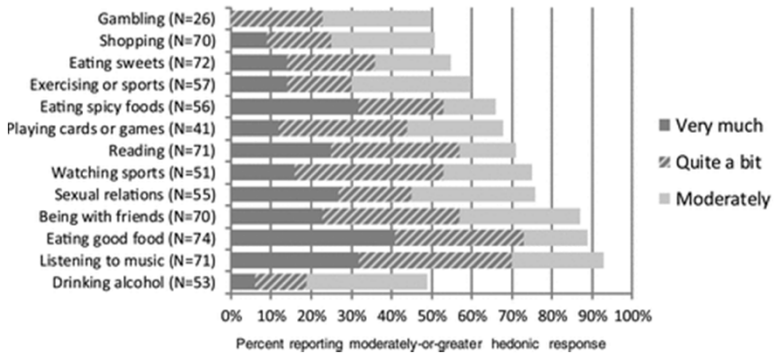
[2]Alkermes, Waltham, Massachusetts
[3]Paladin Consulting Group, Hoboken, New Jersey

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



The American Journal on Addictions
Volume 20, Issue 2, pages 106-112, 28 DEC 2010 DOI: 10.1111/j.1521-0391.2010.00107.x
http://onlinelibrary.wiley.com/doi/10.1111/j.1521-0391.2010.00107.x/full#f1

Vincent Dole, Albert Lasker Award

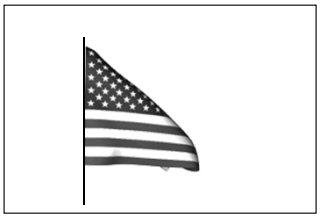
JAMA, 1988 *27 Years Ago

- " 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 addicte*d 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

MEDICATION / PSYCHOSOCIAL

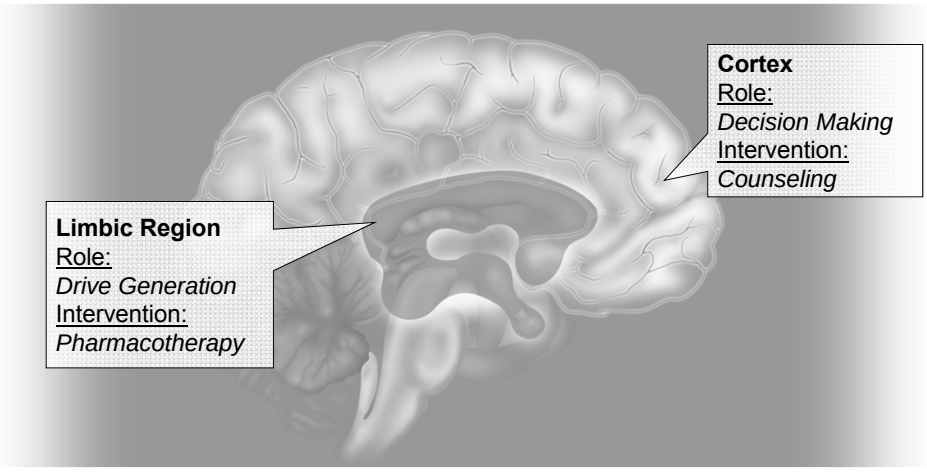
"I medicate first and ask questions later."

MEDICATION / PSYCHOSOCIAL

"Sorry, no water. We're just a support group."

Texting While In Therapy

Comprehensive Addiction Treatment

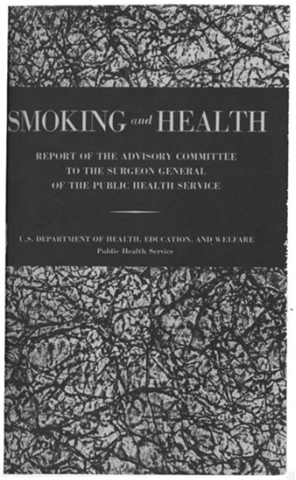


ADDICTION PHARMACOTHERAPY

- 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
- (Rimonabont—cannabinoid antagonist)



1964

Table 1 Premature deaths caused by smoking and exposure to secondhand smoke, 1965–2014

Cause of death	Total
Smoking-related cancers	6,587,000
Cardiovascular and metabolic diseases	7,787,000
Pulmonary diseases	3,804,000
Conditions related to pregnancy and birth	108,000
Residential fires	86,000
Lung cancers caused by exposure to secondhand smoke	263,000
Coronary heart disease caused by exposure to secondhand smoke	2,194,000
Total	20,830,000

Source: Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, unpublished data.

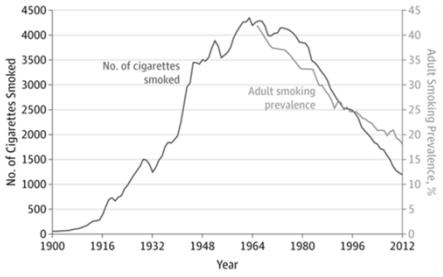


Figure Legend:

US Adult Per Capita Annual Cigarette Consumption (1900-2012) and Smoking Prevalence (1965-2012)Comparable data on smoking prevalence were not collected before 1965.

