Health Effects of Alcohol, Cannabis and Opioids: The Real Deal

Mishka Terplan MD MPH FACOG DFASAM
Professor Departments Obstetrics & Gynecology and Psychiatry
Medical Director MOTIVATE
VCU School of Medicine

Mental Health Mini University
September 6, 2018

Psychoactive Substance Use is Ancient

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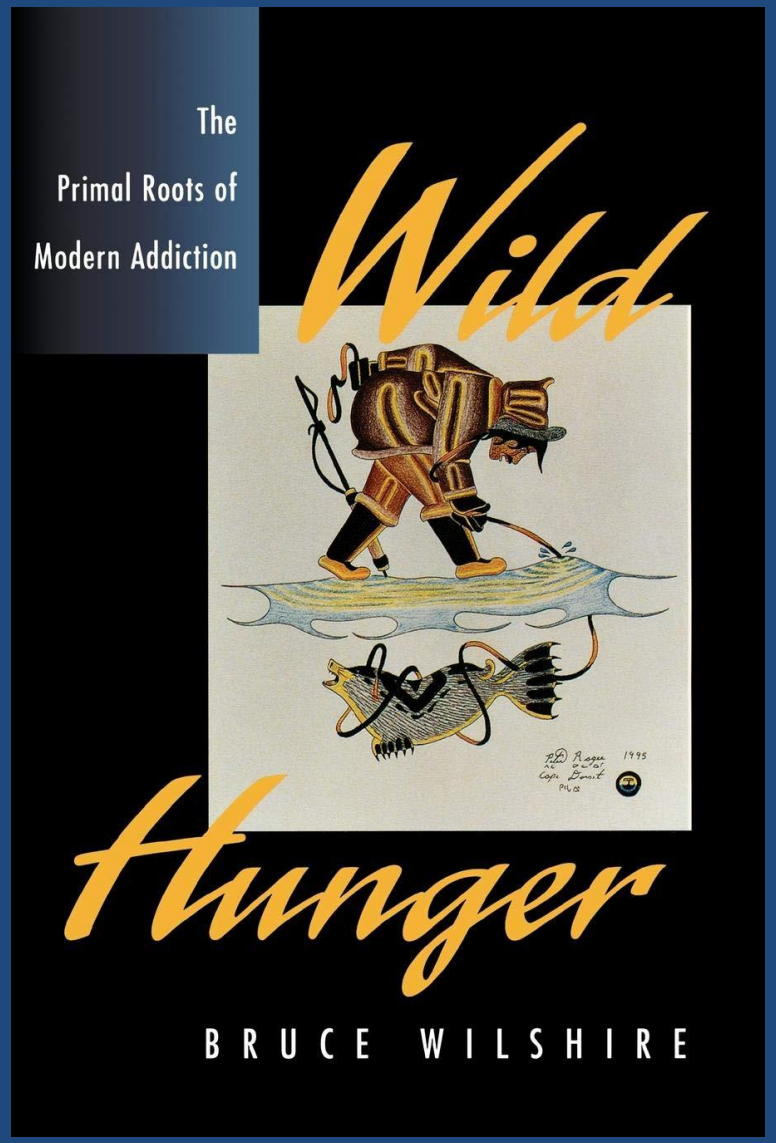
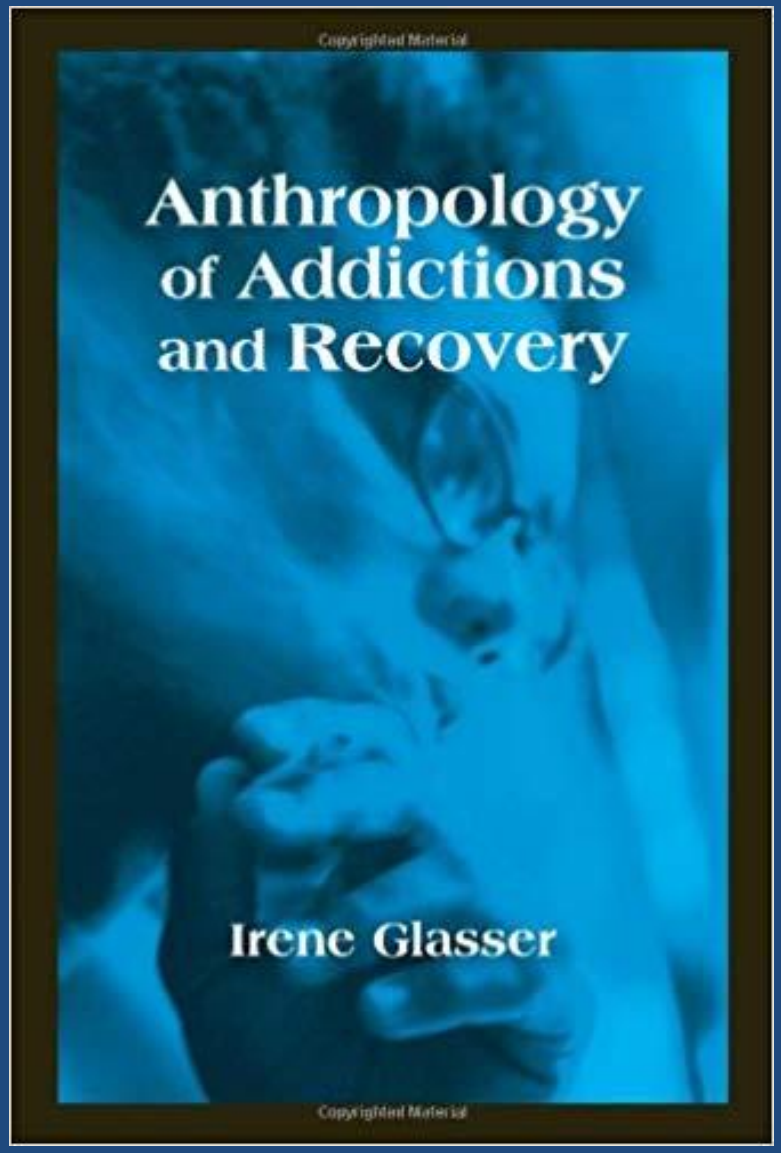
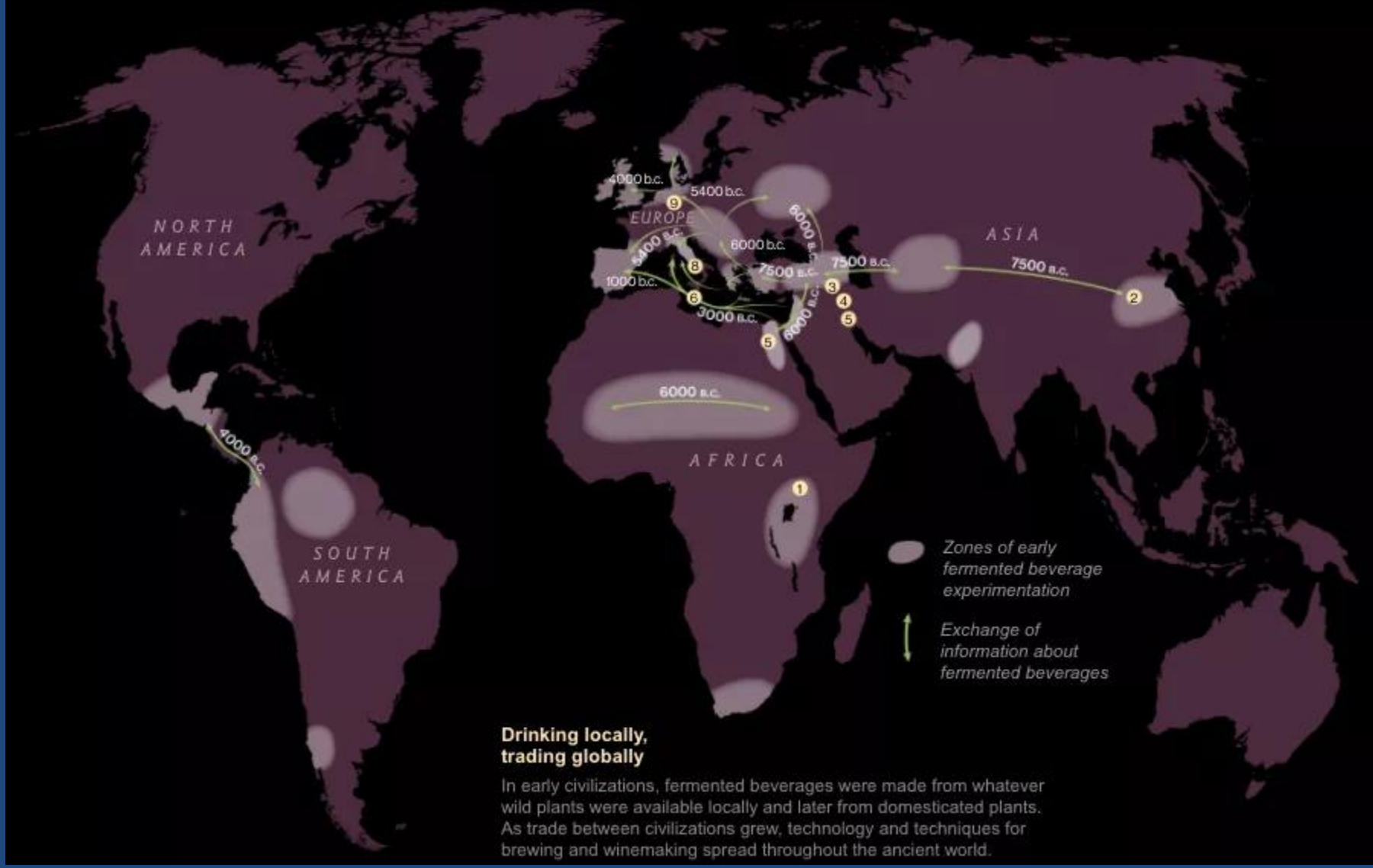




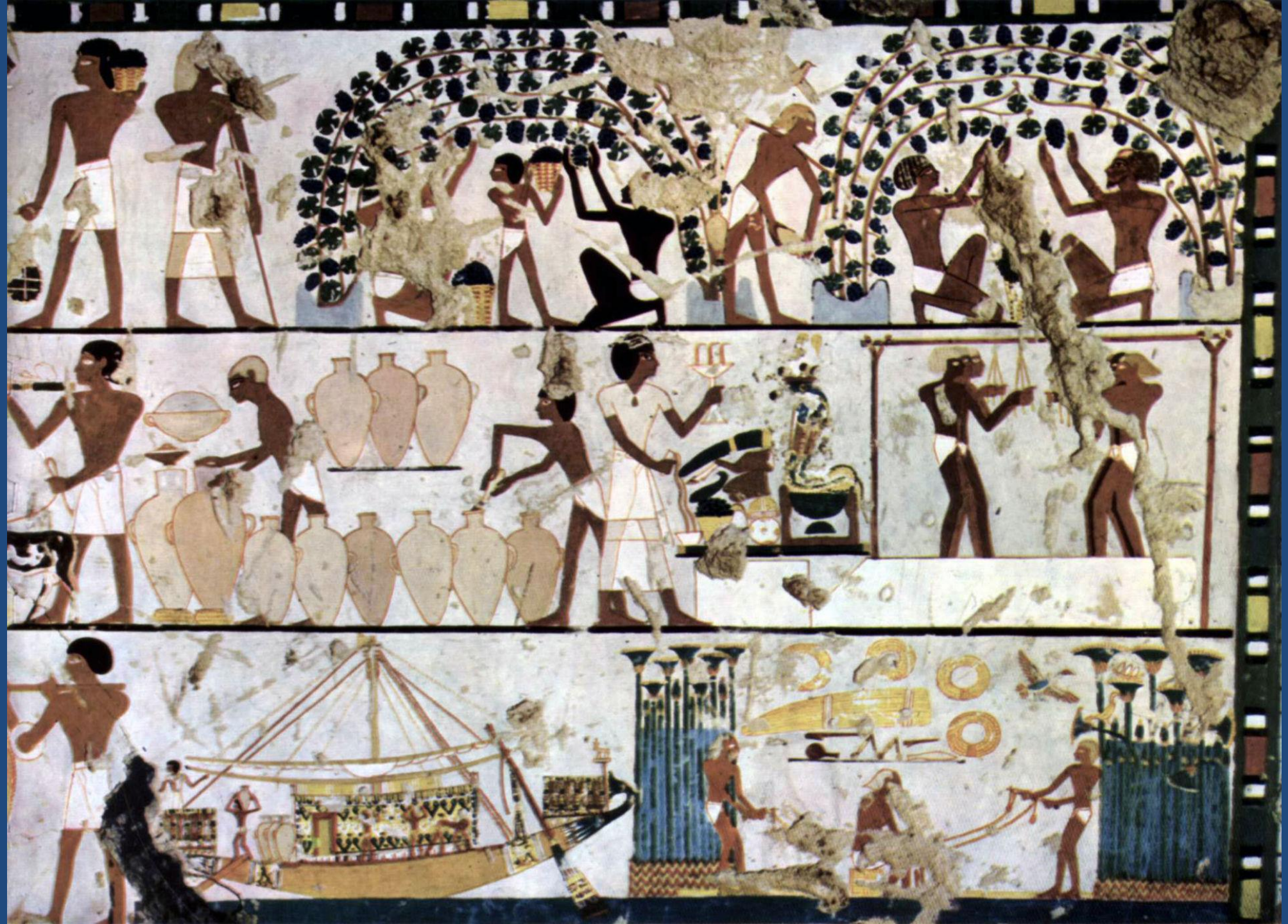
Alcohol Through the Ages

Some 10 million years ago, a shared ancestor of humans and African apes evolved an enzyme that could more rapidly digest the alcohol in fermented fruit. That set the biological stage for the past 10,000 years—in which people all over the world have made alcoholic beverages by fermenting sugars in whatever fruits were available and even by finding ways to ferment starchy grains and roots.



Drinking locally, trading globally

In early civilizations, fermented beverages were made from whatever wild plants were available locally and later from domesticated plants. As trade between civilizations grew, technology and techniques for brewing and winemaking spread throughout the ancient world.



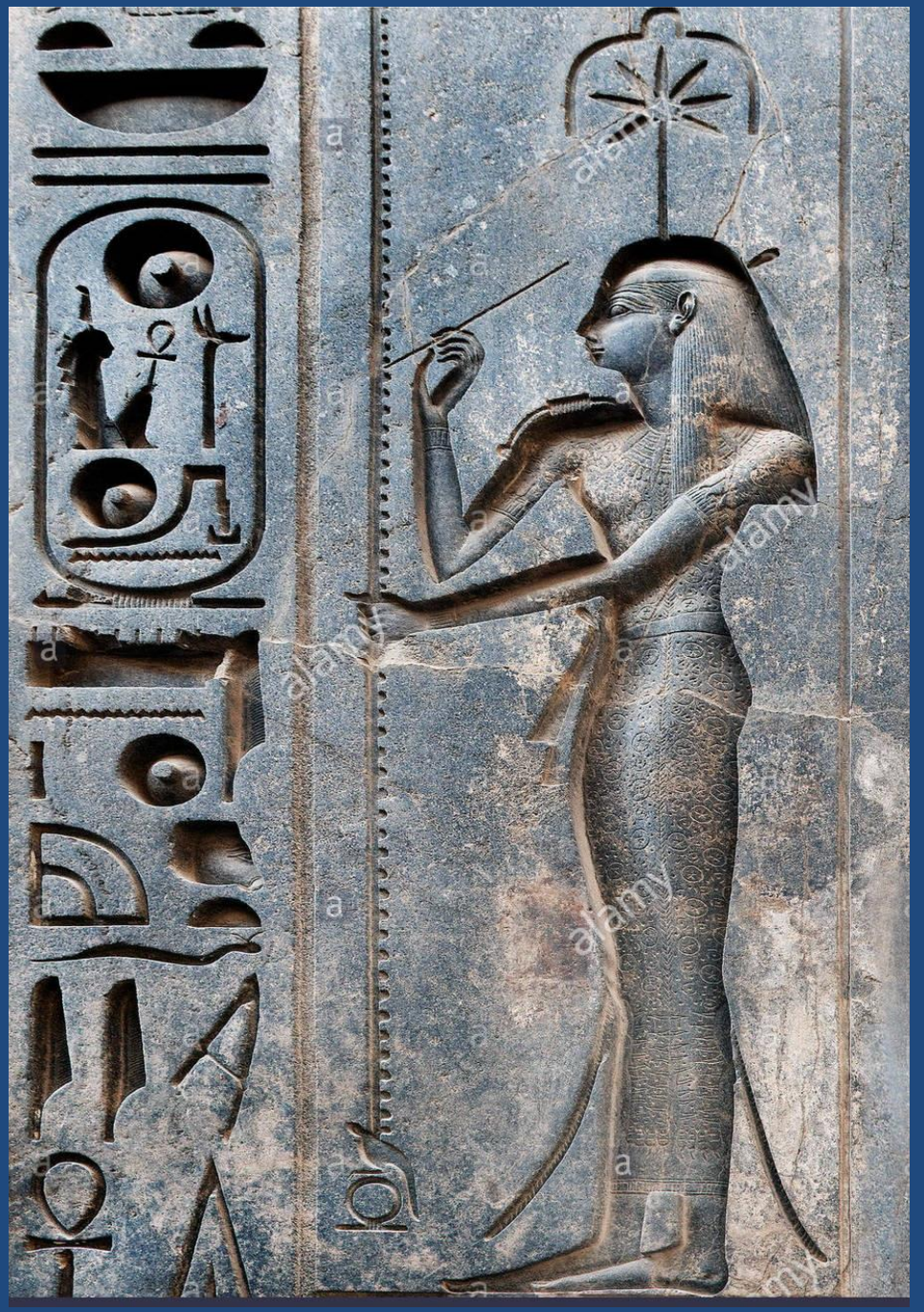
Fermented beverages of pre- and proto-historic China

