

# Benzodiazepine-Induced Brain Injury: The Hidden Prescription Epidemic

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# Session Overview

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## A Bit About Benzos, Dependence, & Withdrawal

- D E Foster

## Inside the Struggle: A Tapering Journey

- John Staight

## Lived Experience, Tolerance, “Detox” and Protracted “Withdrawal” Syndromes

- Nicole Lamberson, PA

## Benzodiazepines: The Hidden Prescription Epidemic

- Alexis Ritvo, MD

## Q & A *(Please submit questions in chat)*



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# A Bit About Benzos, Dependence, & Withdrawal

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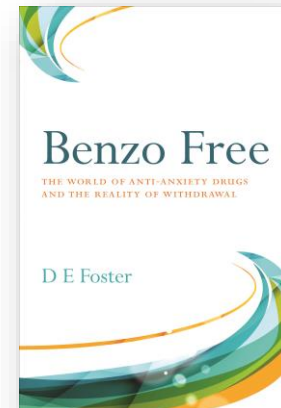
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# A Bit About Benzos, Dependence, & Withdrawal

## Presenter

### D E Foster

- Host / Producer: **The Benzo Free Podcast**
- Author: **Benzo Free: The World of Anti-Anxiety Drugs and the Reality of Withdrawal**
- Lived Experience (12 years on clonazepam)
- Visit our website for more info...



[EasingAnxiety.com](http://EasingAnxiety.com)



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# A Bit About Benzos, Dependence, & Withdrawal

## Intro to Benzos

### Benzodiazepines

- Class of psychoactive medication
- aka Benzos, BZDs, BZRAs, anti-anxiety drugs, minor tranquilizers, etc.
- **Treatment:** Anxiety, Insomnia, Muscle spasms, Epilepsy  
Alcohol detox, Helpful in medical procedures



### Prescribing Stats

- Benzodiazepines are prescribed at about **66 million doctors' appointments** a year \*
- **90% of all benzodiazepines** are prescribed by primary-care providers \*\*

\* Santo L, Rui P, Ashman JJ. Physician Office Visits at Which Benzodiazepines Were Prescribed: Findings From 2014-2016 National Ambulatory Medical Care Survey. Natl Health Stat Report. 2020 Jan;(137):1-16. PMID: 32510318.

\*\* National Institutes of Health (NIH)



# A Bit About Benzos, Dependence, & Withdrawal

## Common Types

### Benzodiazepines

Alprazolam	Clonazepam	Diazepam	Lorazepam	Temazepam
Alprax Neurol Niravam Solanax <b>Xanax</b>	Iktorivil <b>Klonopin</b> Paxam Rivatriil Rivotril	Apaurin D-Pam Ducene Vival <b>Valium</b>	<b>Ativan</b> Lorabenz Lorenin Tavor Temesta	Euhypnos Nocturne Sompam <b>Restoril</b> Tenox

### Nonbenzodiazepines (Z-drugs)

Eszopiclone	Zaleplon	Zolpidem	Zopiclone
<b>Lunesta</b> Lunivia	<b>Sonata</b> Stamoc	<b>Ambien</b> Nytamel Sanval Sublnox	<b>Imovane</b> Zimoclone Zimovane Zioutab



# A Bit About Benzos, Dependence, & Withdrawal

## Types of Benzos

### Types Vary by...

- Potency
- Speed of Effectiveness
- Speed of Elimination (half-life)
- Focus of Treatment

### Affects on Withdrawal

- Tapering Decisions
  - Potency (1mg X/H/K = 20 mg V)
  - Half-Life (V: 20-100 hours)
- Symptomatology varies



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# A Bit About Benzos, Dependence, & Withdrawal

## The Hidden Epidemic

Benzodiazepines have been prescribed for **over 60 years**

- Chlordiazepoxide (**Librium**) - 1960
- Diazepam (**Valium**) - 1969
- Alprazolam (**Xanax**) – 1981

Every decade serious **concerns**  
were raised about  
long-term consequences.

*“...these drugs  
[benzodiazepines] have  
produced a nightmare of  
dependence and addiction,  
both very difficult to treat  
and to recover from.”*

*Sen. Edward Kennedy (1979)  
Senate Sub-committee Hearing*



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# A Bit About Benzos, Dependence, & Withdrawal

## The Hidden Epidemic

### Two Areas of Concern with Benzos

- **Street Use / Overdose**
  - Common in conjunction with Opioids
  - 33.1% of all opioid overdose deaths include a benzodiazepine (2017) \*
- **Long-term Use / Physical Dependence**
  - Usually taken as prescribed

### The Hidden Epidemic

- Long-term use

\* Tori ME, Laroche MR, Naimi TS. Alcohol or Benzodiazepine Co-involvement With Opioid Overdose Deaths in the United States, 1999-2017. JAMA Netw Open. 2020;3(4):e202361. doi:10.1001/jamanetworkopen.2020.2361



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# A Bit About Benzos, Dependence, & Withdrawal

## A Different Kind of Withdrawal

Some people withdraw from long-term benzo use  
**with little or no problem.**

For others, the experience can be **ineffable...**

- **Severity** of Withdrawal
- **Duration** of Withdrawal
- **Life Effects** (career, family, etc.)



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# A Bit About Benzos, Dependence, & Withdrawal

## 12 Categories of Symptoms

### Psychological Symptoms

- Anxiety Symptoms
- Behavioral Symptoms
- Cognitive Symptoms
- Excitability Symptoms
- Perception Symptoms
- Sleeping Symptoms
- Social Symptoms

### Physical Symptoms

- Abdominal / Gastrointestinal
- Symptoms of the Eyes, Ears, Nose, & Mouth
- Symptoms of the Head & Neck
- Symptoms of the Heart & Lungs
- Muscular Symptoms
- Nerve Sensations
- Immune & Endocrine Symptoms



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# A Bit About Benzos, Dependence, & Withdrawal

## Addiction vs. Dependence

### Addiction and Benzos

- Benzodiazepine addiction exists — but rare
  - Often combined with opioids and other prescription meds
- Physical dependence far more common
- Taken as prescribed

*It's rarely addiction.*

**Dr. Steven Wright**  
Addiction Medical Specialist  
BAWG Co-Chair (ret.)



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# A Bit About Benzos, Dependence, & Withdrawal

## Addiction vs. Dependence

### Why is this important?

- Treatment Differs
  - Slow rate of withdrawal (months or years)
  - Abrupt cessation can be **very dangerous**
- Methods Differ
  - Terminology / Protocols
- Length of Recovery Differs



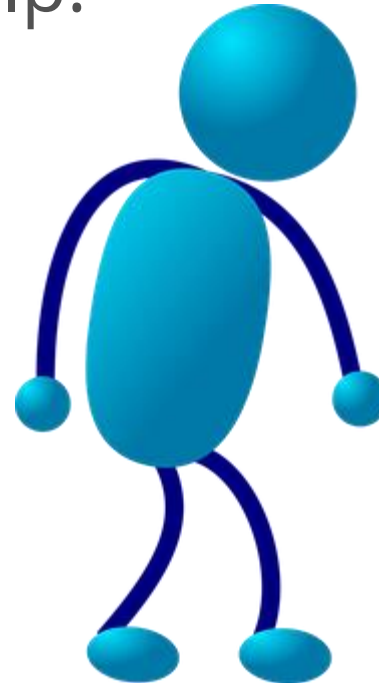
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# A Bit About Benzos, Dependence, & Withdrawal

## The Search for Support

Most long-term benzodiazepine users find themselves isolated and afraid, with no where to turn for help.



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# A Bit About Benzos, Dependence, & Withdrawal

## Benzodiazepine Action Work Group (BAWG)

We're trying to help change that...

### **Benzodiazepine Action Work Group (BAWG)**

*Our mission is to increase benzodiazepine safety  
through education, patient support,  
and informed prescribing and deprescribing practices.*



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# A Bit About Benzos, Dependence, & Withdrawal

## Benzodiazepine Action Work Group (BAWG)

### About BAWG

- Colorado Consortium for Prescription Drug Abuse Prevention
- BAWG Membership
  - Medical and Mental Health Professionals
  - Community Support Leaders
  - Benzo Community Organizers (Alliance, BIC, TSRG, etc.)
- Colorado Focus / National Reach
- **Speakers Bureau (New)**
- **Online Documentation (New)**

[corxconsortium.org](http://corxconsortium.org)



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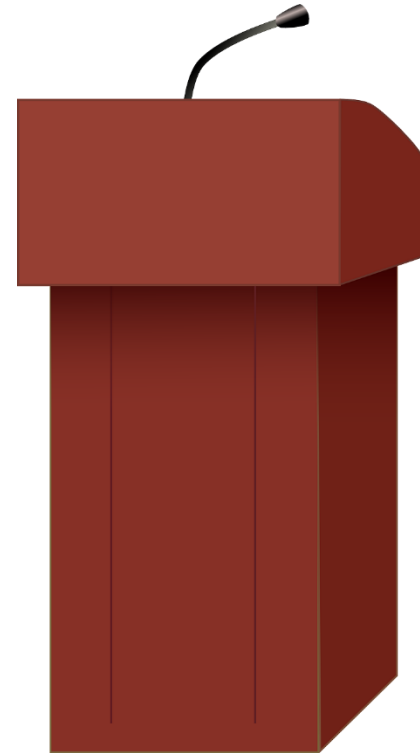
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# A Bit About Benzos, Dependence, & Withdrawal

## Closing

*Enough from me,  
let's hear from our  
other speakers....*



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# Inside the Struggle: A Tapering Journey

John Staight

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# Benzodiazepines: Lived Experience, Tolerance, “Detox” and Protracted “Withdrawal” Syndromes

Nicole Lamberson, PA



Benzodiazepine Information Coalition  
Medical Advisory Board Member,  
Founding Member of Colorado Consortium's  
Benzodiazepine Action Work Group



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# Presentation objectives

- Share my personal testimony of **iatrogenic** (caused by medical treatment) benzodiazepine-induced brain injury
- Define benzodiazepine **tolerance** & why it's important to recognize
- Discuss **over-rapid withdrawal** and **“detox”** from benzodiazepines
- Discuss **protracted “withdrawal” syndromes** & why they're important to recognize



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# My Story

- Prescribed Xanax for “work stress”
- Tolerance developed quickly (unrecognized)
- Misdiagnosis
- Prescribing cascade/polypharmacy x ~5 years
- Discovered benzodiazepine problems on the internet
- “Detox” in October 2010
- Severe withdrawal
- Protracted “withdrawal” syndrome which persists to date
- Medical training did not prepare me for this; Also struggled w/ disbelief from other clinicians



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# Tolerance

- Tolerance to many of the effects of benzodiazepines develops with regular use.<sup>1</sup>
- The body responds to the continued presence of the drug with a series of adjustments that tend to overcome the drug effects.<sup>1</sup>
- The original dose of the drug has progressively less effect and a higher dose is required to obtain the original effect.<sup>1</sup>
- Doctors will sometimes increase the dosage or to add another benzodiazepine—some patients end up taking two benzodiazepines at once.<sup>1</sup>
- **Interdose withdrawal:** withdrawal symptoms start to develop in between scheduled doses.



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# Some Classic Tolerance Symptoms

- Insomnia, sleep disturbances
- Anxiety/panic
- Cognitive decline
- Memory loss
- Agoraphobia
  - Dr. Heather Ashton's clinic: 10/50 became agoraphobic for first time while taking benzodiazepines<sup>1</sup>



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# Some of the Many Other Symptoms I Experienced During Tolerance:

- GI symptoms: diarrhea, “irritable bowel”
- Rashes
- Joint pains, muscle spasticity
- Depression
- Suicidality
- Excessive sleeping
- Fatigue/malaise/lack of motivation
- Isolating
- Agitation/irritability/no stress tolerance
- Mood instability (rage)/personality changes
- Obsessing/compulsing/racing thoughts/paranoia



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# Why Is Tolerance Important to Recognize?

- **Prescribing Cascade:** the situation in which a first drug administered to a patient causes adverse event signs and symptoms, that are misinterpreted as a new condition, resulting in a new medication being prescribed.
- **Polypharmacy:** the simultaneous use of multiple drugs by a single patient, for one or more conditions.



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# Why Is Tolerance Important to Recognize?

- **Medication Spellbinding (intoxication anosognosia):** causes the victim to underestimate the degree of medication-induced mental impairment, to deny the harmful role that the drug plays in the person's altered state, and in many cases compel the individual to mistakenly believe that he/she is functioning better.
  - Belief in medicine/conventional narrative reinforces this
  - Misdiagnosis reinforces this (“Your underlying condition is worsening” or “This is proof you need the meds”)
- **Save time, money, misery**

# Over-Rapid Withdrawal/"Detox"

- Inappropriate for patients not suffering from addiction (those taking as prescribed)
  - Even if patient reports feeling to dose more often/increase dose, it may just be due to tolerance/interdose.
- Patients harmed twice: first by the long-term prescription, second by the medical mismanagement
- Can result in severe withdrawal syndromes: seizures, psychosis, akathisia and even death
- Often fails/patients do poorly: waste of money & can destabilize the CNS where stability can sometimes not be reached again
- Often more polypharmacy
- Can cause support systems to abandon patient/"tough love"



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# Protracted “Withdrawal” Syndromes

- Studies report 10-44% of chronic benzodiazepine users experience moderate to severe protracted “withdrawal” symptoms upon cessation lasting months to years.
- Potential risk factors: cold turkey/rapid tapers, genetics, kindling etc.
- Nomenclature:
  - ‘Protracted’ describes the time sequence but the term ‘withdrawal’ is misleading.
  - Some have suggested calling this phenomena “Benzodiazepine Induced Brain Injury” or “Benzodiazepine Injury Syndrome”.
    - Other names: “Neurotoxicity”



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# Some of My Protracted Symptoms

- Depersonalization/Derealization
- Neuropathy in spine, pelvis, legs, feet
- Burning skin
- Inability to multitask or endure stress
- Anxiety
- Irrational fear/paranoia
- Irritability
- Chronic Fatigue
- Anhedonia (inability to feel pleasure)/Flatness
- Numbness



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# Some of My Protracted Symptoms

- Dizziness/Off-balance/"on a boat" sensation
- Vision problems
- Headaches
- Muscle spasms
- Nausea
- Cognitive impairment
- "Meningitis"/"concussion-like" feeling
- "Switch flipped" feeling
- Insomnia
- Adverse reactions to medications, caffeine, etc.



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# Impact of Protracted Syndrome

- Job loss/unemployment/financial implications (short and long term)
- Impact on relationships
- Women of childbearing age: impact on their ability to have family
- Lost life experiences
- Waking up from “coma”
- Even if eventual complete/near-complete healing, sufferers are left to “clean up the rubble”
- Trauma



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# Why is Recognizing Protracted Syndromes Important?

- Patients need support, validation and hope (some people suicide due to duration and severity)
- Clinicians: keep it in your differential...
  - Avoid more misdiagnosis, mistreatment, polypharmacy, etc.
- Need more research into:
  - causes (how to reduce risk of developing?)
  - treatments/how to best help these patients
  - what % fully resolves?
  - can there be permanent symptoms?



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# Final Thoughts:

- I consider taking benzodiazepines the **single biggest mistake/regret of my life & worst thing that has ever happened to me.**
- The withdrawal and protracted (benzodiazepine injury) syndromes that can result from long-term use can be severe and cause suffering that is indescribable (death seemed like a welcome escape).
- The decision to start (especially) and stop benzodiazepines should not be taken lightly by patient or clinician.



# Resources & References

Find me at Benzodiazepine Information Coalition: [benzoinfo.com](http://benzoinfo.com)



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# References

- <sup>1</sup>Ashton, H., 2002. *Benzodiazepines: How They Work & How to Withdraw, The Ashton Manual*. [online] Benzo.org.uk. Available at: <<http://www.benzo.org.uk/manual/bzcha01.htm>> [Accessed 24 October 2021].
- <sup>2</sup>"Intoxication Anosognosia: The Spellbinding Effect of Psychiatric Drugs," *International Journal of Risk & Safety in Medicine*, 19, 3-15, 2007.



# Benzodiazepines: The Hidden Prescription Epidemic

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# Presentation objectives

1. Increase knowledge about potential harms of prescription benzodiazepines
2. Describe withdrawal, protracted withdrawal and benzodiazepine induced neurological injury
3. Increase knowledge about safer deprescribing (tapering) of benzodiazepines



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# Short vs Long Term Benzodiazepine Use

- Long term benzodiazepine use often begins with treatment of acute distress
- Relatively safe for short-term use (2 to 4 weeks), but their safety has **not** been established beyond that period (Lader 2011)
- Limit initial quantity to 2-3 week bridge while starting other treatment (e.g. SSRI or SNRI for anxiety). (Wyatt 2020)

## Steep Climb In Benzodiazepine Prescribing By Primary Care Doctors

January 25, 2019 - 1:18 PM ET

RHITU CHATTERJEE



The drugs clonazepam and diazepam are both benzodiazepines; they're better known by the brand names Klonopin and Valium. The drug class also includes Ativan, Librium and Halcion.

Bloomberg/Getty Images

The percentage of outpatient medical visits that led to a **benzodiazepine** prescription doubled from 2003 to 2015

Half those prescriptions came from primary care physicians.

Agarwal 2019  
Chaterjee 2019

# Chronic Benzodiazepine Prescription Common

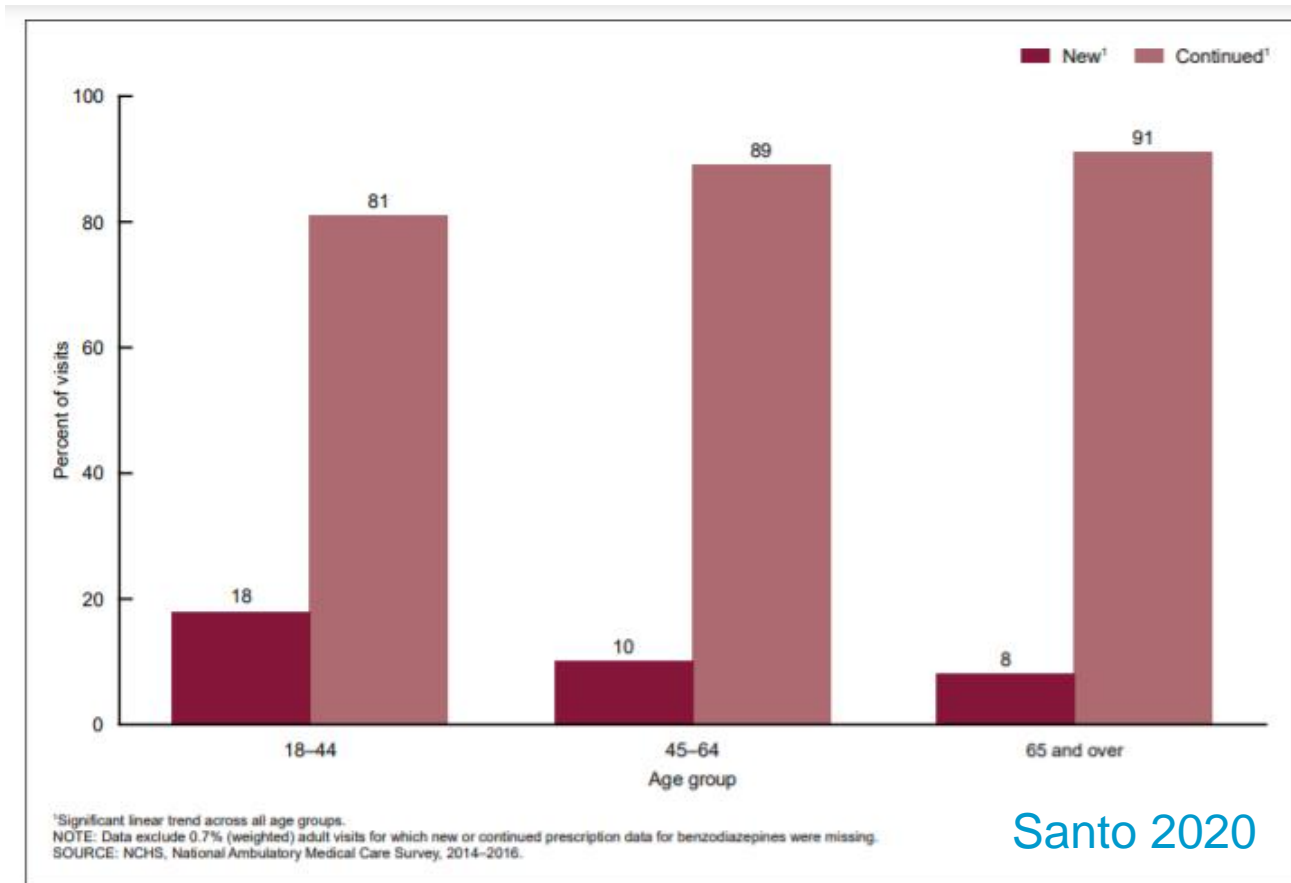


Figure 4. Prescription status for visits at which benzodiazepines were prescribed, by age: United States, 2014–2016



# FDA requiring Boxed Warning updated to improve safe use of benzodiazepine drug class

*Includes potential for abuse, addiction, and other serious risks*

## 09-23-2020 FDA Drug Safety Communication

The current prescribing information for benzodiazepines does not provide adequate warnings about these serious risks and harms associated with these medicines so they may be prescribed and used inappropriately.

Physical dependence can occur when benzodiazepines are taken steadily for several days to weeks, even as prescribed. Stopping them abruptly or reducing the dosage too quickly can result in withdrawal reactions, including seizures, which can be life-threatening.



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# Benzodiazepine Related Harms

- Suicidality and self injurious behavior: two to fourfold increased risk (Dodds 2017)
- Pulmonary conditions (COPD, OSA) (Kroll 2016)
- With aging: increased risk of falls, delirium, and cognitive impairment (Kroll 2016)
- Interdose withdrawal and rebound anxiety/insomnia (Ashton 2004)
- Substance misuse (17.1% BZ users) & substance use disorder (2% of BZ users) (Bianco 2018, NIDA 2018)

# Physical Dependence & Withdrawal

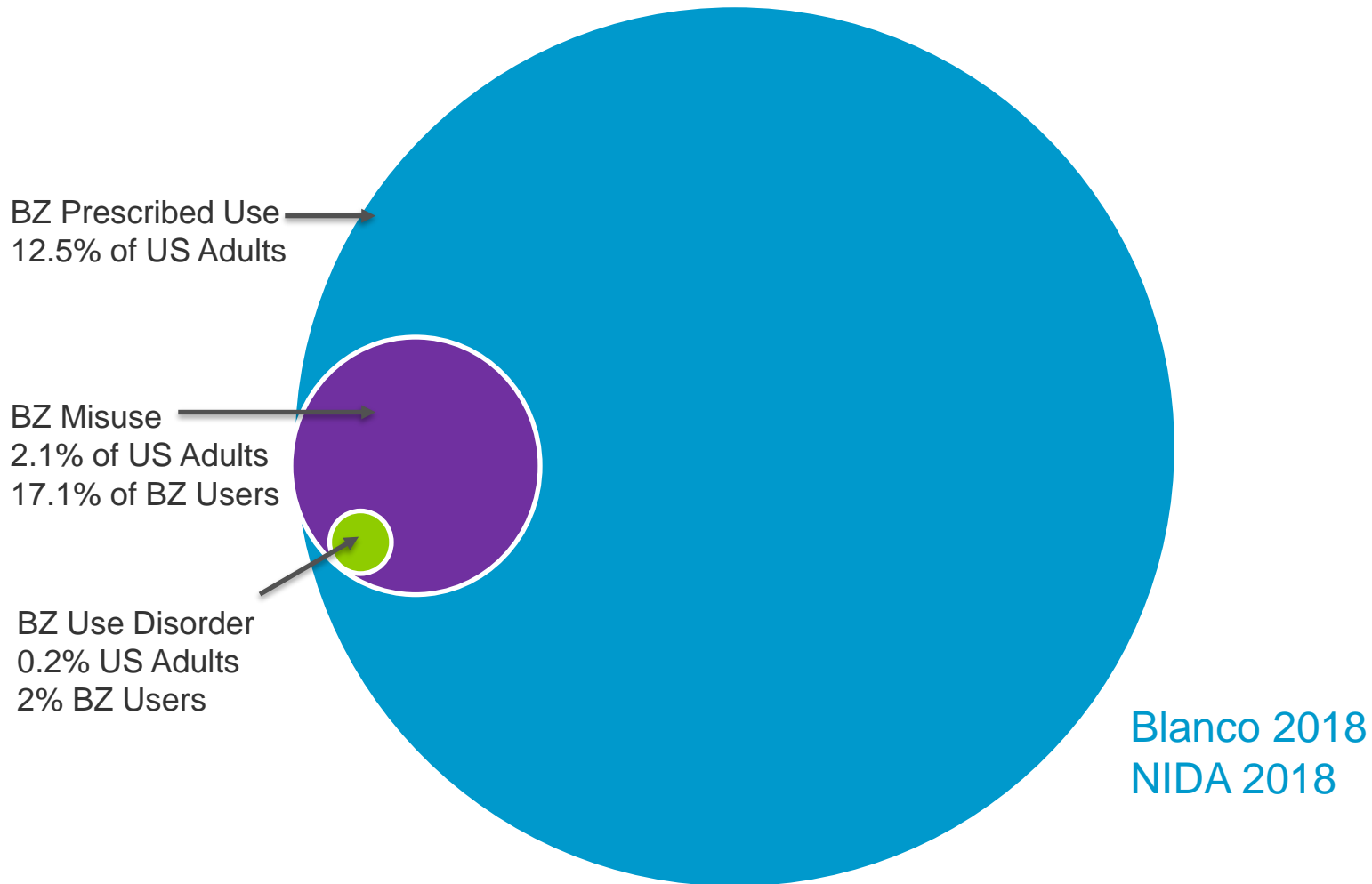
Physical dependence (tolerance and withdrawal) alone is expected with regular prescription use and by itself is NOT addiction.

Addiction (i.e. substance use disorder) must also have impact on one or more of the “**3Cs**”

- ✓ Loss of **Control** of use
- ✓ **Consequences**: social, occupational, recreational psychological, physical
- ✓ **Cravings**

# Research suggests benzodiazepine use is high while use disorder rates are low

October 18, 2018



# Risk of Chronic Use & Abrupt Cessation

1. Patient on clonazepam 1mg daily for anxiety and agitation. Over two years experienced worsening cognitive impairment. