The Essential Primer for Physicians and Healthcare Professionals in Addiction Medicine

ASAM

REVIEW COURSE

in Addiction Medicine



2022 COURSE SCHEDULE & SYLLABUS

COURSE BENEFITS

- Outstanding presentations by experts, authors, and leaders in addiction medicine
- Three years of on-demand access to full-course recordings within 30 days after event
- Curriculum mapped to the addiction medicine exam blueprints
- Complimentary electronic course syllabus with session slides and textbook references
- Dedicated networking time to interact with faculty and colleagues
- Special rate on the 2022 Board Exam Study Tool when registering for the course

ACCME ACCREDITED WITH COMMENDATION

ASAM has been awarded the highest level of Accreditation with Commendation by the Accreditation Council for Continuing Medical Education (ACCME) as a provider of continuing medical education (CME) for physicians.

Welcome to the Course

Message from The ASAM Review Course in Addiction Medicine Course Chairs

Dear Colleague:

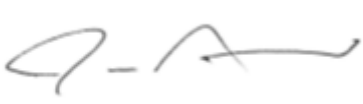
We are pleased to welcome you to the ASAM Review Course in Addiction Medicine! As you know, the field of addiction medicine is expanding rapidly and ASAM is excited to offer an updated version of the Review Course mapped to the 2022 exam blueprints provided by the American Board of Preventive Medicine and the American Osteopathic Association.

This course is widely recognized as the essential primer for physicians and other healthcare professionals who are preparing for a career in addiction medicine, as well as for primary care clinicians who wish to increase their skills in identifying and managing patients with substance use disorders. The Program Planning Committee has invited an outstanding panel of faculty presenters, all of whom are renowned as experts in the field of addiction medicine. Participants of the 2022 ASAM Review Course in Addiction Medicine will gain new knowledge and review important issues across the spectrum of addiction medicine. During two-and-a-half information-packed days, you will have the opportunity to network with fellow colleagues and learn first-hand from faculty experts on topics chosen to help you excel in the field of addiction medicine. We encourage you to get the most out of your experience and take advantage of everything the ASAM Review Course has to offer. We invite you to:

- Participate in the audience-response sessions to test your knowledge and work your way through board-style questions and interesting case scenarios
- Follow presentations in the printed syllabus and/or use the mobile app which allows note-taking
- Meet and network with colleagues and exhibitors to form study groups, establish new connections and discover new developments in the field
- Take your studying to the next level with the Board Exam Study Tool (BEST)
- Review the entire captured course or specific session recordings when you get home in ASAM's eLearning Center
- Engage with fellow learners and faculty members in the Board Exam Preparation Cohort through ASAMConnect as you continue to learn and prepare for the exam after the conclusion of the course

On behalf of the Program Planning Committee, we hope you take the opportunity to engage with colleagues and the phenomenal faculty members in thoughtful discussions to thoroughly prepare for the addiction medicine certification exams and further explore the challenging and rewarding field of addiction medicine. We are delighted to welcome you into the addiction medicine family!

Sincerely,



Jonathan D. Avery, MD
Chair



Erin A. Zerbo, MD, FASAM
Vice-Chair

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2022 Program Planning Committee

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R. Jeffrey Goldsmith, MD, DLFAPA, DFASAM

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REVIEW COURSE
in Addiction Medicine

2022 ASAM Review Course Content Map

	2022 ASAM Review Course Session Title	Associated Principles of Addiction Medicine Chapters
DAY 1	Neurobiology of Addiction	1, 4, 5, 62, 108
	Alcohol Use Disorder	9, 27, 41, 51, 55, 90
	Sedative Use Disorder	10, 52, 56
	Opioid Use Disorder	11, 53, 57, 58
	Tobacco Use Disorder	14, 20, 60
	Cannabis Use Disorder	15, 118
	Stimulant Use Disorder	12, 59
	Other Classes of Drugs	13, 16, 17, 18, 19, 21, 61
DAY 2	Behavioral Addiction	44, 45, 46, 47, 48
	Epidemiology	3
	Ethics and the Law	6, 49, 106, 115, 116, 117, 120
	Psychiatric Co-Morbidities	29, 31, 40, 92, 93, 94, 95, 96, 97, 98, 99
	Prevention and Public Health	22, 24, 25, 28, 36, 37, 42, 73, 107, 121
	Medical Co-Morbidities	29, 31, 39, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 91
	Pharmacology and Toxicology	8, 23, 34, 50, 119
DAY 3	Evolution of Addiction and Treatment	2, 7, 26, 30, 35, 36
	Treatment for Different Stages of Life	43, 54, 107, 109, 110, 111, 112, 113, 114
	Genetics and Gender	38, 90
	Pain and Addiction	100, 101, 102, 103, 104, 105
	Cognitive Behavioral Therapy & Motivational Interviewing	63, 65, 66, 71
	Mutual Help, Psychotherapy, and Social Support	32, 64, 68, 69, 70, 72, 74, 75, 76, 77, 78

ASAM
REVIEW COURSE
in Addiction Medicine

Addiction Medicine Certification

The American Board of Preventive Medicine (ABPM)

The ABPM administers the addiction medicine board exam for MDs. In 2016, the American Board of Medical Specialties (ABMS) recognized addiction medicine as a new medical subspecialty of the ABPM. Physicians certified by any of the 24 ABMS Member Boards can apply for certification through the exam administered by the ABPM. Information about the ABPM exam, application process, and eligibility pathways is available on the ABPM website: www.TheABPM.org/become-certified/

Pathways to Eligibility:
To find out if you're eligible, visit:
www.TheABPM.org/am-i-eligible

Practice Pathway
Until 2025, applicants who complete minimum time in practice or a non-ACGME-accredited fellowship training will be considered for the addiction medicine subspecialty exam.

ACGME-Accredited Fellowship Pathway
After 2025, it will be mandatory that physicians complete an ACGME accredited addiction medicine fellowship in order to be eligible to apply to take the exam.

Applications Accepted: March – June 2022

Exam Administration: Offered in October 2022

The American Osteopathic Association (AOA)

The AOA administers the board exam for addiction medicine certification for DOs. As of May 26, 2021, MDs may also take the AOA addiction medicine certification exams. Information about the AOA exam, application process, and eligibility pathways is available on the AOA website: https://certification.osteopathic.org/addiction-medicine

Pathways to Eligibility:
To find out if you're eligible visit:
https://certification.osteopathic.org/addiction-medicine/board-policies

Clinical Practice Pathway
Until 2023, applicants who complete minimum time in practice, hold an active ABAM certificate, or an ACAAM (formerly TAMF and ABAM) fellowship within five years are eligible to apply to take the exam.

AOA or ACGME-Accredited Fellowship Pathway
After 2023, it will be mandatory that physicians complete an ACGME accredited addiction medicine fellowship in order to be eligible to apply to take the exam.

Applications Accepted: June – October 2022

Exam Administration: Offered in November 2022

Application Resources

In official collaboration with ASAM and the American Board of Preventive Medicine (ABPM), Michigan Collaborative Addiction Resources & Education System (MI CARES) offers tools to help physicians complete the ABPM's requirements for the practice pathway.

For more information, visit: https://micaresed.org/enroll/

Questions? Visit the the Review Course Tabletop Exhibit Hall to interact with representatives from the ABPM, AOA, and MI CARES.

ABPM & AOA Addiction Medicine Exam Blueprints

The ASAM Review Course curriculum is carefully mapped to the ABPM core content areas of the addiction medicine exam blueprint. This also closely relates to the AOA addiction medicine exam blueprint.

ABPM	Exam Core Content	
25%	01	Definitions
	02	Genetics
	03	Pharmacokinetic and Pharmacodynamic Principles
	04	Pharmacology
	05	Neurobiology of Addiction
20%	06	Epidemiological Concepts
	07	Epidemiological Trends of Substance Use Disorders
	08	Prevention
40%	09	Screening, Assessment, and Brief Intervention
	10	Overview of Addiction Treatment
	11	Management of Inpatient and Outpatient Intoxication and Withdrawal
	12	Pharmacologic Interventions for Addictions
	13	Behavioral Interventions
	14	Co-Occurring and Medical Disorders among Patients with Alcohol and Other Drug Use and Addiction
	15	Co-Occurring Psychiatric Disorders among Patients with Alcohol and Other Drug Use and Addiction
	16	Pain and Addiction
15%	17	Ethical, Legal and Liability Issues in Addiction Practice

Addiction Medicine Exam Topics	Target Percentage
Alcohol	15 – 20%
Sedatives	7 – 10%
Stimulants	7 – 10%
Opioids	10 – 15 %
Cannabinoids	7 – 10 %
Nicotine	15 – 20%
Hallucinogens	0.5 – 3%
Dissociatives	0.5 – 3%
Inhalants	0.5 – 3%
Anabolic steroids	0.5 – 3%
Other substances	1 – 3%
Nonsubstance addiction	1 – 3%
General/All substances combined	1 – 5%

AOA Exam Core Content	
1. Pharmacology	24%
2. Epidemiology and Genetics	18%
3. Treatment	15%
4. Legal Aspects	14%
5. Diagnosis	12%
6. Special Populations	11%
7. Prevention	6%

*To view a breakdown of the full AOA exam content outline, visit: https://certification.osteopathic.org/addiction-medicine/wp-content/uploads/sites/34/Addiction-Medicine-Content.pdf

ASAM
REVIEW COURSE
in Addiction Medicine

Schedule-at-a-Glance

Thursday, July 21, 2022 – Pre-Courses

11:00 am – 9:00 pm CT	**ASAM Registration & Education Desk Open**
1:15 pm – 4:30 pm CT	**ASAM Moving Beyond the Barriers of Treating Opioid Use Disorder** *Edwin A. Salsitz MD, DFASAM* *Ruchi M. Fitzgerald, MD, FAAFP*
6:00 pm – 9:15 pm CT	**ASAM Treatment of Alcohol Use Disorder Course** *Stephen Holt, MD, MS, FACP* *Shawn Cohen, MD*

Friday, July 22, 2022 – Day One

6:15 am – 7:15 am CT	**Mutual Help (Open Meeting)** Held each day of the course, these peer-run addiction problem-specific support groups (eg, 12 Step, AA, NA) are open to any registrant.
7:00 am – 5:30 pm CT	**ASAM Registration & Education Desk Open**
7:00 am – 6:30 pm CT	**Tabletop Exhibits Open**
7:00 am – 7:45 am CT	**Continental Breakfast** Networking with colleagues and exhibitors
7:45 am – 8:00 am CT	**Welcome and Opening Remarks** *Jonathan D. Avery, MD* *Erin A. Zerbo*, MD, FASAM
8:00 am – 8:45 am CT	**Neurobiology of Addiction: Key Concepts & Model** *Petros Levounis, MD, MA, DFASAM*
8:45 am – 9:30 am CT	**Alcohol Use Disorder: From Neurobiology to Treatment** *Ricardo Restrepo, MD, MPH*
9:30 am – 10:15 am CT	**Sedative Use Disorder: Key Concepts for Treatmen**t *Ricardo Restrepo, MD, MPH*
10:15 am – 10:45 am CT	**Refreshment Break** Networking with colleagues and exhibitors
10:45 am – 11:30 am CT	**Opioid Use Disorder: Science, History, and Clinical Implications** *Soteri Polydorou, MD*

11:30 am – 12:15 pm CT **Tobacco Use Disorder: Trends and Treatment**
Jonathan D. Avery, MD

12:15 pm – 1:00 pm CT **Cannabis Use Disorder: Science, Trends, and Clinical Implications**
Ruchi M. Fitzgerald, MD, FAAFP

1:00 pm – 2:00 pm CT **Lite-Fare Lunch**
Networking with colleagues and exhibitors

2:00 pm – 2:15 pm CT **Interesting Cases with Audience Response System (ARS)**
Edwin A. Salsitz, MD, DFASAM

2:15 pm – 3:00 pm CT **Stimulant Use Disorder: Trends and Treatment**
Michael H. Baumann, PhD

3:00 pm – 3:45 pm CT **Other Classes of Drugs: Pharmacology and Epidemiology**
Erin A. Zerbo, MD, FASAM

3:45 pm – 4:15 pm CT **Refreshment Break**
Networking with colleagues and exhibitors

4:15 pm – 4:30 pm CT **Interesting Cases with Audience Response System (ARS)**
Edwin A. Salsitz, MD, DFASAM

4:30 pm – 5:30 pm CT **Expert Panel Discussion and Q&A - Day 1**
Jonathan D. Avery, MD (Moderator)
Day One Faculty (See Above)

5:30 pm – 6:30 pm CT **Networking Reception**

Saturday, July 23, 2022 – Day Two

6:15 am – 7:15 am CT **Mutual Help (Open Meeting)**
Held each day of the course, these peer-run addiction problem-specific support groups (eg, 12 Step, AA, NA) are open to any registrant.

7:00 am – 5:30 pm CT **ASAM Registration & Education Desk Open**

7:00 am – 3:30 pm CT **Tabletop Exhibits Open**

7:00 am – 7:45 am CT **Continental Breakfast**
Networking with colleagues and exhibitors

7:45 am – 8:00 am CT **Welcome Back and Board Exam Practice Questions with Audience Response System (ARS)**
Erin A. Zerbo, MD, FASAM

8:00 am – 8:45 am CT	**Behavioral Addiction: From Theory to Treatment** *Faye Chao, MD*
8:45 am – 9:30 am CT	**Epidemiology: Core Concepts and Applications** *Jeffrey J. DeVido, MD, MTS, FAPA, FASAM*
9:30 am – 10:15 am CT	**Ethics and the Law: Principles and Treatment Implications** *H. Westley Clark, MD, JD, MPH, DFASAM*
10:15 am – 10:45 am CT	**Refreshment Break** Networking with colleagues and exhibitors
10:45 am – 11:30 am CT	**Psychiatric Co-Morbidities: Assessment and Treatment** *Kelly J. Kleinert, MD*
11:30 am – 12:15 pm CT	**Prevention and Public Health: Principles and Applications** *Amesika N. Nyaku, MD, MS*
12:15 pm – 1:00 pm CT	**Medical Co-Morbidities: Prevention and Treatment** *Annie Levesque, MD, MSc*
1:00 pm – 2:00 pm CT	**Lite-Fare Lunch** Networking with colleagues and exhibitors
2:00 pm – 2:15 pm CT	**Interesting Cases with Audience Response System (ARS)** *Edwin A. Salsitz, MD, DFASAM*
2:15 pm – 3:00 pm CT	**Pharmacology and Toxicology: Principles, Applications, and Limitations** *Lewis S. Nelson, MD, FASAM*
3:00 pm – 3:45 pm CT	**Becoming Certified: Pathways, Insights and Preparation Strategies** *Ruchi M. Fitzgerald, MD, FAAFP* *Kerri A. Leo, MATD, CAE, CHCP* *Diane Landahl, MSTD, CPCS*
3:45 pm – 4:15 pm CT	**Refreshment Break** Networking with colleagues and exhibitors
4:15 pm – 4:30 pm CT	**Interesting Cases with Audience Response System (ARS)** *Edwin A. Salsitz, MD, DFASAM*
4:30 pm – 5:30 pm CT	**Expert Panel Discussion and Q&A – Day 2** *Erin A. Zerbo, MD, FASAM (Moderator)* *Day Two Faculty (See Above)*

Sunday, July 24, 2022 – Day Three

6:15 am – 7:15 am CT	**Mutual Help (Open Meeting)** Held each day of the course, these peer-run addiction problem-specific support groups (eg, 12 Step, AA, NA) are open to any registrant.
7:00 am – 1:30 pm CT	**ASAM Registration & Education Desk Open**
7:00 am – 10:30 am CT	**Tabletop Exhibits Open**
7:00 am – 7:30 am CT	**Continental Breakfast** Networking with colleagues and exhibitors
7:30 am – 7:45 am CT	**Welcome Back and Board Exam Practice Questions with Audience Response System (ARS)** *Jonathan D. Avery, MD*
7:45 am – 8:30 am CT	**Evolution of Addiction and Treatment: History and Impact** *Paul H. Earley, MD, DFASAM*
8:30 am – 9:15 am CT	**Treatment for Different Stages of Life: Adolescents, Young Adults, and the Elderly** *Maria H. Rahmandar, MD*
9:15 am – 10:00 am CT	**Genetics and Gender: Impacts on Treatment for Women and Newborns** *Leslie A. Hayes, MD*
10:00 am – 10:30 am CT	**Refreshment Break** Network with colleagues and exhibitors
10:30 am – 11:15 am CT	**Pain and Addiction: Past, Present, and Future of Treatment** *Edwin A. Salsitz, MD, DFASAM*
11:15 am – 12:00 pm CT	**Patient Interventions: Cognitive Behavioral Therapy and Motivational Interviewing** *Carla B. Marienfeld, MD, DFAPA, FASAM*
12:00 pm – 12:45 pm CT	**Patient Interventions: Mutual Help, Psychotherapy, and Social Support** *Paul H. Earley, MD, DFASAM*
12:45 pm – 1:30 pm CT	**Expert Panel Discussion and Q&A – Day 3** *Jonathan D. Avery, MD (Moderator)* *Day Three Faculty (See Above)*

Table of Contents

Opening Remarks and Welcome 14

Neurobiology of Addiction: Key Concepts and Models

Presenter Bio: Petros Levounis, MD, MA, DFASAM 15

Presenter Slides 16

Alcohol Use Disorder: From Neurobiology to Treatment

Presenter Bio: Ricardo Restrepo, MD, MPH 23

Presenter Slides 24

Sedative Use Disorder: Key Concepts for Treatment

Presenter Bio: Ricardo Restrepo, MD, MPH 42

Presenter Slides 43

Opioid Use Disorder: Science, History, and Clinical Implications

Presenter Bio: Soteri Polydorou, MD 58

Presenter Slides 59

Tobacco Use Disorder: Trends and Treatment

Presenter Bio: Jonathan D. Avery, MD 71

Presenter Slides 72

Cannabis Use Disorder: Science, Trends, and Clinical Implications

Presenter Bio: Ruchi M. Fitzgerald, MD, FAAFP 84

Presenter Slides 85

Stimulant Use Disorder: Trends and Treatment

Presenter Bio: Michael H. Baumann, PhD 96

Presenter Slides 97

Other Classes of Drugs: Pharmacology and Epidemiology

Presenter Bio: Erin A. Zerbo, MD, FASAM 110

Presenter Slides 111

Expert Panel Discussion and Q&A - Day 1

Panelists 124

Welcome Back and Board Exam Practice Questions with Audience Response System (ARS) - Day 2

Presenter Bio: Erin A. Zerbo, MD, FASAM..... **125**

Behavioral Addiction: From Theory to Treatment

Presenter Bio: Faye Chao, MD **126**

Presenter Slides..... **127**

Epidemiology: Core Concepts and Applications

Presenter Bio: Jeffrey J. DeVido, MD, MTS, FASAM, FAPA..... **138**

Presenter Slides..... **139**

Ethics and the Law: Principles and Treatment Implications

Presenter Bios: H. Westley Clark, MD, JD, MPH, DFASAM..... **151**

Presenter Slides..... **152**

Psychiatric Co-Morbidities: Assessment and Treatment

Presenter Bio: Kelly J. Kleinert, MD..... **162**

Presenter Slides..... **163**

Prevention and Public Health: Principles and Applications

Presenter Bio: Amesika N. Nyaku, MD, MS..... **170**

Presenter Slides..... **171**

Medical Co-Morbidities: Prevention and Treatment

Presenter Bio: Annie Levesque, MD, MSc..... **178**

Presenter Slides..... **179**

Pharmacology and Toxicology: Principles, Applications, and Limitations

Presenter Bio: Lewis S. Nelson, MD..... **185**

Presenter Slides..... **186**

Becoming Certified: Pathways, Insights and Preparation Strategies

Presenter Bio: Christopher J. Ondrula, JD **198**

Presenter Bio: Kerri A. Leo, MATD, CAE, CHCP

Presenter Bio: Ruchi M. Fitzgerald, MD, FAAFP.

Expert Panel Discussion and Q&A – Day 2

Panelists..... **201**

Welcome Back and Board Exam Practice Questions with Audience Response System (ARS) - Day 3

Presenter Bio: Jonathan D. Avery, MD..... **202**

Evolution of Addiction and Treatment: History and Impact

Presenter Bio: Paul H. Earley, MD, DFASAM..... **203**

Presenter Slides..... **204**

Treatment for Different Stages of Life: Adolescents, Young Adults, and the Elderly

Presenter Bio: Maria H. Rahmandar, MD..... **212**

Presenter Slides..... **213**

Genetics and Gender: Impacts on Treatment for Women and Newborns

Presenter Bio: Leslie A. Hayes, MD..... **221**

Presenter Slides..... **222**

Pain and Addiction: Past, Present, and Future of Treatment

Presenter Bio: Edwin A. Salsitz, MD, DFASAM..... **236**

Presenter Slides..... **237**

Patient Interventions: Cognitive Behavior Therapy and Motivational Interviewing

Presenter Bio: Carla B. Marienfeld, MD, , DFAPA, FASAM..... **248**

Presenter Slides..... **249**

Patient Interventions: Mutual Help, Psychotherapy, and Social Support

Presenter Bio: Paul H. Earley, MD, DFASAM..... **256**

Presenter Slides..... **257**

Expert Panel Discussion and Q&A – Day 3

Panelists..... **265**

Course Credits..... **266**

ASAM Publications **268**

ASAM Membership Information..... **269**

ASAM Criteria Course..... **270**

ASAM Career Center..... **271**

ASAM Criteria Assessment Interview Guide..... **272**

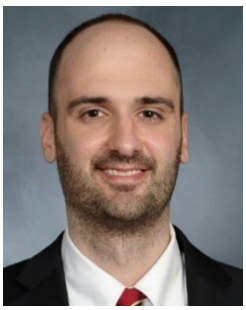
Tobacco Use Disorder..... **273**

*NOTE: Slides included in the Learning Community: Board Exam Preparation Cohort may vary during the live sessions based on the presenters' discretion.

Welcome and Opening Remarks Friday, July 22
7:45 am – 8:00 am CT

Welcome from Review Course Chair Jonathan D. Avery, MD and Vice-Chair Erin A. Zerbo, MD, FASAM.

Faculty Presenters



Jonathan D. Avery, MD
Director of Addiction Psychiatry
Weill Cornell Medical College

Dr. Avery is currently the Director of Addiction Psychiatry and an Associate Professor of Clinical Psychiatry at Weill Cornell Medical College and New York-Presbyterian Hospital. In addition to his clinical work, Dr. Avery teaches addiction psychiatry to the Weill Cornell medical students and residents of New York-Presbyterian Hospital. He has been published on a broad variety of topics in psychiatry, including papers on subjects ranging from clinician attitudes towards patients to how to use buprenorphine. He is the founder of the Addiction Stigma Institute that studies stigma towards individuals with substance use disorders and creates novel interventions to improve these stigmatizing attitudes. He was on the editorial board for the DSM-5 Clinical Cases book and is the editor of the books Co-occurring Mental Illness and Substance Use Disorders: A Guide to Diagnosis and Treatment and The Stigma of Addiction: An Essential Guide. He has won numerous awards for his clinical and academic work, including the American Board of Psychiatry and Neurology Faculty Innovation in Education Award and the Outstanding Faculty Member Award from the New York County Psychiatric Society.



Erin A. Zerbo, MD, FASAM
Director, Northern NJ Center of Excellence in Medication-Assisted Treatment
Rutgers New Jersey Medical School

Erin A. Zerbo, MD, FASAM, received her B.S. in Brain and Cognitive Sciences from the Massachusetts Institute of Technology in 2003, and her M.D. from New York University School of Medicine in 2007. She remained at NYU for a general psychiatry residency and a one-year addiction psychiatry fellowship, graduating in 2012. Since 2014, she has been an Assistant Professor in the Department of Psychiatry at Rutgers New Jersey Medical School and the Associate Director of Medical Student Education in Psychiatry. In addition to managing a large buprenorphine practice dedicated to Newark residents, she is also the director of the Northern New Jersey Center of Excellence in Medication-Assisted Treatment, a new statewide opioid training and education initiative.

Dr. Zerbo serves as the co-Chair of the Council on Education of the New Jersey Psychiatric Association, and she has published and lectured extensively in the field of addiction. Her primary interest is the treatment of substance use disorders in underserved and disadvantaged populations. She is a co-editor of the book "Pocket Guide to Addiction Assessment and Treatment" (APA, 2106), and the lead editor of "Becoming Mindful: Integrating Mindfulness into Your Psychiatric Practice" (APA, 2017).

Neurobiology of Addiction: Key Concepts and Model

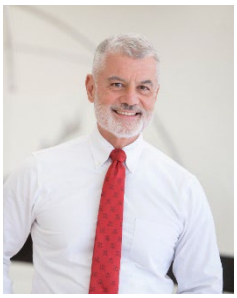
Friday, July 22
8:00 am – 8:45 am CT

Understanding neurobiology is a crucial part of understanding addiction. This session will describe the key neurotransmitters, brain pathways, and brain structures involved in drug use and addiction. The presenter will also explore models for understanding neurobiology and the impact of neurobiology on treatment modalities.

Learning Objective:

- After this session, learners will be able to: Identify key neurotransmitters, brain pathways, and brain structures impacted by the use of drugs, addiction, and addiction treatment.

Faculty Presenter



Petros Levounis, MD, MA, DFASAM
Professor and Chair
Rutgers New Jersey Medical School

Petros Levounis, MD, MA, DFASAM, serves as professor and chair of the Department of Psychiatry and Associate Dean for Professional Development at Rutgers New Jersey Medical School. Dr. Levounis came to Rutgers from Columbia University where he served as director of the Addiction Institute of New York from 2002 to 2013.

Dr. Levounis is a Phi Beta Kappa graduate of Stanford University where he studied chemistry and biophysics before receiving his medical education at Stanford University School of Medicine and the Medical College of Pennsylvania. During medical school, he researched the effects of social class on patient-physician relationships in Oxford, England, and received an MA degree in sociology from Stanford. In 1994, he moved to New York City to train in psychiatry at the New York State Psychiatric Institute of Columbia University. He graduated from Columbia earning the National Institute of Mental Health Outstanding Resident Award and went on to complete his fellowship in addiction psychiatry at New York University.

Dr. Levounis has written numerous articles, monographs, and book chapters; has lectured extensively on addiction topics throughout the United States and abroad; and has been interviewed by CBS, ABC, NBC, CNN, FOX, The Martha Stewart Radio Show, The New York Times, and The Washington Post, among others.

Dr. Levounis is the current President-Elect of the American Psychiatric Association (APA). He has also served on the boards of the American Society of Addiction Medicine (ASAM) and the American Board of Addiction Medicine, and from 2005 to 2009 chaired the national Committee on Addiction Treatment of the APA. Dr. Levounis is a Betty Ford Scholar, a recipient of the Association of Gay and Lesbian Psychiatrists' Distinguished Service Award and the ASAM Educator of the Year Award, and a distinguished fellow of the APA and ASAM. In 2017, he was elected as an honorary member of the World Psychiatric Association.

Dr. Levounis has published thirteen books including the self-help paperback "Sober Siblings: How to Help Your Alcoholic Brother or Sister—and Not Lose Yourself," the textbook of "Substance Dependence and Co-Occurring Psychiatric Disorders," "Motivational Interviewing for Clinical Practice," "The Behavioral Addictions," "Becoming Mindful," "Pocket Guide to LGBTQ Mental Health," and "Office-Based Buprenorphine Treatment of Opioid Use Disorder," now in its second edition. Dr. Levounis is currently working on the first textbook of Technological Addictions. His books have been translated into French, German, Hungarian, Japanese, Portuguese, and Spanish. Dr. Levounis is married to actor Lukas Hassel and lives in New York City.

The Neurobiology of Addiction

Petros Levounis, MD, MA
Professor and Chair, Department of Psychiatry, and Associate Dean
Rutgers New Jersey Medical School
President-Elect
American Psychiatric Association

1

The ASAM Review Course of Addiction Medicine

July 2022

Financial Disclosures



Petros Levounis, MD, MA
No Disclosures

2

Learning Objectives

Identify key neurotransmitters, brain pathways, and brain structures implicated in addiction and addiction treatment.

3

Outline

- Neurotransmitters
- The Basic Model
- The New and Improved Model
- Treatments

4

Neurotransmitters

5

Drug of Abuse	Endogenous Neurotransmitter
Alcohol	GABA / Glutamate*
Amphetamines & Cocaine	Dopamine
Benzodiazepines & GHB	GABA
Cannabis	Anandamide
Hallucinogens & MDMA	Serotonin
Nicotine	Acetylcholine
Opioids	Endorphins
Phencyclidine & Ketamine	Glutamate*

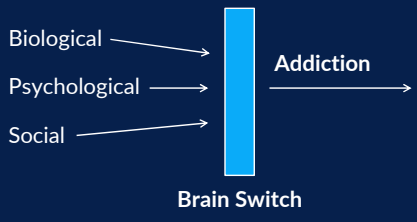
*Drug acts as an antagonist at the NMDA subtype of the glutamate receptor.

6

The Basic Model

7

Addiction: A Biopsychosocial Illness



Olsen and Levounis, Sober Siblings, 2008.

8

The Root Cause of the Disaster

ADDICTION RARE IN PATIENTS TREATED WITH NARCOTICS

To the Editor: Recently, we examined our current files to determine the incidence of narcotic addiction in 39,946 hospitalized medical patients[1] who were monitored consecutively. Although there were 11,882 patients who received at least one narcotic preparation, there were only four cases of reasonably well documented addiction in patients who had no history of addiction. The addiction was considered major in only one instance. The drugs implicated were meperidine in two patients,[2] Percodan in one, and hydromorphone in one. We conclude that despite widespread use of narcotic drugs in hospitals, the development of addiction is rare in medical patients with no history of addiction.

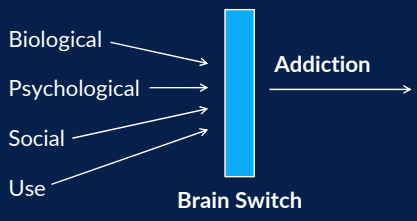
JANE PORTER
HERSHEL JICK, M.D.
Boston Collaborative Drug Surveillance Program
Waltham, MA 02154 Boston University Medical Center

1. Jick H, Miettinen OS, Shapiro S, Lewis GP, Siskind V, Slone D. Comprehensive drug surveillance. JAMA. 1970; 213:1455-60.
2. Miller RR, Jick H. Clinical effects of meperidine in hospitalized medical patients. J Clin Pharmacol. 1978; 18:180-8.

Porter and Jick, N Engl J Med, January 10, 1980.

9

Addiction: A Biopsychosocial Illness



Olsen and Levounis, Sober Siblings, 2008.

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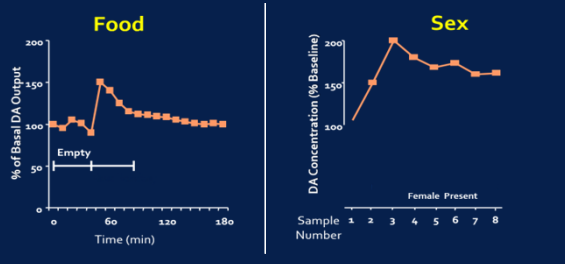
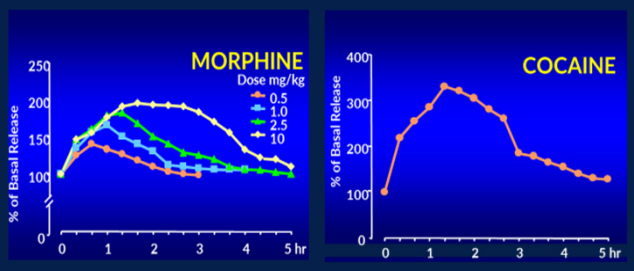
Salience and Natural Rewards



Adapted from: Di Chiara et al, Neuroscience, 1999.
Adapted from: Fiorino and Phillips, J Neuroscience, 1997.

11

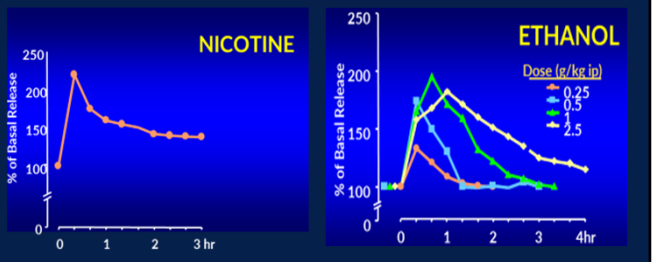
Effects of Drugs on Dopamine Levels



Adapted from: Di Chiara and Imperato, Proceedings of the National Academy of Sciences USA, 1988; courtesy of Nora D Volkow, MD.

12

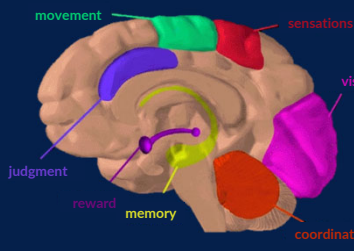
Effects of Drugs on Dopamine Levels



Adapted from: Di Chiara and Imperato, Proceedings of the National Academy of Sciences USA, 1988; courtesy of Nora D Volkow, MD.

13

Executive Function



National Institute on Drug Abuse, NIDA.NIH.gov, 2000.

14

The New and Improved Model

15

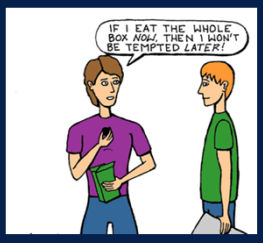
Three Novel Areas

- Motivational Circuitry
- Antireward Pathways
- Interoception

Levounis, Journal of Medical Toxicology, 2016.

16

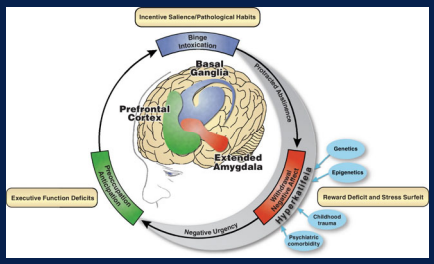
Preoccupation - Anticipation



Levounis, Arnaout, and Marienfeld, Motivational Interviewing for Clinical Practice, 2017.

17

From Reward to Relief



Koob, American Journal of Psychiatry, 2020.

18

Reward Systems

Game #1

A. A sure gain of $250
B. 25% chance to gain $1,000,
75% chance to gain nothing.



Adapted from: Tversky and Kahneman, Science, 1981.

19

Reward Systems

Game #1

A. A sure gain of $250 **84%**
B. 25% chance to gain $1,000,
75% chance to gain nothing **16%**



Adapted from: Tversky and Kahneman, Science, 1981.

20

Reward Systems

Game #2

A. A sure loss of $750
B. 25% chance to lose nothing,
75% chance to lose $1,000.



Adapted from: Tversky and Kahneman, Science, 1981.

21

Reward Systems

Game #2

A. A sure loss of $750 **13%**
B. 25% chance to lose nothing,
75% chance to lose $1,000. **87%**



Adapted from: Tversky and Kahneman, Science, 1981.

22

Human Nature

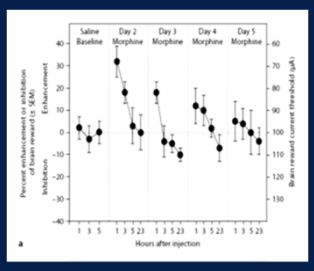
People avoid risks to ensure gains.

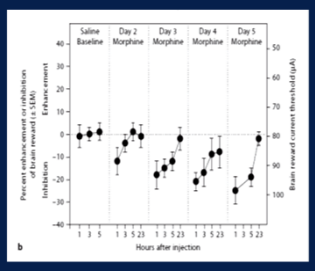
Psychology trumps probability.

Ascher and Levounis , The Behavioral Addictions, 2015.

23

Withdrawal – Negative Affect





Gardner, Chronic Pain and Addiction, 2011.

24

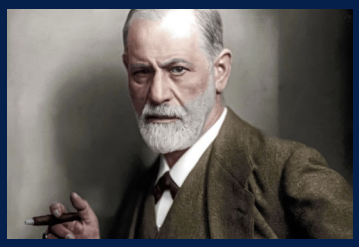


25

Treatments

26

1st Wave: Psychoanalysis



27

2nd Wave: Boot Camps

The prototype, synanon, was founded in California in 1958 to address heroin addiction. The goal was to:

- break down defenses,
- bust through denial, and
- reshape the addict's personality.

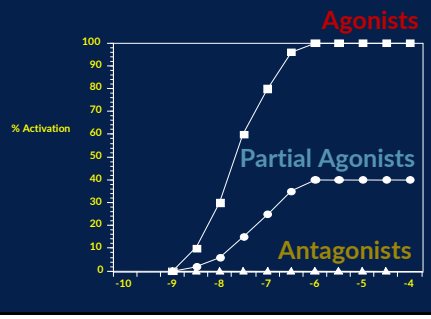
28

3rd Wave: Current Treatments

Medications	Mutual Help	Psychotherapy and Counseling

29

Medications



30

Mutual Help: Medical Staff

1. Housing	2. Government Services	3. Medical Services	4. Outpatient Treatment
5. Job	6. Community	7. Trusting People	8. Inner Peace
9. God	10. Spirituality	11. AA	

Goldfarb, Am J Drug Alcohol Abuse, 1996.

31

Mutual Help: Patients

1. Inner Peace	2. God	3. Medical Services	4. AA
5. Housing	6. Spirituality	7. Outpatient Treatment	8. Community
9. Government Services	10. Trusting People	11. Job	

Goldfarb, Am J Drug Alcohol Abuse, 1996.

32

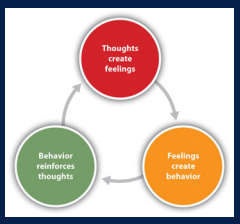
Mutual Help: What Medical Staff Think Patients Think

1. Housing	2. Outpatient Treatment	3. Medical Services	4. Job
5. Trusting People	6. AA	7. Inner Peace	8. Community
9. Government Services	10. Spirituality	11. God	

Goldfarb, Am J Drug Alcohol Abuse, 1996.

33

Cognitive Behavioral Therapy & Motivational Interviewing



Levounis, Zerbo, and Aggarwal, Pocket Guide to Addiction Assessment and Treatment, 2016.

34

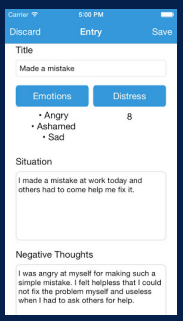
4th Wave: Mindfulness

"Between stimulus and response there is a space. In that space is our power to choose our response. In our response lie our growth and our freedom."

Victor E. Frankl

Frankl, Man's Search for Meaning, 1959.
Zerbo, Schlechter, Desai, and Levounis, Becoming Mindful, 2017.

35

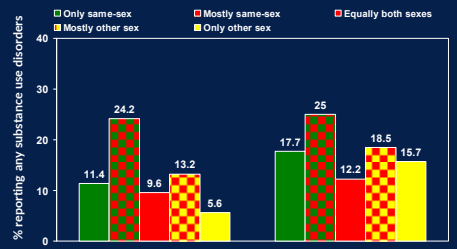


CBT Apps

Mood Tools.org

36

And Back to Psychodynamics . . .



McCabe, Addiction, 2009, Courtesy of Sean E. McCabe, PhD.
Levounis and Yarbrough, Pocket Guide to LGBTQ Mental Health, 2020.

37

Neurotransmitters

38

Drug of Abuse	Endogenous Neurotransmitter
Alcohol	GABA / Glutamate*
Amphetamines & Cocaine	Dopamine
Benzodiazepines & GHB	GABA
Cannabis	Anandamide
Hallucinogens & MDMA	Serotonin
Nicotine	Acetylcholine
Opioids	Endorphins
Phencyclidine & Ketamine	Glutamate*

*Drug acts as an antagonist at the NMDA subtype of the glutamate receptor.

39

In Summary

Addiction is the war between the hijacked salience and reward pathways of the basal ganglia and the executive function of the prefrontal cortex.

Motivational circuitry, the anti-reward pathways, and interoception complete the 2021 model of addiction.

Pharmacological Treatments:
agonists, antagonists, and partial agonists.

Psychosocial Treatments:
mutual help, CBT, Motivational Interviewing, and mindfulness.

Know your neurotransmitters!

40

Alcohol Use Disorder: From Neurobiology to Treatment Friday, July 22
8:45 am – 9:30 am CT

Alcohol use has impacted public health for millennia. This session will start at the beginning with a historical view of alcohol use and how that has progressed to the modern day. Participants will learn how to screen for and identify heavy drinking or alcohol use disorder. The presenter will also discuss key methods of treatment and prevention.

Learning Objective:

- After this session, learners will be able to: Describe the epidemiology of alcohol use, criteria for alcohol use disorder, and evidence-based treatment strategies.

Faculty Presenter



Ricardo Restrepo, MD, MPH, FASAM
Substance Abuse Treatment Program-
SATP/Buprenorphine Clinic Medical Director VA
Long Beach Healthcare System Associate
Clinical Professor, Psychiatry and Human Behaviour, Charles R. Drew University of Medicine and Science, Los Angeles, CA
University of California, Irvine and Riverside
Long Beach VA Healthcare System Associate
Clinical Professor at University of California, Irvine
University of California, Irvine and Riverside (UCI, UCR) and Charles Drew University, Los Angeles, CA

Dr. Restrepo finished his medical school in Medellín, Colombia. He then did his residency training in Psychiatry at Boston University Medical Center where he completed a fellowship in Addiction Psychiatry. He received an MPH in Global Public Health from NYU in 2008, while working at St Luke's/Roosevelt Hospital, where he was Director of the Addiction Psychopharmacology Clinic at the Addiction Institute of New York.

Since 2012, he works at the Long Beach VA Hospital, where he is the Medical Director of the SATP/Buprenorphine Clinic. Ricardo holds an academic position as Associate Clinical Professor of Psychiatry at the University of California (Irvine and Riverside) School of Medicine and most recently at the Charles Drew University, Los Angeles. He teaches and supervises students, psychiatry, family medicine and internal medicine residents. He serves as committee member of the American Academy of Addiction Medicine (AAAP) as well as on the California Society of Addiction Medicine (CSAM) Conference planning committee.

Ricardo's academic interests include the psychotherapy and psychopharmacology of addiction and the teaching of Psychiatry and Addiction Medicine. He is actively involved in issues related to transcultural psychiatry and behavioral addictions. He has worked with immigrant populations in the United States for over 20 years. As a volunteer for Physicians for Human Rights (PHR), he has participated in projects in the United States, Latin America and the Middle East. He has served as a United Nations Consultant since 2005.

Dr. Restrepo has written chapters on addiction and human rights textbooks. He is the co-author of textbooks on buprenorphine as well as women's health and addiction, and he cooperated with the Translation of DSM-5 to Spanish. He is board re-certified in Psychiatry and Addiction Psychiatry and a professional musician.

ALCOHOL

Ricardo Restrepo, MD, MPH

Associate Clinical Professor of Psychiatry
University of California, Irvine and Riverside
Charles Drew University, Los Angeles

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Buprenorphine Clinic Medical Director
VA Long Beach Healthcare System

1

The ASAM Review Course in Addiction Medicine
July 2022

Financial Disclosures

Ricardo Restrepo, MD, MPH
No Disclosures

2

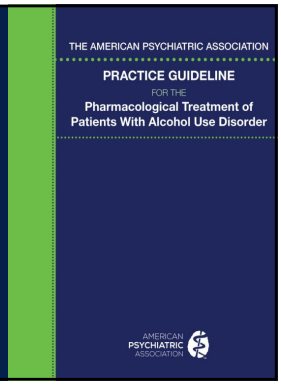
Outline

1. Historical View
2. Neurobiology
3. Epidemiology
4. SBIRT and Clinical Screening Test
5. Diagnosis
6. Biomarkers
7. Phases of Alcohol Treatment and Related Syndromes
8. CIWA-Ar and Management
9. Relapse Prevention Pharmacotherpy and Psychotherapy
10. New Directions
11. Conclusion

3

APA Practice Guideline for the Pharmacological Treatment of Patients With Alcohol Use Disorder

December 2017



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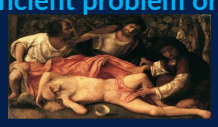
Historical View: Is Alcohol Use Disorder an ancient problem or a disease?





After the flood, Noah plants a vineyard, makes wine and gets drunk. (Genesis 9:21)

"Who hath woe? Who hath sorrow? Who is always fighting? Who is always complaining? Who hath wounds without cause? Who has bloodshot eyes?

They who tarry long at the wine; when it sparkles in the cup.

Don't let the smooth taste deceive you. For in the end it bites like a poisonous serpent. And you will say, 'They hit me, but I didn't feel it.'

Your eyes will see strange visions and you will say strange thoughts. Yet when you awaken, you seek it yet again."

(Proverbs 23:29 (~1,000 BC)

Pliny the Elder: Gaius Plinius Secundus

Naturalis Historia: "drunkeness brings pallor and sagging cheeks, sore eyes, and trembling hands that spill a full cup, of which the immediate punishment is a haunted sleep and unrestful nights…"

5

5

Case: RR

Mr RR is a 58 –year-old, Latino, married, male owner of a music theater in Los Angeles. He is being referred for evaluation to assess his drinking and depression after his older brother, who in the past had problems with alcohol, recommended him.



6

Case: RR

He presents for his evaluation thinking alcohol helps him to manage:

- Depression
- Insomnia
- Irritability and anxiety



7

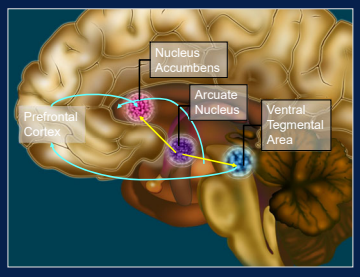
Case: RR

SA history: He reports that he grew up drinking. His first drink was at age four when he tasted the left-over alcohol from a party in his family home. He describes falling in love with the taste of wine and waited every weekend for his family to throw another party.



8

Is Alcohol Use Disorder a disease?



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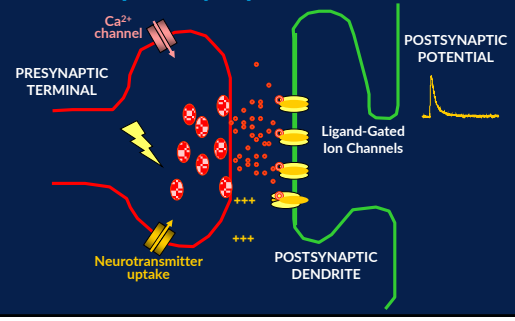
Neurotransmitter Systems

GABA	→	CNS Inhibition
Glutamate	→	CNS Excitation
Opioid	→	Euphoria
Dopamine	→	Addiction
Serotonin	→	Impulsivity
Cannabinoid	→	Pleasant Feeling

10

Steps in Synaptic Transmission



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Case: RR

Substance abuse h/x and symptoms

He then started to drink at age 12 years old on weekends and continued daily for the past 30 years. While he had difficulties quantifying the amount he consumes, he states that he rarely has "too much," although he admits occasionally missing work due to hangovers and driving while intoxicated (luckily, no accidents, no DUI).



12

Case: RR

Substance abuse h/x and symptoms

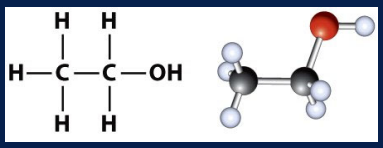
His last drink was the previous night. He explained he often has diarrhea and shakes in the morning, which he attributes to "anxiety" because these symptoms are alleviated with 1 or 2 alprazolam that has been prescribed by his PCP for the past decade.

No other drugs or substance use history.



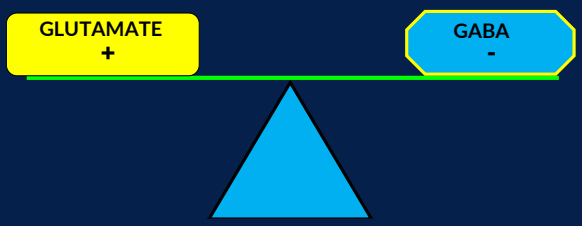
13

Alcohol (Ethanol C2 O1 H6)



14

Acute Alcohol Intake



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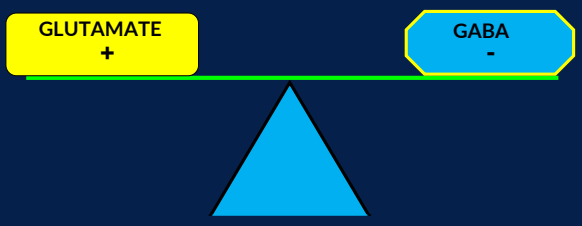
Chronic Alcohol Intake



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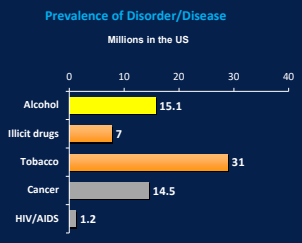
Epidemiology: Scope of Alcohol-Related Problems



- ~95,158 people die (261 per day) annually from alcohol-related causes in the U.S from 2011-2015
- Nearly 15 million adults have AUD people ages 12 and older in 2019
- 414,000 adolescents ages 12 to 17 with AUD in 2019
- 3rd leading preventable cause of death in U.S. with AUD

Sources: Esser et al, MMWR, 2020 ; Prevalence – NSDUH (2019), NCI (2014), CDC (2016); Cost – CDC (2015), National Drug Intelligence Center - National Drug Threat Assessment (2011), 2014 Surgeon General's Report, NHLBI (2012), Hutchinson et al. 2006.

17

Cost and Scope of Alcohol-Related Problems



- ~ 50% of U.S. liver disease deaths attributable to alcohol misuse
- Increase in emergency department visits and hospitalizations related to alcohol in last 10 years

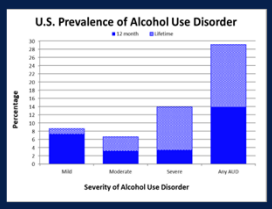
Sources: Prevalence – NSDUH (2015), NCI (2014), CDC (2016); Cost – CDC (2015), National Drug Intelligence Center - National Drug Threat Assessment (2011), 2014 Surgeon General's Report, NHLBI (2012), Hutchinson et al. 2006.

18

Epidemiology/Prevalence

Prevalence:

- Worldwide (Slade et al., 2016)
  - Lifetime 20%
  - 12 month 8.5%
  - In 2012 about 3.3 millions deaths, or 5.9 % of a global deaths, were attributable to alcohol consumption
- U.S. (Grant et al. 2015, 2017)
  - Lifetime 29%, with severe alcohol use disorder (AUD) in about half
  - 12 month 13.9 %
  - 12-month rates of AUD increased by ~50% between 2001-2002 and 2012-2013



Based on data from Grant et al. Epidemiology of DSM-5 alcohol use disorder: results from the National Epidemiologic Survey on Alcohol and Related Conditions III. JAMA Psychiatry. 2015 Aug;72(8):757-66. (Information shared by APA)

19

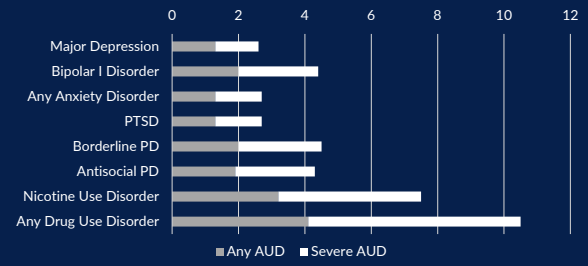
Epidemiology/Demographics

AUD affects individuals of all demographic groups (Grant et al. 2015)

- Onset: 18-29 years
- Ethnicity (12-month prevalence):
  - American Indian/Alaska Native 19.2%
  - African American 14.4%
  - White 14%
  - Hispanic 13.6%
  - Asian-American/Pacific Islander 10.6%
- Gender (12-month prevalence):
  Men 17.6%
  Women 10.4%

20

Adjusted Odds Ratios of Lifetime AUD and Other Conditions



Based on data from Grant et al. JAMA Psychiatry. Aug;72(8):757-66. 2015 (information shared by APA)

21

How much is "too much"?

HEAVY DRINKING	BINGE DRINKING
WOMEN: • 4 or more standard drinks in a sitting. • (8 or more per week.)	**WOMEN:** • 4 or more drinks on same occasion in about 2 hours
MEN: • 5 or more standard drinks in a sitting. • (15 or more per week.)	**MEN:** • 5 or more drinks in same occasion in about 2 hours

22

Prevalence of Alcohol Use Disorder:

Current, Binge, And Heavy Alcohol Use Among People 18 Or Older In The Lifetime And Past Month: 2019

- 85.6% of people ages 18 and older reported that they drank alcohol at some point in their lifetime
- 25.8% of people ages 18 and older reported that they engaged in binge drinking in the past month
- 6.3% reported that they engaged in heavy alcohol use in the past month

NIAAA National Institute on Alcohol Abuse and Alcoholism; SAMHSA NSDUH 2019.

23

COVID and Alcohol Use Disorder:

- Data from a national survey of U.S. adults on their drinking habits found that excessive drinking (such as binge drinking) increased by 21% during the COVID-19 pandemic.
- More than a dozen studies have found that 20% to 40% of individuals surveyed reported consuming more alcohol than usual during the pandemic, based on National Institute on Alcohol Abuse and Alcoholism (NIAAA) information

NIAAA National Institute on Alcohol Abuse and Alcoholism. 2021.

24

Adults are Drinking More Alcohol than a Decade Ago

A binge is defined as four drinks in two hrs for a woman and five drinks in two hrs for a man.

2002

- **65.4%** Past Year Drinking
- **21.5 %** Monthly Binge Drinking

2013

- **72.7%** Past Year Drinking
- **25.8 %** Monthly Binge Drinking

National Epidemiologic Survey on Alcohol and Related Conditions (NESARC). NESARC–III

25

Alcohol Use Is Increasing More In Women Than Men In USA

Percentage of population drinking any alcohol in past year.

Year	Women	Men
2002	59.6%	71.8%
2016	62.0%	68%

Percentage of population drinking any alcohol in past month.

Year	Women	Men
2002	44.9%	57.4%
2016	46 %	55 %

Number of days drinking any alcohol in past month.

Year	Women	Men
2002	6.8 drinks	9.9 drinks
2012	7.3 drinks	9.5 drinks

White AM. Gender Differences in the Epidemiology of Alcohol Use and Related Harms in the United States. *Alcohol Res.* 2020;40(2):01. Published 2020 Oct 29.

26

Population-based Epidemiological Surveys Show Harmful Drinking Levels On The Rise

Age is a known factor in heavy drinking.

Year	*Respondents*	*Past Year*	*Lifetime*	*Source*
1995-2002	adults	6.8% - 8.5%	13% - 23%	NESARC I, II 1997,2004
2011	adults	13.9%	29.1	NESARC III 2015
2011	18-19 years	26.7%	37%	NESARC III 2015

27

DSM-5 : Criteria for Alcohol Use Disorders

1. Use in larger amounts / longer periods than intended
2. Unsuccessful efforts to cut down
3. Excessive time spent taking drug
4. Failure to fulfill major obligations
5. Continued use despite knowledge of problems
6. Important activities given up
7. Recurrent use in physically hazardous situations
8. Continued use despite social or interpersonal problems
9. Tolerance
10. Craving

Severity:
0 to 1 CRITERIA: NO DIAGNOSIS
2 to 3 CRITERIA: MILD
4 to 5 CRITERIA: MODERATE
6 or MORE CRITERIA: SEVERE

28

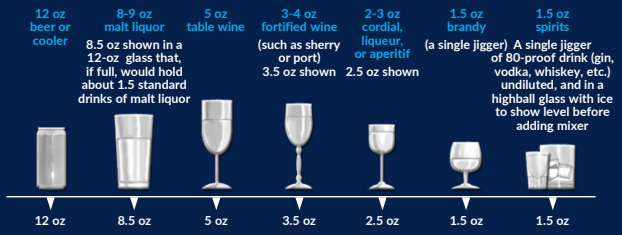
Underdiagnoses and Unmet Treatment Needs

- Physicians are often not comfortable assessing for Alcohol Use Disorders.
- Only 1 in 6 US adults report ever having asked by a clinician about their drinking behavior
- Despite high prevalence, societal cost, and available treatments, AUD remains undertreated
- <1 in 10 with a 12-month AUD diagnosis receive any treatment:
  - Self-help groups
  - Psychotherapy
  - Pharmacological treatments
- Treatment received by patients varies based on geography, insurance coverage, and formulary restrictions

29

What is a Standard Drink?

- **1 Standard Drink = 14 gr. (0.6 oz.) of pure alcohol.**
- **The average person metabolizes about 1 Standard Drink per hour.**



30

BAC

1 drink → BAC = ~15 mg% (0.015 g/dl)

BAC mg%	Clinical Manifestations
20-99	Loss of muscular coordination
100-199	Neurologic impairment with prolonged reaction time, ataxia, incoordination, and metal impairment
200-299	Vey obvious intoxication, except in those with marked tolerance. Nausea, vomiting, marked ataxia

31

BAC

BAC = ~15 mg%

BAC mg%	Clinical Manifestations
300-399	Hypothermia, severe dysarthria, amnesia, Stage I anesthesia
400-799	Onset of alcoholic coma, with precise level depending on degree of tolerance, progressive obtundation, decreases in respiration, blood pressure, and body temperature, urinary incontinence or retention, reflexes markedly decreased or absent
600-899	Often fatal because of loss of airway protective reflexes from airway obstruction by flaccid tongue, from pulmonary aspiration of gastric contents, or from respiratory arrest from profound central nervous system obstruction

32

The Rules of Twenties

- We metabolize 20 mg/dL every 60-90 minutes (zero order kinetics).
- MEN:
  Each drink adds 20 mg/dL to one's BAL.
- WOMEN:
  Each drink adds 40 mg/dL to one's BAL.

33

Women and Pregnancy

- There are three general reasons that females show higher BACs (and greater intoxication) than males if they drink the same amount of alcohol.
- Body composition: In females a greater percentage of body mass is fat compared to males
  Result – The concentration of alcohol is increased in the female bloodstream compared to the male body
- Stomach alcohol dehydrogenase (ADH): Females have very little of this enzyme compared to males
  Result – Females do not metabolize alcohol before it gets out of the stomach.
  Therefore, the blood alcohol concentration (BAC) is higher for females versus males
- Liver ADH: Females have a less active form of this enzyme than males.
  Result – Females do not metabolize alcohol as efficiently as males, thereby. Increasing the BA

34

Women and Pregnancy

Fetal Alcohol Spectrum disorders (FASD): Growth retardation, Facial malformations, Small head, Greatly reduce intelligence.

- FASD is the most commonly known preventable cause of mental impairment.
- The prevalence of FASD : 50 per 1,000 (May et al., 2009 and CDC 2016)
- 40,000 infants per year in US

35

Case: RR

Past Medical h/x: HTN for 10 years, GERD and H/x of pancreatitis.

Medications:
Lisinopril 40 mg qam,
Omeprazole 20 mg daily
Zolpidem XR 6.25 mg qhs prn for insomnia
Alprazolam 1-2 mg tid a day for anxiety.



36

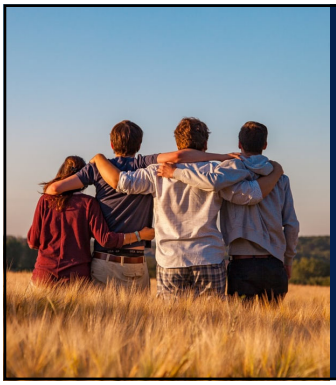
Case: RR

Vital Signs: BP:150/95
Pulse: 90x'

CBC normal with the exception of
Increased MCV equal 102 (80-96)
Electrolytes and renal function: normal
Hepatic function:
GGT 141 (10-42),
AST 60 (15-40)
ALT 40 (10-40)
AST/ALT ratio 1.5
CDT score exceeded the cutoff and so you performed a diagnostic evaluation



37



Preventing and Treating AUD

There are evidence-based interventions for preventing and treating AUD:

- Screening, Brief Intervention, and Referral to Treatment (SBIRT)
- Professionally-led behavioral interventions
- FDA-approved medications
- Mutual support groups, such as Alcoholics Anonymous

38

SBIRT

- Screening quickly assesses the severity of substance use and identifies the appropriate level of treatment.
- Brief intervention focuses on increasing insight and awareness regarding substance use and motivation toward behavioral change.
- Referral to Treatment provides those identified as needing more extensive treatment with access to specialty care.

www.niaaa.nih.gov/guide
http://www.sbirtcolorado.org/healthcare_videosandwebcasts.php

39

Screening Tools
Alcohol Screening is an Effective Prevention Strategy

The CAGE Questionnaire
- Cut Down
- Annoyed
- Guilty
- Eye-Opener

2 or more positive responses are strongly associated with alcohol dependence.

National Institute on Alcohol Abuse and Alcoholism (NIAAA): "Helping Patients Who Drink Too Much"

40

AUDIT-C Questionnaire
(Alcohol Use Disorder Identification Test)

Question	0 Points	1 Point	2 Points	3 Points	4 Points
How often did you have a drink containing alcohol in the past year?	Never	Monthly or less	2–4 times per month	2–3 times per week	4 or more times per week
On days in the past year when you drank alcohol how many drinks did you typically drink?	1–2	3–4	5–6	7–9	10 or more
How often do you have 6 or more drinks on an occasion in the past year?	Never	Less than monthly	Monthly	Weekly	Daily or almost daily

Severity

Abstinence or Low-risk Drinking	Moderate-risk Drinking	High-risk Drinking	Severe-risk Drinking	
AUDIT-C = 0–3	AUDIT-C = 4–5	AUDIT-C = 6–7	AUDIT-C = 8–9	AUDIT-C = 10–12
Health promotion	Brief intervention	Brief intervention +/- Pharmacotherapy +/- Psychosocial interventions	Pharmacotherapy +/- Psychosocial interventions +/- Specialty care management	Specialty care management

41

The Role of Biomarkers in the Treatment of ETOH

- Provide objective outcome measures in alcohol research or evaluating an alcohol treatment program.
- Screen for individuals unable/unwilling to accurately report drinking behavior (e.g., fear, embarrassment, or adverse consequences).
- Evidence of abstinence in individuals prohibited from drinking.
- Enhance patient motivation to stop/reduce drinking.
- Diagnosis tool by assessing contribution of alcohol to the disease.
- Identify relapse early.
- Fear of detection by biomarkers may dissuade drinking.

42

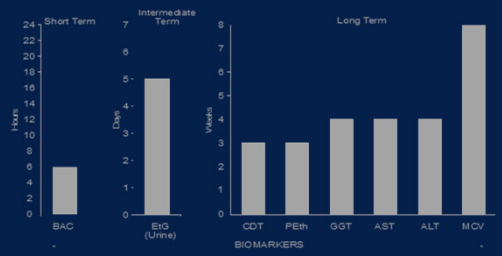
Types of ETOH Biomarkers

- INDIRECT TESTS
- Manifestations of organ damage often due to drinking
  - gamma glutamyltransferase (GGT)
  - aspartate amino transferase (AST, SGOT)
  - alanine amino transferase (ALT, SGPT)
  - macrocytic volume (MCV)
- Reflections of alcohol's effects on other metabolic processes -
  - carbohydrate-deficient transferrin (CDT) - Only FDA Approved alcohol biomarker

- DIRECT TESTS
- Reflections of alcohol use
  - ethyl glucuronide (EtG) and ethyl Sulfate (EtS)
  - Phosphatidylethanol (PEth)

43

Window of Assessment for Various Alcohol Biomarkers



SAMHSA (Substance Abuse and Mental Health Services Administration) The Role of Biomarkers in the treatment of alcohol use disorders, 2012 Revision

44

44

Characteristics of Assessment for Various Alcohol Biomarkers

Marker	*Time to Return to Normal with Abstinence*	*Level of Drinking*	*Comments*	*Blood test normal range*
GGT	2-4 weeks of abstinence	~ 5 drinks (>60g/day) for several weeks	Many sources of false positives—liver disease, diabetes, smoking, obesity, age, anticonvulsants, etc.	W: 0-45 U/L M: 0-53 U/L
SGOT/AST	2-4 weeks of abstinence	Unknown but heavy	Many sources of false positives (see GGT) in addition to excessive coffee consumption	10 - 34 U/L
SGPT/ALT	2-4 weeks of abstinence	Unknown but heavy	Many sources of false positives (see GGT) Less sensitive than AST	8-37 U/L
MCV	Up to several months	Unknown but heavy	Slow return to normal limits even with abstinence renders it a poor independent indicator of relapse. More specific than GGT. Unlike other markers, no strong gender effect	80-100fL
CDT	2-4 weeks	~ 5 drinks(>60g/day) for 2 weeks	Few sources of false positives. Good marker of relapse	<60 mg/L

45

45

Diagnostic Sensitivity and Specificity of Biomarkers

	Sensitivity (%)	Specificity (%)
CDT	69	92
CDT/transferrin	65	93
GGT	73	75
AST	50	82
ALT	35	86
MCV	52	85

Bell, et al. Alcoholism: Clinical and Experimental Research 1994

46

Case: RR

- His last drink was the previous night. He explained he often has insomnia, diarrhea, palpitations, and shakes in the morning, which he attributes to "anxiety" because these symptoms are alleviated with 1 or 2 alprazolam that has been prescribed by his PCP for the past decade.



47

Phases of Alcoholism Treatment

Detoxification:
- Primary goal is to achieve an alcohol-free state
- Wide spectrum of severity
- Drug-specific syndromes: opiates, cocaine, alcohol, benzodiazepines

Relaspe Prevention:
- Primary goal is to maintain an alcohol-free state
- Chronic Treatment

48

Introduction Alcohol Withdrawal

- Epidemiology
- Neurobiology
  - Neurotoxicity
  - Kindling
- Management of Alcohol Withdrawal
  - Benzodiazepines
  - Anticonvulsants
- Real World Implications
  - Outpatient vs. Inpatient
  - Evaluation and Management

49

Epidemiology of Alcohol Withdrawal

- Not well studied
- Significant symptoms occur in 13% to 71% of individuals presenting for detoxification
- Up to 10% of individuals undergoing alcohol withdrawal require inpatient medical treatment
- Estimated mortality up to 2%

Saitz R, Mayo-Smith MF, Roberts MS, Redmond HA, Bernard, DR, Calkins DR. JAMA. 1994;272:519-523.

50

Alcohol Withdrawal and Kindling

- Repeated episodes of alcohol withdrawal likely to worsen
- Exacerbation of symptoms may be due to a kindling process
- Positive relationship of alcohol withdrawal seizures to repeated detoxification

51

Managing Alcohol Withdrawal

- **Principles of treatment**
  - Alleviate symptoms
  - Prevent progression of symptoms
  - Treat underlying comorbidities

52

Alcohol Withdrawal Treatment

- Substitute cross-dependent drug (benzodiazepine)
- Gradually withdraw substitute drug
- Supplement vitamins and minerals
  - Thiamine
  - Folic acid
  - Multivitamin
- Supportive treatment
  - Decrease stimulation, increase fluid and caloric intake

53

Alcohol Withdrawal Treatment

Thiamine Deficiency

- **Thiamine**
  - Important cofactor for several enzymatic reactions
  - Cerebral glucose utilization
  - Glutamate elimination
- **Wernicke's Encephalopathy**
  - Partial to complete paralysis of extra ocular muscles
  - Nystagmus
  - Ataxia
  - Mental disturbances
  - Mortality: 10-20% if untreated
  - Treatment: Thiamine replacement PRIOR dextrose administration
- **Korsakoff's Psychosis**
  - Antegrade amnesia
  - Confabulations

54

States of AWS

1. **Autonomic Hyperactivity**
2. **Hallucinations**
3. **Neuronal excitation**
4. **Delirium Tremens**

There is not necessarily a linear progression.

55

States of AWS

Autonomic Hyperactivity

- Clear Sensorium
- Tremulous
- Diaphoresis
- Anxiety
- Nausea/Vomiting
- Increase cathecolamines in urine, serum and CSF
- Start 6 hrs after last drink Peak 24-48 hrs

Hallucinations

- Most common= VISUAL

Neuronal excitation

- Seizures (Generalized Tonic – Clonic)
- Up to 10%
- Most common in first 12 - 48 hours after last drink

56

States of AWS

DELIRIUM TREMENS (DTs)

- Most often occur within 72 hours after the last drink
- Delirium with Tremor
- Autonomic hyperactivity
- Hallucinations
- Electrolyte abnormalities
- Dehydration
- Hemodynamic instability
- Mortality up to 15%
  Cardiovascular/respiratory collapse

57

CIWA-Ar

(Clinical Institute Withdrawal Assessment of Alcohol, Revised)

- It requires under two minutes to administer
- It requires no medical knowledge
- It provides you with a quantitative score that predicts the severity of withdrawal from alcohol

58

Assessment of Alcohol Withdrawal CIWA-Ar

1. Nausea/Vomiting: 0-7
   - 0 – none
   - 7 – constant nausea and frequently dry heaves and vomiting
2. Tremors: 0-7
   Have patient extend arms & spread fingers.
   - 0 – none
   - 7 – severe, even with arms not extended
3. Anxiety: 0-7
   - 0 – no anxiety, patient at ease
   - 7 - equivalent to acute panic states seen in severe delirium or acute schizophrenic reactions
4. Agitation: 0-7
   - 0 – normal activity
   - 7 – paces back and forth, or thrashes about

59

Assessment of Alcohol Withdrawal CIWA-Ar

5. Paroxysmal Sweats: 0-7
   - 0 – no sweats
   - 7- drenching sweats
6. Orientation and Clouding of Sensorium:0-4
   Ask, "What day is this? Where are you? Who am I?"
   - 0 - Oriented
   - 4 - Disoriented to place and/or person
7. Tactile Disturbance: 0-7
   Ask, "Have you experienced any itching, pins & needles sensation, burning or numbness, or a feeling of bugs crawling on or under your skin?"
   - 0 – none
   - 7 – continuous hallucination

60

Assessment of Alcohol Withdrawal CIWA-Ar

8. Auditory Disturbances: 0-7
   Ask, "Are you more aware of sounds around you? Are they harsh? Do they startle you? Do you hear anything that disturbs you or that you know isn't there?"

9. Visual Disturbances: 0-7
   Ask, "Does the light appear to be too bright? Is its color different than normal? Does it hurt your eyes? Are you seeing anything that disturbs you or that you know isn't there?"

10. Headache: 0-7
    Ask, "Does your head feel different than usual? Does it feel like there is a band around your head?" Do not rate dizziness or lightheadedness.

61

CIWA-Ar Determining Need of Pharmacotherapy

- <8: Minimal – Mild AW, Drug therapy not necessarily indicated
- 8-15: Moderate AW, Drug therapy indicated.
- >15: Severe, Drug therapy absolutely indicated, consider inpatient treatment

http://www.chce.research.va.gov/apps/PAWS/quiz/q1.html

62

Mechanisms Underlying Alcohol Withdrawal

- Multiple neuroadaptive changes in CNS
  - Decreased GABA activity
  - Increased glutamate activity
  - Upregulated calcium channel activity
  - Increased noradrenergic activity
- Alcohol withdrawal is associated with increased CNS activity

CNS=central nervous system; GABA=gamma-aminobutyric acid.
Anton RF, Becker HC, eds. Pharmacotherapy and pathophysiology of alcohol withdrawal. (*Handbook of Experimental Pharmacology*.) 1995.

63

Case: RR

You apply your knowledge and training through Motivational Interviewing. Your open–ended questions and affirmations reviewed with patient's possibilities set the bases for a good rapport with Mr. RR. As part of the treatment dialogue, you showed Mr. RR. his BP elevation 150/90, CIWA:8, and his scores on the CDT , GGT and AST/ALT. You noted that the values were outside the reference ranges for the tests.



64

Case: RR

You then explained, in a direct, yet empathetic manner, the significance of the scores and noted that GGT and AST/ALT levels this high can reflect liver damage and that CDT levels this high usually reflect heavy drinking. Mr. RR then agrees to start an outpatient alcohol treatment program.



65

Treatment Plan

There are several evidence-based options for non-pharmacological treatment that have minimal harms:

- **Motivational Enhancement Therapy (MET):** manualized psychotherapy based on the principles of motivational interviewing; shown to have a small to medium effect size on achieving abstinence
- **Cognitive Behavioral Therapy (CBT):** focusing on the relationships between thoughts, feelings, and behaviors; help manage urges and triggers

66

Treatment Plan

There are several evidence-based options for non-pharmacological treatment that have minimal harms:

- **Medical Management (MM):** manualized treatment that provides education and strategies to support abstinence and promote medication adherence
- **Community based peer support groups** such as Alcoholics Anonymous (AA) and other 12-step programs: helpful in achieving long-term remission but not for replacing formal medical treatment

67

Alcohol Detoxification Use of Benzodiazepines

- **First line agent (gold standard)**
- **Loss of inhibition/sedation due to lack of ETOH**
- **Treatment: Replace the GABA activation (inhibition)**
- **Benzodiazepines:**
  - If hepatic impairment: oxazepam or lorazepam
  - Provide dosing for 24-hour intervals – patient must be re-evaluated before more is provided
    - Vital Signs
    - CIWA-Ar

68

Benzodiazepines Options

- **Chlordiazepoxide** - *Only available in oral form (PO)*
  - Longer half life than most benzos
  - (5-30 hrs)
- **Diazepam**
  - Lipophilic ➡ rapid onset of action
- **Lorazapem**



Available in oral form (PO) and IV
Half life (12-18 hrs)

- Simple metabolism of hepatic glucuronidation (*no active metabolite*)
- Ideal for patients with cirrhosis/liver damage and elderly population

69

Indications For Outpatient Withdrawal Treatment

- CIWA <8 or some with CIWA 8 –15
- No hx. of AW seizures/delirium
- No serious medical/surgical problems
- No serious psychiatric/drug hx
- Social support
- Supervision/housing available

70

Indications For Inpatient Withdrawal Treatment

- History of DTs or withdrawal seizures
- Alcohol withdrawal severity (CIWA>10) + other criteria
- Pregnancy
- Major medical/surgical problems
- Inability to tolerate oral medication
- Imminent risk to harm himself and/or others
- Active psychosis or cognitive impairment
- Recurrent unsuccessful attempts at ambulatory detoxification

71

Treatment of Mild-Moderate Alcohol Withdrawal CIWA-Ar- 8 to 14

- Long-acting Benzodiazepines:
  - Chlordiazepoxide (Librium) 50-100 mg po q 6-8 hrs.
  - Diazepam (Valium) 10-20 mg po q 6-8 hrs.
- Short-acting Benzodiazepines:
  - Lorazepam (Ativan) 2-4 mg po q 1-4 hrs.

72

Treatment of Severe Alcohol Withdrawal CIWA-Ar > 15

- Diazepam 10 mg IV
  - Repeat 5 mg IV q 5 min until calm
- Lorazepam 4 mg po q 1 hr, PRN
  - Moderate to severe liver disease
  - Elderly or confused patients
  - Very ill or debilitated patients

  Can be given po, iv or im

73

Alcohol Detoxification
Use of Anticonvulsants

Anticonvulsants reduce GABA activity.

- CBZ: Reduced rebound withdrawal & post-detox drinking (Malcolm, 2002)
- Gabapentin normalizes alcohol-induced effects on GABA and glutamate; has no hepatic metabolism
- Gabapentin more effective than lorazepam in reducing post-detox drinking (Myrick, 2009)
- Gabapentin, divalproex & vigabatrin may prove useful
- Caution: CBZ & divalproex have limited use in patients with severe hepatic or hematologic disease

74

Alcohol Detoxification
Anticonvulsants Effectiveness and Limitations

Advantages	*Disadvantages*
• No abuse liability • Cognition • Neuroprotective • Protracted Withdrawal	• Limited clinical experience • Hematological side effects • Liver toxicity

75

When to Consider Pharmacotherapy

- Anti-craving Medication as the new standard of care
  - Consider immediately post-detoxification for ALL patients with alcohol use disorder
  - Efficacy requires counseling and/or frequent physician monitoring
- Most FDA approved medications for SUDs can be used in outpatient settings
- Exception: Methadone maintenance therapy: can only be used for treatment of opioid addiction in licensed opioid treatment programs

76

Pharmacogenetics in AUD treatment

Medication	Genetic Variant	Outcome Moderated	Notable Studies
Topiramate	*GRIK1* (rs2832407)	Heavy drinking days (%); side effects	Kranzler et al., 2014 (2); Ray et al., 2009 (4)
Naltrexone	*OPRM1* (Asn40Asp), (rs1799971), DRD4 VNTR	Heavy drinking days (%); abstinence rates; relapse to heavy drinking	Anton et al., 2008 (12); Kim et al., 2009 (13); Oslin et al., 2003 (14); Tidey et al., 2008 (15)
Ondansetron	LL/LS/SS (5-HTTLPR) (rs1042173), *SLC6A4* (5-HTTLPR)	Drinks per drinking day; days abstinent (%)	Johnson et al., 2011 (9)
Sertraline	5-HTTLPR triallelic *SLC6A4*	Heavy drinking days (%); drinking days (%)	Kranzler et al., 2011 (8)
Acamprosate	*GATA4* (rs1327367)	Relapse	Kiefer et al., 2011 (10)
Disulfiram	*DBH* (rs1611115)	Adverse events	Mutschler et al., 2012 (11)

Note: OPRM 1 predictive value for NTX response has not been supported (Schacht, J., Randall, P., Latham, P. *et al* 2017)

Batki & Pennington (2014) Am J Psychiatry
Hartwell and Kranzler (2019)Expert Opinion on Drug Metabolism & Toxicology

77

Alcohol Use Disorder
(Relapse Prevention) FDA Approved

- Naltrexone (Revia): 1994
- Long Acting Naltrexone IM (Vivitrol): 2006

  → ↓ Binge drinking
- Acamprosate (Campral): 2004 → Maintain abstinence
- Disulfiram (Antabuse): 1949 → With supervision improve treatment adherence
- *Nalmefene (2016) * European Medicines Agency (EMA) **

  → ↓ heavy drinking days

78

Alcohol Use Disorder (Relapse Prevention) FDA Approved

- Naltrexone (Revia): 1994
- Long-acting Naltrexone IM (Vivitrol): 2006 → Binge drinking
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- *Nalmefene (2016) * European Medicines Agency (EMA) **

heavy drinking days

79

Neurochemical Targets for AUD

Phenomenon	Neurochemistry	Pharmacotherapy
Reward	Opioids Glutamate 5-HT3 Nicotinic cholinergic	**Naltrexone*** **Acamprosate*** Topitamate, Ondasetron, Varenicline
Protracted withdrawal/dysphoria /anxiety	Glutamate GABA	**Acamprosate** * Topiramate, Gabapentin, Baclofen
Impulsivity	Glutamate Opioids DA	Topiramate? Naltrexone?

80

Pharmacotherapy of Alcohol Use Disorder: Naltrexone-oral/Mechanism of Action

- **Reduces positive reinforcement (reward craving)**
  - Potent inhibitor at mu opioid receptors
- **Modulates the mesolimbic dopamine system in the VTA & projections to the nucleus accumbens**
- There is mixed evidence around markers that predict a favorable response to naltrexone treatment, such as:
  - - Male sex
  - - A positive family history of alcoholism
  - - High levels of craving,
  - - Polymorphism (asp variant) of the opioid receptor gene *OPRM1?*

81

Pharmacotherapy of Alcohol Use Disorder: Naltrexone-oral/Mechanism of Action

- **The patient does not experience the full euphorogenic/reinforcing effect of alcohol.**
  - suppresses/reduces endogenous opioids (beta-endorphin) involved in the reinforcing (pleasurable) and subsequent reduces DA in NAc effects of alcohol and possibly craving
- **Prevents a slip from becoming a full-blown relapse**

82

Pharmacotherapy of Alcohol Use Disorder: Naltrexone-oral / Effectiveness

- Effective in reducing relapse to heavy drinking.
- A meta-analysis of 27 randomized controlled trials found a 36% reduction in the rate of relapse to heavy drinking.
- Medication compliance may be a limiting factor in oral treatment.
- HEAVY DRINKING = 5 or more drinks/day for a man - 4 or more drinks/day for a woman.

Srisurapanont M, Jarusuraisin N. *Cochrane Database Syst Rev* 2005;(1):CD001867.

83

Pharmacotherapy of Alcohol Use Disorder: Naltrexone-oral / Dosing and Safety

- Oral Naltrexone Hydrochloride
- FDA approved dose: 50 mg per day
- Antagonist of mu , delta and kappa opioid receptors.
- Antagonizes opioid-containing agents, but no other significant drug-drug interactions.
- Some have used 100 mg daily with rationale that naltrexone has been effective for heroin addiction at doses of 100mg-100mg-150 mg q Monday, Wednesday, and Friday; an effective plasma concentration can be obtained even if some doses are missed

84

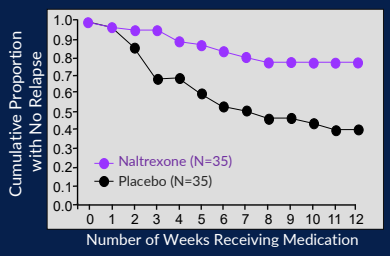
Pharmacotherapy of Alcohol Use Disorder: Naltrexone-oral / Dosing and Safety

- **Side effects**
  - GI: abdominal pain, diarrhea, decreased appetite, nausea
  - Sedation: daytime sleepiness, fatigue, insomnia, headache
- Reversible hepatoxicity
  - LFT's should be monitored closely
- **Works best with complaint patients**
  - Requires counseling (CBT) or frequent MD monitoring visits (Project Combine, 2006)
  - Efficacy questioned in women (O'Malley, 2007)

Physician's Desk Reference (www.PDR.net) and *Epocrates*. Accessed on March 1, 2018.

85

Naltrexone-Oral in the Treatment of Alcohol Use Disorder



Volpicelli et al., Arch Gen Psychiatry, 1992

86

Pharmacotherapy of Alcohol Use Disorder: Long-Acting Naltrexone (IM)

- Extended-Release - Injectable Naltrexone
  - 1 injection per month/ 380 mg
  - 100 µm diameter microspheres of naltrexone and polymeric matrix.
- Advantages: once a month injection can be done in clinician's office
  - Better adherence with once monthly dosing
  - More stable plasma concentrations compared to the oral formulation

Garbutt et al. *JAMA*. 2005;293:1617-1625. *Physician's Desk Reference* (www.PDR.net) and *Epocrates*. Accessed on September 1, 2012.

87

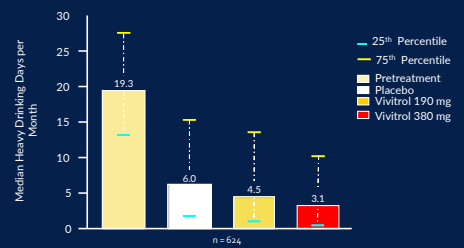
Pharmacotherapy of Alcohol Use Disorder: Long-Acting Naltrexone (IM) Dosing and Safety

- Extended-Release Injectable Naltrexone
  - Side effects: nausea & headaches; more sedation than with the oral formulation
  - LFT's should be monitored closely
  - Injection site reactions possible
  - Best results in patients sober 1 week prior to starting the medication
  - Efficacy shown in more severe alcoholics
  - Reduction in heavy-drinking days (48.9% vs 30.9% on placebo)

Pettinati HM, Alcohol Clin Exp Res, May 2011

88

Naltrexone-injectable in the Treatment of Alcohol Use Disorder Results: Heavy Drinking Days



Garbutt et al., 2005

89

Protracted Withdrawal Symptom

- Sleep dysregulation
- Irritability
- Mood instability
- Anxiety

90

Pharmacotherapy of Alcohol Use Disorder: Acamprosate/ Mechanism of Action

- **Stabilizes glutamatergic neurotransmission altered during withdrawal** (Littleton 1995).
- **Chronic ETOH exposure alters GABA & NMDA systems**
  - Restores balance between inhibitory & excitatory neurotransmission
- **Anticraving, reduced protracted withdrawal**
- **Reduce negative reinforcement (abstinence craving)**
- **No abuse liability, hypnotic, muscle relaxant, or anxiolytic properties**

91

91

Pharmacotherapy of Alcohol Use Disorder: Acamprosate/ Effectiveness

- Effective in improving abstinence.
- The Kranzler and Gage (2008) re-analysis of the European data found that ~20% of patients treated with acamprosate were abstinent after a year of treatment (vs ~10% for placebo).
- The US trial showed efficacy only in patients motivated for abstinence.

Kranzler HR, Gage A. Am J Addict. 2008;17:70-76. Mason BJ et al. *J Psychiatr Res.* 2006;40:383-93.

92

92

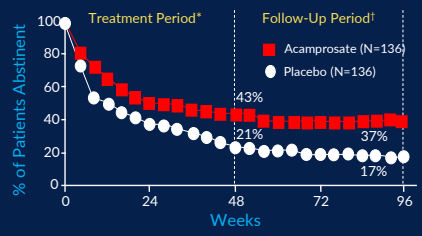
Pharmacotherapy of Alcohol Use Disorder: Acamprosate/Dosing and Safety

- 666 mg three times a day (2000 mg daily)
- Excreted by the kidneys; no liver metabolism
  - Contraindicated: significant renal disease with creat cl <30ml/min or those who are pregnant
- Mild diarrhea (16% acamprosate vs. 10% placebo)
- Recommendation: patients with hepatic disease or those treated with opioids. Advantage when a patient is taking multiple medications
- No drug-drug interactions.

93

93

Acamprosate in the Treatment of Alcohol Use Disorder



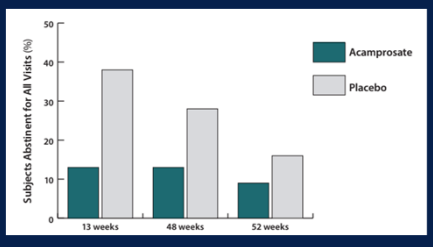
*p=0.001; †p=0.003

Sass et al., *Arch Gen Psychiatry*, 1996

94

94

Acamprosate in the Treatment of Alcohol Use Disorder



Kranzler HR, Gage A. Acamprosate efficacy in alcohol-dependent patients: summary of results from three pivotal trials. Am J Addict. 2008;17(1):70–6.

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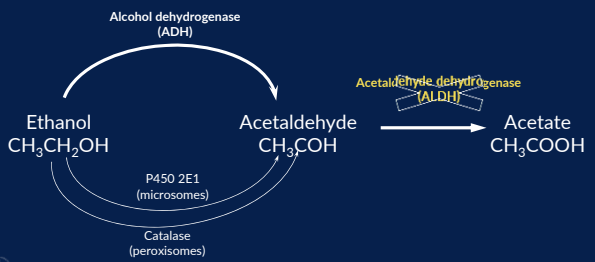
Pharmacotherapy of Alcohol Use Disorder: Disulfiram Mechanism of Action



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Pharmacotherapy of Alcohol Use Disorder: Disulfiram/ Mechanism of Action

- Alcohol → Acetaldehyde → Acetate
- Disulfiram irreversibly binds to acetaldehyde dehydrogenase inhibiting the metabolism of acetaldehyde to acetate.
- Acetaldehyde accumulates resulting in a very unpleasant reaction (tachycardia, headache, nausea, vomiting, flushing).

97

97

Pharmacotherapy of Alcohol Use Disorder: Disulfiram Effectiveness

- Second Line Treatment
- In a meta-analysis of 22 studies was associated with:
  - Sustained abstinent compared to control conditions only in open-label studies
- Double-blind, placebo-control study design is not helpful as both the medication and the placebo pills may (or may not) result in fear of drinking.
- Most studies are negative, but disulfiram may be helpful for a better response than control conditions when medication adherence was *supervised*

Diehl et al. *Alcohol Alcohol.* 2010;45:271-277. Fuller RK et al. *JAMA.* 1986;256:1449-55.
Kranzler HR, Soyka M. Diagnosis and Pharmacotherapy of Alcohol Use Disorder: A Review. *JAMA.* 2018;320(8):815–824

98

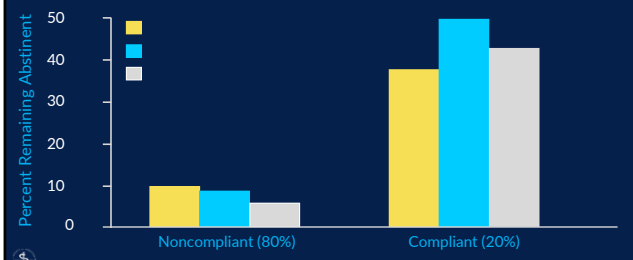
Pharmacotherapy of Alcohol Use Disorder: Disulfiram Dosing and Safety

- **250-500 mg daily.**
- First dose 12 hours after the last drink;
- 500mg PO each morning for 1-2 weeks, then 250mg PO each morning
- **Some liver toxicity; monitor LFTs. Caution with CAD. Contraindicated: psychosis, significant liver disease, esophageal varices, pregnancy, impulsivity** (Barth et al., 2010)
- **Inhibits hepatic microsomal enzymes and increases drug levels (phenytoin, warfarin, isoniazid, metronidazole, TCA and benzodiazepines among others)**
- **SIDE EFFECTS: skin/acneiform eruptions, drowsiness, headache, metallic taste, decreased libido/potency**

Physician's Desk Reference (www.PDR.net) and *Epocrates*. Accessed on March 1, 2018.

99

Disulfiram in the Treatment of Alcohol Dependence
Disulfiram and Abstinence Rates (VA Cooperative Study)



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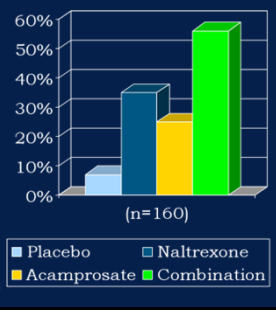
Combinations

- **Naltrexone and acamprosate have different mechanisms of action and may work synergistically on cravings:**
  - **Naltrexone on positive reinforcement**
  - **Acamprosate on negative reinforcement**
- **Medications and psychotherapy.**

Rosner S et al. *J Psychopharmacol.* 2008;22:11-23.

101

Naltrexone/Acamprosate



- Abstinence rates during a 12-week trial with:
  - Naltrexone 50 mg QD,
  - Acamprosate 666 mg TID.
- The **combination** of the two medications helped alcoholics stay abstinent (*P*=0.002) better than each drug alone.

Adapted from Kiefer F et al. Arch Gen Psychiatry. 2003;60:96.

102

Project MATCH

- Compared outcome efficacy for patients matched to treatments based on a prior hypotheses about 11 client attributes.
- Treatment was for 12 weeks; follow-ups continued for years.
- 12-Step programs, CBT and MET were compared.
- Each of the three methods helped in the treatment of alcoholism.
  - However, outpatients who received TSF were more likely to remain abstinent after 1 year following treatment.
- There were a few matching effects, and they were weak.

103

103

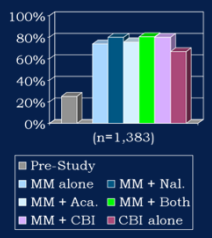
The COMBINE Study

- 1383 patients with alcohol dependence randomized to varying combinations of oral Naltrexone, Acamprosate, combined behavioral intervention (CBI) and medical management (MM)
- Patients received naltrexone, acamprosate, both, or neither
- Half of patients received psychotherapy in addition to medical management
- One patient cohort received psychotherapy alone, no pills

JAMA. 2006;295:2003-2017

104

The COMBINE Study



- Percentage of abstinent days per month during a 16-week treatment trial with:
  - Naltrexone 100 mg QD,
  - Acamprosate 1 g TID.
- All treatment groups had an increase in % days abstinent. Overall effect was from 25% to 73%.

105

The NIAAA COMBINE Study Results

- For patients receiving MM, naltrexone, or CBI therapy, improved outcomes over placebo plus MM
  - Naltrexone + MM had the best outcome
- Acamprosate did not add benefit to naltrexone or CBI, and was no more effective than placebo plus MM
- Taking tablets and seeing a health care professional was more effective than receiving CBI alone (possible placebo effect)
- One-year outcome: no significant differences among the groups

Anton et al. JAMA. 2006;295:2003-2017.

106

Other Pharmacological Agents

- **Anticonvulsants**
  - **Topiramate**
  - **Gabapentin**
  - **Carbamazepine**
  - **Valproic Acid**
- **GABA agonist**
  - **Baclofen**
- **Alpha1 adrenergic blocker**
  - **Doxazosin**
- **Alpha 2 agonists**
  - **Clonidine**
- **Serotonin (5-HT_3) antagonists**
  - **Ondansetron**
  - **Mirtazapine**
- **Selective Serotonin Reuptake Inhibitors**
- **Partial agonist for the α4β2 nicotinic acetylcholine receptor subtype (nACH)**
  - **Varenicline**

- Mu and delta opioid antagonist and partial kappa agonist
  - **Nalmefene**

107

107

Conclusions

- Identify the need of your patients to get treatment
- Substance use disorders are chronic, be ready for relapses
- Prevention is based on screening and early Intervention
- CIWA-Ar is your best ally for AWS
- AWS=BZD most effective, safest and cheapest treatment
- Medications for Alcohol Use Disorder are relatively safe but modestly effective
- Naltrexone is best for "cutting down."
- Acamprosate is best for preventing "the first drink."
- Pharmacotherapy and psychotherapy modalities can be offered by you
- Pharmacotherapy and psychotherapy modalities are effective and scientifically based approaches

108

108

Sedative Use Disorder: Key Concepts for Treatment Friday, July 22
9:30 am – 10:15 am CT

Sedatives are one of the most frequently prescribed and frequently misused substances. This session will review the pharmacokinetics of sedatives and growing prevalence of sedative use. The presenter will discuss the risks and benefits of sedative use including the concerns around related syndromes and polysubstance use. Participants will also learn treatment strategies for sedative withdrawal.

Learning Objective:

- After this session, learners will be able to: Describe the neurobiological impacts of sedatives, criteria for sedatives use disorder, and evidence-based treatment strategies.

Faculty Presenter



Ricardo Restrepo, MD, MPH, FASAM
Substance Abuse Treatment Program-
SATP/Buprenorphine Clinic Medical Director VA
Long Beach Healthcare System Associate
Clinical Professor, Psychiatry and Human Behaviour, Charles R. Drew University of Medicine and Science, Los Angeles, CA
University of California, Irvine and Riverside
Long Beach VA Healthcare System Associate
Clinical Professor at University of California, Irvine
University of California, Irvine and Riverside (UCI, UCR) and Charles Drew University, Los Angeles, CA

Dr. Restrepo finished his medical school in Medellín, Colombia. He then did his residency training in Psychiatry at Boston University Medical Center where he completed a fellowship in Addiction Psychiatry. He received an MPH in Global Public Health from NYU in 2008, while working at St Luke's/Roosevelt Hospital, where he was Director of the Addiction Psychopharmacology Clinic at the Addiction Institute of New York.

Since 2012, he works at the Long Beach VA Hospital, where he is the Medical Director of the SATP/Buprenorphine Clinic. Ricardo holds an academic position as Associate Clinical Professor of Psychiatry at the University of California (Irvine and Riverside) School of Medicine and most recently at the Charles Drew University, Los Angeles. He teaches and supervises students, psychiatry, family medicine and internal medicine residents. He serves as committee member of the American Academy of Addiction Medicine (AAAP) as well as on the California Society of Addiction Medicine (CSAM) Conference planning committee.

Ricardo's academic interests include the psychotherapy and psychopharmacology of addiction and the teaching of Psychiatry and Addiction Medicine. He is actively involved in issues related to transcultural psychiatry and behavioral addictions. He has worked with immigrant populations in the United States for over 20 years. As a volunteer for Physicians for Human Rights (PHR), he has participated in projects in the United States, Latin America and the Middle East. He has served as a United Nations Consultant since 2005.

Dr. Restrepo has written chapters on addiction and human rights textbooks. He is the co-author of textbooks on buprenorphine as well as women's health and addiction, and he cooperated with the Translation of DSM-5 to Spanish. He is board re-certified in Psychiatry and Addiction Psychiatry and a professional musician.

SEDATIVES

Ricardo Restrepo, MD, MPH

Associate Clinical Professor of Psychiatry
University of California, Irvine and Riverside
Charles Drew University, Los Angeles

Substance Abuse Treatment Program-SATP
Buprenorphine Clinic Medical Director
VA Long Beach Healthcare System

1

The ASAM Review Course in Addiction Medicine

July 2022

Financial Disclosures

Ricardo Restrepo, MD, MPH

No Disclosures

2

Outline

1. Historical View
2. Neurobiology
3. Epidemiology
4. Risk and Benefits of Benzodiazepines
5. Phases of Sedative-Hypnotic Treatment and related Syndromes
6. Selective nonbenzodiazepine hypnotic agents
7. Barbiturates
8. GHB
9. Conclusions

3

Historical View

- First half of XX century Barbiturates (starting with Barbital)
- 1950 Meprobomate
- 1950s Benzodiazepine were introduced as substitute for barbiturates (starting with Chlordiazepoxide)
- 1960s Benzodiazepines widely available and prescribed
- 1970s Benzodiazepines became the most commonly prescribed of all medications around the world

4

Historical View

- 1980s Identification of medication losing efficacy over time and became associated with adverse effects
- 1990s Short acting benzodiazepines
- 2000s (drug tolerance and withdrawal) Not sufficient for dependence and nonbenzodiazepine hypnotic agents; elderly population risks
- 2014-present DSM 5 (sedative use disorder); guidelines adopted regarding use

5

Types of Sedatives

- BZ- receptor agonist (BZRA)
  - Benzodiazepines
  - Selective non-benzodiazepine hypnotics (Z-drugs)
- Barbiturates
- Others: GHB and Paraldehyde, chloral hydrate, meprobomate

6



7

Case: RR

A year later, Mr. RR, 59-year-old Latino male with a past history of ETOH use disorder, anxiety, insomnia, and past medical history of HTN, GERD, and pancreatitis, arrives in the emergency department with a friend for confusion and diaphoresis.



8

Neurobiology ($GABA_A$ Receptor)

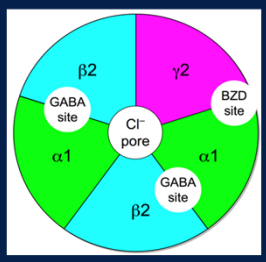
- GABA - the primary inhibitory neurotransmitter system in the CNS
- Transmembrane pentamer composed of:

  2α , 2β

  1γ

9

Neurobiology ($GABA_A$ Receptor)



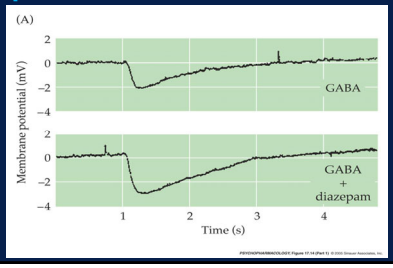
10

Neurobiology ($GABA_A$ Receptor)

- GABA is estimated to be present in 40% of all synapses in the human brain
- It is an inhibitory neurotransmitter opposed to excitatory neurotransmitters such as glutamate.
- It reduces the excitability of the post synaptic side of the synapse
- 2 types : $GABA_A$ ionotropic (prominent target for drugs) and $GABA_B$ metabotropic
- BZDs increase the number of time the Cl- channel opens (frequency)
- BBTs increase the duration of the opening of the Cl-channel

11

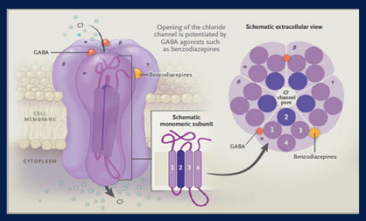
Effects of GABA and diazepam (benzodiazepine) on membrane potentials and chloride flux



12

Neurobiology ($GABA_A$ Receptor)

Benzodiazepines require the presence of GABA
Barbiturates do not require the presence of GABA
Flumazenil blocks effects of benzodiazepine and zolpidem but not Barbiturates



Soyka, N Engl J Med 2017; 376:1147-1157

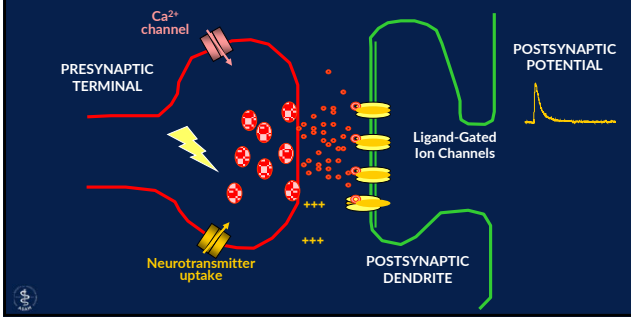
13

Neurobiology ($GABA_A$ Receptor)

- Benzodiazepines
  - Bind a cleft of α and γ subunits
  - Increase the affinity of the receptor for GABA (frequency) : Chloride channel opening
  - BZD needs GABA
- Barbiturates (propofol):
  - Bind α subunit
  - Increase duration of channel opening
  - BBT does need GABA

14

Steps in Synaptic Transmission



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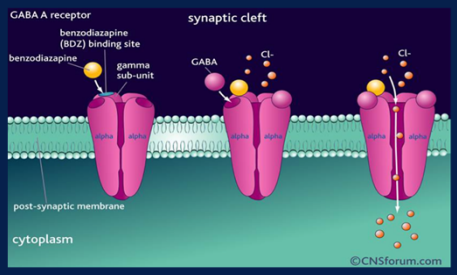
Neurobiology ($GABA_A$ Receptor)



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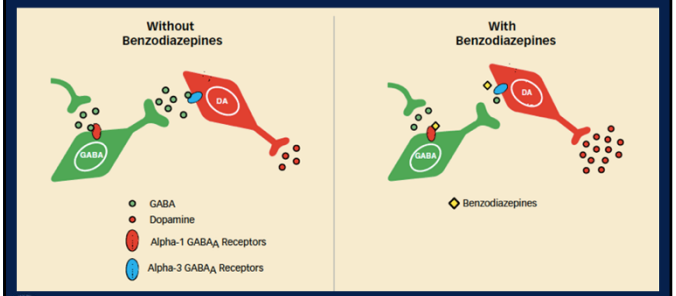
Mechanism of Benzodiazepine Addiction (hypothesis)



NIDA NOTES APRIL 19, 2012

17

Epidemiology

- 80% of pts with benzo use disorder use other drugs
- 30-50% of pts with ETOH use disorders in detox and 44% of IV drug user also use BZD
- Average benzodiazepine use is about 2 c:: 1

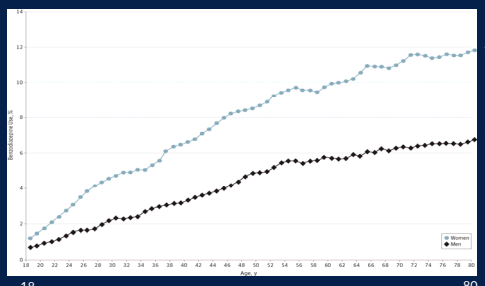


- Use of benzodiazepines increases with age
- In the US, roughly 9 of 10 older adults who use benzodiazepines on a long-term basis are prescribed by PCP

18

Epidemiology

Percentage of Population in the United States in 2008 With Any Benzodiazepine Use by Sex and Age



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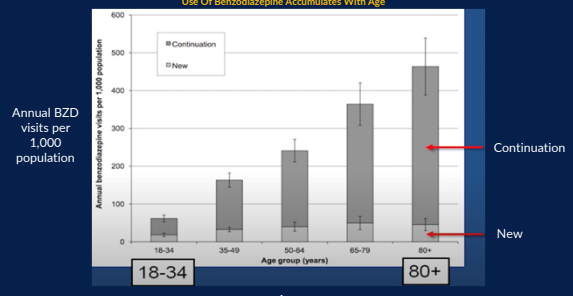
Epidemiology

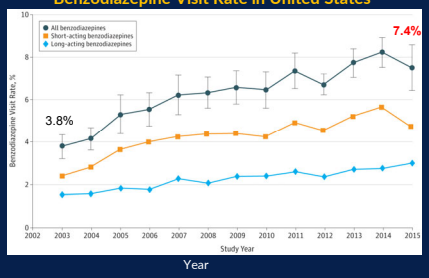
Use Of Benzodiazepine Accumulates With Age



20

Epidemiology

Benzodiazepine Visit Rate in United States



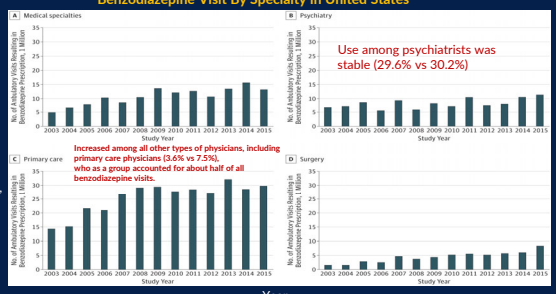
95% increase in BZD-related visits in 12 years

Agarwal SD, Landon BE. JAMA Netw Open. 2019 Jan 4;2(1)

21

Epidemiology

Benzodiazepine Visit By Specialty in United States



Agarwal SD, Landon BE. JAMA Netw Open. 2019 Jan 4;2(1)

22

Concurrent Use of Other Substances

- Rarely the initial or primary substance of abuse
- Rarely used alone to produced intoxication
- Usually abuse with other substances
- Healthy patients prefer placebo to benzodiazepines

- ETOH use disorder patients and their offspring are more likely to experience mood elevation with benzodiazepines

23

Concurrent Use of Other Substances

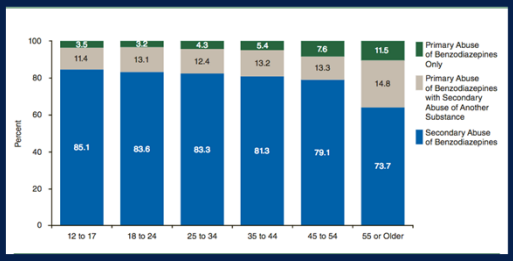
- A high percentage of alcohol dependent patients use benzodiazepines regularly (29-76%)
- 70-96% of patients admitted to inpatient addiction treatment on high dose benzodiazepine use have concurrent dependence on other substances
- It is uncommon to see patients with substance use disorder just on benzodiazepines. Concurrent use with other drugs is common just with benzodiazepine use
- BNZD are prescribed in 1 out of 5 patients on opioids

- Lethality when sedatives-hypnotics are combined with:
  - ETOH + BNZ
  - methadone + BNZ
  - buprenorphine + BNZ
  - Other CNS depressants + BNZ

24

Epidemiology

Primary and Secondary Benzodiazepine Admissions, by Age in 2008



25

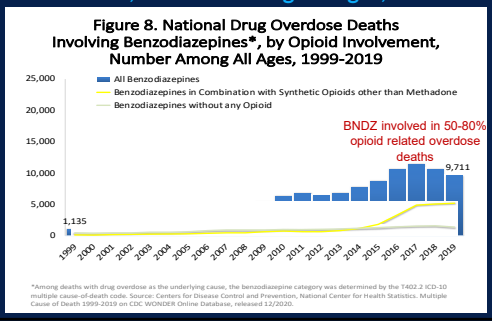
Benzodiazepines + Opioids

- Benzodiazepines (BZs) are the most frequently cited co-intoxicants involved in opioid-related morbidity and mortality.
- In 2010, the CDC reported 16,651 pharmaceutical opioid-related overdose deaths based on death certificate data- almost one of every three opioid-related deaths in 2010 also involved BZs
- On August 31, 2016 FDA issued a drug-safety communication about risks when opioid pain or cough meds are combined with BZs.

(Hwang et al., 2016; Jones, Mack & Paulozzi, 2013; DEA 2013)

26

National Drug Overdose Deaths involving BZDs, by Opioid Involvement, Number among All Ages, 1999-2019



27

Top Five Drugs Most Frequently Involved In Drug Overdose Deaths In United States

2010				2017			
Rank	Reference Drug	Number of Deaths	Percent	Rank	Reference Drug	Number of Deaths	Percent
	N=38,329				N=70,237		
1	Oxycodone	5,256	13.7	1	Fentanyl	27,299	38.9
2	Methadone	4,408	11.5	2	Heroin	15,982	22.8
3	Cocaine	4,312	11.2	3	Cocaine	14,948	21.3
4 →	Alprazolam	3,677	9.6	4	Methamphetamine	9,356	13.3
5	Heroin	3,020	7.9	5 →	Alprazolam	6,647	9.5

Hedegaard H et al. Drugs most frequently involved in drug overdose deaths: United States, 2011–2016. National Vital Statistics Reports; vol 67 no 9. 2018

28

ED Visits: Risk of Serious Outcomes

	12-34 yo	35-44 yo	45-64 yo	65+
BZD alone	28%	30%	37%	39%
BZD + opioids	37%	43%	47%	59%
BZD + alcohol	35%	43%	51%	55%
BZD + opioids + alcohol	39%	47%	57%	70%

SAMHSA, DAWN Report, 12/18/2014

29

Epidemiology

- Most frequent abused pharmaceutical second only to opioids
- Alprazolam is the most frequently abused followed by Clonazepam, Lorazepam, and Diazepam
- BZDs are prescribed at about 65.9 million office-based doctor visits. That's a rate of 27 annual visits per 100 adults

National Health Statistics Report that examined data from the 2014-2016 National Ambulatory Medical Care Survey (NAMCS) 2019.

30

Substances Involved In Drug Related Er Visits For Misuse Or Abuse 2004, 2009, 2011

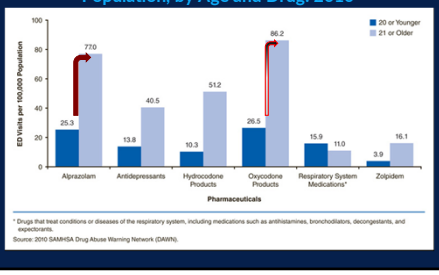
Table 2. Selected Substances Involved in Drug-Related Emergency Department (ED) Visits for Misuse or Abuse of Drugs: 2004, 2009, and 2011

Substances	Number of ED Visits in 2011	Rate of ED Visits per 100,000 Population in 2011	Percent Change, 2004 to 2011	Percent Change, 2009 to 2011
Total ED Visits	**2,442,948**	**780.4**	**52%**	**19%**
Illicit Drugs	1,252,500	402.0	NC	27%
Cocaine	505,224	162.1	NC	NC
Marijuana	455,668	146.2	52%	19%
Heroin	258,482	83.0	NC	NC
Illicit Stimulants	159,840	51.3	NC	68%
Other Illicit Drugs	131,178	42.1	86%	60%
Pharmaceuticals	1,428,145	458.3	114%	13%
Anti-anxiety and Insomnia Medications	501,207	160.9	124%	14%
Alprazolam	154,016	49.4	155%	NC
Clonazepam	76,557	24.6	122%	NC
Lorazepam	50,399	16.2	127%	NC
Zolpidem	37,225	11.9	152%	NC
Narcotic Pain Relievers	420,040	134.8	153%	NC
Oxycodone Products	175,229	56.2	220%	NC
Hydrocodone Products	97,183	31.2	96%	NC
Methadone	75,693	24.3	74%	NC
Morphine Products	38,416	12.3	144%	NC

31

Emergency Department Visits Involving Misuse or Abuse of Selected Pharmaceuticals per 100,000 Population, by Age and Drug: 2010

Faster onset of action and shorter duration greater potential for misuse



32

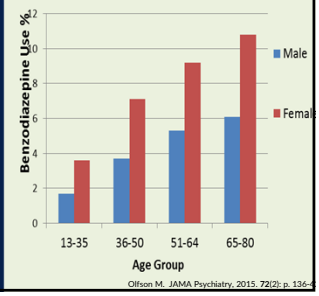
Prevalence of Benzodiazepine Use

Benzodiazepines:

- Use is nearly twice as prevalent in women
- Increased utilization with increasing age
- Proportion of long-term use increases with age
- Prescribed at greater rates than antidepressants for the treatment of depression and anxiety

Olfson M, et al. JAMA Psychiatry. 2015. **72**(2): p. 136-42.; Bernardy NC, et al. J Gen Intern Med. 2013. 28(52): p 5542-8; Demyttenaere, K., et al., J Affect Disord, 2008. **110**1-2): p. 84-93.; Benitez, C.I., et al., Am J Geriatr Psychiatry, 2008. **16**(1): p. 5-13.; Maudsley Prescribing Guidelines in Psychiatry 12th Edition. 2015

Figure 1. Prevalence of benzodiazepine use in the United States

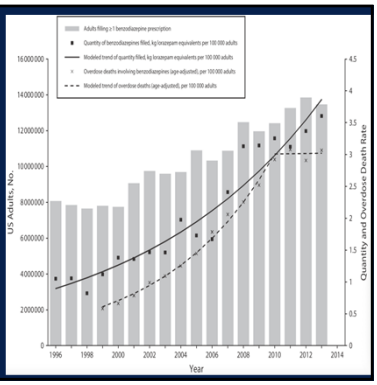


Olfson M. JAMA Psychiatry. 2015. **72**(2): p. 136-42

33

Increasing Benzodiazepine Prescriptions and Overdose Mortality in the United States, 1996–2013

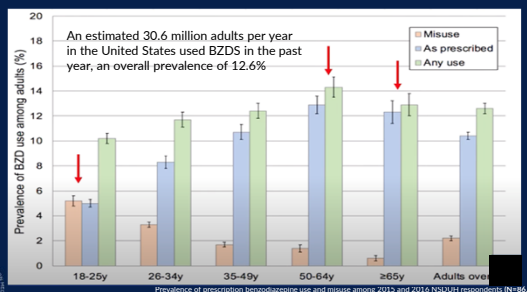
Between 1996 and 2013, the number of adults who filled a benzodiazepine prescription increased by 67 percent, from 8.1 million to 13.5 million.



Bachhuber MA et al Increasing Benzodiazepine Prescriptions and Overdose Mortality in the United States, 1996-2013. Am J Public Health. 2016;106(4):686-688.
Olfson M. JAMA Psychiatry, 2015. 72(2): p. 136-42.

34

BZD Use Accumulates With Age



Prevalence of prescription benzodiazepine use and misuse among 2015 and 2016 NSDUH respondents (**N=86,186**), by age group
*NSDUH, National Survey on Drug Use and Health
Maust DT, Lin LA, Blow FC. Benzodiazepine Use and Misuse Among Adults in the United States. *Psychiatr Serv.* 2019;70(2):97-106. doi:10.1176/appi.ps.201800321

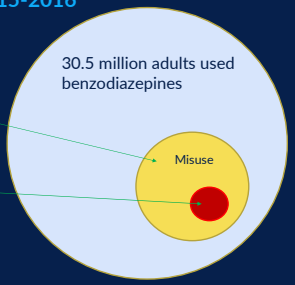
35

Benzodiazepine Use, Misuse, and Use Disorder Among Adults in the United States: Annual Average, 2015-2016

5.2 million adults misused benzodiazepines

0.5 million adults had benzodiazepine use disorders:

- 0.3 million had benzodiazepine dependence
- 0.2 million had benzodiazepine abuse



Blanco C, Han B, Jones CM, et al. Prevalence and correlates of benzodiazepine use, misuse, and use disorders among adults in the United States. J Clin. Psychiatry. 2018; 79(6)

36

Case: RR

Mr. RR did not receive his alprazolam refill from his PCP because, after taper, patient returned to his original dose and ran out of the prescription sooner. Mr. RR is upset and decided to see a psychiatrist who had planned to prescribe medication if ROI to contact PCP is signed.



37

Case: RR

Mr. RR reports that his heart has been racing and his insomnia has worsened; his friend states that, for the past four days, he has been having difficulty following conversations and focusing on daily tasks. He has been off alprazolam for seven days Mr. RR denies any recent psychosocial stressors and does not endorse feelings of guilt, helplessness, or hopelessness. Furthermore, he denies any fever, nausea, vomiting, diarrhea, myalgia, abdominal cramps, or seizures. He denies any recent alcohol or illicit drug use.



38

Factors Associated With Prescribing Benzos

- Anxiety
- Insomnia
- Pain
- Chronic Medical Condition
- Female
- White
- Retirement Low income
- Elderly
- Smoking
- Poor Health
- >1 Prescriber
- Computer prescribing

Agarwal SD, Landon BE. JAMA Netw Open. 2019 Jan 4;2(1)

39

Benzodiazepines and Addiction

Benzodiazepines are often not the primary substance abused and, when combined with other substances (e.g., alcohol ,opioids), can have fatal consequences

- 5-10% - Patients newly started on benzodiazepines develop a substance use disorder
- 50% - Patients with substance use disorder history will develop a benzodiazepine use disorder
- 58-100% - Patients prescribed chronic benzodiazepines become physically dependent

Guina, J., et al., J Psychiatr Pract, 2015. **21**(4): p. 281-303.; *Substance Abuse: A Comprehensive Textbook (4th ed.). Baltimore, MD: Lippincott. Williams & Wilkins. 2004. pp.* 302-312.; Substance Abuse and Mental Health Services Administration. The TEDS Report: Substance Abuse Treatment Admissions for Abuse of Benzodiazepines. . Rockville, MD.; June 2, 2011.

40

Benefits and Risks

- Population
  - Therapeutic dose dependent
  - Prescribed high-dose dependent (sedative use disorder)
  - Recreational benzodiazepine use
- Risk factors for benzo use disorder:
  - Longer duration of BNZ use
  - Higher Benzodiazepine doses
  - Lower level of education
  - Greater insomnia severity
  - Current antidepressant use

41

Benefits and Risks

ACTION		CLINICAL USE
Anxiolytic	Relief of anxiety	Anxiety and panic disorders, phobias
		Agitated Psychosis
Hypnotic	Promotion of sleep	Insomnia
Myorelaxant	Muscle relaxation	Muscle spasms, spastic disorders
Anticonvulsant	Stop fits, convulsions	Fits to drug poisoning, some form of epilepsy, alcohol withdrawal
Amnesia	Impairment of short-term memory	Premedication for operations, sedation for minor surgical operations

42

Benefits and Risks Prior to Prescribing Benzodiazepines

TOLERANCE and DOSE ESCALATION = WITHDRAWAL

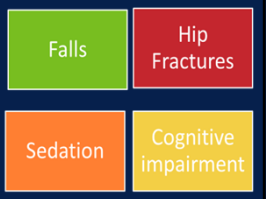
- Examine the risk-benefit ratio
- Avoid nonbenzodiazepine hypnotic
- Short-term use (4 weeks)

43

43

Benefits and Risks (Concerns)

- Long term use have shown deficits in learning, memory, attention, and visual spatial ability
- Anterograde Amnesia
- Adverse effects:
  - May contribute to psychomotor impairment and increase the risk of falls and automobile accidents
  - Psychomotor impairment is characterized by:
  - - Slow reaction time
  - - Diminish speed and accuracy for motor tasks
- Increase risk (50%) of hip fractures and recurrent falls in the elderly population
- OD with Benzodiazepine alone are almost never lethal (high therapeutic index) but OD with BBT alone can be

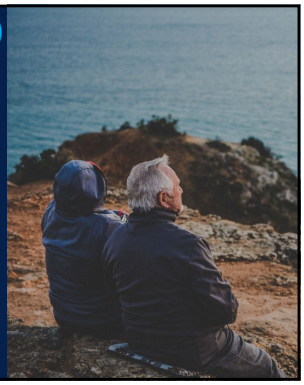


Cumming et al. Benzodiazepines and Risk of Hip Fractures in Older People. *CNS Drugs* 17,2003

44

Benefits and Risks (Concerns)

- The 2015 American Geriatrics Society Beers Criteria recommend avoiding benzodiazepines in this population. Despite these consensus recommendations and known risk factors:
  - Benzodiazepine use is three times more prevalent in older adults compared to younger adults
  - Roughly one-quarter of long-term benzodiazepine use is in patients ≥65 years of age



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Considerations When Prescribing Bzs

- Examine the risk-benefit ratio
- Avoid nonbenzodiazepine hypnotic (Alternative)
- Inform patient of planned duration of therapy
- Prescribe for brief periods
- No refills without follow up
- Use random urine toxicology
- Attempt to taper dose
- Always check the Prescription Drug Monitoring Program (PDMP) before and during the treatment
- Formalize written treatment agreement

46

Phases of Sedative-Hypnotic Treatment and Related Syndromes



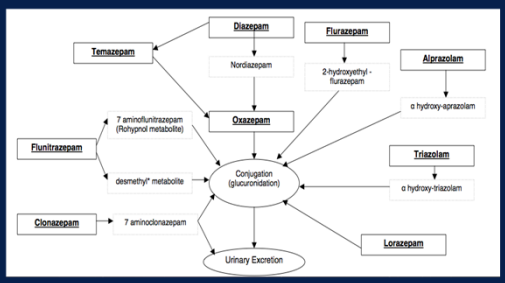
47

Equivalent Doses And Elimination Half-lives Of Benzodiazepines

Benzodiazepines	*Approximately Equivalent Dosage (Mg)*	*Elimination Half-life (Hrs)-(Active Metabolite)*
Alprazolam *	0.5	6-12
Chlordiazepoxide	25	5-30 (36-200)
Clonazepam*	0.5	18-50
Diazepam	10	20-100 (36-200)
Flunitrazepam	1	18-26 (36-200)
Flurazepam	15-30	(40-250)
Lorazepam*	1	10-20
Oxazepam	20	4-15
Temazepam	20	8-22
Triazolam*	0.5	2

48

Benzodiazepine Metabolism



49

Types of Benzodiazepines

- 2-Keto benzodiazepines (Clonazepam, Diazepam, Chlordiazepoxide)
  - All have long half-lives (23-100 hours)
  - All have active metabolites (commonly desmethyldiazepam)
  - Some administered as Prodrug
- 3-Hydroxy Benzodiazepines (Oxazepam, Temazepam, Lorazepam)
  - Intermediate half-lives (most 10-15 hours)
  - No active metabolites (better in elderly/hepatic impaired)
  - Metabolized outside the liver (only need glucoronidation)
- Triazolo Benzodiazepines (Alprazolam, Triazolam)
  - Short to Intermediate half lives (anywhere from <12 hours)
  - Some have active metabolites

50

Pharmacokinetics

BZDs are differentiated by their pharmacokinetic profiles, based on *lipophilicity and metabolism*:

- **Half-life** (short, intermediate, long)
- **Onset-of-action** (rapid, intermediate, slow)
- **Metabolic pathways** (with or without active metabolites, with or without P450 involvement)

Clinical Pharmacology 2017

51

Pharmacokinetics

LONG-ACTING	MEDIUM-ACTING	SHORT-ACTING
• Chlordiazepoxide	• Lorazepam	• Alprazolam
• Diazepam	• Oxazepam	• Triazolam
• Clonazepam	• Temazepam	• Midazolam

52

Case: RR

PE: He was found to be tachycardic (pulse, 110 beats/min) and hypertensive (blood pressure, 170/90 mm Hg). His medical workup, including CBC count, electrolyte panel, liver function tests, blood glucose level, and urine toxicology screen were within normal limits.



53

Case: RR

MSE: Casually dressed male who appeared to be restless and irritable with twitches in his face and complains about tinnitus. He was oriented to time, place, and person. His speech was normal in rate and content. His mood was subjectively anxious and objectively dysphoric, and his affect was congruent with mood. His thought form was linear, and goal directed. There was no evidence of paranoid ideations/delusions. He denied any auditory or visual hallucinations. He scored 30/30 on the Mini-Mental State Examination. He had good insight and judgment. He endorsed passive suicidal ideations, no plan. He denied any homicidal ideations



54

Management of Benzodiazepine Withdrawal

Variable presentation:

- There are no pathognomonic signs and symptoms of benzodiazepine withdrawal
- Assess for subjective and objective symptoms
- May have few concurrently observable hyper-adrenergic signs or vital sign fluctuations (unlike acute alcohol withdrawal)

55

Symptoms Of Anxiety State	*Symptoms Less Common In Anxiety States-relatively Specific To Benzodiazepine Withdrawal*
Anxiety, panic attacks, agoraphobia	Perceptual distortions, sense of movement
Insomnia, nightmares	Depersonalization, derealization
Depression, dysphoria	Hallucinations (visual, auditory)
Excitability, restlessness	Distortion of body image
Poor memory and concentration	Tingling, numbness, altered sensation
Dizziness, light headedness	Formication (skin "crawling")
Weakness "jelly legs"	Sensory hypersensitivity (light, sound, taste, smell)
Tremor	Muscle twitches, jerks, fasciculation
Muscle pain, stiffness	Tinnitus
Sweating, night sweats	Psychotic Symptoms
Palpitations	Confusion, delirium
Blurred or double vision	Convulsions

56

Management of Benzodiazepine Taper

Challenging process for both patients and doctors if you do not have a treatment plan

Strategies:

- Gradual dosage tapering (avoid prn dosing)
- Psychological Support
- Reasons for prescribing
- Lifestyle
- Personality

57

Management of Benzodiazepine Taper

- Consider dosage and type of benzodiazepine
- Environment stresses
- Amount of available support
- Prepare for months or a year for the taper
- Individualize treatment adjusted to patient's needs (personalized treatment)

58

Management of Benzodiazepine Withdrawal /Taper

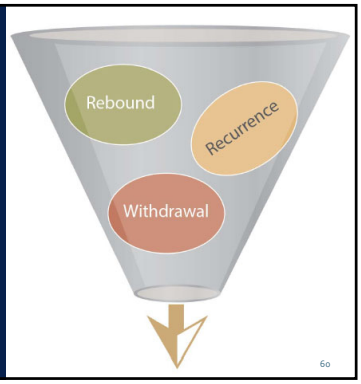
Time course and severity are influenced by:

- Duration of use: short vs. long term use
- Dose: low/therapeutic dose vs. high dose
- Pharmacokinetics: short vs. long acting
- Host factors: comorbid pathology or substance use disorder

59

What is the difference between withdrawal, rebound and recurrence?

- Recurrence: the person experiences the same symptoms and severity of symptoms that existed prior to treatment
- Rebound: occurs when a drug is withdrawn and the individual experiences anxiety symptoms that are more severe than those experience prior treatment
- Withdrawal: the time-limited development of unique symptoms as the result of discontinuing or decreasing the use of a psychoactive drug



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Management of Benzodiazepine Withdrawal

Time and Severity can vary

- Short Acting BZs and those with active metabolites when stopped, can lead to WD sx within hours
- Long Acting BZs with active metabolites can take 48 hours – 7 days for WD sx to emerge
- Severe WD from BZs can be accompanied by delirium

61

61

Management of Benzodiazepine Withdrawal

Duration of use and therapeutic dose:

>10 days use with therapeutic dose:
some experience transient insomnia

<2 weeks with therapeutic dose:
Most experience rebound

>2 months with therapeutic dose:
Most experience mild withdrawal

Of patients who take a benzodiazepine for more than a month, 47% (n=1048) become dependent.

De Las Cuevas et al 2003

62

62

Management of Benzodiazepine Withdrawal

Duration of use and therapeutic dose:

- >4 to 6 months with therapeutic dose;
- Most experience mild to moderate withdrawal

- >12 months with therapeutic dose:
- 20-80% experience moderate to severe withdrawal

63

63

Management of Benzodiazepine Withdrawal: When to Taper

- Over-sedation
- Cognitive impairment
- Concurrent Rxs or use of high-risk CNS depressants medications
  - Other BZs, non-BZ hypnotics, and OPIOIDS
- Alcohol use disorder and other SUDs
- Overuse, misuse, or BZ use disorder
- Patient request
- Other

64

64

MANAGEMENT/Systematic Discontinuation

- Tapering
- Substitution and tapering

65

65

MANAGEMENT/Systematic Discontinuation

- Rate for dosage varies for different types of benzodiazepine pts:
  - Withdrawal shows in 1- 7 days depending on half lives
  - One-eight to one-tenth of the daily dose (10-25% weekly)
  - Taper between 4 weeks to 6 months or even more

66

66

Management of Benzodiazepine Withdrawal

Pharmacological /Strategies Treatment of Withdrawal

- Taper over months:
- Convert to longer acting agent like Clonazepam, Chlordiazepoxide, Diazepam)
- Taper gradually while starting alternative therapies if needed (months)
- Rebound psych meds for anxiety/sleep (Trazadone, Mirtazapine, Buspirone)
- Use of Anticonvulsant carbamazepine or valproate

Ashton H. The diagnosis and management of benzodiazepine dependence. *Curr Opin Psychiatry*. 2005; 18:249-255.

67

When do you see withdrawal symptoms?

- Short acting BZD: oxazepam, triazolam, temazepam, alprazolam
- Short acting sedative-hypnotics: pentobarbital, secobarbital, meprobamate, metaqualone
  - Withdrawal onset in 12-24 hrs with
  - Peak of withdrawal intensity-day 1 to 5
  - Duration of acute withdrawal- 7 to 21 day

68

When do you see withdrawal symptoms?

- Long-acting BZD and sedative-hypnotics: diazepam, chlordiazepoxide, phenobarbital
  - Withdrawal Onset within 5 - 14 days of cessation
  - Peak of Withdrawal Intensity - Days 1 to 9
  - Duration of Acute Withdrawal - 10-28 days
    - Protracted withdrawal symptoms for months

69

Phenobarbital Substitution and Taper

- Substitution of benzodiazepine with equipotent dose of phenobarbital
- For inpatient, medically monitored setting only
- Effective Strategy for:
  - High dose dependent
  - Poly-Substance Dependence
  - Concurrent Alcohol/other Sedative Hypnotic
  - Unknown or erratic polypharmacy drug use

70

Phenobarbital Substitution and Taper

- Establish Stabilization Dose by Computing Phenobarbital equivalents
  - **Alprazolam 1 mg=PB 30 mg**
  - **Clonazepam 2mg=PB 30 mg**
  - **Diazepam 10 mg=PB 30 mg**
  - **Lorazepam 2 mg=PB 30 mg**
  - **Carisoprodol 700 mg=PB 30 mg**
- PB should be give TID or QID
- Maximum PB starting dose 500mg/day

71

Phenobarbital Substitution and Taper

- Monitor patient for signs of toxicity before administering each dose
- Signs of PB toxicity are easy to observe:
  - Sustained horizontal nystagmus
  - Ataxia
  - Slurred Speech
  - If intoxication observed:
    - If 1 sign of toxicity observed, skip one dose
    - If 2 signs of toxicity observed, skip 2 doses
    - Recalculate new daily dose

72

Phenobarbital Substitution and Taper

- Once stabilization dose is established: maintain patient on initial dose for two days
- If patient has neither signs of withdrawal or toxicity, then patient is moved to the withdrawal phase
- Decrease phenobarbital 30 mg/day unless signs of toxicity or withdrawal are seen
- If patient develops objective signs of withdrawal. Daily dose is adjusted upward by 50% and patient is stabilized before continuing withdrawal

73

73

Pregnancy

- Pregnant and lactating women are relatively contraindicated due to:
  - Ability of benzodiazepines to cross fetal placental barrier and to pass into breast milk
  - Teratogenic effects
  - Floppy baby syndrome
  - Neonatal withdrawal

74

74

Flumazenil

- Reverse the sedation produced by a benzodiazepine (Acute O.D with benzodiazepine)
- Nonspecific competitive antagonist of benzodiazepine receptor
- May up regulate BZ receptors
- IV use 1 mg monitor pt every 30-60 minutes
- Adverse effects: seizures, cardiac arrhythmias and acute precipitated withdrawal

75

75

Z-Drugs (Selective Nonbenzodiazepine Hypnotics)

- Zaleplon
- Zolpidem
- Eszoplicone
- Zoplicone*

- Lower the risk for residual daytime drowsiness due to shorter duration of action
- Short term use
- Bind to sub-types of $GABA_A$receptors – *α1 subunit* that specifically modulate sleep and therefore are thought to have less unwanted side effects

- SE: risk of increased sleep- related behaviors

- Apply the general principles prescribing benzodiazepines to the Z-drugs

76

76

Barbiturates

- The oldest sedative hypnotics
- Classified in three different pharmacokinetics category
- In the past used for treatment of anxiety disorders
- BBT: *low therapeutic index*
- Replaced by benzodiazepines
- BBT induce the synthesis of hepatic cytochrome P450, thus alter their own metabolism and the metabolism of other meds

77

77

Barbiturates

Duration of Action	*LS*	*Onset*	*Duration*	*Use*
Ultrashort	H	10-20 s	20-30 min	IV anesthesia
Thiopental				
Methohexital				
Short/Intermediate	M	20-40 min	5-8 h	Surgical anesthesia and sleep induction
Amobarbital				
Secobarbital				
Pentobarbital				
Long	L	Over 1 h	10-12 h	Prolong sedation and seizure control
Phenorbarbital				
Meprobarbital				

78

78

GHB

Gamma-Hydroxy-Butyrate

79

79

"When I wake up,
I feel completely refreshed.
In comparison to the other drugs that
are supposed to be 'clean,'
G really is clean."

80

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81

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Effects

- Sensual drug, like MDMA, but also resulting in "the greatest sex ever."
- Relaxation, tranquility, placidity, mild euphoria, disinhibition.
- Temporary amnesia (hence "the date rape drug").

82

82

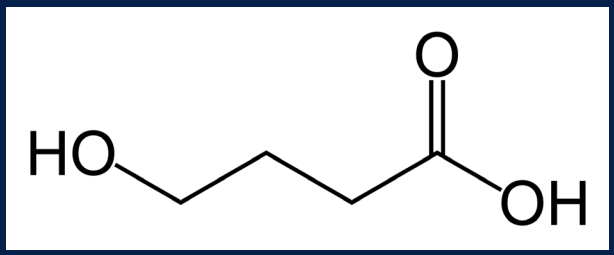
Neurobiology

- GHB is a neurotransmitter.
- It is both a precursor and a metabolite of GABA.
- Activity on both the $GABA_B$ and the GHB binding sites, results in:
  - Temporary suppression of dopamine,
  - Subsequent marked release of dopamine, and
  - Increased release of endogenous opioids.
- It is a highly regulated Schedule III medication for narcolepsy (Xyrem).

83

83

The Molecular Structure



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Intoxication

- Steep dose-response curve:
  - Ataxia, loss of coordination.
  - Respiratory depression, bradycardia.
  - Coma, persistent vegetative states, death
  - Overdose is a real danger (LD50 is only 5 times the recreational dose).
  - Synergistic effect with alcohol/other sedatives.
- Treat as a medical emergency:
  - ABCs, consider Intensive Care Unit admission.
  - Atropine for bradycardia.

85

85

Withdrawal

- Withdrawal is rare but severe.
- Mild withdrawal may persist for several weeks after cessation of use:
  - Anxiety, tremor, insomnia.
  - "Feelings of doom."
- Severe withdrawal resembles barbiturate withdrawal:
  - Treat with benzodiazepines.

86

86

Long Term Features

- Physiological dependence.
- Most patients who overdose on GHB recover completely.
- No FDA approved medications.
- MET and CBT are the major treatment modalities.

87

87

Opioid Use Disorder: Science, History, and Clinical Implications

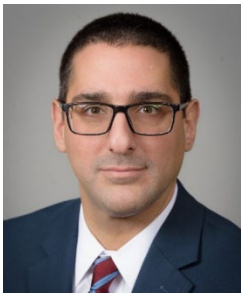
Friday, July 22
10:45 am – 11:30 am CT

Recent data shows that an estimated 10.3 million Americans misused opioids in the past year. This session sets the stage with an overview of the history of opioid use and opioid regulation. The presenter then dives into a deeper exploration of the neurobiology and pharmacology of opioids. The session ends with a thorough review of all treatment options for opioid use disorder and opioid withdrawal.

Learning Objective:

- After this session, learners will be able to: Describe the key opioid regulations, neurobiological impacts of opioids, criteria for opioid use disorder, and evidence-based treatment strategies.

Faculty Presenter



Soteri Polydorou, MD
Medical Director, Addiction Services
Northwell Health
Zucker School of Medicine at Hofstra/Northwell

Dr. Polydorou is a practicing physician with board certifications in Addiction Medicine and Internal Medicine. His involvement in the field of substance use disorder (SUD) treatment and education includes serving as Medical Director of Addiction Services for Northwell Health and Associate Professor at the Zucker School of Medicine at Hofstra/Northwell. Northwell Health is a regional health system of over 20 hospitals and nearly 800 outpatient facilities. Dr. Polydorou is a member of various governmental and professional committees tasked with supporting the delivery and organization of addiction treatment. Dr. Polydorou's interests include public policy initiatives to address substance use disorders, optimizing access to SUD services within health systems, and implementation of innovative opioid use disorder treatments within various healthcare clinical settings.

OPIOIDS

Soteri Polydorou, MD
Associate Professor
Department of Medicine
Department of Psychiatry
Zucker School of Medicine at Hofstra/Northwell

1

The ASAM Board Exam Study Course in Addiction Medicine

2022

Financial Disclosures

Soteri Polydorou, MD
No Disclosures

2

Outline

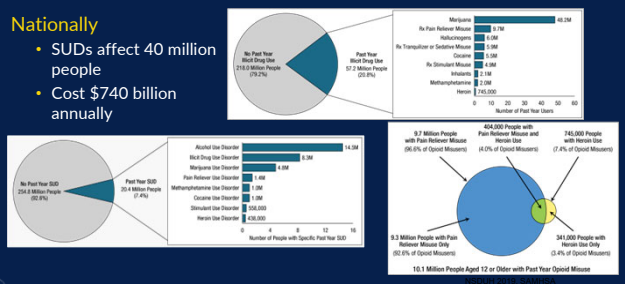
1. Opioid Use Trends
2. History
3. Regulations
4. Neurobiology
5. Intoxication and Withdrawal
6. Medications for Opioid Use Disorder

3

The Need for Treatment is Growing

Nationally

- SUDs affect 40 million people
- Cost $740 billion annually



NSDUH 2019, SAMHSA

4

Unintentional Opioid Overdose

Experienced (non-fatal)

- Lifetime 24% - 94% (mean 45%, median 47%, SD 14%)
- Past Year 9% - 36% (mean 18%, median 17%. SD 10%)

Witnessed (non-fatal and fatal)

- Lifetime 48% - 96% (mean 73.3%, median 70%, SD 14%)

1 Year All Cause Mortality

- 5% of Non-Fatal Opioid Overdose Presentations to ED or Hospital Admission

Martins S et al 2015, Leece P, et al. 2020, Weiner S et al. 2020

5

5

The Need for Treatment is Growing

Nationally

- Over 100,000 lethal ODs in 2021, nearly 15% increase from 2020
- Almost 80% of all overdose deaths involve an opioid of which over 70% include fentanyl
- Heroin users, >100% increase from 2004 to 2016
- 4 out of 5 new recent heroin users previously abused prescription opioids
- >140 OD deaths from opioids daily in US
- 2010 to 2016 heroin related deaths increased by 500%
- 2015 to 2019 fentanyl related deaths increased by over 400%

Leading Causes of Death in US, 2020	Annual Deaths
Heart Disease	696,962
Cancer	602,350
COVID	350,831
Accidents (unintentional injuries)	200,955
Stroke	160,264
Chronic Lower Respiratory Diseases	152,657
Alzheimer's Disease	134,242
Diabetes	102,188
Influenza and PNA	53,544
Renal Disease	52,547

CDC, Health Alert Network, NSDUH, SAMHSA, CSAT, and DOHMH Bureau of Vital Statistics

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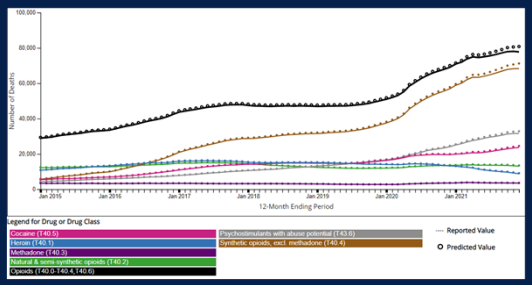
The Need for Treatment is Growing



Based on data available for analysis on 5/12/22.
https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm#dashboard

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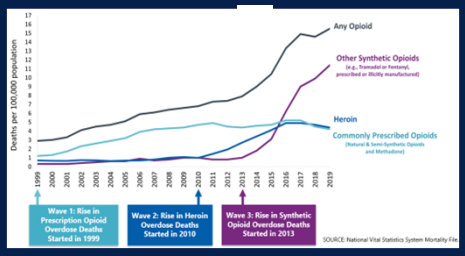
Three Waves of Opioid Overdose Deaths



cdc.gov/drugoverdose 8

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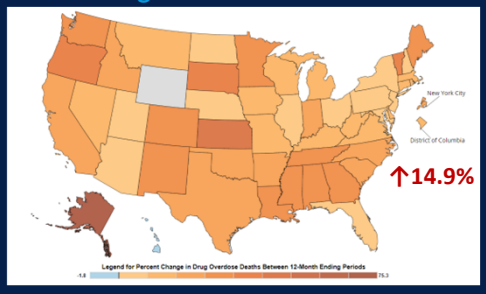
Drug Overdose Deaths 2021



https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm

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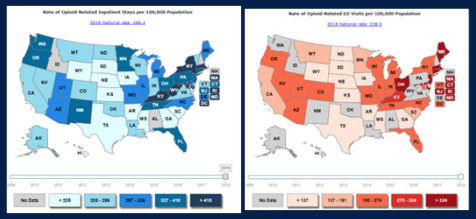
Opioid Related Inpatient Stays and ED Visits



Agency for Healthcare Research and Quality (AHRQ), Healthcare Cost and Utilization Project (HCUP), https://www.hcup-us.ahrq.gov/ 10

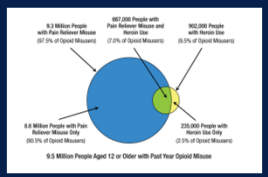
10

The Need for Treatment is Growing

Opioid Use Disorder 2.9 million

- Prescription opioids 2.3 million
- Heroin use 691,000
  - >100% increase from 2004 to 2016
  - Lifetime use 5.7 million, doubled from 2002 to 2018
  - 4 of 5 new heroin users previously used prescription opioids

15-yr reduction in life expectancy
Lewer 2020



NSDUH 2020, SAMHSA

11

Unintentional Opioid Overdose

Experienced (non-fatal)

- Lifetime 24% - 94% (mean 45%, median 47%, SD 14%)
- Past Year 9% - 36% (mean 18%, median 17%. SD 10%)

Witnessed (non-fatal and fatal)

- Lifetime 48% - 96% (mean 73.3%, median 70%, SD 14%)

Martins S et al 2015

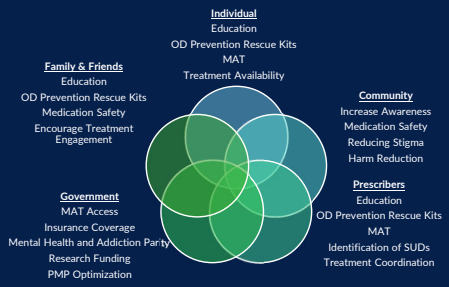
1 Year All Cause Mortality

- 5% of Non-Fatal Opioid Overdose Presentations to ED or Hospital Admission

Leece P et al. 2020, Weiner S et al. 2020

12

Opportunities to Reduce Risk



Hawk K et al 2015

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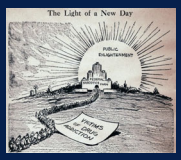
3400 BC



1898



1839



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Opium Poppy: Papaver Somniferum



Alkaloid Content

- **Morphine**, 7-25%, opiate analgesic, named after Morpheus, the Greek God of dreams
- **Noscapine**, 4-15%, central acting antitussive, no morphine-like effect of dependence or tolerance
- **Codeine**, 1-6%, opiate analgesic
- **Thebaine**, 1-6%, important intermediate for the synthesis of semisynthetic opioids e.g., buprenorphine
- **Papaverine**, 1-5%. smooth muscle relaxant
- **Poppy Seeds**: UDS→ + Opiates, Morphine, Codeine (cut-off dependent)

15

U.S. Government Involvement

Congress passes multiple laws aimed at reducing the increase in heroin/morphine/opium addiction.

- **1905**-Opium banned
- **1906**-Pure Food and Drug Act- labeling of all medications by pharmaceutical companies
- **1914**-Harrison Narcotics Act (HNA)
  - **1919**- Supreme Court sides with Treasury interpretation that physician prescribing of opioids for treatment of opioid addiction was violation of HNA
  - Later Supreme Court rulings from **1921 and 1926** reverses interpretation of HNA saying the federal government had overstepped its authority to regulate the practice of medicine



16

U.S. Government Involvement

- 1970-Comprehensive Drug Abuse Prevention & Control Act (Controlled Substances Act)
- 1974 – Narcotic Addict Treatment Act of 1974
- 2000- Drug Addiction Treatment Act (DATA) of 2000– An Amendment to the Controlled Substances Act
  - Allows treatment of opioid dependence with narcotic schedule III, IV, V, or combinations of such drugs
  - Buprenorphine designated Schedule III and FDA approved for treatment of opioid dependence
  - Capacity to refer patients for counseling



17

U.S. Government Involvement

- Approved training programs
  - Complete eight hours of training provided by a pre-approved society or by a society approved by State Medical Licensing Boards or by the Secretary of HHS
  - Providers Clinical Support System, ***PCSSNOW.ORG***
- Apply for waiver from Center for Substance Abuse Treatment (CSAT)
- 2006 – Patient limit increases to 100
- 2016 Comprehensive Addiction and Recovery Act (CARA)
  - Expands buprenorphine prescribing to PA and NP, qualify after taking 24hr of training, until 2021.
  - SAMHSA authorizes patient limit increase to 275

18

18

U.S. Government Involvement

- 2018 Support for Patients and Communities Act
  - Expands buprenorphine prescribing to Clinical Nurse Specialists, Certified Registered Nurse Anesthetists, and Certified Nurse Midwives until 10/1/23
  - Increases number of patients to 100 that can be treated by certain physicians in the first year of obtaining a waiver under specific conditions.
- 2020 HHS Public Health Emergency Declaration, DEA partners with SAMHSA (temporary)
  - Controlled Substances (in accordance with DATA 2000 waivers) can be prescribed using telemedicine or telephone without first conducting an in-person examination while HHS PHED in effect
  - OTP utilization of methadone continues to require an initial on-site examination, but attendance restrictions related to time in treatment have been temporarily modified.

19

19

U.S. Government Involvement

- 2021 HHS Updates Practice Guidelines for the Administration of Buprenorphine for Treating OUD
  - Provides an alternative Buprenorphine Waiver Notice of Intent allowing providers to treat up to 30 patients to forego training requirement, as well as certification to counseling and other ancillary services.
    - https://buprenorphine.samhsa.gov/forms/select-practitioner-type.php

Over 100,000 practitioners hold waivers, 71,000 with 30-limit, 22,000 with 100-limit, <10,000 with 275-limit

20

20



21

DEA Announcement


DEA's Commitment to Expanding Access to Medication-Assisted Treatment

WASHINGTON – Today, Administrator Anne Milgram announced the Drug Enforcement Administration's continued commitment to expanding access to medication-assisted treatment to help those suffering from substance use disorder.

"In this moment, when the United States is suffering tens of thousands of opioid-related overdose deaths every year, the DEA's top priority is doing everything in our power to save lives," said Administrator Milgram. "Medication-assisted treatment helps those who are fighting to overcome substance use disorder by sustaining recovery and preventing overdoses. At DEA, our goal is simple: we want medication-assisted treatment to be readily and safely available to anyone in the country who needs it."

Email DEA Exception Requests: ODLP@dea.gov

Subject Line: Request for Exception to Limitations on Dispensing for OUD

https://www.dea.gov/press-releases/2022/03/23/deas-commitment-expanding-access-medication-assisted-treatment

22

22

Terminology

Endorphins - describes the whole class of endogenous opioid ligands
- Beta-endorphin, enkephalin, dynorphin

Opioid - describes entire class of non-endogenous (natural or synthetic) and endogenous compounds that bind to one or more types of opioid receptors
- Methadone, fentanyl, oxycodone

Opiate - describes compounds naturally derived from the poppy plant
- Morphine, codeine

23

23

Endogenous Opioids & Opioid Receptors

Opioid Class	Opioid Receptor Type
Beta-endorphin Endomorphin	Mu Opioid Peptide Receptor
Dynorphin	Kappa Opioid Peptide Receptor
Enkephalin	Delta Opioid Peptide Receptor
Orphanin/Nociceptin (opiate-like)	*Nociceptin/Orphanin FQ Peptide Receptor, Opioid Receptor Like-1*

Multiple opioid receptor polymorphisms identified

24

24

Overview

- Addictive drugs produce an enhancement in extracellular dopamine levels in the nucleus accumbens and other limbic structures as well as cortical areas.
- Endorphin-Opioid Receptor binding results in an increase in dopamine release in the mesolimbic and mesocortical pathways but unlike exogenous Opioid-OR binding the effect is less robust and does not result in habituation.

25

25

Opioid Receptors

All Opioid Receptors
Seven transmembrane domain
G protein-coupled
Primarily inhibitory pathways

Mu Opioid Receptor (OPRM) Activation (predominantly beta-endorphin)
Reduces cAMP
Inhibits transporter release of GABA, glycine, and glutamate
- Inhibition of GABA in ventral tegmental area (VTA)→increases dopamine release throughout mesolimbic (amygdala, ventral pallidum, hippocampus, NAcc)-mesocortical (prefontal cortex, orbitofrontal cortex, anterior cingulate) dopaminergic fields.

26

26

Opioid Receptors

Mu Opioid Receptor (OPRM) Activation (predominantly beta-endorphin)

- Widely dispersed across a wide variety of brain regions, including cortex, striatum, thalamus, hippocampus, locus coeruleus, ventral tegmental area, nucleus accumbens, amygdala
- Mu receptors also mediate rewarding properties of non-opioid drugs of abuse including cannabinoids, alcohol and nicotine, or even natural reinforcers such as social interactions
- Physiologic effects of **intoxication** and **withdrawal**

27

27

Opioid Receptors

Kappa Opioid Receptor (OPRK) Activation (predominately dynorphin A)

- Identified in various CNS regions such as the nucleus accumbens, caudate–putamen, olfactory tubercle, bed nucleus of the stria terminalis, medial preoptic area, paraventricular nucleus, supraoptic nucleus, dorsomedial, and ventromedial hypothalamus, amygdala, midline thalamic nuclei, periaqueductal gray, raphe nuclei, parabrachial nucleus, locus coeruleus, spinal trigeminal nucleus, and the nucleus of the solitary tract.
- Mediates **dysphoric** activities of both opioids and cannabinoids and therefore opposes mu receptors in regulating the hedonic tone and modulating stress-induced relapse.

28

28

Opioid Receptors

Delta Opioid Receptor (OPRD) Activation (predominately enkephalin)

- Identified in various CNS regions including thalamus, amygdala, NAcc, locus coeruleus, VTA, and others
- Lack of familiar opioid characteristics like respiratory depression, reinforcing effects as measured in self-administration studies, and opioid (mu or kappa) withdrawal symptoms.
- Delta receptors are less directly involved in hedonic control.
- Distinct from mu and kappa receptors, delta receptors may play a role in emotional responses and show **anxiolytic** activity along with benefits in analgesia resulting from inflammatory states.

29

29

Genetics/Pharmacogenomics

Multiple polymorphisms identified in opioid receptor genes and other coding regions which have clinical effect.

- OPRM1 chromosome 6; OPRK1 chromosome 8; OPRD1 chromosome 1
- OPRM1 Gene→SNP,rs1799971: **A118G** (Adenine to Guanine substitution)
- → Asn40Asp(Substitution in the receptor extracellular domain) →
- ↑(?) Binding beta endorphin, ↑ risk OUD, AUD, ↓(?) Analgesic Response
- CYP 2D6: Codeine→Morphine, Hydrocodone→Hydomorphone, Oxycodone→Oxymorphone (Asian heritage: ↓↓ 2D6 Other Groups ~ 10% PM)
- Methadone: CYP 3A4, 2D6, 2B6
- COMT (enzyme) The most widely studied variant is **158Met**, where a G to A nucleotide substitution at codon 158 results in an amino acid change from valine to methionine. Patients with Met/Met genotype have lower morphine requirements than those with a Val/Val expression.

30

30

Role of Endorphin Systems in Normal Physiologic Functions

- Endogenous response to pain
- Neuroendocrine functions
  - Stress-response systems including HPA axis
  - Reproductive function including HPG axis
- Immunologic function
- Gastrointestinal function
- Cardiovascular function
- Pulmonary function
- Mood, affect, cognition

31

31

Additional Opioid Effects

- CNS → Sedation, Analgesia, Euphoria
- GI → Constipation, Nausea
- Endo → ↓Testosterone, ↑Prolactin , ↓FSH, LH
- Urinary → Retention
- Cardiovascular → Vasodilatation, ↑QTc
- Miosis
- Tolerance Varies

32

32

Opioids of Note

- Fentanyl ↑ Temp → ↑Skin Absorption
- Meperidine → Normeperidine→ Neuroexcitation, MAO interactions Serotonin Syndrome
- Tramadol weak mu, ↑5HT, ↑NE, Seizures, (Sched. IV), serotonin syndrome
- Tapentadol mu agonist, ↑ NE (5HT), serotonin syndrome
- Kratom, low dose (1-5g) stimulant resembling caffeine/cocaine, high dose (5-15g) opioid like effects, analgesic/sedation reversed by naloxone, possible assoc with hepatic cholestasis—dose dependent
- Tianeptine, antidepressant similar to TCAs, mu and delta agonist, anticholinergic

33

33

Opioid Potency

Opioid	*Relative Potency*	*Lethal Dose*
Morphine	1x	1 Pea
Diacetylmorphine (heroin)	2x	1 Sunflower Seed
Fentanyl	100x	1 Sesame Seed
Sufentanil	500x	1 Grain of Sand
Carfentanil	10,000x	0.5 Grain of Salt

34

34

Role of Medications in the Treatment of Opioid Use Disorder

Overdose
- Acute intervention, possible reversal, and close monitoring

Withdrawal/Early Stabilization
- Reduction and stabilization of withdrawal symptoms
- Opportunity to initiate and engage in ongoing addiction treatment

Maintenance Therapy
- Prevents or eliminates withdrawal
- Diminishes or eliminates drug craving and use of illicit opioids
- Blocks or attenuates the effects of heroin and other abused opiates
- Risk/harm reduction, reduces overdose risk
- Increased treatment retention and engagement in comprehensive rehabilitation
- Decreased medical and psychiatric symptoms, improves health, reduced risk of HIV and Hep C infection
- Improved social determinants such as employment, family relations
- Decreased criminal behavior

35

35

Opioid Overdose

Classic Triad Seen In Overdose

- ***Miosis (Dilated With Prolonged ↓PO2)***
- ***Decreased level of Consciousness/Coma***
- ***Respiratory Depression***
- Pulmonary Edema (Non-cardiogenic)
- Seizures
  - Meperidine, Tramadol

36

36

Management of Opioid Overdose

- Ventilatory support if needed
- Parenteral Naloxone
- If IV access, bolus 0.1mg/min titrated to
  - RR>10/min
  - Improved level of consciousness
  - No withdrawal
  - If needed ongoing IV infusion 2/3 of initial bolus dose/hr.
- If no IV access, 0.4-0.8mg SQ or IM and observe
- Naloxone OD Prevention Kits

37

37

Opioid Overdose Education and Naloxone Distribution (OEND) Programs

- Improved trainee Strang 2006 knowledge of OD safely and effectively administer naloxone
- Some evidence suggests trainees reduced IV use and were more likely to enter treatment 6 months after training. Seal 2005.
- Chicago, OD deaths reduced after introduction of OOPPs. Maxwell S 2006
- Mass, ⬇ 27% in OD deaths low implementation (1-100/100k) vs ⬆ 46% in high implementation (>100/100k). Walley AY 2013.
- But still…
- Study of >500 MDs reported 54% would NEVER consider prescribing naloxone to an IVDU. Beletsky L 2007.

38

38

Pitfalls Opioid Analgesic ODs

- Need for repeated naloxone treatment with longer acting opioids (methadone), and more potent opioids (fentanyl, carfentanil)
- Check for Fentanyl Patch under clothing
- Fentanyl chest wall/skeletal muscle rigidity
  - Most common with rapid IV administration, not dose related
  - Ventilation, naloxone, neuromuscular blocking agent
- Observation
- Alert to possible acetaminophen or other OD

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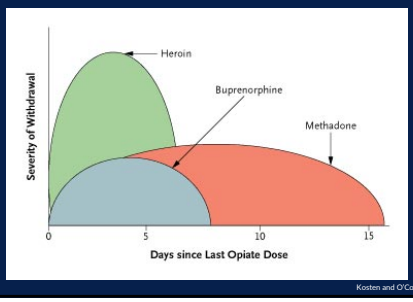
Severity of Opioid-Withdrawal Symptoms after Abrupt Discontinuation of Equivalent Doses of Heroin, Buprenorphine, and Methadone



Kosten and O'Connor, 2003

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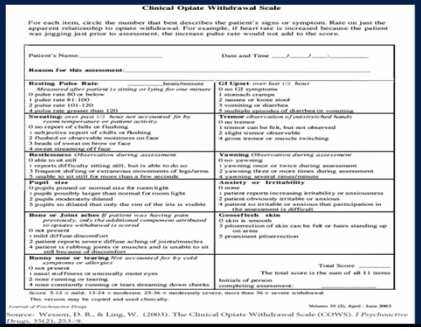
Clinical Opiate Withdrawal Scale (COWS)



Clinical Opiate Withdrawal Scale

For each item, circle the number that best describes the patient's signs or symptom. Rate on just the apparent relationship to opiate withdrawal. For example, if heart rate is increased because the patient was jogging just prior to assessment, the increase pulse rate would not add to the score.