Patrick E. McGovern*†, Juzhong Zhang‡, Jigen Tang§, Zhiqing Zhang¶, Gretchen R. Hall*, Robert A. Moreau‖, Alberto Nuñez‖, Eric D. Butrym, Michael P. Richards††, Chen-shan Wang*, Guangsheng Cheng‡‡, Zhijun Zhao§, and Changsui Wang‡**

*Museum Applied Science Center for Archaeology (MASCA), University of Pennsylvania Museum of Archaeology and Anthropology, Philadelphia, PA 19104; †Department of Scientific History and Archaeometry, University of Science and Technology of China, Hefei, Anhui 230026, China; §Institute of Archaeology, Chinese Academy of Social Sciences, Beijing 100710, China; ¶Institute of Cultural Relics and Archaeology of Henan Province, Zhengzhou 450000, China; ‖Eastern Regional Research Center, U.S. Department of Agriculture, Wyndmoor, PA 19038; **Firmenich Corporation, Princeton, NJ 08543; ††Department of Human Evolution, Max Planck Institute for Evolutionary Anthropology, 04103 Leipzig, Germany; and ‡‡Institute of Microbiology, Chinese Academy of Sciences, Beijing 10080, China

PNAS | December 21, 2004 | vol. 101 | no. 51 |

Seshat – Goddess of wisdom, knowledge, writing



Opioids: The Poppy Goddess

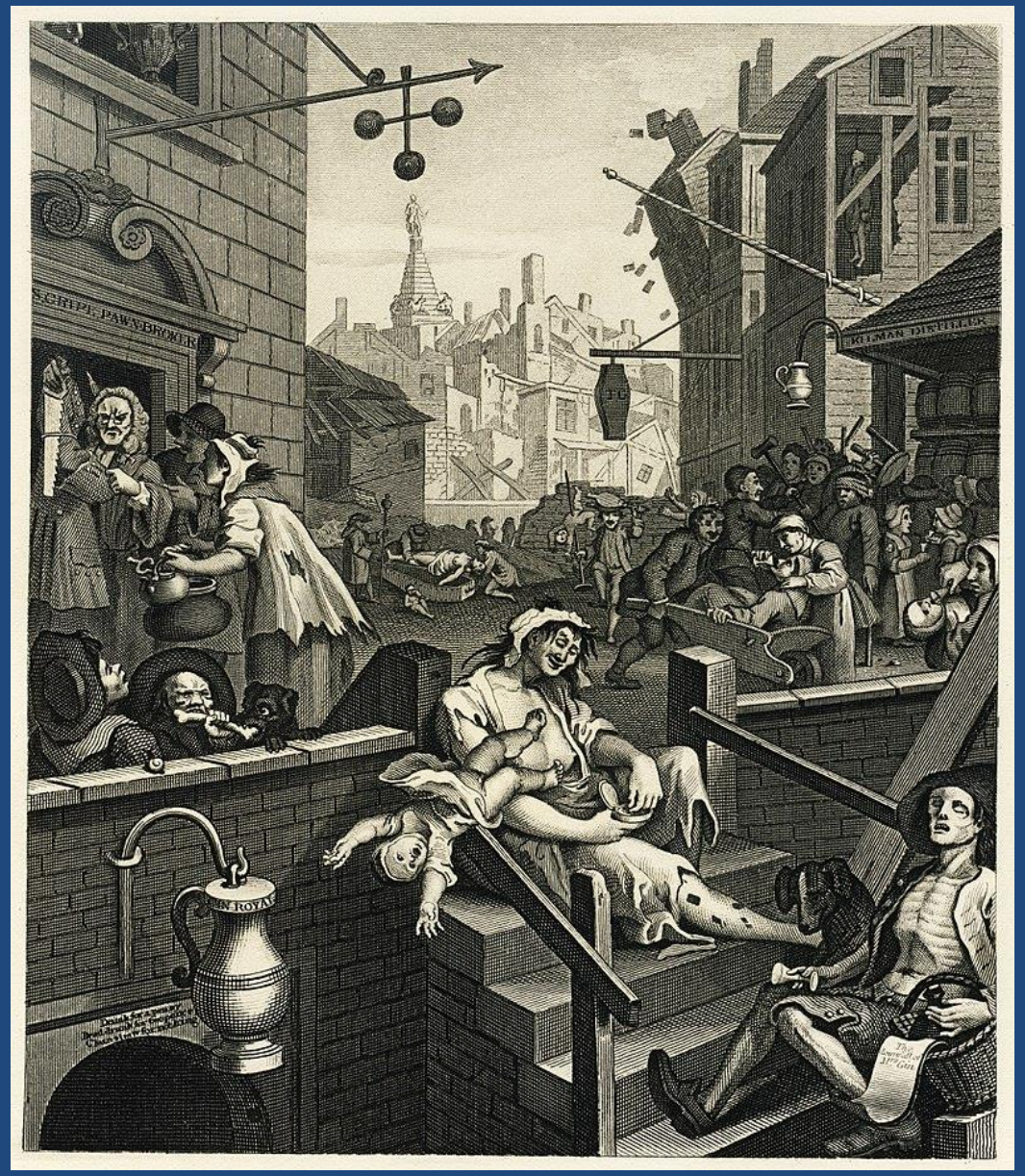
Demeter

Greek “Wine” and the Golden Mean

- Wine technologies in ancient Greece
- Molecular archaeology
- “Golden Mean” / “Moderation” reflected potency of other substance in wine more than avoidance of alcohol intoxication per se

Psychoactive Substance Use is Ancient

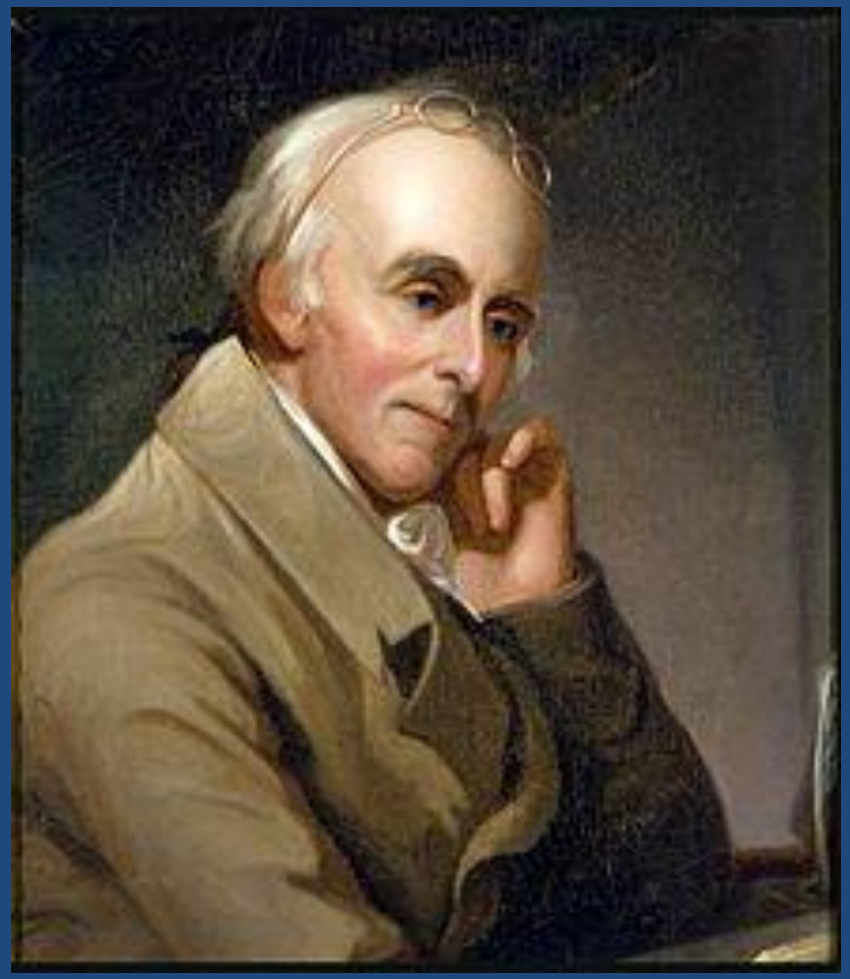
Drug Problems/Addiction,
Modern Phenomena

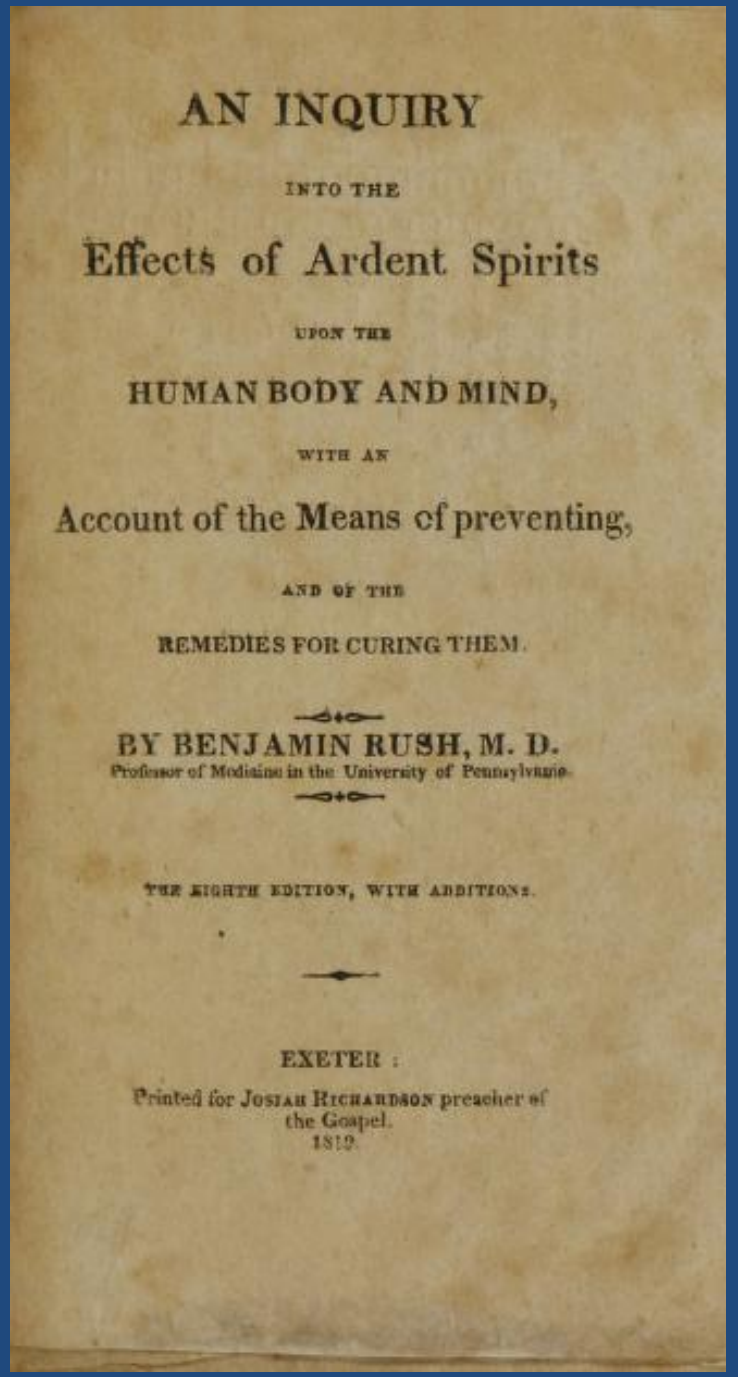


William Hogarth's ***Gin Lane*** 1751

King Alcohol and His Prime Minister c. 1820

Dr Benjamin Rush:
Alcoholism is a medical condition





AN INQUIRY

INTO THE

Effects of Ardent Spirits

UPON THE

HUMAN BODY AND MIND,

WITH AN

Account of the Means of preventing,

AND OF THE

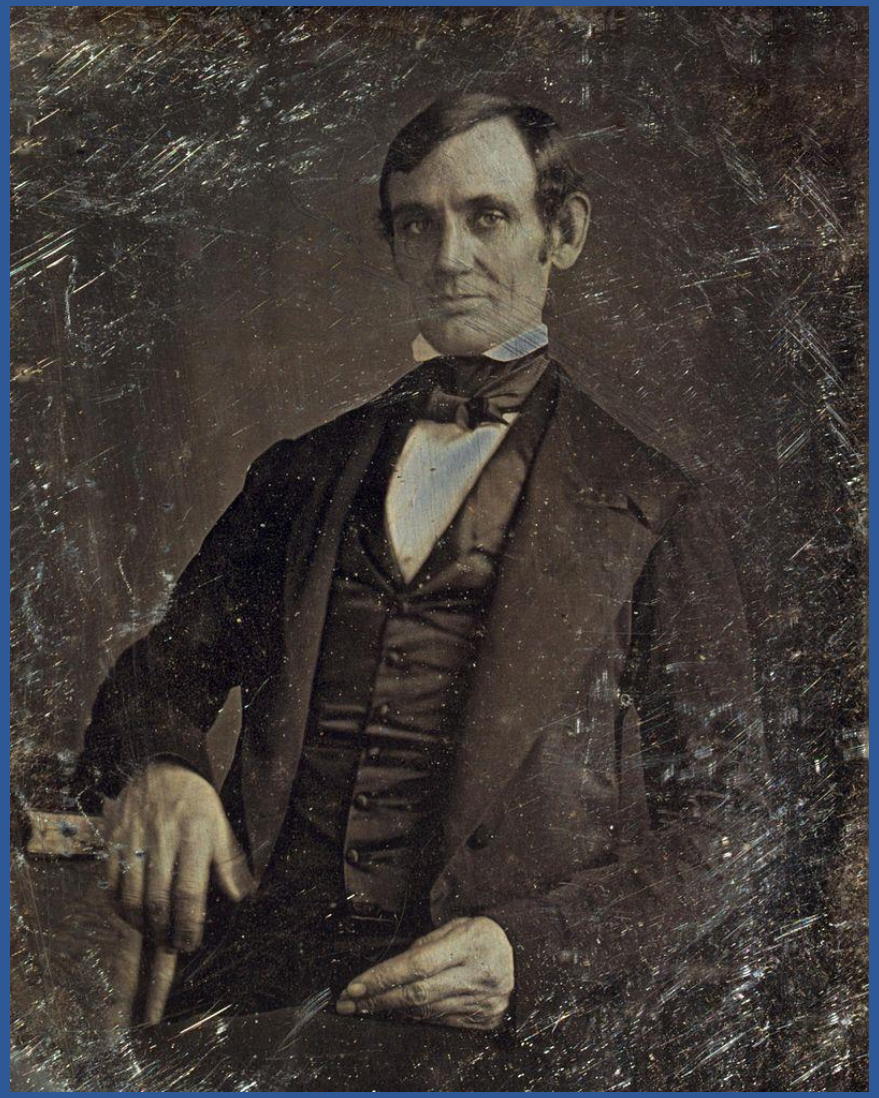
REMEDIES FOR CURING THEM.

BY BENJAMIN RUSH, M. D.
Professor of Medicine in the University of Pennsylvania.

THE EIGHTH EDITION, WITH ADDITIONS.

EXETER:

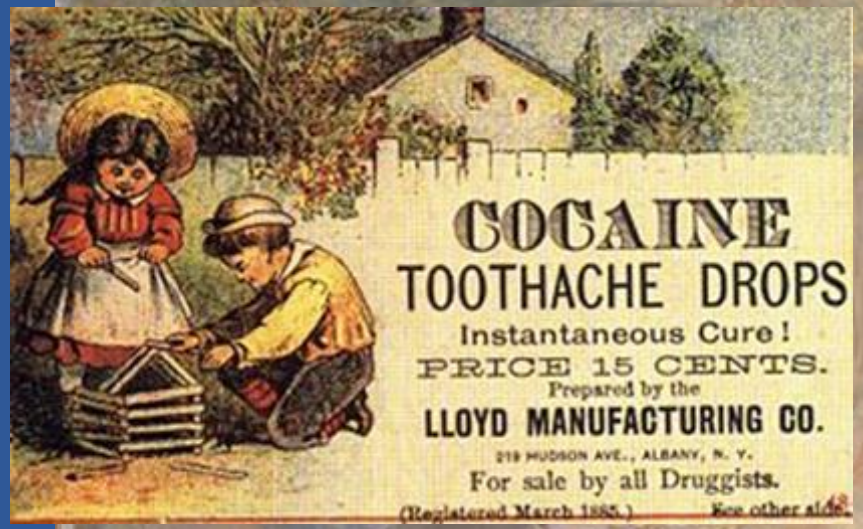
Printed for JOSIAH RICHARDSON preacher of the Gospel.
1819.



The victims to it [spirits] were pitied and compassionated, just as now are…other hereditary diseases.

In my judgment, such of us as have never fallen victims, have been spared more from the absence of appetite, than from any mental or moral superiority over those who have.

A. Lincoln, Address to Springfield Washington Temperance Society
February 22, 1842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TOOTHACHE DROPS
Instantaneous Cure!
PRICE 15 CENTS.
Prepared by the
LLOYD MANUFACTURING CO.
219 HUDSON AVE., ALBANY, N. Y.
For sale by all Druggists.
(Registered March 1885.) See other side.


A Good Friend
AYER'S
Don't take Ayer's Sarsaparilla if you are well. Don't take it simply because you are sick. Take it for what the doctors recommend it and you will like it, become fond of it, for it gives health, strength, vigor.
"I suffered terribly for twelve years. The doctors said my blood was
turning to water. I then tried Ayer's Sarsaparilla, and soon my health was
restored." — Mrs. J. W. FIALA, Hadlyme, Conn.
J. C. AYER CO., Lowell, M


LAUDANUM.--Poison
EACH FLUID OUNCE CONTAINS
45½ GRAINS OPIUM and 40% ALCOHOL
U.S.P. TINCT OPII.
3 mo. old, 1 drop
1 yr. old, 3 drops
4 yrs. old, 5 drops
10 yrs. old, 10 drops
20 yrs. old, 20 drops
Adult, 25 drops
McCORMICK & CO., Baltimore, Md., U.S.A.