Smoking Your Wife to Death

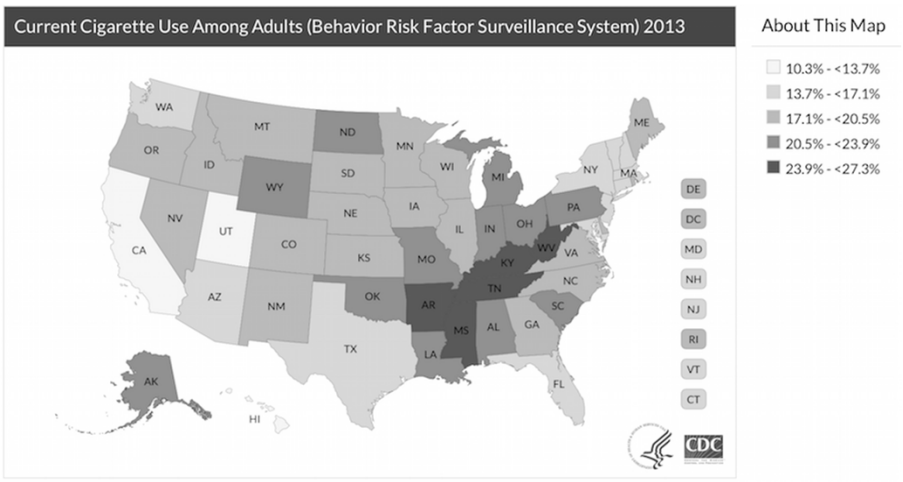
Those personal marriage-solicitation ads listing all the qualities sought in an ideal mate — good looks, brains, tenderness, energy, wealth — sometimes add "nonsmokers only." The smell of stale tobacco can turn off even the most ardent suitor. But now it turns out that there may also be sound medical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

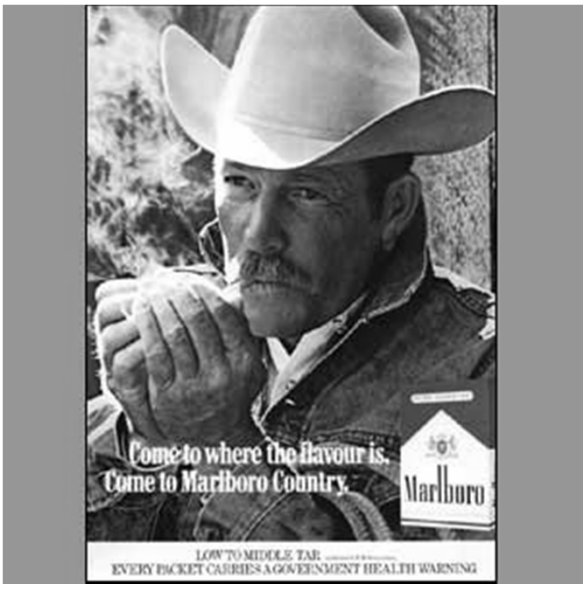
A major study in Japan has found that nonsmoking wives of heavy smokers developed lung cancer at a surprisingly high rate. They had become "passive smokers" who regularly breathed smoke in the air. This study is the best evidence yet that smokers are a menace not just to themselves but to the rest of us as well. The study, spanning 14 years and 265,000 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