Patient's Name: _____ Date and Time: ____/____/____ ____:____

Reason for this assessment: _____

Resting Pulse Rate: _____ beats/minute *Measured after patient is sitting or lying for one minute* 0 pulse rate 80 or below 1 pulse rate 81-100 2 pulse rate 101-120 4 pulse rate greater than 120	**GI Upset:** *over last 1/2 hour* 0 no GI symptoms 1 stomach cramps 2 nausea or loose stool 3 vomiting or diarrhea 5 multiple episodes of diarrhea or vomiting
Sweating: *over past half hour not accounted for by room temperature or patient activity.* 0 no report of chills or flushing 1 subjective report of chills or flushing 2 flushed or observable moistness on face 3 beads of sweat on brow or face 4 sweat streaming off face	**Tremor:** *observation of outstretched hands* 0 no tremor 1 tremor can be felt, but not observed 2 slight tremor observable 4 gross tremor or muscle twitching
Restlessness *Observation during assessment* 0 able to sit still 1 reports difficulty sitting still, but is able to do so 3 frequent shifting or extraneous movements of legs/arms 5 unable to sit still for more than a few seconds	**Yawning** *Observation during assessment* 0 no yawning 1 yawning once or twice during assessment 2 yawning three or more times during assessment 4 yawning several times/minute
Pupil size 0 pupils pinned or normal size for room light 1 pupils possibly larger than normal for room light 2 pupils moderately dilated 5 pupils so dilated that only the rim of the iris is visible	**Anxiety or Irritability** 0 none 1 patient reports increasing irritability or anxiousness 2 patient obviously irritable or anxious 4 patient so irritable or anxious that participation in the assessment is difficult
Bone or Joint aches *If patient was having pain previously, only the additional component attributed to opiates withdrawal is scored* 0 not present 1 mild diffuse discomfort 2 patient reports severe diffuse aching of joints/muscles 4 patient is rubbing joints or muscles and is unable to sit still because of discomfort	**Gooseflesh skin** 0 skin is smooth 3 piloerection of skin can be felt or hairs standing up on arms 5 prominent piloerection
Runny nose or tearing *Not accounted for by cold symptoms or allergies* 0 not present 1 nasal stuffiness or unusually moist eyes 2 nose running or tearing 4 nose constantly running or tears streaming down cheeks	Total Score _____ The total score is the sum of all 11 items Initials of person completing assessment: _____

Score: 5-12 = mild, 13-24 = moderate, 25-36 = moderately severe, more than 36 = severe withdrawal

This version may be copied and used clinically.

Source: Wesson, D. R., & Ling, W. (2003). The Clinical Opiate Withdrawal Scale (COWS). *J Psychoactive Drugs, 35*(2), 253-9.

41

41

Clinical Opiate Withdrawal Scale (COWS)

- Methadone—Hospitalized, OTP, very limited other licensed OP
- Buprenorphine—Hospitalized, Recent HHS Practice Guideline change to Notice of Intent, Waivered MD/DO/PA/NP, OTP
- Symptomatic Meds, e.g., Clonidine, NSAIDS, Imodium, B/Zs
- 72 Hour Rule: Dispense Only

Table 2. Medication Treatment for Opioid Withdrawal.*

Protocol	Examples	Effects and Comments
Medication		
Opioid agonists	Methadone (20 to 35 mg daily) or buprenorphine (4 to 16 mg daily), tapered over several days or weeks	Withdrawal symptoms are decreased in severity. Methadone and other opioid agonists are currently restricted to inpatient settings or licensed programs; buprenorphine is now approved by the FDA for this purpose.
Nonopioid drugs	Clonidine (0.2 mg 3 times daily) or lofexidine (0.2 mg twice daily), administered for approximately 10 days for heroin and 14 days for methadone	Withdrawal symptoms are decreased in severity. Lofexidine is less likely to produce hypotension but is not currently approved by the FDA for this purpose.
Rapid and ultra-rapid detoxification	Protocols include a variety of medications: opioid antagonists (naloxone or naltrexone), clonidine, sedatives, antiemetic agents, analgesics, anesthetics	Withdrawal is precipitated with an opioid antagonist, and symptoms are managed with a variety of adjuvant medications. Patients are awake or lightly sedated for rapid detoxification; they are under heavy sedation or general anesthesia for ultra-rapid detoxification. Both methods require special training, equipment, or both. Research on efficacy is limited.

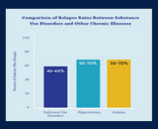
* FDA denotes Food and Drug Administration.

42

42

Opioid Use Disorder Treatment Outcome*

Methadone Maintenance	50 – 80%
Buprenorphine-Naloxone Maintenance	40 – 70%**
Naltrexone Maintenance (oral, depot)	10 – 20%, 20-60%***
"Drug Free" (no pharmacotherapy)	5 – 20%
Short-term Detoxification (any mode) (limited data)	5 – 20%



Methadone and Buprenorphine maintenance treatment reduces overdose risk by 37-86%

>350,000 in OTPs on methadone and est. >800,000 on buprenorphine

Kreek 1996, 2001, 2003, 2006, Krupitsky 2011, Fudala 2003, Weiss 2011, Woody 2008, Mattick 2009, Lee 2016+2017, CSAT

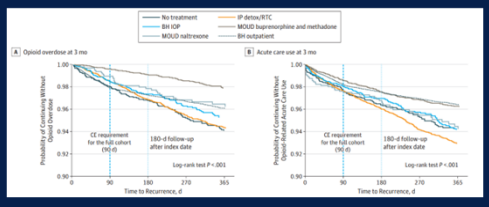
43

Access to Treatment



44

Access to Treatment



Wakeman et al. JAMA 2020

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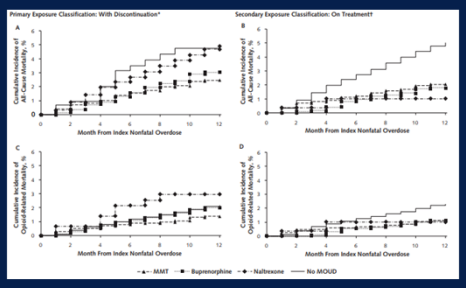
Access to Treatment



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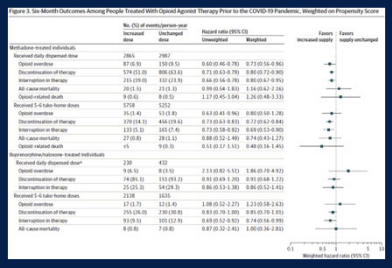
COVID and OUD Treatment Outcomes



No statistically significant increases in opioid-related overdoses over 6 months

47

Buprenorphine

Onset of action 30-60min

Peak effect 90-100min, half-life 24-42 hr

Metabolism via CYP 3A4 isoenzyme

- Those on CYP 3A4 inhibitors (azole, antifungals, macrolide antibiotics, and HIV protease inhibitors) should be closely monitored, and dose adjustments may need to be made
- Those on CYP 3A4 inducers (phenobarbital, carbamazepine, phenytoin, and rifampin) should also be monitored, and dose adjustments may need to be made

Can alter liver enzymes

- Liver function should be monitored periodically depending upon any recent symptoms or history of hepatitis
- Consider dose reduction or transition to mono formulation if ≥3x upper limit of normal

Pregnancy

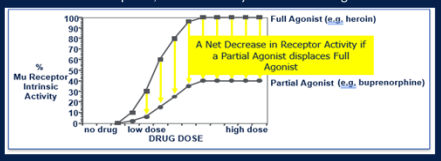
- **MOTHER study**, mono (without naloxone) formulation, reduced morphine/hospitalization/NAS

48

Buprenorphine

Multiple FDA Approved Formulations for OUD: SL film or tablet, monthly SQ, 6-month implant

- Partial agonist of the μ-opioid receptor and antagonist of the κ-opioid receptor.
  - *High affinity* for μ-opioid receptor
    - Competes with other opioids and inhibits their effects
  - *Slow dissociation* from μ-opiate receptor
    - Prolonged therapeutic effect
- At low doses, acts as an agonist; at high doses or in patients dependent on high doses of chronic opioids, it has the ability to act as an antagonist.



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Induction

Opiate Withdrawal Symptoms

- 6-18 hrs after last use of short-acting opioids (heroin, oxycodone), or 24-48 hrs after longer-acting opioids (methadone)
- Clinical Opiate Withdrawal Scale (COWS) score of ≥8-10

Day 1: Start with buprenorphine (+/-naloxone) 2-4 mg SL

- Consider additional 2-4mg after 1-2 hrs if continued elevation of COWS and no precipitated withdrawal
- May consider additional 2-4 mg 6 hrs later if significant OWS persist
- FDA Approved Total Day 1 dose 8 mg, but may clinically increase dose further based on persistent OWS

Day 2: Provide total day 1 dose (routinely given as single dose)

- May increase by 4mg twice daily for ongoing symptoms (8 mg total)
- Total Day 2 dose 16 mg

Adjuvant medications:

- Clonazepam 0.5 to 1mg tid prn, Clonidine 0.1 to 0.2mg q4 prn, Trazadone 100mg qhs prn, NSAIDS, Antiemetics/GI (promethazine 25mg IM, loperamide 4mg PO, octreotide 50 mcg SQ), IVF

Initiated at-home with physician instructions, during hospitalizations, or ED assessments

50

Naltrexone

Antagonist of the μ-opioid receptor

- Withdrawal treatment for those with physical dependence
- POC toxicology
- Induction protocol

Oral formulation FDA approved 1984

- Once daily, 3xweek alternative
- Low adherence limits use to highly motivated populations Comish 1997, Roth 1997

Long-acting injectable formulation (naltrexone-XR), FDA approved for OUD in 2010, *Preferred Formulation*

- More effective than placebo Comer 2006, Krupitsky 2011, Tiihonen 2012
- More effective than treatment as usual in criminal justice population Lee 2016
- Lower medical/surgical related hospitalizations but not overall healthcare utilization found in those in criminal justice system as compared to TAU. Lee 2018
- Non-inferior to buprenorphine, when randomization occurred after opioid detoxification or those successfully inducted onto XR-NTX. Tanum 2017, Lee 2018
- Reported ODs in studies is low, however most did not report how overdose events were measured particularly those lost to follow-up.
  - *Given high dropout rates and known OD risk of interrupted antagonist treatment, rigorous evaluation and reporting of fatal/nonfatal ODs remains needed.* Jarvis 2018

51

When Treating Fentanyl OUD

	Methadone	Buprenorphine	Naltrexone-XR
Initiation	Same day	1-3 days, to minimize risk of precipitated withdrawal	7-14 days for opioid detoxification
Induction withdrawal risk	Low Residual withdrawal may persist during dose titration	Moderate Precipitated withdrawal may last 1-2 days during the induction	Moderate Precipitated withdrawal if given before completion of detoxification Protracted withdrawal may persist 1-2 wks post-induction
Time to full therapeutic dose	2-3 weeks, or longer	2-3 days, or longer	1-day post-administration
Potential to decrease craving	High Dose-related full agonist effect	Moderate Ceiling on the agonist effect (usually at 24-32 mg/d dose)	Variable Mechanism of anti-craving effect poorly understood
Blocking potential	Low	Moderate	High

52

Abuse and Overdose Potential

Buprenorphine has limited abuse potential (epidemiological, human laboratory studies show)

- Relatively low compared to other opioids

Diversion and illicit use of analgesic form (by injection)

Overdose risk low

- Partial μ-OR agonist results in limited CNS and respiratory depression in those with physical dependence
- Risk higher with combined abuse of other sedatives e.g., benzodiazepine
- Deaths more associated with mono formulations dissolved and injected with concurrent benzodiazepine use

53

Induction

Opiate Withdrawal Symptoms

- 6-18 hrs after last use of short-acting opioids (heroin, oxycodone), or 24-48 hrs after longer-acting opioids (methadone)
- Clinical Opiate Withdrawal Scale (COWS) score of ≥8-10
- Toxicology testing:

	Minutes	Hours	Days	Weeks	Months
Blood					
Breath					
Oral Fluid					
Urine					
Sweat					
Hair					

54

Induction

Day 1: Start with buprenorphine (+/-naloxone) 2-4 mg SL
- Consider additional 2-4mg after 1-2 hrs if continued elevation of COWS and no precipitated withdrawal
- May consider additional 2-4 mg 2-4 hrs later if OWS persist
- Total Day 1 dose 8-12 mg

Day 2: Provide total day 1 dose (routinely given as single dose)
- Consider additional 2-4mg increase for ongoing symptoms
- Eval 2-4 hours later and consider additional 2-4 mg for ongoing symptoms
- Total Day 2 dose 16 mg

Low/Micro Dosing Inductions: Typically utilize 0.5mg initial dose while patient continues on full opioid agonist. Slow titration to maintenance doses with d/c of full opioid agonists.

Adjuvant medications:
- Clonazepam 0.5 to 1mg tid prn, Clonidine 0.1 to 0.2mg q4 prn, Trazadone 100mg qhs prn, NSAIDS, Antiemetics/GI (promethazine 25mg IM, loperamide 4mg PO, octreotide 50 mcg SQ), IVF

55

Induction Continued

- Typically initiated for outpatients at-home with physician instructions and availability, and during hospitalizations or ED assessments.
- May be carried out using either Bup/Nal or Bup mono, dependent upon the physician's judgment.
  - Bup/Nal commonly utilized but may consider bup mono formulation for those pregnant, severe liver disease, allergic rxn.

56

56

ED Initiated Buprenorphine Treatment

- Similar to other routine ED-based interventions for medical conditions
  - Buprenorphine induction acutely stabilizes and serves to initiate treatment of OUD
  - Facilitate linkage to community-based providers of OBAT
- From 2009 and 2013, 329 randomized to Screening + Referral, SBIRT, or SBIRT + bup induction in ED and appt for OBAT within 72hrs.
  - At 30 days
    - Increased engagement in addiction treatment: 37%, 45%, 78% (p<.001)
    - Decreased illicit opioid use in past 7 days: 2.3 days, 2.4 days, 0.9 days (p<.001)
  - At 2 months
    - Increased engagement in addiction treatment: 43%, 47%, 74% (p<.001)
    - Decreased illicit opioid use in past 7 days: 1.8 days, 2.0 days, 1.1 days (p=.04)

D'Onofrio 2015, 2017

57

57

Buprenorphine

- Extended-release monthly injection, FDA approved 2017, available 2018
  - Monthly subcutaneous (initial 300mg x 2, followed by maintenance 100mg).
  - Pt initially inducted onto once daily buprenorphine of 8-24mg for 7-10 days.
  - Compared to placebo, increased opi neg tox or self-reported opi use and higher proportion without any evidence of illicit opioid use. (FDA report 2017)

Transdermal and parenteral analgesic formulations not approved for OUD, only pain

58

58

Buprenorphine

- Long-acting subdermal implant, FDA approved 2016
  - Low, steady state dose for 6 months
  - Intended for use only after clinical stability on a daily dose of 8mg or less.
  - 4 approx. 1-inch-long implants requiring a minor surgical procedure for both insertion and removal.
  - Requires completion of in-person training.
  - Non-inferior percentage of urine samples negative for opioids, with favorable findings complete abstinence and time to first use of illicit opioids at 24 weeks compared to SL buprenorphine of 8mg or less.

Rosenthal 2016

59

59

Naltrexone

- Long-acting, competitive, non-selective opioid-antagonist with highest affinity to mu-opioid receptors.
- Metabolism via CYP450
- Excretion predominately urine (53-79%), partial feces. 2% excreted unchanged
- Active metabolite 6-beta-naltrexol
- Half-life 4 hours for naltrexone and 13 hours for 6-beta-naltrexol
- High doses may be associated with hepatic toxicity, contraindicated if elev transaminases, no known hepatic toxicity at standard doses

60

60

Naltrexone

- Oral formulation FDA approved 1984
  - Once daily, 3xweek alternative
  - Low adherence limits use to highly motivated populations (Cornish 1997, Roth 1997)
- Completion of withdrawal treatment must precede naltrexone treatment for those with current physical dependence
- POC toxicology
- Consider induction protocol prior to naltrexone initiation (Sigmon 2012)

61

61

Naltrexone

Long-acting injectable formulation (naltrexone-XR), FDA approved for OUD in 2010

- More effective than placebo Comer 2006, Krupitsky 2011, Tiihonen 2012
- More effective than treatment as usual in criminal justice population Lee 2016
- Lower medical/surgical related hospitalizations but not overall healthcare utilization found in those in criminal justice system as compared to TAU. Lee 2018
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- While the number of reported OD in studies to date is low, most studies did not report clearly how overdose events were measured, particularly in those lost to follow-up.
  - Given high dropout rates and known OD risk of interrupted/stopping treatment, rigorous evaluation and reporting of fatal/nonfatal ODs remains needed. Jarvis 2018

62

62

Naltrexone - XR

Initial Readiness Assessment

- Vital signs, urine toxicology (screen for all opioids including, buprenorphine, oxycodone and methadone), recent opioid use history, pregnancy test, assess for contraindications, e.g., active pain requiring opioids

Last Opioid Use ≥14 days

- IF: Good evidence of opioid abstinence in past 2 weeks, no withdrawal symptoms, and opioid-negative toxicology.
- THEN: Proceed with the XR-naltrexone injection.

XR-Naltrexone: A Step-by-Step Guide, PCSS 2017 63

63

Naltrexone - XR

Last Opioid Use 8-13 days ago, evaluate for withdrawal using COWS

- If COWS >4 treat withdrawal with adjunctive medication and reevaluate in 1-2 days.
- If COWS ≤4 AND opioid-negative toxicology, perform naloxone challenge. If negative, proceed with the XR-naltrexone injection. If positive, adjunctive medication and reevaluate in 1-2 days.

Last Opioid Use ≤7 days

- Patient may still be physically dependent even with opioid-negative toxicology.
- Treat withdrawal with adjunctive medication and postpone evaluation until at least 7 days of no opioid use (See USE within 8-13 days).
- In case of daily opioid use, recommend cessation and conduct buprenorphine-assisted withdrawal management.

XR-Naltrexone: A Step-by-Step Guide, PCSS 2017 64

64

Naltrexone / Naltrexone Challenge Test

Naloxone (IM) Challenge Procedure

- Obtain baseline COWS, if 4 or less proceed with the challenge
- Administer naloxone 0.4 mg (1 cc) IM to deltoid and observe for 20 minutes.
- If no change in COWS administer additional 0.8 mg (2 cc) to the other deltoid and monitor for additional 20 minutes
- Test is considered positive if there is a COWS increase of 2 or more from the pre-injection score

Naltrexone (PO) Challenge Procedure

- Obtain baseline COWS; if 4 or less proceed with the challenge
- Administer naltrexone 25 mg p.o. and observe for 90 minutes
- Test is considered positive if there is a COWS increase of 2 or more

XR-Naltrexone: A Step-by-Step Guide, PCSS 2017 65

65

Naltrexone - XR

Buprenorphine-assisted Withdrawal Management for Naltrexone-XR Initiation

- Wait until the patient is in withdrawal (COWS > 8) and administer buprenorphine (4 mg bid on Day 1)
- Administer adjunctive medications as needed to alleviate residual withdrawal
- Continue adjunctive medication for at least 7 days after the last day of buprenorphine
- Perform naloxone/naltrexone challenge before administering XR-naltrexone

XR-Naltrexone: A Step-by-Step Guide, PCSS 2017 66

66

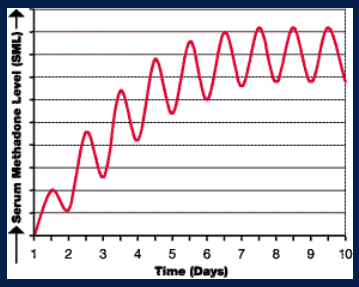
Methadone

- Approved by FDA 1972 for opioid dependence
- Mu opioid receptor agonist and NMDA antagonist (reduces development of tolerance)
- 2 enantiomers in equal amounts
  - *l (R)* active, *d (S)* inactive
  - Rapidly absorbed orally with detectable plasma levels at 30min but has a delayed onset of action with peak levels at 2-4 hours with sustained levels for 24 hours.
- Metabolized by CYP450 – several isoforms:
- CYP2D6 – may explain group who need very high doses
- Excreted in urine and feces
  - Avoids accumulation and reduces risk of toxicity for those with renal or liver dysfunction
- Half-life 24-36 hrs but may range from 4-91 hrs

67

67

Steady State



68

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Methadone

- 2006 Black Box Warning – risk of QTc prolongation and possibly torsades de pointes/polymorphic VT, dose dependent
- Common side effects: ***constipation, diaphoresis, to a lesser extent sexual dysfunction***
- Safety profile well established including during pregnancy
- ***Beware Opioid Conversion Tables!***
- ***Serum Level*** – clinical presentation should direct dosing decisions but SML can serve as aid
  - Peak level drawn 2-4 hours after dosing
  - Trough level drawn prior to daily dosing ~24hrs
  - Peak SML less than twice trough

69

69

Methadone

1. **Initial dose** 10-20mg PO (50% dose IM), 20mg eliminates severe withdrawal (not routinely recommended to exceed 30mg in first 24 hours)
2. **Craving** reduced by increasing methadone dose by 5-10mg q three to seven days (80-120mg or greater)
3. **"Blocking dose"** (often 80-120mg or greater): tolerance that inhibits the euphoric high

After stabilization, methadone and buprenorphine do not produce euphoria or sedation.

ASAM 2017, 2015, SAMHSA TIP 63

70

70

The Basics for all OTPs

- Comprehensive Assessments
- Treatment Plans
- Toxicology Testing
- Diversion Control
- Broadening of MAT options from methadone to incorporation of buprenorphine, etc.
- Attendance schedule for medication dispensing
- Guest Medication
- Confidentiality, 42 CFR Part 2
- Regulatory Oversight

71

71

Medication and Treatment Setting – Selection Considerations

- Abstinence to Harm Reduction Continuum
- Chronic Pain or foreseeable need for opioid analgesia
- Pregnant or planning pregnancy
- Recent Overdose or high risk for overdose behavior
- Medical and Psychiatric Co-occurring Disorders
- Diversion Risk
- Additional substance use disorders
- Alternatives

72

72

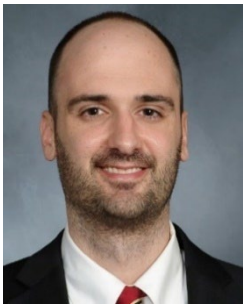
Tobacco Use Disorder: Trends and Treatment Friday, July 22
11:30 am – 12:15 pm CT

While the prevalence of tobacco use is decreasing, smoking still accounts for 20% of all U.S. deaths. This session will review the prevalence and trends of tobacco use, tobacco use disorder, and related co-morbidities. Participants will learn about the different evidence-based treatment options for tobacco use disorder and unique challenges to smoking cessation for special populations.

Learning Objective:

- After this session, learners will be able to: Explain changing trends in nicotine use and evidence-based strategies for prevention and treatment.

Faculty Presenter



Jonathan Avery, MD
Director of Addiction Psychiatry
Weill Cornell Medical College

Dr. Avery is currently the Director of Addiction Psychiatry and an Associate Professor of Clinical Psychiatry at Weill Cornell Medical College and New York-Presbyterian Hospital. In addition to his clinical work, Dr. Avery teaches addiction psychiatry to the Weill Cornell medical students and residents of New York-Presbyterian Hospital. He has been published on a broad variety of topics in psychiatry, including papers on subjects ranging from clinician attitudes towards patients to how to use buprenorphine. He is the founder of the Addiction Stigma Institute that studies stigma towards individuals with substance use disorders and creates novel interventions to improve these stigmatizing attitudes. He was on the editorial board for the DSM-5 Clinical Cases book and is the editor of the books Co-occurring Mental Illness and Substance Use Disorders: A Guide to Diagnosis and Treatment and The Stigma of Addiction: An Essential Guide. He has won numerous awards for his clinical and academic work, including the American Board of Psychiatry and Neurology Faculty Innovation in Education Award and the Outstanding Faculty Member Award from the New York County Psychiatric Society.

TOBACCO

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Weill Cornell Medical College

1

The ASAM Review Course of Addiction Medicine

July 2022

Financial Disclosures

Jonathan Avery, MD
None

2

History

- Native American tribes cultivated and used tobacco for many different purposes for thousands of years before the arrival of the Europeans. [1-2]
- Tobacco became an important economic influence in the British American colonies and the early United States. [1-2]
- The World Health Organization estimates that 1/3 adults smoke, and because tobacco use is on the rise in developing countries, it is one of the few causes of death that is increasing. (CDC, 2005) [3]
- Nicotine and the reinforcing sensory stimulation associated with tobacco use are responsive for the compulsive use of tobacco in the form of cigarettes, bidis, cigars, pipes, snuff, chewing tobacco, etc.

3

Epidemiology of Tobacco

- Prevalence has declined in the US from 42% in 1965 to 14% in 2017 [4,5]
- Men are more likely to be smokers than women (15.8% vs. 12.2%) [6]
- >16 million Americans have smoking-related disease
- Accounts for 20% of coronary-artery disease [7]

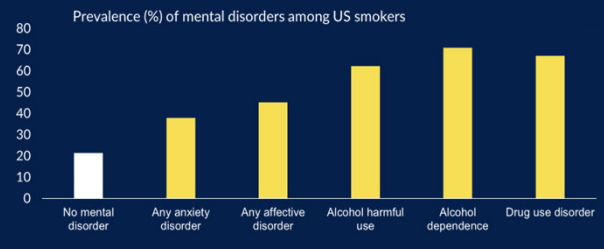
4

Morbidity and Mortality

- Leading cause of preventable death in the United States, accounting for about **440,000 premature deaths annually** [8]
  - **150K from CV disease**
  - **150K from cancer**
  - **150K from non-malignant pulmonary disease**
- Lost years of life: [9]
  - adult men: 13.2 yrs
  - adult women: 14.5 yrs

5

Epidemiology



[10] - Lawrence et al., 2009

6

Compounds in Tobacco Smoke

An estimated 4,800 compounds in tobacco smoke, including 11 proven human carcinogens [11]

Gases [12]

- Carbon monoxide
- Hydrogen cyanide
- Ammonia
- Benzene
- Formaldehyde

Particles [12]

- Nicotine
- Nitrosamines
- Lead
- Cadmium
- Polonium-120

Nicotine is the addictive component of tobacco products, but it does NOT cause the ill health effects of tobacco use.

7

Health Consequences

- Smokers die 10 years earlier than non-smokers on average
- Cancer: oral cavity, pharynx, larynx, bladder, esophagus, cervix, kidney, lung, pancreas, stomach, liver, bowel, acute myeloid leukemia [13]
- Cardiovascular disease, DM type II [14]
- COPD, Asthma [15]
- Osteoporosis, cataracts and macular degeneration, early menopause, erectile dysfunction, gastric and duodenal ulcer disease, skin aging, periodontal disease [16]

8

Tobacco Associated Problems

- Barrier to Recovery
- Financial Hardships
- More Employment Difficulties
- More Housing Difficulties
- Poorer Mental Health
- More Relapse to Drugs and Alcohol
- Social Stigma
- Poorer Appearance
- More Fires in Home

9

Public Health Interventions [17]

- Anti-smoking advertisements
- Increasing taxes
- Age-restrictions
- Tobacco-free laws and policies
- Support for cessation

10

Pharmacology of Nicotine

- Naturally occurring alkaloid [3]
- Triggers the release of a variety of neuroactive hormones
- Acts as a nicotinic acetylcholine receptor (nAChR) agonist [3]
- Stimulant-like effect in the CNS: enhances concentration, alertness, arousal [3]
- Increase of dopamine in brain's reward circuitry [18]
- Enters the CNS in rapidly after inhalation [19]
- Rapid effect on CNS contributes to reinforcement and dependence

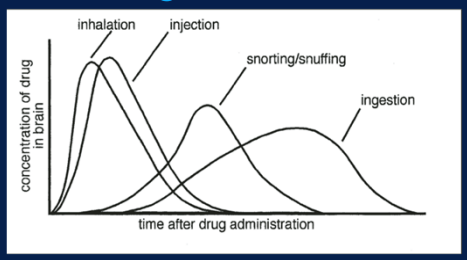
11

Routes of Use

- Nicotine and reinforcing sensory stimulation associated are responsible for the compulsive use of tobacco [20-23]
- Method of administration modifies the addictive potential associated with use [24]
- Compulsive use increases with rapid administration: smoking/vaping >> dermal patch, chewing

12

Smoking is the Fastest Route of Drug Administration



13

Nicotine

- Reaches the brain 20 seconds after inhalation + gradually increases occupancy of the nAChRs **over minutes** [19]
- Smoking 1 cigarette leads to significant occupancy of alpha4beta2 containing nAChRs **for >3 hrs** [19]
- The initial relatively rapid rate of rise of nicotine occurs within minutes, though levels of nicotine-bound receptors continue to rise slowly/are maintained for hours [19]
  - Rapid onset = allows smokers to control nicotine intake (by # of puffs, intensity of puffs, depth of inhalation)

14

Pharmacology of Nicotine

- Half-life is 2 hours [25-26]
- Accumulation in various tissues throughout the body during the day [27]
- Continue to be release from tissues for 6-8 hours after smoking ceases during sleep [25-26]
- Metabolized in the liver via cytochrome P450 enzymes [26]
- Major metabolite is cotinine [26]
- Crosses placenta and is found is breast milk [27]

15

Pharmacology

- Undergoes 1st pass metabolism [26]
- Oral bioavailability is 45% [26]
- Poorly absorbed from stomach 2/2 acidity of gastric fluid, but well absorbed in small intestine 2/2 alkaline environment [26]
- Renal clearance accounts for 2% to 35% (about 10%) of total nicotine clearance [28]
- Nicotine obtained via tobacco reaches high initial concentrations in arterial blood and lungs
  - Nicotine is then distributed to brain, storage adipose, muscle tissue from arterial blood
  - Avg steady-state concentration in body tissue is 2.6x that of the blood [26]

16

Pharmacology

- Once absorbed in bloodstream, nicotine has a volume of distribution of about 180 liters, with less than 5% of it binding to plasma proteins [26]
- Crosses placenta freely
- Found in the amniotic fluid and in the umbilical cord blood of neonates
- Found in breast milk at concentrations approximately 2x those found in blood

17

Sex and Race on Metabolism

- Women metabolize nicotine faster than men, 2/2 estrogen effect on CYP2A6 [29]
  - Even faster during pregnancy
- Related to CYP2A6 gene variants, African Americans obtain on average 30% more nicotine per cigarette, and they clear nicotine and cotinine more slowly than Caucasians. [30]
- Chinese American have a lower nicotine intake per cigarette, and slower metabolism (vs. Caucasians or Hispanics) 2/2 having a higher prevalence of CYP2A6 alleles (associated with slow metabolism) [31-32]
  - Suggest why Chinese American smokers have lower rates of lung cancer than either African Americans or Caucasians [31-32]

18

Biochemical Assessment

- Blood, salivary, and plasma cotinine can be used [33,34]
  - others include expired breath CO, blood carboxyhemoglobin, + plasma/salivary thiocyanate concentrations
- 16-hr ½ life of cotinine makes it useful as a plasma and salivary marker of nicotine intake [35]
- The gold standard for estimating daily nicotine intake from tobacco use is the sum of nicotine and its metabolites in urine. [36]
- Measurement of the minor tobacco alkaloids anabasine and anatabine in urine can be used as a biomarker of tobacco use in individuals who are using nicotine medications. [37]

19

Drug Interactions from Tobacco Smoke

- Affects the pharmacokinetics or pharmacodynamic mechanisms
  - absorption, distribution, metabolism, or elimination
  - potentially causing **altered response or toxicity**
- Accelerates metabolism of many drugs, esp. those metabolize by CYP1A2 [38]
- Might increase CYP2E1 and inhibit CYP2A6 enzymatic activity [38]
- When smokes discontinue abruptly (i.e., when hospitalized) doses of such meds may need to be lowered to avoid toxicity [38]

20

Drug Interactions from Tobacco Smoke

Drugs that may have a decreased effect due to induction of CYP1A2 by tobacco smoke: [39]

- **Caffeine**
- **Clozapine**
- **Olanzapine**
- **Haloperidol**
- **Chlorpromazine**
- **Fluvoxamine**
- **Theophyline**

21

Quitting Smoking Effects on CYP1A2

- Risk for medication toxicity
- May ↑ levels acutely
- Consider dose adjustment
- Clozapine toxicity
  - Seizures
- Reduce caffeine intake

- **Nicotine (or NRT) Does Not** Change Medication Levels
- Nicotine metabolized by **CYP2A6**

22

Pharmacodynamic Interactions: OCPs

- Alter the expected response or action of a drug
- Combined OCPs (estrogen + progestin) w/ smoking is very important
  - Increased risk of serious cardiovascular effects (stroke, MI, thromboembolism) [40]
- Recommended that OCPs are **contraindicated** in women > 35 yrs old AND are a heavy smoker (>15cigs/day) [40]

23

Pharmacodynamic Interactions

- Appear to enhance the procoagulant effect of **estrogens** [41]
- Results in *less sedation* from benzodiazepines and *less analgesia* from some opioids [42]
- Impairs the therapeutic effects of histamine H2 -receptor antagonists used in treating **peptic ulcers** [42]
- Cutaneous vasoconstriction by nicotine can slow the rate of absorption of subcutaneously administered **insulin** [43]

24

Pharmacologic Actions: CNS [44,45]

- Acts on sympathetic system: increase BP, HR, cardiac output, and cutaneous vasoconstriction
- Causes muscle relaxation via simulation of Renshaw cells, via inhibition of motor neurons
- Higher doses: produces ganglionic stimulation -> releases adrenal catecholamines
- Very high doses cause hypotension, slowing of HR

25

Psychoactive Effects

- Causes arousal, relaxation, enhancement of mood/attention/rxn time [46-48]
- Results in relief of withdrawal sx of dependent smokers, rather than direct-enhancing effects [46-48]
  - Smokers may need regular doses of nicotine to feel normal rather than to enhance their capabilities/cognitive effects
- Psychoactive effects dependent on route, speed of administration, environmental factors
  - Subjective effects depend on pre-drug state, level of activity, genetics, history, expectancy [49,50]

26

Genetic Predisposition

- GWAS: single nucleotide polymorphisms on... [51]
  - **CHRNA5-CHRNA3- CHRNB4 nAChR** subunit cluster on chromosome 15q25
    - associated w/ # of cigs/day, serum cotinine levels, lung cancer, peripheral artery disease, chronic lung dz
  - **CYP2A6**, primary enzyme responsible for the oxidation of nicotine and cotinine. [52-53]
    - Reduced function variants of the gene are associated with smoking fewer cigarettes per day and a lower risk of lung cancer
  - **Cell adhesion and ECM molecules** [54]
    - neural plasticity and learning are key determinants of individual differences in vulnerability to drug addictions
- Twin studies: [55,56]
  - monozygotic twins are more similar than dizygotic twins w/ smoking behavior
  - ½ of the total variance (28% to 84%) in smoking behavior are due to genetic effects
  - There is genetic influence on nicotine withdrawal symptoms as well

27

Psychiatric Comorbidities

- **37%** of those w/ a mental illness are smokers vs. **20%** of smokers who do not carry a mental illness. [57]
- Those with Sz, depression, ADHD have higher prevalence of cig smoking compared with general population

Sz: 70-88% are smokers [58]
- Diminished sensory gating to repeated stimuli, smoking can relieve negative sx (blunted affect, emotional withdrawal, lack of spontaneity)
- Smokers experience fewer side effects from antipsychotics (2/2 stimulating effects of nicotine), which might contribute to greater prevalence of smoking in ppl w/ Sz

ADHD: 40% are smokers [59]
- Associated with early initiation of regular cigarette smoking, even after controlling for confounding variables such as socioeconomic status, IQ, and psychiatric comorbidity
- transdermal patches improve the attentional symptoms of ADHD

28

Best Measure of Nicotine Dependence Severity

Heaviness of Smoking Index

- AM (upon awakening) Time to First Cigarette (TTFC) [46]
  - < 30 minutes = moderate
  - < 5 minutes = severe
- Implications for Treatment Outcome
- Need for Medications
- Implications for Dose

29

Tobacco Tolerance

- Causes effects of individual cigarettes tend to lessen throughout the day.
- Overnight abstinence allows considerable, but not complete, re-sensitization of nicotinic receptors to non-desensitized states
- Populations of nAChR subtypes that begin to change as other molecular mechanisms involving neuroadaptations come into play after days and weeks of tobacco use [47,48]

30

Tobacco Cravings

- Powerfully conditioned cues = cravings become associated with everyday events, become linked with mood
- High rates of relapse: [49]
  - Population surveys find that up to 75% of adults who smoke want to stop, but only 1/3 try to stop, and only 3% of those do without aids
  - 50% of individuals w/ past hx of MI, COPD, and other sequelae of smoking, revert to cig smoking days or weeks after leaving the hospital

31

Tobacco Withdrawal

- Nicotine use is continued to avoid the negative sx associated with withdrawal (known as negative reinforcement)
- Majority of withdrawal sx are distressing, but not life-threatening
- Acute withdrawal sxs reach max. Intensity 24 - 48 hrs after cessation and then gradually diminish over weeks [50,51]
- Extrahypothalamic corticotropin-releasing factor (CRF-1) contributes to negative affect during withdrawal [52]
  - CRF released in central amygdala following nicotine withdrawal -> produces anxiety behavior
  - Pharmacological blockade of CRF1 receptors inhibits the anxiogenic effects in withdrawal

32

Tobacco Withdrawal Symptoms [53]

Emerges hours after last cigarette

Can last up to (4) weeks

- Depressed mood
- Insomnia
- Irritability, frustration or anger
- Anxiety
- Difficulty concentrating
- Restlessness
- Increased appetite or weight gain

33

MAO and Nicotine Dependence

- Cig smoking is associated w/ inhibition of monoamine oxidase A + B [54-56]
  - Not caused by nicotine itself, but the condensation products of acetaldehyde with biogenic amines, such as benzoquinones, 2-naphthylamine, harman, + others
- MAOs = metabolize catecholamines, including dopamine
- Rat studies: [57]
  - Pre-tx with MAO-I makes nicotine more rewarding and increases the likelihood and rate of acquisition of nicotine self-administration
  - Important consideration: anti-depressants also inhibit MAOs, therefore smoking-induced inhibition of MAO might contribute to the *perceived benefit* of smoking by some depressed patients

34

Systemic Toxicities

- **Tobacco smoke** = carries volatile and particulate phases that contain substances that are primarily responsible for the human morbidity and mortality [58]
  - Volatile = 500 compounds (nitrogen, CO, carbon dioxide, ammonia, hydrogen cyanide, and benzene)
  - Particulates = >3,500 (alkaloids nornicotine, anabasine, anatabine, myosmine, nicotyrine, and nicotine)
- **Tar:** contains many carcinogens, including polynuclear aromatic hydrocarbons, N-nitrosamines, and aromatic amines [58]

35

Toxicities: Pulmonary

- Causes imbalance between proteolytic and antiproteolytic forces in the lung [59]
- Heightens airway responsiveness
- High rates of COPD in tobacco smokers linked to: [59]
  - Exposure to tar, nitrogen oxides, hydrogen cyanide, and volatile aldehydes
  - These exposures results in oxidative stress and generation of superoxide radicals and hydrogen peroxide and lung damage
- Smokers with DNA damage from polynuclear aromatic hydrocarbons in the WBCs are 3x more likely to be dz with lung cancer than smokers with lower concentrations [60]

36

Toxicities: Cardiovascular

- **Increased risk** of CV toxicity [61]
  - Related to exposure to oxidant chemicals and CO, + hydrogen cyanide, carbon disulfide, cadmium, and zinc
  - CO reduces oxygen delivery to the heart
  - Oxidant chemicals are primarily responsible for endothelial dysfunction, platelet activation, thrombosis, and coronary vasoconstriction

37

Other Effects and Toxicities

- **For women:** [62]
  - lower levels of estrogen
  - earlier menopause
  - increased risk of osteoporosis
  - alkaloids in tobacco smoke decrease estrogen formation by inhibiting an aromatase enzyme in granulosa cells or placental tissue
- **Skin changes:** [63]
  - yellow staining of fingers
  - vasospasm and obliteration of small skin vessels
  - precancerous and squamous cell carcinomas on the lips and oral mucosa
  - enhanced facial skin wrinkling

38

Predictors of Abstinence [64-66]

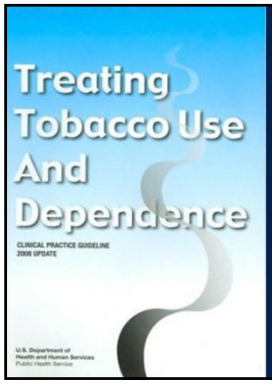
- Lower level of dependence
- Higher socioeconomic status: education, insured
- Older age
- Male gender
- No behavioral health comorbidity
- Fewer smokers in social networks
- Quit in first 7 days / # days quit
- **Use of cessation treatment**

39

Why is it so hard to quit?

- Smoking a drug is highly addicting
- **Treatment options are limited**
  - Few medication types
  - Limited (brief) counseling support
  - No levels of care
- **Utilization of treatment is poor**
  - Most don't use counseling
  - Medications-too low dose, not enough time

40



Brief Intervention

2As and R (Ask, Advise, and Refer)

- Do you use Tobacco?
  - How much? What kinds?
  - Document tobacco use at visits
- How do you feel about quitting?
- Can I give your name to someone to get more information?

41

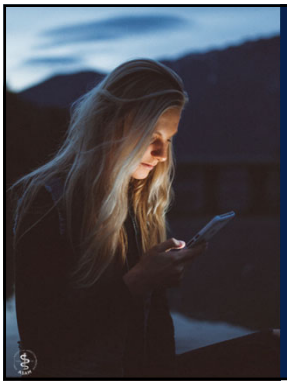
Why Not Quit For One Day?

Or Six Hours?

- Save money
- Try free NRT
- Feel better
- Master a new skill
- Try other coping
- Not go outside in bad weather



42



Quitline
1-800-QUIT-NOW

- Telephone counseling
- Toll-free / state funded
- Assessment
- 4 follow-up calls
- Good for transportation issues
- Scheduled calls from tobacco specialist
- Success rate in smoking cessation
- Many languages, free NRT

43

Pharmacologic Treatments

- First line (FDA-approved): [67]
  - Nicotine replacement therapy (NRT)
  - Bupropion
  - Varenicline
- Second line (not FDA-approved): [67]
  - Nortriptyline

Counseling + Medications= Best Treatment Plan

44

Nicotine Medications [68]

- 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

45

Oral Nicotine Spray [69,70]

- Approved Sept 2019; OTC (Canada & Europe)
- Faster absorption
- 1-2 to two sprays (140/ container; each 1mg nic). Max 4/ hour, 64/ day (most 10-14/ day)
- No evidence product abuse
- Real world and efficacy trials 2X placebo
- Contains tiny amount ethanol. At 64 doses/d, <one tsp (~ 5ml) of wine with 12% alcohol)
- Side effects: hiccups, headache, nausea, mouth/throat irritation, dyspepsia, dizziness

46

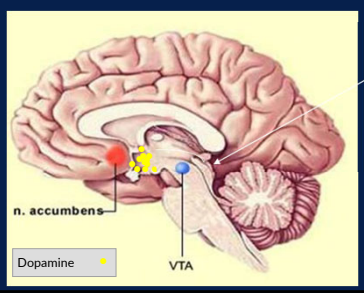
Combination Therapies [71,72]

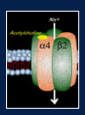
- Improve abstinence rates
- Decrease withdrawal
- Well tolerated

	OR
Patch + gum or spray	**1.9** (1.3-2.7)
Patch + bupropion	**1.3** (1.0-1.85)

47

Varenicline: A selective a4B2 nicotinic receptor partial agonist



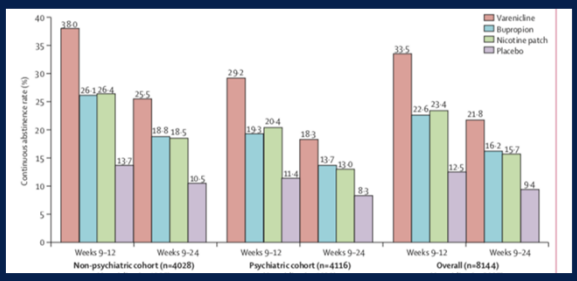


Partial Agonist [73]
Partially stimulates receptor
Some dopamine release
Prevents withdrawal

"Antagonist"
Blocks nicotine binding

48

EAGLES study [74]



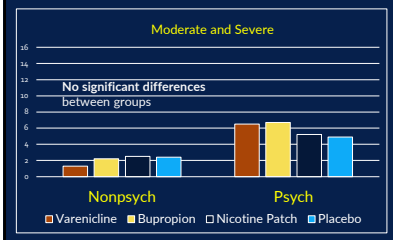
49

Results from 2013 Cochrane Review [75]

Medication	Versus Placebo OR (95% Credible Interval)	Versus other medication OR (95% Credible Interval)
NRT	1.84 (1.71-1.99)	Combination outperformed single formulations
Bupropion	1.82 (1.60-2.06)	NRT: 0.99 (0.86-1.13)
Varenicline	2.88 (2.40-3.47)	Nicotine patches: 1.51 (1.22-1.87) Nicotine gums: 1.72 (1.38-2.13) Other NRT: 1.42 (1.12-1.79) Combination NRT: 1.06 (0.75-1.48)

50

Neuropsychiatric Adverse Events



FDA Approves **Removal** of Boxed Warning Regarding Serious Neuropsychiatric Events from CHANTIX® (varenicline) Labeling [90]

Based on a U.S. Food and Drug Administration (FDA) review of a large clinical trial that we required the drug companies to conduct, we have determined the risk of serious side effects on mood, behavior, or thinking with the stop-smoking medicines Chantix (varenicline) and Zyban (bupropion) is lower than previously suspected. The results of the trial confirm that the benefits of stopping smoking outweigh the risks of these medicines

(December 2016) [76]

Varenicline ↑ Side effects: Nausea, insomnia, abnormal dreams, headaches

51

Summary of Treatment

- All tobacco users should be offered treatment to try to stop
- Counseling + Medications = Best treatment plan
- Better outcomes
  - Education to use medication effectively
  - Combinations of NRT or Varenicline as first line
  - Longer durations (6 mos) effective for relapse prevention

52

Gender Issues

- In any given quit-attempt, women are less likely to successfully quit smoking than men [77]
  - Negative affect/ depression/ socioeconomic issues/ less likely meds
- Women in placebo group less likely than men to quit
- Varenicline was more effective than TNP for women (OR=1.51; 95%CI=0.12,2.05; p=0.007) but not men (OR=0.92; 95%CI=0.65,1.31; p=0.64). [78]
- The advantage of varenicline over bupropion SR and TN is greater for women than men
- Clinical trials and epidemiologic studies

53

Combination Therapy Of Varenicline and Bupropion

- Meta Analysis: 4 RCTs with 1230 smokers.
- Compared with varenicline, combination treatment with varenicline and bupropion could significantly improve the abstinence rate at the end of treatment (RR 1.153, 95% CI 1.019 to 1.305, P = 0.024). [79]

54

Combination Therapy Of Varenicline and Bupropion

- The benefit existed at 6 months follow-up (RR 1.231, 95% CI 1.017 to 1.490, P = 0.033), and was mainly concentrated in highly dependent smokers (RR 1.631, 95% CI 1.290 to 2.061, P < 0.001) and heavy smokers (RR 1.515, 95% CI1.226 to 1.873, P < 0.001) [79]
- For safety outcomes, the combination treatment was associated with more anxiety (RR 1.717, 95% CI 1.176 to 2.505,P = 0.005) and insomnia (RR 1.268, 95% CI 1.076 to 1.494, P = 0.005) symptoms vs varenicline monotherapy. [79]

55

Medication Interaction Tobacco Treatments [79]

Nicotine	CYP_2A6	None
Bupropion	CYP_2B6 CYP_2D6 inhibitor	Many
Varenicline	Excreted in urine	None

56

Special Population: Pregnancy

In 2016, 7.2% of US women who gave birth smoked cigarettes during pregnancy. [80]

Smoking in pregnancy ↑ risks of:

- Spontaneous pregnancy loss
- Placenta abruption
- Ectopic pregnancy
- Placenta previa
- Preterm rupture of membranes
- Low birth weight
- Sudden infant death syndrome
- Low milk volume production and shorter duration of lactation

57

Special Population: Pregnancy [80]

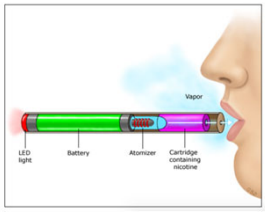
- More likely to quit smoking in pregnancy
- Initiate intervention before conception
- Continue interventions during prenatal care visits
- Counseling is the first-line of treatment
- NRT or bupropion are acceptable second-line options (data lacking but supported by experts comities)
- Limited information regarding safety of varenicline

58

Special Population: Adolescents

- Early intervention is important
- Counseling is the first-line of treatment
- If counseling fails NRT is an acceptable options
- Insufficient data regarding bupropion and varenicline

59



E-Cigarettes

- Battery-operated device
- Heats liquid containing nicotine
- Creates vapor that is inhaled
- Entered US market in 2006 [81]

Image from Rigotti N. et al. E cigarette chapter. Uptodte 2019.

60

Chemicals in Electronic Cigarettes [82,83]

- Propylene glycol, ethylene glycol and glycerin
- Nicotine
- Flavors (sweeteners)
- Most chemicals found at or below 1% of levels in tobacco smoke, and far below safety limits for occupational exposure.
  - Metals (cadmium, chromium, lead, manganese and nickel)
  - Formaldehyde
  - Other carcinogens
  - Solvents
  - Tobacco alkaloids

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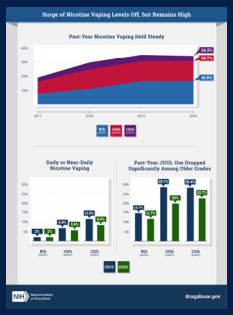



62

Vaping and Youth

- "Vaping" = nicotine, marijuana, just flavoring since 2017
- Increased dramatically in 2018 [84]
  - Nicotine vaping largest ↑ ever recorded for any substance in the 44 years of MTF (2017-2018)
    - 30% of 12th graders vaping nicotine (↑ 11%)
  - Marijuana vaping increased (1-3%) among 8, 10, 12th graders 4%, 12% and 13%
  - Just flavoring increased among 8, 10, 12th graders
    - 15%, 25% and 26%

63

Association of Electronic Cigarette Use With Subsequent Initiation of Tobacco Cigarettes in US Youths

- Prospective cohort (6123=N), mean age 13.4
- Cigarette use at wave 3 was higher among prior e-cigarette users (20.5%) vs no prior tobacco (3.8%). [85]
- Prior e-cigarette use was associated with more than 4 times the odds of ever cigarette use (odds ratio, 4.09; 95%CI, 2.97-5.63) and nearly 3 times the odds of current cigarette use (odds ratio, 2.75; 95%CI, 1.60-4.73) vs no prior tobacco use.
- Supports that e-cigarette use is associated with increased risk for cigarette initiation and use, particularly among low-risk youths.

64

E-cigarette or Vaping Associated Lung Injury (EVALI) [86]

- Lung injury cases associated with e-cigarette, or vaping, to CDC
- Vitamin E acetate -bronchoalveolar lavage (BAL) fluid samples
- Thickening agent in THC-containing e-cigarette
- Most (86%) involved THC products; some (11%) nicotine alone
- 70% of patients are male; 79% are < 35 years old

65

E-Cigarettes

- More frequently used by Americans than other FDA-approved treatments for smoking cessation
- Safer than combustible products, but long-term effects are unknown
- Controversial whether e-cigarette should be used as a first line of treatment, although this is common in UK

66

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72

Cannabis Use Disorder: Science, Trends, and Clinical Implications Friday, July 22
12:15 pm – 1:00 pm CT

Cannabis is becoming more prevalent as states enact new legislation surrounding legal use. This session starts with a broad overview of the epidemiology of cannabis use disorder and the changes in public perception of cannabis use. Participants will understand the physiologic effects of cannabis and how to identify cannabis use disorder. Presenters will end with a thorough review of the options and challenges for treatment of cannabis use disorder.

Learning Objective:

- After this session, learners will be able to: Describe the neurobiological impacts, epidemiological trends, and clinical considerations for cannabis use.

Faculty Presenter



Ruchi M. Fitzgerald, MD, FAAFP
Assistant Professor, Associate Program Director of Addiction Medicine Fellowship Service Chief, Addiction Medicine Consult Service
Rush University/PCC Community Wellness

Ruchi M. Fitzgerald, MD, FAAFP is a family physician and an addiction medicine physician. She is the Service Chief of Inpatient Addiction Medicine at PCC Community Wellness, a federally qualified health center system that serves the West Side of Chicago. Dr. Fitzgerald is an Assistant Professor in the Departments of Family Medicine and Psychiatry and Behavioral Sciences at Rush University, as well as the Associate Program Director of the Rush Addiction Medicine Fellowship. She completed the addiction medicine fellowship at Rush University in 2020. She is a graduate of the University of Michigan Medical School and completed her family medicine residency in 2012 with the Montana Family Medicine Residency. Dr. Fitzgerald developed an interest in provision of care for underserved populations and those affected by substance use disorders during her residency. Dr. Fitzgerald also has extensive experience in telemedicine. During her fellowship, Dr. Fitzgerald worked with the addiction medicine faculty to create RISE-MD (Rush Integrative Substance Use Disorder Education for Medical Doctors), an educational initiative in Rush Medical College that focuses on eliminating stigma while promoting evidence-based treatment of substance use disorders in the next generation of physicians. She has worked with the American Society of Addiction Medicine and the Illinois Society of Addiction Medicine on key advocacy and policy initiatives related to substance use disorders. Dr. Fitzgerald is also an active member of the Federation of State Physician Health Programs and is an advocate for physician health and wellness.

Cannabis Use Disorder

Ruchi Fitzgerald, MD FAAFP
Associate Program Director , Rush Addiction Medicine Fellowship
Assistant Professor, Family Medicine/Psychiatry & Behavioral Sciences, Rush University

1

The ASAM Review Course of Addiction Medicine

July 2022

Financial Disclosures



Ruchi Fitzgerald, MD FAAFP
No Disclosures

2

Learning Objectives

- Name the different formulations of cannabis that impact individuals today.
- Review medications that have an evidence base for treating cannabis withdrawal and cannabis use disorder.
- Increase knowledge about current epidemiological trends in cannabis use in the United States.

3

Epidemiology

4

Cannabis Use/Misuse

- In 2015, estimated 22.2 million Americans – 8.9% of the population aged 12 years or older had used cannabis in the preceding month.
- In 2016, 22.5% of 12th grade students smoked cannabis in the preceding month.
- Cannabis use peaks in the late teens to early 20s, then declines.

5

Increased Risk for Use Disorder

- 9% of people who use marijuana may develop 'pre-substance dependence.'
- The risk increases to 17% in people who start using in adolescence.
- The risk increases to 25 to 50% in people who are daily users (most of whom started using marijuana early in adolescence).

6

Cannabis Basics

- The cannabis plant has 104 cannabinoids; only 2 (THC and CBD) have been extensively studied for potential therapeutic applications.
- THC is the most psychoactive component – (***inhaled, ingested***)
- CBD is postulated to have other mechanisms of action (anti-inflammatory, analgesic, etc.).
- Synthetic cannabinoids vs. Endocannabinoids – they are structurally similar.

7

Cannabis Plant





8



Natural, Plant - Derived Cannabinoids

Most common preparations:

*Marijuana

*Hashish

*Hash Oil

THC Concentrations vary—

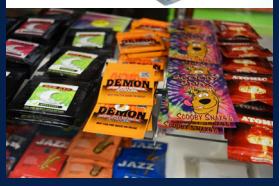
For example, extraction of THC with butane ("dabs") can contain up to 90% THC.

9

Synthetic Cannabinoids

- Higher affinity for cannabinoid receptors than THC
- Have active metabolites that prolong their durations of action
- Increased potential for toxicity
- "Spice" or "K2"
- Not detected on standard UDS





10

Synthetic Cannabinoids





Seely et al. Spice Drugs are More than Harmless Herbal Blends: A Review of the Pharmacology and Toxicology of Synthetic Cannabinoids. Prog Neuropsychopharmacol Biol Psychiatry. 2012;39(2):234-243.
Spice/K2, Synthetic Marijuana. dea.gov.

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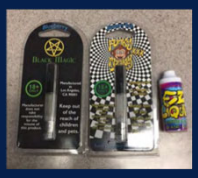
Synthetic Cannabinoids



2019 National Drug Threat Assessment. US Department of Justice Drug Enforcement Administration. December 2019.

12

Cannabinoid Receptor Neurobiology

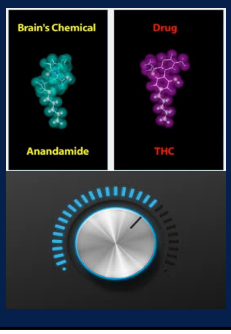
13

The Cannabinoid System

- THC activates the CB1 and CB2 cannabinoid receptors:
  - CB1 has high density in cerebellum, basal ganglia, hippocampus, cerebral cortex. *G protein mediated system.*
  - CB1 has low density in the brainstem, hence low risk of respiratory depression.
  - CB2 is found in spleen, hematopoietic cell lines, mast cells.

14

9-tetrahydrocannabinol (THC)



- Primary psychoactive constituent
- Endocannabinoid system
  - Brain development
- Mimics anandamide
  - Dial down neuron activity

15

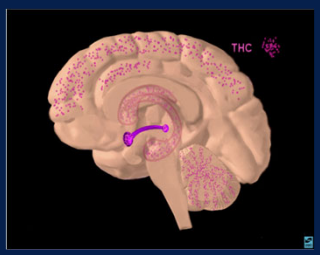
Cannabinoids (CBs)

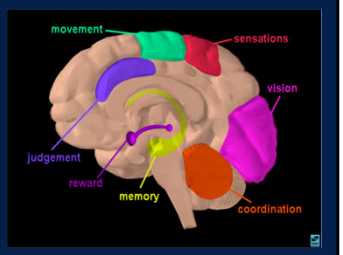
- > 400 chemicals, ↓ neurotransmitter release
- Natural CBs
  - Endogenous – Anandamide ("bliss")
  - Exogenous – Sativa plant (marijuana)
    - Tetrahydrocannabinol (THC) – psychoactive
    - Cannabidiol (CBD) – no effect in brain



16

CB1 Receptor Locations in the Brain





17

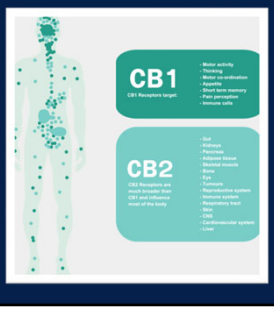
The Endocannabinoid System

- Endocannabinoids (AEA, 2-AG) are naturally produced by the body.
- They bind to cannabinoid receptors.
- Endocannabinoids bind both CB 1 and CB 2.
- Endocannabinoids function as "retrograde messengers."

18

Cannabinoid Receptors

- CB1 – CNS site of CB binding
  - Memory, learning, problem solving, coordination
  - Activated by anandamide, other CBs
  - Modulates neurotransmitters
- CB2 – immune cells outside CNS
  - Anti-inflammatory effects



19

Cannabis Intoxication

- *Desired effects*: relaxation, euphoria, slowed time perception, altered sensory perception, increased appetite.
- *Undesired effects*: impaired concentration, anterograde amnesia, anxiety, panic attacks, paranoia, derealization/depersonalization, psychosis (visual – not auditory hallucinations).

20

	Seizures		Tachycardia
	Agitation	*Cardiovascular*	Hypertension
Central Nervous System	Irritation		Chest pain
	Loss of consciousness		Cardiac Ischemia
	Anxiety		
	Confusion	*Gastrointestinal*	Nausea
	Paranoia		Vomiting
Metabolic	Hypokalemia	*Autonomic*	Fever
	Hyperglycemia		Mydriasis
		Other	Conjunctivitis

Seely et al. Marijuana-based Drugs: Innovative Therapeutics or Designer Drugs of Abuse? Mol Interv. 2011;11(1):36-51.

21

Cannabis Withdrawal

- Reported by up to 1/3 of persons who use cannabis frequently.
- Cannabis withdrawal is recognized by the DSM 5.
- Clinical trials – show reduction of withdrawal symptoms with synthetic THC (dronabinol), nabilone, nabiximol, and gabapentin.

22

Cannabis Withdrawal

Causing distress & ≥ 3 of the following:

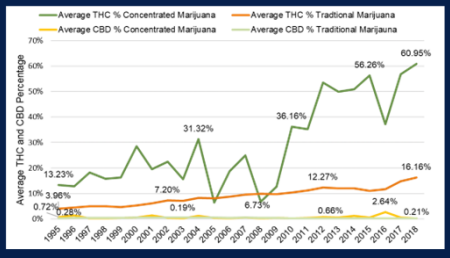
- Irritability
- Anxiety
- Sleep problems
- ↓ Appetite/weight loss
- Depressed Mood
- Restlessness

AND ≥ 1 of the following:

- Abdominal pain
- Sweating
- Shakiness/tremors
- Fever/chills
- Headache

23

THC Percent is Increasing



2019 National Drug Threat Assessment. US Department of Justice Drug Enforcement Administration. December 2019.

24

THC Potency is Increasing

- Up to 31 % in products
- Widespread availability of THC edibles (food and beverage products) and butane-extracted hash oil products ("dabs", "budder", "shatter", "wax")
- Rate of ED visits per 100,000 for cannabis-related adverse reactions has dramatically risen: 96.2 to 146.2 (2004 in 2011).

25

Routes of Administration

- Smoked:
  - Reaches the brain in minutes
  - Effects last 1 - 3 hours
  - Delivers significant amount of THC into the bloodstream

Smoked	*Vaporized*	*Eaten/Drunk*
Smoked in a pipe, bowl, cigarette	Inhaled through machine that converts active compounds into inhalable form	Consumed as ingredient in baked goods, candies, sodas
Rapid effects	Rapid effects	Takes time to reach brain, so effects are delayed

26

Routes of Administration

- Eating or drinking marijuana:
  - Takes ½ - 1 hour to have an effect
  - Effects last up to 4 hours
  - Delivers less THC into the bloodstream

Smoked	*Vaporized*	*Eaten/Drunk*
Smoked in a pipe, bowl, cigarette	Inhaled through machine that converts active compounds into inhalable form	Consumed as ingredient in baked goods, candies, sodas
Rapid effects	Rapid effects	Takes time to reach brain, so effects are delayed

27

Decreased Harm Perception: Adolescents

- 36% of teens think cannabis is harmless
  - 43% favor legalization
  - 80s: 15%
  - 90s-00s: 30%
- Harm perception lowest in 40 yrs
  - Often precedes ↑ prevalence

28

Special Populations and Cannabis

- Adolescents
- Pregnant persons

29

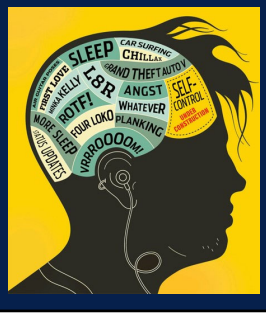
Rates ↑ Across Adolescence

- **Ever tried**
  - ~17% 8th graders
  - ~50%12th graders
- **Past year use**
  - 12% 8th graders
  - 35% 12th graders
- **Current use (past month)**
  - 7% 8th graders
  - 21% 12th graders
  - Surpasses current alcohol and tobacco use

30

Adolescent Brain

- May be vulnerable to the addictive nature of cannabis and neurotoxic effects, including development of psychiatric disorders.
- One study showed decline in IQ among cannabis users before the age of 18, with much less recovery of neuro-psych functioning.
- NSDUH data: risk for cannabis dependence is higher if use begins before age 16 (17% versus 4%)
- Most and latest change in areas of:
  - Reward and motivation
  - Cognition



31

Pregnancy

- THC crosses the placenta (also note effect of smoking)
- Endocannabinoid system plays a role in the control of brain maturation, particularly emotional responses
- Babies exposed to THC:
  - Neurological development effects
  - Reduction in fetal growth, also other negative effects on the infant

32

Pregnancy

- Children exposed to THC:
  - Problem-solving skills, memory, attention deficit
- THC-specific vs. associated environmental factors hard to sort out; ongoing debate and research.

33

Toxicology Testing

- Casual use:
  - Up to 10 days in urine
  - 50% positive in hair samples
- Heavy use:
  - Up to 30 days in urine
  - 85% positive in hair samples
- Measures THC
- Weight loss gives serial UTox spike
- Dronabinol gives positive test
- Passive inhalation gives negative test

34

Effects of Use

35

Neurocognitive Effects

- Short-term memory impairment
- Judgment impairment
- Motor coordination impairment

36

Impaired Cognition

- ↓ Ability to learn
- ↓ Attention, concentration
- ↓ Abstract reasoning and decision-making
- ↓ Memory

37

Physical Health

- Respiratory
  - ↓ Function
  - ↑ Infections
- ↑ Stroke/Temporary brain blood constriction

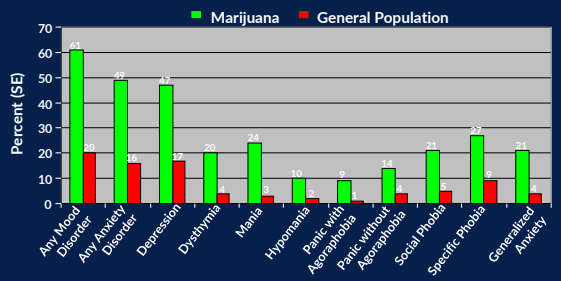
38

Psychiatric

- Anxiety
  - Acute THC → ↓ anxiety
  - Long-term THC → ↑ anxiety
- ↑ Depression
- ↑ Psychosis

39

Psychiatric Co-Morbidity



NESARC. 2005; slide courtesy of Dr. Frances Levin.

40

Diagnosis

41

Substance Use Disorder

In Same Year, ≥2 of:

- Tolerance
- Withdrawal
- Use more/longer
- Unable to ↓ use
- Use despite problems
- Craving
- Failed roles
- Hazardous use
- Social problems
- ↓ Activities
- Lots time use

42

Cognitive Effects

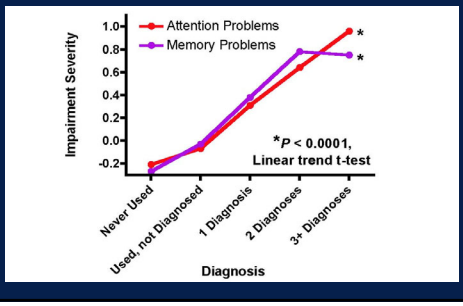
43

Residual Cognitive Effects

- Memory
  - Learning & retaining new information
- Attention and concentration
  - Response speed & variability
- Executive functioning
  - Working memory
  - Verbal fluency

44

Attention and Memory



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Likely Reversible with Abstinence

- Biological markers normalize ~4wks
  - CB receptor density in brain
  - Cortical blood volumes
- Especially in cognitive areas

46

Treatment

47

Treatment for CUD is Challenging

- Few evidence-based supported approaches
- ~ 50% achieve remission
- ~ 70% return to use
- No FDA-approved medications

48

Psychosocial Treatments

- Motivational Enhancement Therapy
- Cognitive Behavior Therapy
- Contingency Management
- Family-Based Programs

49

Medication for CUD

- N-acetylcysteine (NAC)
  - Amino acid derivative, OTC supplement
  - Restores normal glutamate activity
  - Pros: ↓ use in Non-Treatment Seeking adolescents, *not in adults*
  - Cons: did not ↓ craving

50

Pharmacologic Treatment Options

Medication	*Mechanism*	*Comments*	*Literature in Adolescents?*
Atomoxetine	Norepinephrine reuptake inhibitor	• No change in cannabis use • Worsened irritability and GI side effects	• Thurstone et al., 2010[7]
Bupropion	Norepinephrine reuptake inhibitor	• Exacerbated withdrawal (irritability, insomnia)	• Riggs, et al., 2013[8]
Buspirone	Serotonin partial agonist	• Conflicting evidence on cravings and irritability	--
Dronabinol	CB1 receptor agonist	• Reduced symptoms of withdrawal • Contains THC	--
Gabapentin	GABA modulation	• Decrease self-reported cannabis use • Reduced withdrawal symptoms	--
N-acetylcysteine	Correct glutamate dysregulation	• Decreased use in adolescents • Did not show same benefit in adults	• Gray et al., 2012[9]
Naltrexone	Mu-opioid receptor antagonist	• Enhanced subjective effects of cannabis • No change in frequency of cannabis use	--

51

N-acetylcysteine (NAC)

Risks	• Nausea/vomiting • Drowsiness/insomnia • Vivid reams • *Anaphylactoid reactions seen with IV admin, not PO*
Pharmacokinetics	• Bioavailability for oral: 9% • Metabolized to cysteine and glutathione • Half-life: ~ 18 hours

52

Gabapentin

Mechanism of Action	• Blocks alpha-2d subunit of the voltage-gated calcium channel which modulates GABA in the amygdala
Notes	• FDA approved for multiple indications, including partial seizures in ages 3-12
Doses	• Goal of ~1200mg/day Mason (2012) [10]: 50 cannabis-dependent adults (18-65 years old) • Gabapentin 1200mg vs placebo for 12 weeks • Titrated up to 300mg / 300mg / 600mg over the course of 4 days
Clinical benefit	• Increase in negative UDS • Decrease self-reported cannabis use • Reduction in withdrawal symptoms (mood disturbance, craving, and sleep disturbances)

53

Gabapentin

Risks	Well tolerated ☺ Headache, nausea, insomnia and depression

Pharmacokinetics	• Bioavailability: inversely proportional due to saturable absorption
	  • Immediate release
	  • 900mg/day: 60%
	  • 1200mg/day: 47%
	  • 3600mg/day: 33%
	  • 4800mg/day: 27%
	  • Extended release: increased with higher fat content
	• Half-life:
	  • ≤ 12 years old: 5hr
	  • > 12 years: 5-7hr
	  • **Longer in patients with decreased renal function**

54

CB1 Receptor Agonists

Cannabidiol (CBD) Epidiolex ®	Dronabinol (THC) Marinol® Syndros® Nabilone (THC) Cesamet®	Nabixmols (THC + CBD) Stavivex® *not FDA approved*






55

Medicinal Uses of Cannabis/Cannabinoids

- Dronabinol: FDA approved for treatment of anorexia associated with weight loss in patients with AIDS, chemotherapy-induced nausea/vomiting.
- Nabilone: FDA approved for treatment of chemotherapy-induced nausea/vomiting.
- Studies also ongoing re: effects on other disease states (epilepsy, MS).

56

Therapeutic Potential

- Pain (cancer, multiple sclerosis)
- Nausea (cancer)
- Loss of appetite and wasting (HIV/AIDS)
- Increased ocular pressure (glaucoma)
- Inflammation (rheumatoid arthritis, Crohn's disease, ulcerative colitis)
- Epilepsy

57

In Summary

Cannabis includes plants and synthetic cannabinoids.	Cannabis use is common, risk of a use disorder increases with earlier onset of use.	Cannabis contains more THC now than in the past.
Cannabis can affect cognition, but this is reversible in adults, impacts on adolescents less clear.	Most treatment is psychosocial, but several drug targets are being investigated.	

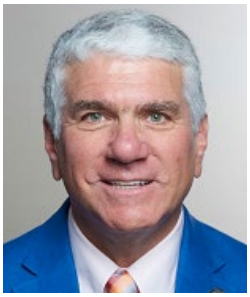
58

Interesting Cases with Audience Response System (ARS)

Friday, July 22
2:00 pm – 2:15 pm CT

Test your critical thinking and problem-solving skills while learning more about the complexities of addiction cases through this interactive session leveraging Audience Response System.

Faculty Presenter



Edwin A. Salsitz, MD, DFASAM
Unit Chief, Inpatient Rehabilitation
Mount Sinai Beth Israel
Icahn School of Medicine at Mount Sinai

Dr. Edwin A. Salsitz has been an attending physician in the Mount Sinai Beth Israel, Division of Chemical Dependency, New York City, since 1983, and is an Associate Clinical Professor of Psychiatry at the Mount Sinai School of Medicine. He is the principal investigator of the Methadone Medical Maintenance (office-based methadone maintenance) research project. Dr. Salsitz is certified in Addiction Medicine by the American Board of Preventive Medicine, as well as by the Board of Internal Medicine and Pulmonary Disease. He has published and lectures frequently on addiction medicine topics.

Dr. Salsitz is a course director for ASAM sponsored Buprenorphine and REMS Opioid trainings, and is a lead mentor in the PCSS-MAT mentoring program. He has co-chaired the ASAM Review Course, the ASAM Common Threads Course, the ASAM State of the Art course and is a reviewer for the Journal of Addiction Medicine and Drug and Alcohol Dependence. He is the chair of the ASAM REMS course on safe and effective prescribing of opioids. Dr. Salsitz was the Co-chair of the ASAM CME committee and Chair of the New York Society of Addiction Medicine CME and Education committee.
Dr. Salsitz is a member of the medical advisory panel, for the New York State Office of Alcohol and Substance Abuse Services. Dr. Salsitz is the recipient of the 2014 ASAM Annual Award, and the 2018 ASAM Annual Educator of the Year Award.

Stimulant Use Disorder: Trends and Treatment Friday, July 22
2:15 pm – 3:00 pm CT

While addiction treatment providers continue to fight the opioid overdose epidemic, there has been a growing resurgence in stimulant use. This session is designed to describe the methods of use, pharmacological effects, and molecular mechanisms of action for stimulant drugs, including cocaine, methamphetamine and newer "bath salts" cathinones. The presenter will also discuss clinical approaches for treating adverse effects and stimulant use disorders.

Learning Objective:

- After this session, learners will be able to: Explain the physiologic effects of stimulants, epidemiology of stimulant use, and emerging options for evidence-based treatment.

Faculty Presenter



Michael H. Baumann, PhD
Chief, Designer Drug Research Unit
IRP/NIDA/ NIH

Michael H. Baumann, Ph.D. is a Staff Scientist and Chief of the Designer Drug Research Unit (DDRU), at the Intramural Research Program (IRP) of the National Institute on Drug Abuse (NIDA) in Baltimore, Maryland. The DDRU collects, analyzes and disseminates the most up-to-date information about the pharmacology and toxicology of newly-emerging synthetic drugs of abuse (i.e., designer drugs), more formally known as new psychoactive substances (NPS). Working with partner organizations such as the Drug Enforcement Administration (DEA) and the National Drug Early Warning System (NDEWS), Dr. Baumann is kept informed about trends in the misuse of NPS. The DDRU has characterized the molecular mechanism of action and pharmacological effects for a diversity of NPS, including “bath salts” (synthetic stimulants), “spice” (synthetic cannabinoids) and synthetic opioids. Findings from the DDRU inform law enforcement personnel, health care workers, clinical toxicologists, forensic scientists, basic researchers, and policymakers who are involved in responding to the global spread of NPS and the associated public health risks.

STIMULANTS

Michael H. Baumann, Ph.D.

