50th Summer Clinical Institute in Addiction Studies

June 9-10, 2021

UCSD Calit2 La Jolla

Center for Criminality & Addiction Research,
Training & Application (CCARTA)
Department of Psychiatry | School of Medicine
University of California, San Diego
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UCSD

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June 9, 2021

Dear Colleagues and Friends:

I want to welcome you to the 50th UCSD Summer Clinical Institute in Addiction Studies. We are excited to host our second virtual institute! We are delighted that you decided to join us.

SCI 2021 is an opportunity for you all to learn from leading experts in substance use disorders worldwide. Please help us by sharing your ideas with our staff in the comments section of the daily evaluations.

We hope that you will be able to implement the knowledge and skills that you will have gained. However, most importantly, thank you for striving to learn and implement the most current science to benefit our patients. I want to thank my UCSD staff, the Qualcomm Institute - Calit2 UCSD production team, and the Scaife Family Foundation for supporting us

Good luck, take good care of yourself and each other.

Igor Koutsenok, MD, MS
Professor of Psychiatry
Director, Center for Criminality & Addiction Research, Training & Application
Director, International Addiction Technology Transfer Center - Ukraine
Co-Director, International Addiction Technology Transfer Center - South East Asia
Vice President, International Consortium of Universities for Drug Demand Reduction

Acknowledgments

We would like to thank the following people who helped make our 50th Annual Summer Clinical Institute in Addiction Studies a success:

California Institute for Telecommunications and Information Technology
The Scaife Family Foundation

The SCI 2021 Faculty

Kathleen Allison, Secretary, CDCR
Barbara Barney-Knox, MBA, BSN, RN, CDCR
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Igor Koutsenok, MD, MS, CCARTA Director
Norman Jackson, MS, Project Manager
Tracy Wilson, Fiscal Manager

	WEDNESDAY, JUNE 9, 2021	THURSDAY, JUNE 10, 2021
8:00	**Welcome and Overview** -– Zafiris J. Daskalakis, MD, Ph.D. Professor and Chair, Department of Psychiatry Dr. Igor and JoAnn Grant Chair in Psychiatry School of Medicine, UC San Diego Health Sciences	**Welcome and Review of Day One** -– Igor Koutsenok, MD, MS
8:30-9:15	**The Use of Incentives and Sanctions in Addiction Treatment** – Douglas B. Marlowe, J.D., Ph.D. National Association of Drug Court Professionals (NADCP)	**International Narcotics and Law Enforcement Affairs Global Vision on Drug Demand Reduction** – Brian Morales, MA Chief of the Criminal Justice Division of the Bureau of International Narcotics and Law Enforcement Affairs, Department of State
9:15-10:00	**Benzodiazepines in Our Brave New World** – Christopher Blazes, MD	**How Genes Influence Alcoholism (and why we should care)** – Marc Schuckit, MD, UCSD
10:00-10:45	**Drivers of Overdose in the U.S. Opioid and Stimulant Epidemics** – Thom Browne, Jr., MA CEO Colombo Plan	**Harm Reduction** – Jon Stiffler, MD, UCSD
10:45-11:30	**Education's Role in Addiction Recovery** – Brantley Choate, Ph.D. California Department of Corrections and Rehabilitation (CDCR)	**Hubert Humphrey Fellowship in Substance Use Disorders – Opportunities and Challenges** – J. Randy Koch, Ph.D. Hubert H. Humphrey Fellowship Program
11:30-12:15	**CDCR Integrated Substance Use Disorder Treatment Panel** – Kathleen Allison, Secretary, CDCR, Renee Kanan, MD, Deputy Director Medical Services, California Correctional Health Care Services (CCHCS), Barbara Barney-Knox, Deputy Director Nursing Services, CCHCS, Lisa Heintz, Director, Legislation and Special Projects, CCHCS	**Evaluations**

The Use of Incentives and Sanctions in Addiction Treatment

—— Douglas B. Marlowe, J.D., Ph.D.
National Association of Drug Court Professionals (NADCP)

Responding to Participant Behavior

Douglas B. Marlowe, J.D., Ph.D.

Incentives *Treatment Adjustments* *Sanctions*

1

Topics

I. Treatment vs. punishment

II. One step at a time case-planning

III. Abstinence violation effect (A.V.E.)

IV. Tangible reinforcement

2

Shaping Behavior

- Treat sick behavior, sanction bad behavior, and reward good behavior — and don't confuse them!
- Don't expect too much
  - Learned helplessness, ratio burden, and ceiling effects
- Don't expect too little
  - Habituation, complacency
- Proximal *vs.* distal vs. mastered goals
- Phase advancement
  - What was once distal becomes proximal, and is eventually mastered

3

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Treat or Punish?

Substance Dependence or Addiction

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Treat or Punish?

Substance Dependence or Addiction

1. Triggered binge pattern
2. Cravings or compulsions
3. Withdrawal symptoms

5

Treat or Punish?

Substance Dependence or Addiction

1. Triggered binge pattern
2. Cravings or compulsions
3. Withdrawal symptoms

} Abstinence is a distal goal until symptom resolution

6

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Treat or Punish?

Substance Dependence or Addiction

1. Triggered binge pattern
2. Cravings or compulsions
3. Withdrawal symptoms

} Abstinence is a distal goal until symptom resolution

Substance misuse

7

Treat or Punish?

Substance Dependence or Addiction

1. Triggered binge pattern
2. Cravings or compulsions
3. Withdrawal symptoms

} Abstinence is a distal goal until symptom resolution

Substance misuse } Abstinence is a proximal goal

8

Treat or Punish?

Substance Dependence or Addiction

1. Triggered binge pattern
2. Cravings or compulsions
3. Withdrawal symptoms

} Abstinence is a distal goal until symptom resolution

Substance misuse } Abstinence is a proximal goal

Collateral needs

- Dual diagnosis
- Chronic medical condition (e.g., HIV+, HCV, diabetes)
- Homelessness, chronic unemployment

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Treat or Punish?

Substance Dependence or Addiction

1. Triggered binge pattern
2. Cravings or compulsions
3. Withdrawal symptoms

} Abstinence is a distal goal until symptom resolution

Substance misuse } Abstinence is a proximal goal

Collateral needs } Regimen compliance is proximal

- Dual diagnosis
- Chronic medical condition (e.g., HIV+, HCV, diabetes)
- Homelessness, chronic unemployment

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Case Planning

Specific Responsivity (timing & sequencing of services)

1. Responsivity needs — interfere with rehabilitation (e.g., mental health disorders, homelessness, withdrawal symptoms)
2. Criminogenic needs — cause or exacerbate crime (e.g., substance use, delinquent peers, criminal thinking, impulsivity)
3. Maintenance needs — degrade rehabilitation gains (e.g., illiteracy, deficient job skills)
4. Restorative justice needs — aid community reintegration (e.g., victim restitution, community service)
5. Non-exigent humanitarian needs — cause distress (e.g., medical or dental problems)

❖ Each successful phase advancement increases the odds of subsequent successes, and vice versa

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Phase Demotion

- Often becomes an issue when services were withdrawn prematurely
- Temporary regression and remedial plan (accelerated redemption)
- Beware the Abstinence Violation Effect (A.V.E.)

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Tangible Rewards

- **Most important for reinforcement-starved participants (4:1 ratio to sanctions)**
- **Density > magnitude**
- **Positive reinforcement > negative reinforcement until reliably clinically stabilized**
- **Symbolic rewards**
- **Fishbowl procedure**

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Readings

Marlowe DB (2007). Strategies for administering rewards and sanctions. In JE Lessenger & GF Roper (Eds.), *Drug courts: A new approach to treatment and rehabilitation* (pp. 317-336). New York: Springer.

Marlowe DB (2008). Application of sanctions. In C Hardin & JN Kushner (Eds.), *Drug Court Quality Improvement Monograph* (pp. 107-114). Alexandria, VA: National Drug Court Institute.

Marlowe DB (2011). Applying incentives and sanctions. In DB Marlowe & WG Meyer (Eds.), *The drug court judicial benchbook* (pp.139-157). Alexandria, VA: National Drug Court Institute.

Marlowe DB (2012). *Behavior modification 101 for drug courts: Making the most of incentives and sanctions*. Alexandria, VA: National Drug Court Institute.

Marlowe DB & Wong CJ (2008). Contingency management in adult criminal drug courts. In ST Higgins, K Silverman & SH Heil (Eds.), *Contingency management in substance abuse treatment* (pp. 334-354). New York: Guilford.

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Benzodiazepines in Our Brave New World

—Christopher KM Blazes, MD, VA Medical Center

Rise of Benzodiazepines Dangers & Answers

Christopher Blazes, MD
OHSU Addiction Psychiatry Fellowship Director
Assistant Professor Dept of Psychiatry & Emergency Medicine OHSU

https://www.youtube.com/channel/UCXTWuTgiIWxSA1F8V2gmXiw/videos?disable_polymer=1

1

Disclosures

- Consulting for the Avisa Group
- I will be discussing ”off label” use of drugs during this presentation

2

Objectives

- Review Historical Perspective
- Review Problems associated with benzodiazepine use
- Review Current Standards for detoxification/deprescribing
- Review some new research challenging these standards

3

- "Kids are different today"
- I hear ev'ry mother say
- Mother needs something today to calm her down
- And though she's not really ill
- There's a little yellow pill
- She goes running for the shelter of a mother's little helper
- And it helps her on her way, gets her through her busy day

4

- That Little yellow pill that helps Mother get through her day is Valium
- Big Pharma has marketed Benzodiazepine to target women—and it worked
- We're going to review this dark history

5

Relative to benzodiazepines…… We May Have Been Mislead by some of these "Facts"

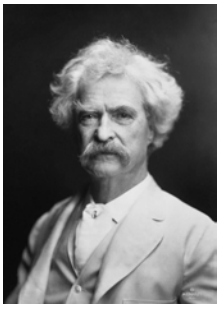
"Facts"

"It ain't what you don't know that gets you into trouble.

It's what you know for sure that just ain't so."

~ Mark Twain

"Facts"



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What's Happening with Benzodiazepines in the modern Western World

- Reminds me of

7

I invite you to remember "Brave New World" – 1932

- Ponder if some sort of collective "**Psychic determinism**" has occurred.

8

Brave New World- Quick Refresher

"A Chemical Dystopia"

- Henry Ford is Worshiped as a prophet
  - Assembly Line Efficiency
  - Homogeneity
  - Predictability
  - **Everyone is Happy because Soma cures all Pain**

Oppression though Making "Happy"

9

Brave New World

- Any Individual effort
  - To Create,
  - To Evolve,
  - To Change
- Is Painful
- If anyone experienced this
  - "Painful call to action"
- Given Soma

Soma Makes Everything Acceptable

Comfortably numb

10

But

- As we know from the Architect in the Matrix,
  - **Pain has a Purpose**
    - It's a Call To Action

11

Anybody Picking up on a trend Here

- "Welcome to the dissociation generation, baby! In this dawning new age, doctors prescribe party drugs, politicians push weed legalization as historic budget deficits loom, and everyone is tripping balls in the name of self-care."
  - There will be consequences to this!

- Oregon Measure 110
- Cannabis Legalization
- Benzodiazepine epidemic

Life is Hard! --- People are escaping in different ways

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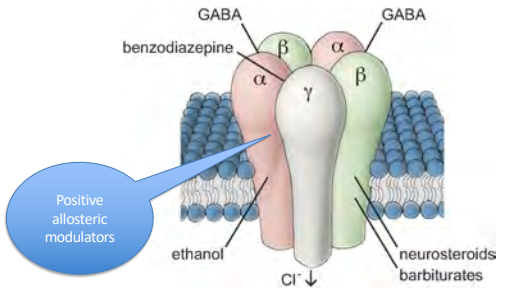
Benzodiazepines act at the
GABA Receptor



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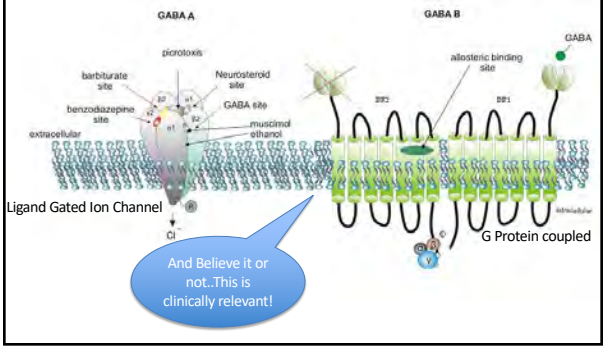
It Gets Much More Complicated

Two Different receptors –Multiple Ligands at multiple Subunits



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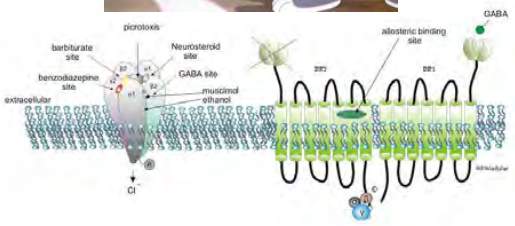

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The Tortoise & the Hare

- **GABAa**
  - Ligand gated ion channel that mediate large and rapid increases neuronal inhibition
    - McDonald and Olsen 1994

  - **All The Usual Suspects**
    - Benzodiazepines
    - Z-Drugs
    - Barbiturates
    - Alcohol

- **GABAb**
  - G-Protein coupled Receptor (GPRC)
  - Slowly maintains the inhibitory tone
    - Bettler et all 2004
    - Bowery et all 2002

  - **Not the Usual Suspects**
    - GHB
    - Baclofen
    - Phenibut
    - Etoh

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GABA is the primary inhibitory Neurotransmitter
Glutamate is the primary excitatory neurotransmitter (acts at the NMDA Receptor)

GABA Glutamate

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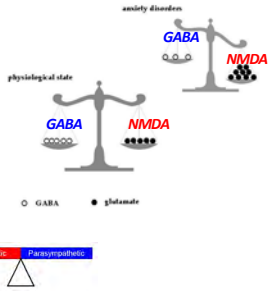
The Balance between the Two is Key

- **GABA = Inhibitory**
  - GABAa, GABAb
- **Glutamate = Excitatory**
  - AMPA, KA, NMDA



- Proper Function of the CNS depends on physiological homeostasis
  - Maintained by two opposite forces acting independently

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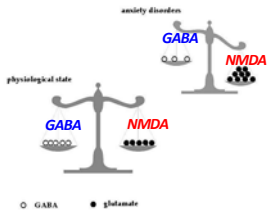
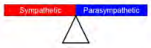
Why is *GABA* So Important

- "GABA and Glutamate are present in practically all functions in the CNS"
- **Together they Make up 90% of all neurotransmission in the brain**



- The Impact of Gabapentin Administration on Brain GABA and Glutamate Concentrations: A 7T 1H-MRS Study, Kejia Cai, Neuropsychopharmacology (2012) 37, 2764–2771



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- So No Wonder why things that affect GABA like Benzodiazepines are so powerful

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Let's Face It…..

Benzo's are powerful--& they really seem to work

- Benzo's Seem to Dissolve Away Anxiety

Temporarily

- Benzo's/Z-drugs seem to make you sleep better

So It Can Seem Very Invalidating When I deny…

"It's the only thing that works!!!"

21

There's No Such Thing As A Free Lunch

- At What Cost?

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Benzodiazepines Uses

Immediately make people with **Anxiety** and **Insomnia** feel better

- **Anxiety & Insomnia**
  - **Anxiety** is most prevalent MH problem in USA
  - 19% 1 yr prevalence in adults
    - National Comorbidity Survey 2017
  - **Insomnia**
    - 30% of people report 1 or more symptoms of insomnia
      - J Clin Sleep Med. 2007 Aug 15; 3(5 Suppl): S7–S10.

- Anxiolysis
- Muscle Relaxant
- Sedation Hypnotic
- Sleep, Anesthesia
- Anticonvulsant
- Alcohol withdrawal

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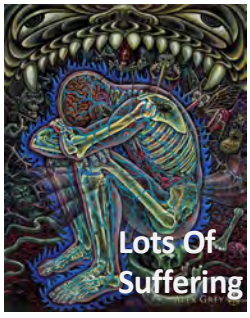

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This Is The Story Of What Happened…..

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Barbiturates Arrived on the Scene

"Facts"

- "New wonder drug **Safer than Opiates** for sleep and anxiety"

The "Facts" we were told and read in the Literature

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Barbiturates

- Pharma's Early attempts to convince us we need a pill to cope

"daytime sedative" for everyday situational stress

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Barbiturates

"Facts"

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But They Weren't Safe


Los Angeles Times FINAL

MARILYN MONROE FOUND DEAD

Sleeping Pill Overdose Blamed

Red Super Bomb Kicks Off Series

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Then Came Benzodiazepines

- **"Safer than Barbiturates"**
  - *Chlordiazepoxide*
  - 1954 Leo Sternbach in Austria synthecized 1960 Roche Pharmaeuticals Released in USA
- Heavily marketed
  - To treat stressors of life
    - **Like going to college**
    - **Raising kids**
    - **Marriage**
    - **"Getting old"**
    - **Responsibilities**
  - Need to take a pill to feel normal

"Facts"

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Mad Marketing

- In a Way, Pharma Created their own demand by pathologizing normal conditions

30

Wyeth showed us how Serax can help this poor woman who is Trapped Behind a Cage of Mops

31

Grand Success Marketing

- The Marketing Destigmatized Anxiety
  - Mostly Directed to Women!!!!!!!
- By 1974, **60 million** Americans were prescribed valium

Just like Prozac destigmatized Depression

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Then Came **Xanax** (alprazolam)

Our favorite palindrome

- 1981---Pfizer/Upjohn capitalized on the fact valium didn't work for panic attacks
- **-Even Popularized the idea of "the panic attack"**
  - Created demand by Popularizing a disorder
    - Iatrogenic Panic attacks
    - **People were encouraged to interpret episodic anxiety as a panic attack**

Pharma needed to find a niche for xanax

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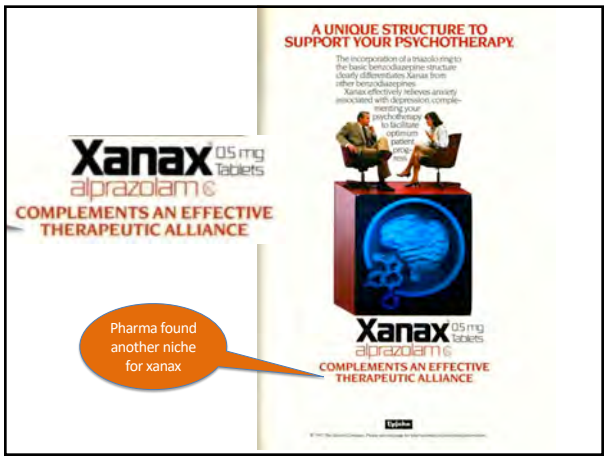

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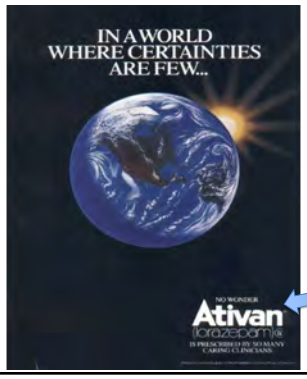
By Now, You get the Idea



"No Wonder Ativan is prescribed By so many caring clinicians"

35

So How effective was all that Marketing?