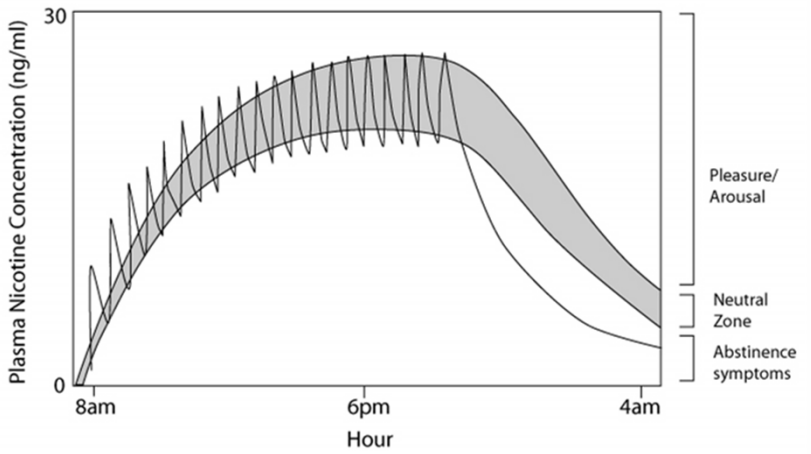




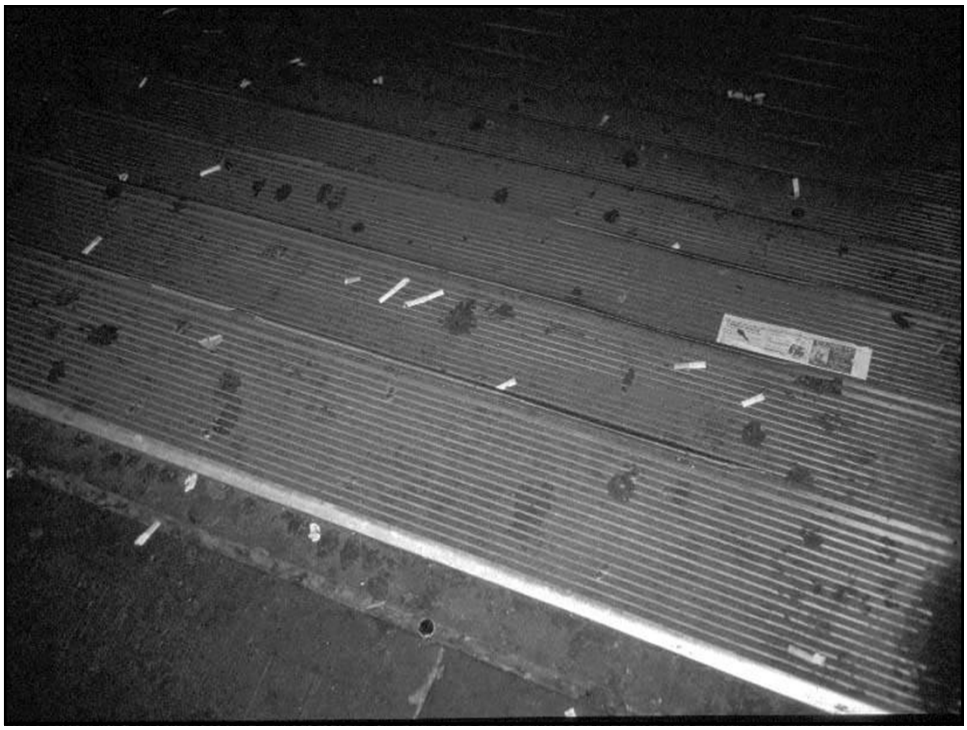
Tobacco Use Disorder Terminology

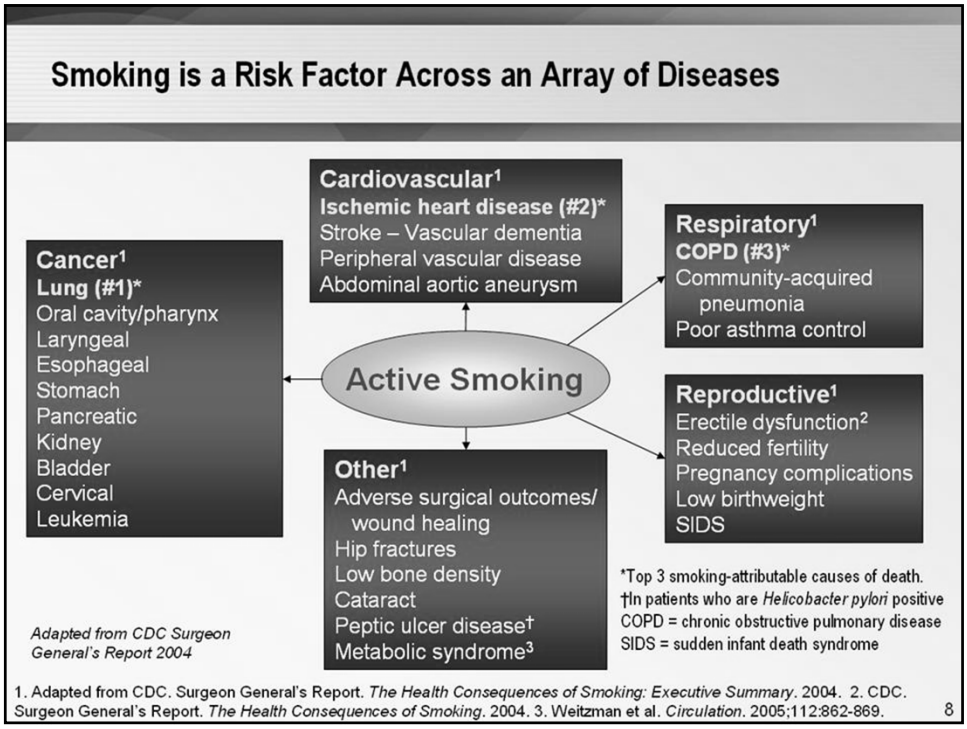
- Tobacco Addiction is the Problem
- Not Nicotine Addiction
- Nicotine dependence ≠ Tobacco Addiction
- Consider NRT Treatment
- ? Harm from Nicotine Alone
  Pregnancy and Apoptosis

Tobacco Addiction Cycle



Benowitz. (1992). *Med Clin N Am* 2:415–437.