Designer Drug Research Unit (DDRU),
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1

The ASAM Review Course of Addiction Medicine
July 2022

Financial Disclosures

Michael H. Baumann, Ph.D.
No Disclosures

2

General Outline

- Cocaine
- Methamphetamine
- Ecstasy
- Bath Salts and RCs
- Summary

3

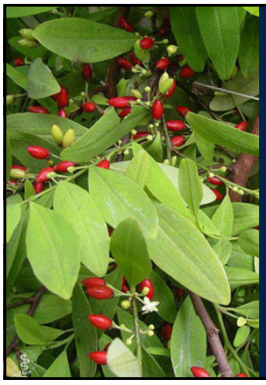
Topics Covered for Each Substance

- Drug Trafficking and Confiscation
- Formulations and Methods of Use
- Pharmacokinetics and Metabolism
- Desired and Adverse Effects
- Chronic and Withdrawal Effects
- Neurobiology
- Treatments

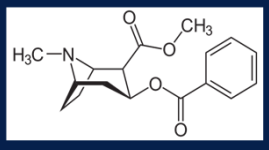
4

Cocaine

5



Cocaine is a Plant Based Alkaloid



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Andean Cocaine is Trafficked on a Global Scale



UNODC World Drug Report. 2020

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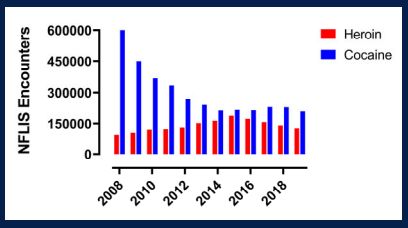
Cocaine Confiscation Remains Relatively Stable



DEA NFLIS, 2020

9

Formulations and Methods of Use

- Cocaine Free Base (i.e., Crack)
  - Smoking of free base "rock" using pipes
- Cocaine HCl
  - Intravenous injection of solutions using needle and syringe
  - Intranasal snorting of powder

10

Pharmacokinetics and Metabolism

- Pharmacokinetics
  - Smoked drug reaches brain within seconds
  - Intravenous drug reaches brain within seconds
  - Intranasal drug reaches brain within minutes
- Metabolism
  - Ester hydrolysis to benzoylecgonine
  - Ecgonine methyl ester

Cone, 1995

11

Rate Hypothesis of Drug Reward

- Smoked and Intravenous Routes
  - Faster rate of drug entry into the brain
  - Enhanced subjective and rewarding effects
- Intranasal and Oral Routes
  - Slower rate of drug entry into the brain
  - Reduced subjective and rewarding effects

12

Desired Effects

- Enhanced Mood and Euphoria
- Increased Attention and Alertness
- Decreased Need for Sleep
- Appetite Suppression
- Sexual Arousal

13

Adverse Effects

- Psychosis
- Tachycardia, Arrhythmias, Heart Attack
- Hypertension, Stroke
- Hyperthermia, Rhabdomyolysis
- Multisystem Organ Failure

14

Tolerance- Blunted Effects

- Acute Tachyphylaxis or "First Dose" Effect
  - Cardiovascular effects blunted
  - Euphoria and sexual arousal diminished
  - But no longer-term tolerance
- Anorexia

15

Sensitization- Enhanced Effects

- Seizures
- Psychosis
  - Paranoid delusions
  - Visual, auditory and tactile hallucinations
  - Virtually indistinguishable from schizophrenia
- Stereotypical Behaviors

16

Withdrawal Effects

- Anhedonia and Depressed Mood
- Increased Appetite
- Anergia and Fatigue
- Vivid or Unpleasant Dreams
- Insomnia or Hypersomnia

17

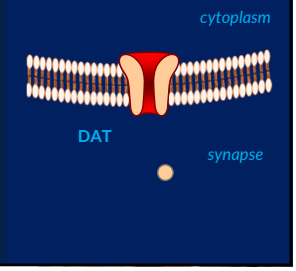
Molecular Sites of Action

- SLC6 Monoamine Transporters
  - Dopamine transporter (DAT)
  - Norepinephrine transporter (NET)
  - 5-HT transporter (SERT)
- Other sites
  - Sodium channels

18

DATs Mediate DA Uptake

- DATs are membrane proteins responsible for uptake of released dopamine (DA)
- Drugs that disrupt DAT function increase synaptic DA
- Increases in DA are rewarding



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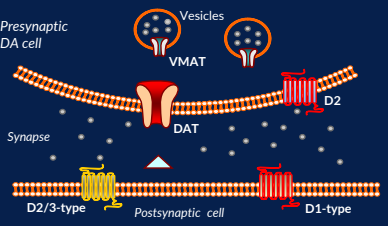
Cocaine is a DAT Blocker (DA Uptake Inhibitor)



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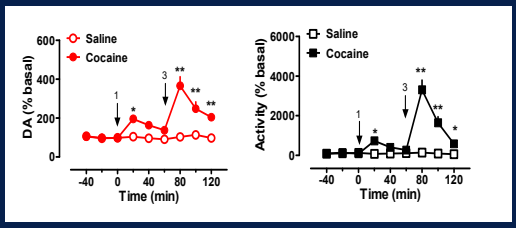
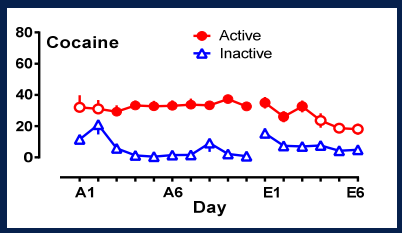
Cocaine Increases Extracellular DA in Rat Nucleus Accumbens



Baumann et al., 1994

21

Rats Will Readily Learn to Self-Administer Cocaine



Schindler et al., 2016

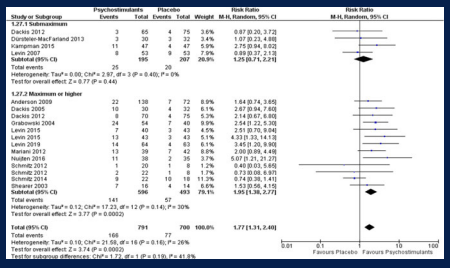
22

Treatment for Cocaine Dependence

- Pharmacotherapy
  - No FDA-approved medication for cocaine dependence
- Psychologically-Based Therapies
  - Cognitive Behavioral Therapy
  - Contingency Management
  - Group & Community Therapies

23

Stimulant Meds- Some Success



Tardelli et al. 2020

24

Methamphetamine

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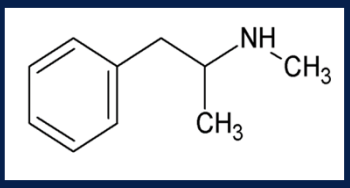
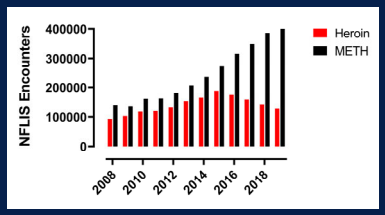
Methamphetamine is a Synthetic Amphetamine Analog





26

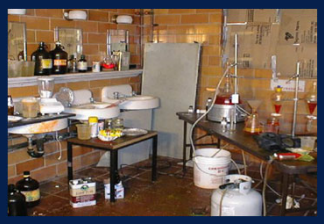
METH Confiscation is Increasing Dramatically in Recent Years



DEA NFLIS, 2020

27

Most METH is Now Trafficked by Mexican Cartels



DEA NFLIS, 2020

28

Formulations and Methods of Use

- Methamphetamine (i.e., Ice or Crystal)
  - Smoking using pipes
- Methamphetamine HCl
  - Intravenous injection of solutions using needle and syringe
  - Intranasal snorting of crystals

29

Pharmacokinetics and Metabolism

- Pharmacokinetics
  - Smoked drug reaches brain within seconds
  - Intravenous drug reaches brain within seconds
  - Intranasal drug reaches brain within minutes
- Metabolism
  - *N*-demethylation to form amphetamine (**bioactive**)
  - Hydroxylation to form inactive metabolites

30

Desired Effects

- Enhanced Mood and Euphoria
- Increased Attention and Alertness
- Decreased Need for Sleep
- Appetite Suppression
- Sexual Arousal

31

Adverse Effects

- Psychosis
- Arrhythmias, Palpitations, Heart Attack
- Hypertension, Stroke
- Hyperthermia, Rhabdomyolysis
- Multisystem Organ Failure

32



33

"METH Mouth"



34

Sensitization- Enhanced Effects

- Seizures
- Psychosis
  - Paranoid delusions
  - Visual, auditory and tactile hallucinations
  - Virtually indistinguishable from schizophrenia
- Stereotypical Behaviors

35

Withdrawal Effects

- Anhedonia and Depressed Mood
- Increased Appetite
- Anergia and Fatigue
- Vivid or Unpleasant Dreams
- Insomnia or Hypersomnia

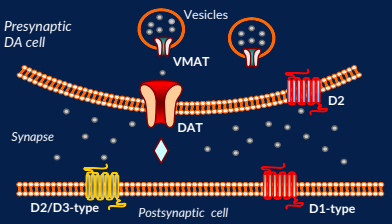
36

Molecular Sites of Action

- SLC6 Monoamine Transporters
  - Dopamine transporter (DAT)
  - Norepinephrine transporter (NET)
  - 5-HT transporter (SERT)
- Other sites
  - Vesicular Monoamine Transporter 2 (VMAT2)
  - Trace amine-associated receptors (TAAR1)

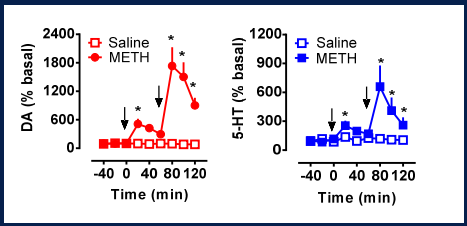
37

METH is a DAT substrate (DA releaser)



38

METH Increases Extracellular DA More Than 5-HT



Baumann et al., 2002

39

Cocaine vs Methamphetamine

COCAINE

Inhibits DAT-mediated reuptake of synaptic dopamine

METH

Inhibits DAT-mediated reuptake of synaptic dopamine

Evokes DAT-mediated release of dopamine

40

Cocaine vs Methamphetamine

COCAINE

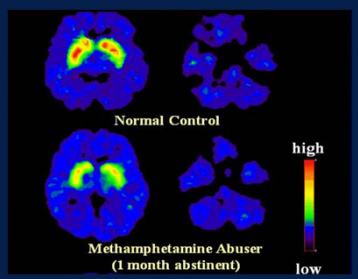
- Rapidly metabolized
- Effects last 1-2 hours
- Withdrawal lasts 1-2 days

METH

- Slowly metabolized
- Effects last 10-20 hours
- Withdrawal lasts many days

41

METH decreases DAT sites in brain



Volkow et al., 2001

42

Role of METH in Gay Subculture

1. METH intoxication
2. Decreased inhibitions and judgment
3. Increased sensation seeking and sexual arousal
4. Unsafe sexual practices
5. HIV transmission

Lee & Rawson, 2008

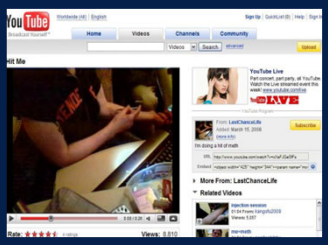
43

METH, Sex, and the Internet

- The Perfect Storm
- Sex, both virtual and real, both safe and unsafe, is only a click away
- Variable Intermittent Reinforcement

44

Internet Websites Foster Risky Behaviors





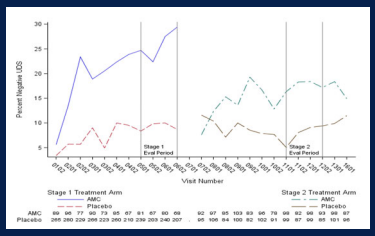
45

Treatment for METH Dependence

- Pharmacotherapy
  - No FDA-approved medication for METH dependence
- Psychologically-Based Therapies
  - Cognitive Behavioral Therapy
  - Group and Community Therapies
  - Twelve Step Programs

46

Bupropion + Naltrexone Reduce METH Use



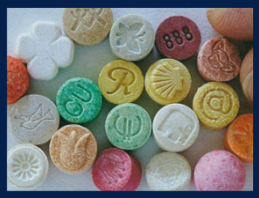
Trivedi et al. 2021

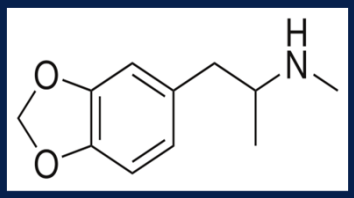
47

Ecstasy

48

Ecstasy (MDMA) is a Synthetic Club Drug

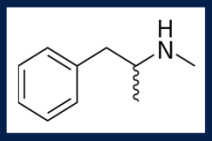




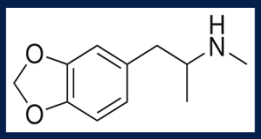
49

MDMA is a Ring-Substituted Amphetamine Analog

Methamphetamine



3,4-Methylenedioxy Methamphetamine (MDMA)



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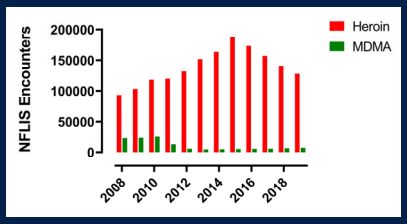
Confiscation of MDMA Remains Low Compared to Other Drugs



DEA NFLIS, 2020

51

Formulations and Methods of Use

- Powders, capsules and tablets
  - Oral ingestion of tablets most common
  - Some intranasal and intravenous use
- "Bumping" or repeated intermittent dosing
- "Stacking" or taking multiple doses at once
- Binge and crash cycling

52

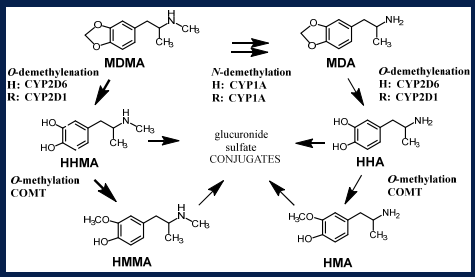
Pharmacokinetics And Metabolism

- Pharmacokinetics
  - Cmax reached within 2 h of oral ingestion
  - Non-linear drug accumulation at doses > 3 mg/kg
- Metabolism
  - *N*-demethylation to form MDA (**bioactive**)
  - *O*-demethylenation to form hydroxylated metabolites

de la Torre et al., 2004

53

MDMA Metabolism is Complex



Baumann et al., 2007

54

Desired Effects

- Combined effects of a stimulant and hallucinogen
  - Enhanced mood and energy
  - Heightened or altered sensory perception
- Feelings of empathy and closeness to others
- Cardiovascular stimulation
- Appetite suppression

55

Adverse Effects

- Psychosis
- Sympathetic Stimulation
  - Palpitations and heart attack
  - Hypertension
- 5-HT Syndrome
  - Hyperthermia and dehydration
  - Treat with hydration, cooling, and sedation
  - Avoid β blockers, which could exacerbate hypertension

56

Withdrawal

- Anhedonia and depressed mood
- Lethargy and fatigue for several days
- Sleep disturbances
- No indication for treatment

57

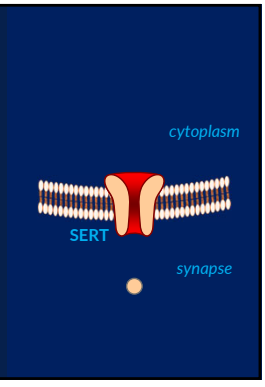
Molecular Sites of Action

- SLC6 Monoamine Transporters
  - 5-HT transporter (SERT)
  - Dopamine transporter (DAT)
  - Norepinephrine transporter (NET)
- Other sites
  - Vesicular Monoamine Transporter 2 (VMAT2)
  - 5-HT2A receptors

58

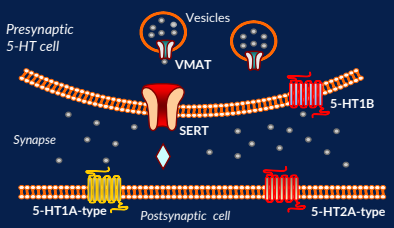
SERTs Mediate 5-HT Uptake

- SERTs are membrane proteins responsible for uptake of released 5-HT
- Drugs that disrupt SERT function increase synaptic 5-HT
- Increases in 5-HT are not rewarding (e.g., SSRIs)



59

MDMA is a SERT substrate (5-HT releaser)



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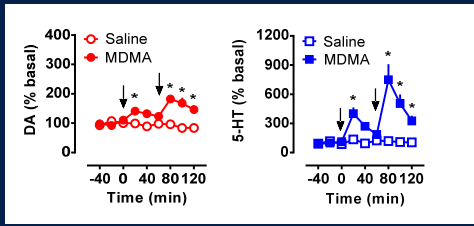
MDMA Increases Extracellular 5-HT more than DA



Baumann et al., 2008

61

Neurotoxic Potential

- MDMA acutely increases synaptic 5-HT
  - SERT-mediated 5-HT release (i.e., reverse transport)
- MDMA chronically impairs 5-HT neurons
  - Depletion of 5-HT stores
  - Inhibition of 5-HT synthesis
  - Loss of SERT sites in brain
- Neurotoxicity?

62

Bath Salts

63

Cathinone is a Plant-Based Alkaloid



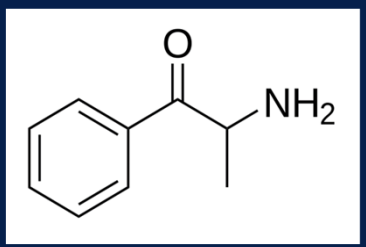
64

Khat Plant *Catha edulis*



65

Cathinone is β-Keto Amphetamine



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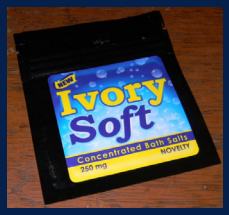
"Bath Salts" Products Contain Synthetic Cathinones



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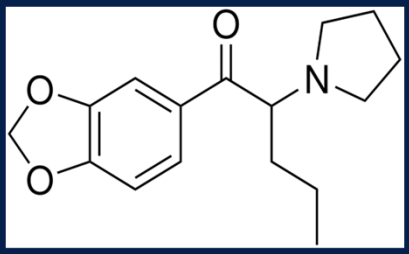
MDPV is an Analog of Pyrovalerone



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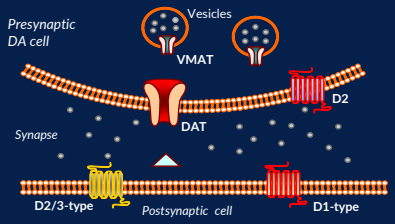
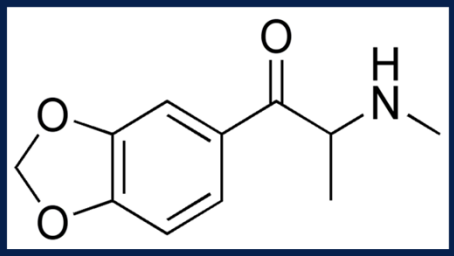
MDPV is a DAT Blocker (DA Uptake Inhibitor)



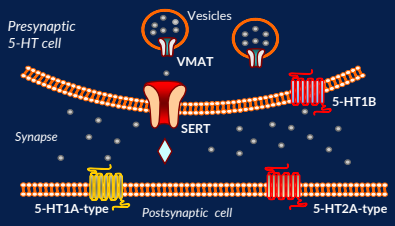
69

Methylone is β-Keto MDMA



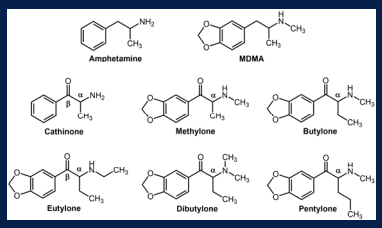
70

Methylone is a SERT substrate (5-HT releaser)



71

Methylone Analogs are now Appearing as Counterfeit MDMA



72

Summary

73

Overall Summary

1. Cocaine is the prototypical dopaminergic stimulant.
2. METH is a powerful stimulant due to its DAT-mediated dopamine release.
3. MDMA acts as a mild stimulant and hallucinogen due to its SERT-mediated 5-HT release.
4. MDPV is cocaine-like while methylone is MDMA-like.

74

Clinical Challenges

1. No FDA-approved medications for stimulant dependence, so treatment is psychosocially-based.
2. No specific antidotes for stimulant intoxication, so treatment is supportive.
3. Stimulant-induced deaths are increasing due to fentanyl co-administration: intentional or accidental?

75

Thank You

76

Other Classes of Drugs: Pharmacology and Epidemiology Friday, July 22
3:00 pm – 3:45 pm CT

Addiction treatment providers are often confronted with a wide array of substance use disorders. This session will cover a diverse group of substances including hallucinogens, dissociatives, inhalants, and steroids. Participants will learn the physiological effects, epidemiology, treatment options and notable examples for each drug class.

Learning Objective:

- After this session, learners will be able to: Identify other classes of drugs, their physiological impacts, and treatment considerations.

Faculty Presenter



Erin A. Zerbo, MD, FASAM
Director, Northern NJ Center of Excellence in Medication-Assisted Treatment
Rutgers New Jersey Medical School

Erin A. Zerbo, MD, FASAM, received her B.S. in Brain and Cognitive Sciences from the Massachusetts Institute of Technology in 2003, and her M.D. from New York University School of Medicine in 2007. She remained at NYU for a general psychiatry residency and a one-year addiction psychiatry fellowship, graduating in 2012. Since 2014, she has been an Assistant Professor in the Department of Psychiatry at Rutgers New Jersey Medical School and the Associate Director of Medical Student Education in Psychiatry. In addition to managing a large buprenorphine practice dedicated to Newark residents, she is also the director of the Northern New Jersey Center of Excellence in Medication-Assisted Treatment, a new statewide opioid training and education initiative.

Dr. Zerbo serves as the co-Chair of the Council on Education of the New Jersey Psychiatric Association, and she has published and lectured extensively in the field of addiction. Her primary interest is the treatment of substance use disorders in underserved and disadvantaged populations. She is a co-editor of the book "Pocket Guide to Addiction Assessment and Treatment" (APA, 2106), and the lead editor of "Becoming Mindful: Integrating Mindfulness into Your Psychiatric Practice" (APA, 2017).

Other Classes of Drugs

Erin Zerbo, MD

Associate Professor, Department of Psychiatry
Rutgers New Jersey Medical School
Newark, NJ

1

The ASAM Review Course of Addiction Medicine

July 2022

Financial Disclosures



Erin Zerbo, MD
No Disclosures

2

Learning Objectives

Identify other classes of drugs, their physiological impacts, and treatment considerations.

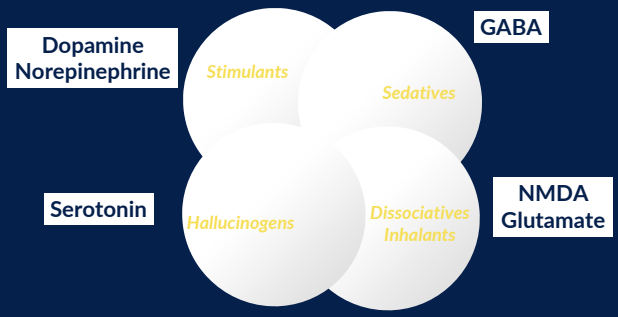
3

Presentation Outline



- Hallucinogens
- Dissociatives
- Inhalants
- Anabolic-Androgenic Steroids

4



5

Hallucinogens

6

Definition of Hallucinogens

- Produce alterations in thought, mood, and perception
- Produce minimal autonomic side effects or craving
- Fail to produce excessive stupor or central stimulation



7

“Illusionogen”

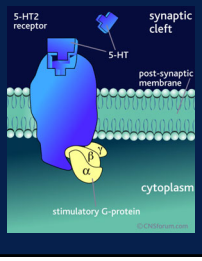


- Illusions = alteration or enhancement of existing sensory perception
- May be more accurate term
  - Reality testing is generally intact
  - Effect varies greatly with expectations and environment

8

Classical Hallucinogens (Serotonergic Hallucinogens)

- 5HT-2A agonists or partial agonists
- Fall within the group of chemical compounds called arylalkylamines
  - Not all are hallucinogenic
  - Stimulants
  - Empathogens



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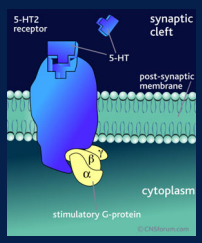
Classical Hallucinogens (Serotonergic Hallucinogens)

- 2 subclasses of arylalkylamines
  - Indolealkylamines (serotonin analogs)
    - Bind at multiple receptors (5HT-2A, 5HT-2B, 5HT-2C, 5HT-1A)
  - Phenylalkylamines (norepinephrine analogs)
    - Fairly selective for 5HT-2A



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Effects of Hallucinogens



Altered shapes and colors	Synesthesia	Alterations in mood (can be tension and anxiety)	Distorted sense of time
Difficulty expressing thoughts	Depersonalization	Dreamlike feeling	

11

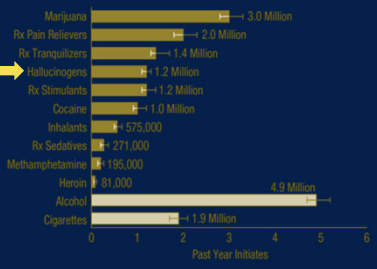
Effects of Hallucinogens Somatic



Dizziness	Weakness	Tremors	Nausea
Drowsiness	Paresthesias	Blurred Vision	

12

Numbers of Past Year Initiates of Substances Among People Aged 12 or Older: 2017 NSDUH



13

DMT

- DMT (N,N-Dimethyltryptamine)
  - Prototype of this subclass of indolealkylamines
    - Naturally occurring (plants, toad)
  - Rapid onset (<5 min), short duration of action (30 min)
    - Inhalation (smoking) or injection (rare)
    - Can be taken orally, but requires MAOI



DMT Crystals

14

Ayahuasca



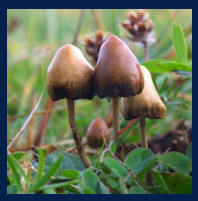


- Brew containing DMT, MAOIs, and other hallucinogens
- Used ceremonially in parts of the Amazon and in some Native American religions
  - Legalized for religious use among Native Americans in the US

15

Psilocybin

- Psilocybin → psilocin
  - Found as naturally occurring tryptamine in certain varieties of mushrooms (shrooms, shrooming)
  - Detachment from reality
    - Inability to discern fantasy from reality
      - Can lead to panic attacks, psychosis
  - Rapid tolerance to effects
    - Cross tolerance with LSD



16

Psilocybin

- Reported mystical-like experiences
  - Inner peace, patience, optimism, self-confidence
- Adverse effects
  - Nausea, vomiting, anxiety
  - May interact with MAOI
- Duration: 4-6 hours



17

Lysergic Acid Diethylamide (LSD)

- Water soluble, clear, white, odorless crystals
  - Thin blotter paper with dried solution of LSD
  - Breath mints/sugar cubes ("dropping" acid), pressed into pills or thin gelatin squares



18

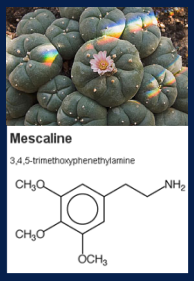
Lysergic Acid Diethylamide (LSD)

- Onset: 30-60 min, Peak: 2-4 hours, Duration: 8-12 hours
- Effects
  - Altered shapes and colors, heightened sense of hearing
  - Depersonalization, visual hallucinations, alterations in mood



19

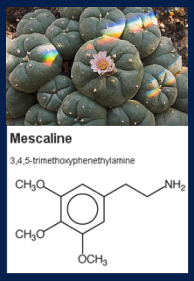
Mescaline/Peyote



- Use legalized within Native American Church
- Buttons from top (crown) of peyote cactus
  - 6-10 buttons for intoxication

20

Mescaline/Peyote

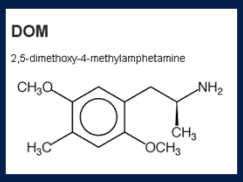


- Slow onset (30-60 min)
  - First hour: minor perceptual changes, increased resp rate, nausea
  - Next several hours (5-10):
    - Visual illusions/hallucinations
    - Synesthesia

21

DOM

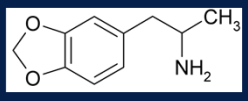
- Results from structural modification of mescaline-like substances
- Extremely potent
- Used as model hallucinogen in drug discrimination studies



22

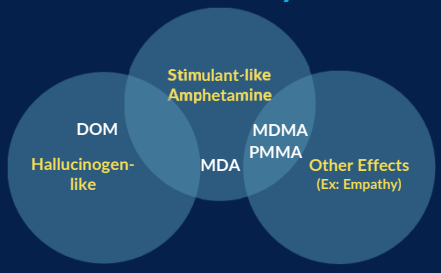
MDMA

- Produces stimulant and hallucinogenic effects
  - Similar to combined effects of cocaine and LSD
- Can be modified to MDMA (ecstasy)
  - Stimulant effects
  - Empathogenic
- Has been represented and sold as MDMA



23

Classification by Effect



24

Salvia

- Herb found in southern Mexico and South
- America, used in healing rituals
  - Traditionally ingested by chewing / drinking juice
  - Sometimes smoked when used as drug of abuse
- Active ingredient in Salvia is salvinorin A, a kappa opioid agonist
- Varied legal status: Banned in 29 states



25

Salvia Effects



- Intense and short-lived
  - Onset < 1 minute
  - Duration < 30 minutes
- Changes in visual perception
- Increased sense of well-being (or not)

26

Hallucinogen Persisting Perception Disorder (HPPD)

- Re-experiencing of perceptual symptoms experienced while intoxicated following cessation of use = flashbacks



29

Salvia Effects



- Feelings of detachment
- Modified perception of external reality and the self
- Decreased ability to interact with surroundings

27

Hallucinogen Persisting Perception Disorder (HPPD)

- Unrelated to dose or number of exposures
- Usually resolves within 1-2 years of last use
- Can be triggered by other substance use



30

Summary: Hallucinogen Intoxication

- Clear Sensorium
- Intact Memory
- Hyperalert
- EEG = arousal
- Intact reality testing
  - Can sometimes be reasoned with or calmed by talking
- Visual Hallucinations >> Auditory

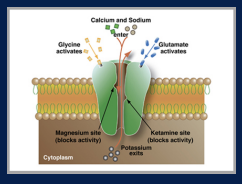
28

Dissociatives

31

Definition

- NMDA receptor antagonists
  - Glutamate activates NMDA receptors to filter sensory stimuli
  - Dissociatives noncompetitively block NMDA receptors → sensory overflow



32

Members of the Class

- Arylcyclohexylamines
  - PCP
  - Ketamine
- Dextromethorphan (DXM)
- Nitrous Oxide







33

Effects

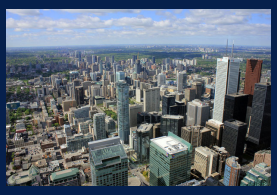


- Dissociation
- Sensory Isolation
- Mental Distortions
- Increased HR, BP, Temp

34

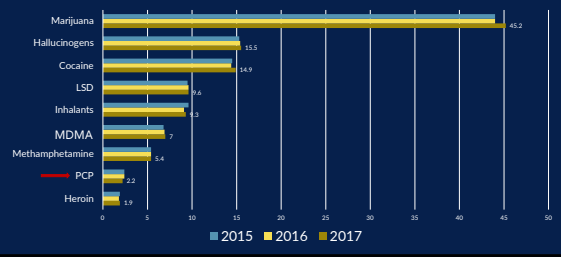
Epidemiology

- Men > Women
- More common in large urban areas
- Often used in combination with alcohol or other illicit substances



35

Lifetime Prevalence of Specific Drug Use: Percentages, NSDUH



36

Phencyclidine (PCP, Angel dust)

- Developed as IV anesthetic
  - No longer FDA-approved; now Schedule I
    - Associated with prolonged delirium



- Risk of seizures or death
- Available as powder, tablets, liquid, and sprayed onto plant leaves and then smoked

37

PCP Effects

- Vary widely with dose

Confusion, delirium, psychosis

⬇

Semi-coma and coma (less common)

⬇

Coma with seizures (rare)

38

PCP

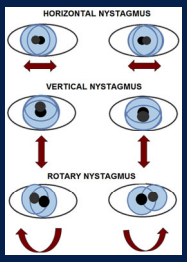
- Psychotomimetic = model of psychosis
  - Positive Symptoms (Delusions, hallucinations)
  - Negative Symptoms (Blunted affect, asociality)



39

PCP

- PCP Intoxication
  - Nystagmus (rotary, vertical, horizontal)
  - Hyperreflexia
  - HTN
  - Feelings of invulnerability
  - Management: low stimulus environment, benzos/antipsychotics as indicated



40

Ketamine (K, Special K)

- FDA-approved for general anesthesia in animals and humans
- Schedule III
- Administered as IV or IM in medical settings
- Used by inhalation, smoking, or oral administration
- Less potent, shorter-acting than PCP



41

Effects of Ketamine

- Analgesia / numbness
- Spacey feeling ("K-hole")
- Amnesia
- Delirium (higher doses)



- Nystagmus (vertical and/or horizontal)
- CV + renal complications
- Long-term
- Dysphoria, memory impairment, apathy, irritability

42

Dextromethorphan (DXM)



- OTC cough medicines
  - Capsules, tablets, lozenges, syrup
  - AKA "skittles"
- Anti-tussive dose: <120mg daily; recommended dose 10-20mg q4hours
- 300-1800mg produces PCP-like effects

43

Effects of DXM

- Euphoria and hallucinations (increasing w/ higher dose)
- Drowsiness, dizziness, blurred vision, slurred speech
- N/V, hypertension, diaphoresis



44

Effects of DXM

- Significant serotonergic properties
  - ↑ serotonin synthesis and release
  - ↓ reuptake



- Deaths have been reported with large doses (200x dose)
  - CNS & respiratory depression, seizure, arrhythmias

45

Summary: Dissociative Intoxication and Overdose

- PCP included on most screening panels (high false positive rate)
  - Need special testing (GC-MS) for ketamine, DXM
- Increased serum CPK & urine myoglobin

46

Summary: Dissociative Intoxication and Overdose

- Rarely see dilated pupils
  - Different from stimulant or hallucinogen intoxication, opioid withdrawal
- Visual hallucinations relatively rare

47

Inhalants

48

Inhalants



Breathable chemicals that can be self-administered, also known as:

- Whippets
- Poppers
- Huff
- Bang
- Kick
- Sniff

49

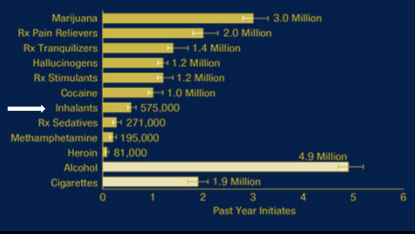
Terminology

- Sniffing = inhaling from an open container
- Huffing = holding fabric soaked in substance to the nose or mouth and inhaling
- Bagging = concentrating vapors in a bag and inhaling



50

Numbers of Past Year Initiates of Substances Among People Aged 12 or Older: 2017 NSDUH



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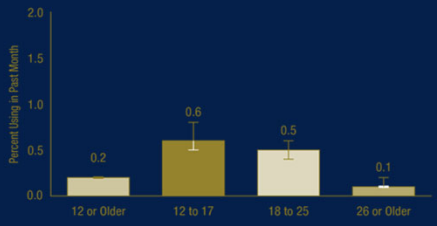
Past Month Inhalant Use Among People Aged 12 or Older, by Age Group: Percentages, 2017 NSDUH



52

Source of Inhalants: Products





Air freshener	Lighter fluid	Household cleaners	Gasoline
Hair spray	Mothballs	Nail polish remover	Paint thinner
Markers	Refrigerant	Rubber cement	Spray paint
	Video head cleaner	Whipped cream canisters	

53

Sources of Inhalants:

Possible Contents

- Amyl, butyl, cyclohexyl nitrite; butane
- Butane
- n-Hexane, tetrachloroethylene, xylene
- Benzene, toluene, xylene, (lead)
- Butane, propane
- Naphthalene, paradichlorobenzene
- Acetone, toluene
- Toluene, trichloroethylene, xylene
- Xylene
- Freon
- Acetone, benzene, n-Hexane, toluene
- Butane, propane, toluene
- Amyl, butyl, cyclohexyl nitrite
- Nitrous oxide

54

Abuse Liability

- Number of factors increase abuse potential
  - Free or low cost
  - Readily available
  - Difficult to test for
  - Perceived as low risk
- Inquire about inhalant use, especially when working with adolescent population
- Provide education regarding consequences of use

55

Inhalant Pharmacology

- Highly lipophilic
- Rapidly absorbed through the lungs
- Crosses blood-brain barrier
- Accumulates in brain, liver and fatty tissue
- Rapid onset, short duration
- Synergistic effect: alcohol, benzos

56

Effects of Inhalants

Acute Effects	Toxic Effects and Overdose
Euphoria	Respiratory depression
Disinhibition	Arrhythmias
Dizziness / lightheadedness	Asphyxia, cardiac arrest and death can occur
Slurred speech	
Ataxia	

57

Chronic Effects of Inhalants

CARDIAC arrhythmia cardiomyopathy	DERMATOLOGICAL perioral infection rash
GASTROINTESTINAL hepatorenal failure	MUSCULOSKELETAL Rhabdomyolysis

58

Chronic Effects of Inhalants

PULMONARY emphysema hypoxia aspiration pneumonia	GENITOURINARY glomerulonephritis hypokalemia
HEMATOPOIETIC aplastic anemia leukemia bone marrow suppression	NEUROLOGICAL peripheral neuropathy delirium/dementia cerebellar atrophy irreversible white matter changes

59

Treatment Considerations

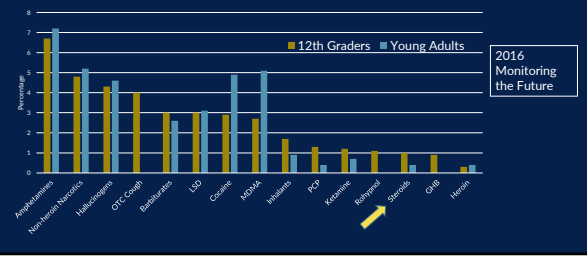
- User may experience prolonged residual effects because chemicals are stored in fatty tissue
- Neurological impairment is often present
  - Cognition should be continually re-assessed
  - Talk therapy / group therapy may not be appropriate

60

Anabolic-androgenic Steroids

61

Annual Prevalence of Various Drugs for 12th Graders and Young Adults (18-25) by % Using



64

Anabolic - Androgenic Steroids (AAS)



- Anabolic = skeletal muscle-building
- Androgenic = masculinizing
- Includes testosterone and >100 related synthetic substances

62

Epidemiology

3 most common populations:

- Athletes
  - Performance enhancement
- Aesthetes
  - Improve physical appearance (often adolescents)
- Fighting Elite
  - Increase aggression and/or job performance (security, law enforcement)

65

Misuse

- Enhance performance and/or improve physical appearance
  - May be taken at 10-100x the intended dose
- Routes of Administration
  - Oral
  - IM



63

Steroid Side Effects

Acne	Liver damage	↑LDL, ↓HDL	Complications of Injections
Aggressive / violent behavior ("Roid Rage")	Hypomania or Mania	Paranoia	Extreme irritability

66

Steroid Side Effects

Women	Men
Deepening of voice	Testicular atrophy
Facial hair	Prostatic hypertrophy
Menstrual changes	Gynecomastia
Male-pattern baldness	Baldness
Genital hypertrophy	Infertility

67

Psychiatric Side Effects

- Aggressive / violent behavior
  - "Roid Rage"
- Hypomania or Mania (high doses)
- Paranoia
- Extreme irritability
- Impaired judgment
- Delusions

Treatment

- Remove AAS
- Use mood stabilizers or anti-psychotics as needed
- Generally, resolves within 1-2 weeks after cessation

68

Other Associated Syndromes & Treatment

- Steroid Withdrawal-Associated Depression
  - Can be responsive to SSRIs
- Comorbid SUD, especially opioid
- Body Dysmorphic Disorder / Muscle Dysmorphia
- Rarely seek treatment
- Not euphorigenic; no immediate high
- Goal is long-term reward associated with physical changes
- May be seen as socially acceptable or positive

69

In Summary

Diverse group of substances with relatively low prevalence, but high abuse liability

Varied but significant effects from use and misuse, including long-term consequences

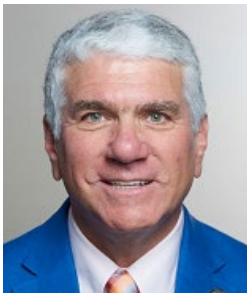
70

Interesting Cases with Audience Response System (ARS)

Friday, July 22
4:15 pm – 4:30 pm CT

Test your critical thinking and problem-solving skills while learning more about the complexities of addiction cases through this interactive session leveraging Audience Response System.

Faculty Presenter



Edwin A. Salsitz, MD, DFASAM
Unit Chief, Inpatient Rehabilitation
Mount Sinai Beth Israel
Icahn School of Medicine at Mount Sinai

Dr. Edwin A. Salsitz has been an attending physician in the Mount Sinai Beth Israel, Division of Chemical Dependency, New York City, since 1983, and is an Associate Clinical Professor of Psychiatry at the Mount Sinai School of Medicine. He is the principal investigator of the Methadone Medical Maintenance (office-based methadone maintenance) research project. Dr. Salsitz is certified in Addiction Medicine by the American Board of Preventive Medicine, as well as by the Board of Internal Medicine and Pulmonary Disease. He has published and lectures frequently on addiction medicine topics.

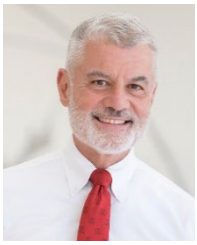
Dr. Salsitz is a course director for ASAM sponsored Buprenorphine and REMS Opioid trainings, and is a lead mentor in the PCSS-MAT mentoring program. He has co-chaired the ASAM Review Course, the ASAM Common Threads Course, the ASAM State of the Art course and is a reviewer for the Journal of Addiction Medicine and Drug and Alcohol Dependence. He is the chair of the ASAM REMS course on safe and effective prescribing of opioids. Dr. Salsitz was the Co-chair of the ASAM CME committee and Chair of the New York Society of Addiction Medicine CME and Education committee.
Dr. Salsitz is a member of the medical advisory panel, for the New York State Office of Alcohol and Substance Abuse Services. Dr. Salsitz is the recipient of the 2014 ASAM Annual Award, and the 2018 ASAM Annual Educator of the Year Award.

Expert Panel Discussion and Q&A - Day 1

Friday, July 22
4:30 pm – 5:30 pm CT

This panel session will provide a prime opportunity for learners to get their questions answered on topics that were presented on the first day of the ASAM Review Course.

Faculty Presenters



Petros Levounis, MD, MA, DFASAM
Panelist

Session: Neurobiology of Addiction: Key Concepts and Model Implications



Ruchi M. Fitzgerald, MD, FAAFP
Panelist

Session: Cannabis Use Disorder: Science, Trends and Clinical



Ricardo Restrepo, MD, MPH, FASAM
Panelist

Sessions: Alcohol Use Disorder: From Neurobiology to Treatment; Sedative Use Disorder: Key Concepts for Treatment



Michael H. Baumann, PhD
Panelist

Session: Stimulant Use Disorder: Trends and Treatment



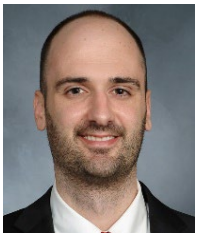
Soteri Polydorou, MD
Panelist

Session: Opioid Use Disorder: Science, History, and Clinical Implications



Erin A. Zerbo, MD, FASAM
Panelist

Session: Other Classes of Drugs: Pharmacology and Epidemiology



Jonathan Avery, MD
Moderator & Panelist

Session: Tobacco Use Disorder: Trends and Treament

Welcome Back and Board Exam Practice Questions – Day 2

Saturday, July 23
7:45 am – 8:00 am CT

Welcome and Board Exam Practice Questions with Audience Response System (ARS) with Vice-Chair, Erin A. Zerbo, MD, FASAM.

Faculty Presenter



Erin A. Zerbo, MD, FASAM
Director, Northern NJ Center of Excellence in Medication-Assisted Treatment
Rutgers New Jersey Medical School

Erin A. Zerbo, MD, FASAM, received her B.S. in Brain and Cognitive Sciences from the Massachusetts Institute of Technology in 2003, and her M.D. from New York University School of Medicine in 2007. She remained at NYU for a general psychiatry residency and a one-year addiction psychiatry fellowship, graduating in 2012. Since 2014, she has been an Assistant Professor in the Department of Psychiatry at Rutgers New Jersey Medical School and the Associate Director of Medical Student Education in Psychiatry. In addition to managing a large buprenorphine practice dedicated to Newark residents, she is also the director of the Northern New Jersey Center of Excellence in Medication-Assisted Treatment, a new statewide opioid training and education initiative.

Dr. Zerbo serves as the co-Chair of the Council on Education of the New Jersey Psychiatric Association, and she has published and lectured extensively in the field of addiction. Her primary interest is the treatment of substance use disorders in underserved and disadvantaged populations. She is a co-editor of the book "Pocket Guide to Addiction Assessment and Treatment" (APA, 2106), and the lead editor of "Becoming Mindful: Integrating Mindfulness into Your Psychiatric Practice" (APA, 2017).

Behavioral Addiction: From Theory to Treatment

Saturday, July 23
8:00 am – 8:45 am CT

While only one behavioral addiction is officially recognized by DSM-5, a second is now a "Condition for Further Study" and many more are likely to follow in subsequent editions of DSM-5. This session will focus on the recognition of behavioral addiction through a deeper understanding the theoretical framework of any addictive disorder. The presenter will provide a thorough review of the neurobiology, prevalence, screening, and treatment of gambling disorder. The session will end with a discussion of the future of behavioral addiction.

Learning Objective:

- After this session, learners will be able to: Describe the theoretical framework for behavioral addiction, criteria for diagnosis and evidence-based treatment strategies.

Faculty Presenter



Faye Chao, MD
Addiction Psychiatrist
James J. Peters VA Medical Center
Icahn School of Medicine at Mount Sinai

Faye Chao, MD is an addiction psychiatrist in the Supported Recovery Service at the James J. Peters VA Medical Center. She attended Jefferson Medical College in Philadelphia and completed her general psychiatry residency training at Harvard Longwood. She went on to an addiction psychiatry fellowship at NYU and worked in inpatient addiction services at both Bellevue Hospital and Mount Sinai West, where she was the unit chief of addiction services. She is board certified in both General and Addiction Psychiatry. Education about addiction topics has been a passion throughout her career, and she has trained medical students, residents, and fellows on clinical rotations, as well as run a motivational interviewing course for residents at Mount Sinai.

Behavioral Addictions

Faye Chao, MD
Assistant Professor, Department of Psychiatry
Icahn School of Medicine at Mount Sinai

1

The ASAM Review Course of Addiction Medicine

July 2022

Financial Disclosures

Faye Chao, MD
No Disclosures



2

Learning Objectives

1. **Describe** the theoretical framework for behavioral addiction, criteria for diagnosis and evidence-based treatment strategies.

3

Presentation Outline

- History
- Impulsivity/Compulsivity Spectrum
- Gambling Disorder
- Internet Gaming Disorder
- Hypersexual Disorder
- Other Behavioral Addictions

4

History

- Classified as:
  - Obsessive-compulsive spectrum disorders
  - Impulse-control disorders
  - By-products of mood disorders
  - Now: substance-related and addictive disorder

5

DSM-5

- Substance-related and Addictive Disorders
  - Gambling disorder
- Conditions for Further Study
  - Internet gaming disorder
- Not included at all ("insufficient evidence")
  - Other internet or technology-related behaviors (social media, TV, etc.)
  - Sex, exercise, shopping, food, etc.

Potenza, M: Non-substance addictive behaviors in the context of DSM-5. *Addict Behav* 2014.

6

Essential Features

- Failure to resist an . . .
  - impulse
  - drive
  - temptation

. . . to perform an act that is harmful to oneself or others.

Potenza, M: Non-substance addictive behaviors in the context of DSM-5. *Addict Behav* 2014.

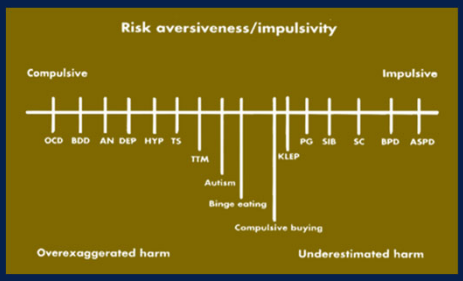
7

Impulsivity vs. Compulsivity

- Both show inability to refrain from repetitive behaviors.
- Impulsivity is driven by an effort to obtain arousal and gratification.
- Compulsivity is driven by an effort to reduce anxiety.

8

Dimensional Approach



Adapted from: Hollander E, Clinical Manual of Impulse-Control Disorders, 2006.

9

Compulsive End

- OCD
- Body Dysmorphic Disorder
- Anorexia Nervosa
- Depersonalization Disorder
- Hypochondriasis
- Tourette's Syndrome
- Trichotillomania
- Autism

- Binge Eating
- Compulsive Buying
- Kleptomania
- Pathological Gambling
- Self-Injurious Behaviors
- Sexual Compulsions
- Borderline Personality Disorder
- Antisocial Personality Disorder

Impulsive End

10

Gender Differences

Women	Men
• Anorexia	• Body Dysmorphic
• Binge Eating	• Sexual Compulsion
• Kleptomania	• Pyromania
• Compulsive Buying	• Gambling
• Trichotillomania	• Problematic gaming

11

Gambling Disorder

12

Gambling Disorder



13

Gambling Disorder

DSM-IV-TR	DSM-5
Pathological Gambling as Impulse-Control Disorder	Gambling Disorder as Substance-Related and Addictive Disorder

American Psychiatric Association: *Diagnostic and Statistical Manual of Mental Disorders, 5th Edition*. Washington, DC: American Psychiatric Association, 2013.

14

Substance-Related and Addictive Disorder



Alcohol	Caffeine	Cannabis
Hallucinogen	Inhalant	Opioid
Sedative	Stimulant	Tobacco
	Gambling Disorder	

15

Clinical Presentation for GD

- Five DSM-5 Addiction Criteria

Plus

- "Chases" one's losses
- Lies to conceal the extent of their gambling
- Relies on others for money
- Gambles when feeling distressed

(Specifiers: episodic or persistent)

Phases

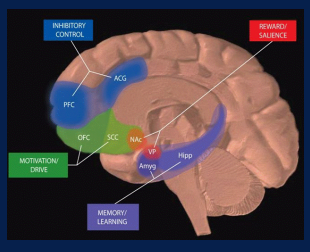
- Winning Phase
- Loss Phase
- Desperation Phase
- Hopelessness Phase

Blanco C, Cohen O, Luján JJ, et al: Pathological gambling and substance use disorders, in Substance Dependence and Co-Occurring Psychiatric Disorders: Best Practices for Diagnosis and Treatment. Edited by Nunes EV, Selzer J, Levounis P, Davies CA. New York, Civic Research Institute, 2010.

16

Neurobiology of GD

- Gambling affects:
  - DA
  - NE
  - Cortisol
  - 5HT
- Neurobiological similarities with substance use disorders



17

Epidemiology

- US Gambling Statistics:
  - $73 billion/year casino gaming revenue
  - 82% of US residents gamble
  - 1% - 2% meet criteria for PG
- Problematic Gamblers:
  - $40,000 average individual debt
  - 25 hours/week average time spent



www.americangaming.org; Dickson-Gillespie L, Rugle L, Rosenthal R, Forgi T: Preventing the incidence and harm of gambling problems. *J Prim Prev* 29:37-55, 2008.

18

The decline of casino slots and the rise of online

theleader.info



The decline of casino slots and the rise of online

For many years the mental image conjured up by the word 'casino' was made up of one of two things. It was either gaming tables surrounded by people rolling dice, holding playing cards or placing bets on a roulette wheel, or it was row upon row of flashing slot machines.

19

State forecasts dip, stagnation of casino tax aid

Projections show state will no longer be able to count on more money from slots, table game for schools

By Lauren Stanforth Published 12:32 pm EDT, Wednesday, March 13, 2019



Albany Times Union, March 2019.

20

What's Available in Your State?



- Opportunities in US:
  - Land-based casinos
  - Internet gambling
  - Nonregulated gambling
  - Online fantasy sports
- More available and accessible now than ever before

21

Screening Tools

- The Lie/Bet Test
  - Have you ever felt the need to bet more and more money?
  - Have you ever had to lie to people important to you about how much you gambled?
    - *99% sensitivity, 91% specificity*



Johnson EE, Hamer R, Nora RM, et al: The lie/bet questionnaire for screening pathological gamblers. Psychological Reports 80:83-88, 1997.

22

Gambling Cognitive Distortions

23

The Odds are Never in Your Favor

- "The house always wins"
- House edge is the ratio of the average loss to the initial bet, essentially the average gross profit the casino expects to make from each game
  - Keno – house edge 25-29%
  - Any craps – 11.11%
  - Ultimate Texas Hold 'Em – 2.19%
  - Blackjack (liberal Vegas rules) – 0.28%
- The longer you play, the greater the odds are that the result of your play will match up with the house edge



www.wizardofodds.com/gambling/house-edge

24

Interpretative Biases



- Attributing wins to skill, losses to flukes
- Wrongly believing that a series of losses increases the chance of subsequent win
- Near misses (“*I was only one number away!*”)
- The “Sunk-Cost” effect

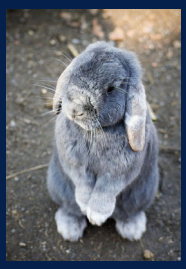
25



26

Superstitious Beliefs

- Believing in:
  - Good luck objects (like animal parts)
  - Behaviors
  - Routines



Gaboury A, Ladouceur R: Erroneous perceptions and gambling. Journal of Social Behaviors and Personality 4:411-420, 1989.

27

Selective Memory



- Remembering wins while ignoring losses
- Totaling wins without correcting for amounts lost

28

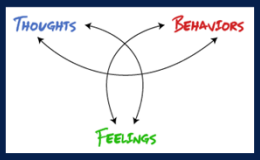
Telescoping

- Temporal:
  - Expecting that naturally occurring—that is, probabilistically expected—wins will happen sooner rather than later.

29

Treatment

- Behavior therapy, cognitive behavioral therapy, family therapy
- Opioid antagonists, SSRIs
- Mutual-help groups (Gamblers Anonymous)



30

Treatment: GD as an Impulsive Disorder

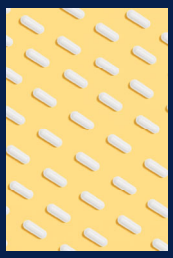
- Opioid Antagonists
  - Naltrexone and Nalmefene
  - Block opioid receptors, decrease dopamine function, and reduce "reward cravings"
  - Best with family history of alcoholism



Grant JE, Kim SW, Hollander E, et al: Predicting treatment response to opiate antagonists and placebo in the treatment of pathological gambling. Psychopharmacol 200:521-527, 2008. Grant JE, Potenza MN: Pathological Gambling: A Clinical Guide to Treatment. Washington, DC, American Psychiatric Publishing, 2004.

31

Treatment: GD as a Compulsive Disorder



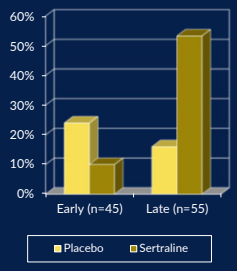
- Selective Serotonin Reuptake Inhibitors
  - Fluvoxamine, Paroxetine, Escitalopram
  - Block serotonin reuptake, increase serotonin function, and reduce "self-medication"
  - Best with co-occurring depression or anxiety

Hollander E, Sood E, Pallanti S, et al: Pharmacological treatments of pathological gambling. *Journal of Gambling Studies* 21:101-110, 2005.

32

Sertraline for Alcohol Use Disorder

- Abstinence rates during a 14-week treatment trial with sertraline 200mg daily
- Helped late-onset drinkers (type 1)
- Worsened early-onset drinkers (type 2)



Pettinati, *Alcohol Clin Exp Res*, 2000.

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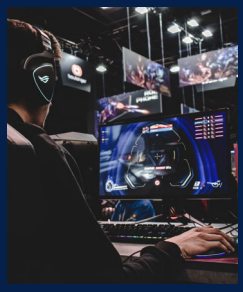


Internet Gaming Disorder

34

The Evolution of IGD

DSM-IV-TR	DSM-5
Not Found	Conditions for Further Study

American Psychiatric Association: *Diagnostic and Statistical Manual of Mental Disorders*, 5th Edition. Washington, DC: American Psychiatric Association, 2013.

35

DSM-5 Criteria

- Seven DSM-5 Addiction Criteria, plus
  - Has deceived family, therapists or others about the amount of gaming
  - Uses games to escape/relieve negative mood
    - (*Excludes Internet gambling, recreational/social Internet use, sexual websites*)

American Psychiatric Association: *Diagnostic and Statistical Manual of Mental Disorders*, 5th Edition. Washington, DC: American Psychiatric Association, 2013.

36

ICD-11 Criteria

- A pattern of persistent or recurrent gaming behavior ('digital gaming' or 'video-gaming'), which may be online (i.e., over the internet) or offline, manifested by:
  - 1) impaired control over gaming (e.g., onset, frequency, intensity, duration, termination, context)
  - 2) increasing priority given to gaming to the extent that gaming takes precedence over other life interests and daily activities
  - 3) continuation or escalation of gaming despite the occurrence of negative consequences.
  - The behavior pattern is of sufficient severity to result in significant impairment in personal, family, social, educational, occupational or other important areas of functioning.
- Modifiers are "predominantly online" and "predominantly offline."

World Health Organization: *International Statistical Classification of Diseases and Related Health Problems, 11th Edition.* Retrieved from https://icd.who.int/, 2019.

37



38

Who's Playing?

- ESA (Entertainment Software Association) 2021 survey
  - 226.6 million Americans play video games
  - 77% of gamers play with others online or in person at least weekly (up from 65% in 2020)
  - 77% play for 3+ hours a week



2021 Essential Facts about the Computer and Video Game Industry. Entertainment Software Association. https://www.theesa.com/. Published July 2021. Accessed April 15, 2022.

39

The Average Player

- Is white (73%)
- May be of either gender
  - Gender breakdown: 55% identify as male, 45% identify as female
- Is age 31
  - 80% of players are over 18 years old
  - In 2021, 28% of those who play video games are over the age of 45.

2021 Essential Facts about the Computer and Video Game Industry. Entertainment Software Association. https://www.theesa.com/. Published July 2021. Accessed April 15, 2022.

40

Clinical Presentation of IGD

- Has more to do with life impact than amount of time played (though this is controversial)
- Often, but not always, occurs in patients with other co-morbidities (especially SUDs and mood disorders)
- Prevalence: Global prevalence appears to be ~2-3% and males 2.5 times as likely to be diagnosed
  - More common in Asian countries esp. China, Taiwan, South Korea. However…



41

Context Matters

- South Korea is the most wired country in the world
  - Greatest number of users
  - First country to achieve over 50% broadband penetration per capita
  - Has the fastest, cheapest broadband in the world
  - Tournament gaming is a viable profession
- Unsurprisingly, one study found that up to 50% of Korean teenagers report problematic internet gaming use (Hur 2006)
- Internet gaming addiction is considered a significant public health concern.

Hur MH. Demographic, habitual, and socioeconomic determinants of Internet addiction disorder: an empirical study of Korean teenagers. *Cyberpsychol Behav.* 2006;9:514–525.

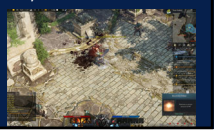
42



43

Problematic Play

- Risk factors include:
  - Personality traits (neuroticism, aggression and hostility, and sensation seeking)
  - Motivations for play (escapism, control, avoiding dissatisfaction)
  - Structural game characteristics (online games, ability to customize virtual game persona, game reinforcement structure).
    - MMORPGs a particular area of interest



44

Imaging Studies

- Internet gaming addicts showed lower resting state functional connectivity between VTA and mOFC (Han 2018)
- Several studies show increased activity in the ACC and mOFC in response to gaming cues in subjects with gaming disorder (Han 2010, Ko 2009)
- Altered gray matter volume in patients with gaming disorder

Han, DH, et al. Bupropion sustained release treatment decreases craving for video games and cue-induced brain activity in patients with Internet video game addiction. *Exp Clin Psychopharmacol.* 2010 Aug;18(4):297-304.
Han, DH, et al. Changes in cue-induced, prefrontal cortex activity with video-game play. *Cyberpsychol Behav Soc Netw.* 2010 Dec;13(6):655-61
Ko, CH, et. al. Brain activities associated with gaming urge of online gaming addiction. *J Psychiatr Res.* 2009 Apr;43(7):739-47

45

Treatment

- Therapy modalities consist mainly of CBT, behavior therapy, and 12-Step approaches
- Psychopharmacologic management is off-label and has poor to middling evidence base for efficacy
  - Potential agents mainly selected from the same medications that are researched for SUDs
- Treatment centers initially arose in Asia and then Europe but now exist in North America as well

46

Treatment Centers in North America

- ReSTART – a residential treatment center near Seattle
- Foothills at Red Oak Recovery in NC
- Last Door in Vancouver
- CGAA – Computer Gaming Addicts Anonymous

47

Hypersexual Disorder

48

The Non-Evolution of HD

DSM-IV-TR	DSM-5
Not Found	Not Found

American Psychiatric Association: *Diagnostic and Statistical Manual of Mental Disorders, 5th Edition*. Washington, DC: American Psychiatric Association, 2013.

49

Proposed Criteria

- Recurrent sexual fantasies/urges/behaviors with three or more:
  - Time spent interferes with other non-sexual obligations
  - Repetitive engaging in response to dysphoric mood states
  - Repetitive engaging in response to stressful life events
  - Repetitive but unsuccessful efforts to control behavior
  - Repetitive engaging while disregarding risk for physical/emotional harm to self or others

Kafka, MP. Hypersexual disorder: A proposed diagnosis for DSM-V. Arch Sex Behav 2010.

50

Proposed Criteria

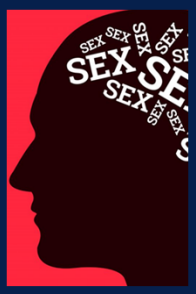
- Specify if:
  - Masturbation, pornography, sexual behavior with consenting adults, cybersex, telephone sex, strip clubs

Kafka, MP. Hypersexual disorder: A proposed diagnosis for DSM-V. Arch Sex Behav 2010.

51

Is it Real?

- Controversy about the criteria, but there is agreement that there is out-of-control, repetitive, and driven sexual behavior (typically with strangers) which leads to distress and dysfunction.



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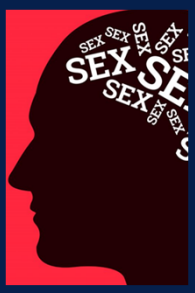
Is it Real?

- Sexual encounter = pleasurable
- Sexually addictive behavior = serves to manage and control negative affect
  - Often poor insight



53

Rapid Fire:
Other Behavioral Addictions

54

Internet Addiction

- Think co-occurring psychiatric disorder
- May use Young's Internet Addiction test

Internet Addiction Test (IAT) by Dr. Kimberly Young.

Internet Addiction Test (IAT) is a reliable and valid measure of addictive use of Internet, developed by Dr. Kimberly Young. It consists of 20 items that measures mild, moderate and severe level of Internet Addiction.

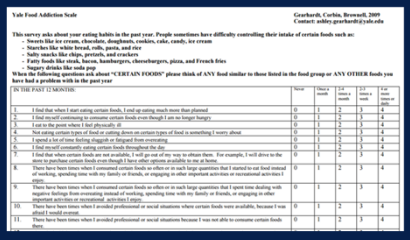
To begin, answer the following questions by using this scale:-

0	Does not apply
1	Rarely
2	Occasionally
3	Frequently
4	Often
5	Always

	Question	Scale					
1	How often do you find that you stay on-line longer than you intended?	1	2	3	4	5	0
2	How often do you neglect household chores to spend more time on-line?	1	2	3	4	5	0
3	How often do you prefer the excitement of the Internet to intimacy with your partner?	1	2	3	4	5	0
4	How often do you form new relationships with fellow on-line users?	1	2	3	4	5	0
5	How often do others in your life complain to you about the amount of time you spend on-line?	1	2	3	4	5	0
6	How often do your grades or school work suffers because of the amount of time you spend on-line?	1	2	3	4	5	0

55

Food Addiction



Yale Food Addiction Scale — Gearhardt, Corbin, Brownell, 2009
Contact: ashley.gearhardt@yale.edu

This survey asks about your eating habits in the past year. People sometimes have difficulty controlling their intake of certain foods such as:
- Sweets like ice cream, chocolate, doughnuts, cookies, cake, candy, ice cream
- Starches like white bread, rolls, pasta, and rice
- Salty snacks like chips, pretzels, and crackers
- Fatty foods like steak, bacon, hamburgers, cheeseburgers, pizza, and French fries
- Sugary drinks like soda pop

When the following questions ask about "CERTAIN FOODS" please think of ANY food similar to those listed in the food group or ANY OTHER foods you have had a problem with in the past year

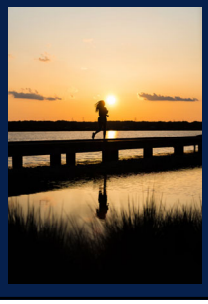
IN THE PAST 12 MONTHS:	Never	Once a month	2-4 times a month	2-3 times a week	4 or more times a week
1. I find that when I start eating certain foods, I end up eating much more than planned	0	1	2	3	4
2. I find myself continuing to consume certain foods even though I am no longer hungry	0	1	2	3	4
3. I eat to the point where I feel physically ill	0	1	2	3	4
4. Not eating certain types of food or cutting down on certain types of food is something I worry about	0	1	2	3	4
5. I spend a lot of time feeling sluggish or fatigued from overeating	0	1	2	3	4
6. I find myself constantly eating certain foods throughout the day	0	1	2	3	4
7. I find that when certain foods are not available, I will go out of my way to obtain them. For example, I will drive to the store to purchase certain foods even though I have other options available to me at home.	0	1	2	3	4
8. There have been times when I consumed certain foods so often or in such large quantities that I started to eat food instead of working, spending time with my family or friends, or engaging in other important activities or recreational activities I enjoy.	0	1	2	3	4
9. There have been times when I consumed certain foods so often or in such large quantities that I spent time dealing with negative feelings from overeating instead of working, spending time with my family or friends, or engaging in other important activities or recreational activities I enjoy.	0	1	2	3	4
10. There have been times when I avoided professional or social situations where certain foods were available, because I was afraid I would overeat.	0	1	2	3	4
11 There have been times when I avoided professional or social situations because I was not able to consume certain foods there.	0	1	2	3	4

- Distinct from binge-eating disorder
- Use the Yale Food Addiction Scale

56

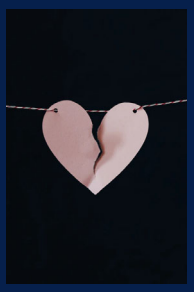
Exercise Addiction

- Apply modified DSM-5 criteria for SUD to diagnose



57

Love Addiction



- Look for conflicted attachments or traumatic experiences in childhood

58

Shopping Addiction (Compulsive Buying Disorder)

- More common among women in developed countries
- 2 - 8% prevalence in the US



59

Tanning Addiction



- Tanning releases endorphins
- Naltrexone was shown to induce withdrawal in a small sample of frequent tanners

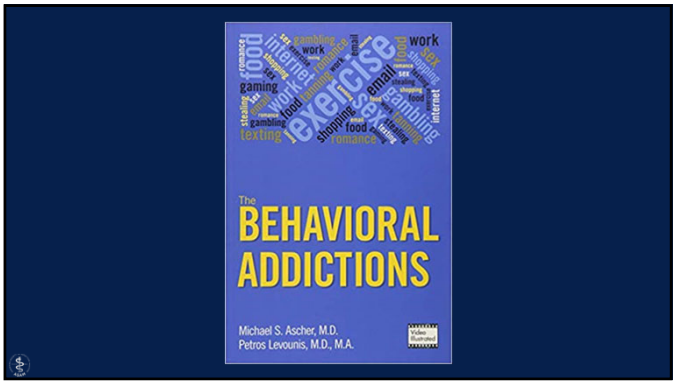
60

Kleptomania

- Possibly an addictive disorder?
- High suicide attempt rate – up to 24%



61



62

In Summary



- Behavioral addictions fall within an impulsivity-compulsivity spectrum of illness.
- DSM-5 only recognizes one disorder officially though one other is included as a condition for further study.
- Psychosocial treatments work.
- Medications have fallen short so far.

63

Epidemiology: Core Concepts and Applications

Saturday, July 23
8:45 am – 9:30 am CT

Epidemiology turns data into usable information. This session will review basic concepts of epidemiology and important addiction-related epidemiological trends. Participants will see examples of epidemiological principles in action and learn how to apply these principles themselves.

Learning Objective:

- After this session, learners will be able to: Explain basic epidemiological concepts related to the field of addiction medicine, their applications, and their limitations.

Presenter



Jeffrey J. DeVido, MD, MTS, FASAM
Chief, Addiction Services//Behavioral Health Clinical Director
Marin County CA Dept of HHS//Partnership HealthPlan of CA
UCSF

Jeffrey J. DeVido, MD, MTS, FASAM is board certified in General Psychiatry, Addiction Psychiatry, and Addiction Medicine and works in Northern California. Upon completion of residency and fellowship training at Massachusetts General and McLean Hospitals/Partners Healthcare, he attended on the psychiatric consultation-liaison services at UCSF, Parnassus Campus for 3 years. For the past 4 years, Dr. DeVido has been Chief of Addiction Services with Marin County CA Department of Health and Human Services and Behavioral Health Clinical Director with Partnership HealthPlan of CA. In both of these roles, he is involved in managing the development of substance use and co-occurring services for Medicaid beneficiaries in 14 counties between the Oregon border and San Francisco. In his free time, he enjoys fly fishing, chasing around his 3 young kids, and Star Trek.

EPIDEMIOLOGY

Jeffrey J. DeVido, MD, MTS (He, Him, His)
Chief, Addiction Services, Marin County Dept. of Health and Human Services
Behavioral Health Clinical Director, Partnership HealthPlan of California
Assistant Professor, UCSF Dept. of Psychiatry and Behavioral Sciences, UCSF Weill Institute for Neurosciences

1

The ASAM Review Course of Addiction Medicine
July 2022

Financial Disclosures

Jeffrey DeVido, MD, MTS, FASAM

Equity shareholder: Altria/Philip Morris/Merck

The opinions expressed in this talk are mine and they do not represent the opinions of my employing institutions or those with whom I am professionally affiliated.

2

Disclosure Information

The ASAM Review Course in Addiction Medicine: EPIDEMIOLOGY

July 23, 2021; 08:45am CST

Jeffrey DeVido, MD, MTS, FASAM, DFAPA



3

Disclosure Information

The ASAM Review Course in Addiction Medicine: EPIDEMIOLOGY

July 23, 2021; 10:45am EST

Jeffrey DeVido, MD, MTS, FASAM, DFAPA



4

Learning Objectives

1. **Review** the dimensions of epidemiology covered in the ABPM exam: 1) basic trends, and 2) epidemiologic concepts.
2. **Establish** different approaches for (re)learning epidemiology as necessary for ongoing professional acumen as well as (unfortunately) things needed to regurgitate on an exam.
3. **Demonstrate** epidemiologic concepts in action through two different common addiction epidemiological questions.
4. **Guide** participants towards resources for ongoing review of epidemiologic data.

5

Presentation Outline

- Consider ways of thinking about and learning about epidemiology.
  - Cheat sheets vs. enduring learning patterns
- Highlight some important epidemiological trends and how to find them yourselves.
- Follow two common questions in addiction medicine as a springboard for reviewing key concepts in epidemiology.

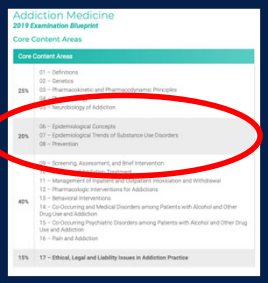
6

Two Ways to Think About Epidemiology

- What do I need to know for the test?
- What might I need to know professionally?

7

The ABPM Exam and Epi





Addiction	Target Percentage
01 Alcohol	15-20%
02 Sedatives	7-10%
03 Stimulants	7-10%
04 Opioids	10-15%
05 Cannabinoids	7-10%
06 Nicotine	15-20%
07 Hallucinogens	5-3%
08 Dissociatives	5-3%
09 Inhalants	5-3%
10 Anabolic steroids	5-3%
11 Other substances	1-3%
12 Nonsubstance addiction	1-3%
13 General/All substances combined	1-5%

https://www.theabpm.org/become-certified/exam-content/addiction-medicine-content-outline/

8

For the Test Strategy:

- Some assumptions:
  - All of you have had some rudimentary epidemiology/biostatistics.
  - Most of you have seen these concepts multiple times.
  - For the most part, you don't use these concepts as much as they come up on tests.
  - You scribble some notes on a cheat sheet to remind yourself as you're studying.
  - When you've been taught these concepts before, it has been shoveled to you in large amounts in short lectures.

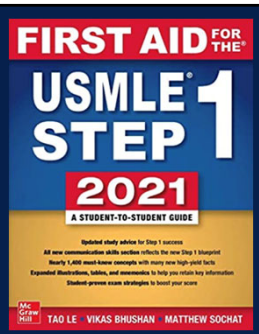
9

For the Test Strategy:



[http://www.bishopmikelowry.com/wp-content/uploads/2013/03/drinking-from-the-firehose.jpg

10



https://www.amazon.com/First-USMLE-Step-2021-Thirty/dp/126046752X/ref=asc_df_126046752X/?tag=hyprod-20&linkCode=df0&hvadid=459537678676&hvpos=&hvnetw=g&hvrand=12792418851990343229&hvpone=&hvptwo=&hvqmt=&hvdev=c&hvdvcmdl=&hvlocint=&hvlocphy=9032089&hvtargid=pla-1113406220592&psc=1

11

Two Ways to Think About Epidemiology

- What do I need to know for the test?
- What might I need to know professionally?

12

Some Important Epidemiological Things That Come up Often in Addictions

- What's the risk of psychosis with cannabis use?
- Why is his urine toxicology screen negative?

13

So…



https://memegenerator.net/instance/26662134/med-student-meerkat-stay-on-your-toes

14

Let's Start With Some Useful Basics:

Primary Prevention

Interventions designed to prevent the onset or future incidence of a specific problem

Secondary Prevention

An early intervention that decreases the prevalence of a specific problem

Tertiary Prevention

Treatment designed to improve quality of life and reduce the symptoms after a disease or disorder has developed
Does not reduce incidence or prevalence

https://press.rebus.community/introductiontocommunitypsychology/chapter/prevention-and-promotion

15

Let's Do A Quick Matching Exercise:

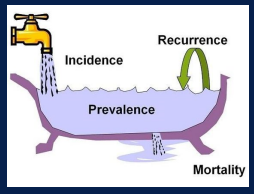
- Incidence
- Prevalence

- #of existing cases/Total #of people (at a point in time)
- Rate: #new cases/#people at risk (during a specified time period)

16

Incidence:

- Represents the RISK of a disease: new cases coming into a population in time
- See people longitudinally (in time) so these data are harder to find for SUDs—**PROSPECTIVE** studies
  - Example: follow-ups on **Epidemiologic Catchment Area** study (1980s)
    - Highest incidence in youngest population (18-29 y/o)



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17

Let's Do A Quick Matching Exercise:

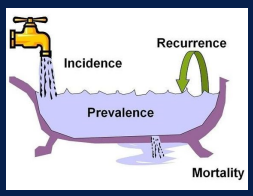
- Incidence
- Prevalence

- #of existing cases/Total #of people (at a point in time)
- Rate: #new cases/#people at risk (during a specified time period)

18

Prevalence:

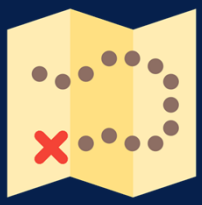
- Represents the *public health burden* of a disease at a particular time
- **CROSS SECTIONAL SURVEYS**
  - Example: annual **National Survey on Drug Use and Health** (NSDUH)
    - Tobacco products, alcohol, illicit drugs



http://image.slidesharecdn.com/measurementinepidemiology-141121024727-conversion-gate01/95/measurements-in-epidemiology-15-638.jpg?cb=1416559706

19

Let's take a quick tour of some prevalence data and important trends to help us put the story together:



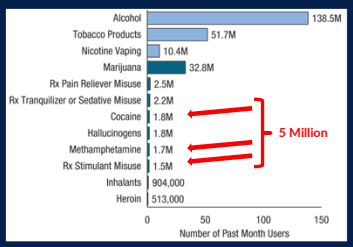
20

First: Big Picture



21

2020 NSDUH Prevalence: Past Month General Substance Use and Nicotine Vaping: Among People Aged 12 or Older; 2020

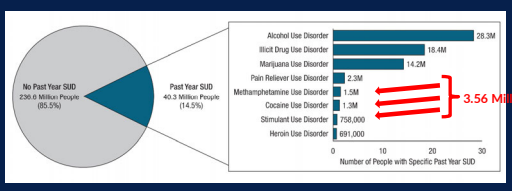


Rx = prescription.
Note: General Substance Use includes any illicit drug, alcohol, and tobacco product use. Tobacco products are defined as cigarettes, smokeless tobacco, cigars, and pipe tobacco.
Note: The estimated numbers of current users of different substances are not mutually exclusive because people could have used more than one type of substance in the past month.

https://www.samhsa.gov/data/data-we-collect/nsduh-national-survey-drug-use-and-health

22

People Aged 12 or Older with a Past Year Substance Use Disorder (SUD); 2020

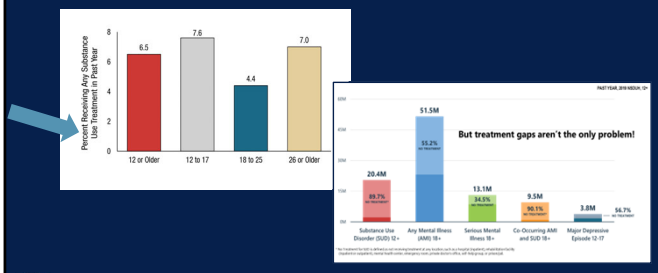


Note: The estimated numbers of people with substance use disorders are not mutually exclusive because people could have use disorders for more than one substance.

https://www.samhsa.gov/data/data-we-collect/nsduh-national-survey-drug-use-and-health

23

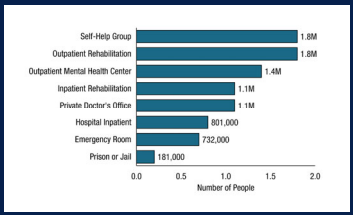
But Do People Get Treatment?



https://www.samhsa.gov/data/sites/default/files/reports/rpt32815/National-BH-Barometer_Volume6.pdf
https://www.samhsa.gov/data/release/2020-national-survey-drug-use-and-health-nsduh-releases

24

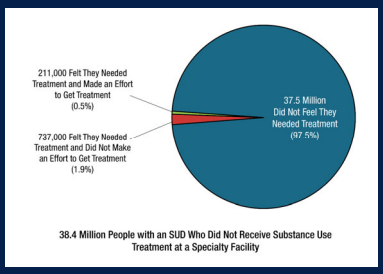
For The People Who do Get "Treatment," Where do They Get It?



https://www.samhsa.gov/data/release/2020-national-survey-drug-use-and-health-nsduh-releases

25

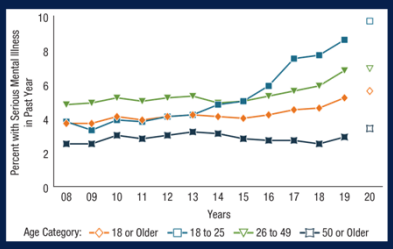
Perceived NEED for Treatment (2020)



https://www.samhsa.gov/data/release/2020-national-survey-drug-use-and-health-nsduh-releases

26

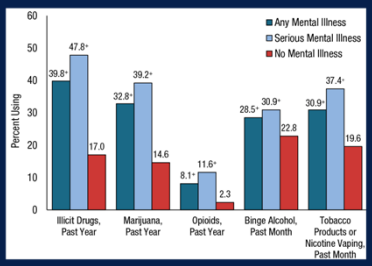
Serious Mental Illness in the Past Year: Among Adults Aged 18 or Older; 2008-2020



https://www.samhsa.gov/data/release/2020-national-survey-drug-use-and-health-nsduh-releases

27

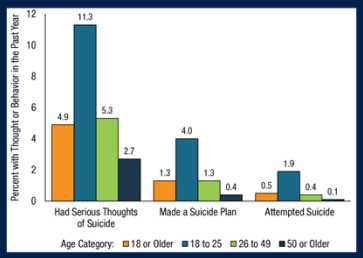
Substance Use: Among Adults Aged 18 or Older; by Mental Illness Status, 2020



https://www.samhsa.gov/data/release/2020-national-survey-drug-use-and-health-nsduh-releases

28

Had Serious Thoughts of Suicide, Made a Suicide Plan, or Attempted Suicide in the Past Year: Among Adults Aged 18 or Older; 2020



https://www.samhsa.gov/data/release/2020-national-survey-drug-use-and-health-nsduh-releases

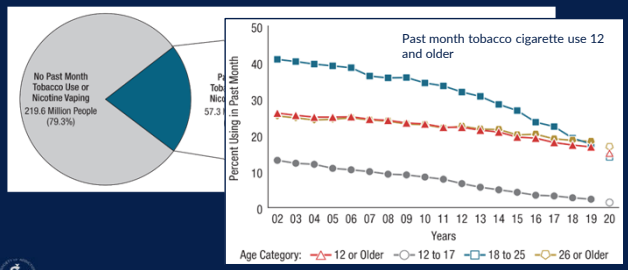
29

Second: Looking a Little Closer by Substance



30

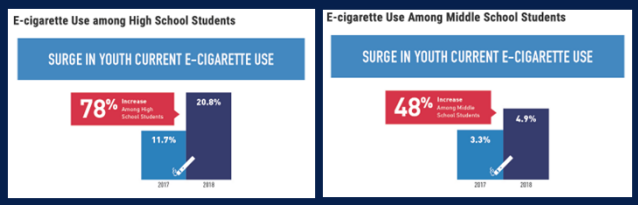
Tobacco



https://www.samhsa.gov/data/release/2020-national-survey-drug-use-and-health-nsduh-releases

31

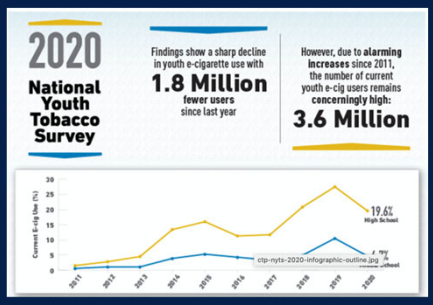
E-Cigarettes



https://www.fda.gov/tobacco-products/youth-and-tobacco/2018-nyts-data-startling-rise-youth-e-cigarette-use

32

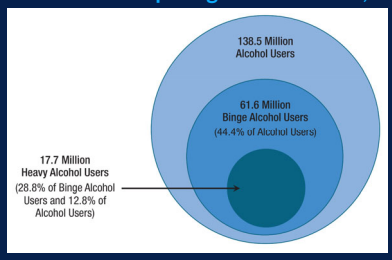
But(t):



https://www.fda.gov/tobacco-products/youth-and-tobacco/youth-tobacco-use-results-national-youth-tobacco-survey

33

Current, Binge, and Heavy Alcohol Use: Among People Aged 12 or Older; 2020

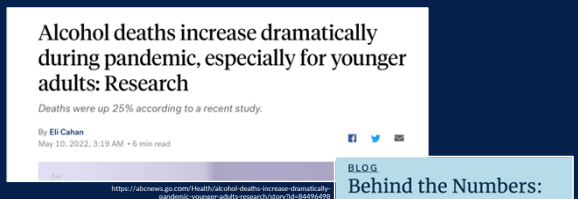


- 73.4% of all SUDs in US are **Alcohol** (may be overlap).
- Half of all drinkers are binge/heavy drinkers.

Note: Binge Alcohol Use is defined as drinking five or more drinks (for males) or four or more drinks (for females) on the same occasion on at least 1 day in the past 30 days. Heavy Alcohol Use is defined as binge drinking on the same occasion on 5 or more days in the past 30 days; all heavy alcohol users are also binge alcohol users.

https://www.samhsa.gov/data/data-we-collect/nsduh-national-survey-drug-use-and-health

34



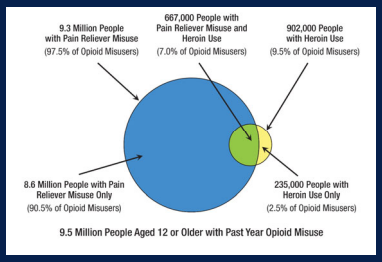
BLOG

Behind the Numbers: Alcohol is Killing More People Than the Opioid Epidemic. Why Aren't We Talking About It?

https://www.caron.org/blog/alcohol-is-killing-more-people-than-the-opioid-epidemic

35

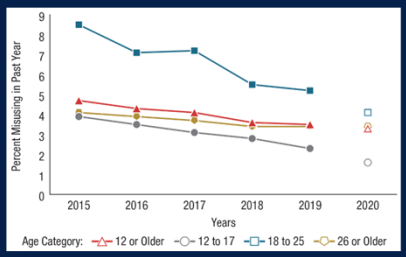
Opioid Misuse—Past Year (2020)



https://www.samhsa.gov/data/data-we-collect/nsduh-national-survey-drug-use-and-health

36

Past Year Prescription Pain Reliever Misuse: Among People Aged 12 or Older; 2015-2020



https://www.samhsa.gov/data/data-we-collect/nsduh-national-survey-drug-use-and-health

37

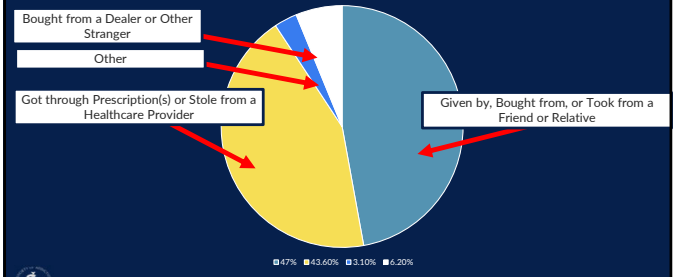
Yet…



38

Opioids—Past Year

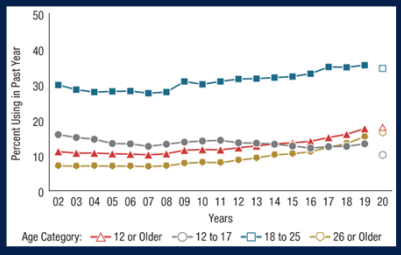
Where'd you get your misused prescription painkiller?



https://www.samhsa.gov/data/data-we-collect/nsduh-national-survey-drug-use-and-health

39

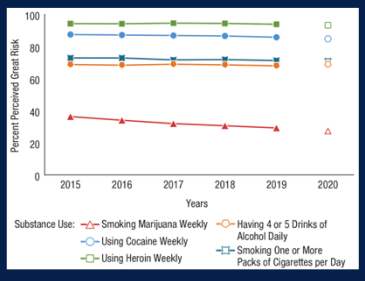
Past Year Marijuana Use: Among People Aged 12 or Older; 2002-2020



https://www.samhsa.gov/data/data-we-collect/nsduh-national-survey-drug-use-and-health

40

Perceived Great Risk from Substance Use: Among People Aged 12 or Older; 2015-2020



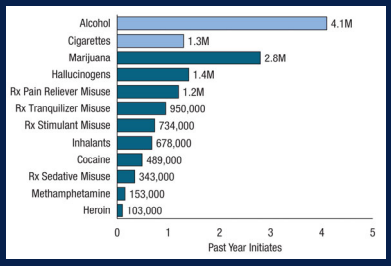
https://www.samhsa.gov/data/data-we-collect/nsduh-national-survey-drug-use-and-health

41



42

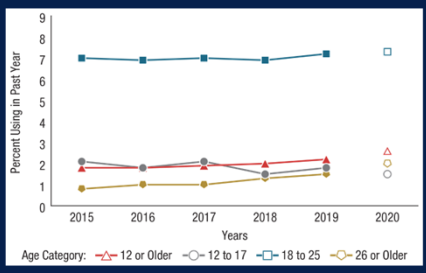
Past Year Initiates of Substances: Among People Aged 12 or Older; 2020



https://www.samhsa.gov/data/data-we-collect/nsduh-national-survey-drug-use-and-health

43

Past Year Hallucinogen Use: Among People Aged 12 or Older; 2015-2020



https://www.samhsa.gov/data/data-we-collect/nsduh-national-survey-drug-use-and-health

44

People who used 'magic mushrooms' less likely to develop opioid use disorder, study finds

USA TODAY

ADRIANNA RODRIGUEZ | USA TODAY

Why Is Everyone Smoking Toad Venom?

How an illegal amphibian-venom-derived psychedelic became the loudest whisper at a dinner party near you.

https://www.townandcountrymag.com/leisure/arts-and-culture/a38687510/toad-venom-bufo-illegal-psychedelic-drug/

Mike Tyson Says He 'Died' After Smoking Psychedelic Toad Venom

https://www.si.com/boxing/2021/11/17/mike-tyson-says-he-died-smoking-psychedelic-toad-venom

45

Third: Other Important Parts of the Story



46

Race/Ethnicity/LGB

	National Average (%)	African American (%)	Asian (%)	American Indian/Alaska Native (%)	Hispanic (%)	Native Hawaiian/ Pacific Islander (%)	Sexual Minority (SM)*
SUD Past Year (18+)	7.7	7.6	4.6	10.2	7.0	8.3	18.3
AUD Past Year (18-25)	9.3 (10.1)	5.3 (5.6)	7.4 (9.1)	12.9 (10.3)	8.7 (9.4)	na	12.0 (12.4)
Marijuana Use Past Year (18+)	18.0 (16.2)	20.0 (18.2)	7.9 (9.3)	20.4 (24.0)	15.2 (13.7)	14.6 (18.6)	43.6 (37.6)
Methamphetamine Past Year (26+)	0.8 (0.7)	0.3 (0.2)	0.1 (0.1)	2.3 (2.6)	0.8 (0.7)	1.6 (2.4)	3.6 (2.9)

RED = ABOVE national average
BLUE = BELOW national average
PURPLE = at national average
( ) = 2018 percentages
* Defined by SAMHSA as people who identify as lesbian, gay, or bisexual—NSDUH began collecting this data in 2015

https://www.samhsa.gov/data/sites/default/files/reports/rpt31104/2019NSDUH-LGB/LGB%202019%20NSDUH.pdf
https://www.samhsa.gov/data/report/2019-nsduh-detailed-tables

47

CENTER ON MEDIA CRIME AND JUSTICE at JOHN JAY COLLEGE | THE CRIME REPORT YOUR CRIMINAL JUSTICE NETWORK

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Nearly Half of State Incarcerees Suffer From Substance Abuse: Survey

By Blake Diaz | July 14, 2021

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https://thecrimereport.org/2021/07/14/nearly-half-of-state-incarcerees-suffer-from-substance-abuse-survey/

48

Gender

- Women tend to initiate substance use later than men
- Women have accelerated course of disorder → "telescoping" (alcohol, marijuana, cocaine, prescription opioids)
- Women with SUDs → more severe impairment in employment, social/family, medical and psychiatric functioning

McHugh RK, et al. Sex and gender differences in substance use disorder. Clin Psychol Rev. 2017 Nov 10.

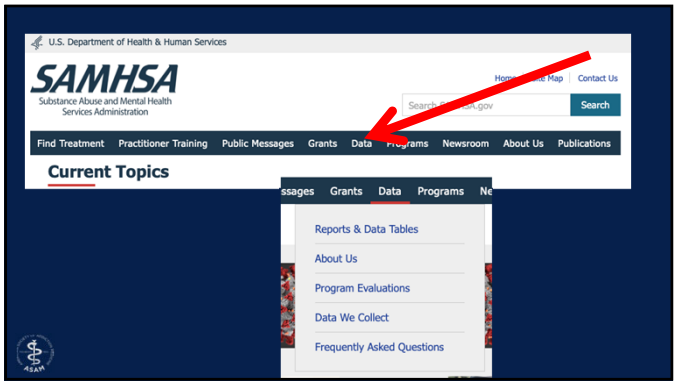
49

So...

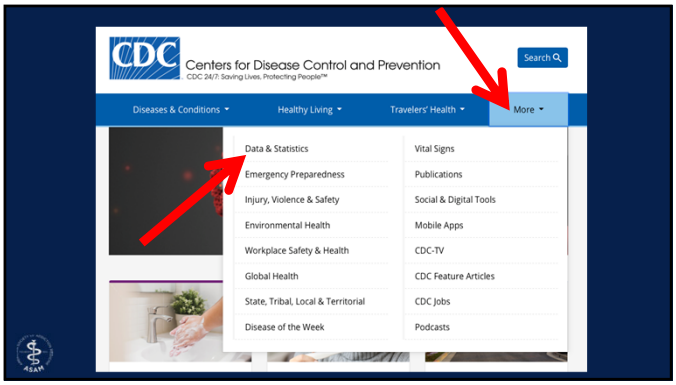


https://memegenerator.net/instance/57246861/wonderful-toys-joker-where-does-he-get-those-wonderful-toys

50



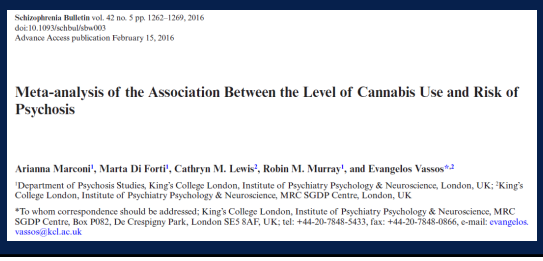
51



52

Let's Look at a Study...

- Question: Does Cannibis use cause psychosis?



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

*To whom correspondence should be addressed; King's College London, Institute of Psychiatry Psychology & Neuroscience, MRC SGDP Centre, Box P082, De Crespigny Park, London SE5 8AF, UK; tel: +44-20-7848-5433, fax: +44-20-7848-0866, e-mail: evangelos.vassos@kcl.ac.uk

53

What is This Study?

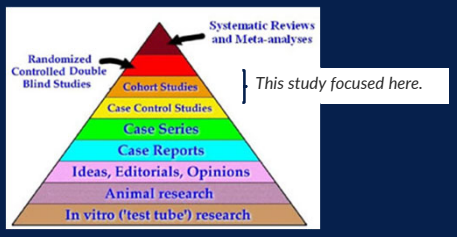
- Performed a systematic review and a meta-analysis
- Included: provided data on cannabis consumption prior to the onset of psychosis
  - 18 for systematic review and 10 for meta-analysis (66,816 individuals)
  - Continuous variable → amount of exposure
  - Cohort and cross-sectional studies included
- Findings:
  - **Odds ratio 3.90** (95% confidence interval 2.84 to 5.34) for risk of schizophrenia and other psychosis-related outcomes among the heaviest cannabis users compared to non-users

54

What can we say about this study?

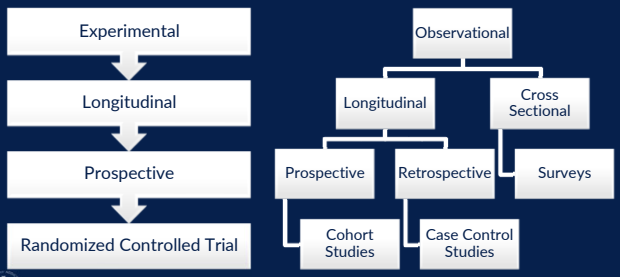
55

1) Quality of evidence, based on study design.



56

Types of Studies



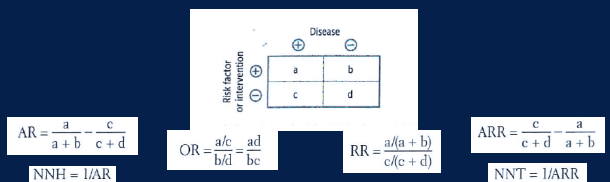
57

Quantifying Risk…



58

Quantifying Risk…



59

Odds Ratio--more

- What is an odds ratio?

Ratio of Odds

- The higher the odds ratio, the stronger the association between the exposure and the outcome appears to be.
- If the odds ratio is 1, then that means that the ratio of the odds shows NO ASSOCIATION between the exposure and the outcome.
- (Those with the disease who were exposed/those with the disease not exposed)/(those without disease exposed/those without the disease not exposed).

60

Odds Ratio—An Example

- Imagine: The relationship between getting breast cancer and driving an American car vs. not.
  - If there is no correlation between these two, then the ratio of those with disease who drove American cars/those with the disease who didn't, would be close to 1, and a ratio of those without disease who drove American cars/those without disease who did not drive American cars would also be close to 1, and the ratio of those two would be one = no relationship.

61

Back To The Cannabis Paper… 2) An ASSOCIATION Was Found

- **Odds ratio 3.90** (95% confidence interval 2.84 to 5.34) for risk of schizophrenia and other psychosis-related outcomes among the heaviest cannabis users compared to non-users.
  - Dose-response effect seen such that increasing exposure to cannabis increases risk of psychosis-related outcomes.

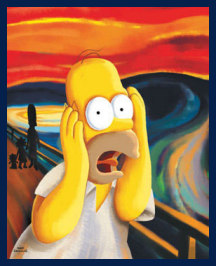
62

What about Confidence Interval?

- (95% confidence interval 2.84 to 5.34)
  - This is the range of values within which the true mean of the population is expected to fall, with a specified probability
  - Probability: 95% CI corresponds to p=0.05
  - If this includes 1, for odds ratio or relative risk, null hypothesis is NOT rejected (no significant difference)

63

Oh No, Not the "Null Hypothesis"!



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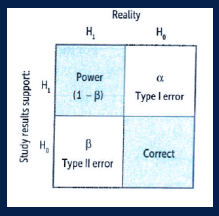
Oh No, Not the "Null Hypothesis"!



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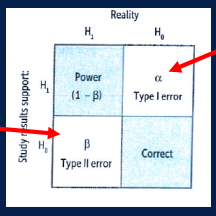
Oh No, Not the "Null Hypothesis"!

Stating that there is not an effect when one does exist: False negative error



Stating that there is an effect when none exist: False positive error

66

2) An Association Was Found

- Does this mean that cannabis causes psychosis, based on this paper?

67

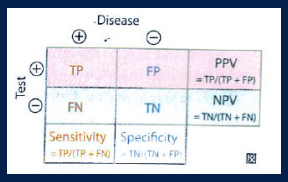
Why is his urine toxicology screen negative?

68

Question:
Patient's ED urine drug screen came back negative for opiates, so he must not have used the methadone he claims to be taking?

69

Sensitivity vs. Specificity



70

High sensitivity screen for opiates (those metabolized to morphine), but low sensitivity for synthetic opioids (methadone).

71

What We've Done

- Briefly reviewed scope of epidemiology covered on ABPM exam
- Examined trends in addictions and explored ways to find that data for future professional or personal use
- Followed two common questions in addiction medicine as a springboard for reviewing key concepts in epidemiology

72

Ethics and the Law: Principles and Treatment Implications

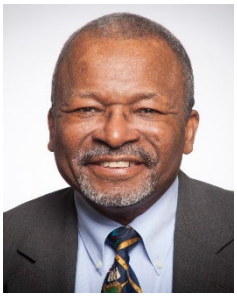
Saturday, July 23
9:30 am – 10:15 am CT

Medical ethics extends far beyond the Hippocratic oath. This session will provide an overview of complex ethical and legal issues that may arise when treating individuals with substance use and other co-occurring disorders. The presenter will also highlight specific medico-legal issues pertaining to special populations including care of justice-involved individuals, impaired professionals, minors, and pregnant women.

Learning Objective:

- After this session, learners will be able to: Describe the ethical and legal considerations that impact treatment of patients with addiction

Faculty Presenter



H. Westley Clark, MD, JD, MPH, DFASAM
Dean's Executive Professor of Public Health
Santa Clara University

H. Westley Clark, MD, JD, MPH is currently the Dean's Executive Professor of Public Health at Santa Clara University in Santa Clara California. He is formerly the Director of the Center for Substance Abuse Treatment, SAMHSA, U.S. Department of Health and Human Service. He contributed to the US Surgeon General's Report on Alcohol, Drug Abuse and Health as a Section Editor for Treatment. He is on the National Advisorry Council of NIAAA. He has served on the National Advisory Council of NIDA. He was a member of the Board of Directors of the non-profit Felton Institute, He was on the Board of Directors of Faces and Voices of Recovery. He was also on the Board of Directors of the Pacific Institute for Research and Evaluation.

He has received numerous awards for his contributions to the field of substance abuse treatment, including: the 2015 Lisa Mojer-Torres Award from Faces and Voices of Recovery, the 2015 James Ralph Memorial Award for Outstanding Public Service from the Black Psychiatrist of America, A 2015 Annual Award, American Society of Addiction Medicine. He was awarded the 2008 John P. McGovern Award from the American Society of Addiction Medicine.

Dr. Clark received a B.A. in Chemistry from Wayne State University; he holds a MD and a MPH from the University of Michigan; where he completed a Psychiatric Residency at University Hospital, Neuropsychiatric Institute. He obtained his Juris Doctorate from Harvard University Law School and completed a two-year Substance Abuse Fellowship at the DVAMC-SF. Dr. Clark received his board certification from the American Board of Psychiatry and Neurology in Psychiatry. He is a Distinguished Fellow of the American Society of Addiction Medicine. He is certified in Addiction Medicine by the American Board of Preventive Medicine. Dr. Clark is licensed to practice medicine in California, Maryland, Massachusetts and Michigan. He is also a member of the Washington, D.C., Bar.

Ethics and the Law

H. Westley Clark, MD ,JD , *MPH*
Dean's Executive Professor of Public Health
Santa Clara University
Santa Clara, California

1

The ASAM Review Course of Addiction Medicine

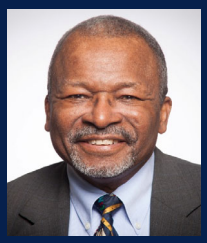
July 2022

Financial Disclosures

H. Westley Clark, MD, JD, MPH

Disclosures:

- Consultant ABInBev Foundation
- Advisor, Responsility.Org
- Single Lecture for Indivior



2

Learning Objectives

Describe the ethical and legal considerations that impact treatment of patients with addiction.

3

Presentation Outline

- Ethical Principles
- Informed Consent
- Privacy and Confidentiality
- Ethical Prescribing
- Special Topics

4

Ethical Principles

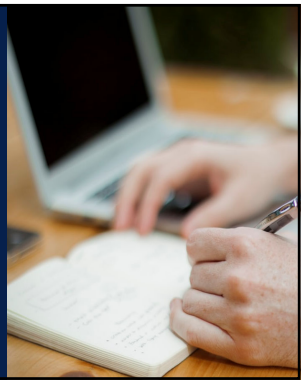
- Autonomy: self-determination, self-governance, moral independence
  - Example: Patient with recurrent upper GI bleed refusing voluntary inpatient addiction psychiatry admission



5

Ethical Principles

- Beneficence: actions should promote patient well-being
  - Example: A patient with a severe heroin use disorder sees PCP who offers him buprenorphine, referral to methadone treatment or inpatient withdrawal management and community recovery resources



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Ethical Principles

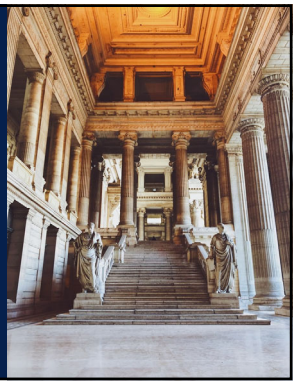
- Non-maleficence: do no harm (or as little as necessary)
  - Examples: (1) Providing benzodiazepines for patients on high dose opioids or (2) prescribing buprenorphine without an exam for cash



7

Ethical Principles

- Justice:
  - Fairness in decisions
  - Equal distribution of resources and new treatments
  - Medical practitioners uphold laws
  - Examples: (1) Advocating for a patient rejected from inpatient addictions treatment when the insurance provider deems it "not clinically indicated" or (2) Accepting cash only for the use of buprenorphine or naltrexone, limiting access to treatment .



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Ethical Principles

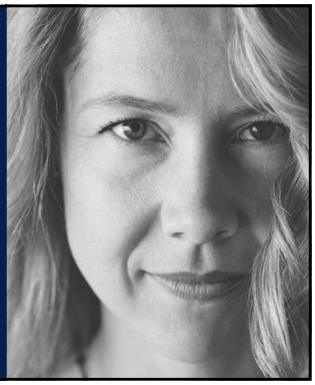
- Respect for people: treating people in a manner that acknowledges their intrinsic dignity
- Truth-telling: honesty, sharing information



9

Complex Ethical Scenario

- 40-year-old female anesthesiologist
- Taking opioid medications meant for patients, replacing with saline
- Has used oral opioids on the job but denies problems
- Asks you to notify nobody



10

Audience Response Question #1

Which of the following is NOT true regarding informed consent?

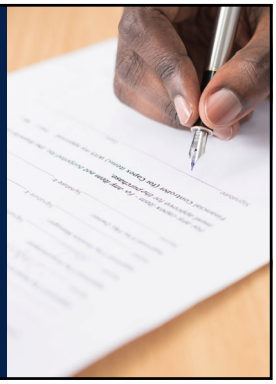
LWO

A. It must be given voluntarily.
B. An individual must possess decisional capacity.
C. Patients with psychosis cannot give informed consent.
D. It involves the disclosure of information between the clinician and the patient.

11

Informed Consent

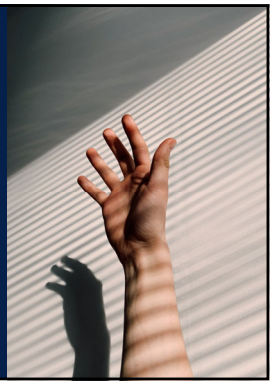
- Voluntariness
- Information disclosure
- Decisional capacity



12

Voluntariness

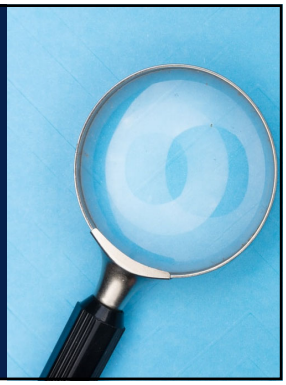
- Freely given
- Coercion: punishment or excessive rewards
- Persuasion
- Influence
- Context-dependent
- Risk of infringing
  - SUDs treatment in custody
  - Drug court
  - Inpatient treatment



13

Information Disclosure

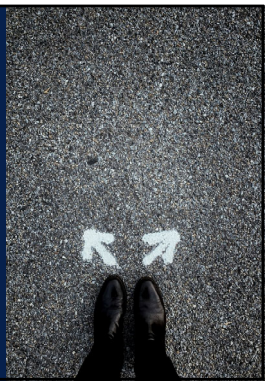
- Nature of illness and proposed treatment
- Risks/benefits
- Alternatives
- Consequences of foregoing treatment
- "Reasonable person" standard
- High standard of disclosure
  - Addictive medications (opioids)
  - Medications with known adverse events (disulfiram)
  - Medication combinations that should be avoided with MAOIs (methadone, bupropion, tramadol, etc.)



14

Decisional Capacity

- Communicate a choice
- Understand the relevant information
- Appreciate the situation and its consequences
- Reason about treatment options
- "Sliding scale" approach
- Potentially impaired
  - Intoxication
  - Substance-related neurocognitive problems
  - Dual diagnosis



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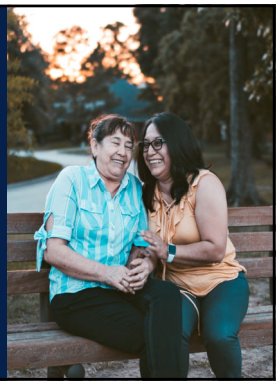
For Those Lacking Capacity

- Durable power of attorney for healthcare decisions (DPOAHC): form identifying surrogate decision-maker if one becomes incapacitated
- Advanced directive/living will: written statement expressing specific wishes, does not designate healthcare POA
- Guardian/conservator of the person: person appointed to make care decisions when patient is incapacitated



16

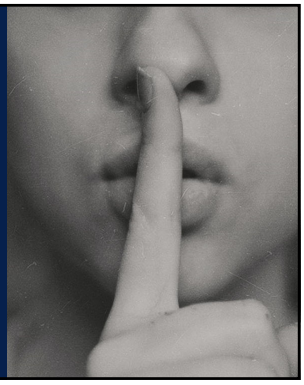
Pearls

- There are various ethical principles underlying medicine and addictions treatment that may come into conflict
- The process of informed consent requires voluntariness, information disclosure, and decisional capacity
- Certain treatment settings have the potential to infringe on voluntariness

17

Privacy and Confidentiality

- Privacy: patient's right to protection of sensitive information
- Confidentiality: clinician's obligation to protect sensitive information
- 42 CFR Part 2: Confidentiality of Alcohol and Drug Abuse Patient Records
- HIPAA



18

42 CFR Part 2 – Covered Programs

- Individual, entity, or identified unit within a general medical facility that provides SUDs diagnosis, treatment, or referral for treatment
- Medical personnel/staff in a general medical facility whose primary function is provision of SUDs diagnosis, treatment, or referral for treatment



19

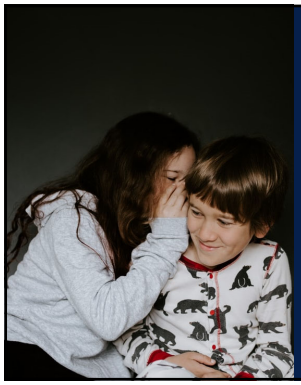
WO

42 CFR Part 2 – Federal Assistance

- Conducted in a federal department or agency
- Supported by federal funds
- Carried out under a license or registration from federal government
  - Medicare providers
  - Authorization to conduct maintenance treatment or withdrawal management
  - Registration under Controlled Substances Act to dispense a substance used in treatment of SUDs



20



Disclosure

- Part 2 programs may only release patient information with the patient's consent
- Exceptions include:
  1. Medical emergency
  2. Error in manufacture, labeling, or sale of a product under FDA jurisdiction
  3. Research
  4. Valid court order with subpoena
  5. Crimes committed on part 2 program premises
  6. Reporting suspected child abuse or neglect
- Failure can result in criminal penalty (a fine)

21

HIPAA ('96), Privacy Rule ('00)

- All PHI protected
- Exceptions related to medical operations and public interest/benefit
- SAMHSA working to revise 42 CFR Part 2

22

Controlled Substance Act (1970)

- Classification and regulation
- Manufacturing
- Distribution
- Exportation and sale

23

CSA Regulation/Classification

- DEA licensure requirement
- Schedule I: illegal, no medical use (cannabis, MDMA, methaqualone, gamma-hydroxybutyric acid (GHB), peyote)
- Schedules II-V: addictive potential
  - II: cocaine, methamphetamine, methadone, phencyclidine, oxycodone, fentanyl
  - III: ketamine, testosterone, buprenorphine, sodium oxybate
  - IV: benzos, zolpidem, tramadol,
  - V: diphenoxylate, pregabalin, *

* As of March 2022, gabapentin is not controlled under the CSA, but a number of states have made it a Schedule V drug. The DEA has been requested to reschedule gabapentin schedule V.

24



Ethical Prescribing

- Patient risks
  - SUDs
  - Diversion
  - Exacerbation of comorbid medical or psychiatric illness
- Practices to address
  - Urine drug testing
  - Medication contract
  - PDMPs

25

Universal Precautions

1. Make a diagnosis with appropriate differential, including a physical exam
2. Psychological assessment (risk of addictive disorders)
3. Obtain informed consent
4. Treatment agreement
5. Pre- and post-intervention assessment of pain level and function
6. Appropriate trial of opioid therapy +/- adjunctive medication
7. Reassess pain score and level of functioning
8. Regularly assess 4 A's: analgesia, activity, adverse effects, aberrant behavior
9. Periodically review diagnosis and comorbid conditions
10. Documentation

26

Audience Response Question #2

Which of the following is NOT an example of misprescribing?

A. Providing a patient opioids at a dangerously high dose.
B. Providing a prescription for three months of opioids following an uncomplicated outpatient surgical procedure.
C. Providing a friend a prescription for Ativan for no medical purpose.
D. Providing a patient a prescription for Ativan for short-term treatment of anxiety, only to later learn via your state's PDMP that she had received multiple prescriptions in the last week from different providers.

27

Legal Consequences

- Misprescribe: inappropriate rationale, dose, quantity, lack of physical examination
- CSA: "unlawful for any person to knowingly or intentionally… manufacture, distribute, or dispense, or possess with intent… a controlled substance"
- Knowingly or Intentionally
- Without legitimate medical purpose
- Outside the usual course of professional practice
  - State medical board sanctions
  - Civil: malpractice
  - Criminal: CSA, murder



28

Recent Case

- James Pierre, MD.
- From June 2015 through July 2016
- Unlawfully prescribing over 1 million pills of hydrocodone
- People paid cash $220 to $500 for each visit.
- Physician convicted by a jury



29

Prescription Drug Monitoring Programs

- 49 states (MO pending), D.C., Guam
- Mitigate abuse/diversion
- Models
  - Non-mandated use
  - Proactive reporting
  - Mandated use
- Criticisms
  - Inadequate information collection
  - Ineffective utilization in clinical settings
  - Limited interstate sharing
- Mixed data on effectiveness, differs by state

30

Pearls

- Confidentiality of substance abuse treatment is governed by 42 CFR Part 2, HIPAA, and the Privacy Rule
- The Controlled Substances Act of 1970 established the DEA regulation and classification of addictive drugs and criminal penalties for distribution of drugs
- There are various models of ethical prescribing that generally involve informed consent, regular assessment and dose planning, and appropriate clinical documentation
- PDMPs, though potentially helpful, differ in their implementation and effectiveness

31

Addiction & the Law: Special Topics

- Adolescents
- Pregnant patients
- Justice-involved populations
- Civil commitment & substance use
- Americans with Disabilities Act (ADA)
- Impaired Clinician

32

Adolescents, Addiction, & the Law

33

Audience Response Question #3

A 15-year-old patient comes to you requesting treatment for alcohol use disorder. Which of the following scenarios most likely requires guardian informed consent before initiating treatment?

A. She is a mature minor
B. She is married
C. She is serving in the military
D. She has run away from home
E. She is experiencing severe withdrawal

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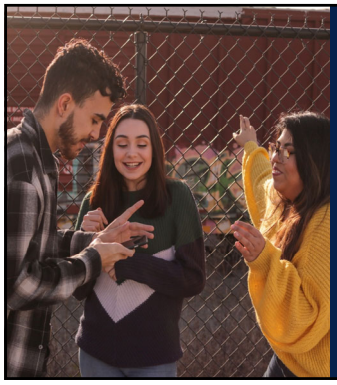


Legal Standards: Minor Informed Consent

- Age of majority
- Minor's ability to consent
  - General medical care
  - Mental health
  - Substance use disorders
- Emancipation
  - Legal
    - Marriage, military
  - Other forms
    - Mature minors
    - Have children
    - High school graduate

35



Mature Minor Doctrine

- Definition
- Assessment of maturity:
  - Age & maturity
  - Emotional capacity
  - Intelligence
  - Risk of procedure/treatment
  - Benefit to minor
- Informed consent assessment:
  - Risks of forgoing treatment
  - Long term consequences
- Brain development, impulsivity & "charged" environments

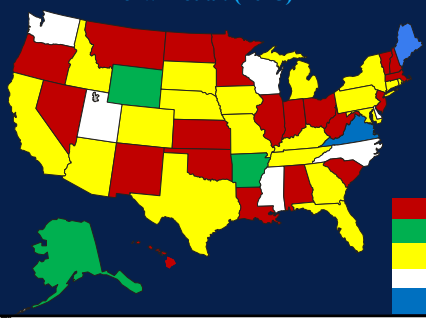
36

Minor Consent for SUD Treatment

- Laws vary by state
- Minimum age of consent can range from age 12-16
- May be able to consent to some services but not others
  - Withdrawal Management
  - Outpatient
    - Buprenorphine for those 16 -18
  - Inpatient
- Parental notification may still be required

37

Consent for Inpatient Substance Treatment
Kerwin et al. (2015)



38

Adolescent Autonomy, Privacy & Confidentiality

- Parental involvement
- Confidentiality can be preserved
- Insurance & privacy



39

Pearls

- State laws vary regarding minor consent requirements and may allow for a mature minor to consent
- Adolescents usually have the greatest autonomy to consent for substance use disorder treatment compared to other medical treatments
- When treating an adolescent patient, involve parents if possible while preserving the adolescent's confidentiality

40

Pregnancy, Substance Use, & the Law

41

Legal Consequences Of Substance Use In Pregnancy

- Criminal
  - Feticide laws (38 states)
  - Chemical endangerment of a child (Amnesty)
  - Direct criminalization of use during pregnancy
- Civil
  - Substance Use = Child Abuse (24 States +DC)
  - Reporting to Child welfare (25 states + DC)
  - Civil commitment (3 states)



42

Reporting Requirements to Child Welfare (Jarlenski, Guttmacher. Org)

- Mandated reporting of child abuse/neglect
  - Standard: Reasonable belief or suspicion for abuse
  - Prenatal drug use & Substance Exposed Newborns
- Clinical & ethical problems
- Guidelines
  - Inform of any mandated reporting requirements & limits of confidentiality
  - Obtain informed consent before drug testing (ACOG)

43

Pearls

- A person who uses substances during pregnancy can be subjected to civil or criminal penalties in many states
- Mandated reporting requirements of perinatal substance use vary across states
- Obtain informed consent before drug testing, including notification of reporting requirements

44

Justice-Involved Populations

45

Audience Response Question #4

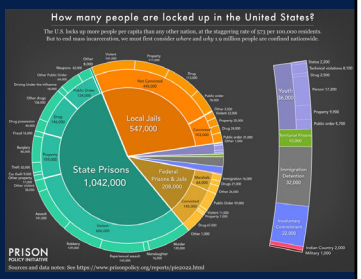
Approximately what percentage of women who are incarcerated in jail have a substance use disorder?

A. 25%
B. 33%
C. 50%
D. 75%
E. 90%

46

Statistics

- In 2019, 6.3 million people under correctional supervision in the U.S.
- History of incarceration in the U.S.
- SUDs & incarceration
  - Over 50% with active SUD
    - >75% of women have SUD
  - ~10- 15% receive treatment



47

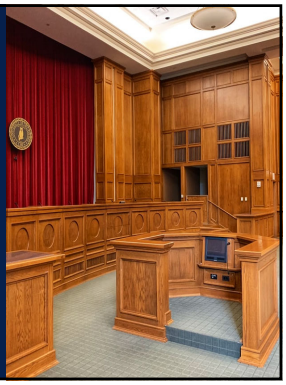
MAT in Corrections

- The Need
  - 75% will relapse within 3 months of release (SAMHSA)
  - 100x more likely to die of overdose within 2 weeks of release (BJS, Binswanger)
- Barriers
  - Lack of education
    - Substituting "one drug for another"/abstinence mentality
  - Diversion concerns
  - Cost
  - Lack of community providers to start or continue MAT
- BUT, more pilots across the US

48

Problem Solving (Treatment) Courts

- Drug, mental health, DUI, veteran's courts
- Therapeutic Jurisprudence
- Judge plays critical role
- Entry & Eligibility
- Structure & sanctions
- Efficacy (Logan)
  - Recidivism decreases
  - Future drug use reduced
- Treatment provider can be in dual role
- Some do not allow MAT (Matusow)



49

FINAL TOPICS

- Civil commitment
- The Americans with Disabilities Act (ADA)
- Impaired Physicians

50



Civil Commitment

- Standards
  - Mentally ill (or substance disorder, below) AND
  - Dangerous to self/others OR
  - Gravely disabled
- Substance use disorders
  - 37 states + DC (NAMSDL)
- Legal process
  - Due process required
  - Hearing occurs in timely manner
  - Committed for specified time by the judge

51



The Americans With Disabilities Act (ADA)

- Disability: Physical or Mental impairment which:
  - Limits in one or more major life activities
  - History of impairment
  - Regarded as having an impairment
- Substance use
  - Alcohol use disorder
  - Other substance use disorders
    - Protected: Not using now but is or has been in treatment for addiction or regarded by others as using drugs
    - Not protected: "Currently using drugs" or casual user
- Exceptions

52

Physician Regulation & Impaired Physicians

- Medical practice acts & state medical boards
- Physician health programs & impaired physicians
  - Exist in nearly every state
  - Goals
  - Voluntary vs. mandated treatment
  - High success rates
- Duty to report impaired physicians:
  - Impairment: physical, mental or substance-related disorder that interferes with abilities to safely and competently perform professional duties
  - Legal standards (have knowledge of or reason to believe) & options
  - Ethical and professional duties

53

Questions?

- hwestleyclark@yahoo.com
- Complete bibliography available on request

54

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15. APA Resource Document on recommended best practices for physician programs. (2017).
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57

Psychiatric Co-Morbidities: Assessment and Treatment

Saturday, July 23
10:45 am – 11:30 am CT

Co-occurring substance use and psychiatric disorders can create additional assessment and treatment complications. This session will use clinical case vignettes to focus on the interactions between disorders, differential diagnoses, and management through both pharmacologic and psychosocial treatments. Participants will receive a framework to assess patients for psychiatric co-morbidities and will be able to identify the mechanism of complications based on direct or indirect drug effects.

Learning Objective:

- After this session, learners will be able to: List the common psychiatric co-morbidities of addiction and their methods for assessment and treatment.

Faculty Presenter



Kelly Kleinert, MD
Associate Unit Director, 4 South Washington Heights Community Service
New York State Psychiatric Institute
Columbia University Vagelos College of Physicians and Surgeons

Kelly Kleinert, M.D. is an Assistant Clinical Professor of Psychiatry at Columbia University Vagelos College of Physicians and Surgeons, board-certified in Psychiatry and Addiction Medicine. She is Associate Unit Director on 4 South, the inpatient unit of the Washington Heights Community Service at New York State Psychiatric Institute, where she works with patients with severe mental illness and often concomitant substance use disorders. Previously, she worked at Janian Medical Care, a nonprofit psychiatric and primary medical care organization in New York City, caring for individuals with co-occurring psychiatric and substance use disorders on a homeless outreach team and on an Assertive Community Treatment (ACT) team. Dr. Kleinert graduated from Columbia University Vagelos College of Physician and Surgeons and completed residency in General Psychiatry at New York University/Bellevue Hospital. Following residency, she returned to Columbia to complete a fellowship in Public Psychiatry.

PSYCHIATRIC CO-MORBIDITIES

Kelly Kleinert, MD
Associate Unit Director, Washington Heights Community Service
Assistant Clinical Professor of Psychiatry
Columbia University Vagelos College of Physicians and Surgeons

1

The ASAM Review Course of Addiction Medicine
July 2021

Financial Disclosures

Kelly Kleinert, MD
No Disclosures

2

Co-Occurring Disorders

- Two diagnoses/disorders
- Two systems
- If applied to all cases, the term has no meaning
- Both psychiatric and substance use disorders need to meet full criteria

3

Dual Disorders

Psychiatric Disorders
- Major Depression
- Bipolar
- Social Anxiety
- Panic
- Schizophrenia
- Attention Deficit Hyperactivity
- Post Traumatic Stress

Substance Use Disorders
- Alcohol
- Stimulants
- Opioids
- Cannabis
- Benzodiazepines

4

Systemic Issues

- Legislation
- Funding
- Personnel
- Training and certification
- Sites
- Culture

5

Twelve-Month Prevalence of Mood and Anxiety Disorders Among Respondents with Substance Use Disorders Who Sought Treatment in the Past 12 Months

Disorder	Respondents, % (SE)
Those With Any Alcohol Use Disorder (5.81%)*	
Any mood disorder	40.69 (4.11)
Major Depression	32.75 (4.01)
Dysthymia	11.01 (2.74)
Mania	12.56 (2.81)
Hypomania	3.07 (1.37)
Any anxiety disorder	33.38 (4.17)
Panic disorder	
With agoraphobia	4.10 (1.54)
Without agoraphobia	9.10 (2.48)
Social phobia	8.49 (3.48)
Specific phobia	17.24 (3.10)
Generalized anxiety disorder	12.35 (3.01)
Any drug use disorder	33.05 (4.23)

*Data in parentheses are the percentages of respondents with the substance use disorders who sought treatment in the past 12 months.

Grant B, JAMA 2004

6

Twelve-Month Prevalence of Mood and Anxiety Disorders Among Respondents with Substance Use Disorders Who Sought Treatment in the Past 12 Months

Disorder	Respondents, % (SE)
Those With Any Drug Use Disorder (13.10%)*	
Any mood disorder	60.31 (5.86)
Major Depression	44.26 (6.28)
Dysthymia	25.91 (5.19)
Mania	20.39 (5.17)
Hypomania	2.48 (1.67)
Any anxiety disorder	42.63 (5.97)
Panic disorder	
With agoraphobia	5.92 (2.19)
Without agoraphobia	8.64 (3.05)
Social phobia	12.09 (3.48)
Specific phobia	22.52 (4.99)
Generalized anxiety disorder	22.07 (5.18)
Any alcohol use disorder	55.16 (6.29)

*Data in parentheses are the percentages of respondents with the substance use disorders who sought treatment in the past 12 months.

Grant B. JAMA 2004

7

NESARC Study

- Limitations of research diagnoses
  - Lay interviewers
  - Underreporting
  - Over-diagnosing
- Possible causal relationships between co-occurring disorders

8

Clarifying the Diagnosis

- Differentiating between substance-induced disorders vs co-occurring psychiatric and substance use disorders
  - Onset of symptoms
  - Periods of abstinence
  - Resolution of symptoms

9

Raphael is a 45-year-old man.

He is in your addictions program for alcohol use disorder. He has a history of recurrent depressive episodes. He started drinking more heavily in his late 20s.

His first depressive episode was in his early 20s.

He has depressive episodes during periods of sobriety.

10

Major Depressive Disorder

- Symptoms: Depressed mood
  Anhedonia
  Changes in appetite, sleep, psychomotor activity, energy, concentration
  Guilt/worthlessness
  Thoughts of death/suicide
- Course: At least 2 weeks
- 15-20% have co-occurring substance use disorder
- Associated with worse substance use outcomes, worse psychiatric symptoms, and increased suicide risk

11

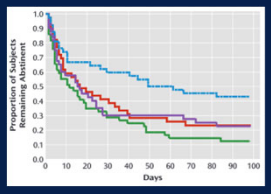
Depression Treatment

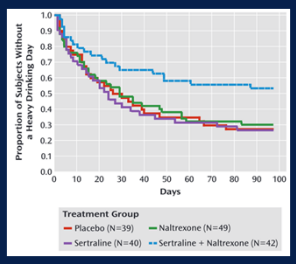
- Psychotherapy: CBT,
- Pharmacotherapy
  - SSRIs
  - SNRIs
  - Atypical antidepressants (bupropion, mirtazapine)
  - TCAs and MAOIs not first-line
- Combination of psychotherapy and pharmacotherapy most effective
- In studies of depression and co-occurring SUD, placebo response moderated effects of medication

12

Sertraline and Naltrexone for Treating Co-Occurring Depression and Alcohol Dependence

Time to first drinking day and time to first heavy drinking day in depressed alcohol-dependent patients.





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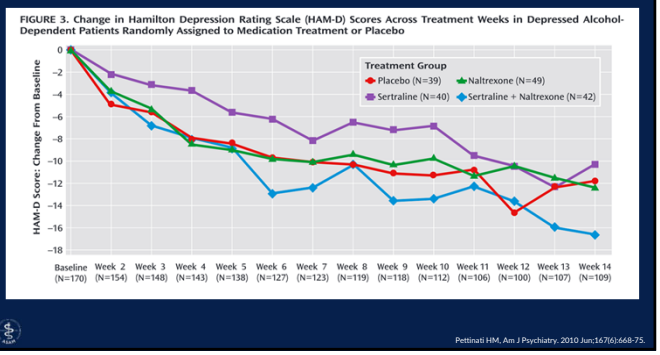


Pettinati HM, Am J Psychiatry. 2010 Jun;167(6):668-75.

14

Serotonin Syndrome

Increased serotonergic activity in the CNS

-Features: clonus (spontaneous or inducible), diaphoresis, agitation, tremor, hyperreflexia, hypertonia, elevated temperature (>38C)

-Treatment: discontinue the offending agent
supportive care + benzos
-> cyproheptadine

15

Serotonin Syndrome vs NMS

	Serotonin syndrome	NMS
Onset	Within 24 hours	Days to weeks
Neuromuscular findings	Hyperactivity	Bradyreflexia, rigidity
Causative agents	Serotonin agonists	Dopamine antagonists
Treatment	Benzos, cyproheptadine	Bromocriptine
Course	Within 24 hours	Days to weeks

Boyer, EW. Serotonin syndrome. In: UpToDate, Post, TW (Ed), UpToDate, Waltham, MA, 2021

16

Justine is a 38-year-old woman.

She presents to methadone clinic for treatment. She has been using IV heroin or other opioids for 20 years. She has a history of depression, suicide attempts, and overdoses.

Do you start an antidepressant in addition to methadone?

17

Co-occurring Depression and Opioid Use Disorder

- Lifetime prevalence of depression is 44-54% (vs 16% in the general population)
- Heterogeneity of effect of antidepressant medication across trials
- Cochrane Review metanalysis: low evidence supporting antidepressant use for depression treatment in individuals on opioid agonists

Pani PP et al. Cochrane Database Syst Rev. 2010 Sep 8;(9):CD008373. doi: 10.1002/14651858.CD008373.pub2

18

Bipolar Disorder

- Definition:
  - Bipolar I – one episode of mania
  - Bipolar II – one episode of hypomania , one depressive episode
- Symptoms of mania:
  - one week of elevated mood and increased energy
  - 3 of the following: grandiosity, decreased need for sleep, talkativeness, racing thoughts, distractibility, increase in goal-directed or psychomotor activity, risk-taking
- Rates of substance use disorder 40%
- Often present depressed - treatment with antidepressant not indicated

19

Anxiety Disorders

- Almost 20% of individuals with SUD have co-occurring anxiety disorder
  - 15% of those with anxiety disorder have a comorbid SUD
  - Double the rates of nicotine and opioid use than general population
- Most common co-occurring disorders
  - Generalized Anxiety
  - Social Anxiety
  - Panic

20

Anxiety Disorder Treatment

- Pharmacotherapy: SSRIs
  - Avoid benzodiazepines
- Psychotherapy: CBT

21

Generalized Anxiety Disorder (GAD)

- Most frequent anxiety disorder seen in primary care, 22%
- 50% have lifetime comorbid SUD
  - 12-22% of individuals with SUD presenting for treatment
- Alcohol use more prevalent than in other anxiety disorders
- Comorbid substance use affects recovery

22

Common Somatic Complaints Of Social Anxiety Disorder



Beidel. *J Clin Psychiatry*. 1998;59(suppl 17):27.

23

Screening for Social Anxiety Disorder

- Does fear of embarrassment cause you to avoid doing things or speaking to others?
- Do you avoid activities in which you are the center of attention?
- Is being embarrassed or looking stupid among your worst fears?

24

Social Anxiety and Substance Use Disorders

- Usually starts in childhood/adolescence
- Risk factor for alcohol use – prevalence of AUD is 48%
- Paradoxically, addiction treatment may worsen social anxiety

25

Integrated Psychiatric Treatment and AA Facilitation

So you thought about going to a meeting last night but were afraid you would panic if you were called on, so you didn't go. Let's work out a strategy:

1. Treat social phobia with medication
2. Rehearsal of what to say in meetings with visualization ("Hi I'm Kelly and I'm glad to be here")
3. Remind patient - no requirement for speaking

Ries RK et al. (2015). Twelve-Step Facilitation: An Adaptation for Psychiatric Practitioners and Patients. In M Galanter et al (Ed). Textbook of Substance Abuse Treatment. Arlington: American Psychiatric Publishing.

26

Marina is a 28-year-old woman.

She complains to her primary care doc about frequent panicky feelings, anxiety, and feeling sweaty in afternoons at work. She states that she feels better once home and after large glass of wine. She is worried because she is drinking more.

She thinks she has panic disorder and that this is causing more drinking.

27

Panic Attack

Surge of fear or discomfort lasting for several minutes to an hour, with 4+ associated symptoms

- Palpitations
- Sweating
- Trembling / shaking
- Shortness of breath
- Chest pain
- Nausea
- Dizziness
- Chills/hot flash
- Paresthesias
- Derealization/depersonalization
- Fear of losing control
- Fear of dying

28

Posttraumatic Stress Disorder

- Diagnosis: all 5 criteria for 1+ month
  - Exposure to traumatic event
  - Re-experiencing
  - Avoidance
  - Negative alterations in mood and cognition
  - Alterations in arousal and reactivity
- Often comorbid depression, anxiety disorders
- Increases likelihood of SUD by 2-4x
- Usually precedes SUD

29

PTSD Treatment

- Psychotherapy
  - Exposure
  - Cognitive therapy (trauma-focused CBT, cognitive processing)
  - EMDR
- Pharmacotherapy
- SSRIs
- Prazosin

30

Attention Deficit Hyperactivity Disorder (ADHD)

- Diagnosis: 5+ symptoms in either inattentive or hyperactive/impulsive domains, in 2+ settings, for 6+ months
  - Inattentive: difficulty paying attention to details, sustaining attention, and organizing, forgetful, loses things, easily distracted
  - Hyperactive/Impulsive: fidgets, restless, driven by motor, talks excessively, difficulty waiting turn
- Rates of SUD 2-3x general population

31

ADHD Treatment

- Typically, amphetamines are first-line treatment
- For individuals with SUD history, atomoxetine
- If active substance use, acutely stabilize/treat substance use first

32

Kelvin is a 28-year-old man.

He presents to urgent care. He is concerned that his computer and phone are bugged. He also is paranoid that police have been following him. He notes these symptoms have been occurring for months. He denies substance use.

Utox is positive for amphetamines. He then acknowledges frequent crystal meth use.

33

Substance-Induced Psychosis vs Schizophrenia

- **Substance-Induced (methamphetamines)**
  - Clear heavy drug use
  - More likely to preserve general function
  - Usually positive symptoms (paranoia, hallucinations), but not many negative symptoms
- **Schizophrenia**
  - Earlier onset
    - Prodrome of withdrawal, negative symptoms, few friends
  - More global impairment, thought disorder

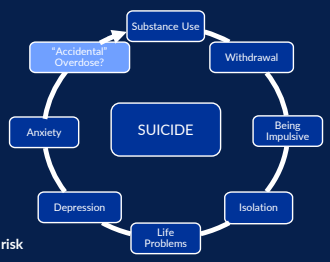
34

Psychotic Disorders

- Up to 15% of substance-induced psychosis can persist after 1mo of abstinence
- Up to 50% of individuals with schizophrenia have co-occurring SUD
  - 75% have tobacco use disorder
- Cannabis use: doubles the odds of developing a psychotic illness
- Substance use in individuals with psychotic disorders
  - Associated with increase in duration of untreated illness
  - Impacts adherence with treatment
  - Leads to increase symptom burden and poorer quality of life

35

Addiction and Suicide



Addiction = 5-10 x risk

Youdelis-Flores 2015

36

Substance Use and Suicide

- Suicides in the U.S. (NVDRS Data)
  - 22% involve alcohol intoxication
  - 20% involve opioids
  - 10% involve cannabis
- Individuals with substance use at 2-100x the risk of general population
- Limitations of suicide research
  - Exclusion of women

SAMHSA/NIMH

37

Suicide and Alcohol

- U.S. study of individuals with AUD
  - 4.5% attempted suicide
  - Related factors: More severe substance use
    Substance-induced psychiatric disorders
    Separated/divorced, prior attempts
- European autopsy study of suicides
  - 40% with alcohol use disorder

SAMHSA/NIMH

38

Opioid Overdose Deaths and Suicide

- About 50,000 deaths from each last year
- In 2017, >40% of all suicides and overdose deaths involved opioids
- Intentionality of ODs dimensional, not categorical

Bohnert and Ilgen. *N Engl J Med.* 380:14, 1379-1380.

39

Suicide and Opioids

- Interventions should address multiple risk factors
  - Quality of pain care
  - Access to psychotherapy
  - Access to medication-assisted treatment for opioid use

Bohnert A and M Ilgen (2019). *N Engl J Med* 2019; 380:71-79.

40

Assessing Imminent Risk

- Withdrawal/cravings
- Changes in pattern of use
- Loss of agency/identity, shame, humiliation, erosion of social supports
- Increased use of other substances
- Stressful life events (recent relapse, legal problems, end of romantic relationship)

Maruti S et al. (2019). *Prev Med* 128: 105854

41

Thank you!

42

Prevention and Public Health: Principles and Applications Saturday, July 23
11:30 am – 12:15 pm CT

Addiction medicine is not only the diagnosis and treatment of addiction but also the prevention of drug use and related issues. This session will discuss some of the core principles of effective prevention and public health initiatives. The presenter will use real examples to demonstrate how different types of prevention can be applied to reduce drug use, related co-morbidities, and mortality.

Learning Objective:

- After this session, learners will be able to: Explain ways the principles of prevention can be applied to addiction medicine and the impact of prevention on public health.

Faculty Presenter



Amesika N. Nyaku, MD, MS
Assistant Professor
Rutgers New Jersey Medical School

Amesika Nyaku, MD MS is an Assistant Professor in the Division of Infectious Diseases at Rutgers New Jersey Medical School and a physician-scientist. She provides clinical care for people living with HIV or other infectious diseases and substance use disorders. Her research interests lie at the intersection of HIV and substance use disorders. She focuses on 1) evaluating long-acting therapeutics for HIV and opioid use disorder, 2) the implementation of integrated care models for HIV and substance use disorders to improve health outcomes, and 3) increasing the inclusion and participation of racial/ethnic minorities in clinical trials research. She is also co-director of the Northern New Jersey Medication-Assisted Treatment Center of Excellence that is tasked with assisting the state in expanding access to medication-assisted treatment for opioid use disorder through education, novel service delivery, and community collaboration.

Prevention and Public Health

Amesika N. Nyaku, MD, MS
Assistant Professor
Rutgers New Jersey Medical School
Co-Director Northern New Jersey Medication Assisted Treatment Center of Excellence

1

The ASAM Review Course of Addiction Medicine

July 2022

Financial Disclosures



Amesika N. Nyaku, MD, MS
No Disclosures

2

Learning Objectives

Explain ways the principles of prevention can be applied to addiction medicine and the impact of prevention on public health.

3

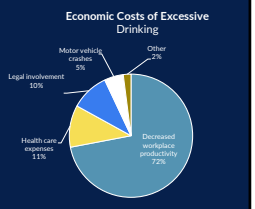
Presentation Outline

- Scope of substance use on public health
- Commonly used public health frameworks of prevention
- Evidence informed prevention interventions

4

Addiction and Public Health

- Mortality
  - Alcohol related deaths – 140,000 deaths/year between 2015-2019
  - Drug related deaths – Since 1999 over 1 million deaths, age-adjusted rate increased by 31% from 2019 to 2020
- Economic impact
  - In 2010, $249 billion related to excessive alcohol use
- Negative impact on chronic diseases
- Exacerbation of social problems



https://www.cdc.gov/alcohol/features/excessive-alcohol-deaths.html
https://www.cdc.gov/drugoverdose/deaths/index.html
https://www.cdc.gov/alcohol/features/excessive-drinking.html
SAMHSA. Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health. 2016

5

What is a Public Health Systems Approach?

- Defines the problem through the systematic collection of data on the scope, characteristics, and consequences of substance misuse
- Identifies the risk and protective factors that increase or decrease the risk for substance misuses and its consequences, and the factors that could be modified through interventions
- Works across the public and private sector to develop and test interventions that address social, environmental, or economic determinants of substance misuse and related health consequences
- Supports broad implementation of effective prevention and treatment interventions and recovery supports in a wide range of settings
- Monitors the impact of these interventions on substance misuse and related problems as well as on risk and protective factors



SAMHSA. Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health. 2016

6

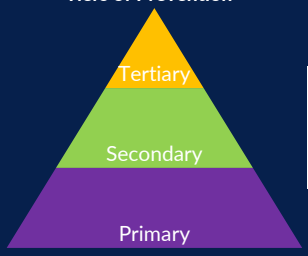
Goals of Prevention

- Preserve or improve the general health and well being
- Reduce mortality
- Reduce co-morbidity
- Improve public health

7

Frameworks in Public Health for Prevention

Tiers of Prevention



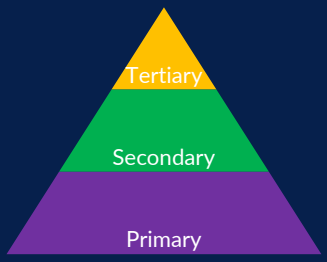
Social-Ecological Model



https://www.iwh.on.ca/what-researchers-mean-by/primary-secondary-and-tertiary-prevention
https://www.atsdr.cdc.gov/communityengagement/pce_models.html

8

Public Health Frameworks: Tiers of Prevention



https://www.iwh.on.ca/what-researchers-mean-by/primary-secondary-and-tertiary-prevention

REVIEW COURSE in Addiction Medicine

9

Tiers of Prevention: Primary Prevention

- Primary prevention aims to prevent disease or injury before it ever occurs.
  - This is done by preventing exposures to hazards that cause disease or injury, altering unhealthy or unsafe behaviors that can lead to disease or injury, and increasing resistance to disease or injury should exposure occur.

https://www.iwh.on.ca/what-researchers-mean-by/primary-secondary-and-tertiary-prevention

10

Tiers of Prevention: Secondary Prevention

Secondary prevention aims to reduce the impact of a disease or injury that has already occurred. This is done by detecting and treating disease or injury as soon as possible to halt or slow its progress, encouraging personal strategies to prevent reinjury or recurrence, and implementing programs to return people to their original health and function to prevent long-term problems.

https://www.iwh.on.ca/what-researchers-mean-by/primary-secondary-and-tertiary-prevention

11

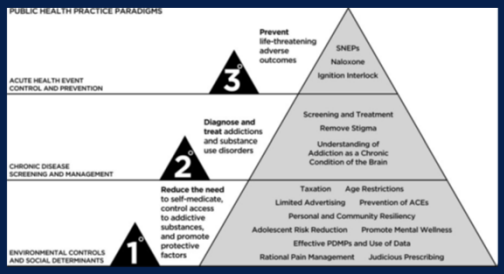
Tiers of Prevention: Tertiary Prevention

- Tertiary prevention aims to soften the impact of an ongoing illness or injury that has lasting effects.
  - This is done by helping people manage long-term, often-complex health problems and injuries (e.g., chronic diseases, permanent impairments) in order to improve as much as possible their ability to function, their quality of life and their life expectancy.
- Tertiary prevention interventions are essentially forms of treatment aimed to prevent worsening conditions and the emergence of secondary problems.

https://www.iwh.on.ca/what-researchers-mean-by/primary-secondary-and-tertiary-prevention

12

Public Health Approaches to Preventing Substance Misuse and Addictions



Butler JC. 2017 ASTHO President's Challenge: Preventing Substance Misuse and Addiction. J Public Health Manag Pract. 2017;23(5):531-536.

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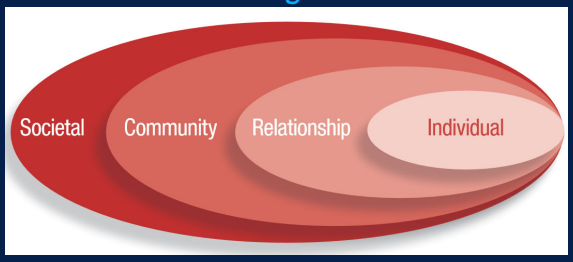
Public Health Frameworks: Social-Ecological Model



https://www.atsdr.cdc.gov/communityengagement/pce_models.html

14

Defining the Levels of SEM

Individual

- Individual biology and other personal characteristics, such as age, education, income, and health history.

Relationship

- Person's closest social circle, such as friends, partners, and family members, all of whom influence a person's behavior and contribute to his or her experiences.

https://www.atsdr.cdc.gov/communityengagement/pce_models.html

15

Defining the Levels of SEM, con't

Community

- Settings in which people have social relationships, such as schools, workplaces, and neighborhoods, and seeks to identify the characteristics of these settings that affect health.

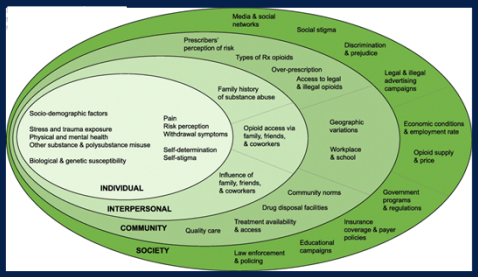
Societal

- Broad societal factors that favor or impair health. This includes cultural and social norms and the health, economic, educational, and social policies that help to create, maintain, or lessen socioeconomic inequalities between groups.

https://www.atsdr.cdc.gov/communityengagement/pce_models.html

16

Social-ecological Framework



Jalali MS, et al. Health Research Policy and Systems 2020;18(1):87.

17

Harm Reduction

Policies, programs and practices that aim to minimize negative health, social, and legal impacts associated with drug use, drug policies, and drug laws. Harm reduction is grounded in justice and human rights – it focuses on positive change and on working with people without judgement, coercion, discrimination, or requiring that they stop using drugs as a precondition of support.



https://www.hri.global/what-is-harm-reduction
Health, Rights, and Drugs UNAIDS 2019

18

Other Prevention Concepts

Environmental Prevention	Limit opportunities for unhealthy or risky behavior or promote the availability of healthier options in order to prevent problems associated with substance use. They do so by altering the environment in ways that can unconsciously influence behavior.
Demand Reduction	Preventing the uptake and/or delaying the onset of use of alcohol, tobacco and other drugs; reducing the misuse of alcohol, tobacco and other drugs in the community and supporting people to recover from dependence through evidence-informed treatment.
Supply Reduction	Preventing, stopping, disrupting or otherwise reducing the production and supply of illegal drugs; and controlling, managing and/or regulating the availability of legal drugs.

19

Environmental Interventions

Actions to minimize future hazards to health and inhibit the establishment factors (environmental, economic, social, behavioral, cultural) known to increase the risk of disease

Examples related to drug use with some evidence base

- Purchase laws
- Price controls
- Restrictions on retail/density
- Controls on advertising

Center for Substance Abuse Prevention (CSAP). 1999. Environmental prevention strategies: Putting theory into practice, training and resource guide. Rockville, MD: National Clearinghouse for Alcohol and Drug Information.

20

Demand Reduction

Preventing the uptake and/or delaying the onset of use of alcohol, tobacco and other drugs; reducing the misuse of alcohol, tobacco and other drugs in the community and supporting people to recover from dependence through evidence- informed treatment

- Criminal sanctions for possession/use
- Drug treatment (coerced and voluntary)
- Drug education and persuasion
- Drug testing and noncriminal sanctions

National Research Council. Informing America's Policy on Illegal Drugs: What We Don't Know Keeps Hurting Us [Internet]. Washington, D.C.: National Academies Press; 2001

21

Supply Reduction

Preventing, stopping, disrupting, or otherwise reducing the production and supply of illegal drugs; and controlling, managing and/or regulating the availability of legal drugs by:

- Crop eradication
- Crop substitution
- Disruption of transport
- Domestic enforcement
- Regulation of pharmaceuticals
- Youth employment programs

National Research Council. Informing America's Policy on Illegal Drugs: What We Don't Know Keeps Hurting Us [Internet]. Washington, D.C.: National Academies Press; 2001

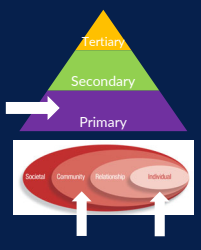
22

What We Know Works

23

Behavioral Interventions: School Based

- Focused on groups that are high risk and aims to strengthen protective factors
  - Good Behavior Game
  - Classroom-Centered Intervention
  - The Fast track Program
  - Life Skills Training
- Delayed early use of alcohol, tobacco, and other substances
- Reduced rates of use

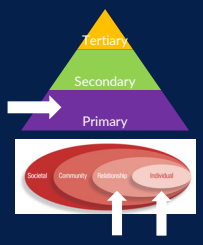


SAMHSA. Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health. 2016

24

Behavioral Interventions: Family Strengthening

- Focus on enhancing parenting skills and adolescent refusal skills
  - Nurse-Family Partnership – this is an early childhood intervention
  - Strengthening Families Program: for Parents and Youth
  - Coping power
  - I Hear What You're Saying
  - Parent Handbook
- Reduced early alcohol and substance use

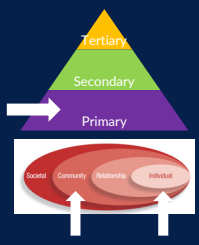


SAMHSA. Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health. 2016

25

Behavioral Interventions: Medical Settings

- Utilizes motivational interviewing and has demonstrated reduction up to 12 months
  - Brief alcohol interventions for all ages
    - Adults 18 years or older – USPSTF Grade B recommendation
    - Adolescents 12 to 17 - USPSTF Grade I recommendation
  - Brief Alcohol Screening and Intervention for College Students
  - Project Share
  - Computerized Alcohol-Related Problems Survey

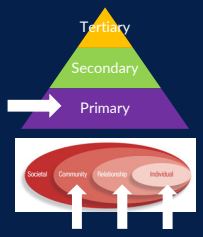


US Preventive Services Task Force et al. JAMA 320, 1899 (2018); Levy, S. J. L. et al. Pediatrics 138, e20161211 (2016).
SAMHSA. Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health. 2016

26

Behavioral Interventions: Community Based

- Communities that Care (CTC)
  - Community stakeholders assessed and prioritized which evidence-based interventions were needed to be implemented for their middle/high school kids
  - Had lower alcohol and tobacco initiation rates
- Promoting School-community-university Partnerships to Enhance Resilience (PROSPER)
  - Collaborative that implemented family strengthening and school based behavioral interventions
  - Had lower marijuana, methamphetamine, inhalant, and prescription opioid use

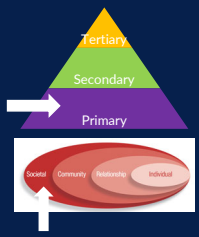


SAMHSA. Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health. 2016

27

Societal Based Interventions

- Pricing and Taxes
  - Largest evidence base is for alcohol
  - Roughly 10% increase in alcohol price reduces drinking by 5%
- Increased alcohol taxes has:
  - Large effect on morbidity and mortality
  - Moderate effect on traffic crashes
  - Smaller effects on crime, violence, and STDs

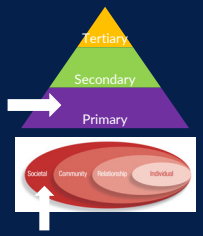


Wagenaar, A. C., et. al. Addiction 104, 179–190 (2009); Wagenaar, A. C., et al. Am J Public Health 100, 2270–2278 (2010);
SAMHSA. Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health. 2016

28

Societal Based Interventions

- Outlet Density
  - Reduction correlated with reduction in alcohol-related crimes
- Commercial Host Liability Policies
  - 6.4% decrease in alcohol-related motor vehicle fatalities
- Limit Days and Hours of Availability
  - Clear correlation between increased availability and increased alcohol-related harms



SAMHSA. Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health. 2016

29

Societal Based Interventions

- Policies to Reduce Drinking and Driving
  - Impaired Driving Laws
  - Checkpoints
  - Ignition Interlocks
  - Treatment programs
- Policies to Reduce Underage Drinking
  - Raising minimum legal drinking age
  - Zero tolerance and/or Use it-Lose it
  - Social host liability (criminal or civil)

Change in Alcohol vs Non-Alcohol-Related Motor Vehicle Deaths: 1982-2013

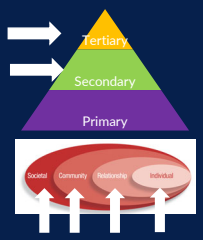


SAMHSA. Facing Addiction in America: The Surgeon General's Report on Alcohol, Drugs, and Health. 2016
https://www.cdc.gov/transportationsafety/impaired_driving/strategies.html

30

Multi-Level Interventions: Naloxone

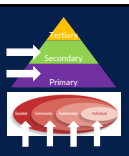
- Opioid antagonist which rapidly reverses opioid related sedation and respiratory depression and may cause withdrawal
- Administration by medical and community members
  - 11 to 21% reduction in opioid overdose deaths
- Good Samaritan Laws
  - 14% reduction in overdose deaths
- Co-prescribing for at-risk patients
  - Decreases opioid-related emergency room visits



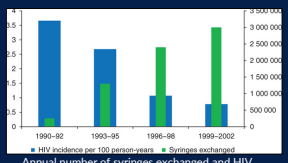
https://www.hhs.gov/opioids/sites/default/files/2018-12/naloxone-coprescribing-guidance.pdf
Walley, A. Y. et al. BMJ 346, f174 (2013).; Townsend, T. et al. Int J Drug Policy 75, 102536 (2020).; McClellan, C. et al. Addict Behav 86, 90–95 (2018).

31

Multi-Level Interventions: Syringe Services Programs



- Benefit and cost-effectiveness is well established
  - 58% reduction in HIV infections in people who inject
  - 56% in HCV infections in people who inject
- Has not been effectively scaled up due to regulations and community norms



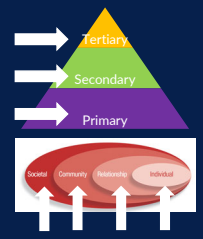
Annual number of syringes exchanged and HIV incidence among PWIDs in NYC, 1990-2002

Aspinall Int J Epidemiol 2014; Des Jarlais AIDS 2016; Platt et al. The Cochrane Review 2017; Broz et al. AJPM 2021

32

Multi-Level Interventions: Medications for Opioid Use Disorder

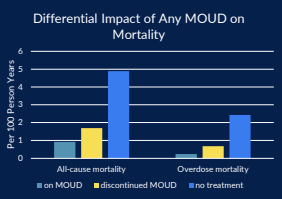
- Tertiary Prevention
  - Decreased mortality
- Secondary Prevention
  - Improves HIV treatment outcomes
- Primary Prevention
  - Prevents HIV and HCV acquisition



33

Medications for Opioid Use Disorder: Tertiary Prevention

- Decreases opioid and non-opioid related mortality
  - Increases quality of life
  - Increases employment
  - Decreases emergency department use



Ma, et al. Molecular Psychiatry 2019; Mattick RP, et al. Cochrane Database Syst Rev 2003 ; Mattick RP, et al Database Syst Rev 2009 ; Mattick RP, et al. Cochrane Database Syst Rev 2014 ; Dupouy J, et al. Ann Fam Med 2017;15(4):355–8. ,

34

Medications for Opioid Use Disorder: Secondary Prevention

Systematic review and meta-analysis of 32 studies showed treatment for OUD (methadone, buprenorphine, naltrexone, other) associated with:



- 69% increase in ART uptake
- 2-fold increase in ART adherence
- 45% increase in viral suppression

Low. Clin Infect Dis. 2016;63:1094.

Slide credit: clinicaloptions.com

35

Medications for Opioid Use Disorder: Primary Prevention

- HIV incidence
  - 54% reduction in people who injected drugs
- HCV incidence
  - 60% reduction in people who injected drugs
  - Strongest effect with agonist forms of MOUD

MacArthur GJ et al. BMJ 2012; 345 :e5945; Hagan et al. JID; 204(1):74-83; Tsui JI, et al. JAMA Intern Med. 2014;174(12):1974–1981

36

Conclusions

Public health prevention interventions for drug use

- Utilize a tiered approached to prevention that considers the individual, interpersonal dynamics, community settings, and societal aspects
- Has a well-established body of evidence-based interventions
- Requires ongoing scale up and systematic monitoring

37

Thank You!

amesika.nyaku@rutgers.edu

38

Medical Co-Morbidities: Prevention and Treatment

Saturday, July 23
12:15 pm – 1:00 pm CT

Many patients with addiction present with other medical co-morbidities that must be addressed in any treatment plan. This session will provide an organ-organized overview of the main medical co-morbidities associated with drug use. Participants will also discuss the importance of routine and preventive health care for patients with substance use disorders.

Learning Objective:

- After this session, learners will be able to: List common co-occurring medical complications associated with drug use and methods for prevention and treatment.

Faculty Presenter



Annie Levesque, MD, MSc
Medical Director, Opioid Treatment Program
Mount Sinai West Hospital
Icahn School of Medicine

Dr. Annie Levesque is the Medical Director of the Opioid Treatment Program at the Addiction Institute at Mount Sinai West. She is also the Associate Director of the Fellowship in Addiction Medicine Program at the Icahn School of Medicine at Mount Sinai. After receiving her medical degree from the University of Montreal, Dr. Levesque completed a Family Medicine and a Clinician-Scholar residency program at the University of Montreal, an Addiction Medicine fellowship at Mount Sinai West Hospital and a Masters in Experimental Medicine at McGill University.

Medical Comorbidities

Annie Lévesque, MD, MSc
Assistant Professor, Department of Medicine, Department of Psychiatry
Mount Sinai West Hospital, Icahn School of Medicine

1

The ASAM Review Course of Addiction Medicine

July 2022

Financial Disclosures

Annie Lévesque, MD, MSc
No Disclosures



2

Learning Objectives

List common co-occurring medical complications associated with drug use and methods for prevention and treatment.

3

Presentation Outline

Routine and preventive care
- History
- Physical examination
- Labs

Comorbidities and consequences of SUD
- Cardiovascular
- GI
- Pulmonary
- Renal
- Infectious
- Neuro
- Traumatic injuries
- Endocrine

4

General Medical Evaluation

Routine/preventive care follows national guidelines (USPSTF)

History and physical evaluation includes categories of assessment employed for all patients, with special focus on the following:

History
- Social and family history
- Emergency Department visits or hospitalizations related to substance use
- Psychiatric history
- Substance related risk behaviors

Physical evaluation
- Vitals
- Observation: signs of intoxication/withdrawal
- ENT: pupils, oral cavity, nasal septum
- Heart: murmur
- Abdomen: liver
- Extremities: injection sites, tremors

5

General Medical Evaluation

Health maintenance labs:

- Complete blood count
- Metabolic panel
- Liver function
- Lipid panel
- HBA1C
- HIV, HBV, HAV, HCV, PPD, RPR
- Vitamin D

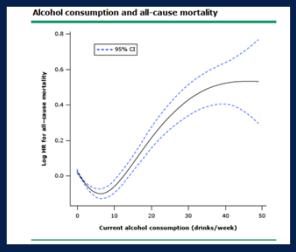
6

Cardiovascular

- TOBACCO → Atherosclerosis, HTN, CAD
- STIMULANTS → Chest pain, HTN, arrhythmia, cardiomyopathy, MI (avoid beta-blockers)
- OPIOIDS → Methadone can increase QTc
- ALCOHOL → Cardiomyopathy, Afib, HTN, CAD

7

Cardiovascular



Moderate alcohol intake and cardiovascular benefits

- Association *vs* Causality
- Antioxidant (phenolic and flavonoid components red wine), antithrombotic, anti-inflammatory
- No recommendation to drink alcohol for health benefits

Xi B et al. J Am Coll Cardiol 2017

8

Gastrointestinal

PANCREATITIS

- Abdominal pain
- ↑ amylase/lipase > 3 times upper limit
- > 100g ETOH per day for 5-10 years

Acute

- Acute inflammatory process
- 28% of cases in women and 59% in men due to ETOH

Chronic

- Progressive inflammatory changes
- Permanent structural damage
- Impairment of endocrine/exocrine functions

9

Gastrointestinal

Alcoholic liver disease

- Risk Factors:
  - Amount of alcohol use
  - Female gender
  - Genetic
  - Obesity
  - Viral hepatitis
  - Hepatotoxins

10

Gastrointestinal

Alcoholic liver disease

Steatosis

- Anorexia, nausea, RUQ pain
- Potentially fully reversible

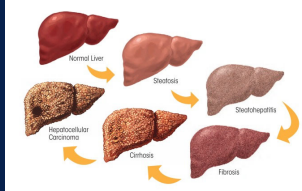
Alcohol-related hepatitis

- Jaundice, bruising, ascites, encephalopathy
- AST/ALT ≥ 2:1, ↑ bilirubin, ↑ INR
- Maddrey score ≥ 32 corticosteroid
- Pentoxifylline may decrease mortality

Cirrhosis

- Late stage of hepatic fibrosis
- Irreversible

Haber PS, Freyer CH. Chapter 81: Liver Disorders Related to Alcohol and Other Drug Use. In: *The ASAM Principles of Addiction Medicine*. Sixth. Wolters Kluwer. Ozuna NA, Donahue TM, Kharbanda KK. Alcoholic Liver Disease: Pathogenesis and Current Management. *Alcohol Res*. 2017;38(2):147-161.



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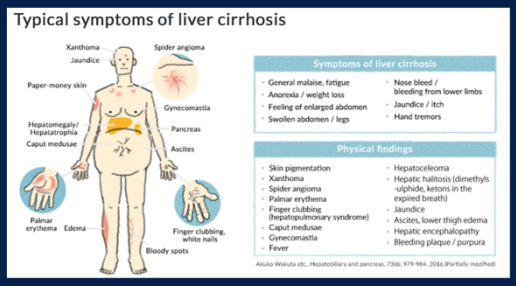
Gastrointestinal



Akuko Wakuta etc., Hepatobiliary and pancreas, 7366, 979-984, 2016 (Partially modified)

12

Gastrointestinal

CANNABIS HYPEREMESIS SYNDROME

- Episodic nausea, vomiting, and abdominal pain
- Relieved by exposure to hot water
- Generally seen in at least weekly users (more often daily users) for at least a year
- Unclear pathophysiology
- Treatment: topical capsaicin on abdomen can relieve acute symptoms, cannabis cessation

13

Pulmonary Complications

Tobacco COPD Asthma Lung Cancer	**Cannabis** Exacerbation of COPD and asthma	**Opioids** Respiratory depression Sleep apnea
Cocaine Pneumothorax "Crack lungs" Chronic toxicity	**Alcohol** Aspiration pneumonia Ascites Hepatopulmonary syndrome	**Sedative-hypnotic** Respiratory depression
Inhalants Respiratory depression Barotrauma Pulmonary edema	**Amphetamines** Pulmonary hypertension Pulmonary edema	**Anabolic steroids** Pulmonary embolism

14

Renal

KETAMINE-INDUCED UROPATHY

- Urge incontinence, decreased bladder compliance, decreased bladder volume, detrusor overactivity, hematuria
- Rarely hydronephrosis or papillary necrosis
- Some injuries are permanent, other improve with medical and surgical treatment
- Mechanism unclear: possible irritation from contact of metabolite with bladder and ureteral mucosa

15

Infectious Complications - Endocarditis

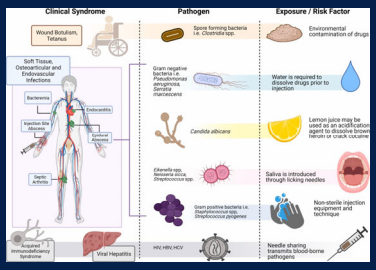


Image from: Marks LR, Nolan NS, Liang SY, Durkin MJ, Weimer MB. Infectious Complications of Injection Drug Use. *Medical clinics of North America.* 2022;106(1):187-200. doi:10.1016/j.mcna.2021.08.006

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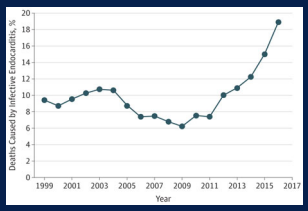
16

Infectious Complications - Endocarditis

Endocarditis in people who inject drugs is associated with rising mortality



Njoroge LW, et al.. *Cardiol* 2018
Ronan MV, Herzig SJ. *Health Aff (MJAMAIlwood)* 2016

Infectious endocarditis should be suspected in patients with fever and risk factors:

- **IV drug use**
  - Tricuspid valve
  - IV cocaine use - vasospasm
- IV lines
- Prior IE
- Prosthetic valve, hx of valvular disease
- Cardiac device
- Immunosuppression
- Recent dental or surgical procedure

Treatment: Antibiotic therapy +/- valve surgery

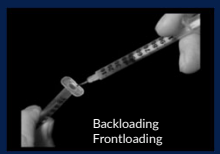
17

Infectious Complications

Sharing of contaminated material is the main driver of HIV and HCV infections among PWID

- Needles
- Auxiliary injection material: dilution water, filters, cookers, backloading, frontloading
- Crack pipes







18

Infectious Complications

HIV	
Type of exposure	**Risk of infection (%) [1]**
Anal receptive	0.5 to 3.38
Anal insertive	0.06 to 0.16
Vaginal receptive	0.08 to 0.19
Vaginal insertive	0.05 to 0.1
Mother-to-child	15 to 45
Accidental puncture	0.33
Sharing of injection equipment	**0.7 to 0.8**

HCV	
Type of exposure	**Risk of infection (%) [2, 3]**
Blood transfusion	Negligible since 1990
Sexual exposure	Low
Sharing of personal items	Low
Tattoo and piercing	Low
Mother-to-child	5 to 6
Accidental puncture	1.8
Sharing of injection equipment	**2.5 to 5**

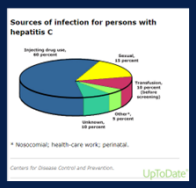
- HIV and HCV viruses can survive several weeks outside of human body
- Viability of virus varies based on virus concentration, medium in which virus is contained, moisture, temperature, sunlight

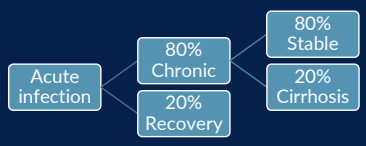
[1]Public Health Agency of Canada, HIV Transmission Risk: A Summary of Evidence.
[2] Noel L et al. INSPQ 2016.
[3] O'Brien et al. Transfusion 2007

19

Infectious complications – Hepatitis C

- Most patients with HCV in North America acquired disease through IV drug use



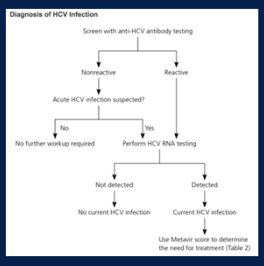


Wilkins T. et al. *Am Fam Physician*. 2015 Jun 15;91(12):835-842.

20

Infectious Complications – Hepatitis C

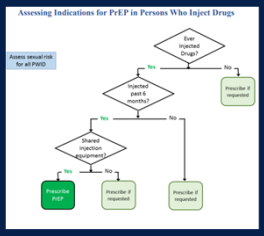
- Annual HCV testing is recommended for PWID with no prior testing or past negative testing and subsequent injection drug use
- Clinical trials among PWID who report current IDU at the start of HCV treatment and/or continued use during therapy demonstrate SVR rates approaching 95%



Wilkins T. et al. *Am Fam Physician*. 2015 Jun 15;91(12):835-842.

21

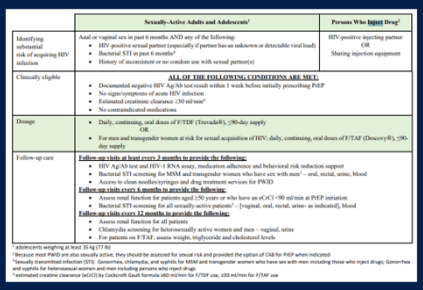
Infectious Complications –PrEP for HIV



Cdc - Preexposure Prophylaxis For The Prevention Of Hiv Infection In The United States – 2021 Update

22

Infectious Complications –PrEP for HIV



	Sexually-Active Adults and Adolescents[1]	Persons Who Inject Drug[2]
Identifying substantial risk of acquiring HIV infection	Anal or vaginal sex in past 6 months AND any of the following: • HIV-positive sexual partner (especially if partner has an unknown or detectable viral load) • Bacterial STI in past 6 months[3] • History of inconsistent or no condom use with sexual partner(s)	HIV-positive injecting partner OR Sharing injection equipment
Clinically eligible	**ALL OF THE FOLLOWING CONDITIONS ARE MET:** • Documented negative HIV Ag/Ab test result within 1 week before initially prescribing PrEP • No signs/symptoms of acute HIV infection • Estimated creatinine clearance ≥30 mL/min[4] • No contraindicated medications	
Dosage	• Daily, continuing, oral doses of F/TDF (Truvada®), ≤90-day supply OR • For men and transgender women at risk for sexual acquisition of HIV; daily, continuing, oral doses of F/TAF (Descovy®), ≤90-day supply	
Follow-up care	**Follow-up visits at least every 3 months to provide the following:** • HIV Ag/Ab test and HIV-1 RNA assay, medication adherence and behavioral risk reduction support • Bacterial STI screening for MSM and transgender women who have sex with men[3] – oral, rectal, urine, blood • Access to clean needles/syringes and drug treatment services for PWID **Follow-up visits every 6 months to provide the following:** • Assess renal function for patients aged ≥50 years or who have an eCrCl <90 mL/min at PrEP initiation • Bacterial STI screening for all sexually-active patients[3] – [vaginal, oral, rectal, urine- as indicated], blood **Follow-up visits every 12 months to provide the following:** • Assess renal function for all patients • Chlamydia screening for heterosexually active women and men – vaginal, urine • For patients on F/TAF, assess weight, triglyceride and cholesterol levels	

[1] adolescents weighing at least 35 kg (77 lb)
[2]Because most PWID are also sexually active, they should be assessed for sexual risk and provided the option of CAB for PrEP when indicated
[3]Sexually transmitted infection (STI): Gonorrhea, chlamydia, and syphilis for MSM and transgender women who have sex with men including those who inject drugs; Gonorrhea and syphilis for heterosexual women and men including persons who inject drugs
[4] estimated creatine clearance (eCrCl) by Cockcroft Gault formula ≥60 mL/min for F/TDF use, ≥30 mL/min for F/TAF use

Cdc - Preexposure Prophylaxis For The Prevention Of Hiv Infection In The United States – 2021 Update

23

Neurologic Complications

SEIZURE
- Intoxication
  - Cocaine, stimulants
- Withdrawal syndromes
  - Alcohol, barbiturates, benzodiazepines
- Opiates: meperidine

STROKE
- At younger age than the general population
- Alcohol, tobacco, cocaine, opioids methamphetamine, LSD, PCP

24

Neurologic Complications

WERNICKE ENCEPHALOPATHY

- Acute complication of thiamine deficiency
- **Classic triad:**
  - Encephalopathy
  - Oculomotor dysfunction
  - Gait ataxia
- Treatment: IV thiamine before administering glucose

KORSAKOFF SYNDROME

- Late neuropsychiatric consequence of WE
- Anterograde and retrograde amnesia
- Apathy
- Intact sensorium
- Confabulation
- No treatment, rarely recovers

25

Sleep Disorders - Changes of Sleep Architecture

	Alcohol	Stimulant or cocaine intoxication	Acute cocaine Withdrawal	Subacute cocaine withdrawal	MDMA intoxication	THC intoxication	THC withdrawal
Sleep latency	↓	↑	↑	↓		↑	↑
Total sleep time	↓	↓	↓	↓	↓		
Sleep efficiency	↓		↓	↓			
Slow wave sleep	↓		↓			↓	↓
REM	↓	↓	↑	↓	↓*	↓	↑

Schierenbeck T, et al. Effect of illicit recreational drugs upon sleep: Cocaine, ecstasy and marijuana. *Sleep Medicine Reviews*. 2008;12(5):381-389. Chakravorty S, et al. Alcohol Dependence and Its Relationship With Insomnia and Other Sleep Disorders. *Alcoholism: Clinical and Experimental Research*. 2016;40(11):2271-2282.

26

Sleep Disorders

- Negatively affects physical and emotional well-being
- Increases risk of relapse
- First-line of treatment is nonpharmacological
- Sleep hygiene
- Avoid benzodiazepines and z-drugs

Nonpharmacological Treatments Of Insomnia

- **Mindfulness meditation.** The patient moves into a state of restful, present-moment alertness, which reduces stress and improves self-control.[33,34]
- **Progressive muscle relaxation.** The patient concentrates on tensing and relaxing groups of muscles.[4,35]
- **Biofeedback.** The patient becomes aware of physiologic stress responses and how to control them.[36]
- **CBT for insomnia.** The patient's dysfunctional beliefs and behaviors are modified to improve his or her emotional state.[26,34]
- **Stimulus control.** The patient reassociates the bedroom with the rapid onset of sleep.[37]
- **Exercise.** Regular physical activity relieves stress and tires the patient.[38]
- **Sleep restriction therapy.** The patient limits sleep to a few hours and progressively increases it until the desired amount of sleep time is achieved.[34]
- **Bright-light therapy.** Exposure to a natural bright light while awake helps promote normal sleep patterns.[38]
- **Dental devices and continuous positive airway pressure machines.** These devices help the patient with obstructive sleep apnea breathe more easily during sleep.[39]

SAMHSA, Treating Sleep Problems of People in Recovery From Substance Use Disorders 2014

27

Acute Traumatic Injuries

- Alcohol and other drugs highly associated with traumatic injuries
- In 2016, 43.6% of people killed in driving accidents tested positive for alcohol and/or other drugs
- Most common drugs = marijuana, cocaine/methamphetamine, opioids, sedatives

SAMHSA. Results from the 2017 National Survey on Drug Use and Health

28

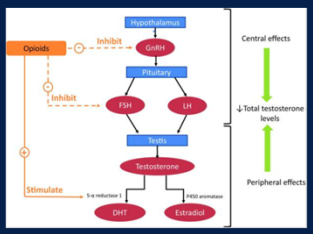
Endocrine and Reproductive

OPIOID INDUCED HYPOGONADISM

- Prevalence estimated between 19% and 86% in individuals chronically taking opioids

Symptoms:

- Change in mood
- Decreased libido/erectile dysfunction
- Decrease muscle strength
- Fatigue
- Osteopenia/osteoporosis
- Menstrual cycle abnormalities
- Hot flashes
- Failure to conceive



Coluzzi F. et al. J Endocrinol Invest. 2018

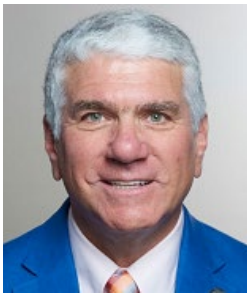
29

Interesting Cases with Audience Response System (ARS)

Saturday, July 23
2:00 pm – 2:15 pm CT

Test your critical thinking and problem-solving skills while learning more about the complexities of addiction cases through this interactive session leveraging Audience Response System.

Faculty Presenter



Edwin A. Salsitz, MD, DFASAM
Unit Chief, Inpatient Rehabilitation
Mount Sinai Beth Israel
Icahn School of Medicine at Mount Sinai

Dr. Edwin A. Salsitz has been an attending physician in the Mount Sinai Beth Israel, Division of Chemical Dependency, New York City, since 1983, and is an Associate Clinical Professor of Psychiatry at the Mount Sinai School of Medicine. He is the principal investigator of the Methadone Medical Maintenance (office-based methadone maintenance) research project. Dr. Salsitz is certified in Addiction Medicine by the American Board of Preventive Medicine, as well as by the Board of Internal Medicine and Pulmonary Disease. He has published and lectures frequently on addiction medicine topics.

Dr. Salsitz is a course director for ASAM sponsored Buprenorphine and REMS Opioid trainings, and is a lead mentor in the PCSS-MAT mentoring program. He has co-chaired the ASAM Review Course, the ASAM Common Threads Course, the ASAM State of the Art course and is a reviewer for the Journal of Addiction Medicine and Drug and Alcohol Dependence. He is the chair of the ASAM REMS course on safe and effective prescribing of opioids. Dr. Salsitz was the Co-chair of the ASAM CME committee and Chair of the New York Society of Addiction Medicine CME and Education committee.
Dr. Salsitz is a member of the medical advisory panel, for the New York State Office of Alcohol and Substance Abuse Services. Dr. Salsitz is the recipient of the 2014 ASAM Annual Award, and the 2018 ASAM Annual Educator of the Year Award.

Pharmacology and Toxicology: Principles, Applications, and Limitations

Saturday, July 23
2:15 pm – 3:00 pm CT

Understanding the pharmacology and toxicology of drugs and medications allows addiction medicine providers to optimize care for their patients. This session provides an understanding of key principles such as tolerance, dependence, hyperalgesia, pharmacokinetics, and pharmacodynamics. Presenters will also discuss applications and limitations including interpretation pitfalls of screening and confirmatory urine drug tests.

Learning Objective:

- After this session, learners will be able to: Describe basic pharmacology and toxicology concepts and their applications or limitations for addiction treatment.

Faculty Presenter



Lewis S. Nelson, MD, FACEP, FACMT, FASAM
Chair, Department of Emergency Medicine
Rutgers New Jersey Medical School

Dr. Nelson is Professor and Chair of the Department of Emergency Medicine and Chief of the Division of Medical Toxicology at Rutgers New Jersey Medical School in Newark, NJ. He is a member of the Board of Directors of the American Board of Emergency Medicine and a Past-President of the American College of Medical Toxicology. He remains actively involved with CDC, FDA, DHS, and with several professional medical organizations including ASAM. Dr. Nelson is an editor of the textbook Goldfrank's Toxicologic Emergencies and on the editorial boards of several journals. In addition to providing direct clinical care to patient in the ED and his efforts at New Jersey Poison Information & Education System, his specific expertise includes the consequences of licit and illicit opioids, emerging drugs of abuse, opioid stewardship, and alcohol withdrawal.

PRINCIPLES OF PHARMACOLOGY & TOXICOLOGY

Lewis S. Nelson, MD, FACEP, FACMT, FASAM

Professor and Chair of Emergency Medicine
Chief, Division of Medical Toxicology
Rutgers New Jersey Medical School

1

The ASAM Review Course of Addiction Medicine

July 2022

Financial Disclosures

Lewis S. Nelson, MD
No Disclosures

2

Learning Objectives

1. **Explain** the differences between and clinical relevance of tolerance, dependence, and hyperalgesia.
2. **Describe** the pharmacologic principles of pharmacokinetics and pharmacodynamics and how each impacts addiction risk and addiction treatment.
3. **Discuss** the interpretation pitfalls of screening and confirmatory urine drug tests in the management of patients with substance use.

3

Addiction Medicine IS Pharmacology

- Drugs must get to the brain to elicit a response.
  - Blood brain barrier is an effective barricade
- The more rapidly the drugs reach the site of action, the greater the reinforcement.
  - Dose and dose rate
  - Route of administration
  - Lipophilicity and other pharmacologic characteristics

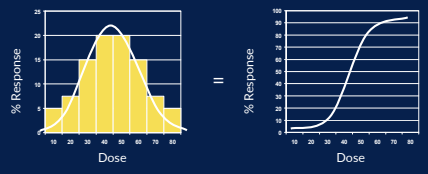
4

Pharmacokinetics and Pharmacodynamics

Absorption (Bioavailability)	Distribution	Elimination
Biotransformation	Dose Response (Clinical Effect)	Potency
Drug interaction	Tolerance	Dependence

5

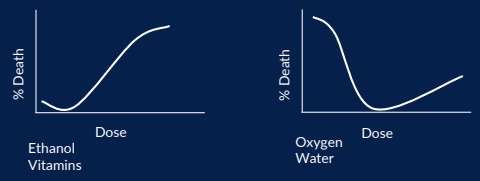
Dose-Response



Response = Anything (Blood pressure, Euphoria, Death)

6

Dose-Response



Response = Death

7

Potency

Rank order the potency at causing death:

Agent	LD50 (mg/kg)
Ethanol	5,000
Morphine	1
Nicotine	1
Botulinum	0.00001

Don't confuse potency with clinical effect

8

Which Has More Potent THC?

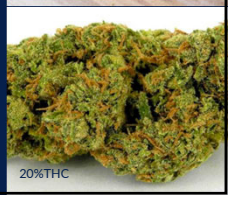
1980's weed

Trick question:
The THC is the same potency
The higher concentration weed is more "potent"

Don't confuse potency of a drug with its concentration

2020 weed





9

Potency Doesn't Really Matter

Agent	Potency (vs morphine)
Tramadol	0.2
Morphine	1
Oxycodone	1.3
Methadone	4
Heroin	4
Buprenorphine	30*
Fentanyl	100
Carfentanil	10,000

Any of these drugs will kill you if you take enough.

10



What is There That is Not Poison?

"What is there that is not poison? All things are poison and nothing [is] without poison. Solely the dose determines that a thing is not a poison"

Paracelsus (1493-1541)
in *Third Defense*

"Dose Makes The Poison"

Philip Theophrastus Bombast von Hohenheim
aka PARACELSUS (1493-1541)

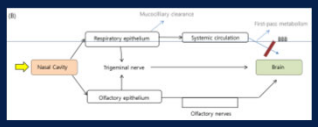
11

Absorption

12

Routes of Administration

- Oral
  - Potentially extensive first-pass
- IV, IN, IM, SC, SL, buccal, inhalational, rectal
  - Bypass hepatic first-pass
- Intrathecal
  - Unique –bypass Blood Brain Barrier
- Transdermal
  - Bypass hepatic first-pass
  - Depot in skin/body fat can influence absorption
- Intranasal
  - May directly access CNS (nose-to-brain)



Hong, S. Pharmaceutics 2019;11:540

13

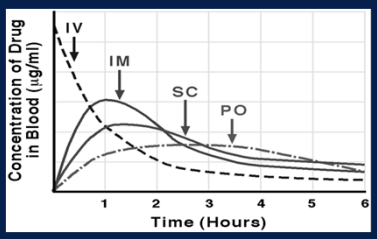
Bioavailability

- The amount of unchanged drug reaching systemic circulation after administration is the bioavailability (F).
- F depends upon:
  - Route (IV is 100%)
  - Site specific membrane permeability
  - Drug transporter activity (p-glycoprotein)
  - First-pass metabolism (oral)

	Route		
	Oral	Sublingual	Buccal
Buprenorphine	10%	30%	50%
	Oral	Sublingual	Intranasal
Naloxone	1%	20%	50%
	Oral		
Morphine	33%		
Oxycodone	75%		

14

Area Under the Curve (AUC)



Wolff K, et al. The SAGE Handbook of Drug & Alcohol Studies

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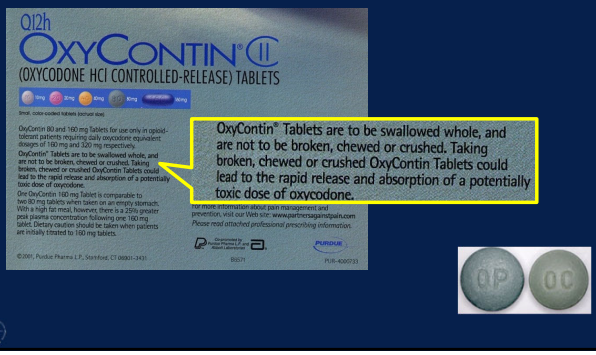

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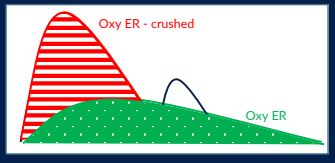
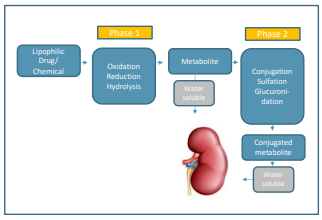
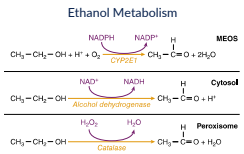


How to Abuse **OP OxyContin**, How to Get High **OP OxyContin** - Bluelight
www.bluelight.org/.../526671-How-to-Abuse-**OP-OxyContin**-How-to-Get-High-**OP-OxyContin**
How to Abuse **OP OxyContin**, How to Get High **OP OxyContin** So far the only legit way to abuse/get high off of the new **OP OxyContin** is what I ...

17

Biotransformation





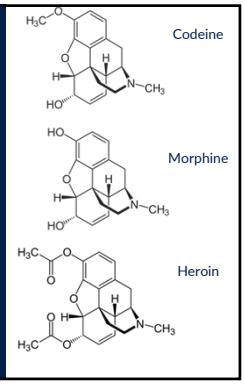
Goldfrank's Toxicologic Emergencies, 11th

18

Activation Through Biotransformation

- Codeine is demethylated in the liver to morphine
  - Occurs via CYP2D6
  - Codeine is a "pro-drug" (drug undergoes hepatic biotransformation or 'metabolism' to its active component)
  - Lisdexamfetamine (Vyvanse™) is another example of a pro-drug

Fun pharm fact: Heroin does not bind to the mu receptor. Metabolism occurs in the CSF.



19

Biotransformation

TABLE 11–1 Characteristics of Different Cytochrome P450 Enzymes[30,34,123]

CYP Enzyme	*1A2*	*2B6*	*2C9*	*2C19*	*2D6*	*2E1*	*3A4*
Percent of liver CYPs	4%–16%	2%–5%	5%–29%	1%–4%	1%–4%	6%–17%	15%–37%
Contribution to enterocyte CYPs	None	None	Minor	Minor	Minor	Minor	70%
Organs other than liver with enzyme	Lung	Kidney	Small intestine, nasal mucosa, heart	Small intestine, nasal mucosa, heart	Small intestine, kidney, lung, heart	Lung, small intestine, kidney	Much in small intestine; some in kidney, nasal mucosa, lung, stomach
Percent of metabolism of typically used pharmaceuticals	9%	7%	13%	7%	20%	3%	30 %
Polymorphisms[a]	No	Yes	Yes	Yes	Yes	No	No
Allelic Frequency							
Decreased Activity							
African American		38%–62%	0%–3%	10%–17%	14%–30%		
Asian	—	14%–25%	2%–8%	25%–39%	47%–94%	—	—
Caucasian		23%–39%	16%–23%	6%–16%	31%–45%		
Increased Activity							
African American		0%–25%		15%–27%			
Asian	—	5%–15%	—	0%–2%	1%	—	—
Caucasian		6%		21%–25%	1%–9%		
Ethiopian					30%		

[a] Polymorphism is a genetic change that exists in at least 1% of the human population. Interpersonal allelic variations exist even in those listed as "No" for polymorphism.

Goldfrank's Toxicologic Emergencies, 11th

20

Biotransformation

Genetically based alterations in gene product function.

Despite rare polymorphism, 3A4 is a major cause of drug interactions

TABLE 11–1 Characteristics of Different Cytochrome P450 Enzymes[30,34,123]

		2B6	*2C9*	*2C19*	*2D6*	*2E1*	*3A4*
		2%–5%	5%–29%	1%–4%	1%–4%	6%–17%	15%–37%
		None	Minor	Minor	Minor	Minor	70%
		Kidney	Small intestine, nasal mucosa, heart	Small intestine, nasal mucosa, heart	Small intestine, kidney, lung, heart	Lung, small intestine, kidney	Much in small intestine; some in kidney, nasal mucosa, lung, stomach
Percent of metabolism of typically used pharmaceuticals	9%	7%	13%	7%	20%	3%	30 %
Polymorphisms[a]	No	Yes				No	No
Allelic Frequency							
Decreased Activity							
African American		38%–62%					
Asian	—	14%–25%				—	—
Caucasian		23%–39%					
Increased Activity							
African American		0%–25%					
Asian	—	5%–15%				—	—
Caucasian		6%					
Ethiopian							

[a] Polymorphism is a genetic change that exists in at least 1% of the human population. Interpersonal allelic variations exist even in those listed as "No" for polymorphism.

Methadone

- Primarily responsible for metabolism
- Some HIV meds induce 3A4
- Variability (despite minimal polymorphism) complicates induction

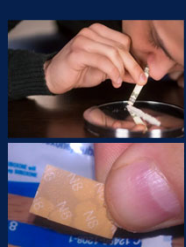
Goldfrank's Toxicologic Emergencies, 11th

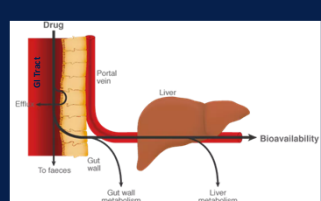
21

Distribution

22

First Pass Hepatic Metabolism





www.doctoralerts.com

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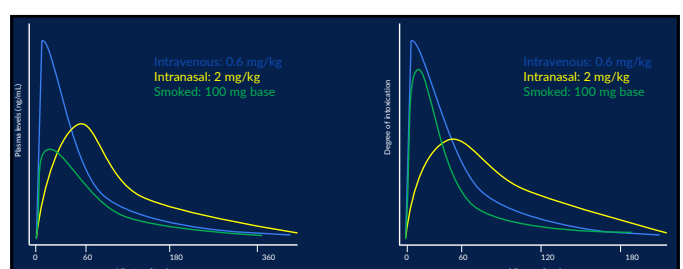


C_{max} and T_{max} depend on route of administration and dose

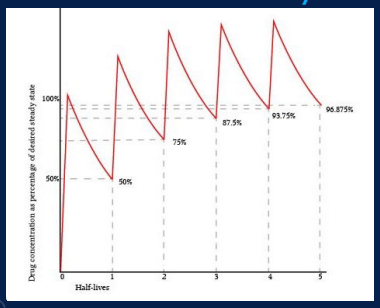
(C_{max} : IV → *Nasal* → *Smoked*)
(T_{max} : IV = *Smoked* → *Nasal*)

Subjective 'high' (0-100) by route
(*IV* → *Smoked* → *Nasal*)

NIDA Research Monograph 1992, 120

24

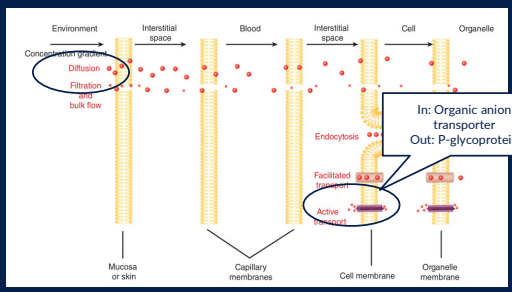
Steady State



- Requires approximately 5 half-lives
  - Regardless of the compound's half-life
- Explains (in part) the risk and difficulty of methadone induction
  - T½ ~24 hr (12-36 hr)

www.derangedphysiology.com/

25



Goldfrank's Toxicologic Emergencies, 11th

26

P-Glycoprotein



"Street pharmacologists" understand these principles.

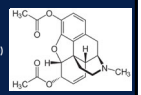
Loperamide and p-glycoprotein inhibitors

27

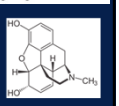
Lipophilicity

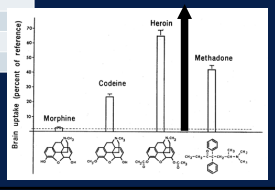
Drug	LogP
Buprenorphine	4.98
Fentanyl	4.05
Methadone	3.93
Naloxone	2.09
Hydromorphone	1.6
Heroin	1.58
Morphine	0.89

Heroin (diacetyl morphine)



Morphine



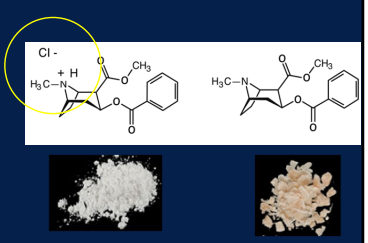


Oldendorf WH. Science. 1972

28

Addiction Medicine IS Pharmacology





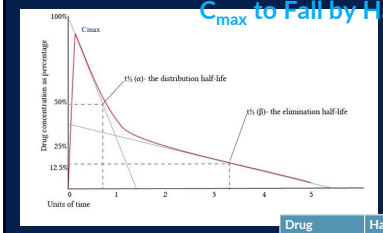
Changes in the pharmacologic properties of a substance and how it is used can lead to dramatically different levels of reward and reinforcement.

29

Elimination

30

T1/2 (Half-life) is The Time For C_{max} to Fall by Half



- Distribution t½
  - Redistribution t½
- Elmination t½
- Context sensitive t½
  - Apparent t½

Drug	Half life (distrib)	Half life (redistrib)	Half life (term)	LogP
Fentanyl	2 min	12 min	480 min	4.05
Methadone	120 min	---	1440 min	3.93

www.derangedphysiology.com/

Note: All half-lives have ranges, not shown.

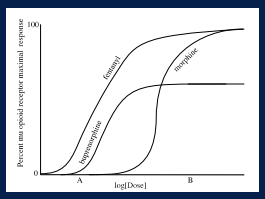
31

Receptor Pharmacology

32

Efficacy

Ligand	% Efficacy
Full agonist	E = 100
Partial agonist	0 < E < 100
Antagonist	E = 0
Inverse agonist	E < 0



33

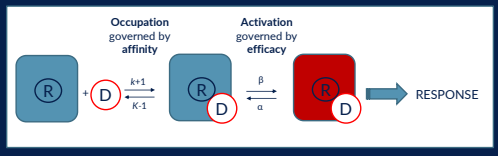
Affinity

Ligand	Ki (Affinity) (nmol)
Hydrocodone	41.58
Oxycodone	25.87
Heroin	9.6
Methadone	3.38
Fentanyl	1.35
Morphine	1.14
Naloxone	1.1
Hydromorphone	0.6
Buprenorphine	0.21

Volpe DA. Uniform assessment and ranking of opioid Mu receptor binding constants for selected opioid drugs. Reg Toxicol Pharmacol 2011

34

Receptor kinetics
On-Off



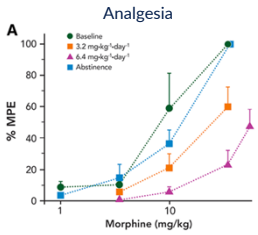
35

Pharmacodynamics

36

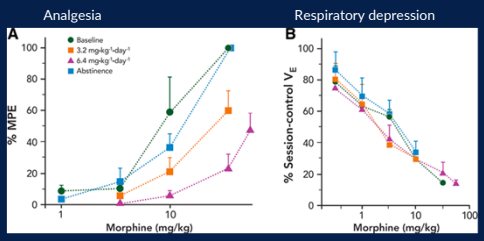
Tolerance

- Tolerance is the reduction in response to a drug after its repeated administration
- Tolerance shifts the dose-response curve to the right
  - Higher doses than initial doses to achieve the same effect



37

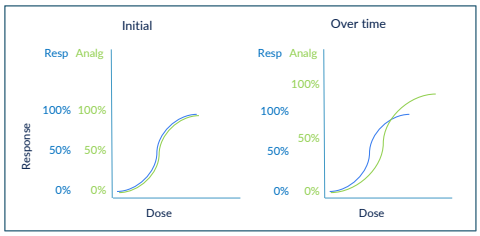
Differential Tolerance



Hayhurst. Anesthesiology 2016;124:483-8

38

The Paradox of Differential Tolerance

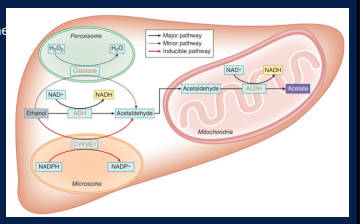


Tolerance to analgesia is rapid
Tolerance to respiratory depression is slow

39

Pharmacokinetic Tolerance

- A consequence of increased metabolism after a drug is repeatedly administered
- Results in less drug being available at the receptor for drug activity.
- Ethanol
  - Although ADH is not inducible, CYP2E1 is
  - Accounts for more rapid elimination of alcohol in heavy, chronic users

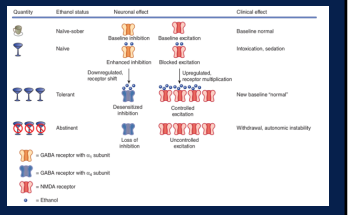


Goldfrank's Toxicologic Emergencies, 11th

40

Pharmacodynamic Tolerance

- Down-regulation of receptors (higher drug concentration needed)
  - Desensitization of GABA (ethanol)
    - Receptor conformation
  - Desensitization of MOR (opioid)
    - Signal transduction
    - Decreased density (internalization)
- Up-regulation of receptors
  - Increased number of NMDA



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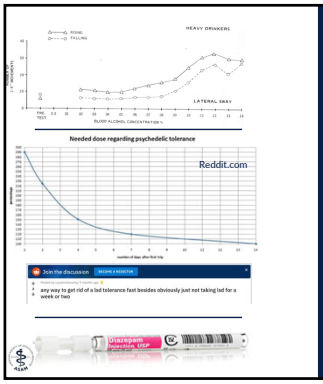
41

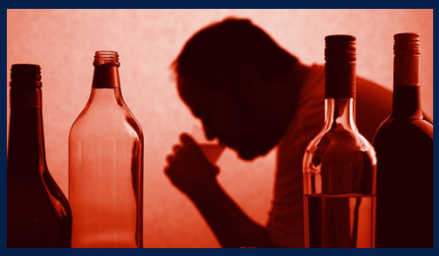


Other Clinical Examples of Tolerance

- Mellanby effect
  - Less "intoxicated" on descending limb of BAC curve
- MDMA, psilocybin, and LSD
  - Serotonergic
- Resistant alcohol withdrawal from IV (not really PO) diazepam

42

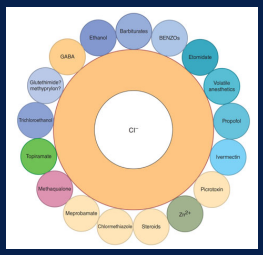
Conditioned Tolerance



43

Cross-Tolerance

- Tolerance to the repeated use of a specific drug in a given category is generalized to other drugs with the same structural or mechanistic category.



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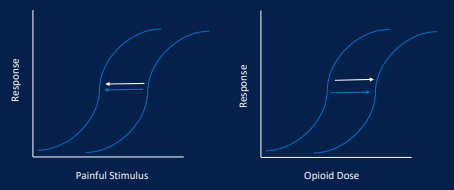
44

Opioid-induced Hyperalgesia / Opioid Tolerance



Lowering of the pain threshold

Decreased efficacy of the opioid

Superficially clinically indistinguishable

45

Physical Dependence

- A state that develops as a result of adaptation and the resetting of homeostatic mechanisms
- Withdrawal syndrome can occur in a physically dependent person when the drug is abruptly stopped
  - Typically improves on restarting the drug
  - Can be a point of no-return
- Can occur with both addictive and non-addictive use of drugs
  - Clonidine, caffeine
- Can occur with therapeutic use

46

Drug Interactions

47

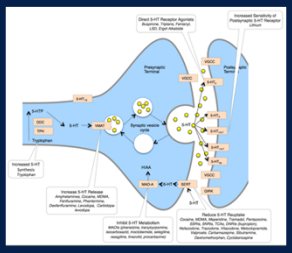
Physiological Drug Interactions





48

PK/PD Drug Interactions



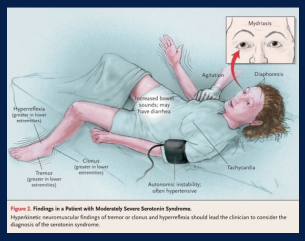


Figure 2. Findings in a Patient with Moderately Severe Serotonin Syndrome.
Hyperkinetic neuromuscular findings of tremor or clonus and hyperreflexia should lead the clinician to consider the diagnosis of the serotonin syndrome.

www.real-psychiatry.blogspot.com
Boyer E. NEJM 2005

49

Exposure Pathway


Los Angeles Times

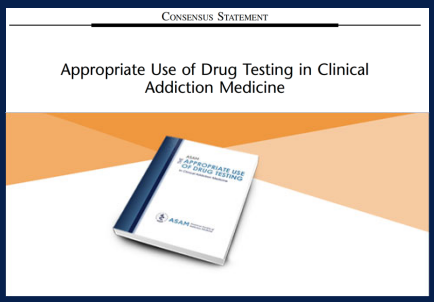
Possible fentanyl exposure sends police officer to hospital in Silicon Valley

A police officer in the Silicon Valley city of Los Altos was taken to a hospital Monday after possible being exposed to fentanyl, authorities said.





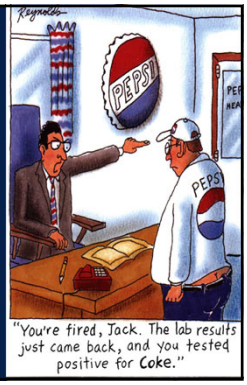
50



51

Clinical Considerations

- Testing is not meant to "catch" the patient
  - Testing identifies recent use it does NOT identify addiction or impairment
  - A positive finding suggests a need to review treatment plan
    - A positive finding is not to prevent, limit, or punitively change treatment
- Tests must be interpreted in the context of patient self-report and other information from observed behaviors or reliable sources
- Language is important
  - e.g., clean vs dirty, pass/fail



52

Screening and Confirmatory Tests

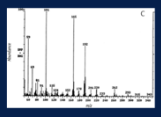


Screening (Presumptive) Assays – indicate the presumptive presence of drugs

Highly sensitive

Rapid, inexpensive

Cutoff: Yes/No



Confirmatory (Definitive) Assays – specifically identify the drug detected in the screening assay

Highly specific

Quantitative

Complicated, expensive

53

Screening Tests for Drugs of Abuse

- Enzyme immunoassay
  - Based on a substance's structure.
  - Relatively inexpensive, easily automated
- Analytical false positives are possible
  - Confirm positive screens in some clinical situations
- Analytical false negatives are less common
  - Clinical false negatives occur

02/28/2017 23:09	Amphetamines Urine	N	[Not Detect-]	Final

Not Detected * Interpretive Data:
Drug Screen results are provided for medical management only. No chain of custody documentation. Testing does not meet NIDA standards. Positive results are not confirmed.

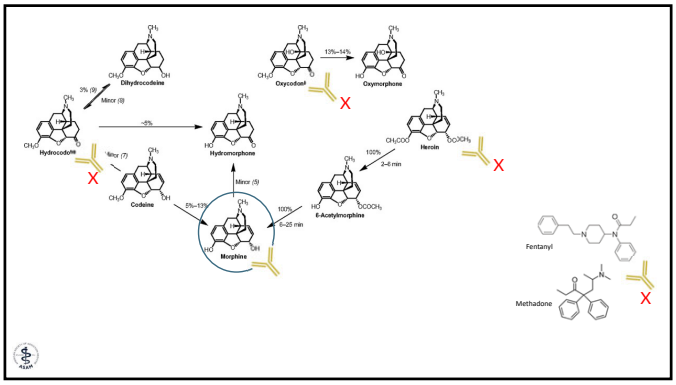
54

Drugs of Abuse Screening

NIDA/SAMHSA 5
- Opiates
- Amphetamines
- Cocaine
- Marijuana
- Phencyclidine

NIDA-9 (Extended)
- Opiates
- Amphetamines
- Cocaine
- Marijuana
- Phencyclidine
- Barbiturates
- Benzodiazepines
- Methadone
- Propoxyphene

55



56

The "Opiate" Assay: Not So Good for "Opioids"

	Online DAT opiates IP assay	EMIT II+ opiate assay[2]	TDx/TDx-flex opiate opiate assay[3]	Architect/ Aeroset	Acsym opiate[3]	CEDIA opiate[4]	DRI opiate[4]	DRI oxycodone[4]
Morphine	100	100	100	100	100	100	100	<29
Codeine	134	98	>3.6	167	>3.6	125	167	<20
Ethyl morphine	101		<10		>100			
Diacetyl morphine (heroin)	82					53	86	<33
6-Acetylmorphine	78	69	>20	67	<30	81	79	<200
Dihydrocodeine	69	103	>3.6	106	>3.6	50	67	<100
Morphine-3-glucuronide	54	48	>57	47	>57	81	50	<11
Morphine-6-glucuronide			>5.7		<8.6	47	100	
Hydrocodone	28	121	>8.0	158	>12	48	18	<133
Hydromorphone	21	60	>4.4	54	>6.7	57	7.5	<333
Norcodeine	2							<10
Meperidine							0	<10
Oxycodone	0	12	>1.1	11	<1.7	3.1	1.9	100
Oxymorphone		1.5	<10	0	<15	1.9	0.7	103
Noroxycodone								<0.1
Noroxymorphone								<0.1
Meperidine	0	<0.6	<2.0	0	<3.0	0.2	0	
Levallorphan		<4	<6.0	13	<6.0			
Levorphanol		29	>6.0	27	>6.0		2.1	<50
Nalorphine		3	<20	2.3	<30			
Naloxone	0	0.04	<20	0	<30		0	<50
Imipramine	0					1.6		
Ranitidine						0	0	
Thebaine	25		<20		<30		<15	
Naltrexone	0						0	<20
Fentanyl			<60		<60			

57

TABLE 7–4 Performance Characteristics of Common Urine Drug Screening Immunoassays*

Drug/Class	Detection Limits (ng/mL)*	Confirmation Limits (ng/mL)*	Detection Interval†	Comments
Amphetamine/ methamphetamine	500	500	1–2 days (2–4 days)	Decongestants, ephedrine, L-methamphetamine, selegiline, and bupropion metabolites are reported to give false-positive test results with some assays; MDA, MDEA, and MDMA are variably detected.
Barbiturates	200		2–4 days	Phenobarbital detection interval is up to 4 weeks.
Benzodiazepines	100–300		1–30 days	Benzodiazepines vary in reactivity and potency. Hydrolysis of glucuronides increases sensitivity. False-positive test results are reported with oxaprozin.
Cannabinoids	50	15	1–3 days (1 month)	Screening assays detect inactive and active cannabinoids; confirmatory assay detects inactive metabolite THCA. Duration of positivity is highly dependent on screening assay detection limits.
Cocaine	150	100	2 days (1 wk)	Screening and confirmatory assays detect inactive metabolite BE. False-positive test results caused by cross-reactive compounds are unlikely.
Opiates			1–2 days (1 week)	Semisynthetic opioids derived from morphine show variable cross-reactivity. Fully synthetic opioids (eg, fentanyl, meperidine, methadone, tramadol) have minimal cross-reactivity. Quinolones are known to cross-react with some assays.
Codeine/morphine	2,000	2,000		
Hydrocodone/hydromorphone	300	100		
Oxycodone/oxymorphone	100	50		
6-Acetylmorphine	10	10		
Methadone	300		1–4 days	Doxylamine is reported to cross-react with some assays.
Phencyclidine	25	25	4–7 days (1 month)	Dextromethorphan, diphenhydramine, ketamine, and venlafaxine is reported to cross-react with some assays.

*Performance characteristics vary with manufacturer and may change over time. For the most accurate information, consult the package insert of the current kit or contact the manufacturer. †Substance Abuse and Mental Health Services Administration recommendations[1] are shown for amphetamines/methamphetamines, cannabinoids, cocaine, opiates, and phencyclidine immunoassays. Other commercial immunoassay cutoffs are also listed. Other cutoffs may be set by individual laboratories. ‡Values are after typical use; values in parentheses are after heavy or prolonged use.
BE = benzoylecgonine; MDA = methylenedioxyamphetamine; MDEA = methylenedioxyethylamphetamine; MDMA = methylenedioxymethamphetamine; THCA = tetrahydrocannabinolic acid.

Goldfrank's Toxicologic Emergencies, 11th Edition

58

Interpretation of a True Positive Opioid Screen

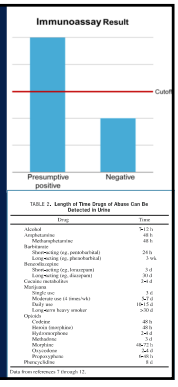
- Patient uses an opioid
  - However:
    - Unclear which opioid
    - Does not correlate with effectiveness or impairment
    - Cannot tell route, time of use, or amount used
- Clinical false positive
  - Not a false positive



59

Interpretation of a True Negative Opioid Screen

- Patient is not using
  - Diversion away
- Clinical false negative
  - Collection/Lab error
  - Wrong assay used
    - e.g., "Opiate" assay for oxycodone
  - Cutoffs are often used
  - Detection periods are short

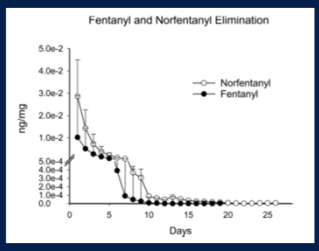


60

Protracted renal clearance of fentanyl in persons with opioid use disorder

Andrew S. Huhn[a,b,c,*], J. Gregory Hobelmann[a,b], George A. Oyler[c], Eric C. Strain[a]

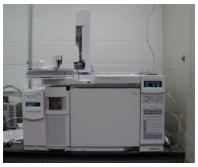
[a] Department of Psychiatry and Behavioral Sciences, Johns Hopkins University School of Medicine, Baltimore, MD, 21224, USA
[b] Ashley Addiction Treatment, Havre de Grace, MD, 21078, USA
[c] Department of Chemical and Biomolecular Engineering, Johns Hopkins University, Baltimore, MD, 21218, USA



- Analytically correct
  - True positive
- Clinically incorrect
  - False positive

Huhn AS, et al. Drug Alcohol Depend 2020;108:147

61





The Gold Standards for Confirmation

- Gas Chromatography/Mass Spectrometry
  - Gold standard for confirmation
  - Chemical "fingerprint" of drugs
  - Sensitive and specific
  - Legally defensible
- Liquid Chromatography/Tandem Mass Spectrometry (LC/MS/MS)
  - Emerging Standard for Confirmation
  - Less sample preparation

62

Buprenorphine analysis

- Can only generalize about expected levels
  - No credible way to say "X" dose should give "Y" level
  - Patients tend to stay within a certain range over time unless dose changes
    - Trending helpful and can detect aberrancy
- Adulterated specimen
  - Bup without metabolite (always)
  - Bup >1000 ng/mL, even with metabolite (suggestive)
- Higher Bup levels than Norbup levels due to:
  - Dosing shortly before urine test
  - CYP 3A4 inhibitor or substrate which slows conversion to metabolite

63

Matrix Considerations

- Window of detection
- Time to obtain results (availability of POCT)
- Ease of collection (need for trained personnel, collection facilities)
- Invasiveness/unpleasantness of collection
- Availability of the sample (e.g., renal health, shy bladder, baldness, dry mouth)
- Susceptibility of the sample to tampering

64



Drugs and metabolites are concentrated in urine
Can compare to creatinine



Drugs are found in much lower concentrations
Easy to observe



Drugs and metabolites incorporated into hair
Concentrations of drugs low with sporadic use



Prospective collection, 1-2 weeks
Inter and intraindividual variability



Invasive and expensive to test
More direct relationship to impairment



Easy to collect and observe
Essentially limited to ethanol

65

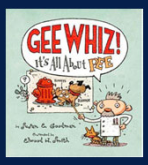
TABLE 4. Comparing Testing Characteristics Across Matrices

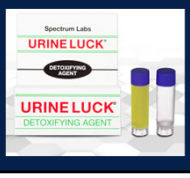
	Blood	Breath	Oral Fluid	Urine	Sweat	Hair
General detection period	<24 hours [2] 1–8 hours [75] 1–48 hours [26]	~1 hr per standard drink	<24 hours [2] 12–24 hours [27] 1–36 hours [28] 5–48 hours [29] 12–48 hours [25]	1.5–4 days [29] 1–3 days [25,26,30]	Continuous, usually 1–4 weeks [2,76]	7–90 days [2] 7–100 days [76]
POCT/On-site immunoassay available	Yes, primarily used for alcohol	For alcohol	Yes	Yes	No	No
Primarily detects	Parent drug compound; blood alcohol concentration	Parent drug compound; blood alcohol concentration	Parent drug compound	Drug metabolite	Parent drug compound	Parent drug compound
Best use in treatment setting	Determination of acute impairment or intoxication for alcohol	Determination of acute impairment or intoxication for alcohol	Short-term detection in ongoing treatment	Intermediate-term detection in ongoing treatment	Medium-term prospective monitoring	Long-term monitoring; 3-month drug use history
Ease of collection	Requires staff trained in phlebotomy	Easily collected	Easily collected	Requires specialized collection facility (restroom)	Easily collected	Easily collected
Intrusiveness of collection	High for intravenous access	Low	Low	High	Low	Low
Resistance to tampering	High	High	High, but some uncertainty	Low	High, but some uncertainty	High when chemically untreated
Retesting same sample	Difficult	Generally not possible	Difficult	Possible	Possible depending on patch used	Easy

ASAM Appropriate Use of Drug Testing in Clinical Addiction Medicine, 2017

66

Specimen Validity Testing









67

Where Can I Get Help With Interpretation?



- Medical or forensic toxicologist
- Staff at the testing laboratory
- A physician with MRO certification

68

References

1. Nelson LS, Howland MA, Lewin NA, Smith SW, Goldfrank LS, Hoffman RS. Goldfrank's Toxicologic Emergencies, 11th Edition. New York, McGraw Hill, 2019.
2. Hayhurst CJ, Durieux ME. Differential Opioid Tolerance and Opioid-induced Hyperalgesia: A Clinical Reality. *Anesthesiology*. 2016;124(2):483-488.
3. Oldendorf WH. Some Relationships Between Addiction and Drug Delivery to the Brain. NIDA Research Monograph 120: Bioavailability of drugs to the brain and the blood brain barrier. 1992.
4. ASAM Appropriate Use of Drug Testing in Clinical Addiction Medicine, 2017

69



Lewis.Nelson@Rutgers.edu
@LNelsonMD

70

Becoming Certified: Pathways, Insights and Preparation Strategies

Saturday, July 23
3:00 pm – 3:45 pm CT

Being a certified addiction specialist has many benefits from increased practice-based and clinical efficiencies, to being a part of bridging the gap between almost 22 million people struggling with addiction and approximately only 5,500 specialists nationwide. This session provides an overview of the different pathways to becoming board certified in addiction medicine and the resources available to support candidates in the certification process. Presenters will also discuss tips and tricks for preparing for the addiction medicine exams.

Learning Objective:

- After this session, learners will be able to: Identify the different pathways and requirements to certification in Addiction Medicine through ABPM and AOA and recognize good practices and resources available for preparing for the exam.

Faculty Presenters



Christopher J. Ondrula, JD
Executive Director
American Board of Preventive Medicine

Currently, Mr. Ondrula is the Executive Director for the American Board of Preventive Medicine (ABPM). As Executive Director, Mr. Ondrula works with the ABPM Board of Directors to develop and operationalize overall ABPM strategic initiatives through the planning and coordination of projects designed to advance ABPM's goals. That work includes the creation and implementation of a key performance indicator report that contains operational metrics and outcome measures that quantify organizational productivity and provides a platform for improved operational performance. Mr. Ondrula is also responsible for formulating policies and strategic plans intended to identify fertile areas for the ABPM's continued growth within the House of Medicine.

Previously, Mr. Ondrula was the Strategic Business Affairs & Legal Advisor for the American Board of Medical Specialties (ABMS). In that role, Mr. Ondrula planned, organized and coordinated projects supporting key ABMS organizational strategic objectives, focusing on ways to improve efficiency. Mr. Ondrula's responsibilities at ABMS also included the CertLink Initiative where, among other things, he was chiefly responsible for development of the economic model to assess its viability, as well as his collaborative work with the Ethics and Professional Committee, and strategic efforts in support of the ABMS Legislative Team.

Prior to joining ABMS in 2015, Mr. Ondrula served as the Chief Executive Officer and Director at Heartland Food Corporation which, at the time was the 2nd largest Burger King franchisee in the -World, and, before that he was the Chief Operating Officer and General Counsel for Spence Group Services. Mr. Ondrula received his undergraduate degree in business from Miami University in Oxford, Ohio, and received his Juris Doctorate from Valparaiso University School of Law.



Kerri A. Leo, MATD, CAE, CHCP
Certification Director
American Osteopathic Association

Kerri Leo is the Certification Director for the American Osteopathic Association's Conjoint Committee on Addiction Medicine. As Certification Director, she works with the AOACAM to develop and implement all certification exams, as well as communicating with diplomates and candidates. Kerri also serves as the Certification Director for the American Osteopathic Board of Family Physicians.

Previously, Kerri was the Director of Education Development for the American Association of Clinical Endocrinology. In that role, Kerri was responsible for the planning and implementation of all live education activities and all grant activities. She has over 20 years of experiencing in managing adult education activities for various professional associations and has planned meetings on five continents. Kerri received her undergraduate degree in French from Marquette University in Milwaukee, WI, and received her master's degree in Training and Development from Roosevelt University in Chicago, IL.



Ruchi M. Fitzgerald, MD, FAAFP
Assistant Professor, Associate Program Director of Addiction Medicine Fellowship Service Chief, Addiction Medicine Consult Service
Rush University/PCC Community Wellness

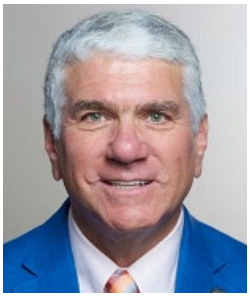
Ruchi M. Fitzgerald, MD, FAAFP is a family physician and an addiction medicine physician. She is the Service Chief of Inpatient Addiction Medicine at PCC Community Wellness, a federally qualified health center system that serves the West Side of Chicago. Dr. Fitzgerald is an Assistant Professor in the Departments of Family Medicine and Psychiatry and Behavioral Sciences at Rush University, as well as the Associate Program Director of the Rush Addiction Medicine Fellowship. She completed the addiction medicine fellowship at Rush University in 2020. She is a graduate of the University of Michigan Medical School and completed her family medicine residency in 2012 with the Montana Family Medicine Residency. Dr. Fitzgerald developed an interest in provision of care for underserved populations and those affected by substance use disorders during her residency. Dr. Fitzgerald also has extensive experience in telemedicine. During her fellowship, Dr. Fitzgerald worked with the addiction medicine faculty to create RISE-MD (Rush Integrative Substance Use Disorder Education for Medical Doctors), an educational initiative in Rush Medical College that focuses on eliminating stigma while promoting evidence-based treatment of substance use disorders in the next generation of physicians. She has worked with the American Society of Addiction Medicine and the Illinois Society of Addiction Medicine on key advocacy and policy initiatives related to substance use disorders. Dr. Fitzgerald is also an active member of the Federation of State Physician Health Programs and is an advocate for physician health and wellness.

Interesting Cases with Audience Response System (ARS)

Saturday, July 23
4:15 pm – 4:30 pm CT

Test your critical thinking and problem-solving skills while learning more about the complexities of addiction cases through this interactive session leveraging Audience Response System.

Faculty Presenter



Edwin A. Salsitz, MD, DFASAM
Unit Chief, Inpatient Rehabilitation
Mount Sinai Beth Israel
Icahn School of Medicine at Mount Sinai

Dr. Edwin A. Salsitz has been an attending physician in the Mount Sinai Beth Israel, Division of Chemical Dependency, New York City, since 1983, and is an Associate Clinical Professor of Psychiatry at the Mount Sinai School of Medicine. He is the principal investigator of the Methadone Medical Maintenance (office-based methadone maintenance) research project. Dr. Salsitz is certified in Addiction Medicine by the American Board of Preventive Medicine, as well as by the Board of Internal Medicine and Pulmonary Disease. He has published and lectures frequently on addiction medicine topics.

Dr. Salsitz is a course director for ASAM sponsored Buprenorphine and REMS Opioid trainings, and is a lead mentor in the PCSS-MAT mentoring program. He has co-chaired the ASAM Review Course, the ASAM Common Threads Course, the ASAM State of the Art course and is a reviewer for the Journal of Addiction Medicine and Drug and Alcohol Dependence. He is the chair of the ASAM REMS course on safe and effective prescribing of opioids. Dr. Salsitz was the Co-chair of the ASAM CME committee and Chair of the New York Society of Addiction Medicine CME and Education committee.
Dr. Salsitz is a member of the medical advisory panel, for the New York State Office of Alcohol and Substance Abuse Services. Dr. Salsitz is the recipient of the 2014 ASAM Annual Award, and the 2018 ASAM Annual Educator of the Year Award.

Expert Panel Discussion and Q&A - Day 2

Saturday, July 23
4:30 pm – 5:30 pm CT

This panel session will provide a prime opportunity for learners to get their questions answered on topics that were presented on day two of the ASAM Review Course.

Faculty Presenters



Faye Chao, MD
Panelist

Session: Behavioral Addiction: From Theory to Treatment



H. Westley Clark, MD, JD, MPH, DFASAM
Panelist

Session: Ethics and the Law: Principles and Treatment Implications



Jeffrey J. DeVido, MD, MTS, FASAM
Panelist

Session: Epidemiology: Core Concepts and Applications



Kelly Kleinert, MD
Panelist

Session: Psychiatric Co-Morbidities: Assessment and Treatment



Annie Levesque, MD, MSc
Panelist

Session: Medical Co-Morbidities: Prevention and Treatment



Lewis S. Nelson, MD
Panelist

Session: Pharmacology and Toxicology: Principles, Applications, and Limitations



Amesika N. Nyaku, MD, MS
Panelist

Session: Prevention and Public Health: Principles and Applications



Erin A. Zerbo, MD, DFASAM
Moderator

Welcome Back and Board Exam Practice Questions – Day 3 Sunday, July 24
7:30 am – 7:45 am CT

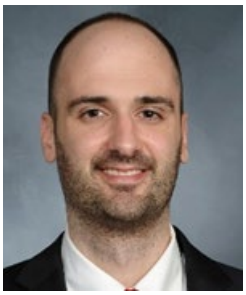
Welcome and Board Exam Practice Questions with Audience Response System (ARS) with Review Course Chair, Jonathan D. Avery, MD.

The ASAM Review Course is widely recognized as the essential primer for physicians and other healthcare professionals who are preparing for a career in addiction medicine, as well as for primary care providers who wish to increase their skills in identifying and managing patients whose medical problems are exacerbated by substance use disorders.

Learning Objective:

- After this session, learners will be able to: Understand how to maximize your Review Course experience for the third day of the course.

Faculty Presenter



Jonathan D. Avery, MD
Director of Addiction Psychiatry
Weill Cornell Medical College

Dr. Avery is currently the Director of Addiction Psychiatry and an Associate Professor of Clinical Psychiatry at Weill Cornell Medical College and New York-Presbyterian Hospital. In addition to his clinical work, Dr. Avery teaches addiction psychiatry to the Weill Cornell medical students and residents of New York-Presbyterian Hospital. He has been published on a broad variety of topics in psychiatry, including papers on subjects ranging from clinician attitudes towards patients to how to use buprenorphine. He is the founder of the Addiction Stigma Institute that studies stigma towards individuals with substance use disorders and creates novel interventions to improve these stigmatizing attitudes. He was on the editorial board for the DSM-5 Clinical Cases book and is the editor of the books Co-occurring Mental Illness and Substance Use Disorders: A Guide to Diagnosis and Treatment and The Stigma of Addiction: An Essential Guide. He has won numerous awards for his clinical and academic work, including the American Board of Psychiatry and Neurology Faculty Innovation in Education Award and the Outstanding Faculty Member Award from the New York County Psychiatric Society.

Evolution of Addiction and Treatment: History and Impact Sunday, July 24
7:45 am – 8:30 am CT

Approaches to describing and treating addiction have changed dramatically over the years. This session will begin by presenting a brief history of addiction treatment, focusing on the lessons learned from each approach. Next, the presenter will review the current definition of addiction and its importance in directing modern policy and treatment. Finally, the session will review The ASAM Criteria, a critical tool for standardizing evidence-based care.

Learning Objective:

- After this session, learners will be able to: Describe key milestones in developing addiction, addiction treatment and developing standardized, evidence-based, care.

Faculty Presenter



Paul H. Earley, MD, DFASAM
Medical Director
Georgia Professionals Health Program, Inc.

Paul H. Earley, MD, DFASAM has worked in Addiction Medicine for 35 years. He treats all types of addictive disorders and specializes in the assessment, treatment, and management of health care professionals. As a therapist, he works with patients already in recovery, providing long term therapy for those who suffer from this disease. His professional expertise extends to advocacy for professionals before agencies and licensing boards.

Dr. Earley is a dynamic speaker and educator; he speaks and trains on topics of addiction, its treatment and addiction among health care professionals. In addition, he trains therapists about the neurobiological basis of psychotherapy. In his travels, he has provided training in the United States, Canada, the United Kingdom, Italy, Iceland and Switzerland.

He is the author of three books and numerous research articles on addiction and its treatment. His two most recent books, RecoveryMind Training and the RecoveryMind Training Implementation Guide describe an innovative and comprehensive system designed to reengineer addiction treatment. He is a contributing author to the American Society of Addiction Medicine (ASAM) Textbook: Principles of Addiction Medicine, as author of the chapter: Physician Health Programs and Addiction among Physicians and a contributing author to the ASAM Criteria. His work was featured in the documentary series on addiction entitled Close to Home by Bill Moyers.

Dr. Earley is the Immediate Past President of the American Society of Addiction Medicine (ASAM). He is the Medical Director of the Georgia Professionals Health Program, Inc., the Physicians Health Program (PHP) for the state of Georgia and the Immediate Past President of the North American Federation of State Physician Health Programs (FSPHP). With Earley Consultancy, LLC, he works with treatment facilities, providing training in cohesive care, treatment effectiveness and staff development using RecoveryMind Training.

EVOLUTION OF ADDICTION AND TREATMENT: HISTORY AND IMPACT

Paul H. Earley, M.D., DFASAM
Immediate Past President, American Society of Addiction Medicine
Past President, Federation of State Physician Health Programs
Medical Director, Georgia Professionals Health Program, Inc.

1

The ASAM Review Course of Addiction Medicine
July 2021

Financial Disclosures

Paul H. Earley, M.D., DFASAM
Medical Director - Georgia Professionals Health Program, Inc: Salary
Principal - Earley Consultancy, LLC: Salary
DynamiCare Health, Inc: Stock

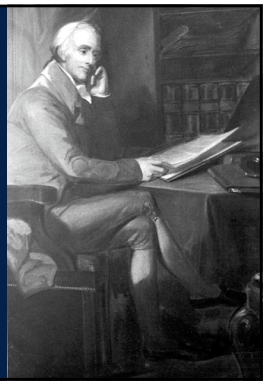
2

Addiction Treatment History

3

Benjamin Rush, M.D.

- Published: *Inquiry into the Effects of Ardent Spirits on the Human Mind and Body* in 1784
- Asserted that alcohol was the causal agent in alcoholism
- Asserted that loss of control over drinking is the characteristic symptom of inebriety
- Stated that total abstinence from alcohol was the only effective cure
- Called for creation of a "Sober House" for the care of the confirmed drunkard (1810)



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The 19th Century

- In the early 1800's, an increase in grain supply, rapid crop spoilage, and an emerging entrepreneurial spirit increased the supply of distilled alcohol.
- As a result, drinkers increased their consumption of distilled alcohol.
- Definitive data is missing, but alcoholism seemed to increase, especially in urban areas.
- In the 1840s, the temperance movement took on the alcohol problem.

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New York State Inebriate Asylum



1864 - Containment

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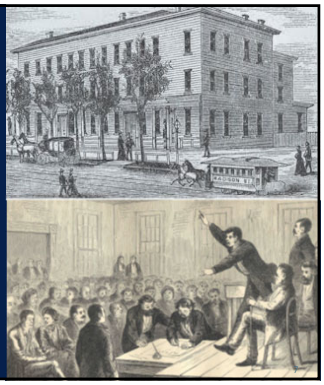
The Washingtonians

- Social network
- Public recitation of stories
- Faith-based change

1840 to 1855



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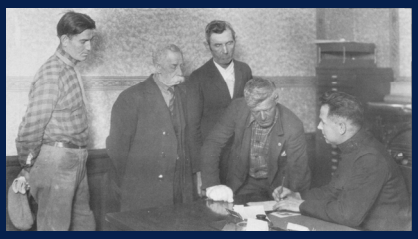
The Salvation Army



Founded in 1865, it continues to be the largest addiction treatment system in the world.

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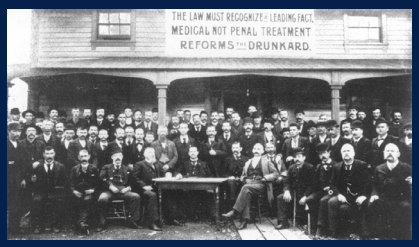
The Keeley League



- 1879 - First franchised, private, for-profit addiction treatment system
- 1891 – Keeley forms first patient mutual aid society

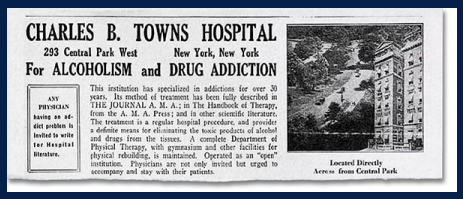
9

Keeley League

- Keeley used repeated "double chloride of gold" injections. Followed up with "take home bottles."
- This was part of the dangerous patent medicine industry that led to subsequent regulation and development of science-based medications.
- However, other elements became part of later addiction treatment programs:
  - Regular sleep, exercise, health recreation
  - Abstinence and careful selection of friends
  - Continued socializing by graduates
  - Viewed inebriety as a disease
  - "Recovered" alcoholics worked in his centers

10

Towns Hospital


CHARLES B. TOWNS HOSPITAL
293 Central Park West New York, New York
For ALCOHOLISM and DRUG ADDICTION

ANY PHYSICIAN having an addict problem is invited to write for Hospital literature.

This institution has specialized in addictions for over 20 years. Its method of treatment has been fully described in THE JOURNAL A. M. A.; in The Handbook of Therapy, from the A. M. A. Press; and in other scientific literature. The treatment is a regular hospital procedure, and provides a definite means for eliminating the toxic products of alcohol and drugs from the tissues. A complete Department of Physical Therapy, with gymnasium and other facilities for physical rebuilding, is maintained. Operated as an "open" institution. Physicians are not only invited but urged to accompany and stay with their patients.

Located Directly Across from Central Park

1901

- Focused on removing the craving and restoring physical health and diet
- Varied from NY Inebriate Asylum about issues of treatment coercion
- Physicians were not only invited but urged to accompany and stay with their patients

11

Prohibition

- Based upon the concept that alcohol itself is the cause of alcoholism (and what was described at the time as personal and social evil), thus no one should drink.
- In the U.S., lasted from
  - 1919 until 1933



12

Drugs and the Legal System

- At the turn of the century, the sale of drugs was not controlled in any manner.
- Starting in the late 1800's, home remedies containing alcohol, opium, morphine, cocaine, and cannabis professing "cures" for any number of illnesses.
- Sigmund Freud experiments with cocaine and winds up recommending it for the treatment of morphinism for his friend and colleague Ernst von Fleischl-Marxow.
- The Pure Food and Drug Act, and later the Harrison Act (1914), created a split between legal and illegal drugs consumed by U.S. citizens.

13

13

The Harrison Act

- Drugs deemed legal (and thus, taxed): alcohol and tobacco (Nicotine)
- Illegal drugs placed into a hierarchy
  - Heroin, cocaine, and many hallucinogens were placed as Schedule I. This includes peyote; however, Native Americans can apply for special dispensation as a religious sacrament.
  - Misplacements of certain drugs, notably marijuana. This increased the belief that the legal system does not understand addiction risk and is uninterested in medical or social safety.
- Paradoxically, the two legal drugs are the most medically toxic to the body.

14

14

The Legal System

- The brain center that drives addiction was unaltered by the Harrison Act.
  - Once addicted, economics of supply and demand describes use of substances in such individuals as "inelastic demand."
  - As a result, many individuals who develop addiction violate laws and become criminals.
- Today, the prison industry flourishes, and the treatment industry is all but defunct.
  - 65% of prison inmates meet criteria for SUDs.
  - Recent evolution of state and local drug court programs promise innovative and effective solutions.

†Shoveling Up II: The Impact of Substance Abuse on Federal, State and Local Budgets, CASA (2009)

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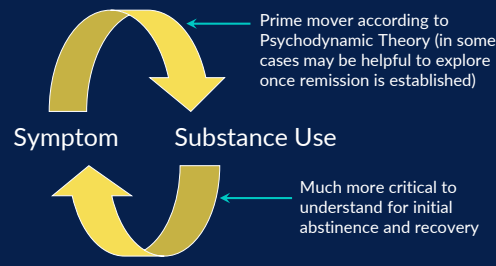
Self-Medication Theory



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Bob Smith and Bill Wilson



Met in 1935

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17

Innovations from A.A.

- Emancipated spirituality from its roots in religious institutions.
- Legitimized varieties of spiritual experiences in recovery.
- Found alternatives to religious antidotes for guilt including self-inventory, confession, acts of restitution, and acts of service.
- Encouraged service work and working with others.
- Established the first chronic care system for a chronic disease.
- A.A. was a peer-led social movement that used a spiritually-based program with explicit instructions.

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Hazelden and the Minnesota Model

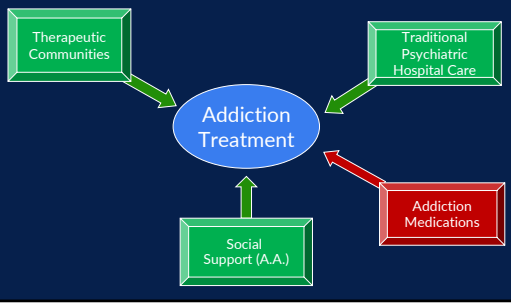


A centralized treatment system that focused on detoxification and the principles of A.A.

Opened 1949

19

The Origins of Addiction Treatment



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Elements of the Minnesota Model

- Alcoholism is an involuntary, primary, chronic, progressive biopsychosocial spiritual disease.
- Recovery is the goal of treatment, not abstinence.
- Focus on treatment of a central disease process, abandoning the psychoanalytic and moral models of addiction.
- Addiction is best treated in a milieu of dignity and respect.
- A revised view of motivation: initial motivation (or lack thereof) is not a predictor of outcome. Also, motivation is as much the responsibility of the milieu as the patient.

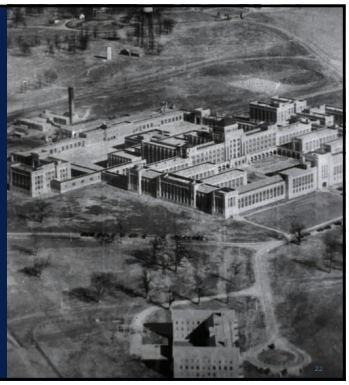
21

Federal Narcotics Farm

Lexington, Kentucky

For a long period of time, this was the world's epicenter for addiction research and drug treatment . Convicts did time alongside individuals who volunteered to enter the center for treatment.

1935 to 1970



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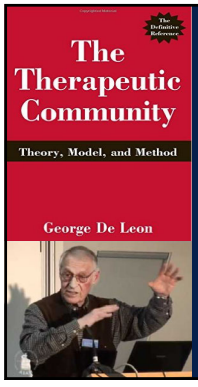


The Therapeutic Community

- Whole person focused, centered on lifestyle changes
- Goals are:
  - Becoming pro-social
  - Honesty
  - Taking responsibility for self
  - Willingness to learn from others
- Democratically run, everyone, including staff, are part of the community
- Drives individual change through "community as method"
- Introduced the concept of ongoing support, most often lifelong disease management

23

Synanon's Dederich

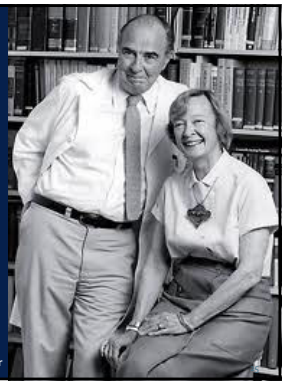
- Rebuilding character through community, peer pressure and confrontation.
- "Don't mess with us – you can get killed dead, physically dead."
- Founded 1958



24

Medications for the Treatment of OUD

- Heroin dispensing in England and Switzerland.
- Methadone therapy in the U.S. (1964)
  - Humane treatment in an era of discrimination and legal interdiction
  - Biological disease model
  - Although A.A. took this stand earlier, this was the first medical treatment that took a firm stand that addiction is a chronic disease.
  - In *The ASAM Criteria*, it is referred to as Opioid Treatment Services (OTS)



Drs. Dole and Nyswander

25

Addiction is a Brain Disease

- Alan Leshner, Ph.D. and former head of NIDA, began describing addiction as a **brain disease** in 1996
- He stated that addiction is a *disease of the brain* that has several important components:
  - A social context
  - Behavioral, psychological and spiritual aspects
- Recovery takes time, time measured in years

26

Lessons From History

- Addiction is an ever-present phenomenon, changing focus from time to time on different substances and behaviors. (Don't believe that the current drugs abused will be the primary drug of misuse!)
- Treatment has focused on religious conversion, psychotherapy, characterological manipulation, legal interdiction, and pharmaceutical intervention at various times—a single modality, universally applied, has, inevitably, failed.
- Short-term interventions **do not work.** Addiction is a chronic condition requiring long-term care.
- The illness is very complex and has multiple antecedents. The clinician must adapt his or her approach to each patient.

27

The ASAM Criteria

28

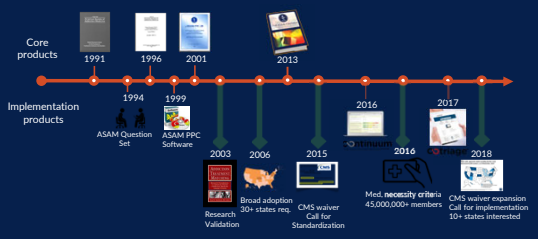
The Evolution of the ASAM Criteria



For the least intensive or restrictive care that meets the patient's multi-dimensional needs and to ensure ongoing care and the optimal treatment outcome.

29

The ASAM Criteria
Widespread adoption & validation



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The ASAM Criteria – Treatment Axis

Digits demarcate major types of treatment with decimal places defining intensity. The system is designed for increased granularity and refinement in the future.

- **Level 0.5** Early Intervention ← Prevention Services
- **Level 1** Outpatient Treatment ← Less than three times per week, commonly individual services
- **Level 2.1** Intensive Outpatient
- **Level 2.5** Partial Hospitalization ← Group-based treatment at a specialized center
- **Level 3.1** Clinically Managed Low Intensity Residential Services
- **Level 3.3** Clinically Managed Medium Intensity Residential Treatment
- **Level 3.5** Clinically Managed High Intensity Residential Treatment
- **Level 3.7** Medically Monitored Intensive Inpatient Treatment
  ← Residential Services
- **Level 4** Medically Managed Intensive Inpatient Treatment ← Medical Hospital

31

31

The ASAM Criteria – The Dimensional Axis

- Dimension 1: Acute Intoxication and/or Withdrawal Potential
- Dimension 2: Biomedical Conditions and Complications
- Dimension 3: Emotional, Behavioral or Cognitive Conditions and Complications
- Dimension 4: Readiness to Change
- Dimension 5: Relapse, Continued Use or Continued Problem Potential
- Dimension 6: Recovery/Living Environment

32

32

Putting the ASAM Criteria Axes Together

Dimensions of Care	Levels of Care: 0.5	1	2.1	2.5	3.1	3.3	3.5	3.7	4
Dimension 1									
Dimension 2									
Dimension 3									
Dimension 4									
Dimension 5									
Dimension 6									

33

33

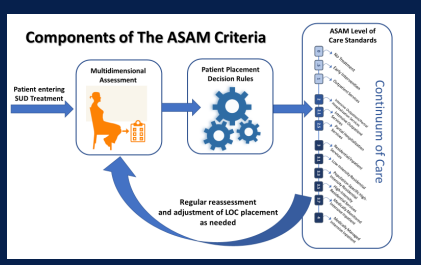
Disease Typology

- In many levels, there are specialty services outlined for:
  - Co-Occurring Capable services (a COC Program)
  - Co-Occurring Enhanced services (a COE Program)
  - Biomedical Enhanced services (a BIO Program)
  - Withdrawal Management services (a program with WM)
  - Opioid Treatment services (OTS must be available in all levels of care, some levels can do this through liaison with opioid treatment services - OTS)

34

34

Assessment & Care Placement



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Integrated or Available Biomedical Care

- Pain and Addiction
- Care for Medical Complications of Addiction
- Treatment of addiction during pregnancy
- Consult liaison services at every major hospital
- Physician Involvement – when indicated – in all levels of care.

36

36

The ASAM Criteria

- Provides a template for the type and intensity of addiction treatment.
- Reiterates the importance of long-term management.
- Ensures cost-effective care.
- Ensures adequate staffing for the different levels of care.
- Emphasizes the importance of patient evaluation and ongoing reevaluation.
- Is the emerging national standard that will reengineer our disorganized and chaotic addiction treatment system in the U.S.

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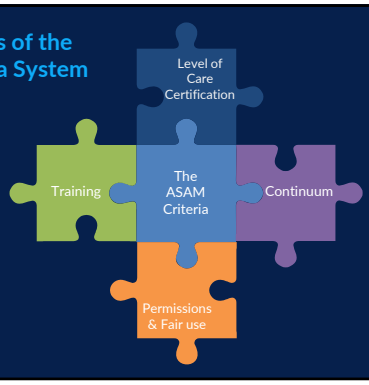
Components of the ASAM Criteria System



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The ASAM Criteria System

- Definitions of Levels and Types of Care
- Implementation Training to ensure fidelity
- Treatment System Certification
- Proper Use of ASAM Criteria Language
- Assessment using the ASAM Continuum, a research-based assessment tool.

39

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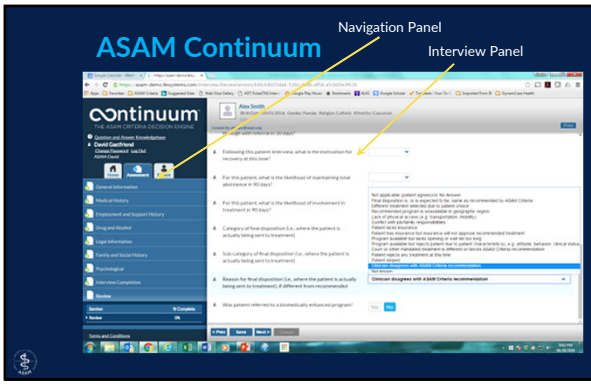
ASAM Continuum



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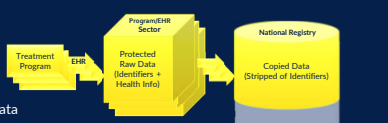
Future Goals: The ASAM Continuum & Repository



CONTINUUM™ Raw Program Data
- ✓ Referral, Placement, Care Planning
- ✓ HITECH Act, ACA population expansion

ASAM LOC Recommendation
- ✓ Parity Act monitoring & compliance
- ✓ MCO Prior Authorization & UR reform

State Databases & National Registry
- ✓ Needs analysis, Value-Based Contracting
- ✓ CMS 1115 Waiver requirements
- ✓ SAMHSA STR reporting requirements



41

41

The Fourth Addition of The ASAM Criteria

- The levels of care will be expanded and become more consistent.
- Increased integration of medical care and medications for treatment.
- Dimensions will be rearranged for mor logical assessment.
- Treatment will be extended in scope and time frame in recognition of the need for long term care of this chronic condition.

42

42

The ASAM Definition of Addiction

43

43

The Definition of Addiction

Recently Revised

- Addiction is a treatable, chronic medical disease involving complex interactions among brain circuits, genetics, the environment, and an individual's life experiences. People with addiction use substances or engage in behaviors that become compulsive and often continue despite harmful consequences.
- Prevention efforts and treatment approaches for addiction are generally as successful as those for other chronic diseases.

44

44

The Definition of Addiction

- Note that ASAM's definition of addiction is distinctly different that the criteria in the DSM-5.
  - DSM-5 uses characteristic signs and symptoms to make a diagnosis.
  - The ASAM definition used the word Addiction and outlines causation and characteristics of the disease.
- ASAM's definition emphasizes
  - Addiction is chronic
  - Addiction is treatable
  - The illness is complex, and its many etiologies are important in its genesis and treatment
  - The response to prevention and treatment is similar to other chronic conditions.

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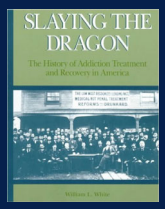
Further Reading







46

46

Treatment for Different Stages of Life: Adolescents, Young Adults, and the Elderly Sunday, July 24
8:30 am – 9:15 am CT

Patients in different stages of life may require different treatment considerations. Adolescents tend to lack insight into the social, school and legal problems that result from substance use, while the elderly are often isolated and are most susceptible to the health consequences of substance use. This session will review epidemiology, screening, complications of use, and unique treatment issues for adolescents, young adults, and the elderly.

Learning Objective:

- After this session, learners will be able to: Describe how the different life stage of a patient can impact the development, diagnosis, and treatment of addiction.

Faculty Presenter



Maria H. Rahmandar, MD
Medical Director, Substance Use & Prevention Program
Lurie Children's Hospital of Chicago, Division of Adolescent & Young Adult Medicine
Northwestern University, Feinberg School of Medicine

Maria Rahmandar, MD, is an attending physician in The Potocsnak Family Division of Adolescent and Young Adult Medicine at Anne & Robert H. Lurie Children's Hospital of Chicago, and an Assistant Professor of Pediatrics at Northwestern University Feinberg School of Medicine, with a secondary appointment in Psychiatry and Behavioral Sciences. Dr. Rahmandar serves as the founding Medical Director for the Substance Use & Prevention Program, and and Overdose Education & Naloxone Distribution Program. Her clinical, research, education and advocacy interests include adolescent substance use, mental health and contraception. Among her leadership roles, Dr Rahmandar serves as an E-Cigarette Faculty Expert for the American Acadmeny of Pediatrics and serves on the Illinois Society of Addiction Medicine Board of Directors.

Treatment for Different Stages of Life

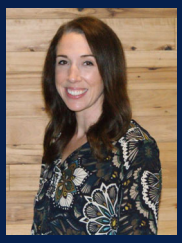
Maria Rahmandar, MD
Lurie Children's Hospital of Chicago
Northwestern University Feinberg School of Medicine

1

The ASAM Review Course of Addiction Medicine

July 2022

Financial Disclosures



Maria Rahmandar, MD
No Disclosures

2

Learning Objectives

Describe how the different life stage of a patient can impact the development, diagnosis, and treatment of addiction.

3

Presentation Outline

Adolescents (10-19) and Young (10-24 per World Health Organization)

Elderly (someone much older than yourself)

4

Adolescence

- Biologic growth and development
- Increased social pressures
- Increased decision making
- Search for self

5

Adolescents Are Vulnerable

- Earlier substance use = higher risk of addiction
- Adolescent immaturity during critical development period = vulnerability
  - Impulsiveness and excitement seeking
  - Difficulty delaying gratification
  - Poor executive function and inhibitory control

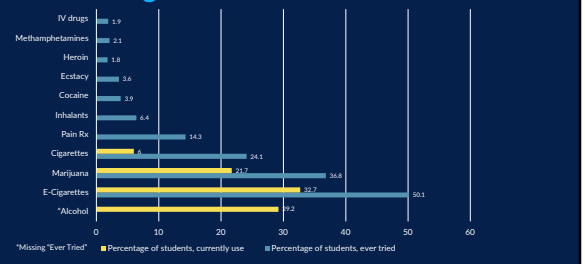
6

Associated Factors

- Having a parent/sibling with substance use disorder
- Mood disorder
- Learning disorder/poor school performance
- Low self-esteem
- Substance use among peers
- Availability of substances in community
- Poor family relationship, family conflict

7

Substances Used by US High School Students



Centers for Disease Control and Prevention. Youth Risk Behavior Survey Data. 2019

8

Recent Trends

- **Overall, from 2020 to 2021, teen substance use reportedly declined**
  - Johnston, L. D., Miech, R. A., O'Malley, P. M., Bachman, J. G., Schulenberg, J. E., & Patrick, M. E. (2022). Monitoring the Future national survey results on drug use 1975-2021: Overview, key findings on adolescent drug use. Ann Arbor: Institute for Social Research, University of Michigan.
- **Overdose deaths increased 94% 2019 to 2020, largely due to fentanyl**
  - Friedman J, Godvin M, Shover CL, Gone JP, Hansen H, Schriger DL. Trends in Drug Overdose Deaths Among US Adolescents, January 2010 to June 2021. *JAMA*. 2022;327(14):1398–1400. doi:10.1001/jama.2022.2847

9

CRAFFT 2.1 + N

- During the past 12 months, on how many days did you:
  - Alcohol
  - Marijuana or synthetic marijuana
  - Anything else to get high
  - Vaping device containing nicotine and/or flavors, or any tobacco products
    - www.crafft.org

10

CRAFFT 2.1 + N

- C - Have you ever ridden in a CAR driven by someone (including yourself) who was "high" or had been using alcohol or drugs?
- R - Do you ever use alcohol or drugs to RELAX, feel better about yourself, or fit in?
- A - Do you ever use alcohol/drugs while you are by yourself, ALONE?
- F - Do your family or FRIENDS ever tell you that you should cut down on your drinking or drug use?
- F - Do you ever FORGET things you did while using alcohol or drugs?
- T - Have you gotten into TROUBLE while you were using alcohol or drugs?

**2 or more yes answers suggests a significant problem.*

11

CRAFFT 2.1 + N

Ask about use of vaping device containing nicotine and/or flavors, or any tobacco products.

1. Ever tried to QUIT
2. Use NOW because hard to quit
3. Felt ADDICTED
4. CRAVINGS
5. Felt like NEEDED to vape/use tobacco
6. Hard to keep from using in PLACES where you shouldn't
7. When you HAVEN'T used
   a. Hard to CONCENTRATE
   b. IRRITABLE
   c. NEED/urge
   d. NERVOUS, restless, anxious

12

Do We Care About Cannabis?

- Vulnerable populations: youth, psychiatric illness, other substance use disorders
- Consequences of intoxication, e.g., MVCs
- Impact on learning
- Psychiatric consequences of use
- Progression to cannabis use disorders and other substance use disorders

13

Vulnerability in Youth

- Daily use of cannabis <age 17 associated with substantially increased risk of:
  - Later cannabis dependence
  - High school non-completion
  - Use of other drugs
  - Suicide attempts

Silins E, Horwood LJ, Patton GC, Fergusson DM, Olsson CA, Hutchinson DM, Spry E, Toumbourou JW, Degenhardt L, Swift W, Coffey C, Tait RJ, Letcher P, Copeland J, Mattick RP; Cannabis Cohorts Research Consortium. Young adult sequelae of adolescent cannabis use: an integrative analysis. Lancet Psychiatry. 2014 Sep;1(4):286–93

14

Can We Establish Credibility Despite Historic Exaggeration & Racist Cannabis Regulations?

15

Messaging - Overcoming Societal Attitudes

- Cannabis is addictive (but not everyone gets addicted)
- Cannabis can be harmful (but not everyone gets harmed)
- This is not your grandmother's cannabis
- Broader use leads to broader problem use through access and decreased perceived harm
- This is a huge problem for youth and other vulnerable populations

16

Features of Adolescent Treatment

- Developmental barriers to treatment engagement
  - Invincibility
  - Immaturity
  - Motivation and treatment appeal
  - Salience of burdens of treatment
- Variable effectiveness of family leverage (or not)
- Pushback against sense of parental dependence and restriction
- Prominence of co-morbidity

17

Developmentally Informed Treatment -1

- Remember that adolescents rely on the support of adults, but also acknowledge that they are striving for autonomy
- Emphasize rewards and praise
- Emphasize adolescent learning styles, using energetic and fun activities while preserving therapeutic content
- Emphasize social alternatives to drug use
- Acknowledge normative attraction of thrill-seeking, risk, deviance
- Management of disruptive behavior is expected and essential, balancing limits
- Weave a safety net of supports: families (or surrogates), but expect some resistance

18

Developmentally Informed Treatment - 2

- Encourage adolescents to formulate their own solutions
- Natural consequences: Give some rope (but not too much) and don't enable
- Emotion regulation training
- Address sleep deprivation
- Skills rehearsal
- Treatment = habilitation, not rehabilitation
- Not effective- "Just grow up!", "Just say no."

19

Motivational Approaches

- Do you know other kids who have been in trouble?
- What are the pros and cons for you?
- How much do you think is too much?
- What do you know about health risks?
- If it did become a problem in the future, how would you know?
- Do you know why I or your parents might think it's a problem?
- If you can stop anytime, would you be willing to see what it's like…
- Let's schedule you to come back and see how it's going…

20

Families

- Monitoring and supervision
- Modeling of prosocial behaviors
- Support for treatment
- Communication and negotiation
- Difficult balance of zero tolerance and accommodation of normative experimentation
- We need to work hard to engage families

21

Vignette

- 17-year-old male began prescription opioids at 15, progressing to daily use with withdrawal within 8 months; nasal heroin age 16, injection heroin 6 months later
- 3 episodes residential tx, 2 AMA, 1 completed
- Presents in crisis seeking detox ("Can I be out of here by Friday?")
- How should you care for him?

22

Adolescents and Opioids

- Medications feasible and effective (buprenorphine better than heroin)
- Adolescents with non-fatal opioid overdose should be strongly considered for buprenorphine treatment
- Naltrexone requires acceptance with concern over retention
- Longer duration buprenorphine better
- XR buprenorphine can be considered

23

Older Adults

24

Older Adults-"Hidden Problem"

- Lack of screening in primary care
- Lack of guidelines for assessing older adults
- Signs and symptoms of harmful use overlap with other conditions
- Ageist bias

25

Detecting Problematic Substance Use

- Psychiatric symptoms: sleep changes, mood changes
- Physical symptoms: nausea/vomiting, poor coordination, tremors
- Physical signs: injuries, falls, bruises, malnutrition, self-neglect (ie poor hygiene)
- Cognitive changes: confusion/disorientation, memory impairment, daytime drowsiness, impaired reaction time
- Social/behavioral changes: withdrawn, family discord, early refills

Lehman S, Fingerhood M. Substance use disorders in later life. New England Journal of Medicine 2018; 378:2351-60.

26

Challenges in Detecting Problematic use

- Relying on older patient's report of frequency and quantity of substance use can lead to underestimation of the problem
- Older adults and family members may not appreciate deleterious consequences of long-time patterns of drinking or drug use
- Harm can come from lower amounts of substances

Lehman S, Fingerhood M. Substance use disorders in later life. New England Journal of Medicine 2018; 378:2351-60.

27

Patient Vignette

- EB is a 72-year-old female seen for her initial visit. She has a history of chronic pain in her hips and knees. Her previous provider will no longer prescribe oxycodone because, for the past two months, her 30-day script ran out after two weeks. She is fearful that providers won't help her. She cannot take NSAIDs and admits that she often takes oxycodone when she is upset.
- She lives alone in a senior housing apartment; she has two daughters- both with difficulties (medical and social). Non-smoker; no alcohol.
- How should you care for her?

28

Opioids and Aging

- Older adults who were prescribed opioids (vs NSAIDs), had significantly higher rates of:
  - Cardiovascular events
  - Fractures
  - Hospitalizations
  - Death
  - (risk for gastrointestinal bleeding was similar)

Solomon DH, Rassen JA, Glynn RJ, Lee J, Levin R, Schneeweiss S. The Comparative Safety of Analgesics in Older Adults With Arthritis. *Arch Intern Med.* 2010;170(22):1968-1978. doi:10.1001/archinternmed.2010.391

29

American Geriatrics Society Beers Criteria

- Avoid chronic NSAIDs, muscle relaxants and use tramadol with caution (added 2019)
- Avoid opioids if history of falls or fracture
- Avoid tricyclics- amitriptyline

American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2019 Apr;67(4):674-694. doi: 10.1111/jgs.15767. Epub 2019 Jan 29. PMID: 30693946.

30

Patient Vignette

- BR is an 82-year-old female brought to the ER by neighbor with "syncope." It is noted that she has alcohol on her breath and her BAL is 228 mg/dl. When confronted, she becomes tearful. Her son goes to her home and finds hidden miniatures throughout her apartment.
- How do you approach caring for her?

31

Short Michigan Alcoholism Screening Test-Geriatric Version (SMAST-G)

In the past year:

1. When talking with others, do you ever underestimate how much you actually drink?
2. After a few drinks, have you sometimes not eaten or been able to skip a meal because you didn't feel hungry?
3. Does having a few drinks help decrease your shakiness or tremors?
4. Does alcohol sometimes make it hard for you to remember parts of the day or night?
5. Do you usually take a drink to relax or calm your nerves?

32

SMAST-G

6. Do you drink to take your mind off your problems?
7. Have you ever increased your drinking after experiencing a loss in your life?
8. Has a doctor or nurse ever said they were worried or concerned about your drinking?
9. Have you ever made rules to manage your drinking?
10. When you feel lonely, does having a drink help?

**2 or more "yes" responses indicative of alcohol problem.*

33

Patient Vignette

- RT is a successful 79-year-old businessman with HTN and recurrent depression with poor sleep and worries about his memory. At initial evaluation, he performs well on cognitive testing, but you learn that he has two "stiff drinks" every evening, and often has a third after a stressful day. He is defensive about his drinking because this has been a longstanding pattern that he enjoys.
- How concerned are you about his drinking?

34

Alcohol: the Most Commonly Used Substance

- Alcohol Use Disorder in Older Adults
  - Early Onset: more common; Men>Women
  - Late Onset: more likely to be triggered by stressful life event (loss of spouse, retirement, medical disability, pain, sleep problem) ; Women>Men

Lehman S, Fingerhood M. Substance use disorders in later life. New England Journal of Medicine 2018; 378:2351-60.

35

National Institute on Alcohol Abuse and Alcoholism

Drinking Guidelines for Older Adults (65 & older)

- Should not have more than:
  - 3 drinks on a given day
  - 7 drinks in a week

36

Alcohol Use Trends

- Increased in past 2 decades for adults 60+, particularly women
- Binge drinking prevalence:
  - 20% of 60-64yo
  - 11% of 65+

www.niaaa.nih.gov/alcohols-effects-health/special-populations-co-occurring-disorders/older-adults

37

Increased Risks of Alcohol Even at "Low Consumption"

- Increased vulnerability to physiological effects
  - Decreased lean muscle mass
  - Decreased total body water
  - Less efficient liver enzymes that metabolize alcohol
  - Increased effective concentration of alcohol, higher and longer lasting blood alcohol levels
- Additional risks
  - Alcohol-medication interactions
  - Co-morbid chronic illnesses
  - Women experience alcohol-related harms at lower levels than men

38

Patient Vignette

- SL is a 78-year-old male with Alzheimer's dementia being cared for at home by his daughter and son-in-law. He has had increasing episodes of agitation and his daughter inquires about the use of cannabis to help with agitation.
- What do you advise?

39

Patient Vignette

- CR is an 82-year-old male with HTN, GERD, and recurrent depression which is being treated with two different antidepressants. His depression is much improved, but he continues to experience anxiety and stress, primarily related to worries about his wife's cancer and her poor health. He reports that he has decided to go to a marijuana dispensary and try cannabis to see if it can help his mood and his anxiety.
- How do you respond?

40

Cannabis Use is Increasing Among Older Adults

- Prevalence of cannabis use increased from 2002/2003 to 2012/2013
  - 45-64 age group.....increased from 1.6% to 5.9%
  - 65+ age group.....increased from 0.0% to 1.3%
- Adults age 50+ with cannabis use
  - Frequently began use in teen years
  - Often have other co-morbid substance use and mental disorders
- Majority of older people who use cannabis perceive no risk or slight risk from frequent use (e.g., 3 times/week)

Choi NG, DiNitto DM, Marti CN. Older adults who use or have used marijuana: Help-seeking for marijuana and other substance use problems. J Subst Abuse Treat. 2017 Jun;77:185-192.

41

Impact of Cannabis on Physical and Mental Health

- Older adults often see marijuana as "safer" alternative to alcohol, opioids, or pharmaceutical medications
- Short term use is associated with
  - Impaired short-term memory, impaired judgment/motor coordination, driving skills
  - Injury, paranoia, and psychosis

Lehman S, Fingerhood M. Substance use disorders in later life. New England Journal of Medicine 2018; 378:2351-60.

42

Patient Vignette

- KT is a 70-year-old male seen for initial visit. He has a history of Type 2 diabetes mellitus and hypertension. He lives with his wife and has three daughters and eight grandchildren that he sees regularly. He enjoys watching sports and getting together with friends every Friday night to play pinochle and most times there is crack cocaine use- "we just unwind and have a good time."
- How should you address cocaine use? What if he instead drank 3-4 beers to unwind?

43

Treatment Approach for Older Adults

- Don't minimize
- Confront with compassion
- Remove shame
- Build self-esteem
- Give encouragement/hope
- Undo isolation
- Work on coping skills
- Facilitate finding new ways to stay busy with use of peers

44

Conclusions: Treatment for Youth and the Elderly is Effective, but…

- We need to learn to improve it
- There isn't enough of it
- Access and engagement is a problem
- **Treatment works!**
- **We are at a crossroads -- we have an obligation to do better!**

45

References

1. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2019 Apr;67(4):674-694. doi: 10.1111/jgs.15767. Epub 2019 Jan 29. PMID: 30693946
2. Cavacuiti CA. Principles of Addiction Medicine: The Essentials (2011). LWW: Philadelphia, PA
3. Centers for Disease Control and Prevention. Youth Risk Behavior Survey Data. 2019
4. Choi NG, DiNitto DM, Marti CN. Older adults who use or have used marijuana: Help-seeking for marijuana and other substance use problems. J Subst Abuse Treat. 2017 Jun;77:185-192. doi: 10.1016/j.jsat.2017.02.005. Epub 2017 Feb 16. PMID: 28216197
5. Friedman J, Godvin M, Shover CL, Gone JP, Hansen H, Schriger DL. Trends in Drug Overdose Deaths Among US Adolescents, January 2010 to June 2021. *JAMA*. 2022;327(14):1398–1400. doi:10.1001/jama.2022.2847
6. Johnston, L. D., Miech, R. A., O'Malley, P. M., Bachman, J. G., Schulenberg, J. E., & Patrick, M. E. (2022). Monitoring the Future national survey results on drug use 1975-2021: Overview, key findings on adolescent drug use. Ann Arbor: Institute for Social Research, University of Michigan
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9. Solomon DH, Rassen JA, Glynn RJ, Lee J, Levin R, Schneeweiss S. The Comparative Safety of Analgesics in Older Adults With Arthritis. *Arch Intern Med*. 2010;170(22):1968–1978. doi:10.1001/archinternmed.2010.391
10. www.crafft.org
11. www.niaaa.nih.gov/alcohols-effects-health/special-populations-co-occurring-disorders/older-adults

46

Genetics and Gender: Impacts on Treatment for Women and Newborns Sunday, July 24
9:15 am – 10:00 am CT

While much of substance use disorder presentation is similar for both women and men, understanding the differences can help improve treatment outcomes. Genetics can also play a role in the development and presentation of addiction. This session will review genetic and gender-based considerations for assessing and treating addiction in women and discuss substance-related treatment for pregnant or post-partum patients and newborns.

Learning Objective:

- After this session, learners will be able to: Describe genetic and gender differences impacting the assessment and treatment of addiction in women and list evidence-based treatment strategies for pregnant patients and newborns.

Faculty Presenter



Leslie A. Hayes, MD
Family Physician
El Centro Family Health

Dr. Leslie A. Hayes, MD, works for El Centro Family Health in Espanola, NM. She is board-certified in both addiction and family medicine. While Dr. Hayes enjoys all aspects of family medicine, her particular passion is taking care of people with opioid use disorder. She especially enjoys working with pregnant women and new mothers who have had drug problems and works hard to make sure that they and their babies receive compassionate and appropriate medical care. She got much of her training in substance use disorders through Project ECHO and now considers herself extremely fortunate to have been able to give back to Project ECHO, and she now provides training for other providers around the state of New Mexico and nationally in substance use disorder and use of buprenorphine. She recently started an ECHO in her own organization with the goal of getting 90% of providers trained to prescribe buprenorphine and provide compassionate, evidence-based care for Substance Use Disorder. She was named a White House Champion of Change in April of 2016 for her work with substance use disorder and pregnancy. Her work was also featured in The Providers, an award-winning documentary about rural health care.

Pregnancy, Genetics, & Womens' Health

Leslie Hayes, MD
Family Physician and Addiction Medicine
El Centro Family Health
Espanola, NM

1

The ASAM Review Course of Addiction Medicine

July 2022

Financial Disclosures

Leslie Hayes, MD
No Disclosures



2

Learning Objectives

Describe genetic and gender differences impacting the assessment and treatment of addiction in women and list evidence-based treatment strategies for pregnant patients and newborns.

3

Presentation Outline

- Genetics and substance use disorder
- Gender differences in substance use disorder
- Pregnancy and the postpartum period
- Effects of substance use during pregnancy on the newborn
- Neonatal opioid withdrawal syndrome

4

Genetics and Substance Use Disorder

5

Three Ways That Genetics Influences Substance Use Disorder

- Direct effect of genes on susceptibility to substance use disorder
- Pharmacogenetics affects how drugs affect an individual
- Epigenetics affects which genes are expressed

6

Genetics of Substance Use Disorder

- Nature vs. nurture, better phrased as nature and nurture, for substance use disorder. A person's likelihood of developing substance use disorder is a result of a dynamic interaction between genes and the environment.[1]
- Heritabilities of SUD's range from 0.39 for hallucinogens to 0.72 for cocaine.

[1]Genetics and Epigenetics of Addiction. in DrugFacts. https://www.drugabuse.gov/publications/drugfacts/genetics-epigenetics-addi
[2]Bevilacqua and Goldman. Genes and Addictions. Clin Pharmacol Ther. 2009 APril; 85(4) pp 359-361

7

Twin Studies – Direct Effect of Genes

- Both the Swedish and Vietnam twin studies showed significantly higher concordance rates for substance use disorder in monozygotic twins than in dizygotic twins.[1,2]

[1]Gelernter et Kranzler. Chapter 2. Genetics of Addiction in Galanter et al. Textbook of Substance Abuse Treatment. The American Psychiatric Publishing 2015 pp. 26-45
[2]Bevilacqua and Goldman. Genes and Addictions. Clin Pharmacol Ther. 2009 April; 85(4) pp 359-361

8

Pharmacogenetics

- Both the ADH1 B2-His47 ARG allele of Alcohol Dehydrogenase 1B and ALDH-Glu487 Lys allele of Aldehyde Dehydrogenase 2 can cause flushing, nausea, and headache with alcohol, due to accumulation of acetaldehyde.[1]
  - More common in people of South Asian descent and those of Jewish ancestry.
  - Homozygotes nearly completely protected from alcoholism.

[1]Zajicek and Karan. Pharmacokinetic and Pharmacodynamic Principles in Miller et al. The ASAM Principles of Addiction Medicine. Wolters Kluwer 2019. p. 97-98

9

Pharmacogenetics of Medication Therapy Of OUD

- The A118G SNP (single nucleotide polymorphism) of the opioid mu receptor (OPRM1) enhances the therapeutic response to naltrexone for alcohol dependence.[1]
  - A118G is also much more common in people with heroin use disorder.[2]
- Increased length of stay and increased need for pharmacotherapy in Neonatal Opioid Withdrawal Syndrome have recently been observed among neonates with variations in the A118G SNP in the mu opioid receptor OPRM1 gene and various SNP's in the COMT (Catechol-O-methyltransferase – enzyme that degrades dopamine, norepinephrine, and epinephrine.)[3]

[1]Haile et al. Pharmacogenetic Treatments for Drug Addiction: Alcohol and Opiates, The American Journal of Drug and Alcohol Abuse, 34:4, 355-381 [2]Ibid
[3]Wachman et al. Association of OPRM1 and COMT single-nucleotide polymorphisms with hospital length of stay and treatment of NAS. JAMA 2013;309(17):1821-1827

10

Pharmacogenetics of Medication Therapy Of OUD

- Methadone is metabolized in part by CYP2D6.
  - Ultrarapid metabolizers do not do well on methadone.[1]

[1]Haile et al. Pharmacogenetic Treatments for Drug Addiction: Alcohol and Opiates, The American Journal of Drug and Alcohol Abuse, 34:4, 355-381

11

Epigenetics

- Epigenetics is the study of epigenomes which are markers that turn genes on or off or express them more or less strongly.
  - Changes to the epigenomes can be passed down anywhere from 2-12 generations.
  - Environmental factors like diet, stress, and prenatal drug use can cause epigenetic changes which predispose to substance use disorder.

John Cloud. Why Your DNA Isn't Your Destiny. *Time*. 1/6/2010

12

Gender Differences in Substance Use Disorder

13

Gender Differences And Substance Use Disorder

- Men are more likely than women to use almost all types of illicit drugs.[1]
  - Women probably use prescription drugs at greater rates than men.[2]
  - Men are 1.9 times more likely to have drug dependence.[3]
- Men have higher rates of alcohol use, including binge drinking, than women, except for teens, where rates are similar.[4]

[1]Substance Use in Women Research Report Sex and Gender Differences in Substance Use https://www.drugabuse.gov/publications/research-reports/substance-use-in-women/sex-gender-differences-in-substance-use Accessed 2/18/2021
[2]Greenfield et al. Substance Abuse in Women. Psychiatr Clin Nort Am. 2010 June; 33(2): 339-355 [3]Ibid
[4]Substance Use in Women Research Report Sex and Gender Differences in Substance Use https://www.drugabuse.gov/publications/research-reports/substance-use-in-women/sex-gender-differences-in-substance-use Accessed 2/18/2021

14

Gender Differences And Substance Use Disorder

- Women are more likely to be introduced to injection drug use by their male sexual partner, whereas men are more likely to be injected by a friend.[1]

[1]Greenfield et al. Substance Abuse in Women. Psychiatr Clin Nort Am. 2010 June; 33(2): 339-355

15

Gender Differences And Substance Use Disorder

- Women are more likely to use prescription opioids to self-medicate for anxiety or stress.[1] Men are more likely to use prescription opioids for experimentation or to get high.[2]
- Women are more likely to drink in response to stress and negative emotions whereas men are more like to drink to enhance positive emotions or conform to a group.[3]

[1]Final Report: Opioid Use, Misuse, and Overdose in Women. Office on Women's Health. July 19, 2017
[2]Greenfield et al. Substance Abuse in Women. Psychiatr Clin Nort Am. 2010 June; 33(2): 339-355
[3]Ibid

16

Women and Alcohol

- Women get drunker faster than men:
  - Decreased body weight[1]
  - Decreased alcohol dehydrogenase[2]
  - Decreased volume of water compartment distribution[2]
  - Less muscle than then men

[1]Zweben. Special Issues in Treatment: Women in Miller et al. The ASAM Principles of Addiction Medicine. Wolters Kluwer 2019 p. 529
[2]Ibid

17

Health Risks For Women with Substance Use Disorder

- Women have a "telescoped course" for alcohol use disorder.[1]
  - They develop pathologic effects of alcohol more rapidly.
- Women have a 50-100% higher death rate from alcohol use disorder, including deaths from suicide, alcohol-related accidents, heart disease, stroke, and liver damage.[2]

[1]Zweben. Special Issues in Treatment: Women in Miller et al. The ASAM Principles of Addiction Medicine, Sixth Edition. Wolters Kluwer 2019 p. 529
[2]Substance Use in Women Research Report Sex and Gender Differences in Substance Use https://www.drugabuse.gov/publications/research-reports/substance-use-in-women/sex-gender-differences-in-substance-use Accessed 2/18/2021

18

CDC Guidelines For Risky Drinking[1]

- Excessive drinking (or risky drinking or at-risk drinking) is defined as the following:
  - Binge drinking, the most common form of excessive drinking, is defined as consuming:
    - For women, 4 or more drinks during a single occasion.
    - For men, 5 or more drinks during a single occasion.
  - Heavy drinking is defined as consuming
    - For women, 8 or more drinks per week.
    - For men, 15 or more drinks per week.
- Most people who drink excessively are not alcoholics or alcohol dependent.
- Recent commentary by Lowik et al in the Journal of Addiction Medicine discussed whether adjustments are needed for these guidelines.

[1]https://www.cdc.gov/alcohol/fact-sheets/alcohol-use.htm accessed 2/17/2021
[2]Lowik et al. **Where is the Science? A Critical Interrogation of How Sex and Gender are Used to Inform Low-Risk Alcohol Use Guidelines.** *J. Addict Med* Vol 14, No. 5, Sept/Oct 2020

19

Incarceration And Substance Use Disorder

- A population-based study showed that 22% of patients with substance use disorder had been incarcerated before.
- 10.6% of the general population reported a history of incarceration.

Tsai, J., Gu, X. Utilization of addiction treatment among U.S. adults with history of incarceration and substance use disorders. *Addict Sci Clin Pract* **14**, 9 (2019).

20

Incarceration And Substance Use Disorder

- Men with SUD were found to be more likely to have a history of incarceration than women with SUD.[1]
- Blacks and Latinos are far more likely to be incarcerated for drug law violations than whites, even though rates of drug use and drug selling are similar.[2]

[1]Tsai, J., Gu, X. Utilization of addiction treatment among U.S. adults with history of incarceration and substance use disorders. *Addict Sci Clin Pract* **14**, 9 (2019).
[2]http://www.drugpolicy.org/resource/drug-war-mass-incarceration-and-race-englishspanish Accessed 02/16/2021

21

Women, Violence, and SUD

- Women with a history of childhood sexual abuse are three times as likely to develop an addictive disorder as women without that history.[1]
- One study showed lifetime intimate partner violence victimization was reported by 46.7% of women and 9.5% of men entering SUD treatment.

[1]Zweben. Special Issues in Treatment: Women in Miller et al. The ASAM Principles of Addiction Medicine. Wolters Kluwer 2019 p. 532
[2]Schneider et al. Violence and Victims. Volume 24, Number 6, 2009 744 © 2009 Prevalence and Correlates of Intimate Partner Violence Victimization Among Men and Women Entering Substance Use Disorder Treatment

22

Pregnancy and Substance Use Disorder

23

Definition Of Terms For Providers Not Regularly Doing Obstetric Care

- G = Gravida = total number of pregnancies
- P = Para = total number of deliveries
- XX weeks = weeks since last menstrual period or weeks since conception + 2
- Full-term = 37-41 weeks gestation
- IUGR = Intrauterine growth restriction = fetal weight by ultrasound < 10th percentile
- SGA = small for gestational age = weight of newborn baby < 10th percentile for gestational age

24

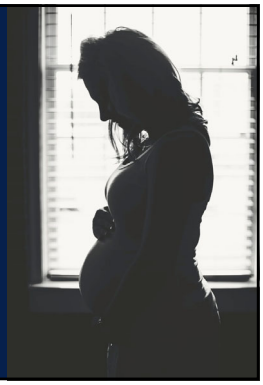
Definition Of Terms For Providers Not Regularly Doing Obstetric Care

- Preterm labor = labor at < 37 weeks
- Preterm delivery = delivery at < 37 weeks
- Placental abruption = placenta pulls away from the wall of the uterus. Small abruptions can cause IUGR or preterm labor. Large abruptions can be fatal for mother and baby.

25

Case Study

33 yo G4P3 had been stable on buprenorphine-naloxone for four years. Presented to her buprenorphine provider for routine appointment and was discovered to be pregnant. Her buprenorphine provider did not give her a script because of this. She relapsed to heroin. She presented to our clinic at 25 weeks gestation, but because of transportation difficulties, she was unable to get restarted on buprenorphine and delivered a premature infant at 31 weeks. She restarted buprenorphine postpartum, and both she and baby did well.



26

Case Study

22yo G1P0 presents at 9 weeks gestation. Actively using heroin. Desperately wanted to keep this pregnancy and this child. Started on buprenorphine maintenance, did well. Child with no signs of Neonatal Opioid Withdrawal Syndrome at birth. Currently seven years old, doing well.



27

Substance Use In Pregnancy

- Use of alcohol, tobacco, and drugs during pregnancy is the leading preventable cause of mental, physical, and psychological impairments in children.
- Between 1998-2011, there was a 127% increase in opioid-dependent pregnant women presenting for delivery.[1]
- Opioid-dependent pregnant women have an unintended pregnancy rate of 86%.[2]
  - Please provide or refer for contraception if you are treating female patients.

[1]McCarthy et al. Opioid dependence and pregnancy: minimizing the stress on the fetal brain. American Journal of Obstetrics and Gynecology. 3 December 2016. pp 1-6
[2]Weaver et al. Alcohol and Other Drug Use During Pregnancy: Management of the Mother and Child in Miller et al. The ASAM Principles of Addiction Medicine. Wolters Kluwer 2019 P. 1315

28

Perinatal SBIRT: 4 Ps Plus

4Ps Plus:

Parents	Did either of your parents ever have a problem with alcohol or drugs?
Partner	Does your partner have a problem with alcohol or drugs?
Past	Have you ever had a problem with alcohol or drugs in the past?
Past 30 days	In the past month, have you drunk any alcohol or used any substances?

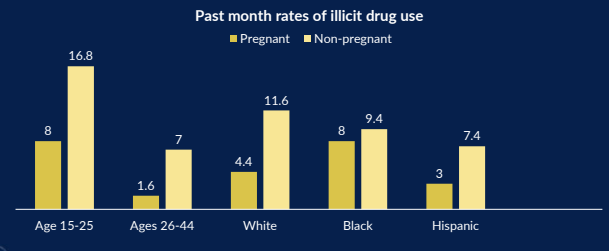
[1]ACOG committee opinion 711. 2017
[2] J Perinatol. 2005 Jun;25(6):368-74.

29

1. What are medical implications of substance use disorder with pregnancy?
2. What is the significance of pregnancy for any substance use disorder?

30

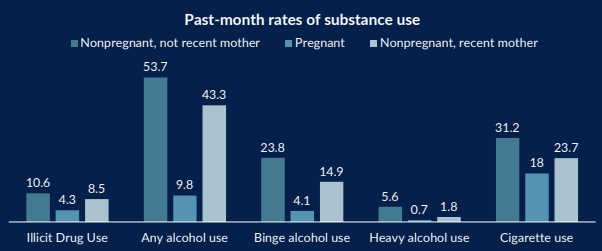
Percentages Of Past-month Illicit Drug Use In Pregnant And Non-pregnant Women



Helmbrecht et al. Management of Addiction Disorders in Pregnancy. *J Addict Med*; Vol 2, Number 1, March 2008, pp 1-16

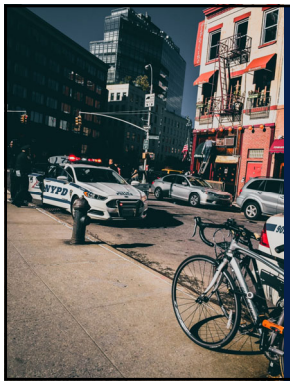
31

Percentages Among Women Aged 15-44 Years Who Reported Past-month Substance Use By Pregnancy And Recent Motherhood Status



Helmbrecht et al. Management of Addiction Disorders in Pregnancy. *J Addict Med*; Vol 2, Number 1, March 2008, pp 1-16

32



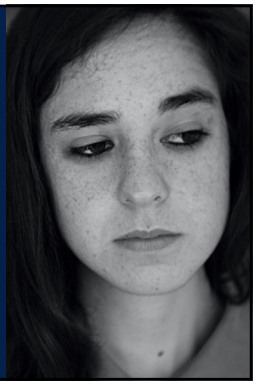
Case Study: Pregnancy and Substance Use Disorder

28 yo G5P4, on methadone maintenance, disappeared from care at about 20 weeks, returned at 38 weeks in labor. Stated she had been at a methadone clinic in another community, but urine was negative for methadone and positive for opiates. Baby went into horrible withdrawal at birth, child protective services involved and took child. Mother was arrested when she and her cousin, who was foster mother, got in fight on OB floor.

33

Case Study: Pregnancy and Substance Use Disorder

23 yo G2P1 presented using heroin. Started on buprenorphine with good response. Metabolite testing confirmed patient was taking medication. Incarcerated. Patient found with large quantities of methamphetamine and heroin and drug paraphernalia in her cell. Jail wished to stop buprenorphine. Told it needed to be continued. She was placed in solitary because of this.



34

- What are psychosocial implications of substance use disorder with pregnancy?

35

Implications Of Substance Use Disorder With Pregnancy

- Psychosocial:
  - Most mothers have a high motivation to change.
  - Lot of guilt/shame for many women
  - Legal implications around custody of baby and older children
  - Most substance-using pregnant women have very poor self-care behaviors. If they continue to use drugs, they are unlikely to take good care of themselves during the pregnancy

36

Implications Of Substance Use Disorder With Pregnancy

- Co-occurring disorders
  - Depression.
    - Both substance use disorder and depression cause poor self-care.
  - Domestic violence
    - Second-leading cause of trauma-related death in pregnancy.

37

Implications Of Substance Use Disorder With Pregnancy

- Psychosocial:
  - Often have history of childhood sexual abuse or physical abuse (with implications for parenting)
  - High incidence of PTSD
  - Most women who abuse drugs start using because their partners use drugs. If they are still with that partner, it can be difficult for them to quit unless he quits as well.

38

Prenatal Care

- In a study in the Journal of Perinatology, it was found that women with illicit drug use and no prenatal care had the highest risk for prematurity, low-birth weight and small for gestational age infants. As prenatal care increased, risk for prematurity, low birth weight and small for gestational age babies dropped.[1]
- Women will often delay or not get prenatal care because of stigma and fear of consequences, including being reported to child protective services.[2]

[1]El-Mohandes et al. Prenatal Care reduces the Impact of Illicit Drug use on Perinatal Outcomes. Journal of Perinatology. 2003; 23:354-360
[2]Bishop et al. Pregnant Women and Substance Use. Overview of Research and Policy in the United States. Bridging the Divide: A Project of the Jacobs Institute of Women's Health. February 2017

39

Effects of Specific Substances on Pregnancy

40

Birth Defects With Substances

- The drug with the most teratogenic potential is alcohol.[1]

[1]Weaver et al. Alcohol and Other Drug Use During Pregnancy: Management of the Mother and Child in Miller et al. The ASAM Principles of Addiction Medicine. Wolters Kluwer 2019 P 1317

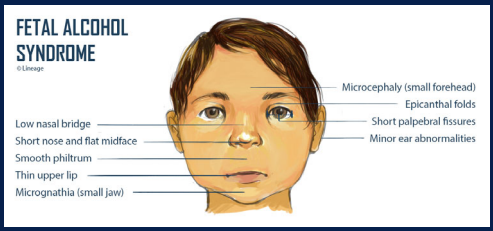
41

Fetal Alcohol Syndrome

- Evidence of growth restriction (prenatal and/or postnatal)
  - Height and/or weight <= 10th percentile
- Evidence of deficient brain growth and/or abnormal morphogenesis
  - Structural brain anomalies or head circumference <=10th percentile
- Characteristic pattern of minor facial anomalies
  - Short palpebral fissures, thin vermillion border upper lip, smooth philtrum

42

Fetal Alcohol Syndrome



43

Fetal Alcohol Effects

- Incidence of fetal alcohol syndrome = 6-9/1000 children[1]
- Incidence of partial fetal alcohol syndrome = 11-17 per 1000 children[2]
- Incidence of fetal alcohol spectrum disorder = 24-48 per 1000 children[3]

1. Weaver et al. Alcohol and Other Drug Use During Pregnancy: Management of the Mother and Child in Miller et al. The ASAM Principles of Addiction Medicine. Wolters Kluwer 2019 p. 1319

44

Tobacco and Pregnancy

- Neonates born to mothers who smoke weigh an average of 200 gm less than neonates born to mothers who don't smoke.[1]
- 22% of SUIDs (Sudden Unexpected infant deaths) can be directly attributed to maternal smoking during pregnancy.[2]

[1]Weaver et al. Alcohol and Other Drug Use During Pregnancy: Management of the Mother and Child in Miller et al. The ASAM Principles of Addiction Medicine. Wolters Kluwer 2019P 1318

[2]Anderson TM, Lavista Ferres JM, Ren SY, et al. Maternal Smoking Before and During Pregnancy and the Risk of Sudden Unexpected Infant Death. Pediatrics. 2019; 143(4):e20183325

45

Cannabis and Pregnancy

- Difficult to get definitive answers on effects:
  - Women often using other substances, especially alcohol and tobacco
  - Psychosocial variables, such as income, age, and education, vary
  - Pre-existing conditions, such as ADHD or anxiety
  - Many studies done before level of THC was as high as now
- Cannabis use is common – the prevalence of self-reported marijuana use is 2-5%, and it increased from 2.37% in 2002 to 3.85% in the 2014 NSDUH.[1]
  - One study showed 2.6% use by self-report, 22.4% by umbilical blood sampling.[2]



1. Thompson R, DeJong K, Lo J. **Marijuana Use in Pregnancy: A Review.** *Obstet Gynecol Surv.* 2019 Jul;74(7):415-428
2. Nashed et al. **Cannabinoid Exposure: Emerging Evidence of Physiological and Neuropsychiatric Abnormalities** *Frontiers in Psychiatry.* 11/2021

46

Cannabis and Pregnancy

- Most common reasons to use cannabis in pregnancy are morning sickness and to manage anxiety/depression
  - Cannabis can lead to cannabis hyperemesis syndrome.[1]
- Data is mixed on effect of cannabis on pregnancy.
  - Studies have given varied results on effect on birthweight[2,3], birth defects[4], and other outcomes.
  - There does seem to be a pattern of neurobehavioral effects on the fetus, with hyperactivity and sleep problems in toddlers, ADHD in pre-teens, and emotional dysregulation in adolescents.[5,6,7]

1. Badowski S, Smith G. Cannabis use during pregnancy and postpartum. *Can Fam Physician.* 2020;66(2):98-103.
2. Gunn JK et al. **Prenatal exposure to cannabis and maternal and child health outcomes: a systematic review and meta-analysis.** BMJ Open. 2016 Apr 5;6(4):e009986. doi: 10.1136/bmjopen-2015-009986.
3. Conner et al. Maternal Marijuana Use and Adverse Neonatal Outcomes: A Systematic Review and Meta-analysis. Obstet Gynecol. 2016 Oct;128(4):713-23. doi: 10.1097/AOG.0000000000001649.
4. Weaver et al. Alcohol and Other Drug Use During Pregnancy: Management of the Mother and Child in Miller et al. The ASAM Principles of Addiction Medicine. Wolters Kluwer 2019P 1325
5. Thompson R, DeJong K, Lo J. **Marijuana Use in Pregnancy: A Review.** *Obstet Gynecol Surv.* 2019 Jul;74(7):415-428
6. Nashed et al. **Cannabinoid Exposure: Emerging Evidence of Physiological and Neuropsychiatric Abnormalities** Frontiers in Psychiatry. 11/2021
7. Roncero et al. **Cannabis use during pregnancy and its relationship with fetal developmental outcomes and psychiatric disorders. A systematic review.** *Reprod Health.* 2020;17(1):25. 2020 Feb 17.

47

Cannabis And Pregnancy – What We Need To Tell Our Patients

- Pregnant women complain about hearing mixed messages from healthcare providers. They also state that want more research on the safety and effects of cannabis with pregnancy.[1]
- There is no recognized "safe" amount of marijuana with pregnancy.
  - Although marijuana hasn't been found definitively to be dangerous, it has also most definitely not been found to be safe.
- There is very likely a risk of long-term neurocognitive effects.
- While it may help with morning sickness, it can lead to cannabinoid hyperemesis syndrome, which is way worse, and there are better treatments.

Barbosa-Leiker et al. Daily Cannabis Use During Pregnancy and Postpartum in a State With Legalized Recreational Cannabis, *Journal of Addiction Medicine:* November/December 2020 - Volume 14 - Issue 6 - p 467-474

48

Stimulant Use and Pregnancy

- Methamphetamine[1] and cocaine[2] use are associated with the following:
  - Preterm delivery
  - Low birth weight
  - Small for gestational age infants



1. Kalaitzopoulos et al. Effect of Methamphetamine Hydrochloride on Pregnancy Outcome: A Systematic Review and Meta-analysis. *Journal of Addiction Medicine*: May/June 2018 - Volume 12 - Issue 3 - p 220-226
2. Smid MC et al. Stimulant Use in Pregnancy: An Under-recognized Epidemic Among Pregnant Women. *Clin Obstet Gynecol.* 2019;62(1):168-184.

49

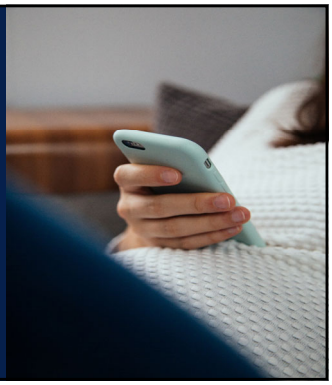
Implications Of Opioid Use Disorder With Pregnancy

- Medication: Both use and withdrawal have fetal effects. **Withdrawal effects usually considered more serious.**
  - Withdrawal causes a hyperadrenergic state which causes constriction of blood vessels in placenta. Exacerbated by cocaine and methamphetamine use. Can cause preterm labor and placental abruption.
  - Biggest direct effect of opioid use is Neonatal Opioid Withdrawal Syndrome at birth.

50

Comorbid Medical Conditions Case Study Pregnancy and Opioid Dependence

25 yo G2P1 presents at 26 weeks, stating, "I'm addicted to heroin." Scared that she will lose baby to child protective services or have medical complications. She wants to get into treatment.



51

1. Is medication therapy an option for her?
2. Which is better, buprenorphine or methadone?
3. What about weaning off the heroin and using abstinence-based therapy?

52

Abstinence-based therapy is not recommended during pregnancy for anyone who is actively using opioids.[1]

[1]Kampman and Jarvis. American Society of Addiction Medicine (ASAM) National Practice Guideline for the Use of Medications in the Treatment of Addiction Involving Opioid Use. J Addict Med 2015;9 358-367

53

Medication Therapy and Pregnancy

Medication therapy for opioid use disorder (MOUD) is standard of care for pregnancy.

54

Medication Therapy and Pregnancy

- Medication therapy can be done with either methadone or buprenorphine.
  - Methadone has been used longer, but most providers prefer to start with buprenorphine if available.
- Data regarding naltrexone is limited, but it is probably safe to continue in pregnancy if patient wishes. It should not be started in pregnancy.

55

Buprenorphine vs. Methadone in Pregnancy

- 2010 NEJM study showed significantly less Neonatal Opioid Withdrawal Syndrome in buprenorphine group than the methadone group[1]
  - Babies exposed to buprenorphine required 89% less morphine, had a 43% shorter hospital stay, and shorter duration of treatment than babies exposed to methadone[1]

[1]Jones, H. et al. Neonatal Opioid Withdrawal Syndrome after Methadone or Buprenorphine Exposure. *NEJM*. Vol 363, 12/9/10 pp 2320-31.

56

Buprenorphine vs. Methadone in Pregnancy

- Buprenorphine vs buprenorphine-naloxone
  - ASAM: "While the evidence on the safety and efficacy of naloxone in pregnant women remains limited, the combination buprenorphine/naloxone product is frequently used and the consensus of the guideline committee is that the combination product is safe and effective for this population."[1]
  - CDC: Combination pills containing both buprenorphine and naloxone are not recommended for treatment of OUD in pregnant women due to limited evidence at this time.[2]
  - SAMHSA: "Positions are evolving on using the combination product (buprenorphine/naloxone) throughout the pregnancy, rather than transitioning the pregnant woman to the buprenorphine-only product for the duration of her pregnancy. …Evidence is now building that newborn outcomes are not negatively affected by using the combination product during gestation and that pregnant women may not need to transition to the buprenorphine-only product during pregnancy to protect the fetus …Pregnant women and their healthcare professionals should make a decision with regard to the use of the buprenorphine/naloxone combination product in the context of pregnancy based on the benefit vs. the risk to the dyad."

1. The ASAM NATIONAL PRACTICE GUIDELINE For the Treatment of Opioid Use Disorder 2020 Focused Update
2. https://www.cdc.gov/pregnancy/opioids/treatment.html Accessed 3/26/2022
3. Substance Abuse and Mental Health Services Administration. Clinical Guidance for Treating Pregnant and Parenting Women With Opioid Use Disorder and Their Infants. HHS Publication No. (SMA) 18-5054. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2018.

57

Buprenorphine and Pregnancy

- Does buprenorphine need to be started in a monitored environment?
  - ASAM: "Hospitalization during initiation of treatment with buprenorphine may be advisable due to the potential for adverse events, especially in the third trimester."[1]
  - SAMHSA: "Many clinics now offer induction to buprenorphine as an outpatient service and sometimes as partial home induction. Partial home induction for pregnant women lacks sufficient evidence at this time."[2]
  - Recent study showed no cases of precipitated withdrawal in the home induction group and one in the observed induction group with successful induction onto buprenorphine for all.[3]

1. The ASAM NATIONAL PRACTICE GUIDELINE For the Treatment of Opioid Use Disorder 2020 Focused Update
2. Substance Abuse and Mental Health Services Administration. Clinical Guidance for Treating Pregnant and Parenting Women With Opioid Use Disorder and Their Infants. HHS Publication No. (SMA) 18-5054. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2018.
3. Kelly JC et al. **Home Induction of Buprenorphine for Treatment of Opioid Use Disorder in Pregnancy.** Obstet Gynecol. 2021 Oct 1;138(4):635-639.

58

Access To Buprenorphine While Pregnant

- A 2020 study of obstetricians showed that only a third of obstetricians always recommend MOUD and a fourth never recommend it.[1]
- MOUD providers are far less likely to accept pregnant patients than non-pregnant patients.[2]
  - Methadone 97% vs 91%
  - Buprenorphine 83% vs 51%

1. Ko, J.Y., Tong, V.T., Haight, S.C. *et al.* Obstetrician–gynecologists' practice patterns related to opioid use during pregnancy and postpartum—United States, 2017. *J Perinatol* **40**, 412–421 (2020).
2. Stephen W. Patrick et al. (2018): Barriers to accessing treatment for pregnant women with opioid use disorder in Appalachian states, Substance Abuse

59

Morning Sickness and Methadone

- Both ondansetron and methadone cause QT prolongation, so use other treatments first.
- Lifestyle changes:
  - Small frequent meals
  - Avoid fluids with meals
  - Eat something before getting out of bed
  - Popsicles
- Ginger
- Pyridoxine, 10 mg + Doxylamine, 10mg tid

60

What about medically monitored withdrawal?

61

Medically Monitored Withdrawal

- Most studies show a high rate of relapse to opioid[1,2]
  - Rates range from 17-96%[3,4,5]
  - Relapse rate is lower on medication therapy[6]
- No study of medically monitored withdrawal has examined maternal outcomes postpartum[7]

[1]Dashe et al. Opioid detoxification in pregnancy. Obstetrics and Gynecology. Volume 92, Issue 5, November 1998, pp 854-858
[2]Bell et al. Detoxification from opiate drugs during pregnancy. Am J Obstet Gynecol 2016;215:374.e1-6
[3]Dashe et al. pp. 854-858
[4]Jones et al. Medically Assisted Withdrawal (Detoxification): Considering the Mother-Infant Dyad. J Addict Med 2017 DOI 10.1097
[5]Bell et al. Ibid.
[6]Jones et al. Ibid
[7]Jones et al. Ibid

62

1. The previous patient has made it to term and is about to go into labor.
2. Do you need to do anything special to manage her labor?
3. What can you expect for the baby?
4. Can she breastfeed?
5. What can she expect post-partum?

63

Labor and Delivery

- Method of delivery should be based solely on obstetric considerations.
- Epidural is preferred method of pain relief.
- If you use opioids, you need to use a full agonist with strong binding potential, or you risk making pain relief less.
  - Fentanyl is preferred agent.

64

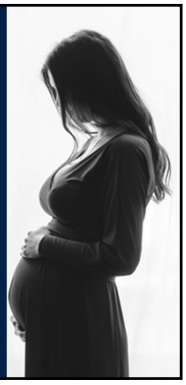
Post-partum Mothers and Substance Use Disorder

- High risk of relapse. Encourage them to continue with recovery behaviors and medication.
- Often do not have good parenting skills. Consider home nursing, parenting classes.
- May have a fussier baby than average – need a lot of support.

65

Comorbid Medical Conditions Case Study: Pregnancy and Opioid Dependence

34 yo G2P1 had been on buprenorphine-naloxone for heroin use disorder. She moved away, got pregnant, and weaned herself off the buprenorphine. Moved back and declined to restart buprenorphine because "I am not going to ever go back to drugs." NSVD of healthy baby with negative urine drug screens throughout pregnancy. Died of an overdose about one year post-partum.



66

Maternal Mortality and Opioid Use Disorder

- Studies from Maryland, Tennessee, Colorado, Utah, Ohio, and Massachusetts have found that postpartum overdose is one of the top causes of maternal mortality, causing 15-33% of deaths.

[1]https://phpa.health.maryland.gov/mch/Documents/Health-General%20Article,%20%C2%A713-1207,%20Annotated%20Code%20of%20Maryland%20-%202015%20Annual%20Report%20%E2%80%93%20Maryland%20Maternal%20Mortality%20Review.pdf. Accessed 2/18/2021
[2]Tennessee Maternal Mortality Review of 2Maryland Maternal Mortality Review. 2014 Annual Report. MD Dept of Health and Mental Hygiene. Prevention and Health Promotion Administration.
[3]Metz et al. Maternal Deaths from Suicide and Overdose in Colorado, 2004-2012. Ob Gyn. Vol 128. No. 6. December 2016. pp 1233-1240
[4]Smid et al. Pregnancy-Associated Death in Utah: Contribution of Drug-Induced Deaths. Obstet Gynecol. 2019 Jun; 133(6): 1131-1140
[5]Hall et al. Pregnancy-Associated Mortality Due to Accidental Drug Overdose and Suicide in Ohio, 2009-2018. Obstetrics and Gynecology. Vol 136, No 4 October 2020
[6]Schiff et al. Fatal and Nonfatal Overdose Among Pregnant and Postpartum Women in Massachusetts. Obstet Gynecol. 2018

67

Maternal Mortality and Opioid Use Disorder

- Suicide is also a substantial contributor to postpartum mortality.[1]
- Risk factors for postpartum opioid overdose and postpartum suicide have significant overlap.[2]
- Three of the most common include depression, intimate partner violence, and substance use disorder.
- Screen for depression postpartum. Use Edinburgh Postpartum Depression Screen or another tool.

[1]Campbell et al. Pregnancy- Associated Deaths from Homicide, Suicide, and Drug Overdose: Review of Research and the Intersection with Intimate Partner Violence. *Journal of Women's Health*. Volume 30, Number 2, 2021.
[2]Mangla et al. Maternal self-harm deaths: an unrecognized and preventable outcome. American Journal of Obstetrics and Gynecology. October 2019.

68

Increased Maternal Mortality Continued For Many Years After Delivery in 2019 Study

Mothers in Ontario and England with babies who had neonatal abstinence syndrome have a mortality rate that is over ten times as high as mothers who did not have an affected baby.

Roughly 1 in 20 mothers died over the next decade.

Top cause of death was unintentional injuries, but there were also high rates of murder and suicide, drug-related deaths, and unavoidable deaths.

Guttmann A et al. Long-term mortality in mothers of infants with neonatal abstinence syndrome: A population-based parallel-cohort study in England and Ontario, Canada. PLoS Med 16(11): e1002974. November 26, 2019.

69

Neonatal Opioid Withdrawal Syndrome

70

Neonatal Opioid Withdrawal Syndrome Definition

- Neonatal Opioid Withdrawal Syndrome = physical withdrawal.
- Neonatal Opioid Withdrawal Syndrome ≠ baby is addicted to drugs.

71

Clinical Definition of Opioid Withdrawal in the Neonate from The AAP

- Presence of clinical elements 1 and 2
- **(1) In utero exposure** to opioids with or without other psychotropic substances (recommended to be collected via confidential maternal self-report; toxicology testing also acceptable with maternal informed consent)
- **(2)Clinical signs** characteristic of substance withdrawal; any 2 of the following 5 signs qualify:
  - Excessive crying (easily irritable)
  - Fragmented sleep (<2-3 h after feeding)
  - Tremors (disturbed or undisturbed)
  - Increased muscle tone (stiff muscles)
  - Gastrointestinal dysfunction (hyperphagia, poor feeding, feeding intolerance, loose or watery stools)

Jilani et al. Standardizing the Clinical Definition of Opioid Withdrawal in the Neonate. *The Journal of Pediatrics*. September/October 2020 - Volume 14 - Issue 5

72

Neonatal Opioid Withdrawal Syndrome

- Neonatal Opioid Withdrawal Syndrome is highly treatable if diagnosed early, limited in duration, and, as far as we know, has limited long-term effects compared to the effects of untreated opioid use disorder.
- We should never use the possibility of NOWS to justify not properly treating opioid use disorder.
- We should also make sure that all pregnant women who are under treatment with medication facing the possibility of a baby with NOWS understand that they are doing the best possible thing for their baby.

73

Non-pharmacologic Treatment Of Neonatal Opioid Withdrawal Syndrome

- Non-pharmacologic treatment includes the following:
  - Small, frequent feeds.
  - Quiet, dim light.
  - Swaddling or skin-to-skin.
  - Prenatal education for parents.
- Studies from Dartmouth[1] and Yale[2] showed substantial improvements in cost and length of stay using non-pharmacologic treatment.

[1]Holmes et al. Rooming-In to Treat Neonatal Opioid Withdrawal Syndrome: Improved Family-Centered Care at Lower Cost. Pediatrics 2016; pp 2015-2029
[2]Grossman et al. An Initiative to Improve the Quality of Care of Infants with Neonatal Opioid Withdrawal Syndrome. Pediatrics 2017;139(60)

74

Breastfeeding

- The Academy of Breastfeeding Medicine, the American Academy of Pediatrics, the American College of OB-GYN, the Substance Abuse and Mental Health Services Administration, and the American Society for Addiction Medicine recommend breastfeeding for women with substance use disorder who are in a treatment program and have had negative drug screens for 2 months prior to delivery.[1,2,3,4,5]
  - This includes women on MOUD.

[1]Jansson, L. et al, Methadone Maintenance and Breastfeeding in the Neonatal Period PEDIATRICS Vol. 121 No. 1 January 2008, pp. 106-114
[2]Reece-Stretman et al. ABM Clinical Protocol #21: Guidelines for Breastfeeding and Substance use or Substance Use Disorder, Revised 2015 Breastfeeding Medicine: Vol 10, November 3, 2015, pp 135-141
[3]Substance Use, Misuse, and Use Disorders During and Following Pregnancy, with an Emphasis on Opioids. ASAM Policy Statement. January 18, 2017
[4]Clinical Guidance for Treating Pregnant and Parenting Women with Opioid Use Disorder and Their Infants. SAMHSA. HHS Publication No. (SMA) 18-5054
[5]ACOG Committee Opinion. Opioid Use and Opioid Use Disorder in Pregnancy. Number 711. August 2017.

75

Child Protective Services and Mental Health

A study in Manitoba showed that losing custody of a child-to-child protective services is associated with significantly worse maternal mental health outcomes than experiencing the death of a child

Risk of depression was 1.90 times greater for women who had lost a child-to-child protective services.

Risk of substance use was 8.54 times greater for women who had lost a child-to-child protective services.

Wall-Wieler, Elizabeth et al. Maternal Mental Health after Custody Loss and Death of a Child: A Retrospective Cohort Study Using Linkable Administrative Data. The Canadian Journal of Psychiatry. 2018, Vol. 63(5) 322-328.

76

Comprehensive Addiction and Recovery Act

CARA requires states to identify and report on the following:

- Number of substance-exposed infants born
- Number of substance-exposed infants for whom a Plan of Care was created
- Number of infants with a Plan of Care for whom referrals were made to appropriate services, including services for affected family members or caregivers

77

To Call Child Protective Services or not

- Know your state's laws
- Child Welfare Information Gateway has a page that will let you look up your state's laws:
- https://www.childwelfare.gov/topics/systemwide/laws-policies/state/
- Know your local hospitals' policies.

78

To Call Child Protective Services or Not

- Discuss child protective service involvement during pregnancy
  - What will trigger a referral
  - What will likely happen with a referral
- Discuss with your patient what to do if a referral is made:
  - Be honest with child protective services
  - Have a plan for SUD treatment
  - Have a plan to ensure the baby is safe

79

Take Home Messages

There is a substantial genetic component to substance use disorder.	Women are less likely than men to use drugs and alcohol but have worse outcomes when they do.	Alcohol and tobacco are the most dangerous drugs for the fetus in pregnancy.
Medication treatment is recommended for opioid use disorder in pregnancy.	The postpartum period and after is a high-risk time for relapse and death in women with SUD.	Use non-medical treatments first for neonatal opioid withdrawal syndrome.

80

Pain and Addiction: Past, Present and Future of Treatment

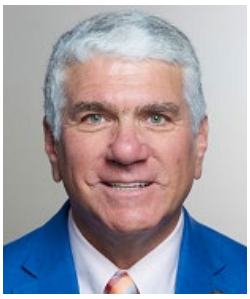
Sunday, July 24
10:30 am – 11:15 am CT

The complex overlap of pain and addiction presents several public health and clinical challenges. This session will review the evolution of the prescription opioid epidemic, which led to the heroin and fentanyl epidemics. The presenter will then review data and clinical practice guidelines regarding the treatment of chronic non-cancer pain and the effectiveness of opioid therapy. Participants will also learn about options to simultaneously treat opioid use disorder and chronic pain.

Learning Objective:

- After this session, learners will be able to: Explain the conceptual overlap, assessment, and evidence-based treatments for pain and addiction.

Faculty Presenter



Edwin A. Salsitz, MD, DFASAM
Unit Chief, Inpatient Rehabilitation
Mount Sinai Beth Israel
Icahn School of Medicine at Mount Sinai

Dr. Edwin A. Salsitz has been an attending physician in the Mount Sinai Beth Israel, Division of Chemical Dependency, New York City, since 1983, and is an Associate Clinical Professor of Psychiatry at the Mount Sinai School of Medicine. He is the principal investigator of the Methadone Medical Maintenance (office-based methadone maintenance) research project. Dr. Salsitz is certified in Addiction Medicine by the American Board of Preventive Medicine, as well as by the Board of Internal Medicine and Pulmonary Disease. He has published and lectures frequently on addiction medicine topics.

Dr. Salsitz is a course director for ASAM sponsored Buprenorphine and REMS Opioid trainings, and is a lead mentor in the PCSS-MAT mentoring program. He has co-chaired the ASAM Review Course, the ASAM Common Threads Course, the ASAM State of the Art course and is a reviewer for the Journal of Addiction Medicine and Drug and Alcohol Dependence. He is the chair of the ASAM REMS course on safe and effective prescribing of opioids. Dr. Salsitz was the Co-chair of the ASAM CME committee and Chair of the New York Society of Addiction Medicine CME and Education committee.
Dr. Salsitz is a member of the medical advisory panel, for the New York State Office of Alcohol and Substance Abuse Services. Dr. Salsitz is the recipient of the 2014 ASAM Annual Award, and the 2018 ASAM Annual Educator of the Year Award.

PAIN AND ADDICTION

Edwin A. Salsitz, MD, DFASAM
Associate Clinical Professor of Psychiatry
Mount Sinai Beth Israel, NYC

1

The ASAM Board Exam Study Course in Addiction Medicine

July 2022

Financial Disclosures

Edwin A. Salsitz, MD, DFASAM
No Disclosures

2

"PRINCIPLES" 6th Edition

Comprehensive, Complete, Clear, References

- Chap. 37: Misuse All Controlled Medications
- Chap. 100: Basic Science and Overlap P & A
- Chap. 101: Psychological Issues
  - "If life is empty, pain will fill it up."
- Chap. 102: Rehabilitation Modalities
- Chap. 103: Non-Opioid Pharmacotherapy
- Chap. 104: Opioid Therapy
- Chap. 105: Co-Occurring Pain and Addiction
- Chap. 106: Legal & Regulatory Issues in Opioid Prescribing

3



JAMA. 2015;314(20):2123



JAMA. 2016;315(17):1826

4

The Epidemic of Untreated Pain

5

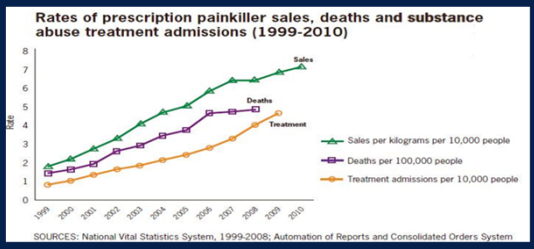
Alleviating Suffering 101 Pain Relief in the USA

- 2011 IOM Report: 116 Million Americans have pain which persists for weeks to years
- $560 - $635 Billion per year
- Some physicians overprescribe opioids, while others refuse to prescribe
- Lack of education: Providers and Patients
  - Headache, LBP, Neck Pain, Joint Pain, Fibromyalgia

NEJM 366:3 Jan 19,2012

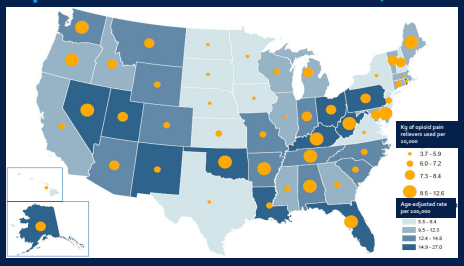
6

Rates of Opioid Overdose Deaths, Sales, and Treatment Admissions, United States, 1999–2010



7

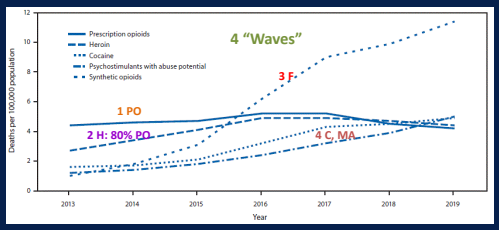
Drug Overdose Death Rate, 2008, and Opioid Pain Reliever Sales Rate, 2010



National Vital Statistics System, 2008; Automated Reports Consolidated Orders System, 2010.

8

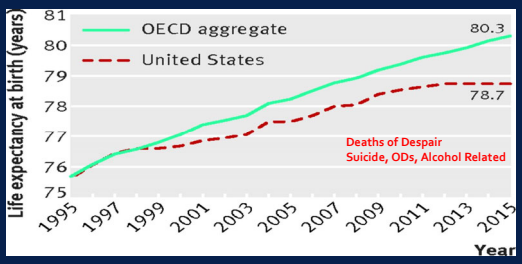
Age-Adjusted Rates of Drug Overdose Deaths Involving Prescription Opioids, Heroin, Cocaine, Psychostimulants with Abuse Potential, and Synthetic Opioids Other than Methadone—United States, 2013–2019



MMWR Morb Mortal Wkly Rep 2021;70:202–207

9

Life Expectancy at Birth in the US and the Organisation for Economic Cooperation and Development, 1995-2015.

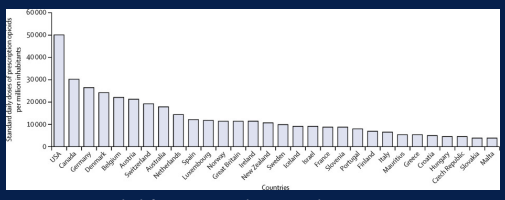


Members of the Organisation for Economic Coordination and Development include Australia, Austria, Belgium, Canada, Chile, Czech Republic, Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Iceland, Ireland, Israel, Italy, Japan, Korea, Latvia, Luxembourg, Mexico, the Netherlands, New Zealand, Norway, Poland, Portugal, Slovak Republic, Slovenia, Spain, Sweden, Switzerland, Turkey, the UK, and the US.

Steven H Woolf, and Laudan Aron BMJ 2018;360:bmj.k496

10

Avoiding Globalization of the Prescription Opioid Epidemic



Top 30 Opioid-Consuming Nations 2012-2014

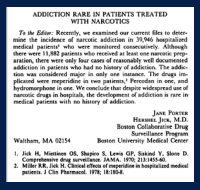
Lancet, Vol 390, 29 July–4 August 2017, Pages 437-439, Keith Humphreys

11

How Did We Get Here?

12

"Perfect Storm"

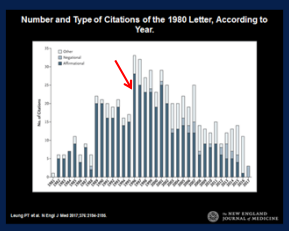


ADDICTION RARE IN PATIENTS TREATED WITH NARCOTICS

To the Editor: Recently, we examined our current files to determine the incidence of narcotic addiction in 39,946 hospitalized medical patients[1] who were monitored consecutively. Although there were 11,882 patients who received at least one narcotic preparation, there were only four cases of reasonably well documented addiction in patients who had no history of addiction. The addiction was considered major in only one instance. The drugs implicated were meperidine in two patients,[2] Percodan in one, and hydromorphone in one. We conclude that despite widespread use of narcotic drugs in hospitals, the development of addiction is rare in medical patients with no history of addiction.

JANE PORTER, M.D.
HERBERT JICK, M.D.
Boston Collaborative Drug Surveillance Program
Boston University Medical Center
Waltham, MA 02154

1. Jick H, Miettinen OS, Shapiro S, Lewis GP, Siskind V, Slone D. Comprehensive drug surveillance. JAMA. 1970; 213:1455-60.
2. Miller RR, Jick H. Clinical effects of meperidine in hospitalized medical patients. J Clin Pharmacol. 1978; 18:1804.



- **1980→ 2017: 608 citations** : ~75% used as evidence that addiction is rare with COT and made no mention that these were hospitalized patients with few doses of opioids.
- 11 other letters from 1980 were cited on average, 11 times.

N Engl J Med 1980; 302: 123.
N Engl J Med 376:22 June 2017

13

"Perfect Storm"

- 1995: Introduction of Oxycontin
- 1995: Pain is Fifth Vital Sign
- Publications indicating low risk of addiction
- Thought Leaders with Financial/Pharma Conflicts
- Patient Satisfaction Surveys: "…staff did everything they could to help you with your pain"
- Physicians successfully sued for not treating pain
- No Evidence long term Effectiveness COT → CNCP
- Physical Dependence vs Addiction

14

Doctor liable for not giving enough pain medicine

June 14, 2001 Posted: 12:28 AM EDT (0428 GMT)



HAYWARD, California (CNN) -- **In a civil case that could have broad ramifications for how patients in pain are treated, a California jury Wednesday found a doctor liable for recklessness and abuse for not prescribing enough pain medication to a patient, who later died of cancer.**

The jury in Alameda County Superior Court called on the doctor to pay the patient's family $1.5 million dollars for pain and suffering of the patient. Under California law, however, the cap for such awards is $250,000, and the judge will likely reduce the jury's award.

A Doctor Who Prescribed 500,000 Doses of Opioids Is Sent to Prison for 40 Years

Dr. Joel Smithers was convicted of more than 800 counts of illegally prescribing opioids, and jurors found that the drugs he prescribed caused the death of a woman.

By Adeel Hassan

Oct. 2, 2019

A Virginia doctor who prescribed more than 500,000 doses of opioids in two years was sentenced to 40 years in prison on Wednesday for leading what prosecutors called an interstate drug distribution ring.

15



ORIGINAL RESEARCH

Prescription Opioid Use among Adults with Mental Health Disorders in the United States

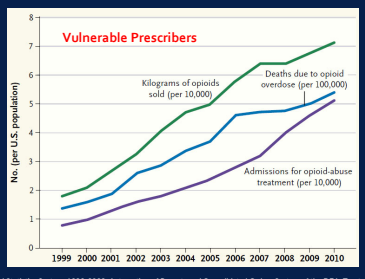
Conclusions: **The 16% of Americans who have mental health disorders receive over half of all opioids prescribed in the United States.** Improving pain management among this population is critical to reduce national dependency on opioids.

Adverse Selection

J Am Board Fam Med 2017;30:407– 417

16

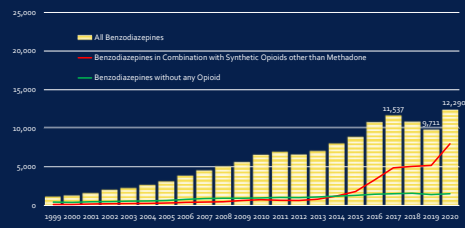
Prescription Opioid Trends: 1999-2010



National Vital Statistics System, 1999-2008; Automation of Reports and Consolidated Orders System of the DEA; Treatment Episode Data Set

17

National Drug Overdose Deaths Involving Benzodiazepines, by Opioid Involvement, Number Among All Ages, 1999-2020



*Among deaths with drug overdose as the underlying cause, the benzodiazepine category was determined by the T402.2 ICD-10 multiple cause-of-death code. Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2020 on CDC WONDER Online Database, released 12/2021.

18

New Safety Measures Announced for Opioid Analgesics, Prescription Opioid Cough Products, and Benzodiazepines FDA: August 2016

Table 1. The Danger of Combining Opioids And Benzodiazepines

FDA Warning: Risks From Concomitant Use With Benzodiazepines or Other CNS Depressants
Concomitant use of opioids with benzodiazepines or other central nervous system (CNS) depressants, including alcohol, may result in profound sedation, respiratory depression, coma, and death.
• Reserve concomitant prescribing of (opioid) and benzodiazepines or other CNS depressants for use in patients for whom alternative treatment options are inadequate
• Limit dosages and durations to the minimum required
• Follow patients for signs and symptoms of respiratory depression and sedation

Source: US Food and Drug Administration website. Available at: http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm518697.

19

FDA Drug Safety Communication: FDA urges caution about withholding opioid addiction medications from patients taking benzodiazepines or CNS depressants: careful medication management can reduce risks

This provides updated information to the FDA Drug Safety Communication: FDA warns about serious risks and death when combining opioid pain or cough medicines with benzodiazepines; requires its strongest warning (/Drugs/DrugSafety/ucm518473.htm) issued on August 31, 2016.

Safety Announcement

[9-20-2017] Based on our additional review, the U.S. Food and Drug Administration (FDA) is advising that the opioid addiction medications buprenorphine and methadone should not be withheld from patients taking benzodiazepines or other drugs that depress the central nervous system (CNS). The combined use of these drugs increases the risk of serious side effects; however, the harm caused by untreated opioid addiction can outweigh these risks. Careful medication management by health care professionals can reduce these risks. We are requiring this information to be added to the buprenorphine and methadone drug labels along with detailed recommendations for minimizing the use of medication-assisted treatment (MAT) drugs and benzodiazepines together.

Buprenorphine and methadone help people reduce or stop their abuse of opioids, including prescription pain medications and heroin. Methadone and buprenorphine have been shown to be effective in reducing the negative health effects and deaths associated with opioid addiction and dependency.[1] These medications are often used in combination with counseling and behavioral therapies (https://www.samhsa.gov/medication-assisted-treatment/treatment#counseling-behavioral-therapies), and patients can be treated with them indefinitely. Buprenorphine and methadone work by acting on the same parts of the brain as the opioid that the patient is addicted to. The patient taking the medication as directed generally does not feel high, and withdrawal does not occur. Buprenorphine and methadone also help reduce cravings[2] (see Table 1. List of Buprenorphine and Methadone MAT Drugs).

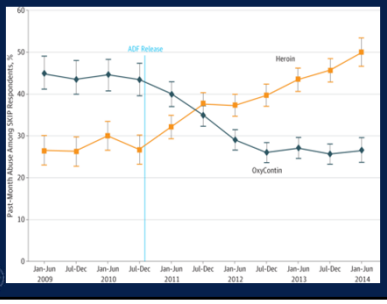
20

Intended/Unintended Consequences in Reaction to the Prescription Opioid Epidemic

- Prescription Drug Monitoring Programs: PDMP
- Limits on the quantity and dosage prescribed
- UDTs become standard of care
- Education of prescribers: FDA REMS course on Safe and Effective Opioid Mgt.
- CDC Guidelines
- Tamper Resistant/Abuse Deterrent Formulations
- Patients Physically Dependent on Opioids Left in the Lurch
- **HEROIN: Cheaper, Readily Accessible**
- **FENTANYL/Fentanyl Analogues**

21

Abuse-Deterrent Formulations and the Prescription Opioid Abuse Epidemic in the United States: Lessons Learned From OxyContin



Respondents Who Endorsed Past-Month Use of OxyContin or Heroin Before and After the Introduction of an Abuse-Deterrent Formulation (ADF). Respondents include 10 784 participants in the Survey of Key Informants' Patients (SKIP) program (mean number per half-year, 991). Data are presented in 6-month increments from January 1, 2009, through June 30, 2014, and are expressed as percentages (95% CI [error bars]), with a χ^2 test for trend significance of $P < .001$ during the study period. The ADF was released in August 2010. OxyContin is a proprietary formulation of oxycodone hydrochloride.

JAMA Psychiatry. 2015;72(5):424-430.

22

CDC Guideline for Prescribing Opioids for Chronic Pain—3/16

Type 1 evidence: Randomized clinical trials or overwhelming evidence from observational studies.
Type 2 evidence: Randomized clinical trials with important limitations or exceptionally strong evidence from observational studies.
Type 3 evidence: Observational studies or randomized clinical trials with notable limitations.
Type 4 evidence: Clinical experience and observations, observational studies with important limitations, or randomized clinical trials with several major limitations.

- **NonPharmacologic** and **NonOpioid** therapy is preferred (Type 3)
- Before starting opioid therapy, **establish realistic treatment goals (Type 4)**
- Before starting and periodically during opioid therapy, discuss **risks, benefits,** and **responsibilities** for managing therapy **(Type 3)**
- **Immediate Release Opioids** should be used when starting therapy (Type 4)
- When opioids are started, the **Lowest Effective Dose should be used 50/90 MME (Type 3)**
- Quantity prescribed: **Acute Pain < 3 days supply, Rarely >7 days (Type 4)**
- **Evaluate Benefit vs Harm** in patient within 1-4 weeks of starting opioids (Type 4)

23

CDC Guideline for Prescribing Opioids for Chronic Pain—3/16

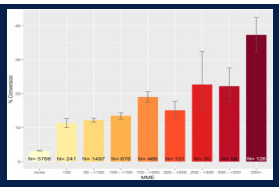
Type 1 evidence: Randomized clinical trials or overwhelming evidence from observational studies.
Type 2 evidence: Randomized clinical trials with important limitations or exceptionally strong evidence from observational studies.
Type 3 evidence: Observational studies or randomized clinical trials with notable limitations.
Type 4 evidence: Clinical experience and observations, observational studies with important limitations, or randomized clinical trials with several major limitations.

- Before starting and during therapy, **Evaluate Risk Factors (Type 4)**
- Review patient's history of controlled substance use by using the state's automated **Prescription Drug Monitoring System (PDMP) (Type 4)**
- When prescribing opioids for chronic pain, clinicians should use **Urine Drug Screens (UDS) (Type 4)**
- Avoid prescribing opioid medications with **Benzodiazepines (Type 3)**
- Offer **Substance Use Disorder Treatment** for patients when needed (Type 2)

24

Conversion to Persistent or High-Risk Opioid Use After a New Prescription From the Emergency Department: Evidence From Washington Medicaid Beneficiaries

Zachary F. Meisel, MD, MPH*; Nicoleta Lupulescu-Mann, MS; Christina J. Charlesworth, MPH; Hyunjee Kim, PhD; Benjamin C. Sun, MD, MPP
*Corresponding Author. E-mail: zfm@wharton.upenn.edu, Twitter: @zacharymeisel.

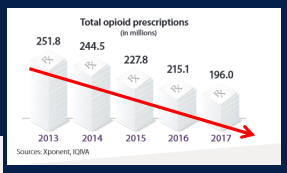


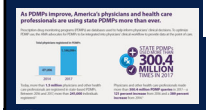
Frequency of persistent or high-risk opioid conversion by quantity of morphine milligram equivalents prescribed at the index ED visit

Ann Emerg Med. 2019;-:1-11

25

Physicians' Progress to Reverse the Nation's Opioid Epidemic
AMA Opioid Task Force 2018 Progress Report

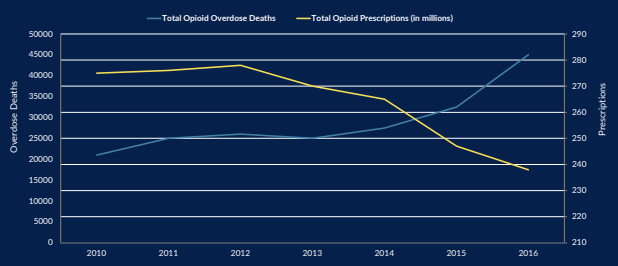






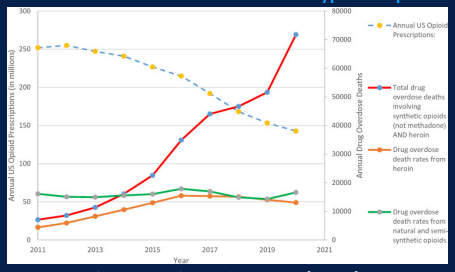
26

Opioid Overdose and Prescribing Trends



27

Changes in Annual Opioid Prescriptions Compared to Overdose Death Rates from Different Types of Opioids



CDC Drug Overdose: US Opioid Dispensing Rate Map [Internet]. CDC. Nov 2021

28

Start With Non-Pharmacologic Therapy

- Physical Therapy, Exercise
- Cold, Heat
- CBT, MI
- Meditation, Mindfulness
- Acupuncture
- Biofeedback
- Massage
- Aquatic Therapy
- Spinal Cord Stimulation (SCS)

29

Effective Analgesic



30

Next Option: Non-Opioid Pharmacotherapy

- Acetaminophen (Efficacy), NSAIDS (Adverse Effects, Cardiac, Elderly)
- Anti-Depressants: TCAs, SSRIs, SNRIs
  - Neuropathic Pain, Nociplastic Pain (e.g., Fibromyalgia), Pain + Depression
- Anti-Convulsants: Gabapentanoids, Topiramate, Carbamazepine
  - Neuropathic Pain, Nociplastic Pain, Migraine Prophylaxis
- Topicals: Lidocaine Patch, NSAIDS, Capsaicin
- "Muscle Relaxants:" Baclofen, Cyclobenzadrine, Methocarbamol, Tizanidine
  - Avoid Benzodiazepines, Carisoprodol (Schedule IV)
- Ketamine: Acute Pain (e.g., ED)
- Interventional Procedures: Epidurals, Nerve Blocks, Neuro-Modulation

31

Gabapentanoids: Conclusions

- Significant Misuse Among Patients with SUDs, Primarily OUD Receiving Methadone or Buprenorphine Maintenance.
- Significant Adverse Effects With Therapeutic Doses, and Increased Adverse Effects With Supra-Therapeutic Doses
- Must Adjust for Renal Function
- Full Recovery From Adverse Effects Is The Rule
- **Death Is Uncommon, But Increased In Combination With Opioids**
- Gabapentin Bioavailability ↓ With Increasing Dose
- Weak Evidence For Off Label Pain Treatment
- Should Gabapentin Be Listed On PDMPs (e.g., Ohio, NJ)
- Pregabalin Schedule 5 listed
- Add Gabapentanoids To UDT Screens

32

Opioid Pharmacotherapy

- Acute Pain: e.g., Post-Operative
- Limit Duration: NYS-7days
- Cancer Pain
- Palliative Care, Hospice
- End of Life Care
- **Chronic Opioid Therapy (COT) for**
  - **Chronic Non-Cancer Pain (CNCP)**
    - **Effectiveness, Safety, Adverse Effects,**
    - **IR vs. ER**

33

Long Term(>16wks.) COT for CNCP

Long-term Opioid Treatment of Chronic Nonmalignant Pain: Unproven Efficacy and Neglected Safety.

- "..No high-quality evidence on the efficacy of COT for CNCP." no RCT lasting >3mos
- "Until 2003, opioid addiction associated with the treatment of CNCP was clearly a neglected topic of publication."

- **Reported Rates of Iatrogenic OUD 3-5%**
- **Currently 30-40%**

Kissin, Igor Journal of Pain Research, 2013:6 513-529

34



REVIEW — Annals of Internal Medicine

The Effectiveness and Risks of Long-Term Opioid Therapy for Chronic Pain: A Systematic Review for a National Institutes of Health Pathways to Prevention Workshop

Roger Chou, MD; Judith A. Turner, PhD; Emily B. Devine, PharmD, PhD, MBA; Ryan N. Hansen, PharmD, PhD; Sean D. Sullivan, PhD; Ian Blazina, MPH; Tracy Dana, MLS; Christina Bougatsos, MPH; and Richard A. Deyo, MD, MPH

Conclusion: Evidence is insufficient to determine the effectiveness of long-term opioid therapy for improving chronic pain and function. Evidence supports a dose-dependent risk for serious harms.

Conclusion: Evidence is insufficient to determine the effectiveness of long-term opioid therapy for improving chronic pain and function. Evidence supports a dose-dependent risk for serious harms.

35

Initiating Opioid Treatment: CNCP

- Prescribers should regard initial treatment as a therapeutic trial
  - May last from several weeks to several months; **start with IR Opioid**
  - Decision to proceed w/ long-term treatment should be intentional and based on careful consideration of outcomes during the trial
    - Progress toward meeting therapeutic goals
    - Functional Improvement
    - Presence of opioid-related adverse effects
    - Changes in underlying pain condition
    - Changes in psychiatric or medical comorbidities
    - Identification of aberrant drug-related behavior, addiction, or diversion

Chou R, et al. *J Pain.* 2009;10:113-30.

36

Guidelines for Opioid Rotation

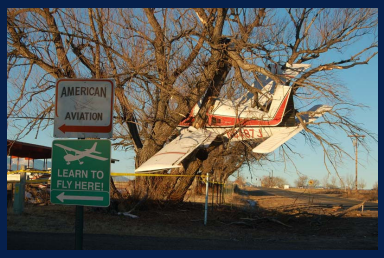
- Calculate equianalgesic dose of new opioid from EDT
- Reduce equianalgesic dose by 25%-50%: **incomplete cross tolerance**
- **Methadone: EDTS Not Helpful**
  Start Low, Go Slow
  2% of sales / 30% of Overdose Deaths: Pain, not OTPs

- **Opioid Induced Hyperalgesia (OIH): counterintuitive but real**
  - Differentiate from Opioid Tolerance ↑Dose → ↓Pain or ↑Pain

Fine PG, et al. *J Pain Symptom Manage.* 2009;38:418-25.

37

Can You Land the Opioid Plane?



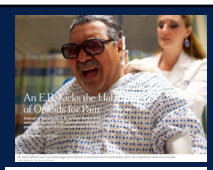
38

Opioid Tapering/Deprescribing Strategies

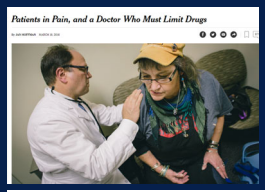
- Patient Requests/Agrees vs Patient Resists
- Alternative Treatment if Pain Still Present
- Clonidine/Lofexidine Tablets and Patches
- alpha 2 centrally acting adrenergic agonists→ ↓LC→ ↓NE
- Switch to Methadone
- Switch to Buprenorphine
- Symptomatic Meds: NSAIDS, Loperamide, Benzos(short course), non-benzo sleep meds
- Patients report favorable outcomes after tapering

JAMA Internal Medicine May 2018 Volume 178, Number 5
The Journal of Pain, Vol 18, No 11 (November), 2017

39









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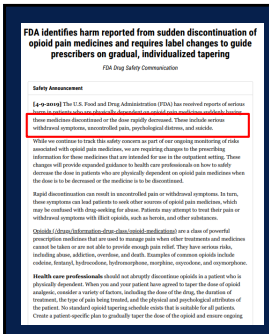
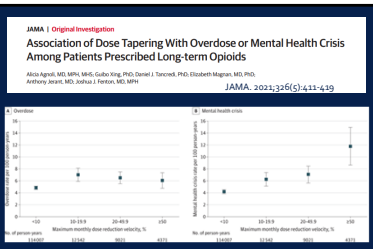




CONCLUSIONS: Among patients prescribed stable, long-term, higher-dose opioid therapy, tapering events were significantly associated with increased risk of overdose and mental health crisis

41

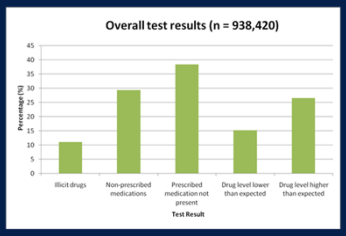
HHS Guide for Clinicians on the Appropriate Dosage Reduction or Discontinuation of Long-Term Opioid Analgesics

Oct. 2019

- The CDC Guideline for Prescribing Opioids for Chronic Pain **does not recommend opioid discontinuation when benefits of opioids outweigh risks.**
- Avoid misinterpreting cautionary dosage thresholds. Guideline recommends avoiding or carefully justifying increasing dosages **above 90 MME/day, it does not recommend abruptly reducing opioids from higher dosages.**
- **Avoid dismissing patients from care.**

42

Urine Toxicology Results in Chronic Pain Patients on Opioid Therapy

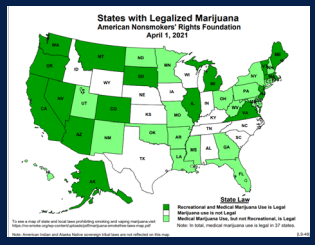


Couto JE, Goldfarb NI, Leider HL, Romney MC, Sharma S. High rates of inappropriate drug use in the chronic pain population. *Popul Health Manag*. 2009;12(4):185–190.

43

Cannabis/Cannabinoids





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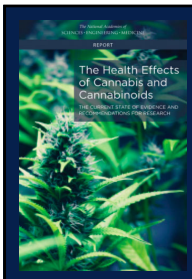


- In adults with chemotherapy induced nausea and vomiting, oral cannabinoids are effective antiemetics.
- In adults with chronic pain, patients who were treated with cannabis or cannabinoids are more likely to experience a clinically significant reduction in pain symptoms
- In adults with multiple sclerosis (MS) related spasticity, short-term use of oral cannabinoids improves patient-reported spasticity symptoms.
- For these conditions the effects of cannabinoids are modest; for all other conditions evaluated there is inadequate information to assess their effects.

Opioid Use Disorder: Conflicting reports. No RCTs Controversies About Listing as Eligible Disorder for Medicinal Cannabis by Some States

National Academy of Science, Engineering and Medicine. 2017.

45

Prescription Drug Monitoring Programs: PDMPs

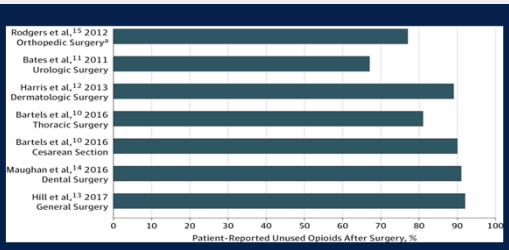
- All states are operational
- Some states mandatory at time of Rx, e.g., N.Y.
- Some state PDMPS include bordering and other states
- OTPs are exempt: both Methadone and Buprenorphine
- OBOT Buprenorphine included in PDMPs
- ↓ Doctor shopping and Rx opioid prescribed since 2010
- Evidence of ↓ OD deaths
- Unintentional consequences: ↑Heroin, ↑Pain, Abrupt Rx Cessation

46

The JAMA Network

From: **Prescription Opioid Analgesics Commonly Unused After Surgery: A Systematic Review**

JAMA Surg. Published online August 02, 2017.



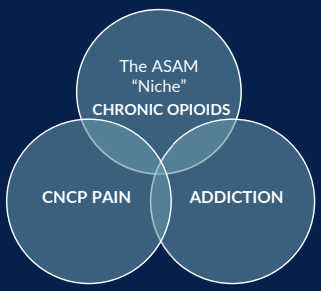
47

Opioid Rx Disposal

- DEA Take Back Programs
- Some Pharmacies, Some Police Stations
- Mix with cat litter/coffee grounds, then seal in plastic bag and throw out in trash
- Flush down toilet: environmental issues
  - Fentanyl Patch: Flush only
- DO NOT throw out in trash in Rx bottle

48

Complex Intersection



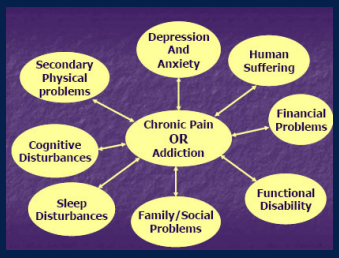
49

Pain and Addiction: Definitions

- "Pain is viewed as a biopsychosocial phenomenon that includes **sensory, emotional, cognitive, developmental, behavioral, spiritual and cultural components."** (IASP website)
- Addiction is a treatable, chronic medical disease involving **complex interactions among brain circuits, genetics, the environment, and an individual's life experiences.** People with addiction use substances or engage in behaviors that become compulsive and often continue despite harmful consequences.

50

Pain and Addiction



Ann Quinlan-Colwell, PhD, PCSS-O Webinar. 2011.

51

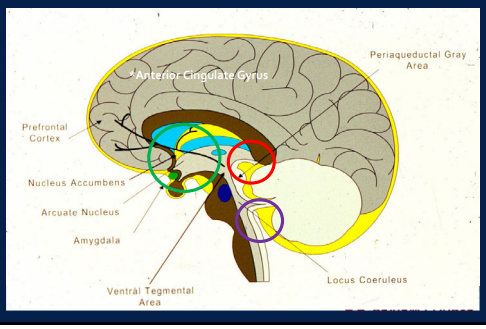
Pain and Addiction
Limited (e.g., UDT) Objective Measurements





52

Opioid Sites of Action in the Brain



53

"Exaggerated Response"
What Did It Feel Like The First Few Times?

- "All my problems disappeared."
- "Felt like I was under a warm blanket."
- "Thought this is how normal people feel."
- "Forgot about all the abuse."
- "Felt like the world was at peace."
- "Totally relaxed." "Not shy."
- "Looking at a beautiful sunset."
- "I was energized!"
- *Liking opioids: this is a vulnerability.*

54

Treating Pain in the Addicted Patient

- "Pain patients with a coexisting SUD are among the most challenging patients in medicine."
- Universal Precautions
- "Real Pain" may make opioids less rewarding/euphorogenic
- Addicted Patients Have Pain: Trauma, Lower Thresholds, Medical
- Screening Tests: ORT, SOAPP, others
- Untreated Pain is a trigger for relapse
- Address both pain and addiction
- Significant other to secure and dispense opioid meds
- Psychiatric Co-morbidity
- Active Addiction recovery program
- UDS, pill counts, agreements, etc.
- **Multidisciplinary Pain Program**

Bailey, et al. *Pain Medicine* 2010; 11: 1803-1818

55

Buprenorphine Formulations: FDA Approved for Pain not OUD

- Buprenex® Parenteral (IV, IM)
- Butrans® Transdermal (7 Day)
- Belbuca® Buccal Film (75—900mcg q12h)

- Approved for pain but **NOT** OUDs
- **Can NOT be used OFF LABEL** for OUDs: Violates DATA 2000

56

JAMA Network Open. JAMA Network Open. 2021;4(9)

Original Investigation | Substance Use and Addiction

Evaluation of Buprenorphine Rotation in Patients Receiving Long-term Opioids for Chronic Pain
A Systematic Review

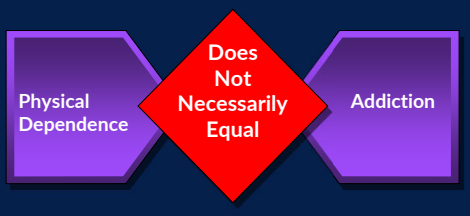
Victoria D. Powell, MD; Jack M. Rosenberg, MD; Avani Yagantl, BS; Claire Garpestad, MD; Pooja Lagisetty, MD, MSc; Carol Shannon, MPH; Maria J. Silveira, MD, MA; [illegible]

CONCLUSIONS AND RELEVANCE: In this systematic review, buprenorphine was associated with reduced chronic pain intensity without precipitating opioid withdrawal in individuals with chronic pain who were receiving LTOT. Future studies are necessary to ascertain the ideal starting dose, formulation, and administration frequency of buprenorphine as well as the best approach to buprenorphine rotation.

MEANING: These findings suggest that buprenorphine rotation may be a viable option for mitigating the harms of long-term opioid therapy in individuals with chronic pain who were receiving unsafe opioid analgesic regimens; further studies are needed to examine the best way to accomplish buprenorphine rotation.

57

Pain and Addiction



58

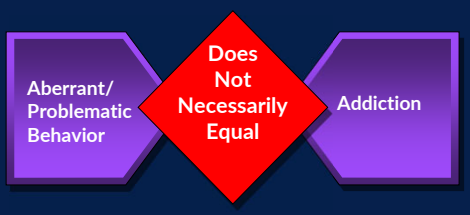
Definitions: Complex Physical Dependence

"Dependence on opioid pain treatment is not, as we once believed, easily reversible; it is a complex physical and psychological state that may require therapy similar to addiction treatment, consisting of structure, monitoring, and counseling, and possibly continued prescription of opioid agonists. Whether or not it is called addiction, **complex persistent prescription opioid dependence** is a serious consequence of long-term pain treatment that requires consideration when deciding whether to embark on long term opioid pain therapy as well as during the course of such therapy.

Opioid Dependence vs Addiction: A Distinction Without a Difference? Ballantyne J, Sullivan M, Kolodny A, Arch Intern Med, 2012

59

Pain and Addiction



60

Pain and Addiction

Chronic Pain

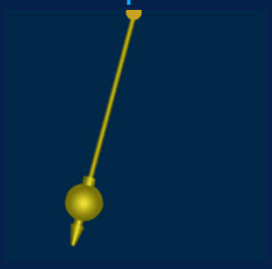
Does Not Necessarily Equal

Suffering

61

Evolution Of Opioid Prescribing

Opioid Phobia



Opioid Philia

Opioid Cautious

Multidimensional Pain Treatment

62



Baby Boomers

OK, BOOMERS!

63

Pain Quotes

- "To have great pain is to have certainty. To hear that another person has pain is to have doubt." "Seeing Pain," Nicola Twilley (2018)
- "Physical Pain does not simply resist language, but actively destroys it." -"The Body in Pain" by Elaine Scarry (1985)
- "Morphine is God's own medicine" Sir William Osler
- We can't live without opioids; we have to learn to live with them.

64

Good luck on the exam and in your careers!



65

Patient Interventions: Cognitive Behavioral Therapy and Motivational Interviewing Sunday, July 24
11:15 am – 12:00 pm CT

Non-pharmacologic modalities are often used in addiction treatment. This session reviews common terminology and concepts in Cognitive Behavioral Therapy (CBT) and Motivational Interviewing (MI). Participants will also learn about other evidence-based modalities like Dialectical Behavioral Therapy, Network Therapies, and case management as they relate to addiction treatment.

Learning Objective:

- After this session, learners will be able to: Identify the basic principles of common behavioral interventions and applications to addiction treatment.

Faculty Presenter



Carla Marienfeld, MD, DFAPA, FASAM
Medical Director Addiction Recovery and Treatment Program
University of California San Diego

Carla Marienfeld, MD, is a board-certified addiction psychiatrist and Clinical Professor at the University of California, San Diego who supports recovery in an evidence based, harm-reduction approach through therapy, motivational interviewing, and medication treatment. Her research involves analysis of electronic medical record data for individuals with substance use disorders. She has authored or co-authored over 35 peer reviewed articles, book chapters, practice guidelines, and invited commentaries, and she edited two books: Motivational Interviewing for Clinical Practice and Absolute Addiction Psychiatry Review: An essential board exam study guide. She has been highly involved in education of colleagues and trainees about addiction psychiatry and effective interventions including buprenorphine treatment and motivational interviewing, and she is the fellowship director for the UCSD Addiction Psychiatry Fellowship. Dr. Marienfeld completed a fellowship in addiction psychiatry and residency training in psychiatry at Yale. During her residency, she was chief resident of psychiatry and founded (and later led) the Yale Global Mental Health Program. She earned a medical degree with honors from Baylor College of Medicine in Houston.

Cognitive Behavioral Therapy & Motivational Interviewing

Carla Marienfeld, MD, FASAM, DFAPA
Clinical Professor of Psychiatry
Medical Director Addiction Recovery and Treatment Program
University of California, San Diego

Thank you to Drs. Finch, Earley, and Lasswell adapting their slides!

1

The ASAM Review Course of Addiction Medicine

July 2022

Financial Disclosures

Carla Marienfeld, MD
No Disclosures



2

Learning Objectives

Identify the basic principles of common behavioral interventions and applications to addiction treatment.

3

Models for Addiction: *Past and ~Present*

- **Moral:**
  - The addict is weak or bad.
  - The drug itself is evil.
- **Psychological/Sociological:**
  - "Addictive personality"
  - Learned behavior: Reward theory
  - Family and cultural norms
- **Medical "brain disease":**
  - Genetic predisposition
  - Chemical imbalance or neuro-adaptation

4

Behavioral Therapies: *Groups*

- Modal format for much SUD therapy:
  - Cost effective
  - Increase Access
  - Peers are a powerful agent of change
  - Better fidelity to model
- Advantages:
  - Modeling, varied coping skills
  - Public affirmations, confession, support
  - Networks of support

5

Behavioral Therapies: *Individual*

- Privacy
- Flexibility to address issues as they arise
- Focus on unique individually relevant issues
- More practical for some providers
- Avoidant patients (e.g., schizophrenia, trauma, socially anxious)

6

Selected Evidence-Based Psychosocial Treatments

- Motivational Interviewing (MI)
- Cognitive-Behavioral Treatment (CBT)
- Mutual Help (AA, NA, Smart Recovery, Women for Sobriety)
- Community Reinforcement Approach (CRA)
- Community Reinforcement And Family Therapy (CRAFT)
- Contingency Management (CM)
- Behavioral Couples Treatment
- Acceptance and Commitment Therapy (ACT)
- Dialectical Behavioral Therapy (DBT)
- Supportive Therapy

7

What is Motivational Interviewing About?

"MI is about arranging conversations so that people talk themselves into change based on their values and interests."

Miller and Rollnick, *Motivational Interviewing: Helping People Change, 3rd Edition*, 2013.

8

A Range of Styles

Directing ↔ Guiding ↔ Following



- Teach
- Assess
- Prescribe
- Lead



- Draw out
- Encourage
- Motivate



- Listen
- Understand
- Go along with

Miller and Rollnick, *Motivational Interviewing: Helping People Change, 3rd Edition*, 2013.

9

Spirit (PACE)

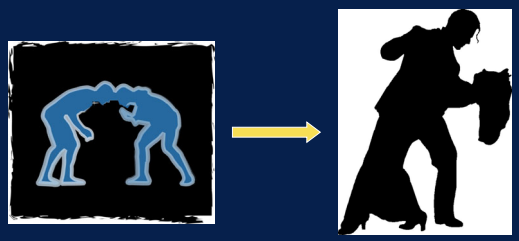
Emphasis on spirit rather than techniques.

- **P**artnership
- **A**cceptance
- **C**ompassion
- **E**vocation

Miller and Rollnick, *Motivational Interviewing: Helping People Change, 3rd Edition*, 2013.

10

The Spirit of MI: Wrestling vs. Dancing



Source of metaphor: Jeff Allison

11

Four Foundational Processes of MI

- Planning (how will we get there?)
- Evoking (why are we going there?)
- Focusing (where shall we go?)
- Engaging (shall we walk together?)

12

Core Skills (OARS + I&A)

- **O**pen Ended Questions
- **A**ffirming
- **R**eflecting (simple and complex)
- **S**ummarizing
- **I**nforming & **A**dvising (with permission, elicit-provide-elicit)

Miller and Rollnick, *Motivational Interviewing: Helping People Change*, 3rd Edition, 2013.

13

Reflective Listening

"Right now, drinking doesn't help me feel better the way it used to. In fact, I feel worse now."

- Echo: Drinking makes you feel worse now.
- Rephrase: So, you find that drinking is no longer helping you to feel better, the way it used to.
- Double-sided: In the past, drinking helped you to feel better. Now it makes matters worse.
- Continuation: … and you want to find some way to feel better instead of drinking.

14

Facilitating Change

- Change talk: as a person argues on behalf of one position, he or she becomes more committed to it; we talk ourselves into (or out of) things.
- Sustain talk: the more of it is evoked during a counseling session, the more likely that the person will continue the status quo.



15

Encourage & Reinforce Change Talk

DARN CAT

- D: desire -- Want, wish, like
- A: ability -- Can, could, able
- R: reason -- Specific reason for change
- N: need -- Need to, have to, must, important



COMMITMENT LANGUAGE PREDICTS CHANGE

- C: commitment — Will, intend to, going to
- A: activation — Ready to, willing to (w/o specific commitment)
- T: taking steps — Report recent specific action toward change

16

Motivational Enhancement Therapy (MET)

- From the founders: "[MET] is a systematic intervention approach for evoking change in problem drinkers. It is based on principles of motivational psychology and is designed to produce rapid, internally motivated change. This treatment strategy does not attempt to guide and train the client, step by step, through recovery, but instead employs motivational strategies to mobilize the client's own change resources."
  – Miller et al., 1999
- Adapted from Motivational Interviewing
- 4 session protocol – great for short-term therapeutic relationships
- Used as a tailored approach for substance misusers
- Three phases
- Manual available here: https://casaa.unm.edu/download/MET.pdf

17

Cognitive Behavioral Therapy (CBT) Efficacy

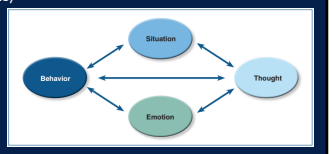
- CBT models
  - among the most extensively evaluated interventions for SUDs
- Based primarily on Marlatt and Gordon's 1985 model of relapse prevention
  - target cognitive, affective, and situational triggers for substance use
  - provide skills training specific to coping alternatives

18

Cognitive Behavioral Therapy

- CBT says: Substance use is reinforcing; this interacts with psychological or behavioral coping deficits to produce increase in substance use
- SUD develops when pattern is repeated
- Solution: more effective coping
- Also deals with expectancies (cognitions)
- Stages of treatment:
  - Building rapport and alliance
  - Preparing for Change
  - CBT Strategies
  - Maintaining Change/Termination





https://www.treatmentworksforvets.org/wp-content/uploads/2018/04/CBT-SUD-Therapist-Manual.pdf

19

Core Elements of Cognitive Behavioral Therapy:

1. **Recognize**: triggers and cues, external and internal
2. **Anticipate/Avoid**: high risk situations-people-places
3. **Cope:** skills for relaxing, dealing with stress, tolerating dysphoria
4. **Connect:** options for support, socializing, fun, and meaning

20

Cognitive Behavior Therapy: Basic Treatment Components (1):

- Identification of high-risk situations
  - "people, places, and things"
- Development of coping skills
  - To manage risks and triggers, as well as negative emotional states
- Development of new lifestyle behaviors
  - To decrease the need for and the role of substance use
- Development of sense of self-efficacy
  - Build on small successes in coping and positive choices

21

Cognitive Behavior Therapy: Basic Treatment Components (2):

- Communication skills
  - Refusal skills
  - Asking for help
- Preparation for lapses
  - Process to be learned from "lapses"
  - Prevent lapse from becoming relapse
  - Identify and manage patterns of thinking that increase risk
- Dealing with relapse
  - Relapse is not a catastrophe
  - Minimize consequences

22

Twelve-Step Facilitation (TSF)

- From the founders: "This therapy is grounded in the concept of alcoholism as a spiritual and medical disease. The content of this intervention is consistent with the 12 Steps of Alcoholics Anonymous (AA), with primary emphasis given to Steps 1 though 5. In addition to abstinence from alcohol, a major goal of the treatment is to foster the patient's commitment to participation in AA."

  - Nowinski, Baker, & Carroll, 1999

- Emphasizes concepts like acceptance, surrender, the moral inventory
- Covers strategies like HALT
- Includes sessions for family members covering enabling and detaching
- Available here: https://pubs.niaaa.nih.gov/publications/projectmatch/match01.pdf

23

CRA vs CRAFT

- Both are evidence supported behavioral treatments for SUD
- Community Reinforcement Approach (CRA)
  - Intended for the person
    - Based on the belief that a drinker's "community" (e.g., family, social and job environment) plays a critical role in supporting or discouraging use
    - Consequently, the environment needs to be restructured such that a sober lifestyle is more rewarding than a using lifestyle
- Community Reinforcement and Family Therapy (CRAFT)
  - An outgrowth of CRA
  - Helps the family
    - Method for working with concerned family members in order to get a treatment-refusing person to enter treatment

24

Community Reinforcement Approach (CRA)

- Based on operant conditioning: substance use as learned behavior
- Naturalistic: uses contingencies already operating in the individual's natural environment to support change and abstinence (e.g., giving or withholding praise for behaviors)
- Functional analysis of both healthy and substance use behaviors in terms of ability to reward or be aversive
- Refining problem-solving and goal-setting efforts for individual and/or family (teaching positive communication, contracting skills)

25

CRAFT

- From the founder: "The Community Reinforcement Approach and Family Training (CRAFT) intervention is a scientifically based intervention designed to help concerned significant others (CSOs) to engage treatment-refusing substance abusers into treatment."
  - Robert J. Meyers, 2019
- Goal: treatment engagement for the substance user
- "Positive approach" that avoids confrontation
- Culturally sensitive: works with cultural mores/beliefs to develop treatment plan
- Teaches CSOs to use positive reinforcers (rewards)
- Encourages CSOs to allow the substance user to suffer natural consequences of using behavior
- Includes: functional analysis, sobriety sampling, CRA treatment plan, behavioral skills training, job skills, social/rec counseling, relapse prevention, and relationship counseling

26

Contingency Management

- Uses therapeutically applied incentives and other reinforcements to increase one or more target behaviors
- Variety of reinforcement schedules, contingency types, and variations
- Standard treatment includes twelve weeks of CM
- Adjunct to on-going therapy or stand-alone
- Can be implemented by case managers to trained specialists
- Clinical trials indicate:
  - Increase attendance in programming
  - Medication adherence
  - Drug abstinence
  - Helps stimulant use disorder

27

Contingency Management (CM)

- Based on operant conditioning: substance use as learned behavior
- Uses contingencies set in place explicitly and exclusively for therapeutic purposes
- Examples:
  - Earning vouchers exchangeable for retail products contingent on negative urine toxicology results
  - Earning methadone take-home privileges for negative urine drug screens

28

Behavioral Couples Therapy

- From the founders: "BCT tries to increase and reward behaviors that support abstinence and long-term recovery."
  - Fals-Stewart, O'Farrell, Birchler, & Gorman, C. (2006)
- Stand alone or in concert with another treatment
- 12 sessions
  - Support for Recovery
  - Relationship Enhancement
  - Communication Skills
  - Continuing Recovery
- Skills include establishing shared goals, catching partner(s) doing something nice, share rewarding activities, employing problem-solving, generating an action plan for moving forward

29

Acceptance and Commitment Therapy (ACT)

- Has some studies for use with SUDs
- Six Core Processes
  - Acceptance
  - Cognitive Diffusion
  - Being Present
  - Self As Context
  - Values
  - Committed Action



- Useful in helping pts consider how their substance use disconnects them from their values.
- Comparing "sober values" to "using values" or reconnecting to values

30

Dialectical Behavior Therapy (DBT)

- Manual driven behavioral treatment utilizing validation and motivational enhancement techniques
- Often combination of group and individual elements
- Addresses enhancement of four basic capabilities:
  - Interpersonal effectiveness
  - Emotional and self regulation capacities
  - Ability to tolerate distress
  - Mindfulness

31

Dialectical Behavioral Therapy (DBT)

- From the founder: "When DBT is successful, the patient learns to envision, articulate, pursue, and sustain goals that are independent of his or her history of out-of-control behavior, including substance abuse, and is better able to grapple with life's ordinary problems."

  - Linehan, 2008

- Core processes: Change & acceptance
- Emphasis on abstinence
  - Change: pushing for immediate and permanent cessation of drug abuse
  - Acceptance: a relapse, should it occur, does not mean that the patient or the therapy cannot achieve the desired result
- Key skills: Cope ahead, Failing well
- Addict Mind → Clean Mind

32

Psychotherapy in Everyday Practice

Basic Elements of Psychotherapy:

- Expectation of receiving help
- Therapeutic relationship
- Obtaining external perspective/support
- Encouraging positive choices
- Frame of understanding

All available in the medical encounter.

Supportive Psychotherapy

Uses direct measures to ameliorate symptoms - to maintain, restore, or improve self-esteem, ego functions, and adaptive skills.

Focuses on developing adaptive capacities

Take into account the patient's limitations:
- Deficits in character structure
- Defense mechanisms
- Native ability
- Life circumstances

33

Monitor for Effectiveness and Outcome

- Monitor not just in terms of sobriety/abstinence
- Monitor in terms of functional improvement:
  - Emotional
  - Interpersonal
  - Medical ***(Don't rely entirely on self-report)***
  - Occupational
  - Legal
- Is there progress toward patient's identified goals?
- Is there active participation in treatment?

34

Case Management: Adapt Treatment Based on Ongoing Assessment of Outcome

- Increase level of care
- Improve recovery environment
  - Joblessness / Homelessness
  - Substance users in living environment
- Assess and access treatment for co-morbid psych problems
- Increase skills for tolerating negative affects
- Is there now a need for medication treatment?

35

Co-Occurring Psychiatric Disorders

- General guidelines
  - Concurrent treatment post-stabilization is best!
- PTSD
  - Cognitive Processing Therapy (CPT)
  - Eye Movement Desensitization and Reprocessing (EMDR)
  - Prolonged Exposure (PE)
    - Concurrent Treatment of PTSD and SUDs using Prolonged Exposure

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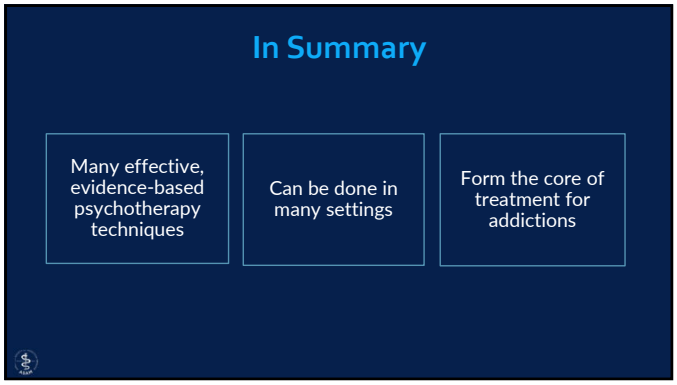
In Summary
Many effective, evidence-based psychotherapy techniques
Can be done in many settings
Form the core of treatment for addictions

37

Patient Interventions: Mutual Help, Psychotherapy, and Social Support Sunday, July 24
12:00 pm – 12:45 pm CT

Effective addiction treatment should be comprised of multiple approaches, varied to meet the changing needs of each patient. This session will describe the principles, supportive research, applications, and challenges for a variety of common psychosocial interventions including 12-step support models.

Learning Objective:

- After this session, learners will be able to: List different types of evidence-based psychosocial treatments and their applications.

Faculty Presenter



Paul H. Earley, MD, DFASAM
Medical Director
Georgia Professionals Health Program, Inc.

Paul H. Earley, MD, DFASAM has worked in Addiction Medicine for 35 years. He treats all types of addictive disorders and specializes in the assessment, treatment, and management of health care professionals. As a therapist, he works with patients already in recovery, providing long term therapy for those who suffer from this disease. His professional expertise extends to advocacy for professionals before agencies and licensing boards.

Dr. Earley is a dynamic speaker and educator; he speaks and trains on topics of addiction, its treatment and addiction among health care professionals. In addition, he trains therapists about the neurobiological basis of psychotherapy. In his travels, he has provided training in the United States, Canada, the United Kingdom, Italy, Iceland and Switzerland.

He is the author of three books and numerous research articles on addiction and its treatment. His two most recent books, RecoveryMind Training and the RecoveryMind Training Implementation Guide describe an innovative and comprehensive system designed to reengineer addiction treatment. He is a contributing author to the American Society of Addiction Medicine (ASAM) Textbook: Principles of Addiction Medicine, as author of the chapter: Physician Health Programs and Addiction among Physicians and a contributing author to the ASAM Criteria. His work was featured in the documentary series on addiction entitled Close to Home by Bill Moyers.

Dr. Earley is the Immediate Past President of the American Society of Addiction Medicine (ASAM). He is the Medical Director of the Georgia Professionals Health Program, Inc., the Physicians Health Program (PHP) for the state of Georgia and the Immediate Past President of the North American Federation of State Physician Health Programs (FSPHP). With Earley Consultancy, LLC, he works with treatment facilities, providing training in cohesive care, treatment effectiveness and staff development using RecoveryMind Training.

PATIENT INTERVENTIONS: MUTUAL HELP, PSYCHOTHERAPY, AND SOCIAL SUPPORT

Paul H. Earley, M.D., DFASAM
Immediate Past President, American Society of Addiction Medicine
Past President, Federation of State Physician Health Programs
Medical Director - Georgia Professionals Health Program, Inc.

1

The ASAM Review Course of Addiction Medicine
July 2022

Financial Disclosures

Paul H. Earley, M.D., DFASAM
Medical Director - Georgia Professionals Health Program, Inc: Salary
Principal - Earley Consultancy, LLC: Salary
DynamiCare Health, Inc: Stock

2

A Very Brief Introduction

- Recovery Support Services
- Relapse Prevention Training
- Twelve-step Support Systems
- Recovery Coaching
- Contingency Management
- Affect Recognition & Regulation – DBT
- Addressing Trauma - EMDR
- Recovery-based Partner Therapy

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Recovery Support Services

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Recovery Support Services[1]

- Translation and Transportation
- Housing & Family
- Parenting & Childcare
- Cultural and Gender Discrimination
- Employment
- Financial and Legal
- Schooling and Training

[1] Laudet, A. B. and K. Humphreys (2013). "Promoting recovery in an evolving policy context: what do we know and what do we need to know about recovery support services?" J Subst Abuse Treat 45(1): 126-133.

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Relapse Prevention Training

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Principles of Relapse Prevention Training

- Relapse prevention provides definitive skills that can be taught and practiced.
- Research has validated two specific techniques
  - Cognitive Behavioral Approach[1]
  - Mindfulness-based Approach[2]
- Both arose from the University of Washington, G. Alan Marlatt's group.

[1] Marlatt, A., & Donovan, D. (2007). *Relapse Prevention, Maintenance Strategies in the Treatment of Addictive Behaviors (Second ed.): Guilford Press.*
[2] Bowen, S., Chawla, N., & Marlatt, G. A. (2011). *Mindfulness-based relapse prevention for addictive behaviors : a clinician's guide. New York: Guilford Press.*

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7

Recognizing Cravings

- Cravings are a normal part of the human experience.
- Addiction disorders simply grab onto this process. In addiction recovery, they can be quite intense and/or persistent.
- The strength, frequency, and duration of cravings vary from person to person and from time to time and are not necessarily predictors of relapse.
- Cravings may never completely disappear.
- Learning to manage cravings, then, is a central part of successful remission.

8

8

Types of Cravings

- Environmental cues (e.g., seeing a drug, smelling tobacco smoke, hearing addiction-related music).
- Visceral events (body sensations, taste, or smell)
- Emotional events (a feeling that the alcoholic "used to drink over")
- Memory tapes (scenes that play in the mind, especially those with strong visual "tapes").

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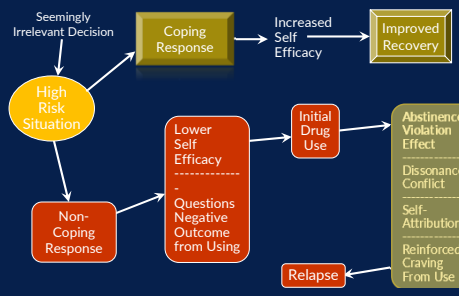
Process Model of Relapse



[1] Modified from Marlatt, A., & Donovan, D. (2007). *Relapse Prevention, Maintenance Strategies in the Treatment of Addictive Behaviors (Second ed.): Guilford Press.*

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Essential Elements of the Process Model

- Collating a list of High-Risk Situations and clues for when they may occur is important for remission.
- Considering the best coping response for the most likely HRSs ahead of time is powerful medicine.
- Negative self talk (self-attribution) is counterproductive.
- Enacting coping responses decreases the probability of future relapse.

11

11

Mindfulness Model of Relapse Prevention

- Teaches Mindfulness - a mental state achieved by focusing one's awareness on the present moment, while calmly acknowledging and accepting one's feelings, thoughts, and bodily sensations.
- Meditation reduces impulsivity and teaches a calming self-awareness of one's current state.
- MBRP teaches patients to focus on increasing awareness, decreasing judgment, and shifting from "reacting" to "skillful responding."[1]

[1] Bowen, S., Chawla, N., Collins, S. E., Witkiewitz, K., Hsu, S., Grow, J. Marlatt, A. (2009). Mindfulness-Based Relapse Prevention for Substance Use Disorders: A Pilot Efficacy Trial. *Substance Abuse, 30(4), 295-305.*

12

12

Twelve Step Support Systems

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13

Mutual or Peer Support Groups

Twelve-step programs:

- Alcoholics Anonymous / Narcotics Anonymous / Cocaine Anonymous / Crystal Meth Anonymous / Nicotine Anonymous
- Al Anon / Nar Anon
- ACOA (Adult Children of Alcoholics)

Other national support groups:

- Smart Recovery
- Women for Sobriety
- Refuge Recovery

Local, religiously affiliated and/or less formalized programs

- Celebrate Recovery & Church groups
- Continuing care groups at a treatment center

14

14

Alcoholics Anonymous

- AA helps individuals recover through common process mechanisms associated with enhancing self-efficacy, coping skills, and motivation, and by facilitating adaptive social network changes.[1]
- Focuses individual on long-term goals and provides a holding place for that patience.
- Teaches relapse prevention skills.
- Normalizes the experience of loss of control, slippage of moral values, and substance-induced trauma.
- Sets discontinuation of abusable substances as the primary goal.
- Provides a path for reconciliation of the past.
- Provides a social network that is (relatively) free of substance use.

[1] Kelly, J. F., Magill, M., & Stout, R. L. (2009). How do people recover from alcohol dependence? A systematic review of the research on mechanisms of behavior change in Alcoholics Anonymous. *Addiction Research & Theory, 17*(3), 236-259.

15

15

Why Won't My Patients go to AA?

- A focus on spiritual principals and, by some, religious tenets.
- Spiritual references often turn off the agnostic or atheist if they do not mesh with spiritual beliefs of other members.
- Many patients with addiction disorders suffer from varying levels of social phobia.
- Newcomers find the format unusual, look for hierarchical structures where none exist.
- Most patients are not naturally drawn to AA, as its values and system is antithetical to the mindset and worldview that their illness has induced previously.

16

16

Why do Patients Dislike AA?

How patients approach their issues and situation:	What AA teaches:
Focus on short-term goals	Focus on long-term goals
Quick fix	Gradual change
I'm different	We are all the same
Pleasure (or relief from pain) is paramount	Pain helps you grow
I can do this	We can do this
Fight harder	The solution emerges when you admit defeat.
My problems will improve if external things get better.	Problems will only improve when you approach the world in a different manner.
Substances are the problem	I am the problem

17

17

What do Patients Like in AA?

- Listening to stories of hope and transformation
- Not being forced to talk
- No obligatory dues or fees
- Ease of access: many cities have hundreds or even thousands of meetings throughout the day.
- A sense of warmth and belonging
- Acceptance and often unconditional love
- Coffee & cigarettes

18

18

Core Concepts of AA

- Proper implementation requires familiarity with the core concept and terms
  - Acceptance of the illness; working through "denial" and accepting "powerlessness"
  - Mentoring: Obtaining a sponsor who provides support and helps the individual understand the process.
  - Attendance at meetings must be frequent at first ("like old fashioned antibiotics, effective but has to be taken often for it to work")
  - Spirituality: Surrender to "higher power" of ones own choosing (often the group in its wisdom is that power)
- Explore what is helpful and what, at first, is not

19

19

Twelve-Step Facilitation

- Handoff can be cold, warm or with training.
  - Cold: "You should go to an AA meeting, look it up online."
  - Warm: " I know of a meeting at 8 pm on Pine St every weeknight. Would you consider going there twice between now and when we next meet?"
  - Manualized: "We are going to walk through a manual that teaches you how to use 12-Step programs to support your recovery. I will help you find a meeting locally. Then you can go to a meeting and report back next week and we will discuss what happened."
- Handoff with training is best implemented using a structured process and can be manual-driven.
  - Manual developed for project MATCH available through NIAAA[1]
  - MAAZE - Making Alcoholics Anonymous Easier[2]

[1] Nowinski, J., et al. (1995). *Twelve Step Facilitation Therapy Manual.* Rockville, Maryland, U.S. Department of Health and Human Services
[2] Kaskutas, L. A., et al. (2009). "Effectiveness of Making Alcoholics Anonymous Easier: a group format 12-step facilitation approach." *J Subst Abuse Treat* 37(3): 228-239.

20

20

The 2020 Cochrane Review

- March 2020 Cochrane Review (authors Kelly, Humphreys & Ferri)
- 27 Studies, 10,566 participants, 21 RCT or quasi-RCT
- Compared MET & CBT with twelve step programs and twelve step facilitation.
- Concluded that AA/TSF:
  - Usually produced **higher** rates of continuous abstinence than the other established treatments investigated.
  - May be superior to other treatments for increasing the percentage of days of abstinence, particularly in the longer-term.

[1] Kelly, John F., Keith Humphreys, and Marica Ferri. "Alcoholics Anonymous and other 12-step programs for alcohol use disorder." Cochrane Database of Systematic Reviews (2020).

21

21

The 2020 Cochrane Review[1]

- Concluded that AA/TSF:
  - Performs as well as other treatments for reducing the intensity of alcohol consumption.
  - Four of the five economics studies found substantial cost-saving benefits for AA/TSF, these interventions reduce healthcare costs substantially.
- This is a clear evidence base for this modality for those with alcohol use disorder.
- Kelly stated, "It's the closest thing in public health we have to a free lunch."
- In addiction medicine, the term "Evidence-based medicine" has become conflated with MAT. Everyone should add AA to the category of Evidence-based medicine for AUD.

[1] Kelly, John F., Keith Humphreys, and Marica Ferri. "Alcoholics Anonymous and other 12-step programs for alcohol use disorder." Cochrane Database of Systematic Reviews 3 (2020).

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Outcomes Using ROSC in OUD

- Benefits of active referral to twelve step programs in opioid use disorder less clear.
- One large recent review of ~21,000 patients provided three types of care[1]
  - Medication management (MM) only
  - Limited psychosocial (LP) therapy
  - Recovery-oriented, 12-step orientation (RO)
- Urine drug tests negative for opioids at the time of the second buprenorphine prescription were 34% for MM, 56% for LP, and 62% for RO (P < .001)

[1] Galanter, M., et al. (2020). "Buprenorphine Treatment for Opioid Use Disorder in Community-Based Settings: Outcome Related to Intensity of Services and Urine Drug Test Results." *American Journal on Addictions*

23

23

Recovery Coaching

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24

Recovery Coaching

- Recovery Coaching is provided by a paraprofessional and designed to sustain connection and help with day-to-day choices and actions.
- A Recovery Coach is a non-judgmental individual who encourages self-reflection and promotes actions that promote or endorse remission behaviors and recovery.
- RCs can work with individuals who are actively using and those in early remission.
- Recovery coaches do not offer primary treatment for addiction, do not diagnose, and are not associated with any particular method or means of recovery.
- Services provided include strengths-based support (as opposed to disease-focused assistance).

25

25

Recovery Coaching

- Recovery coaching is ad hoc, often conducted via telephone or via electronic communication.
- May be linked with Contingency Management, urine drug screening and social services.
- Limited research[1] shows:
  - Improved relationships with providers and social supports
  - Increased satisfaction with the treatment overall
  - Reduced rates of relapse
  - Increased retention in treatment

[1] Reif, S., et al. (2014). "Peer recovery support for individuals with substance use disorders: Assessing the evidence." *Psychiatric Services* **65(7): 853-861.**

26

26

Contingency Management

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Contingency Management

- Contingency Management (CM) is a treatment tool that is:
  - Among the most thoroughly researched behavioral approach to SUD treatment (>100 RCTs and multiple meta-analyses).
  - Among the most effective clinical approaches.
  - Cost-effective
  - Can be used with patients across the change spectrum (from decreasing use to attaining and maintaining remission.
  - Increases compliance with medications that treat addiction.

And yet, it is *rarely* utilized.

28

28

Contingency Management

- Is based upon operant conditioning or behavioral economics
- Breaks down the recovery process into a series of goals that are:
  - Concrete
  - Attainable
  - Realizable
- This sidesteps the hopelessness of many individuals with addiction diseases
- Subtly and subconsciously establishes priorities for recovery by:
  - Rewarding critical recovery behaviors
  - Prioritizes critical behaviors through reward intensity
- Important elements are:
  - Pro-remission or recovery behaviors are reinforced in close temporal proximity to the event.
  - Monetary reinforcers are the most simple and universal rewards, but other reinforcers (e.g., food vouchers) work in some situations.

29

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Contingency Management

- Rewards should be:
  - Immediate - immediate rewards are twice as effective as delayed rewards.[1]
  - Tangible - and matched to participant needs.
  - Intermittent - e.g., pulling a ticket from a punch bowl that may contain a prize of varying values are just as effective as constant reinforcement but is more cost effective.
  - Valuable - low value rewards are half as effective as high-value rewards.[1]
- Importantly, CM does not increase gambling.[2]

[1] Lussier, J. P., et al. (2006). "A meta-analysis of voucher-based reinforcement therapy for substance use disorders." *Addiction* **101(2): 192-203.**
[2] Petry, N. M., et al. (2006). "Prize-based contingency management does not increase gambling." *Drug Alcohol Depend.* **83(3): 269-273.**

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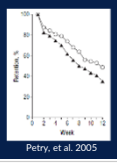
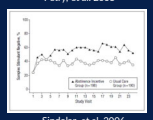
Examples of Efficacy in Different Venues

- 800 cocaine/methamphetamine-using patients across 14 clinics
- Prize-based CM, in a 12-week study
- Psychosocial clinics: $70/month/patient
  - Retention: 49% (CM) vs. 35% (Control)
  - Mean consecutive weeks abstinent: 4.4 vs 2.6
- Methadone clinics: $40/month/patient
  - 24% of patients reached cocaine abstinence in CM group, versus 9% in controls.
  - Mean consecutive abstinent period: 2.8 weeks in CM group versus 1.2 weeks in controls.



Petry, et al. 2005



Sindelar, et al. 2006

Petry, N. M., Peirce, J. M., Stitzer, M. L., & et al. (2005). Effect of prize-based incentives on outcomes in stimulant abusers in outpatient psychosocial treatment programs: A national drug abuse treatment clinical trials network study. *Arch Gen Psychiatry, 62(10), 1148-1156.*

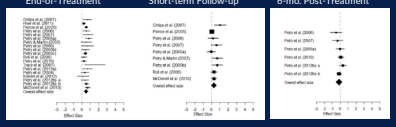
Sindelar, J. L., Olmstead, T. A., & Peirce, J. M. (2007). Cost-effectiveness of prize-based contingency management in methadone maintenance treatment programs. *Addiction, 102(9), 1463-1471.*

31

Limitations of CM

- Research studies reported a cost of about $100 per month per patient in prizes (Petry, 2013)
- Studies were mostly 3-month trials
- Effects dissipate after 6 months (Benishek 2014).
  - Possibly CM shapes, but does not transform behavior

End-of-Treatment | Short-term Follow-up | 6-mo. Post-Treatment



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Implementing Contingency Management

- Staff may have concerns about "paying patients to do the right thing."
  - This is overcome by pragmatic discussions. Motivation is a scarce commodity for many patients!
- The logistics are complex
  - Setting up measurable, concrete goals
  - Recording responses
  - Tracing and dispensing rewards
- The easiest method of implementation comes from technology.

33

Affect Regulation and Recognition

34

Affect Regulation and Recognition

- Many individuals have difficulties with either:
  - Recognizing and understanding feeling states
  - Responding in a productive manner to those feelings
- Addiction entraps and induces strong emotions and difficulties handling emotions trigger relapse and continued use.
- Therapy in emotions management is helpful in preventing relapse in such individuals.[1]
- Alexithymia (the inability to recognize and name feeling states) plays a role in a different population of those with substance use disorders.[2]

[1] Hsu, S. H., Collins, S. E., & Marlatt, G. A. (2013). Examining psychometric properties of distress tolerance and its moderation of mindfulness-based relapse prevention effects on alcohol and other drug use outcomes. *Addict Behav, 38(3), 1852-1858.*

[2] Morie, K. P., Yip, S. W., Nich, C., Hunkele, K., Carroll, K. M., & Potenza, M. N. (2016). Alexithymia and addiction: a review and preliminary data suggesting neurobiological links to reward/loss processing. *Current addiction reports, 3(2), 239-248.*

35

Dialectic Behavioral Therapy

- The best studied, evidence-based technique is Dialectic Behavioral Therapy (DBT). [1]
- Four basic skills in DBT, commonly taught in a class setting:
  - Emotion regulation
  - Mindfulness
  - Interpersonal effectiveness
  - Distress tolerance
- DBT combines cognitive-behavioral and mindfulness techniques to emotional regulation.
- Helpful in patients with problems in emotional regulation, including those with borderline personality disorder.

[1] McClintock, Andrew S., and Marianne Marcus. "Mindfulness-based approaches in addiction treatment." *Textbook of Addiction Treatment* (2021): 391-400.

36

Partner Therapy

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Partner / Couples Therapy

- Several partner therapies have been studied and shown to be effective in increasing remission.[1]
- Important to explore the partner's relationship to substances as well as others in the home.
- Encourage reasonable accommodations by the partner to support remission. The partner's definition of "reasonable" is important!
- Remission is problematic when the identified patient is on the downside of a significant power differential.

[1] Powers, M. B., Vedel, E., & Emmelkamp, P. M. (2008). Behavioral couples therapy (BCT) for alcohol and drug use disorders: A meta-analysis. *Clin Psychol Rev, 28(6), 952-962.*

38

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Trauma Symptom Abatement - EMDR

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Trauma & Addiction

- Physical, emotional, sexual, or religious trauma co-migrates with addiction disorders (incidence of addition higher in traumatized populations).[1]
- …with a suggestion that trauma especially childhood trauma contributes to the development of addiction disorders.
- Addiction often traumatizes its victim. Random flashbacks of intense addiction-related memories may trigger relapse.

[1] Khoury, L., Tang, Y. L., Bradley, B., Cubells, J. F., & Ressler, K. J. (2010). Substance use, childhood traumatic experience, and Posttraumatic Stress Disorder in an urban civilian population. *Depress Anxiety, 27(12), 1077-1086.*

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Eye Movement Desensitization and Reprocessing (EMDR)

- Developed in 1987, the therapist gently guides the patient to briefly focus on the trauma memory.
- …while simultaneously engaging eye movements and/or other forms of rhythmic left-right stimulation.
- The process is highly structured and repeatable with multiple sessions that
  - Gather the history
  - Qualify the target memory
  - Process the memory to an adaptive resolution
  - Evaluate the outcome

41

41

Eye Movement Desensitization and Reprocessing (EMDR)

- Individuals with a trauma history often begin using substances to manage flashbacks and emotional unrest produced by their trauma.
- Trauma victims abuse alcohol, sedatives and dissociatives but, paradoxically use stimulants and cocaine.
- EMDR may be helpful in disengaging and disaffecting addiction-related memories.[1]
- EMDR and other interventions reduce trauma flashbacks and thus the substance use triggered by their recall.
- This in turn improves the prognosis of the addiction disorder.
- Other trauma-resolution techniques may also prove helpful.

[1] Hase, M., Schallmayer, S., & Sack, M. (2008). EMDR reprocessing of the addiction memory: Pretreatment, posttreatment, and 1-month follow-up. *Journal of EMDR Practice and Research, 2(3), 170-179.*

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42

Conclusions

- A wide variety of psychosocial interventions are available to assist in recovery from substance use disorders.
- Careful assessment is the first and most important step in matching treatment to a particular individual's issues.
- Not addressing psychosocial issues leads to a worse prognosis and is bad medicine.
- Engaging patients with all psychosocial interventions requires an approach based upon compassion and concern.
- Physicians should have a basic understanding of the many types of therapeutic interventions in order to help patients engage in them when indicated.



43

Expert Panel Discussion and Q&A – Day 3

Sunday, July 24
12:45 pm – 1:30 pm CT

This panel session will provide a prime opportunity for learners to get their questions answered on topics that were presented on the final day of the ASAM Review Course.

Faculty Presenters



Paul H. Earley, MD, DFASAM
Panelist

Session: Evolution of Addiction and Treatment: History and Impact; Patient Interventions: Mutual Help, Psychotherapy, and Social Support



Leslie A. Hayes, MD
Panelist

Session: Genetics and Gender: Impacts on Treatment for Women and Newborns



Carla Marienfeld, MD, DFAPA, FASAM
Panelist

Session: Patient Interventions: Cognitive Behavioral Therapy and Motivational Interviewing



Maria H. Rahmandar, MD
Panelist

Session: Treatment for Different Stages of Life: Adolescents, Young Adults, and the Elderly



Edwin A. Salsitz, MD, DFASAM
Panelist

Session: Pain and Addiction: Past, Present and Future of Treatment



Jonathan D. Avery, MD
Panel Moderator

Course Credits

ASAM has been awarded the highest level of Accreditation with Commendation by ACCME as a provider of CME

ASAM Review Course in Addiction Medicine

ACCME Accreditation Statement
The American Society of Addiction Medicine (ASAM) is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education (CME) for physicians.

AMA Credit Designation Statement
The American Society of Addiction Medicine designates this live activity for a maximum of **19.25 AMA PRA Category 1 Credits™.** Physicians should claim only the credit commensurate with the extent of their participation in the activity.

American Academy of Family Physicians (AAFP)
The AAFP has reviewed The ASAM Review Course in Addiction Medicine and deemed it acceptable for up to 19.25 Live AAFP Prescribed credits. Term of Approval is from 07/22/2022 to 07/24/2022. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

American Board of Medical Specialties MOC Approval Statement
Through the American Board of Medical Specialties ("ABMS") ongoing commitment to increase access to practice relevant Continuing Certification Activities through the ABMS Continuing Certification Directory (https://www.continuingcertification.org/), the ASAM Review Course in Addiction Medicine has met the requirements as a MOC Part II CME Activity (apply toward general CME requirement) for the following ABMS Member Boards: Allergy and Immunology, Anesthesiology, Colon and Rectal Surgery, Family Medicine, Medical Genetics and Genomics, Nuclear Medicine, Physical Medicine and Rehabilitation, Plastic Surgery, Preventive Medicine, Psychiatry and Neurology, Radiology, Thoracic Surgery, Urology.

NAADAC, the Association for Addiction Professionals
This activity has been approved by the American Society of Addiction Medicine, as a NAADAC Approved Education Provider, for educational credits. NAADAC Provider #295, ASAM is responsible for all aspects of the programming.

Continuing Education Credits (CEUs)
Non-physician participants will receive a certificate of attendance upon completion of the activity and an online evaluation confirming their participation. Participants should submit his/her certificate of attendance to their professional organization/institute.

Maintenance of Certification / Continuing Certification Program (CCP)

The ASAM Review Course and 2 pre-courses meet the CME requirements for the following primary boards:

- American Board of Medical Specialties (ABMS)
- American Board of Preventive Medicine (ABPM)
- American Board of Anesthesiology (ABA)
- American Board of Pediatrics (ABP)
- American Board of Internal Medicine (ABIM)
- American Board of Surgery (ABS)
- American Board of Psychiatry and Neurology (ABPN)
- American Board of Addiction Medicine (ABAM)
- Royal College of Physicians and Surgeons of Canada (RCPSC)

ASAM Moving Beyond the Barriers of Opioid Use Disorder Pre-Course

ACCME Accreditation Statement

The American Society of Addiction Medicine (ASAM) is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education (CME) for physicians.

AMA Credit Designation Statement

The American Society of Addiction Medicine designates this live activity for a maximum of **3 AMA PRA Category 1 Credits™**. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

ASAM Treatment of Alcohol Use Disorder Pre-Course

ACCME Accreditation Statement

The American Society of Addiction Medicine (ASAM) is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to provide continuing medical education (CME) for physicians.

AMA Credit Designation Statement

The American Society of Addiction Medicine designates this live activity for a maximum of **3 AMA PRA Category 1 Credits™**. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Disclosure Information

In accordance with disclosure policies of ASAM and the ACCME, the effort is made to ensure balance, independence, objectivity, and scientific rigor in all CME activities. These policies include mitigating all possible relevant financial relationships with ineligible companies for the Planning Committees and Presenters. All activity Planning Committee Members and Presenters have disclosed relevant financial relationship information. The ASAM CME Committee has reviewed these disclosures and determined that the relationships are not inappropriate in the context of their respective presentations and are not inconsistent with the educational goals and integrity of the activity.

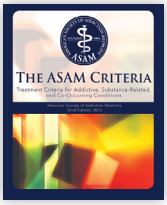
ASAM American Society of Addiction Medicine

Publications Buy & Learn Today!
www.ASAM.org/Publications

Books. News. Podcasts. Journal.

ASAM WEEKLY

ASAM Weekly is a digital source of timely, useful addiction news, covering everything from treatment practices, addiction research, advocacy, and social issues. Delivered Tuesday to subscribers emails.



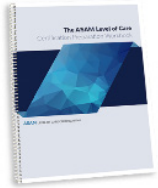
The ASAM Criteria, 3rd Edition

The most widely used and comprehensive set of guidelines for placement, continued stay and transfer/discharge of patients with addiction and co-occurring conditions that improve the quality of addiction treatment.



Level of Care Certification Manual

This manual describes the LOC standards derived in The ASAM Criteria™, the rating elements assessed during the certification survey, and the policies, procedures, and systems a programs to meet the certification standards.



Level of Care Preparation Workbook

This companion manual facilitates self-assessments of programs to identify strengths and areas for improvement.



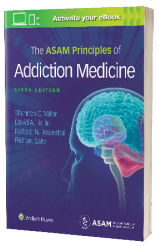
Journal of Addiction Medicine (JAM)

The Journal of Addiction Medicine is a peer-reviewed publication focusing on the latest research developments in addiction medicine, as well as on treatment innovations and ethical, economic, forensic, and social topics.



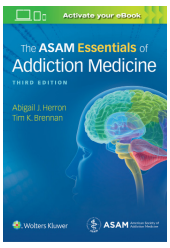
Beyond the Abstract: Addiction Medicine Podcast

An Ideal opportunity for readers and others interested in addiction medicine to get a closer look at the perspective behind research articles.



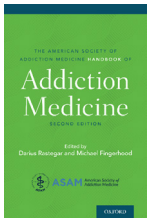
Principles of Addiction Medicine, 6th edition

The Principles of Addiction Medicine (PAM) has provided the core knowledge in the specialty field by blending underlying scientific principles with practical essentials of clinical management.



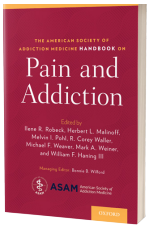
Essentials of Addiction Medicine, 3rd Edition

The companion book to Principles of Addiction Medicine, Essentials is streamlined in a concise, easy-to-navigate format for quick reference and access to authoritative information on pharmacology, diagnosis, assessment, and early intervention.



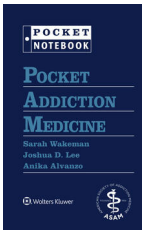
Handbook of Addiction Medicine, 2nd Edition

Ideal for the general practitioners, this handbook is also an excellent reference for addiction medicine community. Handbook provides practical, evidence-based guidance for identifying and treating substance use disorders.



Handbook of Pain and Addiction

The Handbook provides authoritative clinical guidance addressing the complex relationship between addiction and pain. General practitioners and ADM professionals will find this book useful in their practices.



Pocket Addiction Medicine

This handbook provides must-know information on everything from screening for and diagnosis of substance use disorder to managing intoxication and withdrawal, to ongoing treatment of substance use disorder, including caring for special populations—all designed for quick reference at the point of care.

Learn more about ASAM Resources today!
www.ASAM.org/Publications

ASAM American Society of Addiction Medicine

Membership Join Today!
www.ASAM.org/Membership

Connect | Advocate | Educate | Treat



About ASAM

ASAM, founded in 1954, is a professional medical society representing over 7,000 physicians, clinicians and associated professionals in the field of addiction medicine. ASAM is dedicated to increasing access and improving the quality of addiction treatment, educating physicians and the public, supporting research and prevention, and promoting the appropriate role of physicians in the care of patients with addiction.

7,000 +
Members strong

40
State/Regional Chapters

Join ASAM, the leading medical society for addiction medicine.

Connect

ASAM membership offers the opportunity to develop public policies, design continuing education programs, educate legislators, network with peers, and attend world-renowned courses in the field of addiction medicine.

Advocate

ASAM is leading the movement to transform America's addiction treatment infrastructure and expand access to research-validated, results-based care.

Educate

ASAM is an ACCME-accredited provider of continuing education and is a recognized leader of educational events in the addiction medicine field. ASAM's educational programs prepare physicians and clinicians to translate the power of science into high-quality treatment care for patients, their families, and communities.

Treat

ASAM is the leader in setting standards and disseminating research for the addiction field.



ASAM CRITERIA COURSE

The ASAM Criteria Course comprises a comprehensive suite of competency-based learning activities that meets the learning needs of the multiple audiences.

This is a practical training designed to help beginner, intermediate, and advanced clinical staff develop patient-centered service plans and make objective decisions about patient admission, continuing care, and transfer/discharge for individuals with addictive, substance-related, and co-occurring conditions.

Content is based on information found in *The ASAM Criteria*® and incorporates an opportunity for participants to practice applying the information through case-based activities.

- Describe the underlying principles and concepts of The ASAM Criteria.
- Identify the six dimensions of the ASAM Criteria's multidimensional patient assessment.
- Determine treatment priorities based on risk assessment to guide treatment and service planning.
- Determine an appropriate level of care and treatment priorities based on risk assessment.
- Implement the ASAM Criteria, in the context of system challenges, for patients with addiction to ensure appropriate level of care and treatment outcomes.

Monthly Virtual-Live Courses

The ASAM Criteria Course is presented monthly in a virtual-live format. Select an upcoming date. New dates added monthly. Register today!

Register: www.asam.org/CriteriaCourse

ASAM American Society of Addiction Medicine

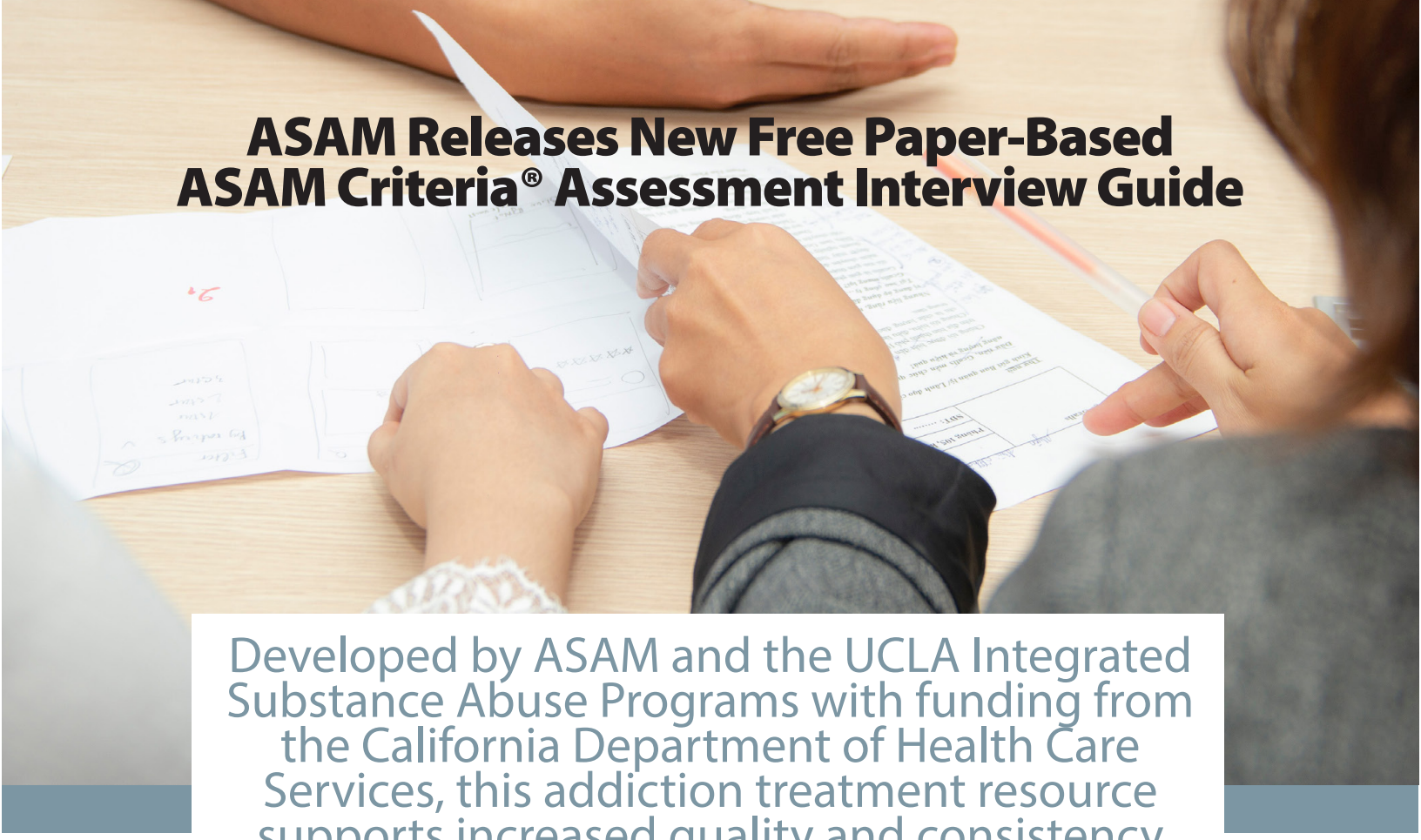


The ASAM CAREER CENTER

WWW.ASAM.ORG/CAREERS

Whether you are a job seeker or an employer, ASAM's Career Center is your gateway to explore job opportunities and qualified professionals in the field of addiction medicine.

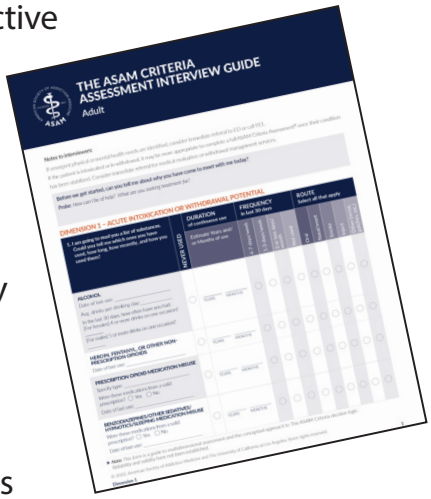
- Apply for 500+ jobs from over 200 employers hiring today
- Receive new jobs sent to your inbox with a Job Alert
- Post your resume to all employers confidentially
- Attract top industry employers with your ASAM membership
- Hire the most qualified who are up-to-date on the latest treatments in the field of addiction medicine



ASAM Releases New Free Paper-Based ASAM Criteria® Assessment Interview Guide

Developed by ASAM and the UCLA Integrated Substance Abuse Programs with funding from the California Department of Health Care Services, this addiction treatment resource supports increased quality and consistency of patient assessments and individualized, patient-centered care.

The American Society of Addiction Medicine and the University of California, Los Angeles Integrated Substance Abuse Programs released a new, paper-based resource to support more consistent and effective implementation of The ASAM Criteria®, a national framework for patient-centered, evidence-based addiction care.



The ASAM Criteria Assessment Interview Guide is the first publicly available standardized version of The ASAM Criteria assessment. With this release, ASAM and UCLA hope to increase the quality and consistency of patient assessments and treatment recommendations.

This resource can also help assist states looking to facilitate continuity and consistency in substance use disorder (SUD) treatment delivery and coverage. Because it is paper-based, offered free to all clinicians, and can be used in many different clinical contexts, the Guide enhances the public utility of The ASAM Criteria's multidimensional assessment approach for the addiction treatment community.

The ASAM Criteria assessment addresses the broad biological, psychological, and social factors that influence the patient's prognosis, evaluating the patient's needs related to substance use and co-occurring physical and mental health problems, as well as social and environmental factors that influence risk.

Learn More About the Guide visit: **www.ASAM.org/InterviewGuide**

SCAN ME

Tobacco Use Disorder

- **Between 65-87% of patients in addiction treatment smoke tobacco, compared to about 21% of the general population.** These high rates of tobacco use contribute to significant patient suffering and early death.
- **Over 53% of people with substance use disorder (SUD) die of tobacco-related causes.** Most of these deaths occur before age 60, while only about 30% of the general population die of tobacco-related deaths and typically after age 70.
- Highly effective interventions that target tobacco use are available; however, they are not sufficiently integrated into addiction treatment programs.



Common misconceptions have limited the use of tobacco use disorder interventions in addiction treatment settings.

Many clinicians mistakenly believe that encouraging patients to address their tobacco use disorder may disrupt the treatment for other SUDs. However, research has clearly demonstrated the efficacy of treating tobacco use disorder in parallel with other SUDs.

The American Society of Addiction Medicine has released brief guidance on integrating tobacco use disorder interventions in addiction treatment. The guidance points to four primary recommendations.

1. Screen all patients for tobacco use disorder.
2. Offer evidence-based treatment to all patients with tobacco use disorder.
3. Use motivational and harm reduction strategies for patients ambivalent about quitting.
4. Implement organizational policies to support treatment of tobacco use disorder.

AMERICAN SOCIETY OF ADDICTION MEDICINE
FOUNDED 1954
ASAM

SCAN ME

Learn more and download the guidance at: **www.ASAM.org/Tobacco**

ASAM Upcoming Education, Resources & Membership

ASAM
ANNUAL CONFERENCE
Innovations in Addiction Medicine and Science
April 13-16, 2023 | Washington DC

Registration & Abstracts Open August 2022!

ASAM State of the Art Course
September 29 - October 1, 2022 | Washington DC



ASAM Review Course Resources

2022 Board Exam Study Tool (BEST)
Access or purchase the 2022 BEST by visiting
https://elearning.asam.org/p/ASAMBEST2022

Textbooks Available
The ASAM Principles of Addiction Medicine, Sixth Edition, is the leading textbook in the field of addiction medicine and a great reference for the ASAM Review Course. *The ASAM Essentials of Addiction Medicine, Third Edition*, is a concise, easy-to-navigate text that includes authoritative information on everything addiction medicine. These books are available at www.LWW. com or 1.800.638.3030.

ASAM Membership

ASAM is the leading and largest national medical society representing over 7,000 physicians, clinicians, and associated professionals in the field of addiction medicine. To join ASAM or renew your membership, visit: www.ASAM.org/membership

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www.ASAM.org | 301.656.3920