- ***Prevalence of Benzodiazepine use***
  - **12.6% in 2018**
    - **Maust 2018**

NSDUH
National Survey on Drug Use and Health

NSDUH 2017—
-70,000 People surveyed in person

- **2:1 Female : Male**

- ***Prevalence of Benzodiazepine use***
  - **West 2014**
    - **High School Seniors**
      - **5%** prescribed BZDs
      - **8%** Illicit BZDs
      - **F>M 2:1**
- **Nielsen 2007**
  - **Disproportionately High in Suboxone/Methadone/Opiate patients**
  - Up to **25%!!!**

I think its higher

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Corroborative Data

Recent Study from Spain 2020

- The dispensing prevalence of BZDs use in 2015 was:
  - 14.2% overall
  - 18.8% in women
  - 9.6% in men
  - 36% in those over 65 years.

Lleida

Trends in the consumption rates of benzodiazepines and benzodiazepine-related drugs in the health region of Lleida from 2002 to 2015 F. Torres-Bondia, J. de Batlle, L. Galván, M. Buti, F. Barbé & G. Piñol-Ripoll BMC Public Health volume 20, Article number: 818 (2020)

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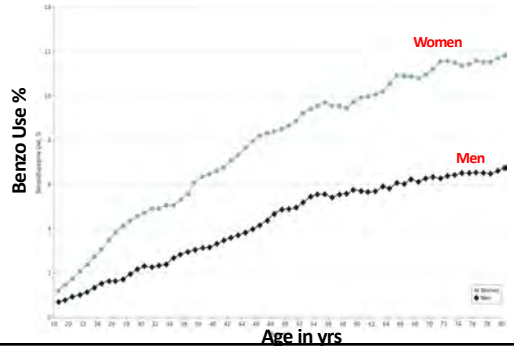
Two Disturbing trends

JAMA Psychiatry - Olfson 2015



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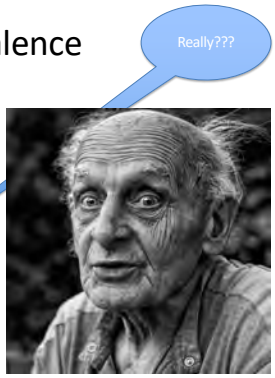
Prevalence



- Chronic daily use also increases with age
  - 14.7 % young adults who use
  - 31.4% elderly

- **Benzodiazepine use in the United States.** Olfson M[1], King M[2], Schoenbaum M[3]. JAMA Psychiatry. 2015 Feb;72(2):136-42. doi: 10.1001/jamapsychiatry.2014.1763.

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We Continue to Prescribe Inappropriately

- Only 20–30% of prescription of BZDs prescriptions were judged to be appropriate.
  - Wrong Diagnosis
  - Wrong duration

Pek EA, Remfry A, Pendrith C, Fan-Lun C, Bhatia RS, Soong C. High prevalence of inappropriate benzodiazepine and sedative hypnotic prescriptions among hospitalized older adults. J Hosp Med. 2017;12:310–6.

Batty G, Hooper R, Oborne C, Jackson S. Investigating intervention strategies to increase the appropriate use of benzodiazepines in elderly medical in-patients. Br J Clin Gov. 2001;6:252–8.

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Pakistan Study of Resident Physicians

- BENZODIAZEPINE USE AMONG RESIDENT DOCTORS IN TERTIARY CARE HOSPITAL, Aftab Alam Khan, J Ayub Med Coll Abbottabad 2019;31(4)
- 278 Residents in the Study
  - 48.7% use BZD's
  - Primary reasons
    - #1) Insomnia
    - #2) Anxiety

If we're taking it ourselves, unconsciously we might be less likely to discourage its use in our patients

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There's More?

But

- **It's not just the Drug Companies to blame……**

DEA Schedule ---?

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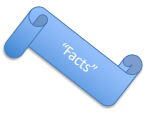
DEA Schedule IV

- " Low potential for abuse and low risk of dependence."



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BZD's Activate Classic Abuse Pathways

- Tan et all Nature 2010
  - BZD's activate dopaminergic neurons in VTA by modulating GABAa receptors in neighboring interneurons.
  - Bottom Line
    - Increase Dopamine levels in Nucleus Accumbens through disinhibition
      - Similar to Opioids, cannabinoids, GHB

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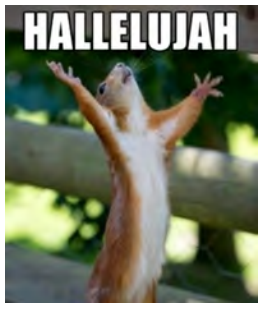
New Black Box Warning

- FDA Drug Safety Communication, Sept 23, 2020
  - Forced all benzodiazepine package inserts to include a boxed warning:
    - "serious risks of abuse, addiction, physical dependence, and withdrawal reactions"



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Pay For Performance

PRESS GANEY

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How does this all add up?

- 1)Less stigma—from marketing
  - Cool to be on Xanax
- 2)Direct dopamine release into reward pathway
- 3)Possible Inappropriate Scheduling by DEA
- 4)Pay for performance

Incentive Salience

47

"I need my Xanax just like I need my Insulin"

- Most prescribed Psych medication in America
  - #1—Xanax
  - #2---Ambien

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What else?

- **A lot of people get addicted**
  - 50 % of chronic BZD users met criteria for BZD dependence (DSM4)
    - Guerlais 2015

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Benzodiazepine Addiction

- **And it only takes a month to get addicted**
  - BZD dependence (addiction) Happens in 50% of patients taking for greater than one month
    - De la Cuevas Psychopharmacology 2003

The old DSM 4 definition

50

Not all Benzo's are Equal

- Can Buy in the **Tenderloin**
  - Xanax>>Klonopin> Ativan
- Can't Buy in the **Tenderloin**
  - Oxezapam
  - Librium(Chlordiazepoxide)
  - Chlorazepate

"You can Have these Back"

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So Who Is The Most Evil

52

"A Review of Alprazolam Use, Misuse, Withdrawal"

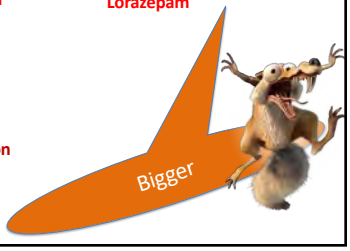
Nassima Ait Daoud J Add Med 1/18

- Great Review Article Describing the idiosyncrasies of Alprazolam
  - **Worse Withdrawal than other benzo's**
  - **More Misused**
  - **More toxic in overdose**
    - Twice as likely to end up in ICU
  - **Can become dependent in 7 days**

53

Alprazolam

- SAMHSA 2013, Grohol 2016
  - **Xanax is related to more ED visits than any other Benzo from analysis of PDMP data**
    - 1 in 311 Xanax
    - 1 in 321 Klonopin
    - 1 in 540 Ativan
    - 1 in 517 Valium
  - **ED visits related to misuse/prescription written**
- Ferrer et al 2001
  - **Alprazolam created greater dopamine release in striatum than Lorazepam**

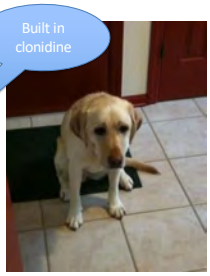


54

Alprazolam-----Why So BAD?

- Low Lipophilic and not Protein Bound
  - Doesn't stay around long
  - Short Half Life
- High Potency
  - Previous slide
  - Just plain works
- Rapid onset Withdrawal
  - No metabolites to ease the withdrawal
  - People need more sooner just to feel normal
- Withdrawal More severe (Idiosyncratic)
  - Browne and Hauge 1986, Kantor 1986
  - Psychosis-- Zipursky et al 1985
  - Suicidal-- Risse et al 1990
  - **Alprazolam Activates Alpha 2 receptors (other benzos don't)-- Erikson et al 1986**
- ***Can Become Physiologically dependent in one week***
  - Galpern et all 1989—animal study
- More Likely to Cause BZD induced hyperanxiety
  - Fyer at al 1987
  - Pecknold et al 1988

Built in clonidine



What??

55

Ever More Scary

- **Withdrawal Sx's can't be treated effectively by other Benzos**
  - Lorazepam
  - Chlordiazepoxide
  - Diazepam
  - **All ineffective at treating Xanax withdrawal**
    - Schweizer et al 1993
    - Sachdev et al 2014
    - Risse et al 1990
    - Albeck 1987
  - Limited Data that:
    - Clonazepam will work (Paterson 1990)
    - Carbamezapine and Clonidine (Klein et al 1986)

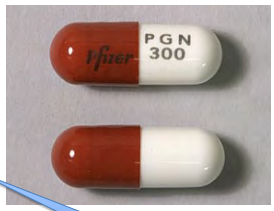
56

What's The Deal With Gabapentin?

57

Gabapentin/Pregabalin

- Mechanism?
  - Indirectly results in increased GABA activity
    - Halts the formation of new synapses?
    - May increase GABA biosynthesis
    - ***NMDA receptor antagonist Activity***
- Can Buy in the Tenderloin
  - Followed on PDMP



Intriguing

58

Is it Addictive

- Probably doesn't cause Dopamine release in Nucleus Accumbans
- Very commonly hear Anecdotally & 3 references….
  - Enhances the euphoria of opiates
  - "It doubles the High"
  - the use of gabapentin and an opioid together **increased the risk of opioid related deaths by 60%**

-Bonnet U[1], Scherbaum N[2] **How addictive are gabapentin and pregabalin? A systematic review.** Eur Neuropsychopharmacol. 2017 Dec;27(12):1185-1215. doi: 10.1016/j.euroneuro.2017.08.430. Epub 2017 Oct 5.

-Gomes T, Juurlink DN, Antoniou T, et al. Gabapentin, opioids, and the risk of opioid-related death: a population-based nested control study. PLoS Med. 2017;

-Gabapentinoid Abuse in order to Potentiate the effects of methadone: A survey amongst substance Misusers. Colin Baird Eur Addict Res 2014;20:115-118

59

61

"Facts"

Z Drugs

"The Safer Alternative to Benzodiazepines"

- Sleeping Pills
  - Zolpidem, Zopiclone, esZopiclone, zaleplon
- Just like Benzo's Z-drugs are..
  - Positive Allosteric Modulators of GABA receptor

Sound Familiar

62

Z drugs

- Growing body of literature establishing their addictive qualities
- Commonly studied together w BZD's
- Rehabs frequently seeing patients addicted solely to zolpidem

63

Some **Z-Drug Abuse** References For Your Records

- Zolpidem abuse.
- Madrak, Leslie N; Rosenberg, Mark. **The American Journal of Psychiatry; Washington** Vol. 158, Iss. 8, (Aug 2001): 1330-1.
- Victorri-Vigneau C, Dailly E, Veyrac G, et al. Evidence of zolpidem abuse and dependence: results of the French Centre for Evaluation and Information on Pharmacodependence (CEIP) network survey. Br J Clin Pharmacol 2007;64:198-209.
- Cubala WJ, Landowski J. Seizure following sudden zolpidem withdrawal. Prog Neuropsychopharmacol Biol Psychiatry 2007;31:539-540
- Freudenreich O, Menza M. Zolpidem-related delirium: a case-report. J Clin Psychiatry 2000;61:449-450.
- Aragona M. Abuse, dependence and epileptic seizures after zolpidem-withdrawal: review and case-report. Clin Neuropharmacol 2000;23:281-283.
- Repeated Zolpidem Treatment Effects on Sedative Tolerance, Withdrawal, mRNA Levels, and Protein Expression
- Wright, Brittany T.. The University of Tennessee Health Science Center, ProQuest Dissertations Publishing, 2016. 10131840
- 2. Hajak G, Müller WE, Wittchen HU, Pittrow D, Kirch W. Abuse and dependence potential for the non-benzodiazepine hypnotics zolpidem and zopiclone: A review of case reports and epidemiological data. Addiction 2003;98:1371-8.
- 5. Licata SC, Mashhoon Y, Maclean RR, Lukas SE. Modest abuse-related subjective effects of zolpidem in drug-exp… Behav Pharmacol 2011;22:160-6.
- **High-dose zolpidem dependence - Psychostimulant effects? A case report and literature review**
- Chattopadhyay, Abhijna; Shukla, Lekhansh; Pandasamy, Arun; Tengasi, Vivek, Industrial Psychiatry Journal, **Mumbai** Vol. 25, Iss. 2, (Jul/Dec 2016): DOI:10.4103/ipj.ipj_80_14
- Review of Safety and Efficacy of Sleep Medicines in Older Adults
- Schroeck, Jennifer L; Ford, James; Conway, Erin L; Kurtzhalts, Kari E; Gee, Megan E; et al. **Clinical Therapeutics; Bridgewater** Vol. 38, Iss. 11, (Nov 2016): 2340-2372
- **ZOLPIDEM: INTRAVENOUS MISUSE IN DRUG ABUSERS** EMMANUEL BRUNELLE et al Addiction Sept 2005
- **Psychiatric Morbidity in Dependent Z-Drugs and Benzodiazepine Users, Yin et al**, International Journal of Mental Health and Addiction, 6/2017
- **Cimolai N. 2007.** Zopiclone: is it a pharmacologic agent for abuse?. *Canadian Family Physician Medecin de Famille Canadien* . 2007. **53(12):** 2124-2129.
- **Nordfjærn T, Bjerkeset O, Bratberg G, Moylan S, Berk M, Gråwe R. 2013.** Socio-demographic, lifestyle and psychological predictors of benzodiazepine and z-hypnotic use patterns. *Nordic Journal of Psychiatry* . 2013. **68(2):** 107-116.
- Potentially inappropriate use of benzodiazepines and z-drugs in the older population-analysis of associations between long-term use and patient-related factors. Aleksandra Maktabi, Ylikas Tillenburg, Jörg Dirmaier, Silke Kuhn, Martin Härter and Uwe Verthein. PeerJ. (y 22, 2018): pe4614.

Not Even Really Debatable Any More

64

Let's Summarize the Bad News?

65

Cognitive Impairment

- Cognitive Impairment while taking
  - Vignola 2000,
  - Sakol 1998,
  - Golombok 1998
  - McAndrews 2002

66

Dementia

- 10 Recent Studies showed increased risk of dementia with BZD and Z- drug use
  - High Dose
  - Long term use
  - Long acting BZDs
  - **If use > 3yrs—**
    - **highest risk—**
    - **no recovery**
- Tapainen,2018
  - Nationwide case control
  - 350k patients

Billioti de Gage S, Moride Y, Ducruet T, Kurth T, Verdoux H, Tournier M, et al. Benzodiazepine use and risk of Alzheimer's disease: case–control study. BMJ. 2014;349:g5205.
Billioti de Gage S, Begaud B, Bazin F, Verdoux H, Dartigues JF, Peres K, et al. Benzodiazepine use and risk of dementia: prospective population based study. BMJ. 2012;345:e6231.
Zhong G, Wang Y, Zhang Y, Zhao Y (2015) Association between Benzodiazepine Use and Dementia: A Meta-Analysis. PLoS ONE 10(5): e0127836
The risk of Alzheimer's disease associated with benzodiazepines and related drugs: a nested case–control study
X. Tapiainen, Acta Psychiatrica Scandanavia, 2018

67

Dementia – Controversial

- Anticholinergic and benzodiazepine medication use and risk of incident dementia: a UK cohort study, Grossi et al. BMC Geriatrics (2019) 19:276

- In a cohort study with 10-year follow-up (N=8216) we did not find any evidence of an increase in risk of dementia associated with the use benzodiazepines or anticholinergics

68

2020 Paper
Dementia – Controversial

- **Associations of Benzodiazepines, Z-Drugs, and Other Anxiolytics With Subsequent Dementia in Patients With Affective Disorders: A Nationwide Cohort and Nested Case-Control Study,** Merete Osler, Martin Balslev Jørgensen, Am J Psychiatry **2020** Jun 1;177(6):497-505.

- 235,465 patients over age 20 in the Danish National Patient Registry between 1996 and 2015.
  - Median f/U 6 yrs
  - Did not reveal associations between use of benzodiazepines or Z-drugs and subsequent dementia
  - Some results were compatible with a protective effect.
    - Insomnia and anxiety are known risk factors for dementia

69

Drug Interactions

- Safe Medications like **Buprenorphine** become dangerous when combined with Benzodiazepines.
  - Kintz-"Forensic Science" International 121 (2001) 65±69
  - Reynaud- "Addicton",1998
  - **Nielsen**, "Drug and Alcohol Dependence", 2005
  - **Lintzeris,** "American Journal on Addictions" 2010
  - **Lee**, "Drug and Alcohol Dependence", 2014
  - …….

Pinray, "Basic & Clinical Pharmacology & Toxicology" 2008

70

The Benzodiazepine Suboxone Issue

- **It's complicated**
  - **FDA placed a "Black Box" warning in 2016 on the buprenorphine package insert**
    - BPN should be avoided in combination with benzodiazepines and other CNS suppressants
  - **FDA Drug Safety Communication 2017**
    - Buprenorphine should not be withheld from patients who are already taking benzodiazepines as prescribed because the risks of overdose from opiates outweigh the risks of concomitant benzodiazepine and buprenorphine use
  - **2020 Warning persists**
    - **No longer Boxed**

Mixed signals from the government makes it hard to interpret

No Green light to start Benzos if already on sboxone

71

BZD Z-drugs MVAs

- "Overwhelming evidence both experimental and epidemiological, BZD and Z-drugs being implicated in fatal and non fatal MVA's"
  - Brandt 2017

72

Impairment

- Z drugs "significantly impaired driving performance, cognitive, memory, and psychomotor performance the morning following bedtime administration"
  - Mets Sleep, 2011

73

Benzo's and Z drugs Mortality

- Weich BMJ 2014
  - **34,721** Patients in Primary Care **followed for 7.6 yrs**
  - Age Adjusted hazard ratio all cause mortality
    - 3.46 after adjusting for confounders

- In other words
  - You're 3 and a half times more likely to die if you're on a benzo or z drug

74

JAMA Dec 2020

- This retrospective cohort study used a large, nationally representative US data set (the National Health and Nutrition Examination Surveys [NHANES]) from 1999 to 2015.
- 5212 participants followed up for a median of 6.7 years
- a significant increase in all-cause mortality was associated with benzodiazepine and opioid cotreatment (hazard ratio, 2.04 [95%CI, 1.65-2.52]) and benzodiazepines without opioids (hazard ratio, 1.60 [95%CI, 1.33-1.92]).

Association Between Benzodiazepine Use With or Without Opioid Use and All-Cause Mortality in the United States, 1999-2015, Kevin Y. Xu,MD et al JAMA Network Open.2020;3(12):e2028557.

75

Prescribed BZDs Increases risk of Suicide

- Dodds 2017
  - Review Article of 17 studies
  - Majority of studies found that benzodiazepine use was associated with increased suicide risk.
- Thought to be mediated by increasing Aggression & Behavioral Disinhibition

Once I became aware of this, it was striking how often I see this association in practice—esp clonazepam, Esp within the first few months of initiation

76

Zolpidem & Suicide

- **Case control of 2199** pts who attempted or completed suicide b/n 2001 and 2011 in Taiwan and 10 controls for each

- Ambien Use was associated with a **2-fold greater risk of suicide** after adjustment for:
  - age, sex, urbanization, occupation, history of BZD and antidepressant use, various mental disorders, insomnia

Sun, Yu, et al. "Association between zolpidem and suicide: a nationwide population-based case-control study." *Mayo Clinic Proceedings* 91.3 (2016): 308+

77

Falls

- Decades of evidence implicating them in Falls
  - **Falls are a big deal!!!!**

Article

December 15, 1999

Benzodiazepines of Long and Short Elimination Half-life and the Risk of Hip Fracture

1. Herings et al., Arch Int Med 1995. 2. Wagner AK et al., Arch Int Med 2004.
2. 3. Wang PS et al., AJP 2001.

78

Benzodiazepines and Pneumonia

- Benzodiazepines have been shown to increase the relative risk of pneumonia
- Meta-analysis of 10 studies involving more than 120,000 pneumonia cases were included
  - The odds for developing pneumonia were 1.25-fold higher (odd ratio, OR = 1.25; 95% confidence interval (CI), 1.09-1.44) in BZD users compared with individuals who had not taken BZD.

Benzodiazepines or related drugs and risk of pneumonia:
A systematic review and meta-analysis
Guo-qing Sun, Int J Geri atr Psychiatry. 2019;1–9.

79

Prescriptions Increasing in # and Size

- Bachhuber 2016
  - Am J Public Health

–1996 to 2013

- BZD scripts increased from **4.1-5.6%** of population in USA
- **Quantities tripled**

Yikes

80

There's some scary Data There…. What Do We Do Now?

81

Sometimes its best to get people off these meds

82

Options Summary

- #1) Convert to long acting Benzo using equivalency chart
  - Taper over Weeks to months
    - Requires motivated and compliant patient
    - Often challenging in use disordered people
- #2) Prolonged taper on Same Benzo
  - 50% initially
  - 10% per week after
- #3)Convert to Anti-epileptic (Phenobarbital, carbamazepine) then taper that med
  - May be Better If Pt has Use D/O
- #4)Water Taper
  - Dissolve in Water
  - Minimal Daily Decreases in dose

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"Standard of Care" Recommendations for Taper

- "The overall consensus is that BZD's should be discontinued gradually over a period of several **weeks to avoid Sz's and severe withdrawal Sx's**"
  - Soyka NEJM 2017 quoting Cochrane review
- Change to long acting BZD
  - Although never been shown to actually make a difference in final outcomes
    - Lader BMJ 2014
    - Soyka Medikamentabhangigheit 2015
- Taper over 4-12 weeks
  - 10-50% reductions at a time

84

"Standard of Care" Recommendations for Taper

- **Controversy**
- **Paucity of Data**

Two Most Quoted Reviews Used to Justify The use of Benzodiazepines as Tapering agent in Helping People Detox from BZD's

Not even about tapering from benzodiazepines!!!

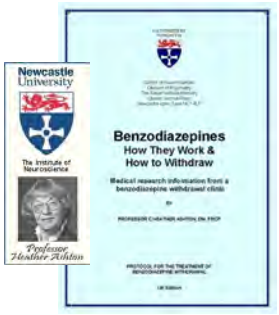
- **Amato Cochrane Review 2010 is relative to BZD safety in Tx of Alcohol Withdrawl**

- **Darker Cochrane Review 2015 Meta analysis of CBT + taper vs taper alone for BZD withdrawal**
  - **CBT + taper was better**

"Facts"

85

Heather Ashton



- First to argue switch to long acting and slow taper for months
- Years of clinical experience
- No Studies done
- Best for non Use-disordered patients

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Long Tapers are Effective?

- I Invite you to question this?
- Is this consistent with your experience?
- Not Mine

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Don't Forget
Long Tapers are a marathon

- **Tapering patients, most often, will be uncomfortable throughout the entire taper..& long after**
- **Supportive measures Throughout taper & PAWS**

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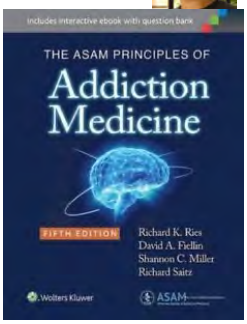
Alternative Discontinuation

- Rapid taper of Benzo over 3 days
  - 1/3—1/3—0
    - **Usually Inpatient**
- Cross Titrating
  - Depakote 500mg tid or
  - Carbamezapine 200mg tid or
  - Gabapentin 800mg tid
- Continue Antiepileptic for at least 1 month
- Start SSRI's for rebound anxiety
  - Ries J. Psychoactive Drugs 1998
  - Garcia-Borreguero, Eu Arch Psych 1990



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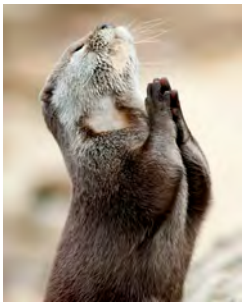
Controversy

- Nothing comparing slow "standard of care" taper to the "Ries" style rapid taper-Cross Titration to anti-epileptic Meds



Please somebody do this study!

90

Hospitalization?

- **If it were my family member……**
- Recommended for people on supratherapeutic doses
  - National Center for PTSD
    - **Ptsd.va.gov 2013**
- **Soyka NEJM 2017**
  - **Recommends hospitalization for Diazepam dose >100mg/day**

91

Inpatient Barbiturate Taper For BZD detox.

Very Simple Safe & Effective

- Johns Hopkins Reviewed 300 inpatient rapid Detox from Only BZD's using 3 day Fixed dose Phenobarbital taper
  - Been used at Bayview for 20 years
  - Maintain doses of methadone/bup
    - Might have to hold doses for sedation

Table 2
Phenobarbital protocol and percentage of doses held

Dose/Interval	No. of doses in protocol	Percentage who received all doses *	Percentage of doses held because of sedation *
200 mg once	1	86	14
100 mg every 4 hours	5	58	17
60 mg every 4 hours	4	70	14
60 mg every 8 hours	3	56	25

* Patients who were discharged against medical advice were not included.

Main outcomes	
Seizures	0 (0%)
Delirium	3 (1.0%)
Falls	0 (0%)
Sedation	84 (27.1%)
Left against medical advice	53 (17.1%)
ED visits within 30 days	22 (7.1%)
Readmission with 30 days	19 (6.1%)

Kawasaki J. Sub. Ab Tr 2012

92

Add some Alpha 2 Agonist

- Maldonado Article 2017
  - Emphasizes the use of Alpha 2 agonists combined with antiepileptics to treat **alcohol** withdrawal (Similar pathophys to benzo withdrawal)
- **Elegantly describes how antiepileptics & alpha 2 agonists more closely address the underlying pathophysiological derangements that underlie withdrawal syndromes than do benzos**
  - **Elevated NE & glutaminergic state**

Novel Algorithms for the Prophylaxis and Management of Alcohol Withdrawal Syndromes-Beyond Benzodiazepines José R Maldonado. Crit Care Clin 2017 Jul;33(3):559-599.

93

I use a Modified Maldonado

Pheno's can be dangerous used for Outpt detox

- Residential/Inpatient
  - Immediate discontinue Benzo
  - **Phenobarbitol**
    - Loading dose 64-192mg
      - Age, weight comorbidity
    - Fixed dose 32-64mg qid + additional doses prn based on CIWA-B protocol
    - 4-10 days
  - **Clonidine Patch 0.1-0.2**
    - 7-14 days
    - 0.1 oral tid prn
  - PAWS – when necessary
    - Gabapentin 100-300 tid for 1-6 months
    - Oxcarbamezapine 150 bid for 1-6 months
- Outpatient
  - **Clonidine Patch**
    - 0.1-0.2 for 7 or 14 days
  - **Oxcarbamezapine**
    - 150 bid
  - Rapid 3-7 day taper of benzo
  - PAWS – when necessary
    - Gabapentin 100-300 tid for 1-6 months
    - Oxcarbamezapine 150 bid for 1-6 months

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How Do We Chose?
Will a taper be successful

- **Discontinuation Factors**
  - Duration of use
  - Dose
  - MOTIVATION
  - Addiction
  - DOC- Is it their Primary Addiction
  - Number of Withdrawal episodes in past
  - **Coach-partner**

95

Why All This Debate?

- Withdrawal is Bad News!

96

Benzodiazepine Withdrawal is Dangerous

- No controversy Here
  - Hollister, Psychophamacologia, 1961
    - Sudden Withdrawal of BZD's causes:
      - Seizures
      - Psychosis
      - Delirium
  - Dangerous and miserable

Does BZD Withdrawal cause DT'S?

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Withdrawal Symptoms

Non Specific Sx's	Frequency %
Insomnia	71%
Anxiety	56%
Mood Swings	49%
Myalgia/Twitching	49%
Headache, Tremor	38%
N/V, Anorexia	36%
Sweating, Blurred Vision	22%
Complications	
Psychosis	7%
Seizures	4%

Hypersensitivity	
Noise	38%
Light	24%
Smell/Touch	15%/7%
Hyposensitivity	
Smells/Taste	15%/4%
Qualitative Changes	
Movement	24%
Vision, Taste	13%
Derealization	24%

Janhsen, Deutsches Arzteblatt Intnl 2015

98

Withdrawal Review

- Benzo Withdrawal is widely variable and unpredictable!
- We often underestimate how bad it can be

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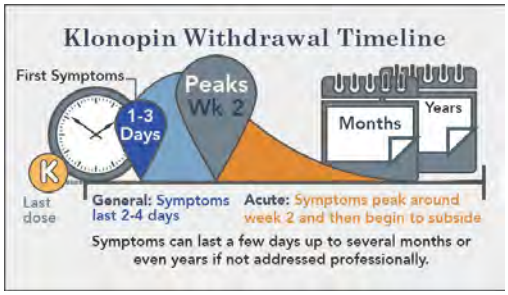
Kindling Effect

- Not "Largely theoretical"
- Sensitization
  - Multiple withdrawals lead to more severe withdrawals
- Inpatients who get Psychotic

100



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PAWS

- Post-Acute-Withdrawal Syndrome (PAWS) is a set of impairments that can persist for weeks, months, or years after the abstaining from a substance of abuse.
- Also known as:
  - post-withdrawal syndrome
  - prolonged withdrawal syndrome
  - protracted withdrawal syndrome.

102

PAWS

- Not DSM 5 Diagnosis
  - Very small amount of Literature
  - More Literature (Old) for Protracted withdrawal from Alcohol
    - Miller FT (Mar–Apr 1994). "Protracted alcohol withdrawal delirium". *J Subst Abuse Treat*. **11** (2): 127–30.
    - Satel SL (May 1993). "Should protracted withdrawal from drugs be included in DSM-IV?". *American Journal of Psychiatry*. **150** (5): 695–704.

103

Benzodiazepine PAWS references

- "Benzodiazepine withdrawal—An unfinished Story"
  - "**Complete recovery may take a year or more**"
    - Ashton BMJ 1984
  - Coming off Tranquilizers: A **Sisyphean** Toil
    - Lader Addiction 2009
- Post acute withdrawal syndrome, More than just return of pre-treatment Sx's
  - Higgit, Fonagy 1990

104

PAWS

- Estimated that 90% of people recovering from Drugs of Abuse experience this
- Wax and Wane in Severity
  - may disappear altogether only to reappear at a later time

105

Sx's Are Many --- & often Non-Specific

- **Difficulty with cognitive tasks**
  - **learning, problem solving, or memory**
- **Irritability**
- Feelings of anxiety or panic
- Depression
- Psychosis
- Obsessive-compulsive behaviors
- Difficulty maintaining social relationships
- Craving originally abused substances
- **Apathy or pessimism**
- **Disturbances in sleep patterns**
- **Increased sensitivity to stress**

Benzo Brain

- Fatigue
- Decreased energy
- Lack of motivation
- **Hypersensitivity**
  - **Pain**
  - **Anxiety**
  - **Sound**
- Anhedonia
- Autonomic Disturbances

106

PAWS

- These symptoms tend to increase in severity when triggered by stressful situations, but might flare up even without any clear stimulus.
  - Looks like emotional Dysregulation
  - Personality disorder
- Can Lead to Mis-diagnosis

107

PAWS- Treatment

Most research is in Alcohol PAWS

- Medications
  - Strongest Evidence is for anti-epileptic meds
    - **Carbamezapine, Oxcarbamezapine, Topiramate**
    - Trileptal/gabapentin
  - Some limited evidence
    - Baclofen
    - Acamprosate
    - Atomoxetine
- How long?
  - Not much guidance from literature
  - I often do 6 months

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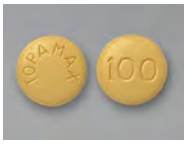
Antiepileptics for PAWS

- "Well suited for managing the symptoms of altered hedonic function, stress reactivity, and cravings " present in PAWS
- Anticonvulsants may facilitate homeostasis and restorative changes (in the GABA/glutamate) system once a subject has obtained sobriety
  - Hammond et all 2015



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PAWS Treatment

- Keep Lots of tools in the toolbox
- Slow and Steady
  - Medications of course
- But don't forget – Treat the anxiety/insomnia that they took the Benzo's for in the first place
  - SSRI's etc…
  - Psychotherapy
    - CBT-I
  - Behavioral therapy
  - Group Therapy/12 Step
  - Alternative

110

Attention to PAWS

- Why?

111

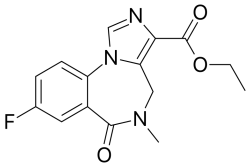
PAWS causes Relapses

112

PAWS Treatment-- Future

- Flumazenil
  - Selective $GABA_A$ Antagonist
  - Speeds up the process
    - L. Saxon; S. Borg & A. J. Hiltunen (August 2010). "Reduction of aggression during benzodiazepine withdrawal: effects of flumazenil". *Pharmacology Biochemistry and Behavior*. 96 (2): 148–151.
    - Sean David Hood, Benzodiazepine dependence and its treatment with low dose flumazenil, Br J Clin Pharmacol. 2014 Feb; 77(2): 285–294.

Danger



113

Future

- Big Fail
  - Oude 2006
    - **88% recommenced use after taper within 15 months**
    - **--Likely PAWS**
  - We're Doing Something Wrong
    - Much More research needed
    - Have to do Better

Opinion alert

114

Pollman BMC Pharma & Tox 2015 Meta-analysis

- Our review revealed that benzodiazepine and Z drug deprescribing interventions are numerous, largely heterogeneous and poorly described. The pace of publication annually remains stable, indicating maintained interest in the field. Generalizability is problematic.

First Honest Acknowledgement I've seen Of the state of affairs

115

Designer Benzos

- Immunoassays generally have good cross-reactivity for non-FDA approved benzodiazepines
  - Some exceptions are:
    - Fortazolam
    - Ketazolam
- Many of these will not show up on GCMS
- 1 Swedish study showed that 40% of with benzodiazepines results actually contained a nonapproved benzodiazepine

116

Summary

- Benzodiazepines were heavily marketed esp. to treat Women.
  - The marketing was quite successful
- Benzodiazepines use leads to collateral damage
  - Falls, mortality, drug interactions
  - Dementia?, Cognitive impairment
  - Suicide, Pneumonia, MVA's
- De-prescribing is necessary for some and is problematic for many when attempted
  - Limited guidance from the literature on best practices
  - May be worth reconsidering the standard of care taper
  - Cross titration to antiepileptic with alpha 2 agonists
- PAWS is very real and managing this can help limit relapses

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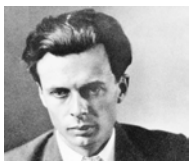
The End



"But I don't want
comfort.
I want God,
I want poetry,
I want real danger,
I want freedom,
I want goodness.
I want sin."

– Aldous Huxley, Brave
New World

118

Drivers of Overdose in the U.S. Opioid and Stimulant Epidemics

—Thom Browne, Jr., MA, Colombo Plan

Drivers of Overdose in the U.S. Opioid and Stimulant Epidemics

UCSD Summer Clinical Institute in Addiction Studies

Thom Browne Jr.
President & CEO
Colombo Plan Secretariat
Rubicon Global Enterprises
June 2021

1

Role of Fentanyl in Drug Overdoses

- **A 2016 CDC study found that fentanyl was detected in over half (56%) of the 5,152 opioid overdose deaths in ten states between July – December 2016.***
- **However, in 2017 there were an estimated 72,306 drug overdose deaths according to CDC, of which 29,406 (41%) were due to synthetic opioids such as fentanyl.****
- **Thus, fentanyl was undoubtedly contributing to overdose rates, but it was far from their only cause.**

*O'Donnell JK, Halpin J, Mattson CL, Goldberger BA, Gladden RM. Deaths Involving Fentanyl, Fentanyl Analogs, and U-47700 — 10 States, July–December 2016. MMWR Morb Mortal Wkly Rep 2017;66:1197–1202.

**NIDA, Overdose Death Rates, revised August 2018

2

Increased Role of Multiple Drug Combos in Overdose

- **Overdose deaths resulting from a dangerous combination of cocaine and opioids are outpacing fatalities linked to cocaine abuse alone.***
  - **75.5% of all cocaine-related deaths also involved one or more opioids in 2019***
- **A similar trend has been observed with the combined abuse of both methamphetamines and opioids.***
  - **54% of all meth-related deaths in 2019 also involved opioids***

*U.S. National Center for Health Statistics (NCHS) Data Brief, April 2021

3

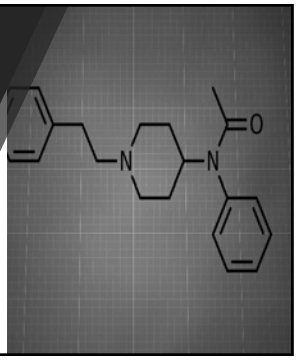
Overdose deaths have now reached record levels, with 88,000 people dying from a drug overdose between August 2019 and August 2020. That equates to more than 240 people each day, and a 26.8% increase from the prior year.*

*U.S. National Center for Health Statistics (NCHS) Data Brief, April 2021

4

Fentanyl

- Fentanyl is a ***highly potent*** synthetic opioid
- Fentanyl is 80 to 100 times stronger than morphine and 50 times more potent than heroin
- Carfentanil is estimated to be 10,000 X more potent than morphine
- Fentanyl's effects include ***respiratory depression*** and ***arrest***



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Lethal Dose of Fentanyl

6

Lethal Doses of Fentanyl

- It has been determined that it would only take 2 – 3 milligrams of fentanyl to induce respiratory depression, arrest, and possibly death **(see photo of penny on previous slide)***
- When visually compared, 2 to 3 milligrams of fentanyl is about the same as five to seven individual grains of table salt*

_____

* Fentanyl: A Briefing Guide for First Responders, U.S. Department of Justice, DEA

7

NOVEL OPIOIDS

- Etonitazene
  (1,000 – 1,500 X morphine)
- Isotonitazene
  (500 X morphine)
- Metonitazene
  (100 X morphine)

8

Diltiazem

- Diltiazem is a medication belonging to a class of calcium-channel blockers and it is commonly used to treat high blood pressure
- Double-depressant effect with heroin
- As an adulterant, it can cause severe adverse cardiovascular reactions, including angina, bradycardia, hypotension, and arrhythmia*
- Potentiates cocaine toxicity & toxic cardiac effects (possibly due to hypoxemia)*

_____

*Brunt T. Monitoring illicit psychostimulants and related health issues. Oisterwijk, The Netherlands: BOXPress, 2012.

9

Acetaminophen

- Acetaminophen is an over-the-counter pain relief medication responsible at high chronic doses for liver damage
- When mixed with heroin, it can dramatically depress heart rate and breathing
- When cut into cocaine, it can increase hepatoxicity (liver damage)

10

Diphenhydramine

- When mixed with opioids (double depressant effect), it can dramatically depress heart rate and respiration
- Can cause prolongation of the QT interval, which can lead to a life-threatening cardiac arrhythmia called Torsades des Pointes (TdP)*
- The combination of cocaine and H1-antihistamines like diphenhydramine can be synergistic in terms of super-additive reinforcing effects with regard to potency**

*Husain Z, Hussain K, Nair R, Steinman R. Diphenhydramine induced QT prolongation and torsade de pointes: an uncommon effect of a common drug. Cardiol J 2010;17(5):509–11

**Wang Z, Woolverton WL (2007) Self-administration of cocaine-antihistamine combinations: super-additive reinforcing effects. Eur J Pharmacol 557: 159–160.

11

Xylazine

- **Xylazine is a nonnarcotic sedative commonly used as an adulterant in heroin, cocaine, and fentanyl**
- **It is only approved as an animal tranquilizer and used as a sedative, analgesic and muscle relaxant***
- **The most common side effects in humans associated with xylazine administration include bradycardia, respiratory depression, hypotension, CNS depression, and other changes in cardiac output****

*Ruiz-Colón K, Chavez-Arias C, Díaz-Alcalá JE, Martínez MA (July 2014). "Xylazine intoxication in humans and its importance as an emerging adulterant in abused drugs: A comprehensive review of the literature". Forensic Science International. 240: 1–8.

**Reyes JC, Negrón JL, Colón HM, Padilla AM, Millán MY, Matos TD, Robles RR (June 2012). "The emerging of xylazine as a new drug of abuse and its health consequences among drug users in Puerto Rico". Journal of Urban Health. 89 (3): 519–26.

12

Metamizole/Dipyrone

Metamizole is a pain reliever, fever reducer, and spasm reliever

Side effect of agranulocytosis (a dangerously suppressed immune system that places user at very high risk for serious infections due to a severely lowered white blood cell count)*

Combining dipyrone with opiates like heroin results in analgesic potentiation and produces supra-additive effects**

* Brack A, Rittner HL, Schäfer M (March 2004). "Nichtopioidanalgetika zur perioperativen Schmerztherapie" [Non-opioid analgesics for perioperative pain therapy. Risks and rational basis for use]. Der Anaesthesist (in German). 53 (3): 263–80.

** Hernandez-Delgadillo G & Cruz S. (2004). Dipyrone potentiates morphine-induced antinociception in dipyrone-treated and morphine-tolerant rats. Eur. J. of Pharmacol. 502, 67-73.

13

TRAMADOL

Tramadol is an opioid pain medication used to treat moderate to severe pain

Can cause respiratory distress and death when taken in high doses or when combined with alcohol or other drugs (heroin, fentanyl) that cause drowsiness or slow breathing

Taking Tramadol with benzodiazepines and other similar dugs can cause very serious effects (slowed breathing, coma, death)

14

Benzodiazepines

Benzodiazepines (alprazolam, diazepam) are a type of medication known as tranquilizers used to treat anxiety, panic disorders, & insomnia.

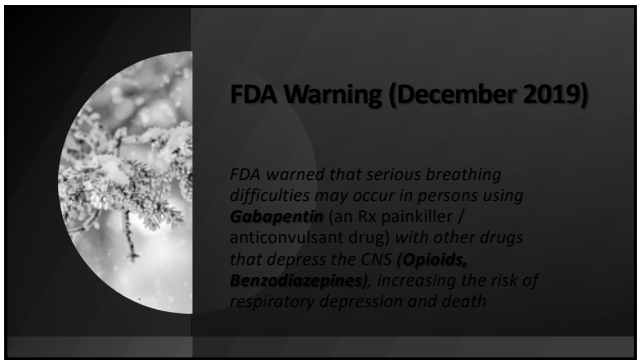
Combining opioids and benzodiazepines can be unsafe because both types of drug sedate users and suppress breathing—the cause of overdose fatality.*

Clinical evidence suggests that benzodiazepines can inhibit respiration, and when combined with the respiratory-depressive effects of opioids, may increase likelihood of death.**

* Dasgupta N, Funk MJ, Proescholdbell S, Hirsch A, Ribisl KM, Marshall S. Cohort Study of the Impact of High-Dose Opioid Analgesics on Overdose Mortality. *Pain Med Malden Mass*. 2016;17(1):85-98. doi:10.1111/pme.12907.

** Alzal, A & Klystkin, E. Interactions of benzodiazepines with heroin: Respiratory depression, temperature effects, and behavior. Neuropharmacology. 2019 Nov 1;158:107677

15



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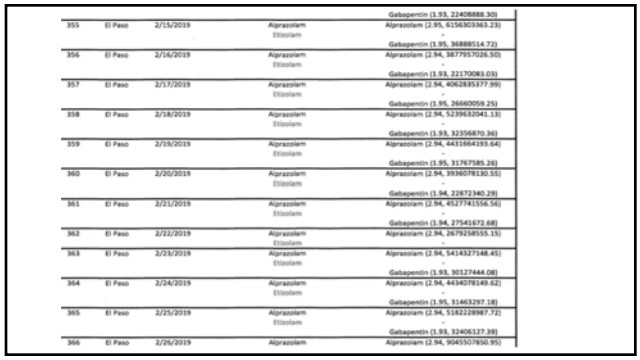
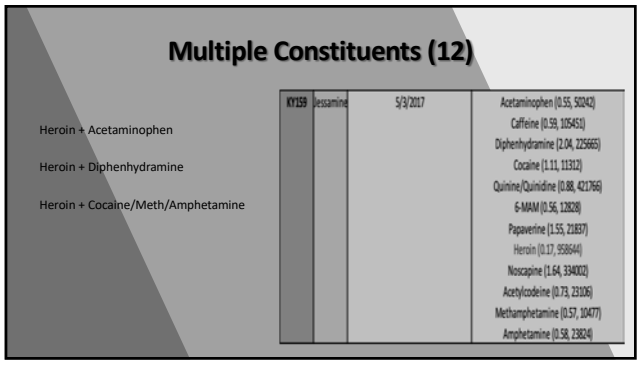


				Gabapentin (1.93, 22408888.30)
355	El Paso	2/15/2019	Alprazolam Etizolam	Alprazolam (2.95, 6156303363.23) - Gabapentin (1.95, 36888514.72)
356	El Paso	2/16/2019	Alprazolam Etizolam	Alprazolam (2.94, 3877957026.50) - Gabapentin (1.93, 22170083.03)
357	El Paso	2/17/2019	Alprazolam Etizolam	Alprazolam (2.94, 4062835377.99) - Gabapentin (1.95, 26660059.25)
358	El Paso	2/18/2019	Alprazolam Etizolam	Alprazolam (2.94, 5239632041.13) - Gabapentin (1.93, 32356870.36)
359	El Paso	2/19/2019	Alprazolam Etizolam	Alprazolam (2.94, 4431664393.64) - Gabapentin (1.95, 31767585.26)
360	El Paso	2/20/2019	Alprazolam Etizolam	Alprazolam (2.94, 3936078130.55) - Gabapentin (1.94, 22872340.29)
361	El Paso	2/21/2019	Alprazolam Etizolam	Alprazolam (2.94, 4527741556.56) - Gabapentin (1.94, 27541672.68)
362	El Paso	2/22/2019	Alprazolam Etizolam	Alprazolam (2.94, 2679258555.15) -
363	El Paso	2/23/2019	Alprazolam Etizolam	Alprazolam (2.94, 5414327148.45) - Gabapentin (1.93, 30127444.08)
364	El Paso	2/24/2019	Alprazolam Etizolam	Alprazolam (2.94, 4434578149.62) - Gabapentin (1.95, 31463297.18)
365	El Paso	2/25/2019	Alprazolam Etizolam	Alprazolam (2.94, 5182228987.72) - Gabapentin (1.93, 32406127.39)
366	El Paso	2/26/2019	Alprazolam	Alprazolam (2.94, 9045507850.95)

17



18

Multiple Constituents (14)

Heroin + Diltiazem

Heroin + Tramadol

VT150	Windsor	2/2/2017	Caffeine (0.6, 442400 Aminopyrine (0.56, 254713) Tramadol (0.84, 281569) Morphine (0.56, 56) Acetylcodeine (0.76, 12423) 6-MAM (0.55, 2421) Heroin (0.78, 237471) Fentanyl (1.99, 163814) Quinine/Quinidine (0.88, 182947) Noscapine (1.64, 1187745) Quetiapine (2.06, 555857) Ketamine (0.63, 3215) Papaverine (1.55, 10128) Diltiazem (2.12, 43384)

19

Vermont & Kentucky Street-level Drug Samples (2016 - 2017)

VT #156	VT #160	KY #26	KY #105
Heroin	Heroin	Heroin	Heroin
Cocaine	Cocaine	Cocaine	Cocaine
Tramadol	Fentanyl	Tramadol	Fentanyl
Ketamine	Levamisole	Fentanyl	4-ANPP
Fentanyl	Acetaminophen	4-ANPP	Acetaminophen
Aminopyrine	Quinine	Aminopyrine	Diphenhydramine
Diltiazem	Lidocaine	Diphenhydramine	Levamisole
Quinine	Procaine	Quinine	Phenacetin
Quetiapine	Caffeine	Lidocaine	Quinine
Caffeine	Acetylcodeine	Metamizole/Dipyrone	Caffeine
Acetylcodeine	6-MAM	Caffeine	Acetylcodeine
6-MAM	Papaverine	Acetylcodeine	6-MAM
Noscapine	Noscapine	6-MAM	Papaverine
Papaverine		Papaverine	Noscapine
Morphine		Noscapine	

Legend:

Black = controlled drugs

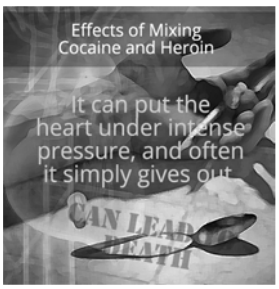
Purple = fentanyls

Red = adulterants

Green = impurities from heroin manufacturing process

20

Speedballs are Dangerous



21

Super Speedball Effect
[Quintuple Depressant / Double Stimulant]

KY100	Franklin	3/20/2017	Methamphetamine (0.57, 21175)
			Cocaine (1.12, 2315)
			Morphine (0.57, 181)
			Acetylcodeine (0.75, 32444)
			6-MAM (0.56, 15581)
			Heroin (0.78, 933919)
			Papaverine (1.55, 8458)

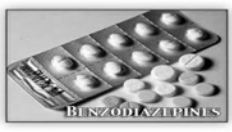
22

23

Adulterant Effects on Naloxone Administration

Naloxone will not reverse overdose resulting from non-opioid drugs, like benzodiazepines (e.g., alprazolam)*

*Bureau of Justice Assistance. Law Enforcement Naloxone Toolkit. BJA National Training and Technical Assistance Center.

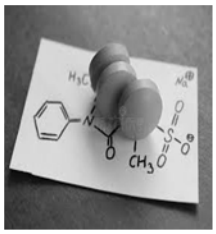


Naloxone only partially reverses the toxic effects of Tramadol overdose and may increase the risk of seizures**

**Rossi, S. ed. (2013). Australian Medicines Handbook (2013 ed.). Adelaide: The Australian Medicines Handbook Unit Trust. ISBN 978-0-9805790-9-3.

24

Metamizole/Dipyrone Effects on Naloxone Administration



- One study found that naloxone was unable to reverse the effect of **metamizole/dipyrone** alone or in combination with morphine.*
- Another study found that a dose of naloxone that is completely effective to block morphine is only partially effective in blocking the supra-additive effects of morphine plus **metamizole**.**
- To almost abolish the potentiated effect produced by this combination, it is necessary to administer higher naloxone doses.**

*Taylor J, et al. (1998). Metamizole potentiates morphine effects on visceral pain and evoked c-Fos immunoreactivity in spinal cord. Eur. J. Pharmacol. 351, 39-47.

**Hernandez-Delgadillo G & Cruz S. (2006). Endogenous opioids are involved in morphine and dipyrone analgesic potentiation in the tail flick test in rats. Eur. J. of Pharmacol. 546, 54-59.

25

26

Levamisole's Effect on Naloxone

- A Colombo Plan-funded study by the research institute Cinvestav (UNAM – Mexico) reported *"**Levamisole** significantly potentiates the lethal, analgesic and hematological effects of heroin."*
- Potentiation for lethality can be prevented by *"a dose of Naloxone higher than that needed to antagonize heroin's effect."*
- Alternatively, potentiation may be prevented by administration of two antagonists: Naloxone (NAL) and Mecamylamine (MEC)

27

Levamisole is Toxic

- **Levamisole** is a veterinary pharmaceutical used primarily to treat worm & parasitic infestations in livestock.
- It has also been used experimentally and historically to treat various autoimmune disorders and cancers in humans.
- Withdrawn from the Canadian (2003) and USA (1999) markets due to **toxicity.**
- Results in a decrease of white blood cells that can ***lower immunity and increase opportunist infections*** **(e.g., CV-19).**

28

Levamisole: Role as an Adulterant

- It is suggested that levamisole increases the number of D1 dopamine receptors in the brain and potentiates the euphoria, psychostimulant effects, and intense "high" of cocaine.*
- Levamisole has at times been detected in up to 79% of the cocaine street supply in the U.S. and overseas.

*Hofmaier T, et al, Aminorex, a metabolite of the cocaine adulterant levamisole, exerts amphetamine like actions at monoamine transporters. Neurochem Int (2014) Jul; 73:100- 32-41.

*Tallarida CS, et al, Levamisole and cocaine synergism: a prevalent adulterant enhances cocaine's action in vivo. Neuropharmacology, 2014 Apr; 79:590-5.

*Katarzyna M, et al, Acute coronary syndrome after levamisole-adulterated cocaine abuse. Journal of Forensic & Legal Medicine, 21 (2014) 48-52.

*Larocque A & Hoffman RS, Levamisole in cocaine: Unexpected news from an old acquaintance. Clin Toxicol, 2012 Apr; 50(4):233-41.

29

Naloxone Inhibiting Street-level Drug Samples (2020 - 2021)

OH #56 (7)	FL #792 (6)	NH #1099 (5)	Illinois #1452 (3)
Heroin	***Heroin***	Heroin	Heroin
Cocaine	Ketamine	***Tramadol***	MDMA
Tramadol	Fentanyl	Acetylfentanyl	Fentanyl
Xylazine	Acetyl Fentanyl	Fentanyl	Acetyfentanyl
Fentanyl	Butyryl Fentanyl	Levamisole	Alprazalom
Acetylfentanyl	Metamizole	Xylazine	Gabapentin
Butyryl Fentanyl	Tramadol	Gabapentin	***Diphenhydramine***
Metamizole	Xylazine	Phenacetin	Acetaminophen
Levamisole	Phenacetin	Lidocaine	Quetiapine
Diphenhydramine	Aminopyrine	Eutylone	Quinine
Lidocaine	Procaine	Caffeine	Acetylcodeine
Quinine	Lidocaine	Acetylcodeine	6-MAM
6-MAM	Quinine	6-MAM	
Acetylcodeine	6-MAM, Acetylcodeine		
Morphine	Morphine, Codeine		

Legend:

Black = drugs, adulterants, and impurities

Red = naloxone inhibitors

Underline/Italics = primary constituent

30

Naloxone Inhibiting Street-level Drug Samples (2020 - 2021)

NH #1074 (5)	NH #1198 (6)	OH #22 (7)	OH #130 (6)	Illinois #1555 (6)
Fentanyl	*Fentanyl*	Heroin	Heroin	Heroin
Acetyl Fentanyl	Acetyl Fentanyl	Cocaine	Oxycodone	*Diphenhydramine*
Tramadol	Butyryl Fentanyl	Ketamine	Fentanyl	Fentanyl
Xylazine	Levamisole	Fentanyl	Acetyl Fentanyl	Acetyl Fentanyl
Levamisole	Tramadol	Acetyl Fentanyl	Tramadol	Tramadol
Phenacetin	Metamizole	Butyryl Fentanyl	Levamisole	Levamisole
Lidocaine	Heroin	Levamisole	Metamizole	Metamizole
Quinine	Acetaminophen	Metamizole	Xylazine	Xylazine
Caffeine	Phenacetin	Tramadol	Phenacetin	Ketamine
	Procaine	Xylazine	Quinine	Quetiapine
	Caffeine	Aminopyrine	Diphenhydramine	Acetaminophen
	Codeine	Lidocaine	Ephedrine	Amionpyrine
	Morphine	Quinine	Lidocaine, Procaine	Trazodone
	Acetylcodeine	Morphine, Caffeine, Ephedrine	Codeine, Morphine	Codeine, Morphine
	6-MAM	6-MAM, Acetylcodeine	6-MAM, Codeine, Acetylcodeine	6-MAM, Acetylcodeine

Legend:

Black = drugs, adulterants, and impurities

Red = naloxone inhibitors

Underline/Italics = primary constituent

31

Education's Role in Addiction Recovery

—Brantley Choate, Ph.D., California Department of Corrections and Rehabilitation (CDCR)

CDCR Integrated Substance Use Disorder Treatment Panel

—Kathleen Allison, Secretary, CDCR
Renee Kanan, MD, Deputy Director Medical Services, California Correctional Health Care Services (CCHCS),
Barbara Barney-Knox, Deputy Director Nursing Services, CCHCS,
Lisa Heintz, Director CCHCS

CALIFORNIA CORRECTIONAL HEALTH CARE SERVICES

California Department of Corrections and Rehabilitation

Road To Recovery

Integrated Substance Use Disorder Treatment Program

University of California, San Diego
Summer Clinical Institute in Addiction Studies

Kathleen Allison, Secretary, CDCR
Renee Kanan, Deputy Director, Medical Services
Barbara Barney-Knox, Deputy Director, Nursing Services
Lisa Heintz, Director, Legislation and Special Projects

June 9, 2021

1

Introduction of Presenters

Kathleen Allison
Secretary
California Department of Corrections and Rehabilitation

2

2

Lisa Heintz
Director, Legislation and Special Projects

3

3

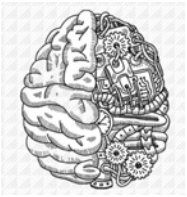
Presentation Overview

- Problem: Context for Change
- Solution: Integrated Substance Use Disorder Treatment Program
- Sustainability: Enhanced Pre-Release and Transition Services
- Measuring Success

4

4

Context for Change



Big Problem in this Country

- CDC data from May 2020 show an 18% increase in fatalities or more than 81,000 drug-related deaths - the highest ever recorded in a 12-month period (mostly OUD)

Big Problem in California

- More than 7,000 overdose deaths in early 2020 and climbing

Bigger Problem for CDCR

- Overdose deaths tripled between 2015 and 2019
- Majority of incarcerated individuals suffer from SUD

5

5

Context for Change

The majority of incarcerated individuals:

- Committed offenses to meet their drug needs
- Incarcerated for an alcohol or drug violation
- Committed offenses under the influence of alcohol/other drugs

The majority of incarcerated individuals have experienced significant TRAUMA including neglect, and physical, emotional and sexual abuse (often beginning in childhood)

- 62-87% of incarcerated men
- 77-90% of incarcerated women

6

6

Context for Change

Bruce Perry, MD obtained from Gwualagucci (2015)

Incarcerated Adults:

- **62-87% men**
- **77-90% women**

7

7

Context for Change

SUD involves the dysregulation of dopamine in certain parts of the brain.

- 70% of carceral populations have a substance use disorder.
- Almost 100% of those have adverse childhood events or suffer adverse adult events by just being incarcerated over and over again.

We need dopamine to survive. It is our motivation.

- Average normal dopamine levels range from 40 to 100 nanograms per deciliter.
- We know how much dopamine is required to get out of bed in the morning (approximately 15 nanograms per deciliter).
- While addiction initially provides elevated levels of dopamine - causing an unnatural "high" - eventually the brain stops producing dopamine.

8

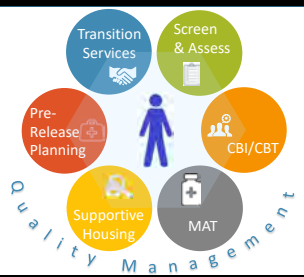
8

Renee Kanan
Deputy Director, Medical Services

9

9

ISUDT Program Components



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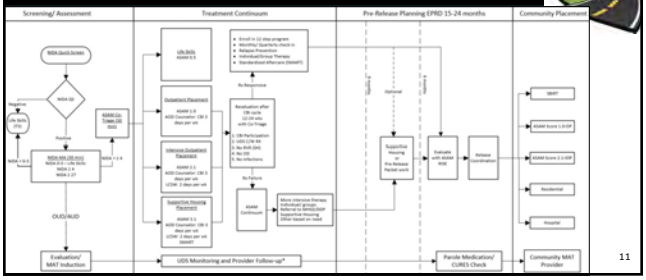
10

ISUDT Program Overview



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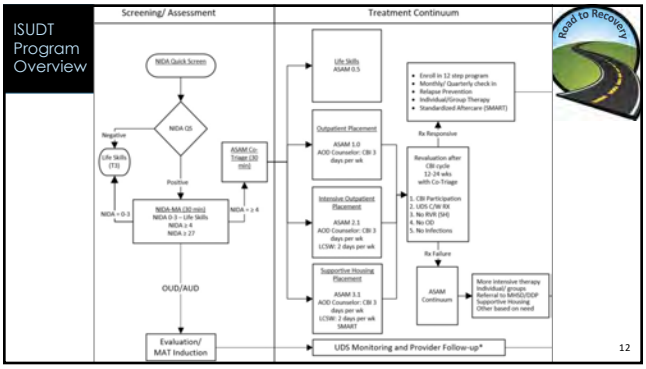
ISUDT Program Overview



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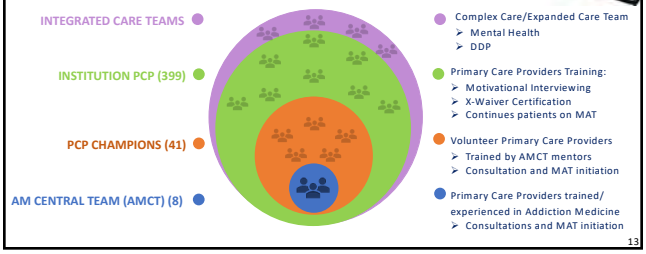
Preparing CCHCS Provider Workforce



- Complex Care/Expanded Care Team
  - Mental Health
  - DDP
- Primary Care Providers Training:
  - Motivational Interviewing
  - X-Waiver Certification
  - Continues patients on MAT
- Volunteer Primary Care Providers
  - Trained by AMCT mentors
  - Consultation and MAT initiation
- Primary Care Providers trained/ experienced in Addiction Medicine
  - Consultations and MAT initiation

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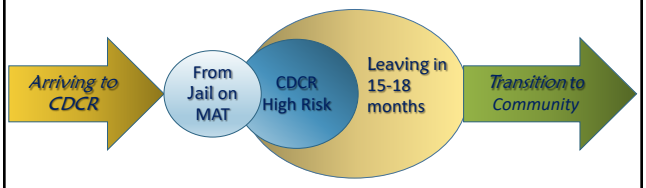
ISUDT Program

Patients at Highest Risk of Death



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Barbara Barney-Knox
Deputy Director, Nursing Services

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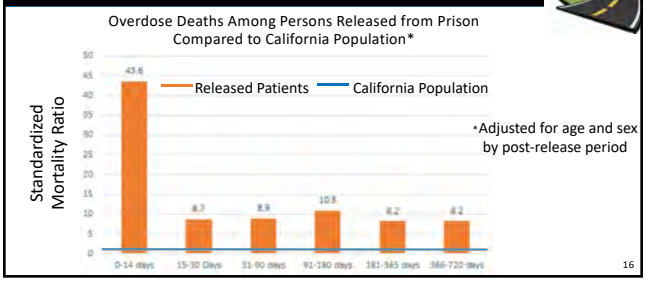
Sustainability



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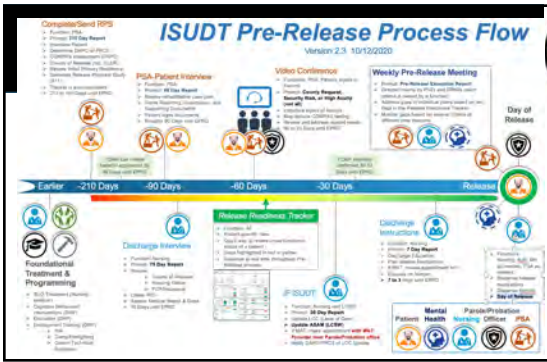
ISUDT Pre-Release Process Flow



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Transition Services

Patient Population Risk, Needs and Services

- 75% of eligible patients released will receive Naloxone.
- 50% of patients released will be scheduled for 14-day follow up with community provider for MAT.
- 50% of scheduled patients will attend their follow up appointment.

Transition Services Infrastructure

Harm/Risk reduction plans:

- Food, Clothes, Shelter, Transportation and Employment
- 85% of patients will have a signed Release of Information prior to release
- 50% of patients will have Benefit Information on file 30-days prior to release

Counties will participate in Data Sharing Warehouse

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Transition Services

- Enroll & Activate Medi-CAL
- Secure Housing
- Schedule Health Care Appointments
- Transportation Arrangements

- Engage Family & Peer Support
- Transitional Guidance as Needed
  - Finances
  - Employment
  - Education

Whole Person Care

Care Management & Care Coordination for Successful Reintegration Back to Community

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Transition Services

California

- Drug Medi-Cal Organized Delivery System (DMC-ODS)
- County Data Sharing Portal

CDCR/CCHCS

- Naloxone For All Leaving CDCR
- ASAM Assessment
- Community Transition

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Measuring Success

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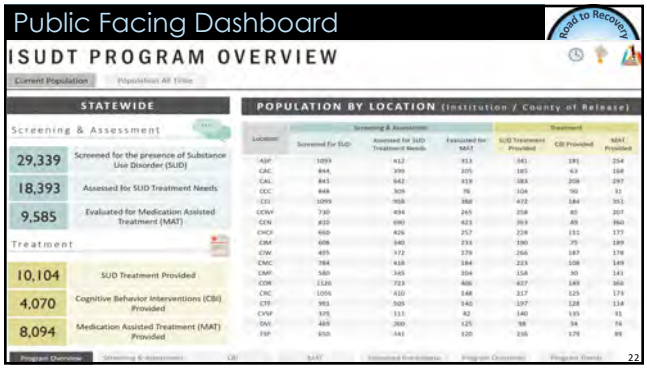
Public Facing Dashboard



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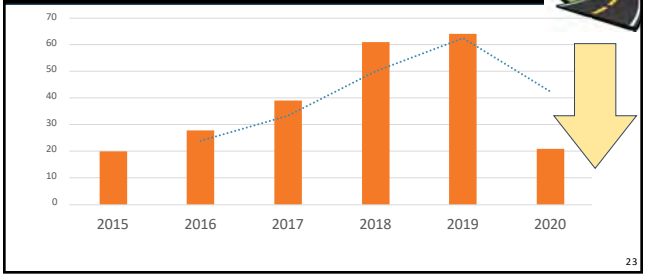
CCHCS Overdose Deaths



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Whole Person Care

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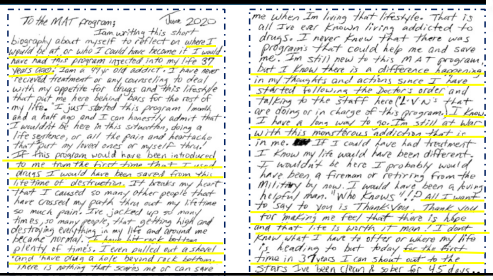
Life Transformations



To the MAT Programs June 2020

I am writing this short biography about myself to reflect on where I would be at or who I could have become if I would have had that program injected into my life 37 years ago! I am a 49 yr old addict. I have never received treatment or any counseling to deal with my appetite for drugs and this lifestyle that put me here behind bars for the rest of my life. I just started this program 1 month and a half ago and I can honestly admit that I would be here in this situation, doing a life sentence, or all the pain and heartache that I put my loved ones or myself thru. If this program would have been introduced to me from the first time that I used drugs I would have been saved from this lifetime of destruction. It breaks my heart that I caused so many other people that have crossed my path thru out my lifetime so much pain. I've jacked up so many times, so many people, shot, getting high and destroying everything in my life and around me because normal. I have hit rock bottom plenty of times. I even pulled out a shovel and have dug a hole beyond rock bottom. There is nothing that scares me or can take me when I'm living that lifestyle. That is all I've ever known living addicted to drugs. I never knew that there was programs that could help me and save me. I'm still new to this MAT program but I know there is a difference happening in my thoughts and actions since I have started following the Doctor's order and talking to the staff here (I've a long way to go. I'm still at war with this monstrous addiction that is in me. If I could have had treatment I know my life would have been different. I would've to have I probably would have been a fireman or retiring from the Military by now. I would have been a living helpful man. Who knows?! All I want to say to you is Thank You. Thank you for making me feel that there is hope and that life is worth it man! I don't know what I have to offer or where my life is heading to but today for the first time in 37 years I can shout out to the stars I've been clean & sober for 45 days.

25

25

Life Transformations

…reflect on where I would be at or who I could have become if I would have had this program injected into my life 37 years ago! I am a 49 year old addict. I have never received treatment or any counseling to deal with my appetite for drugs and this lifestyle that put me here behind bars for the rest of my life.

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Any
Questions
28

International Narcotics and Law Enforcement Affairs Global Vision on Drug Demand Reduction

—— Brian Morales, MA, Chief of the Criminal Justice Division of the Bureau of International Narcotics and Law Enforcement Affairs, Department of State

INL GLOBAL VISION ON DRUG DEMAND REDUCTION

JUNE 2021

INL – BUREAU OF INTERNATIONAL NARCOTICS AND LAW ENFORCEMENT AFFAIRS
U.S. DEPARTMENT OF STATE

STATE/INL

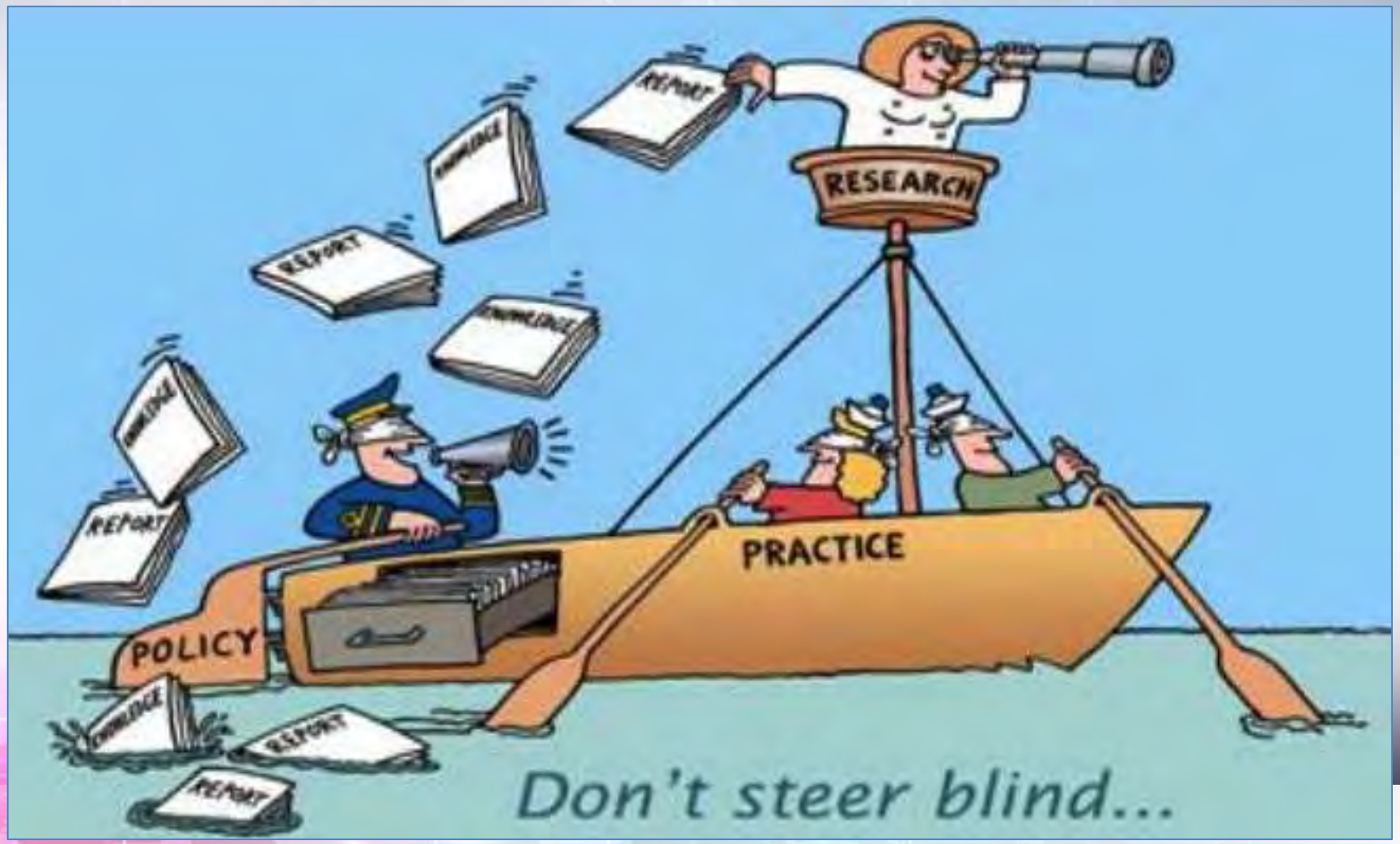
- Foreign Assistance authority to address substance use globally
- Objective: Reduce demand for drugs and drug-related criminal behavior
- Partnerships in 110 countries, all sectors

RESEARCH → POLICY → PRACTICE

- United States leads in substance use research
- Our message is positive/optimistic: body of research, confidence in evidence-based practices

RESEARCH, POLICY, PRACTICE

- Disconnect
- Research does not translate into policy or practice
- Limited success leads to disappointment experiments in radical policies



Source: Rannsoknir & Greining, Center for Social Research and Analysis

CONSORTIUM OF INTERNATIONAL ORGANIZATIONS

5 Specialized Organizations with Drug Demand Reduction Expertise

Colombo Plan
(Sri Lanka)

Organization of American States
(Washington, DC)

African Union
(Addis Ababa, Ethiopia)

United Nations Office on Drugs and Crime
Drug Prevention and Health Branch
(Vienna, Austria)

World Health Organization
(Geneva, Switzerland)

Today's Greatest Global Challenges in Addressing Drug Use and Drug Use Disorders

1. Education and Professionalization of the the Workforce
2. Quality of Treatment and Prevention Services
3. Access / Barriers to Treatment and Prevention Services
4. Insufficient Services for People with Special Clinical Needs
5. Lack of Adequate Data – Insufficient Epidemiological Research
6. Limited or Non-Existent Recovery Oriented Systems of Care
7. Continued Stigma and Discrimination of People Who Use Drugs
8. Insufficient Investment by Governments in Drug Demand Reduction
9. Extreme Policy Experiments Not Based on Evidence
10. Misconception about Drug Harms Propagated by Popular Culture

1. Education and Professionalization of the Global Workforce

UNIVERSAL CURRICULUM

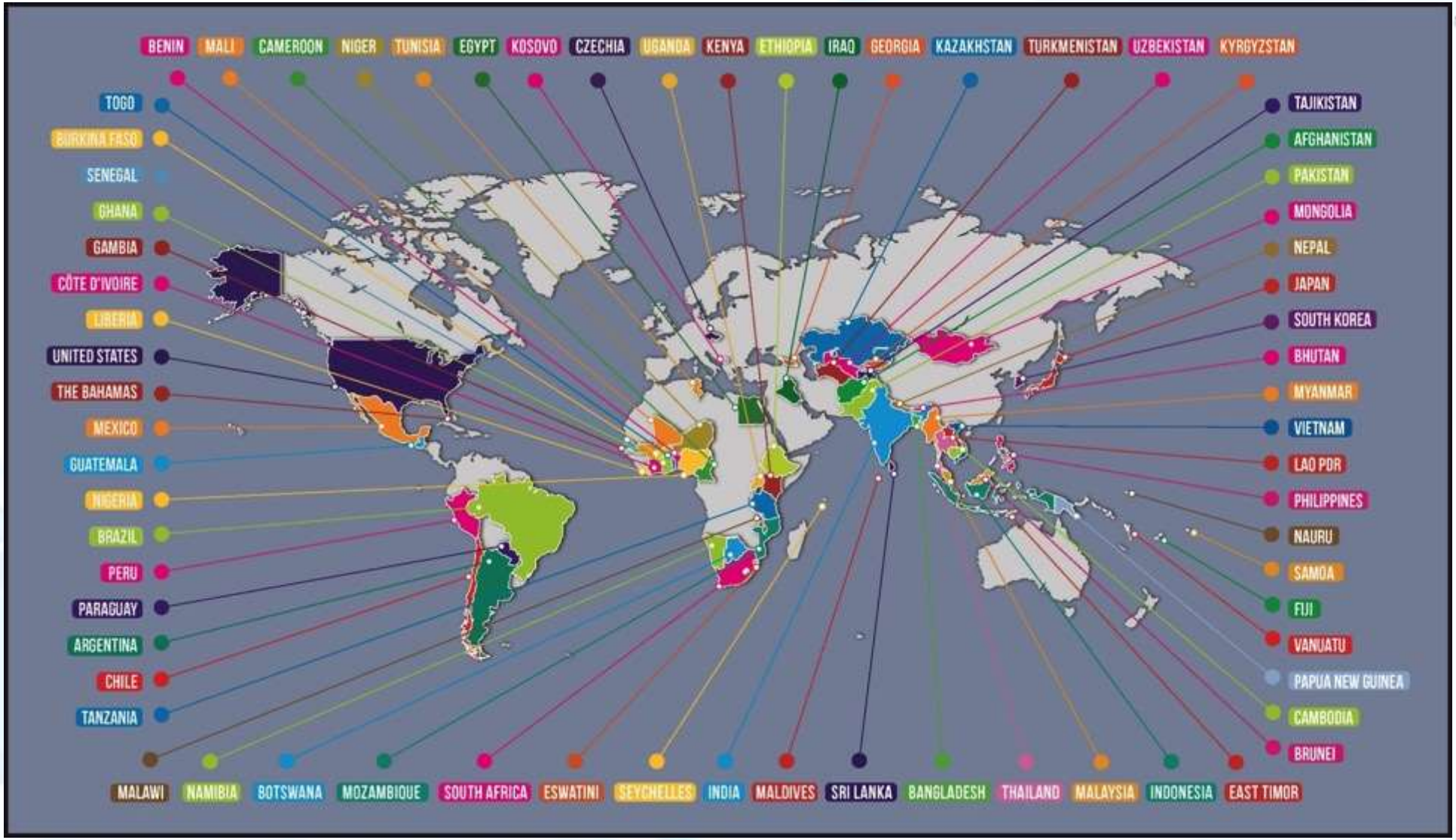
Universal Treatment Curricula

Universal Prevention Curricula

Adaptation and Translation of Manuals

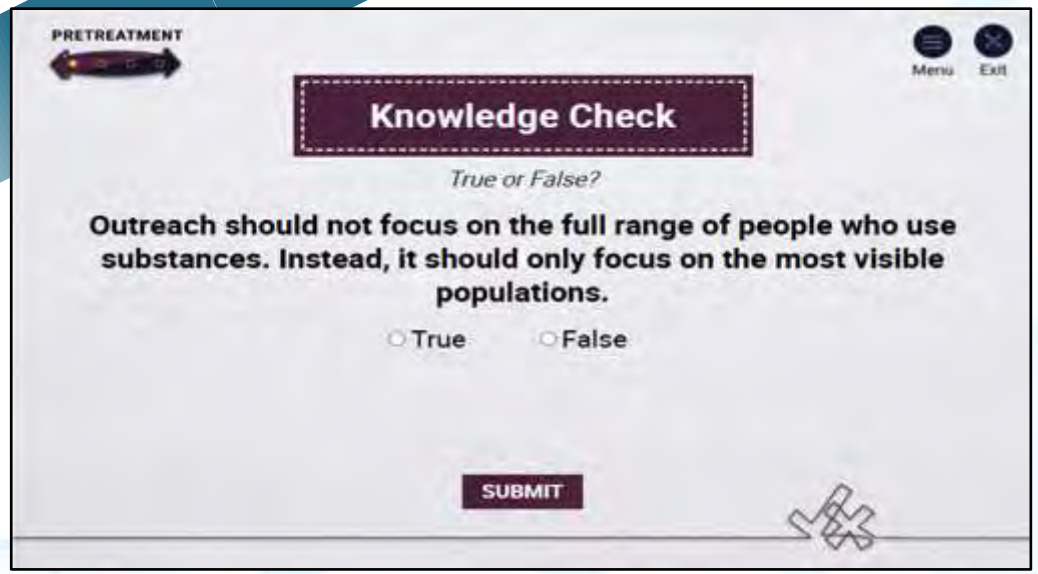
Afghanistan | Pakistan | Central Asia | Sri Lanka | Korea | Indonesia | Malaysia | Liberia | The Bahamas

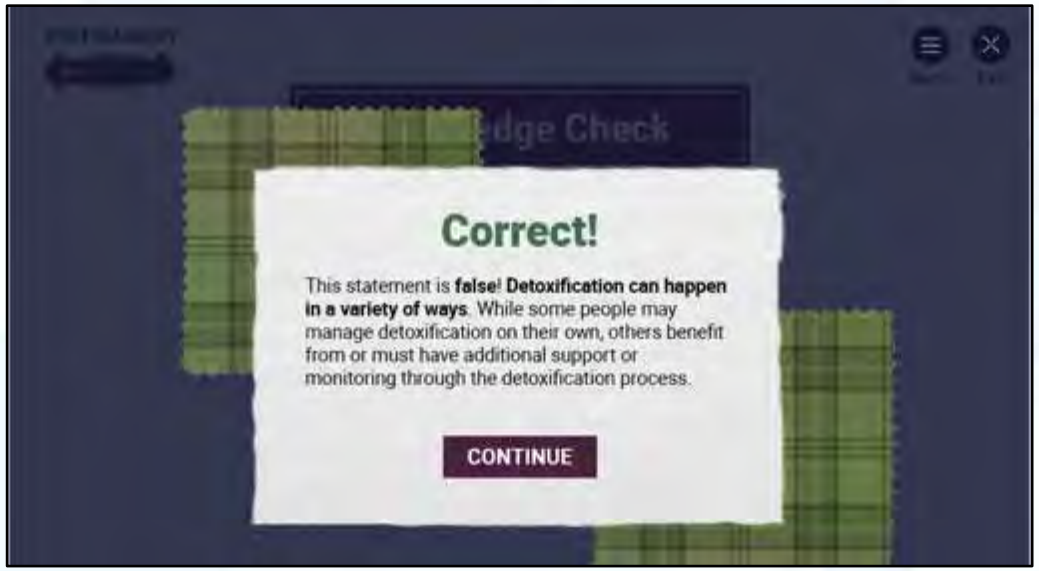
UNIVERSAL CURRICULUM (2010-2021)

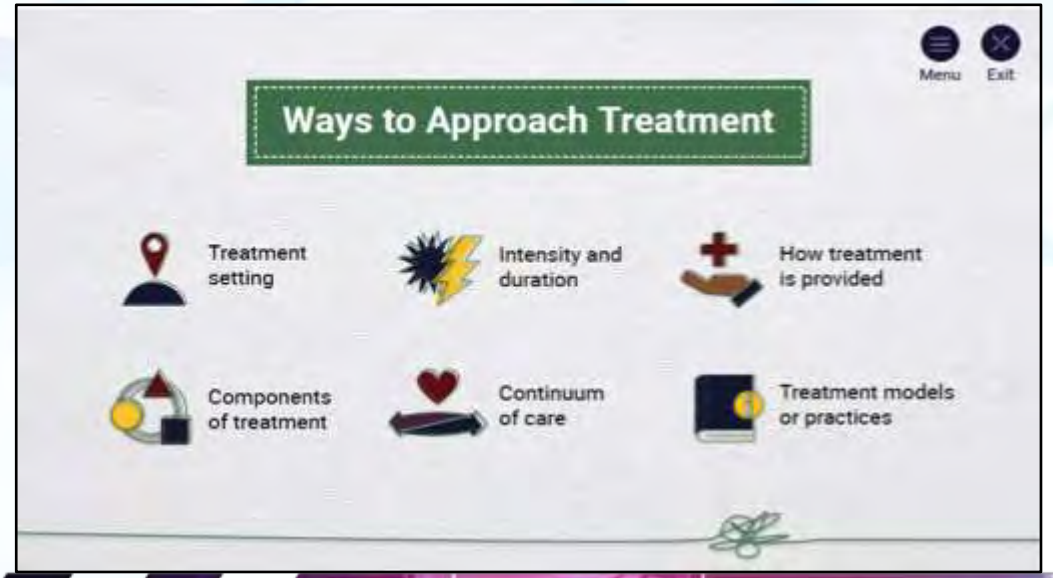


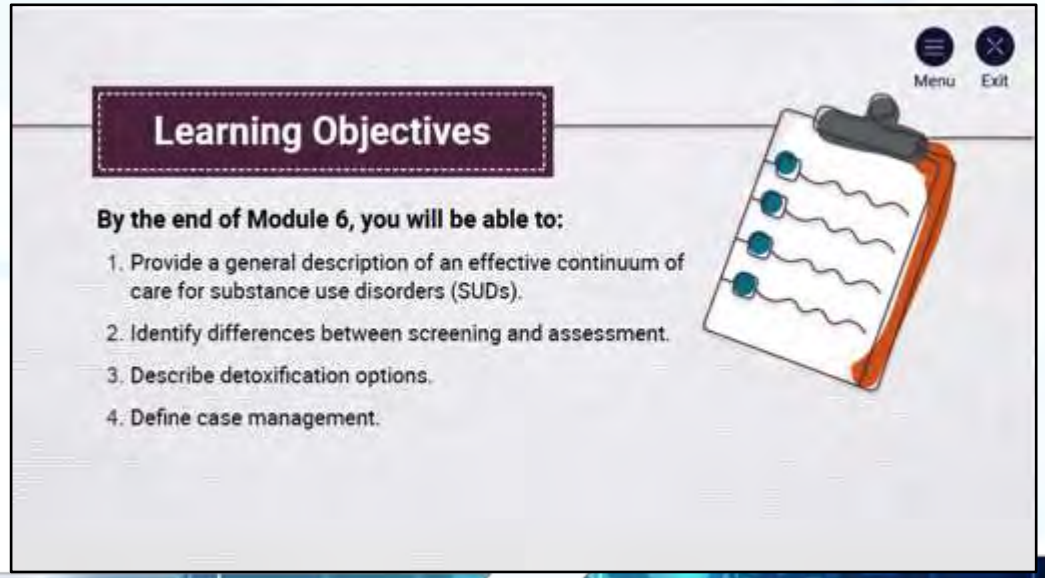
- 3 UC Series
- 121 Courses
- 2,660 Total Training Hours
- 4 Editions
- 24 Languages
- 69 Countries
- 177 Training Providers (27 in U.S.)

2021: LAUNCHING TRAINING HUB







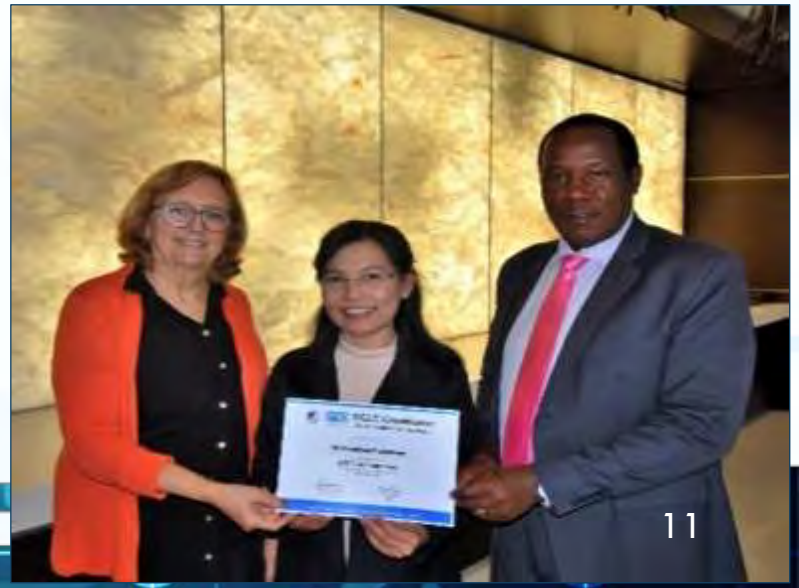


INTERNATIONAL CREDENTIALING

www.globalccc.org

Global Centre for Credentialing and Certification (GCCC)

- International Certified Addiction Professional (ICAP)
- Remote Proctoring – *coming soon*
- Prevention Certificate – *coming soon*
- 2,000+ Credentialed Professionals from 69 countries



INTERNATIONAL SOCIETY OF SUBSTANCE USE PROFESSIONALS (ISSUP)

www.issup.net

INTERNATIONAL SOCIETY OF SUBSTANCE USE PROFESSIONALS

Website

- 220,000 - Website visitors
- 940,000 - Website page views
- 9,350 - Social media followers

National Chapters

INTERNATIONAL SOCIETY OF SUBSTANCE USE PROFESSIONALS

Online Events

- **2020: Record of 70 ISSUP webinars** in 6 languages
- **2020:** ISSUP's African Regional Event with **5,054 attendees from 117 countries.**

- Organized by UAE, U.S. (INL), 5 international organizations
- Plenaries and 24 concurrent events (symposia, training, workshops) bringing together the global workforce to translate research into practice
- Inviting you to largest in-person reunion of the addiction field since the COVID-19 pandemic

INTERNATIONAL CONSORTIUM OF UNIVERSITIES FOR DRUG DEMAND REDUCTION (ICUDDR)

www.icuddr.org

Launched 2016

- Promotes **Addiction Studies** at the University Level
- Advances Applied **Addiction Research** through UTC/UPC training
- **Supports Networking:**
  - community-university partnerships
  - faculty and student exchanges among universities

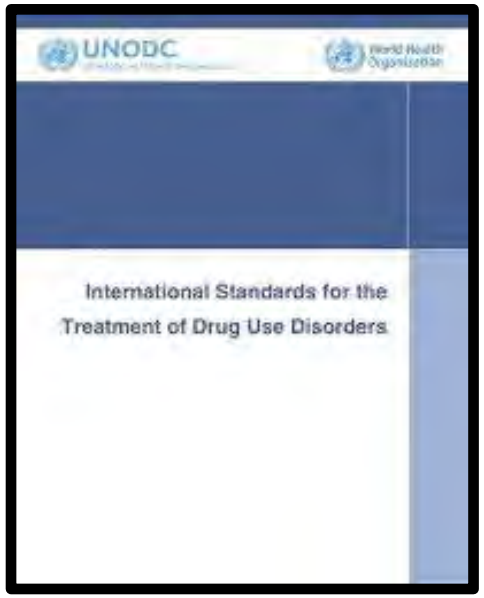
- Members: 260+ universities from 60+ countries.
- Supported development of 52 new substance use programs at the university level.
- Awarded NIDA grant for ISAJE support to promote DDR research publications worldwide.

2. Quality of Treatment and Prevention Services

UNODC/WHO QUALITY ASSURANCE PROGRAM

World Health Organization

Developed Int'l Standards for Treatment → **Established Quality Standards** → **Providing Technical Assistance to governments in accreditation of treatment services/facilities**

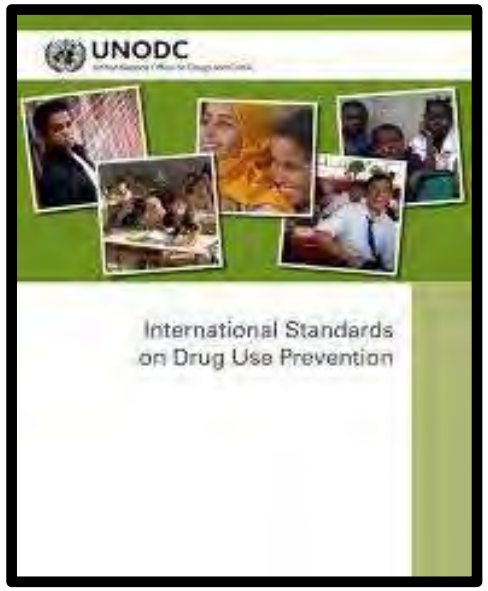


- Fall 2021: UNODC/WHO Global Quality Assurance Conference
- Winter 2021: Planning to launch consortium of quality assurance agencies to adopt a common standard

FUTURE PREVENTION QUALITY ASSURANCE PROGRAM

World Health Organization

Developed Int'l Standards for Prevention → **Establish Global Quality Standards for Prevention** → **Providing Technical Assistance to governments in accreditation of prevention organizations**



- Goal for the next 5-10 years: establish quality standards for prevention organizations.
- Mapping of prevention systems and organizations worldwide
- Training and technical assistance for prevention workforce and organizations

3. Access and Barriers to Prevention and Treatment Services

INTERNATIONAL TECHNOLOGY TRANSFER CENTERS (ITTC)

Launched 2021

www.ittcnetwork.org

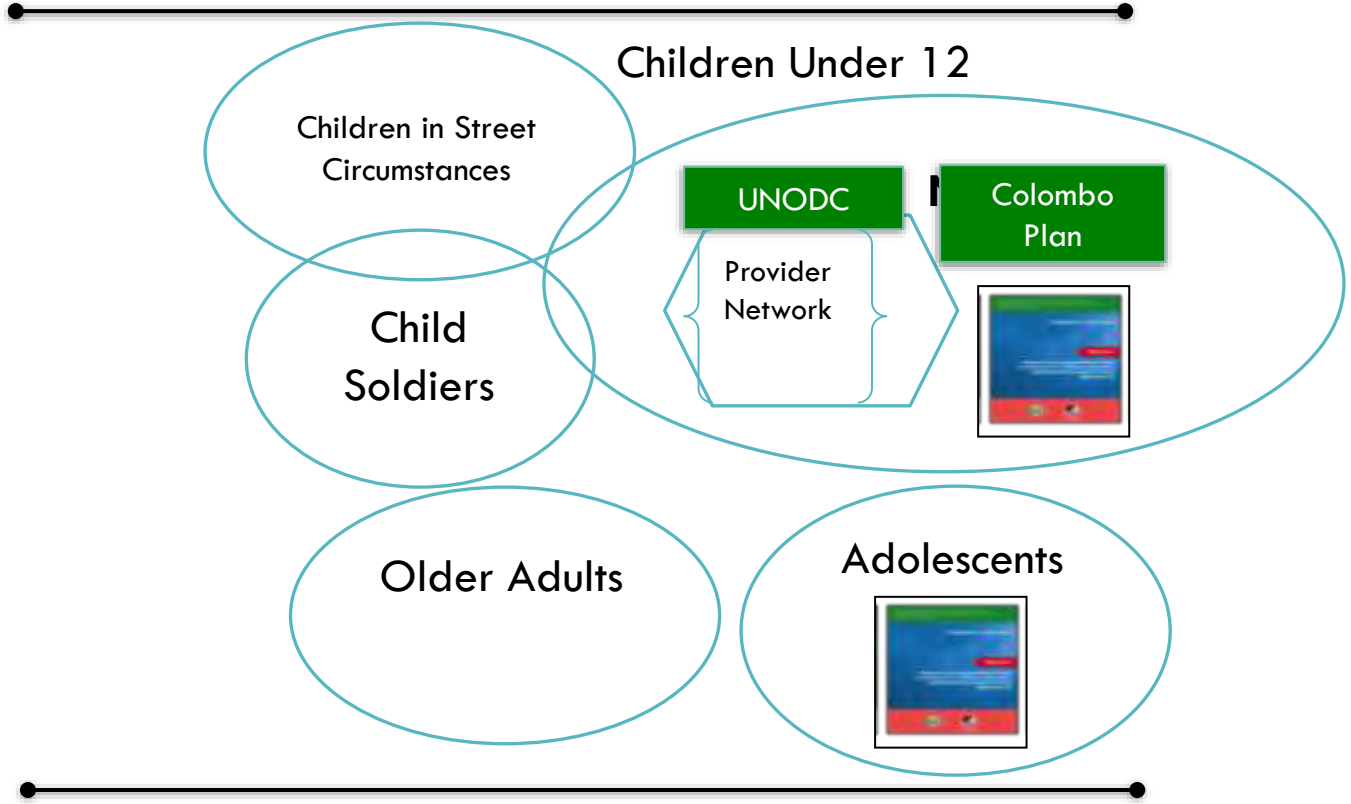
- Based on U.S. ATTC model
- Adopts a systems analysis in conducting assessments and epidemiological studies.
- Identifies barriers and gaps in treatment access and coverage
- Provides mentoring and technical assistance
- Incorporates comprehensive prevention, treatment and recovery interventions.

- Current Members: South Africa, Ukraine, U.S., Vietnam (4)
- In Progress: Colombia, Czechia, Indonesia, Mexico, Peru (5)

4. Insufficient Services for People with Special Clinical Needs

Populations with Special Clinical Needs

1. Age



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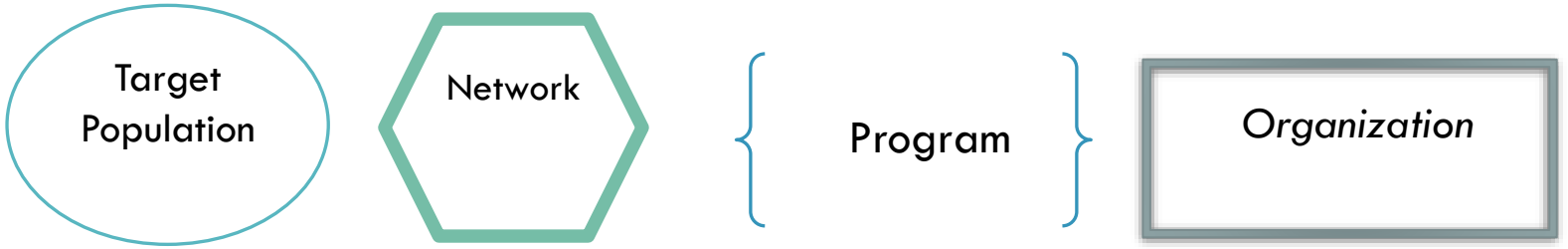
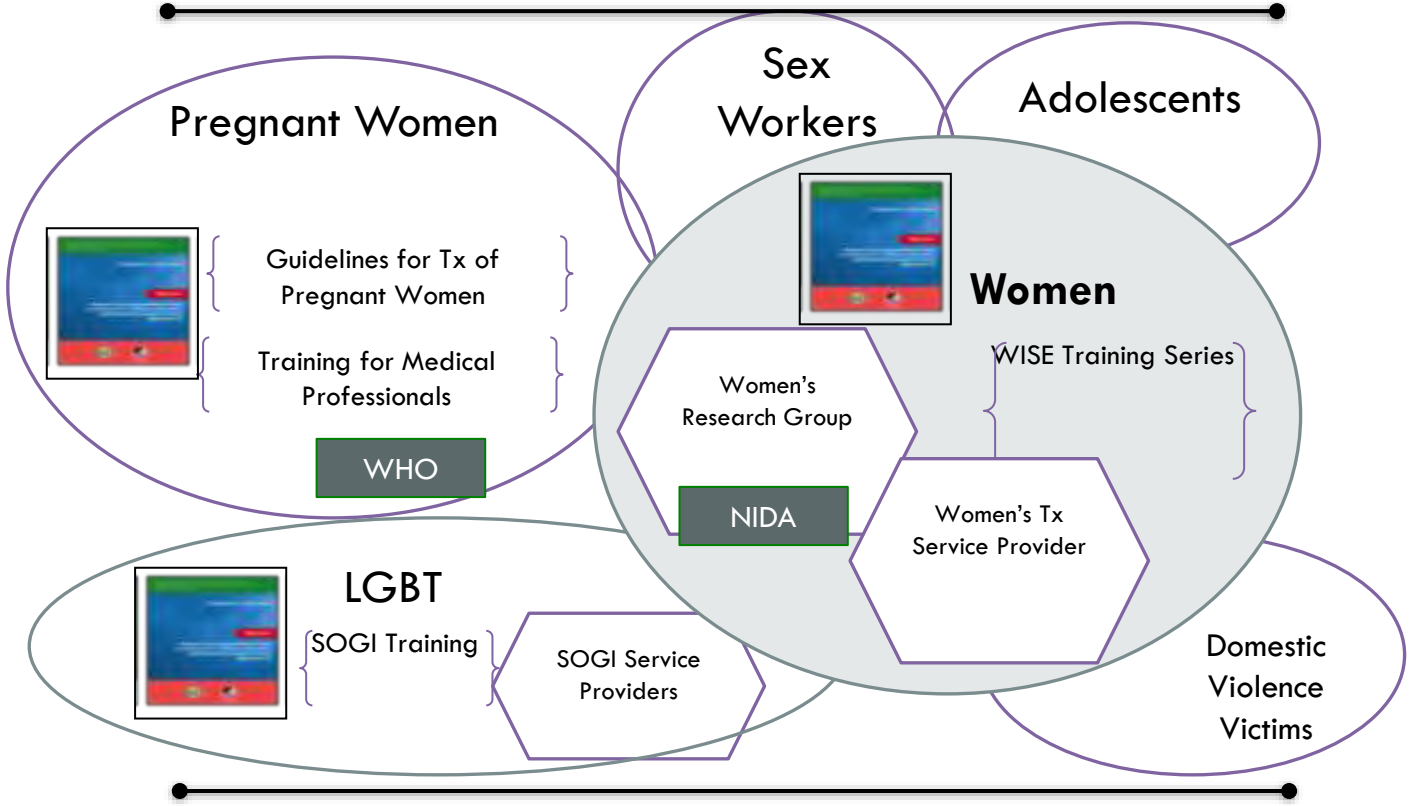


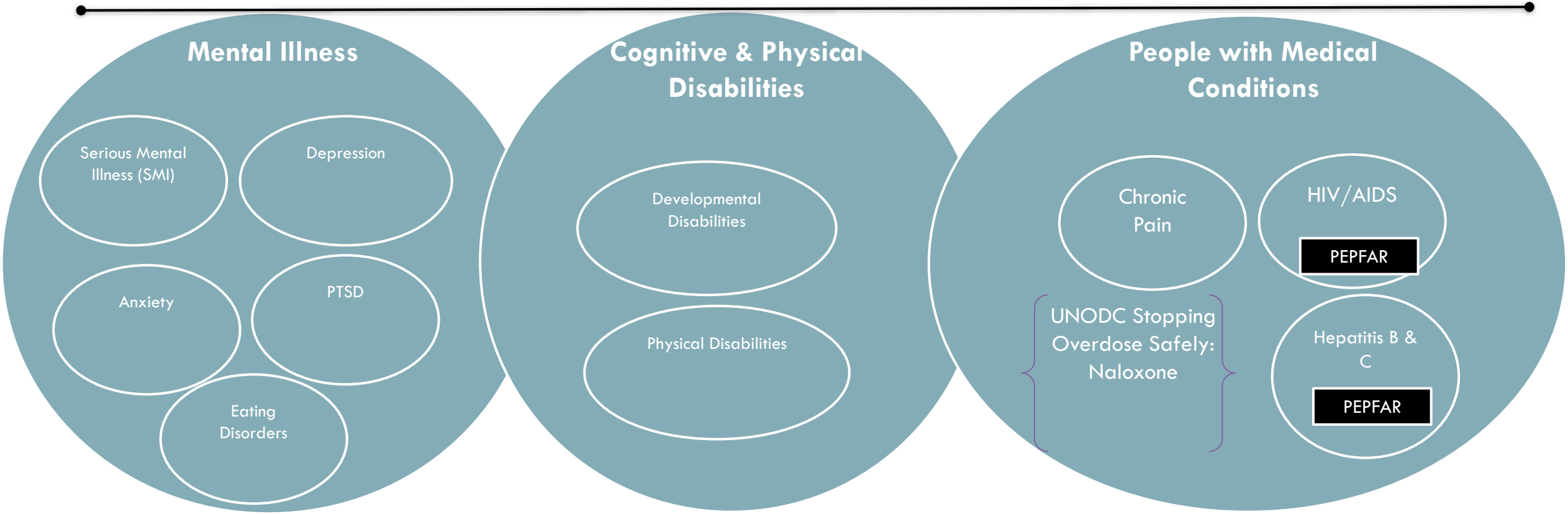
Populations with Special Clinical Needs

2. Gender and Gender Identity



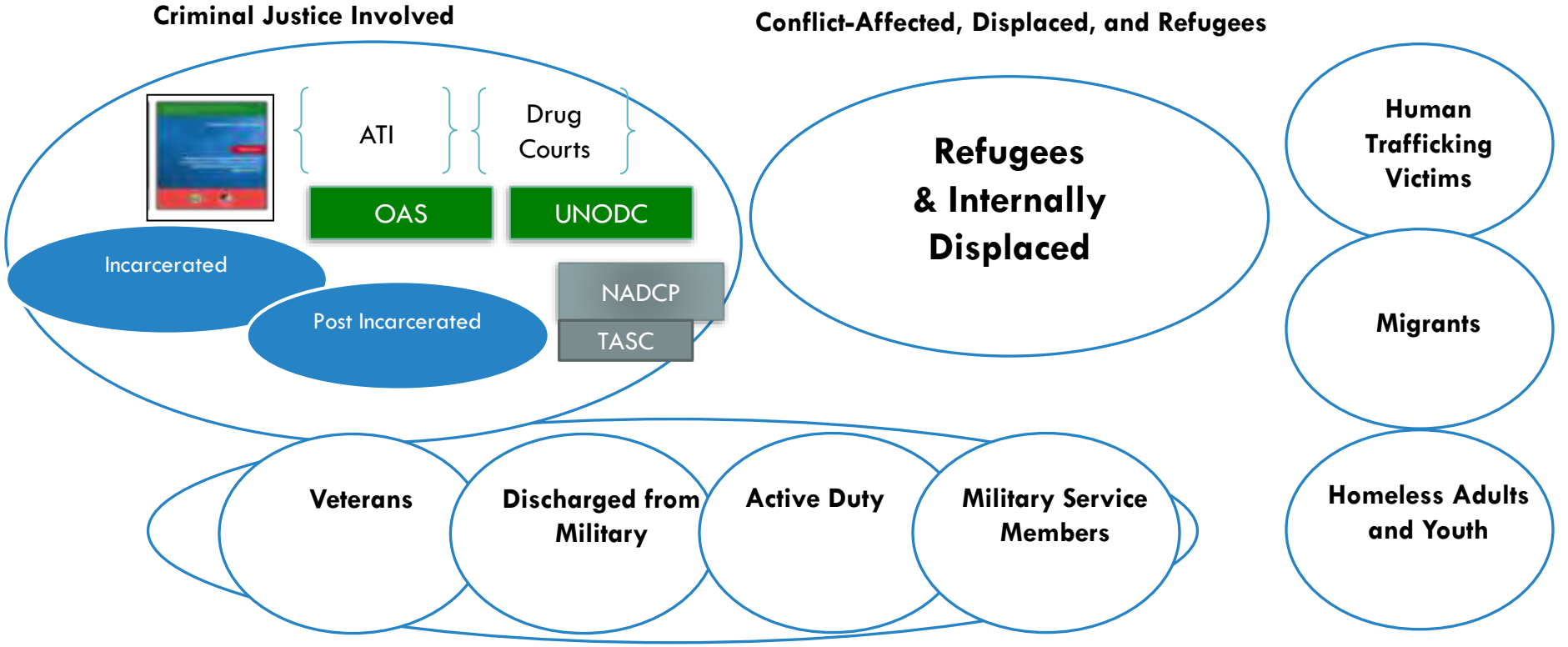
Populations with Special Clinical Needs

3. People with Disabilities and Mental and Psychiatric Conditions



Populations with Special Clinical Needs

4. Dislocation/Displacement from Home Environment



Populations with Special Clinical Needs

5. Culturally, Geographically, and Professionally Diverse Groups

Gangs

Law Enforcement and Criminal Justice Workers with Substance Use Dependence

People Living in Deprivation

Minority Groups of Ethnic, Religious, Racial, Tribal, Nationality (including indigenous)

Populations at Risk for Extremism

Outreach Drop In Centers

Colombo Plan

Rural Populations

Rural Program Network

Colombo Plan

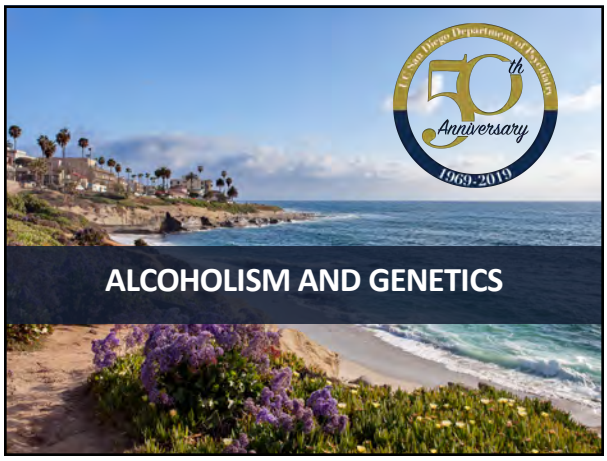
UNODC

Thank You

BRIAN MORALES
U.S. Department of State
DemandReduction@state.gov

How Genes Influence Alcoholism (and why we should care)

—Marc Schuckit, MD, UCSD



LECTURE COVERS

- Background
- Do genes affect the risk?
- What is inherited?
- Low alcohol response
  - How environment contributes
  - Searching for genes
- How to use the information

LECTURE COVERS

- Background
- Do genes affect the risk?
- What is inherited?
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  - How environment contributes
  - Searching for genes
- How to use the information

SUBSTANCE USE DISORDER Dx

In same year 2+ of:

Failed roles

Hazardous use

Social problems

Tolerance

Withdrawal

Use longer/more

Unable to ↓

Lots time use

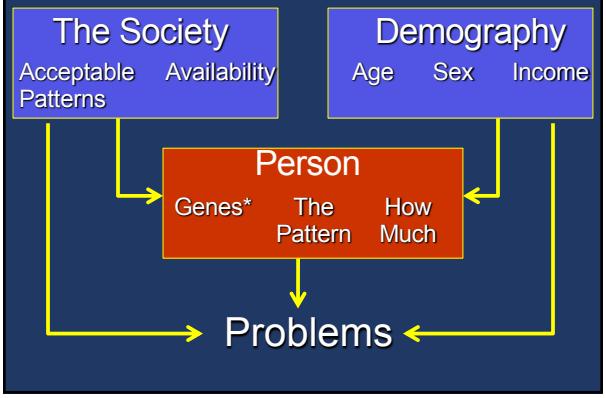
↓ activities

Use despite probs

Craving

If alcohol, is AUD, etc.

ALCOHOL USE & PROBLEMS



LECTURE COVERS

Background

Do genes affect the risk?

What is inherited?

Low alcohol response

How environment contributes

Searching for genes

How to use the information

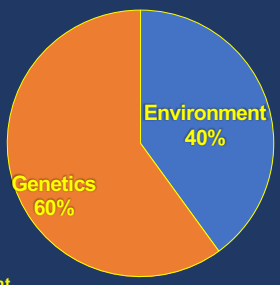
GENES AND AUDs

4 x ↑offspring risk

4 x ↑ if adopted out

Risk > for MZ vs DZ twins

ALCOHOLISM RISK



Multiple Characteristics

Each with Genes & Environment

PREDISPOSING RISK FACTORS

Alcohol metabolizing enzymes

Impulsivity

Psychiatric disorders

Sensitivity / Level of Response (LR)

ALCOHOL METABOLISM

~10% excreted via lungs/urine/sweat

90% metabolized by stomach & liver enzymes:

alcohol → acetaldehyde (ADH)

acetaldehyde → CO_2 and H_2O (ALDH)

PREDISPOSING RISK FACTORS

Alcohol metabolizing enzymes

Impulsivity

Psychiatric disorders

Sensitivity / Level of Response (LR)

LECTURE COVERS

Background

Do genes affect the risk?

What is inherited?

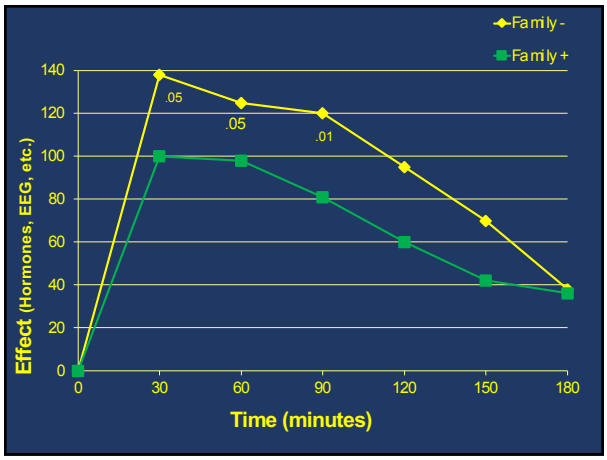
Low alcohol response

- How environment contributes
- Searching for genes

How to use the information

LR RATIONALE

Youth drink for effects
If need more for effect
will drink more
Then heavy drinking affects
Peers
Expectations
Stress



SELF REPORT OF EFFECTS

	1st 5 Times	Recent 3 Months	Heaviest
Feel Effect			
Feel Dizzy or Slur Speech			
Stumble			
Fall Asleep			

SRE CORRELATES: AGE 12*

Maximum drinks	.49
Frequency	.11
Problems	.28

* Avon Longitudinal Study of Parents and Children

LR PREDICTS OUTCOMES

San Diego Prospective Study

San Diego Prevention Study

Collaborative Study of Genetics AUDs

Avon Longit Study Parents & Children

Plus Australian twins, Danish cohort

ENVIRONMENT/ATTITUDE MEASURES

LR: Self Report of Effects of alcohol

Alcohol challenge

Peer drinking: Important People Scale

Expectancies: Alcohol Expect Questionnaire

Coping: Drinking to Cope

PREVENTION STUDY (N=500)

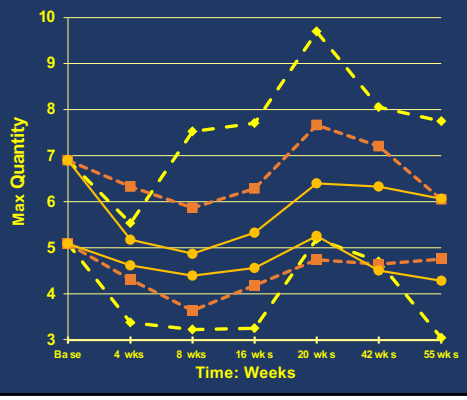
Questionnaire to students
- ~73% response
- Select matched low and high LR

3 prevention groups
- LR-Based (LRB)
- State of the Art (SOTA)
- Control

Four 45-min Internet videos

Follow for 55 weeks

Maximum Drinks



Harm Reduction

—J. David Stiffler, MD, UCSD

Harm Reduction

J. David Stiffler, MD
HS Clinical Assistant Professor of Psychiatry
Assistant Director, UCSD Addiction Psychiatry Fellowship Program
University of California, San Diego

Disclosures

- None

Goals of the Talk

- Definition of harm reduction
- Harm reduction – how and why
- Models of Addiction (biopsychosocial model in harm reduction)
- Examples
- Principles
- What it takes to practice harm reduction

Harm Reduction - Definition

Interventions reduce problematic **effects** of behaviors or decisions
(Logan 2010)

Keys to a harm reduction approach:

- Non-judgmental approach to meet patient "where he/she is"
- Engagement in treatment is a primary goal
- Do NOT require abstinence as a goal or prerequisite of Tx
- Provider's goals secondary to patient's goals
- Supports any step in the direction of less harm

Harm Reduction

How?

- Can use various styles or interventions: directive, MI, CBT
- Can be used for prevention, interventions, maintenance
- Do not always/solely focus on the substance use behavior

Why?

- Many with SUD are not in treatment
- Extend Tx to those unwilling/unable to pursue abstinence

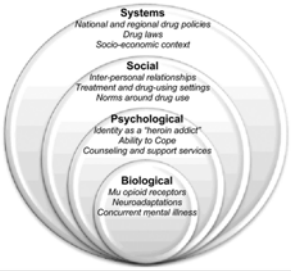
Models of Addiction

- Moral
  - Substance use and quitting are matters of will power
  - Drug use and people who use drugs are bad, weak, sinners
- Enlightenment
  - People are responsible for their addiction
  - Need to seek a higher power to recover
- Disease
  - (NIDA) Addiction is chronic disease characterized by drug seeking/use that is compulsive, or difficult to control, despite harmful consequences
  - Simple
  - People are not viewed as weak or flawed

Biopsychosocial Model of Addiction

(Buchman, Skewes)

- Biological
- Psychological
  - Childhood risk factors
  - Personality and temperament
  - Gender/sexuality
- Social
  - Family
  - Peers, intimate relationships
  - Culture
- Systemic



Examples of Harm Reduction Interventions

(Walley 2019)

- Syringe needle exchange programs
- Overdose education and naloxone distribution
- Opioid replacement therapy for opioid use disorder

- Designated drivers
- Naltrexone for alcohol use disorder

- Sun screen!

Principles for Practice in Health Care Settings

(Hawk 2017)

- Humanism
- Pragmatism
- Individualism
- Autonomy
- Incrementalism
- Accountability without termination

Principles - Humanism

- Patients are individuals
- Harmful behaviors have some benefit
- Understanding pts decisions is empowering for providers

- Approach
  - Moral judgements do not lead to (+) health outcomes
  - Provider accepts patient's choices
  - Do not hold grudges

Principles - Pragmatism

- Nobody will ever achieve perfect health behaviors
- Behavior and ability to change are influenced by social and community norms

- Approaches
  - Abstinence neither prioritized nor assumed to be pts goal
  - Range of supportive approaches is provided
  - Care about actual harms to pts (vs moral/societal standards)
  - Realize might experience moral ambiguity

Principles - Individualism

- Every patient presents with own needs and strengths
- Pts present with spectrum of harm and receptivity → need spectrum of interventions

- Approach
  - Strengths/needs assessed for each patient, no assumptions made
  - No universal protocol/messaging
  - Tailor treatment, maximize options

Principles - Autonomy

- Offer suggestions, education about Tx, but patient makes *choice
  (*to the best of pts abilities, beliefs, priorities)
- Approach
  - Pt-provider partnerships are important
    - Patient-driven care
    - Shared decision making
    - Reciprocal learning
  - Care negotiations based on the current state/goals of the patient

Principles - Incrementalism

- Any (+) change is step towards improved health
- Need to understand and plan for backward movement
- Approaches
  - Help pts celebrate and (+) change
  - (+) reinforcement is valuable
  - At times, everyone experiences plateaus or (-) trajectories

Principles - Accountability without termination

- Pts are responsible for their choices and health behaviors
- Pts are not “fired” for not achieving goals
- Pts have right to make harmful health decisions and providers can help pts understand that consequences are their own
- Approach
  - Help pts understand the impact of their choices
  - Backwards movement is not penalized

What does it take to practice harm reduction? (1)

(Denning 2012)

- Willingness to
  - Practice radical neutrality
  - Grapple with ethical gray area
  - Tolerate, accept, attempt to understand difficult behaviors
  - Be taught by patients
  - Relinquish the role of authority, judge or expert
  - Partner with patients

What does it take to practice harm reduction? (2)

(Denning 2012)

- Belief that:
  - People know what they need
  - People will tell the truth
  - Any step is progress
  - Power of relationship over technique
  - Complexity is good
  - Ambivalence and resistance are natural and useful

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Hubert Humphrey Fellowship in Substance Use Disorders – Opportunities and Challenges

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Andia Meksi, MS
Hubert H. Humphrey Fellowship Program

The Hubert H. Humphrey Fellowship Program in Substance Abuse Prevention, Treatment and Policy

Summer Clinical Institute in Addiction Studies
University of California, San Diego
June 10, 2021

VCU

History and Organization

- Established in 1978 by President Jimmy Carter
- A Fulbright Exchange Program
- Funded by the U.S. State Department and administered by the Institute of International Education
- Program areas include human rights, public health, agriculture, law, journalism, economics, etc.

Who are the Fellows

- Mid-career professionals from different sectors
- Primarily from low and middle income countries
- Very competitive. In FY 21:
  - Over 4,500 applications--150 selected
- 6,017 alumni of the program since 1978, representing 162 countries

Program Design

- Fellowships are for 10 months--August to June
- Non-degree program
- Focuses on:
  - Professional development in the fellow's individual field
  - Leadership training
  - Cultural exchange

The VCU Humphrey Fellowship Program

- VCU was selected as a host university in 2006
- Major focus on substance abuse (including alcohol and tobacco), but includes a broad range of other healthcare issues such as HIV/AIDS, children's mental health, and healthcare policy
- NIDA is a key collaborator

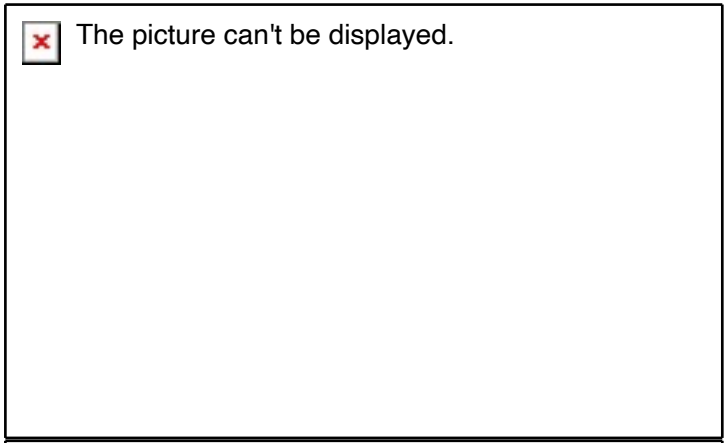
VCU

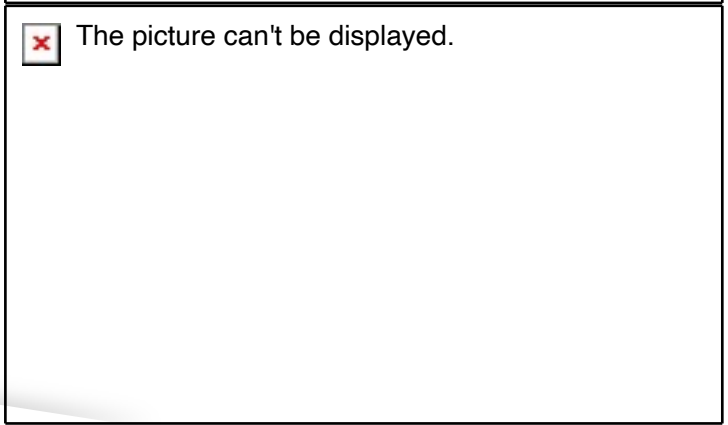
Our Approach

- Many requirements, but relatively unstructured and flexible—individual program plans
- Classroom and experiential learning
- Focus on the use of culturally appropriate, science-based interventions and the need for evaluation
- “Change Agents”

Professional Development

- Humphrey Seminar
- Academic Coursework
- Professional Development Activities
  - Conferences, workshops, field trips & roundtable discussions
- Professional Affiliation (internships)





Cultural Exchange

VCU

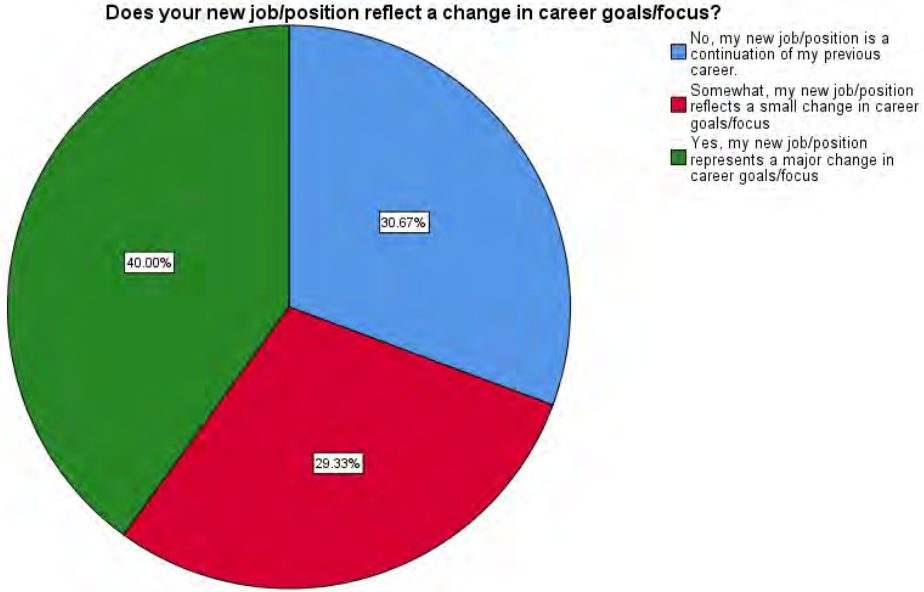
One Year Follow-up Data

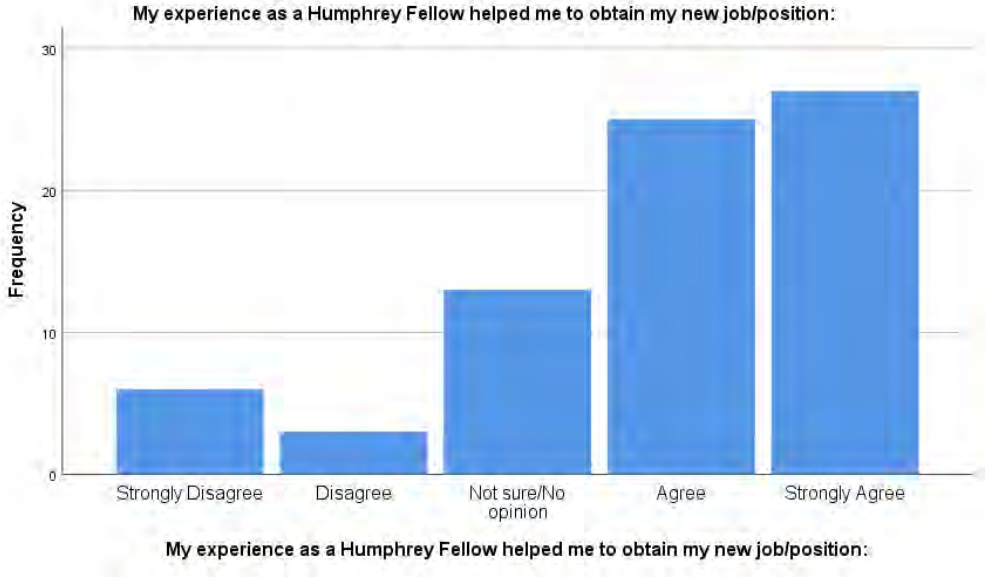
Cohort 2007-2019

N=108

Started a New Job

69.4% (N=75) started a new job/position





Project Collaborations

Anyone from the US

- 40.6% (N=43) collaborated/worked on a project with someone from the US

Other Humphrey Fellows

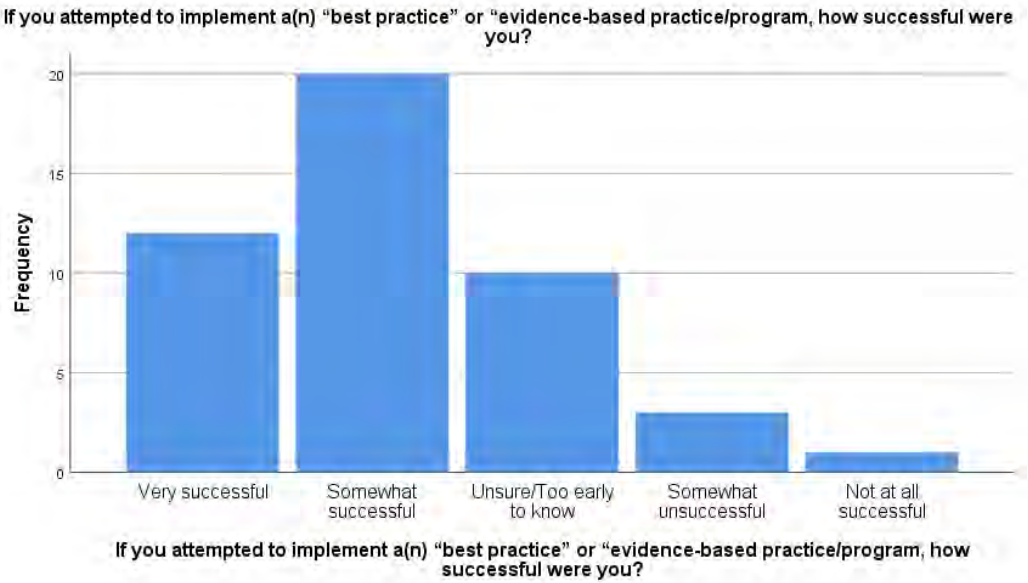
- 19% (N=20) have collaborated/worked on a project with any other Humphrey Fellow

Missing Data: N=3

Project Implementation

- 83.9% (N=47) implemented one or more best practices/programs

**Cohorts 2009-2013 were not assessed for this question*



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Mission Statement

Devoted to workforce competence in addiction and mental health services by bringing research to practice — our clients deserve the best!

www.ccarta.com

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Continuing Education Units

APA
The UCSD Department of Psychiatry is approved by the American Psychological Association Sponsor Approval System to provide continuing education for psychologists. This course has been approved for **13** continuing education hours. The UCSD Department of Psychiatry maintains sole responsibility for this course. You will need to provide your license number.

CAADE
This course can account for **13** continuing education units (CEUs) for California Association of Alcoholism and Drug Educators (CAADE). You will need to provide your certificate number.

CCAPP
This course can account for **13** continuing education units (CEUs) for California Consortium of Addiction Programs and Professionals (CCAPP). You will need to provide your certificate number.

Please complete the viewing and registration requirements to be issued your professional certificate.