Prevalence of Smoking Among Patients With Mental Illness and Substance Abuse

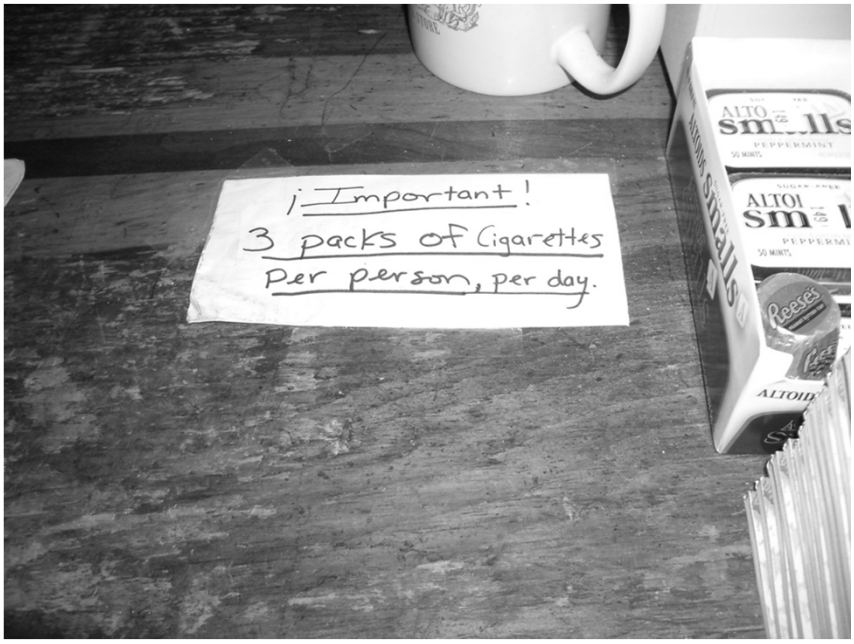
Table 1. Prevalence of Smoking Among Patients With Mental Illness and Substance Abuse

Condition	Smoking Prevalence, %
Schizophrenia[4,5]	45-88
Major depression[5]	40-60
Bipolar disorder[5]	55-70
Anxiety disorder[5]	19.2-56
Panic attacks[5,6]	38-46
Attention-deficit/hyperactivity disorder[7]	41-42
Posttraumatic stress disorder[5,6,8,9]	45-66
Alcohol abuse[5,10]	43-80
Drug abuse[5,10]	49-98
General population[11a]	19.8

[a]General population includes all the above categories of mental illness.

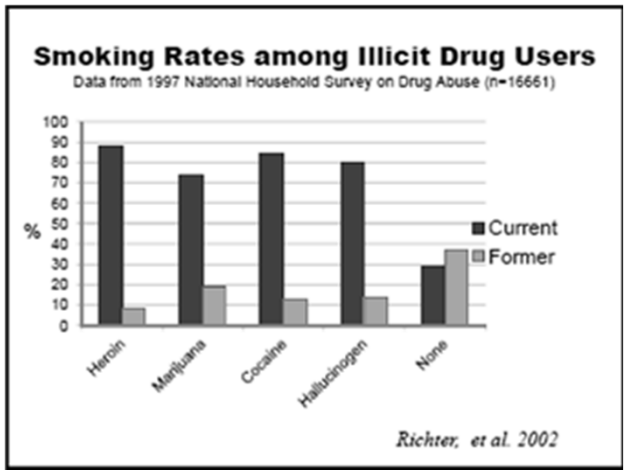
Schroeder, S. A. JAMA 2009;301:522-531.

JAMA



GOULD FARM

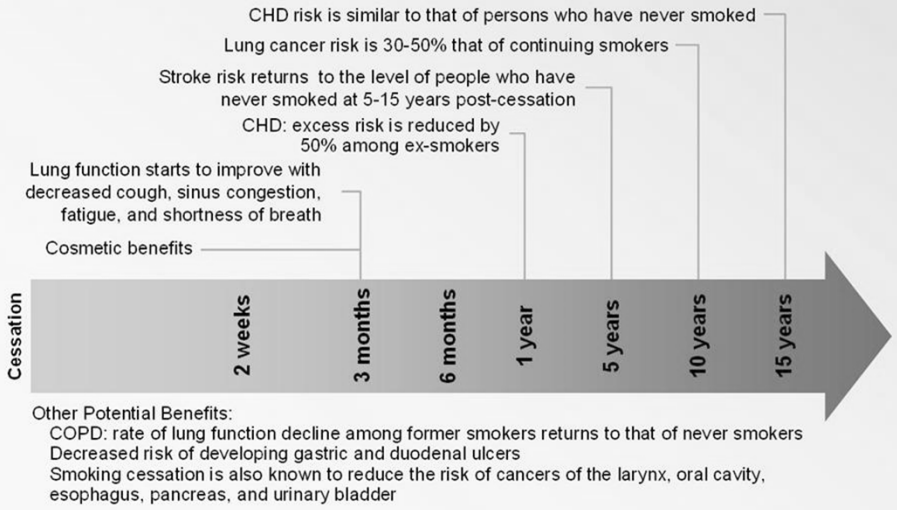
Harvesting Hope • Promoting Recovery



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 Life Time Health Benefits of Smoking Cessation



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

1. Fiore MC et al. *U.S. DHHS, U.S. Public Health Service*, 2000. 2. CDC. Surgeon General Report 2004: http://www.cdc.gov/tobacco/sgr/sgr_2004/sgranimation/flash/index.html . 3. CDC. *MMWR*. 1990;39:viii-xv.

12


NEW YORK POST
25 CENTS
LATE CITY FINAL
SMOKIN'
Marlboro men kick butt in Fallujah
FULL STORY: PAGES 6-7

2004


At the 1907 Hill County Rodeo, Montana Mary asked the boys to show her the ropes about smoking cigarettes
The boys obliged
You've come a long way, baby.
VIRGINIA SLIMS
VIRGINIA SLIMS


"Reach for a Lucky instead"
Lucky Strike, the finest Cigarette you ever smoked, made of the finest tobaccos—The Cream of the Crop—"IT'S TOASTED." Lucky Strike has an extra, secret heating process. Everyone knows that heat purifies and so 20,679 physicians say that Luckies are less irritating to your throat.
LUCKY STRIKE
CIGARETTES
"It's toasted"
Your Throat Protection—against irritation—against cough.
*We do not say smoking Luckies reduces flesh. We do say when tempted to overindulge, "Reach for a Lucky instead."


THE ROANOKE TIMES
Monday, September 20, 2004
Stealing Cheese
STEPHANIE KLEIN-DAVIS | The Roanoke Times
Mellisa Williamson, 35, a Bullitt Avenue resident, worries about the effect on her unborn child from the sound of jackhammers.

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**

Hurt RD, et al. JAMA 275:1097, 1996

Nicotine Medications

- **Not a carcinogen**
- Use high enough dose
- Scheduled better than PRN
- Use long enough time period
- Can be combined with bupropion
- Can be combined with each other
- Have almost no contraindications
- Have no drug-drug interactions
- Safe enough to be OTC

Nicotine Patch

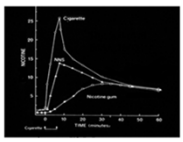
Slow onset of action
Continuous nicotine delivery
24 or 16 hour dosing
Easy, good compliance
No strict tapering or timeline
Side effects- skin reaction, insomnia
OTC

Oral Forms of Nicotine

Dose frequently – every 1-2 hours
Slow, buccal absorption
Acidic foods ↓ absorption
Mild side effects- mouth, throat burning
GI upset if swallowed (bite and park gum)
Rx for Nicotine Inhaler

Nicotine Nasal Spray

Rapid delivery though nasal mucosa
Most side effects (nasal irritation, rhinitis, coughing, watering eyes)
2 sprays= 1 dose; up to 40 doses/day
Some dependence liability
Rx needed

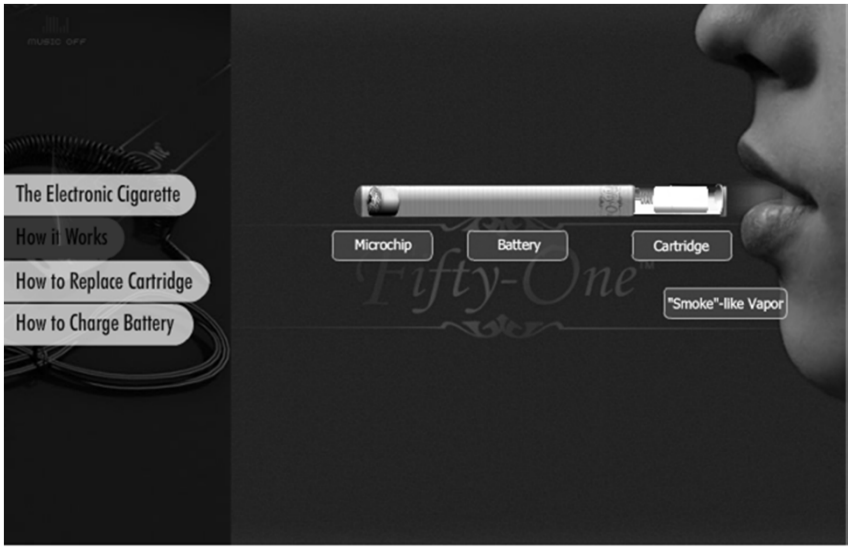


Effectiveness of First Line Medications

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

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

PHS Clinical Practice Guideline 2008 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

Hays JT & Ebbert JO. Mayo Clin Proc 78:1020, 2003

Varenicline
Mode of Action

- **Partial agonist with specificity for the α4B2 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.

***Cochrane Database of Systematic Reviews* 2006 Issue 3**

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.

***Cochrane Database of Systematic Reviews* 2006 Issue 3**

Obama pledges not to smoke in White House

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

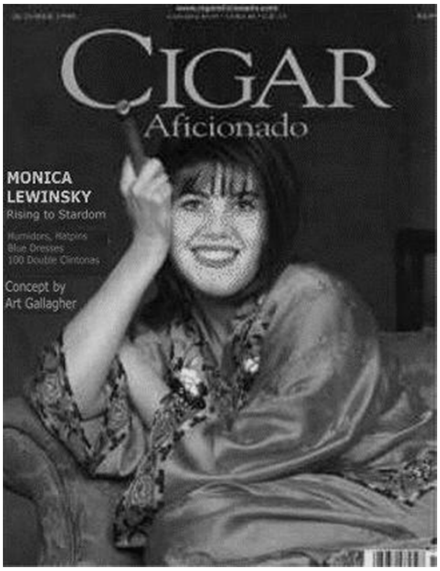
AP Associated Press
updated 2:54 p.m. ET, Sun., Dec. 7, 2008

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.

Obama on White House no-smoking rules
Dec. 7: President-elect Barack Obama talks about smoking in the White House with Tom Brokaw on "Mee


CIGAR
Aficionado
MONICA
LEWINSKY
Rising to Stardom
Humidors, Ratpins
Blue Dresses
100 Double Clintonas
Concept by
Art Gallagher

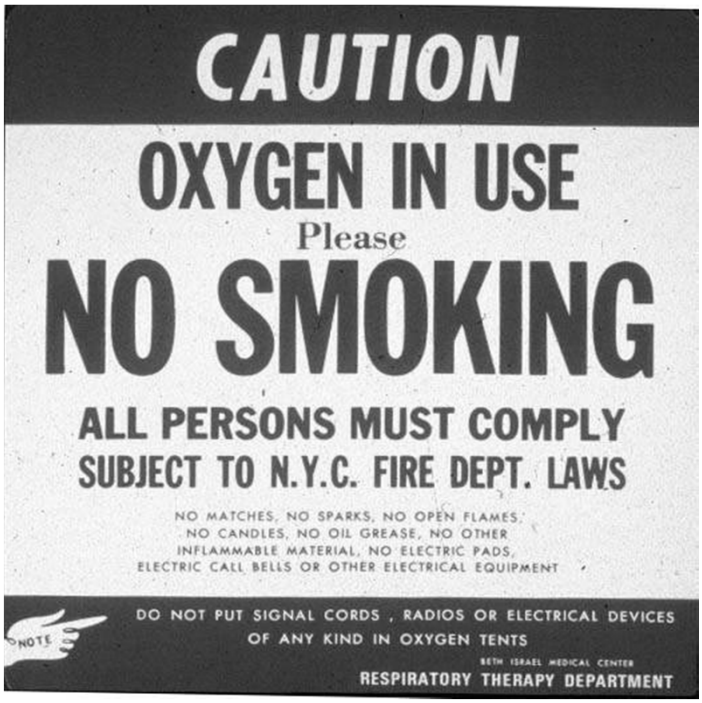

WOPICO
blogspot.com

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

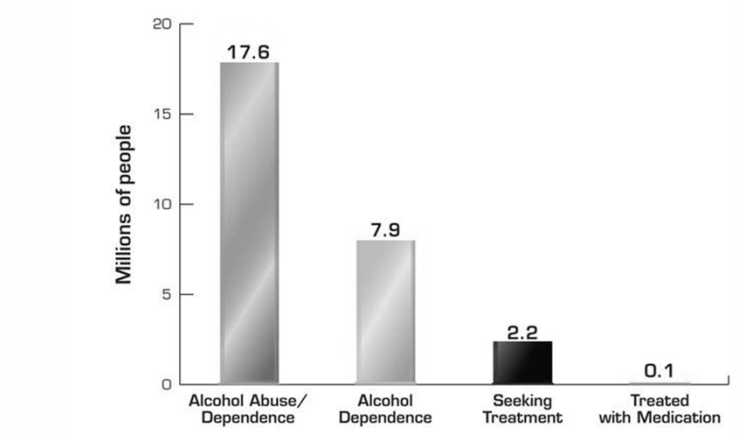
At a MINIMUM, Do Not SMOKE During Your Work Time



ALCOHOL ADDICTION

- Disulfiram (Antabuse)
- Naltrexone tablets
- Naltrexone injectable (Vivitrol)
- Acamprosate (Campral)
- Topiramate* (Topamax)
- Varenicline* (Chantix)
  *not FDA approved

Undertreatment of Alcohol Use Disorders



Grant BF et al. *Arch Gen Psychiatry.* 2004;61:807-816.

SAMHSA, Office of Applied Studies. Substance Dependence, Abuse and Treatment Tables; 2003

Grant BF et al. Arch Gen Psychiatry. 2004;61:807-816.
SAMHSA, Office of Applied Studies. Substance Dependence, Abuse and Treatment Tables; 2003

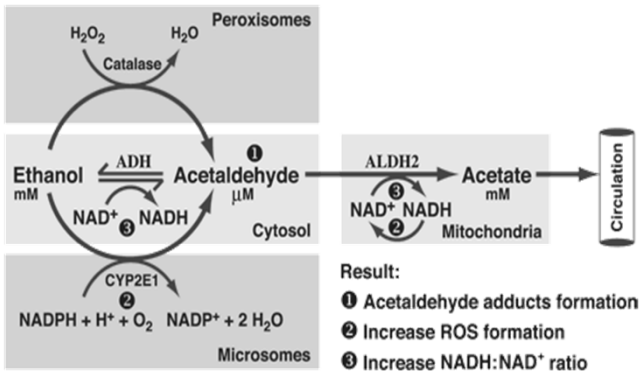
IMS - MAT March 2006

IMS - MAT March 2006

DISULFIRAM

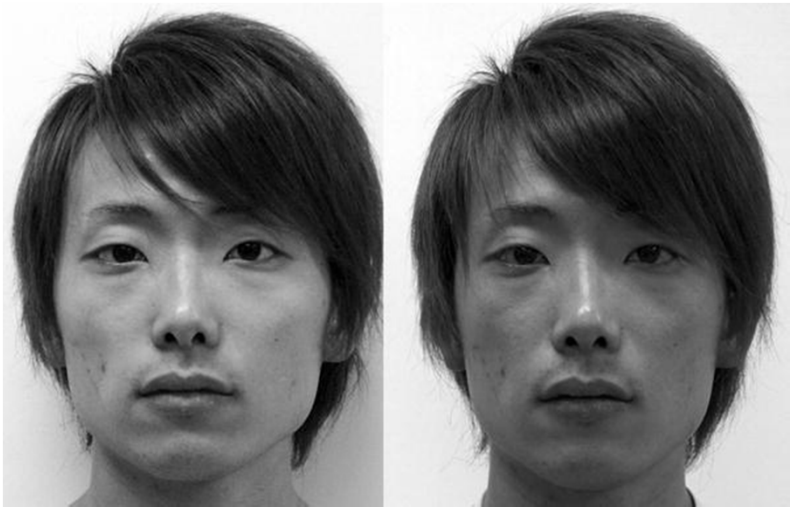
- ALDH irreversibly inactivated
- Flushing in 5-10 minutes after EtOH
- Abstain from EtOH for 12 hours prior
- Adverse Effects—Headaches, Dizziness, Tremor, Metallic Taste, Neuropathy, Optic Neuritis, Hepatitis(can be fulminant)
- Drug/Drug Interactions(phenytoin)
- Sensitization may last 14 days until ALDH is regenerated

Alcohol Metabolism



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

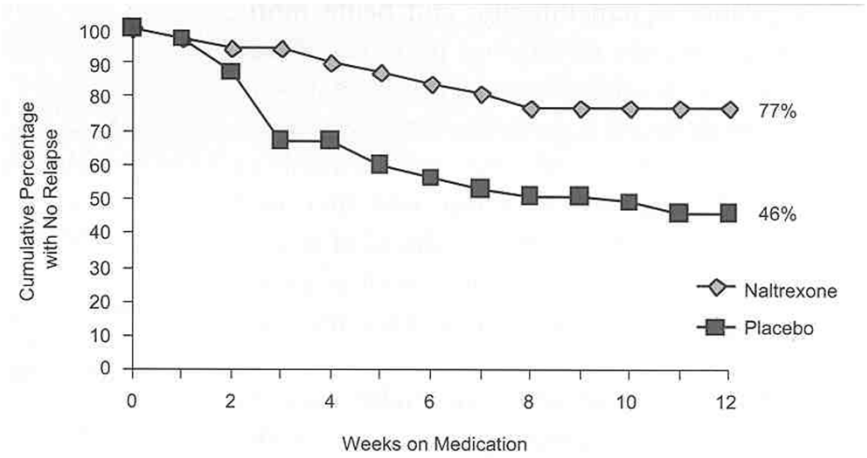


Facial flushing in a 22-year-old ALDH2 heterozygote before (left) and after (right) drinking alcohol. The individual pictured in this figure has given written consent for publication of his picture using the PLoS consent form.

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



Volpicelli et al., Naltrexone in the treatment of alcohol dependence, Arch Gen Psych, 1992; 49:876-880.

ORIGINAL CONTRIBUTION

Efficacy and Tolerability of Long-Acting Injectable Naltrexone for Alcohol Dependence

A Randomized Controlled Trial

James C. Garbutt, MD
Henry R. Kranzler, MD
Stephanie S. O'Malley, PhD
David R. Gastfriend, MD
Helen M. Pettinati, PhD
Bernard L. Silverman, MD
John W. Loewy, PhD
Ellen W. Ehrich, MD
for the Vivitrex Study Group

Context Alcohol dependence is a common disorder associated with significant morbidity and mortality. Naltrexone, an opioid antagonist, has been shown to be effective for treatment of alcohol dependence. However, adherence to daily oral pharmacotherapy can be problematic, and clinical acceptance and utility of oral naltrexone have been limited.

Objective To determine efficacy and tolerability of a long-acting intramuscular formulation of naltrexone for treatment of alcohol-dependent patients.

Design, Setting, and Participants A6-month, randomized, double-blind, placebo-controlled trial conducted between February 2002 and September 2003 at 24 US public hospitals, private and Veterans Administration clinics, and tertiary care medical centers. Of the 899 individuals screened, 627 who were diagnosed as being actively drinking alcohol-dependent adults were randomized to receive treatment and 624 received at least 1 injection.

Intervention An intramuscular injection of 380 mg of long-acting naltrexone (n = 205) or 190 mg of long-acting naltrexone (n = 210) or a matching volume of placebo (n = 209) each administered monthly and combined with 12 sessions of low-intensity psychosocial intervention.

Main Outcome Measure The event rate of heavy drinking days in the intent-to-treat population.

Results Compared with placebo, 380 mg of long-acting naltrexone resulted in a 25% decrease in the event rate of heavy drinking days ($P = .03$) and 190 mg of naltrexone resulted in a 17% decrease ($P = .07$). Sex and pretreatment abstinence each showed significant interaction with the medication group on treatment outcome, with men and those with lead-in abstinence both exhibiting greater treatment effects. Discontinuation due to adverse events occurred in 14.1% in the 380-mg and 6.7% in the 190-mg group and 6.7% in the placebo group. Overall, rate and time to treatment discontinuation were similar among treatment groups.

Conclusions Long-acting naltrexone was well tolerated and resulted in reductions in heavy drinking among treatment-seeking alcohol-dependent patients during 6 months of therapy. These data indicate that long-acting naltrexone can be of benefit in the treatment of alcohol dependence.

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See also Patient Page.

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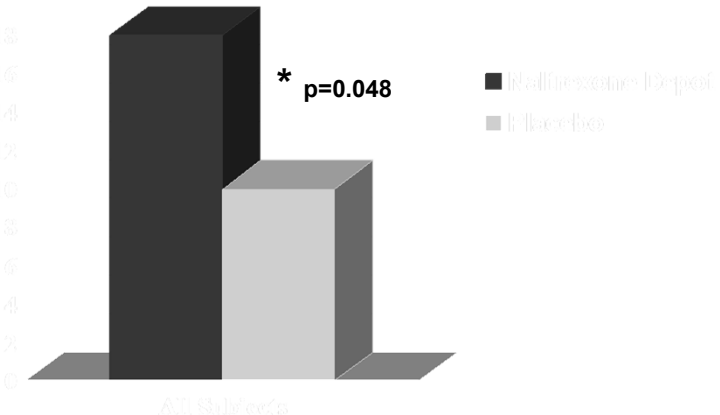
Percentage of Subjects Abstinent Through 3 Months

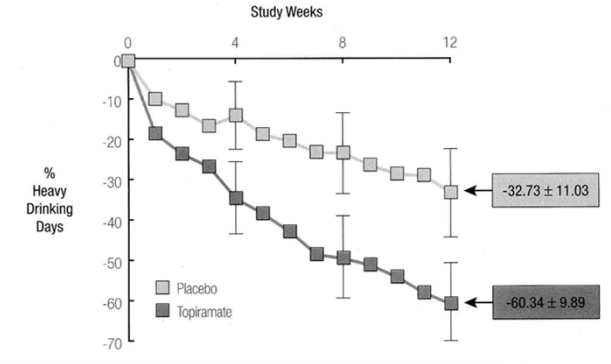


Acamprosate (N - acetylhomotaurine)

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

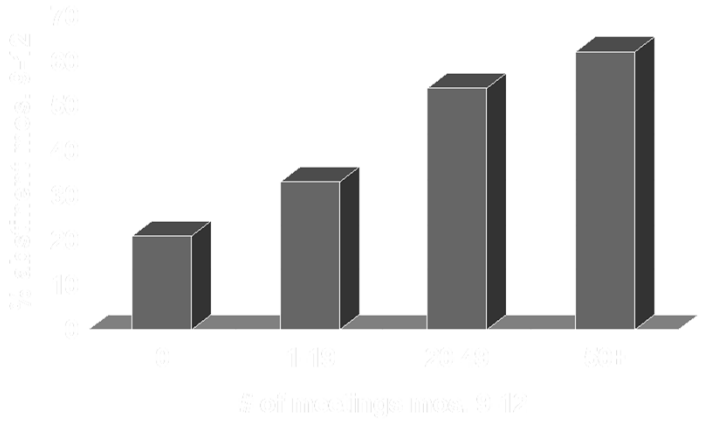
Topiramate

Figure 10. Mean Change (±95% CI) From Baseline in Percent Heavy Drinking Days[22]



At study end, $F(1,98) = 13.47$; $P=.0003$; effect size (ES)=0.70.
Baseline: 68.34% (topiramate) vs 60.84% (placebo).
Adapted with permission from Johnson BA, Ait-Daoud N, Bowden CL, et al. Oral topiramate for the treatment of alcohol dependence: a randomised controlled trial. *Lancet*. 2003;361:1677-1685.

Abstinence & AA meeting amount



Male VA residential patients
n = 2376

Moos et al., *J Clin Psychol* 2001

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

MethadoneMaintenance 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 irrestible craving and enable him to progress in AA toward social and emotional recovery.

COCAINE 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
- (Rimonabont—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