CREST
BRAND
LAUDANUM
POISON
DIRECTIONS
Three months old 2 drops
One year old 4 drops
Four years old 6 drops
Ten years old 14 drops
Twenty years old 25 dps.
Adults 30 drops

MORPHINISM

AND

NARCOMANIAS FROM OTHER DRUGS

THEIR

ETIOLOGY, TREATMENT, AND MEDICOLEGAL RELATIONS

BY

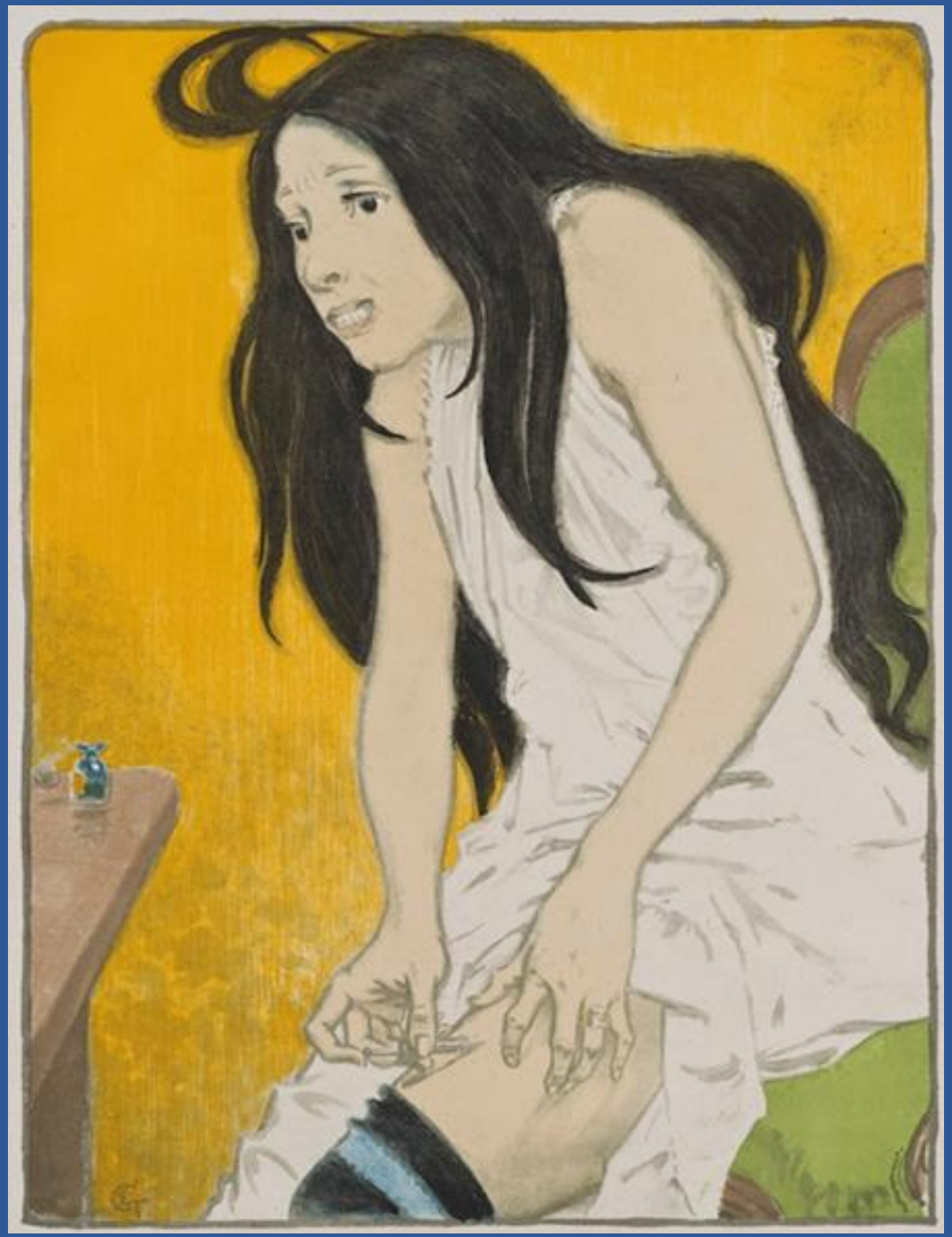
T. D. CROTHERS, M.D.

Superintendent of Walnut Lodge Hospital, Hartford, Conn.; Editor of the Journal of Inebriety; Professor of Mental and Nervous Diseases, New York School of Clinical Medicine, etc.

PHILADELPHIA AND LONDON
W. B. SAUNDERS & COMPANY
1902

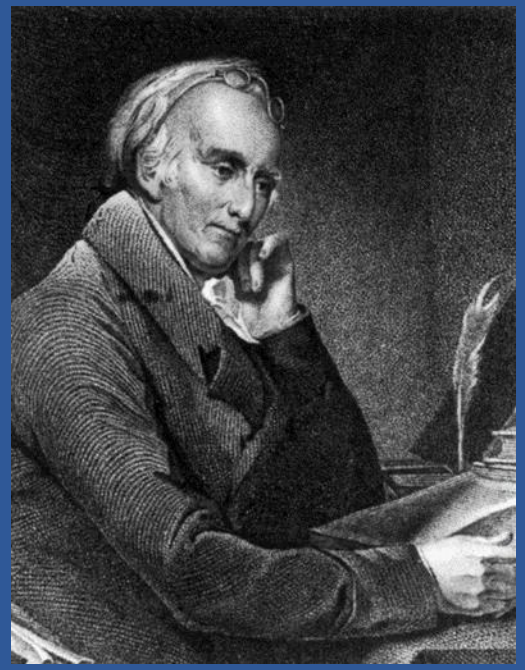
Within a few years many authorities have pointed out the danger of morphinism in women who come under treatment for gynecologic disorders. The impulse to secure relief from pain and to induce sleep is so imperative that morphin is taken without regard to its perils. The patient is both physiologically and psychologically impressed with the intense satisfaction of rapid relief, and ever after this impression becomes dominant in pain and suffering. All control of the will, feelings, and emotions is overcome by it. The desire to escape pain and suffering becomes in many cases a mania.

Capriciousness of mind, irritability, selfishness, restlessness, and excitability are the natural characteristics of many women, who quickly become morphinists, especially if under treatment for disorders of the generative organs. Such persons



Turn of the century treatment: Addiction is a disease

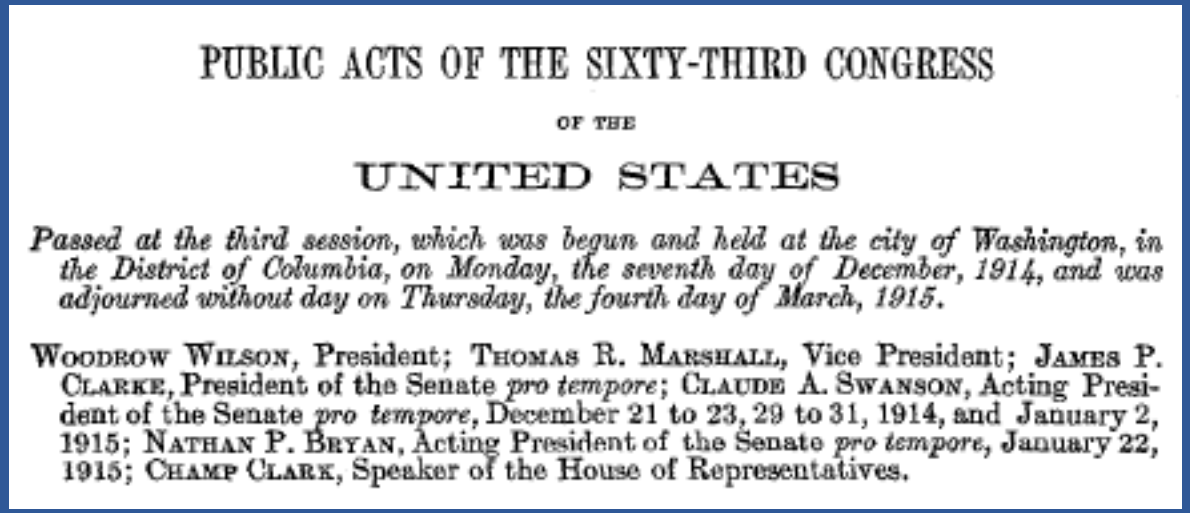
- Addiction – seen as medical condition and treated like one
  - Short acting opioids
  - Specialty clinics – detoxification and “maintenance”
  - 44 communities had morphine clinics (run by both public health and police departments) to care for “medically infirm addicts”



Dr Benjamin Rush

Early 20th Century

- 1914 Harrison Narcotics Tax Act
  - Regulated manufacture and distribution of opioids (and cocaine)
  - Licensing of pharmacists and physicians
  - Permitted dispensing opioids “to a patient in the course of [the physician’s] professional practice only”
- 1919 Supreme Court Cases – contesting/clarifying role of opioid prescribing for individuals with addiction
  - Rendered illegal the prescribing/dispensing of opioids for “maintenance” of opioid use disorders
- 1919 - 1935 c 25,000 physicians indicted for violation of Harrison Act
- All morphine maintenance clinics closed



PUBLIC ACTS OF THE SIXTY-THIRD CONGRESS

OF THE

UNITED STATES

Passed at the third session, which was begun and held at the city of Washington, in the District of Columbia, on Monday, the seventh day of December, 1914, and was adjourned without day on Thursday, the fourth day of March, 1915.

WOODROW WILSON, President; THOMAS R. MARSHALL, Vice President; JAMES P. CLARKE, President of the Senate *pro tempore*; CLAUDE A. SWANSON, Acting President of the Senate *pro tempore*, December 21 to 23, 29 to 31, 1914, and January 2, 1915; NATHAN P. BRYAN, Acting President of the Senate *pro tempore*, January 22, 1915; CHAMP CLARK, Speaker of the House of Representatives.

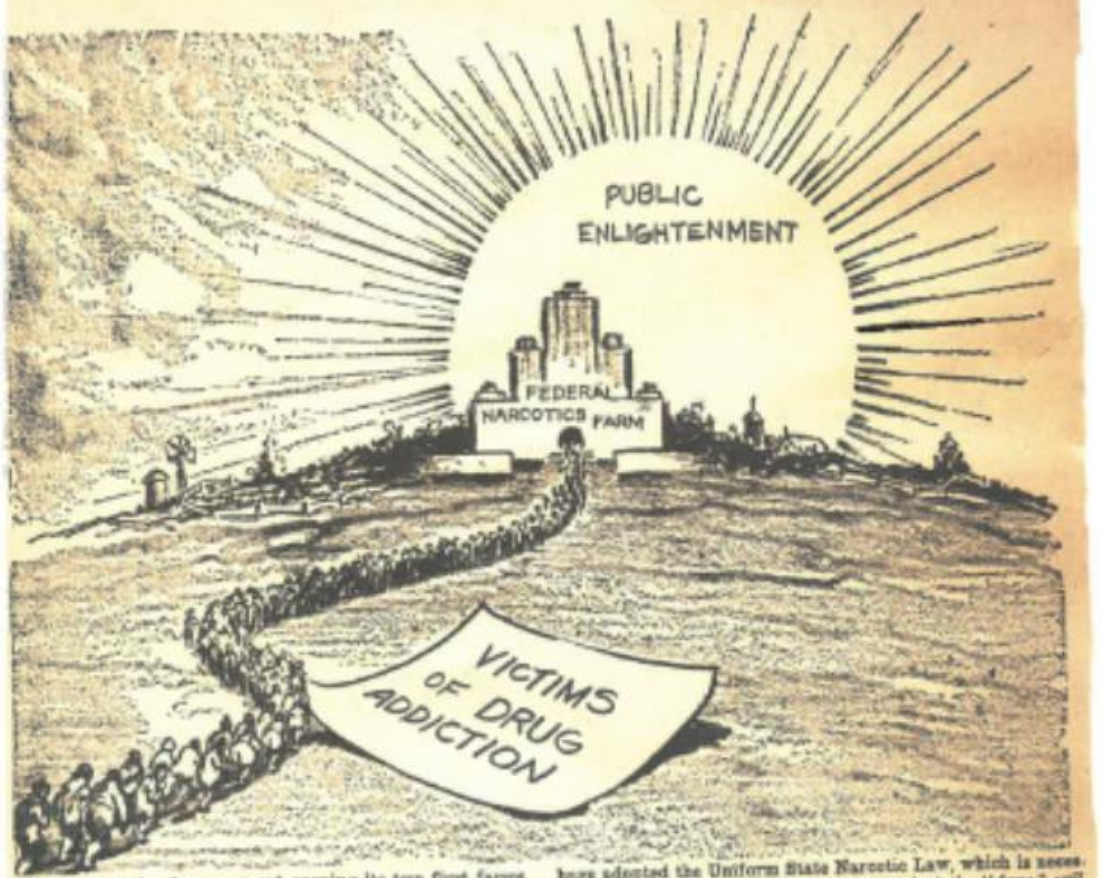
The original *New York World-Telegram and Sun* caption reads: "Out of the paddy wagons and into the Police Headquarters go some of the 88 dope addicts and pushers rounded up last night in biggest mass drive against narcotics in the city's history. They come from all over the city except Staten Island and in their possession cocaine, heroin, marijuana." Photo by Ed Ford, November 12, 1955.

Eight men declare themselves drug addicts before a Lexington judge in order to be sent to Narco to receive the six-month "cure." The original caption from this photograph reads: "Several times a week, the scene shown here is repeated in one of the courts . . . Like most groups of addicts, this group contains men from several cities who come here to seek help." The men in this photo come from New York, Chicago, Philadelphia, and Richmond, Virginia. 1951

ARCH 4, 1935

ATLANTA GEORGIAN

The Light of a New Day



With the federal government opening its two first farms
r the cure of narcotic victims, historic progress is recorded
the humanitarian treatment of a serious problem.

This movement should be carried rapidly on. There
hould be a narcotic-cure farm in every state of the Union.

It is a deplorable fact that ONLY A FEW of the states have adopted the Uniform State Narcotic Law, which is necessary to build up the nation's defenses against the "dope" evil.

Numerous legislatures are now in session. In each of the laggard states IMMEDIATE enactment of the Uniform State Narcotic Law should be compelled by local public opinion.

Failure to adopt the measure will be inexcusable.

Why do people take drugs?

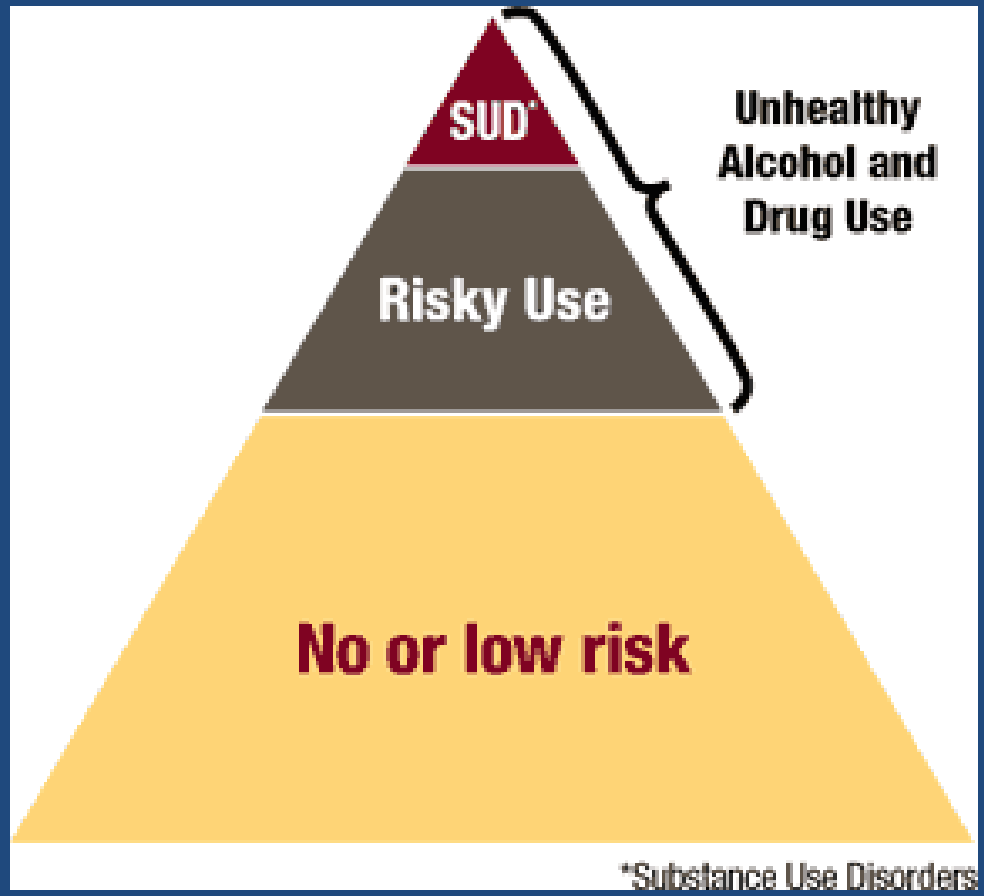
Why do people take drugs?

- To feel good
- To feel better
- To do better
- To fit in
- Curiosity

If taking drugs makes people feel good or better, makes people do better, what’s the problem?

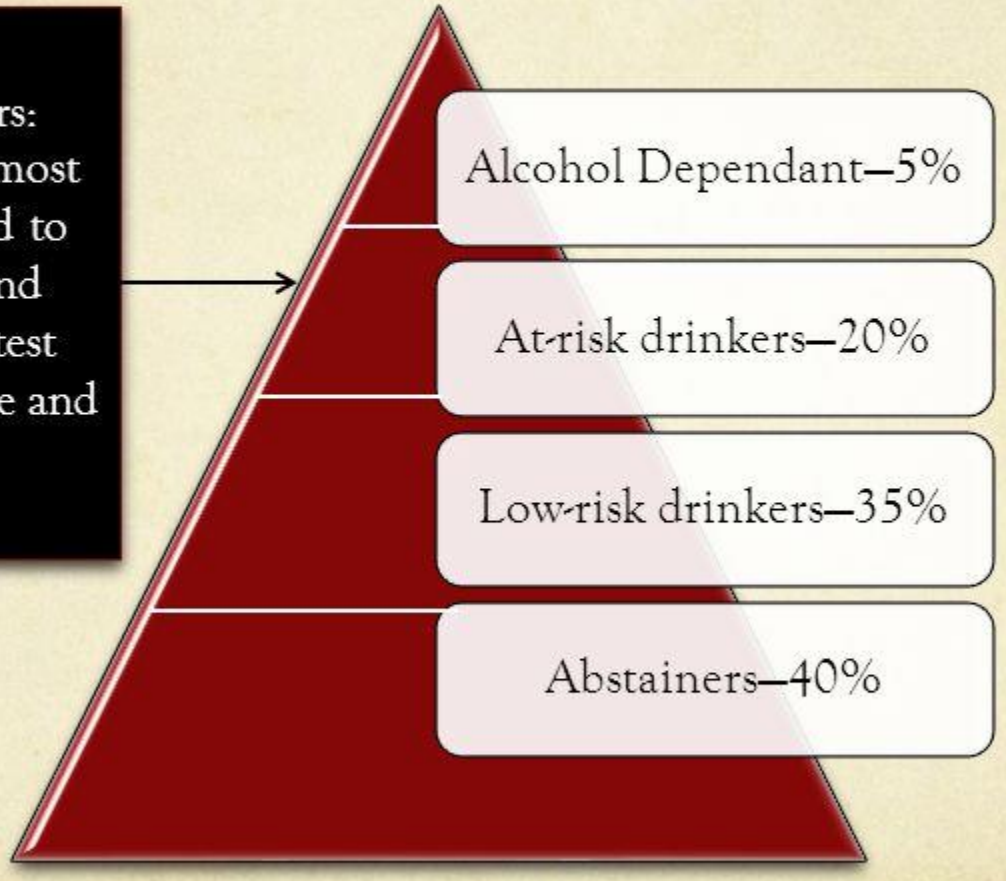
Substance Use Harms

- Substance use harms
  - Medical: biological and individual
  - Social
- Clinical Assessment
- Benefits?



Drinkers' Pyramid

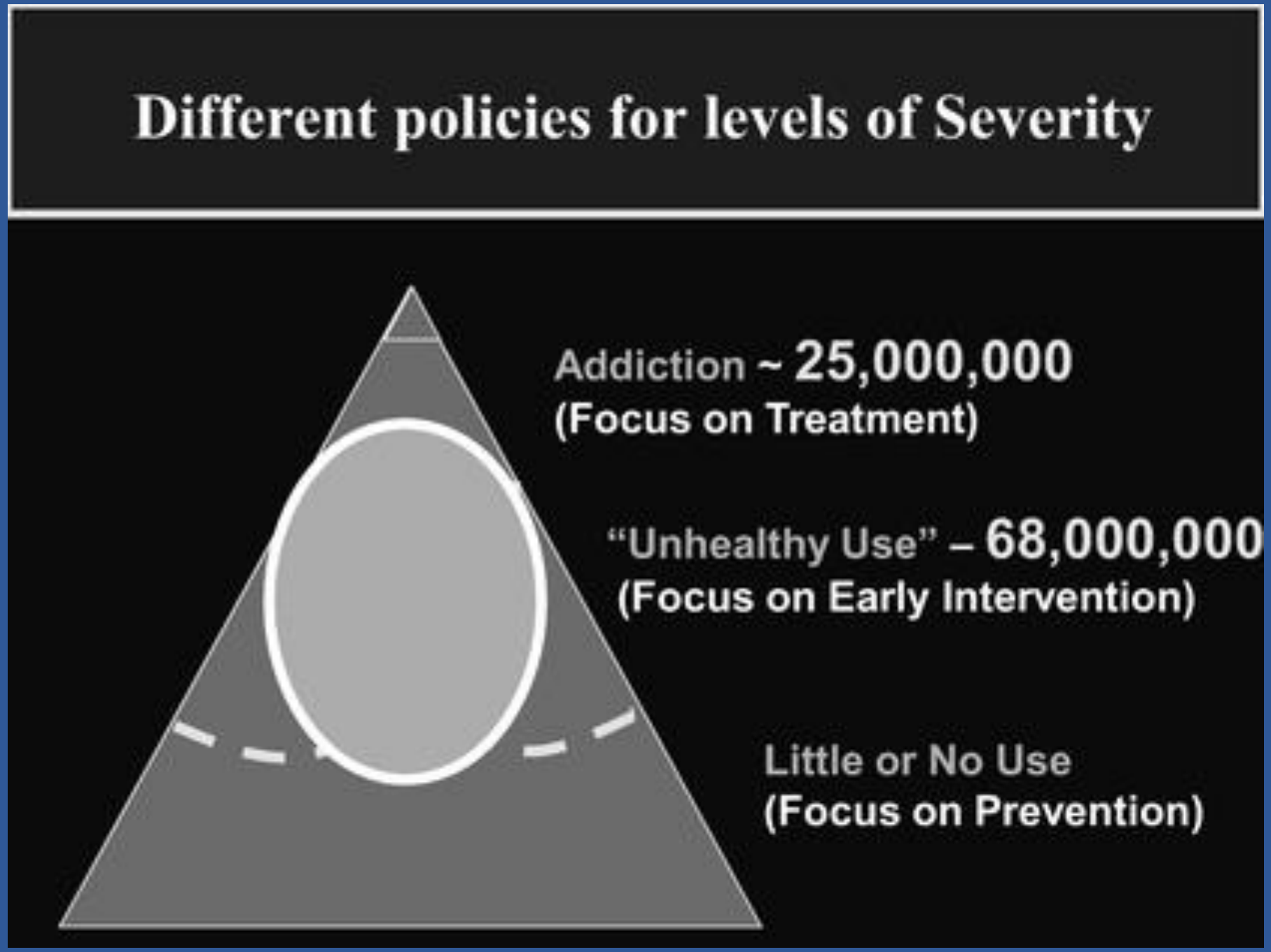
At-risk drinkers: targeted group, most likely to respond to intervention and represents greatest savings in care use and prevention.



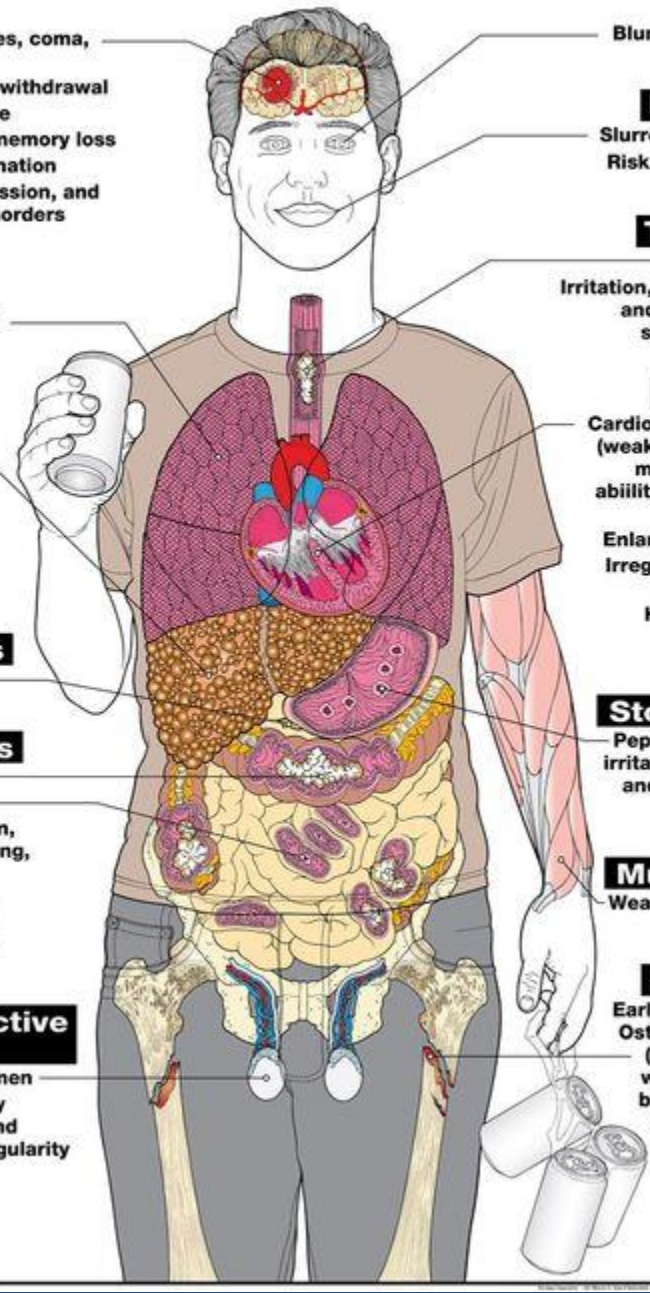
Source: Center for Substance Abuse Treatment: Background Paper, Screening, Brief Intervention, and Referral to Treatment (SBIRT)

Brief intervention, treatment, and recovery support services for Americans who have substance use disorders: An overview of policy in the Obama administration.

By Humphreys, Keith,McLellan, A. Thomas
Psychological Services, Vol 7(4), Nov 2010, 275-284



Harmful effects of Alcohol



Brain
- Stroke, seizures, coma, and death
- Addiction and withdrawal
- Brain shrinkage
- Learning and memory loss
- Loss of coordination
- Anxiety, depression, and personality disorders

Lungs
- Breathing may stop, then death

Liver
- Cirrhosis
- Fibrosis
- Alcoholic hepatitis
- Liver failure
- Fatty liver

Pancreas
- Pancreatitis

Intestines
- Cancer
- Ulcers
- Abdominal pain, nausea, vomiting, and diarrhea
- Inflammation, irritation, and hemorrhaging

Reproductive system
- Impotence in men
- Infertility, early menopause, and menstrual irregularity in women

Eyes
- Blurred vision

Mouth
- Slurred speech
- Risk of cancer

Throat
- Cancer
- Irritation, bleeding, and difficulty swallowing

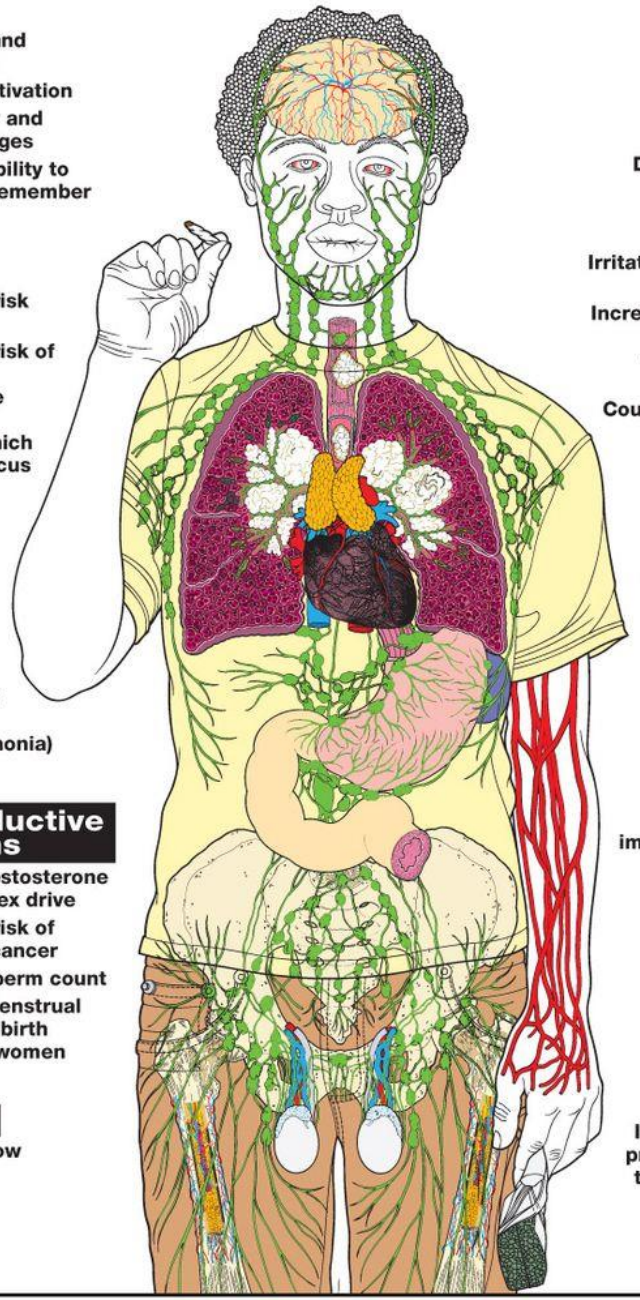
Heart
- Cardiomyopathy (weakens heart muscle and abiility to pump blood)
- Enlarged heart
- Irregular heart beat
- High blood pressure

Stomach
- Peptic ulcers, irritated lining, and bleeding lesions

Muscles
- Weak and soft

Bones
- Early onset of Osteoporosis (bones are weak, soft, brittle, thin and more easily broken)

Harmful effects of Marijuana



Brain
- Addiction and withdrawal
- Lack of motivation
- Personality and mood changes
- Reduced ability to learn and remember

Lungs
- Increases risk of cancer
- Increases risk of Chronic Obstructive Pulmonary Disease which causes mucus build up in airways, chronic coughing, wheezing, and shortness of breath
- Increases risk of lung infections (like pneumonia)

Reproductive systems
- Reduces testosterone and male sex drive
- Increases risk of testicular cancer
- Reduces sperm count
- Irregular menstrual cycles and birth defects in women

Bones
- Bone marrow damage

Eyes
- Sleepy, blood shot eyes

Mouth
- Dry and burning

Throat
- Irritates lining of the esophagus
- Increases chance of cancer in the esophagus and larynx
- Coughing, burning, and phlegm

Heart
- Increases blood pressure and heart rate
- Increases risk of heart attack and stroke

Immune system
- Weakens immune system's ability to protect the body against infections and diseases (like cancer)

Blood vessels
- Increases blood pressure leading to higher risk of strokes

Schizophrenia Bulletin vol. 42 no. 5 pp. 1262–1269, 2016
doi:10.1093/schbul/sbw003
Advance Access publication February 15, 2016

Meta-analysis of the Association Between the Level of Cannabis Use and Risk of Psychosis

Arianna Marconi[1], Marta Di Forti[1], Cathryn M. Lewis[2], Robin M. Murray[1], and Evangelos Vassos[*,2]

[1]Department of Psychosis Studies, King's College London, Institute of Psychiatry Psychology & Neuroscience, London, UK; [2]King's College London, Institute of Psychiatry Psychology & Neuroscience, MRC SGDP Centre, London, UK

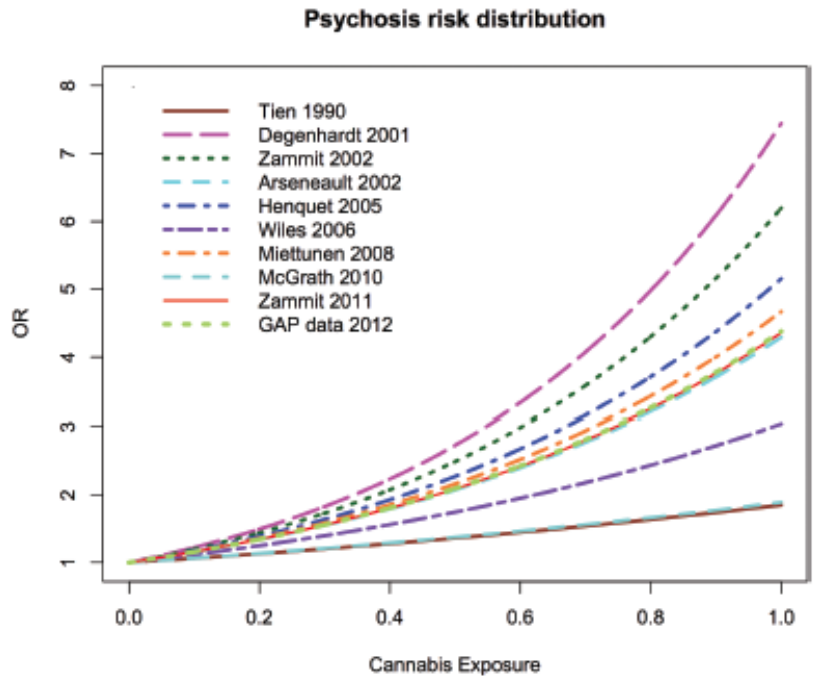


Fig. 2. Estimated risk ratio of psychosis by level of cannabis use in original studies.

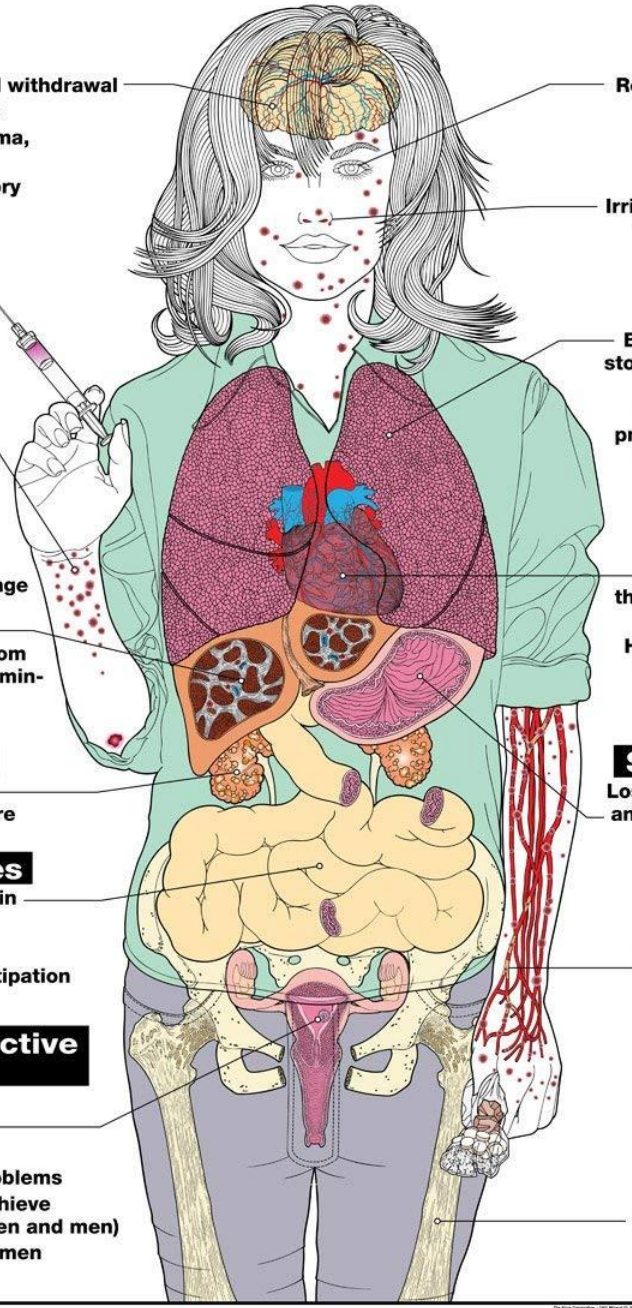
Cannabis and the Development of Psychosis

10+ longitudinal studies – all show an association between canna bis use and psychosis

Risk in context:

- Individual: Increase from 1-2%
- Population: Additional 3,000,000 events

Harmful effects of Heroin



Brain
- Addiction and withdrawal
- Brain damage
- Overdose, coma, and death
- Loss of memory
- Depression
- Insomnia

Skin
- Sores and scars (tracks) from injections
- Bruises
- Infections

Liver
- Disease/damage caused by Hepatitis C and/or HIV (from sharing contaminated needles)

Kidneys
- Disease and possible failure

Intestines
- Abdominal pain
- Diarrhea
- Nausea
- Chronic constipation

Reproductive system
- Miscarriages
- Still births
- Birth defects
- Menstrual problems
- Inability to achieve orgasm (women and men)
- Impotence in men

Eyes
- Reduced vision and watery

Nose
- Irritated nostrils from snorting

Lungs
- Breathing may stop, then death
- Respiratory illnesses (like pneumonia and tuberculosis)

Heart
- Infections of the heart lining and valves
- Heart disease, heart failure, and death

Stomach
- Loss of appetite and weight loss
- Vomiting

Blood vessels
- Scarred and/or collapsed arteries and veins
- Blood clots

Bones
- Arthritic pain

amfAR MAKING AIDS HISTORY | Opioid & Health Indicators Database ABOUT | Find Your State | Find Your Congressional District | Share On:

Increases in Acute Hepatitis C Virus Infection Related to a Growing Opioid Epidemic and Associated Injection Drug Use, United States, 2004 to 2014

Jon E. Zibbell, PhD, Alice K. Asher, PhD, Rajiv C. Patel, MPH, Ben Kupronis, MPH, Kashif Iqbal, MPH, John W. Ward, MD, and Deborah Holtzman, PhD

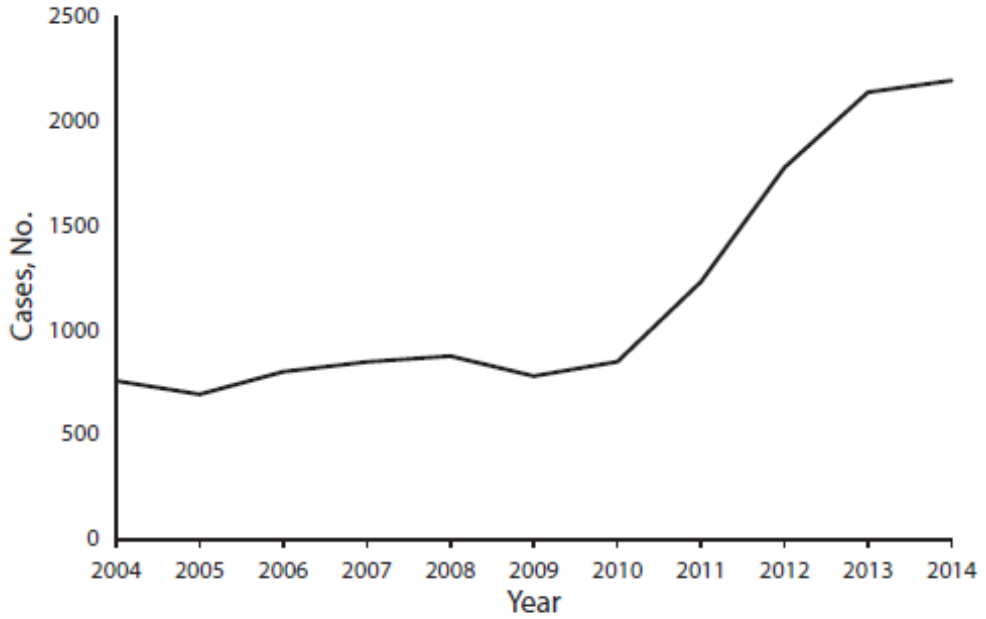
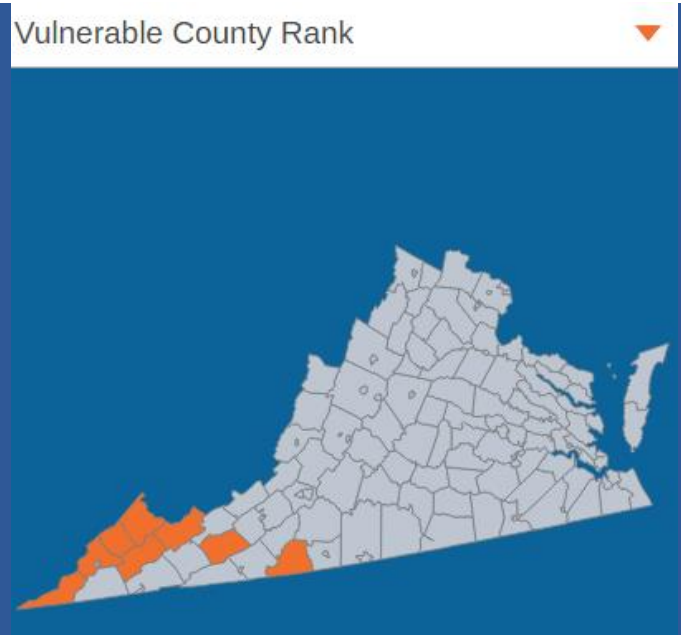
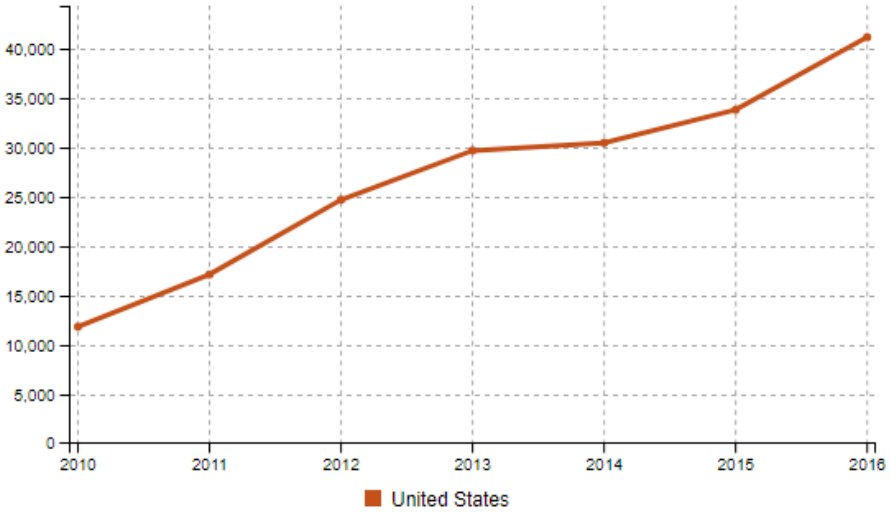


FIGURE 1—Reported Cases of Acute HCV Infection by Year: National Notifiable Disease Surveillance System, United States, 2004–2014



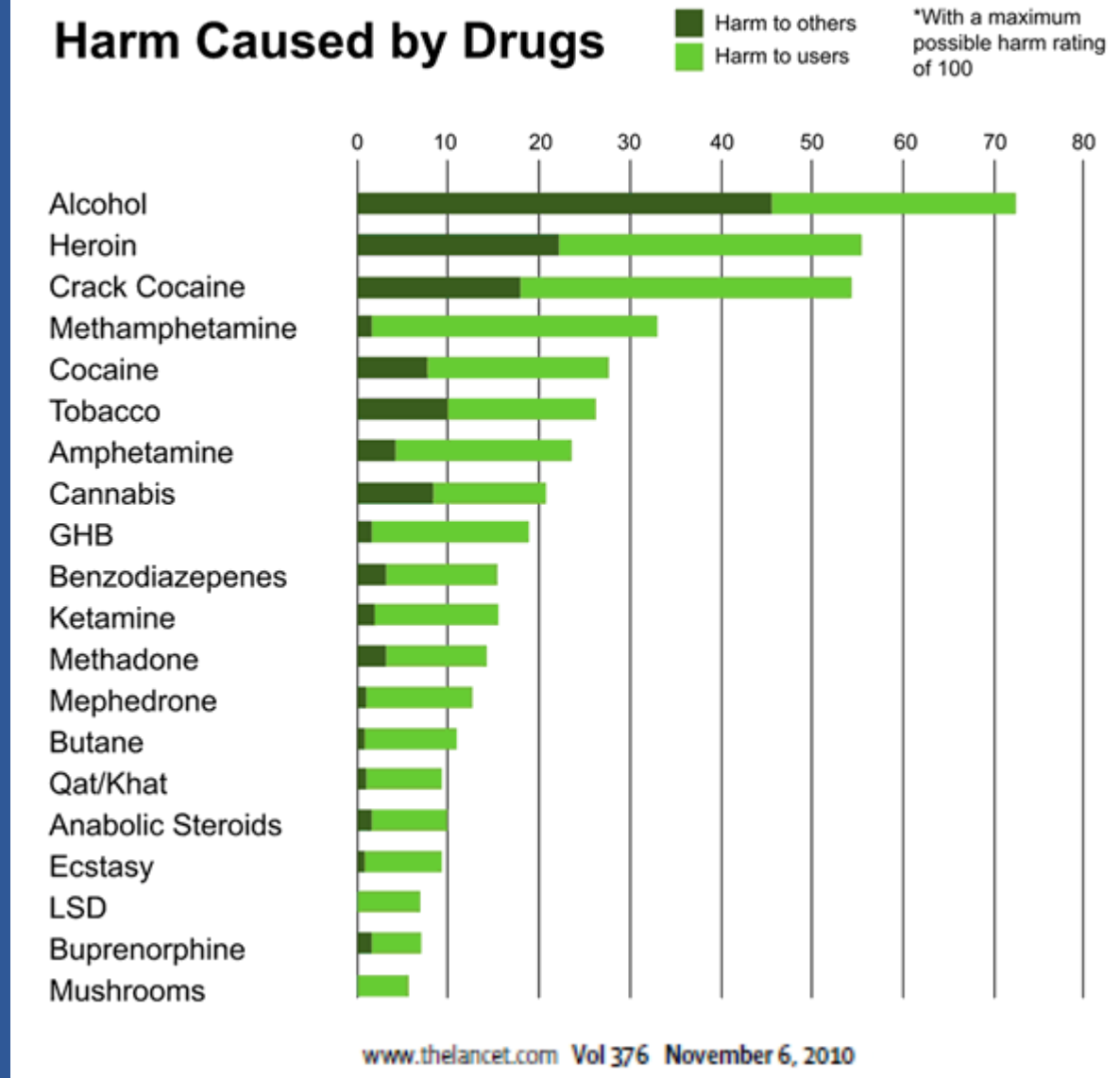


Harms – Operationalized:

Harms to people who use drugs
vs.
Harms to others

Drug harms in the UK: a multicriteria decision analysis

David J Nutt, Leslie A King, Lawrence D Phillips, on behalf of the Independent Scientific Committee on Drugs



www.thelancet.com Vol 376 November 6, 2010

Am J Prev Med 2015;49(5):e73–e79

2010 National and State Costs of Excessive Alcohol Consumption

Jeffrey J. Sacks, MD, MPH,[1] Katherine R. Gonzales, MPH,[2] Ellen E. Bouchery, MS,[3] Laura E. Tomedi, PhD, MPH,[4] Robert D. Brewer, MD, MSPH[5]

Table 1. Excessive Alcohol Consumption Costs (in Millions), by Category, U.S., 2010

Category of cost	Total costs ($)	Government costs ($)	Binge drinking ($)	Underage drinking ($)	Drinking while pregnant ($)
Total	249,026.4	100,674.8	191,126.9	24,268.3	5,494.1
Health care	28,379.1	16,915.1	16,273.8	3,795.8	2,830.0
Specialty care for abuse/ dependence	12,044.6	9,031.3	8,245.2	2,120.4	–
Hospitalization	5,948.5	2,828.1	2,007.5	198.9	48.6
Ambulatory care	1,524.5	524.0	1,070.8	144.4	7.0
Nursing home	1,166.8	691.6	863.4	2.1	0.5
Drugs/services	1,545.5	471.6	1,085.5	146.4	7.1
Fetal alcohol syndrome	2,750.0	1,248.5	1,160.5	449.5	2,750.0
Prevention and research	1,048.8	1,048.8	496.1	454.4	10.1
Training	34.8	11.5	16.4	6.3	–
Health insurance administration	2,315.6	1,059.7	1,328.5	273.3	6.7
Lost productivity	179,084.9	57,219.0	134,035.4	13,666.6	2,290.0
Impaired productivity at work	76,858.6	25,440.2	52,614.1	1,924.3	–
Impaired productivity at home	6,218.0	–	4,256.6	205.0	–
Absenteeism	4,619.9	1,529.2	4,619.9	201.5	–
Impaired productivity while in specialty care	1,983.4	656.5	1,358.6	349.1	–
Impaired productivity while in hospital	228.4	75.6	64.1	6.4	2.6
Mortality	75,204.5	24,892.7	58,373.4	6,044.2	170.7
Incarceration of perpetrators	9,150.5	3,028.8	9,150.5	3,855.3	–
Crime victims	2,704.8	895.3	2,704.8	734.7	–
Fetal alcohol syndrome	2,116.8	700.6	893.3	346.0	2,116.8
Other	41,562.5	26,540.7	40,817.7	6,806.0	374.1
Crime victim property damage	559.4	–	559.4	216.1	–
Criminal justice: corrections	15,865.9	15,865.9	15,865.9	1,842.0	–
Criminal justice: alcohol-related crimes	2,160.0	2,160.0	1,631.4	478.6	–
Criminal justice: violent and property crimes	5,998.8	5,998.8	5,998.8	2,117.6	–
Criminal justice: private legal	228.1	–	228.1	72.8	–
Motor vehicle crashes	13,461.9	–	13,461.9	1,490.2	–
Fire losses	2,914.3	2,142.0	2,914.3	527.5	–
Fetal alcohol syndrome (special education)	374.1	374.1	157.9	61.1	374.1

The Underestimated Cost of the Opioid Crisis

The Council of Economic Advisers

November 2017

Table 2: Estimated Cost of the Opioid Crisis in 2015 (2015 $)

VSL Assumption	Fatality Costs	Non-fatality Costs	Total Costs
Age-dependent	$431.7 billion	$72.3 billion	$504.0 billion
Low	$221.6 billion	$72.3 billion	$293.9 billion
Middle	$393.9 billion	$72.3 billion	$466.2 billion
High	$549.8 billion	$72.3 billion	$622.1 billion

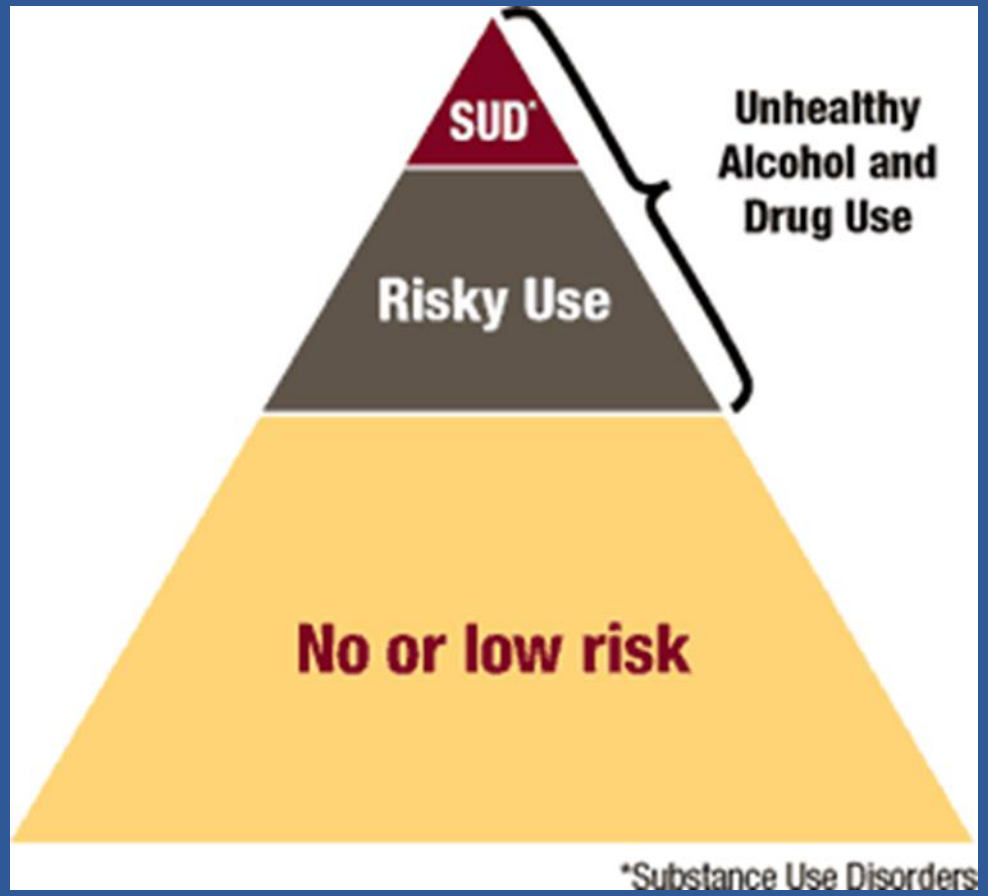
Comparing and Contrasting Alcohol use and Opioid use During Pregnancy

	Opioid Use During Pregnancy	Alcohol Use During Pregnancy
Prevalence of use	1.6%-8.5% of pregnant women use opioids; however, it's on the rise[1]	Approximately 8.5% of pregnant women drink alcohol at some point during pregnancy[1]
Likelihood of developing	NAS is seen in 30-80% of infants born to women who used opioids in the third trimester[2]	2-5% of school age children may have FASDs [3]
Negative effects/Disabilities	Neonatal Abstinence Syndrome (NAS) [4]	Fetal Alcohol Spectrum Disorders (FASDs)[1]
Duration of effects	Unknown[4]	FASDs last a lifetime [5]

Comparing and Contrasting Alcohol use and Opioid use During Pregnancy (Continued)

	Opioid Use During Pregnancy	Alcohol Use During Pregnancy
Cost of Care	Average of $90,000 per case of NAS[6]	Estimate $1.2-2.5 million per case of FAS[7]
Screening and Brief Intervention	Universal screening using the 5 P's tool, and brief intervention[8]	Universal screening using the AUDIT (US) tool, and brief intervention[9]
Ethics	Avoid separation of mother and child[10]	Avoid separation of mother and child [10]
Treatment	Medication-assisted therapy (MAT)[2]	Appropriate treatment referral for alcohol use disorder *

*See treatment resource directories on ACOG website: https://www.acog.org/About-ACOG/ACOG-Departments/Tobacco--Alcohol--and-Substance-Abuse/Fetal-Alcohol-Spectrum-Disorders-Prevention-Program/Provider-Resources/FASD-Resource-Directory


SUD*
Risky Use
No or low risk
Unhealthy Alcohol and Drug Use
*Substance Use Disorders

Not everyone who uses drugs becomes addicted

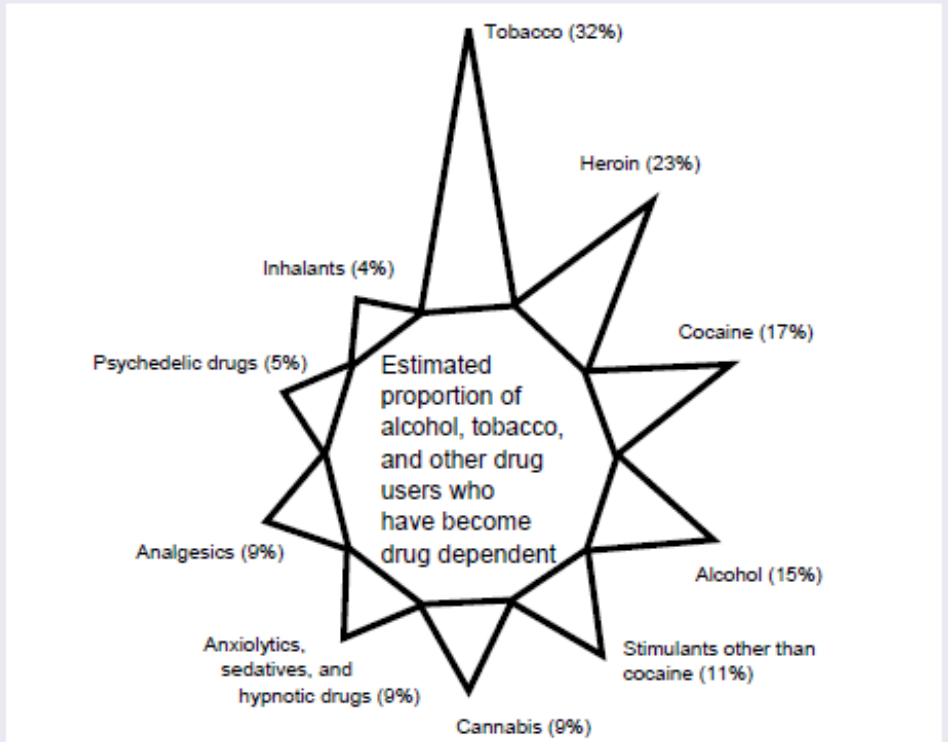


Figure 2 Estimated proportion of alcohol, tobacco, and other drug users who have developed clinical syndromes of drug dependence as defined according to the American Psychiatric Association's *Diagnostic and Statistical Manual of Mental Disorders, Third Edition, Revised*. The data were obtained from the National Comorbidity Survey, 1990–1992.

SOURCE: Adapted from Anthony et al. 1994.

Experimental and Clinical Psychopharmacology
1994, Vol. 2, No. 3, 244–268

In the public domain

Comparative Epidemiology of Dependence on Tobacco, Alcohol, Controlled Substances, and Inhalants: Basic Findings From the National Comorbidity Survey

James C. Anthony, Lynn A. Warner, and Ronald C. Kessler

What is the risk of opioid addiction among individuals prescribed opioids for pain?

What is the risk of opioid addiction among individuals prescribed opioids for pain?

Rates of opioid misuse, abuse, and addiction in chronic pain: a systematic review and data synthesis

Kevin E. Vowles[a,*], Mindy L. McEntee[a], Peter Siyahhan Julnes[a], Tessa Frohe[a], John P. Ney[b], David N. van der Goes[c]

PAIN

April 2015 • Volume 156 • Number 4

Rates of misuse 12-29% (95%CI:13-38%)
Rates of addiction averaged between 8-12% (95% CI: 3-17%)

Table 4

Opioid addiction—unweighted and weighted means, SD, and 95% confidence interval (CI).

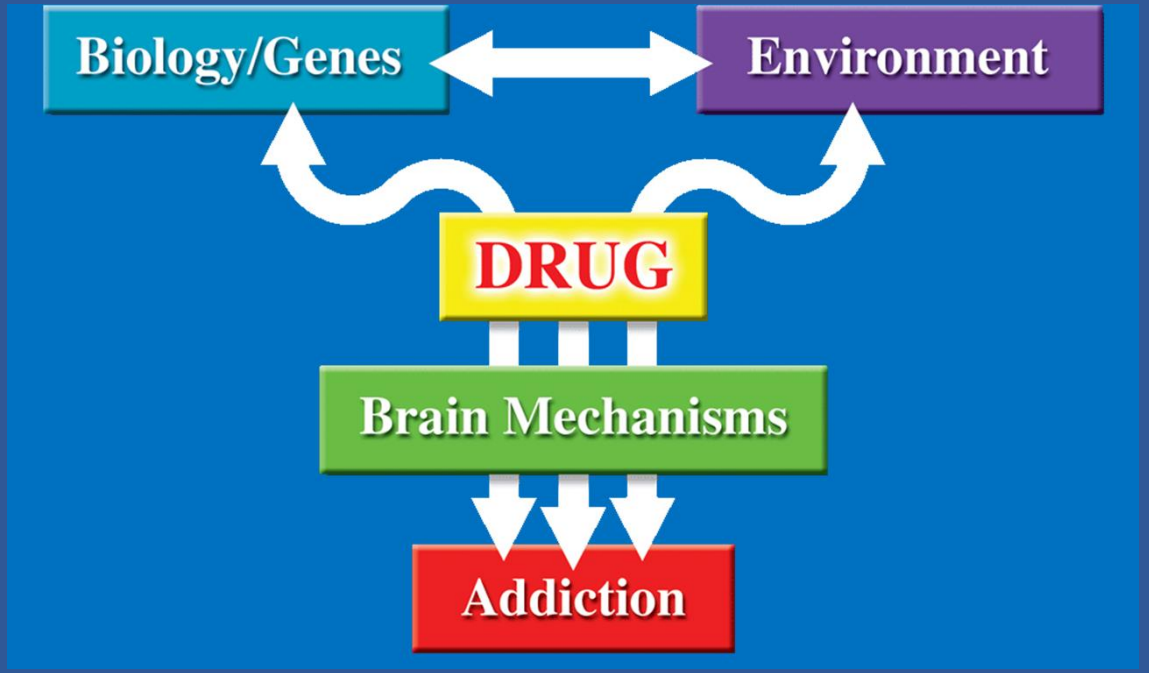
	Minimum, %		Maximum, %	
	Mean (SD)	95% CI	Mean (SD)	95% CI
Unweighted	10.9 (9.8)	5.3-16.5	11.7 (9.9)	6.1-17.3
Weighted means				
Sample size	4.3 (6.2)	0.8-7.8	4.7 (6.5)	1.0-8.4
Log sample size	10.1 (9.5)	4.7-15.5	10.8 (9.6)	5.4-16.2
Winsorized	7.8 (8.2)	3.2-12.4	8.6 (8.3)	3.9-13.3
Quality rating	10.5 (8.8)	5.5-15.5	10.4 (8.9)	5.4-15.4
Sample size × quality*	9.9 (8.7)	5.0-14.8	10.7 (8.9)	5.7-15.7
Quality				
High-quality studies	8.8 (7.3)	4.3-13.3	9.8 (7.8)	5.0-14.6
Low-quality studies	23.1 (12.9)	3.4-39.2	23.1 (12.9)	3.4-39.2

*Interaction term the product of standardized scores for the log transformed sample size and quality rating.

Why do some people become addicted and not others?

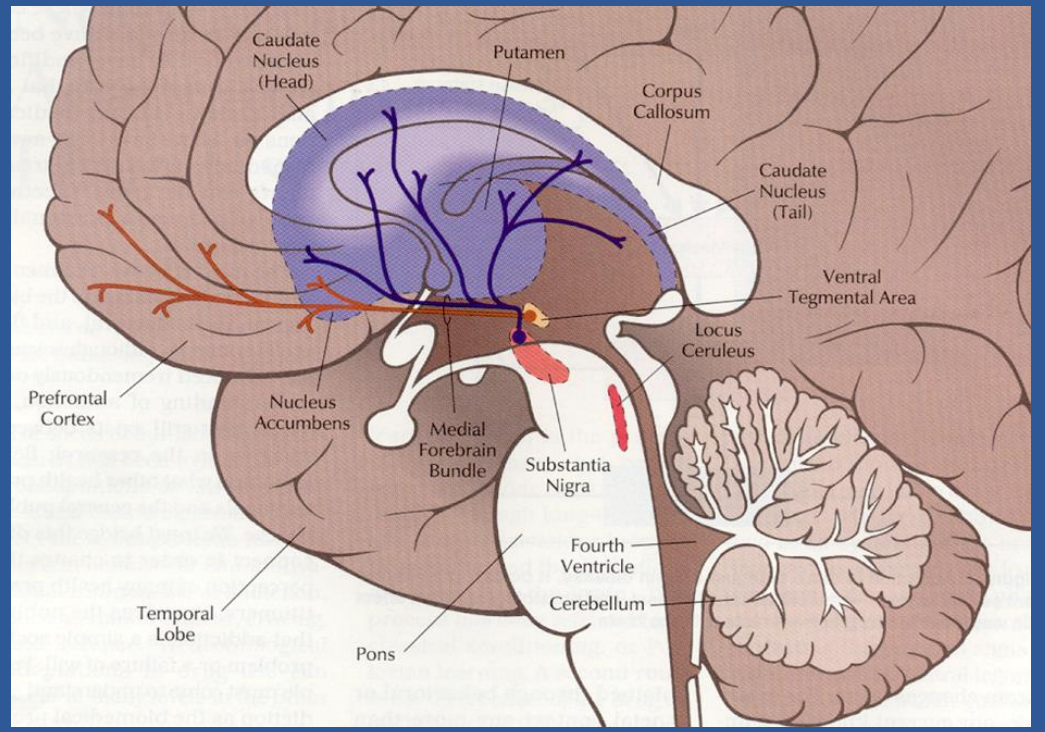
Why do some people become addicted and not others?

- Genetic
- Home environment/neighborhood
- Age of onset
- Psychiatric co-morbidities – Trauma
  - Childhood sexual and/or physical abuse (>60% of individuals w addiction)
  - PTSD (c 50% of individuals w PTSD lifetime addiction)
- Violence – history/current violent relationship

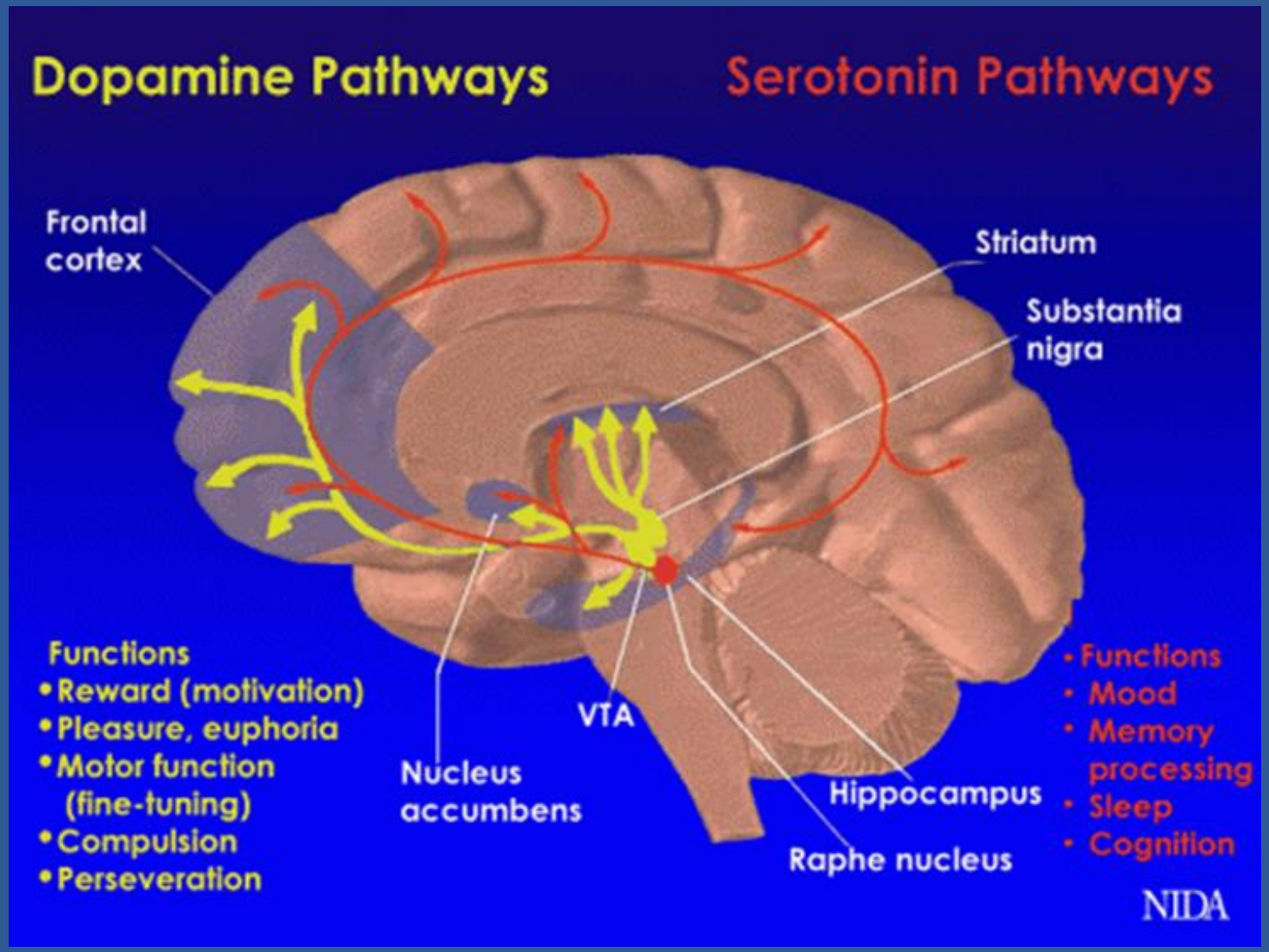


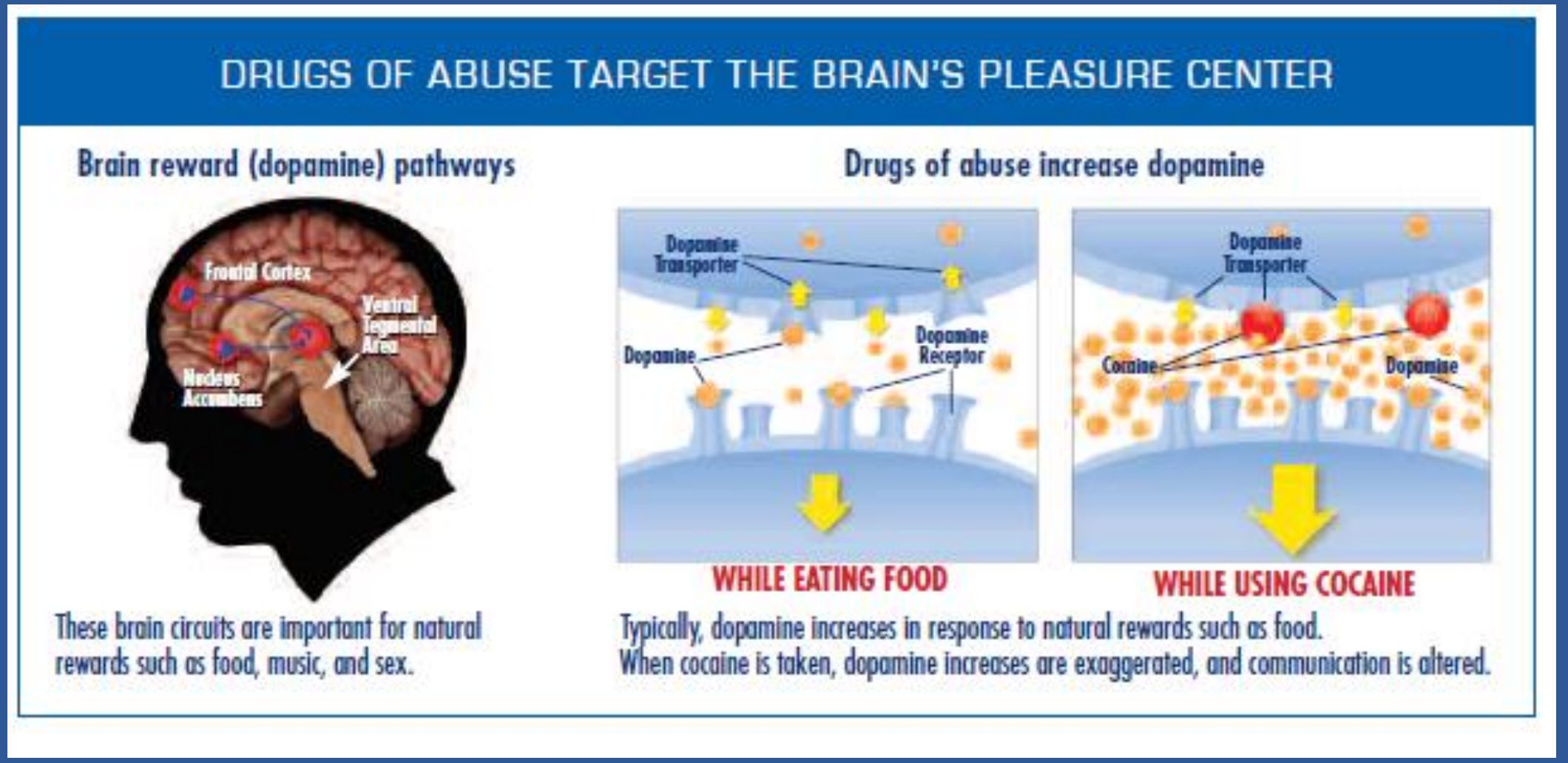
Reward/Reinforcement

- Reward/Reinforcement Pathway:
  - Ventral Tegmental Area (VTA)
  - Nucleus Accumbens with projections to Prefrontal Cortex
  - Dopaminergic system



Dopamine and the “Hijacked Brain” Hypothesis

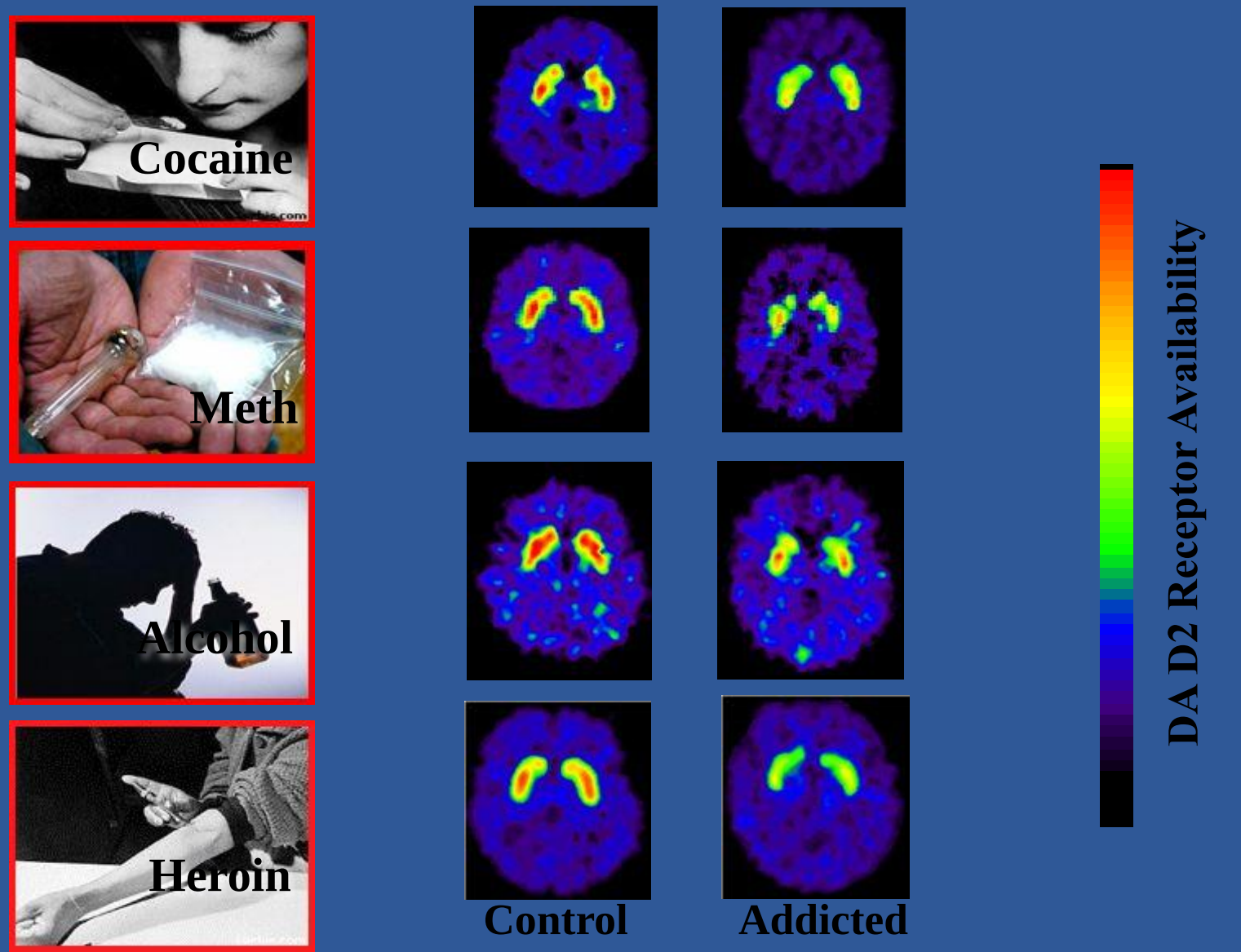




Drugs – release 2-10 times more dopamine than natural rewards such as eating and sex

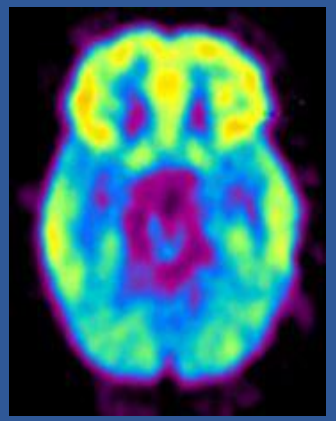
Prolonged drug use changes the brain: Functionally…

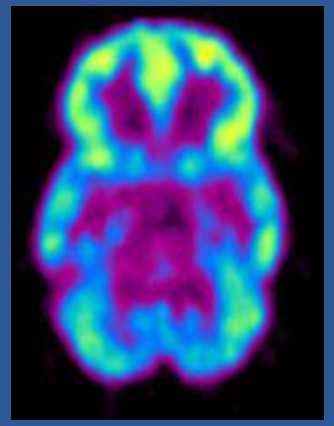
Dopamine D2 Receptors are Decreased by Addiction



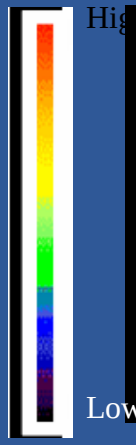
Addiction Changes Biology

Decreased Brain Metabolism in *Drug User*

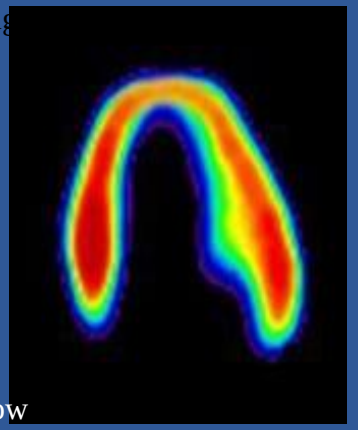




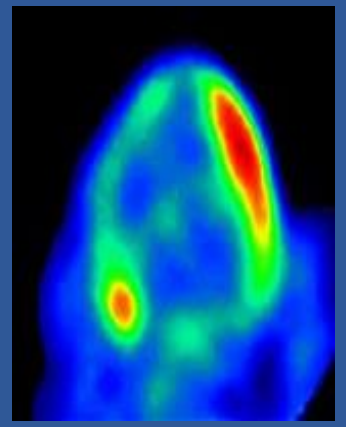
Diseased Brain/ Cocaine User



Decreased Heart Metabolism in *Heart Disease Patient*



Healthy Heart



Diseased Heart

Research supported by NIDA addresses all of these components of addiction.

NIDA

Heroin Addiction—A Metabolic Disease

Vincent P. Dole, MD, and Marie E. Nyswander, MD, New York

THE METHADONE Maintenance Research Program[1-3] began three years ago with pharmacological studies conducted on the metabolic ward of the Rockefeller University Hospital. Only six addict patients were treated during the first year, but the results of this work were sufficiently impressive to justify a trial of maintenance treatment of heroin addicts admitted to open medical wards of general hospitals in the city.

Methadone therapy was started in low dosage (10 to 20 mg/day in divided portions) and increased slowly over a period of four to six weeks to avoid narcotic effects. After the patients had reached the stabilization level (80 to 120 mg/day) it was possible to maintain them with a single, daily, oral ration, without further increase in dose. At the end of the six weeks of hospitalization the patients were discharged to outpatient clinics where they received their daily

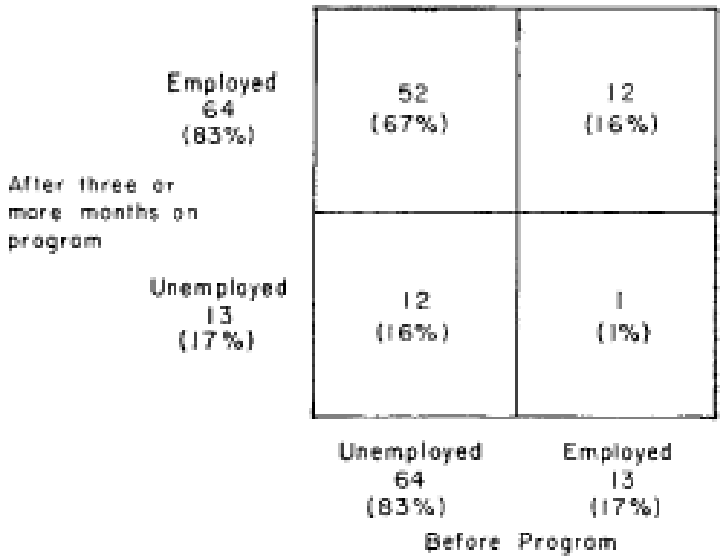


Fig 6.—Employment of 77 male patients in the program for 3 to 27 months as of April 15, 1966, compared with their status before starting treatment.

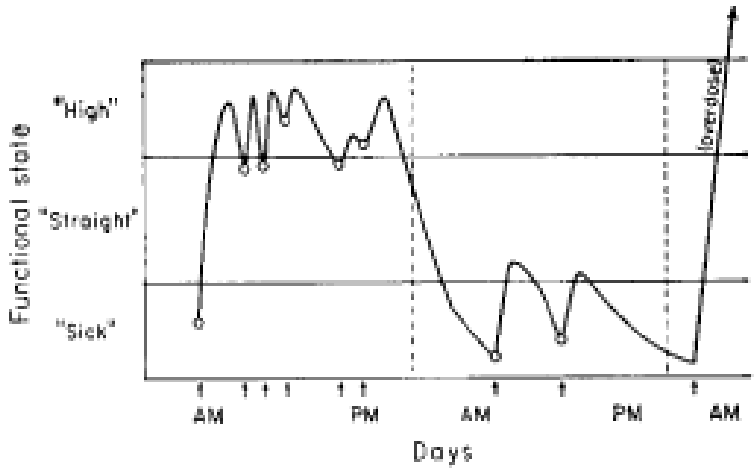


Fig 1.—Diagrammatic summary of functional state of typical "mainline" heroin user. *Arrows* show the repetitive injection of heroin in uncertain dose, usually 10 to 30 mg but sometimes much more. Note that addict is hardly ever in a state of normal function ("straight").

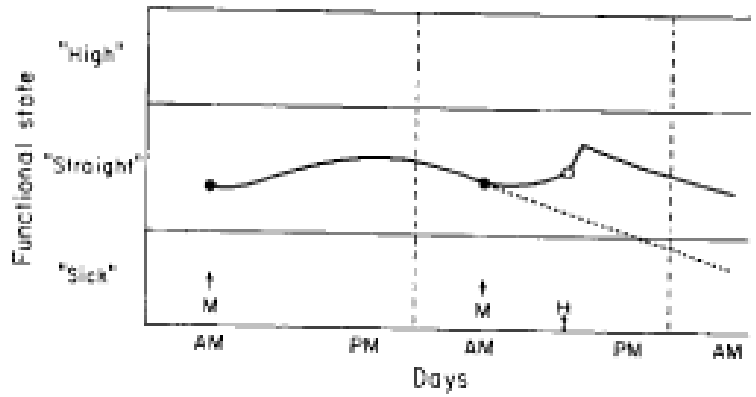


Fig 2.—Stabilization of patient in state of normal function by blockade treatment. A single, daily, oral dose of methadone prevents him from feeling symptoms of abstinence ("sick") or euphoria ("high"), even if he takes a shot of heroin. *Dotted line* indicates course if methadone is omitted.

Overtime Addiction from Reward Seeking to Relief Seeking

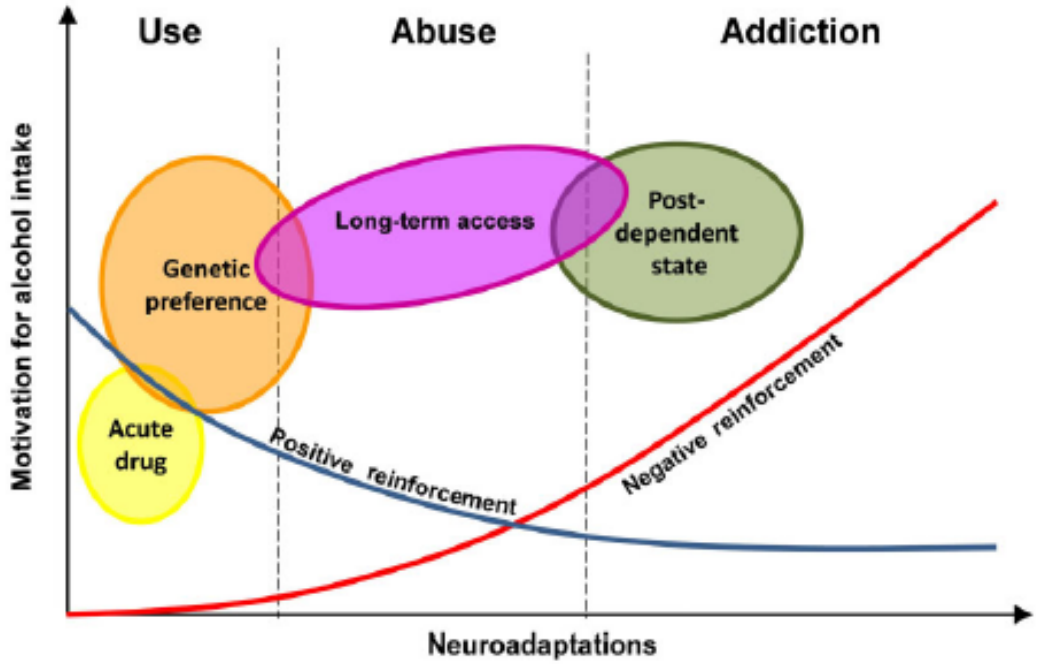
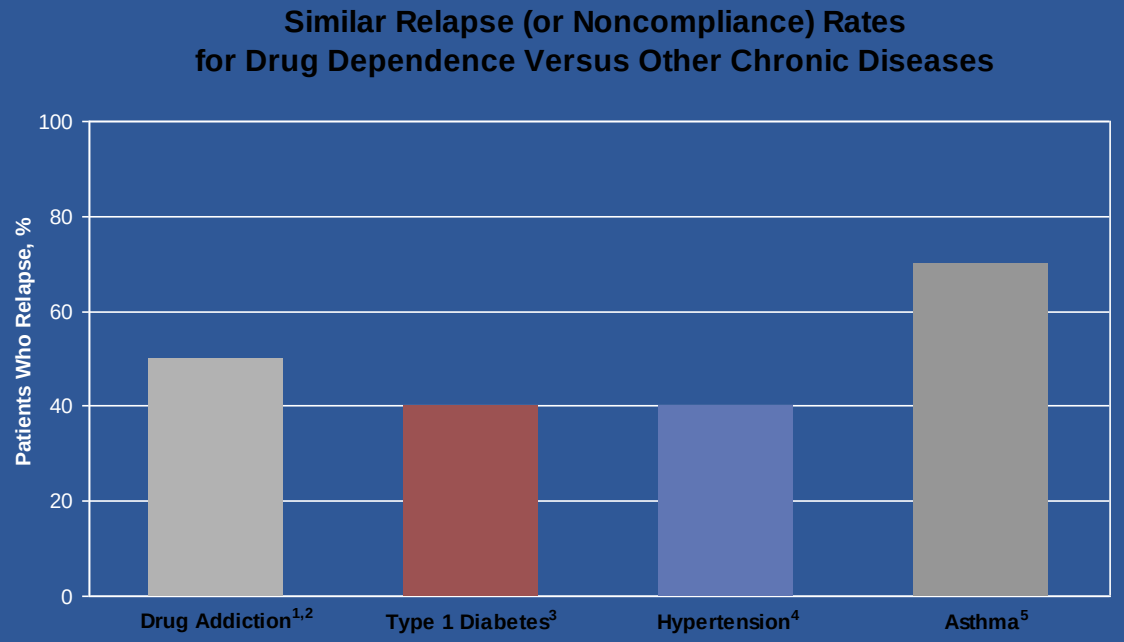


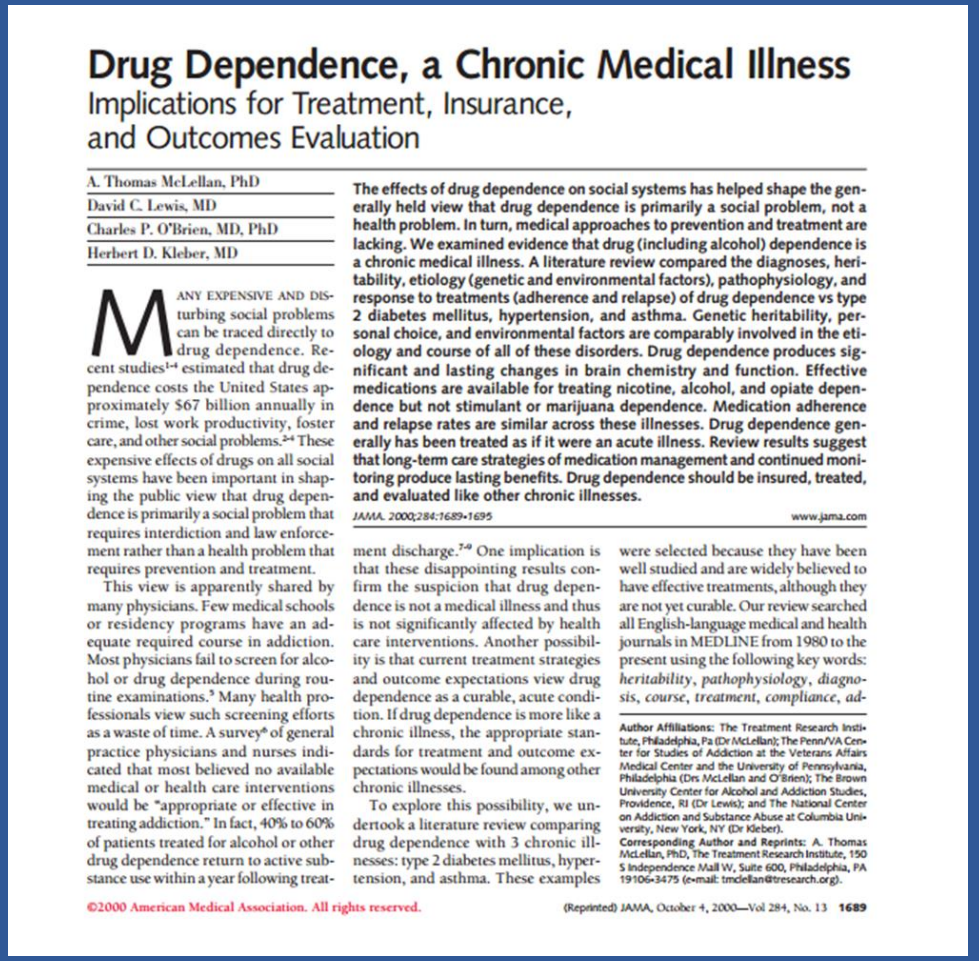
Figure 1 Conceptual framework placing common animal models along the trajectory of alcohol addiction. Alcohol dependence progresses over time from initial, largely positively reinforcing, pleasurable alcohol effects (reward), to be maintained by relief from a negative emotional state (negative reinforcement). The different animal models address distinct aspects of the addiction trajectory. Acute alcohol administration, e.g. for the development of conditioned place preference, or basic genetic models are mainly grounded on the positive reinforcing effects of alcohol, but do not likely encompass neuroadaptations characterizing the progression into addiction. These are better modeled by long-term (several months and more) alcohol consumption or forced intoxication procedures, the former covering the spectrum of adaptive and maladaptive processes from drug initiation to relapse-like behaviors. Because rodents, in contrast to humans, rarely drink to intoxication, and consequently do not develop noticeable withdrawal symptoms, forced chronic intermittent exposure leading to a postdependent state has been instrumental for studying the emergence of negative motivational processes and their role in the pathophysiology of addiction. Both, long-term access and post-dependent models exhibit predictive validity for medication development in alcoholism

If left untreated, addiction lasts a lifetime

- The natural history of addiction:
  - Relationship failure
  - Parenting failure
  - Inability to function in workforce
  - Incarceration
  - Homelessness
  - Untreated medical and psychiatric co-morbidities
  - HIV HCV acquisition and transmission
  - Overdose
  - Death

How effective is treatment?





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

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

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.[2-4] 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 requires interdiction and law enforcement rather than a health problem that requires prevention and treatment.

This view is apparently shared by many physicians. Few medical schools or residency programs have an adequate required course in addiction. Most physicians fail to screen for alcohol or drug dependence during routine examinations.[5] Many health professionals view such screening efforts as a waste of time. A survey[6] of general practice physicians and nurses indicated that most believed no available medical or health care interventions would be "appropriate or effective in treating addiction." In fact, 40% to 60% of patients treated for alcohol or other drug dependence return to active substance use within a year following treatment discharge.[7-9] One implication is that these disappointing results confirm the suspicion that drug dependence is not a medical illness and thus is not significantly affected by health care interventions. Another possibility is that current treatment strategies and outcome expectations view drug dependence as a curable, acute condition. If drug dependence is more like a chronic illness, the appropriate standards for treatment and outcome expectations would be found among other chronic illnesses.

To explore this possibility, we undertook a literature review comparing drug dependence with 3 chronic illnesses: type 2 diabetes mellitus, hypertension, and asthma. These examples were selected because they have been well studied and are widely believed to have effective treatments, although they are not yet curable. Our review searched all English-language medical and health journals in MEDLINE from 1980 to the present using the following key words: *heritability*, *pathophysiology*, *diagnosis*, *course*, *treatment*, *compliance*, *ad-*

Author Affiliations: The Treatment Research Institute, Philadelphia, Pa (Dr McLellan); The Penn/VA Center for Studies of Addiction at the Veterans Affairs Medical Center and the University of Pennsylvania, Philadelphia (Drs McLellan and O'Brien); The Brown University Center for Alcohol and Addiction Studies, Providence, RI (Dr Lewis); and The National Center on Addiction and Substance Abuse at Columbia University, New York, NY (Dr Kleber).
Corresponding Author and Reprints: A. Thomas McLellan, PhD, The Treatment Research Institute, 150 S Independence Mall W, Suite 600, Philadelphia, PA 19106-3475 (e-mail: tmclellan@tresearch.org).

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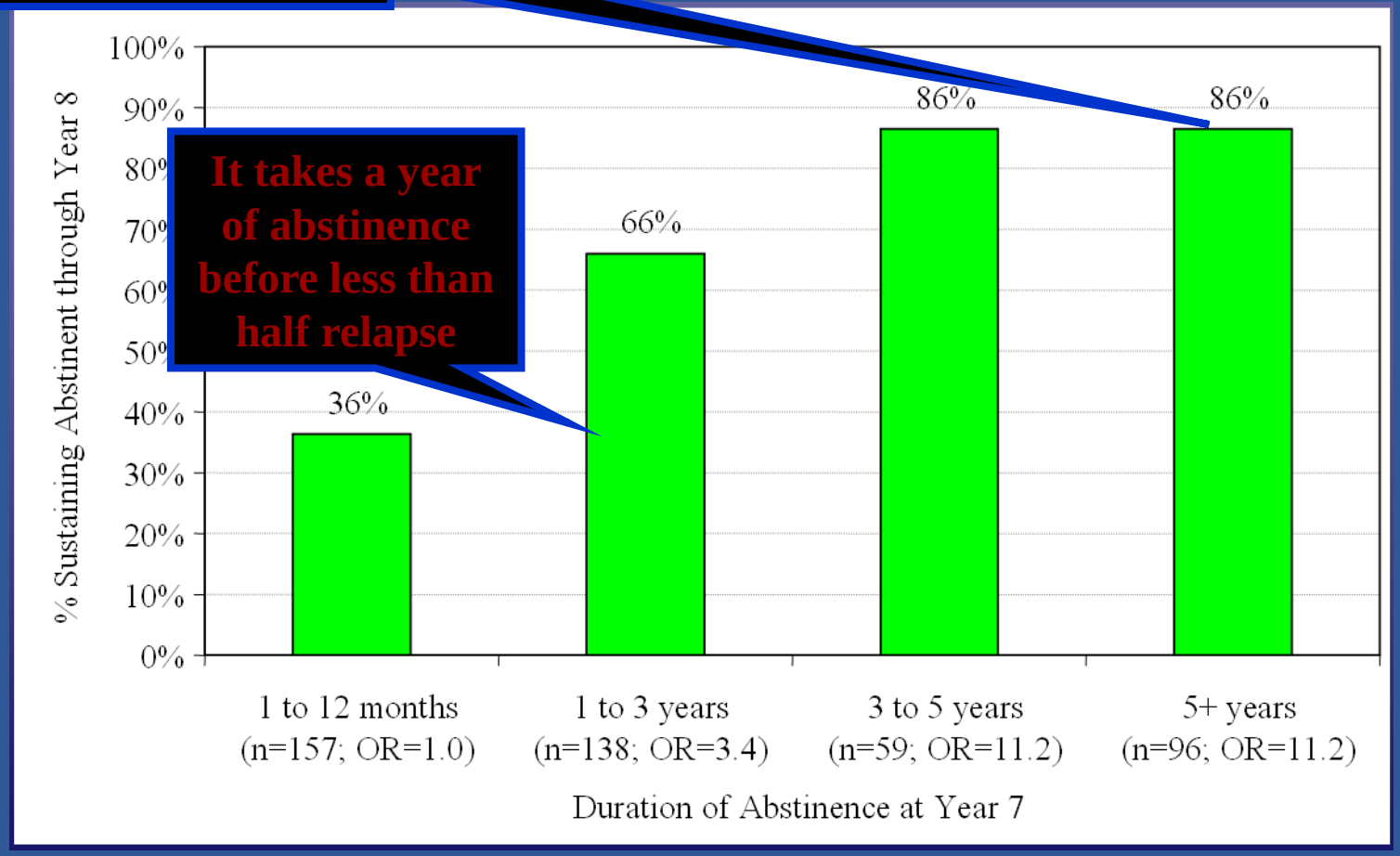
Graph adapted from Caron Foundation. http://www.caron.org/pdfs/RelapseRecovery-2003.pdf., 2. Hoffman NG, Miller NS. *Psychiatr Ann.* 1992;22(8):402-408. 3. Graber AL et al. *Diabetes Care*. 1992;15(11):1477-1483., 4. Clark LT. *Am Heart J*. 1991;121(2 pt 2):644-669., 5Dekker FW et al. *Eur Respir J*. 1993;6(6):886-890.

Extended Abstinence is Predictive of Sustained Recovery

After 5 years – if you are sober, you probably will stay that way.

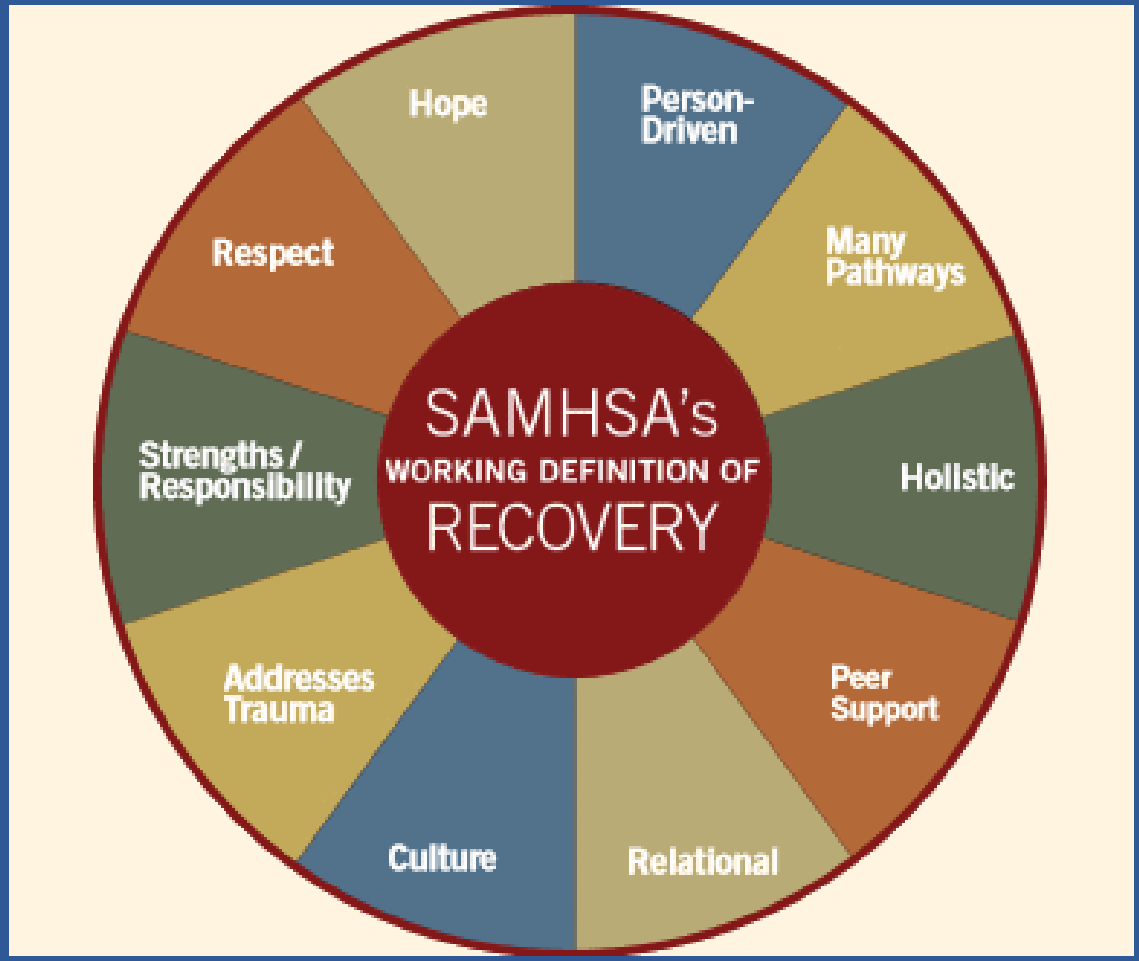
It takes a year of abstinence before less than half relapse



Dennis et al, Eval Rev, 2007

Recovery is the Goal of Treatment

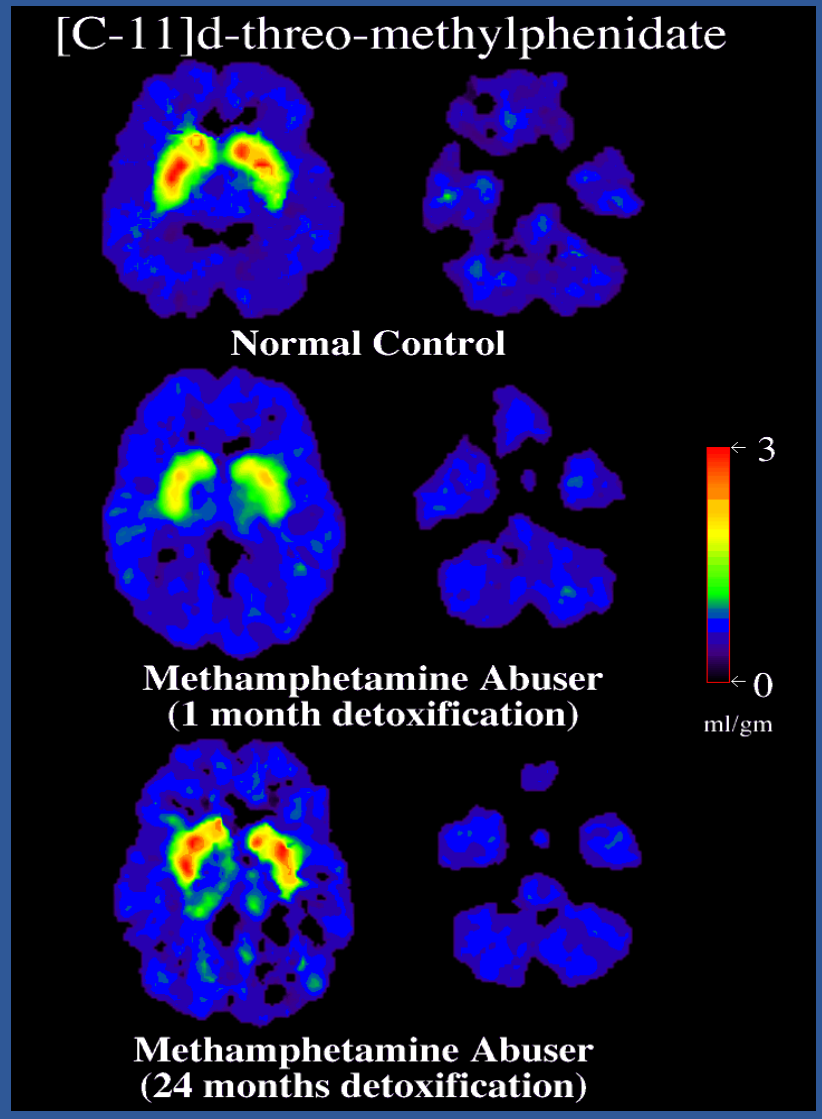
- Recovery is more than abstinence
- Building a life of integrity,
- Connection to others,
- Purpose and
- Serenity
- Recovery is fully compatible with the use of medications



Recovery Leads to Return of Normal Brain Structure and Function

DAT Recovery with prolonged abstinence from methamphetamine

Volkow et al., J. Neuroscience, 2001.



Conclusion(s)

- Substance use is ancient, but harmful use, especially addiction, is a more recent phenomena
- Substance harms as health concerns – not new
- Harms of substances not limited to addiction
- The future is synthetic

Thank You

- Mishka Terplan
-  @do_less_harm
- Mishka.Terplan@vcuhealth.org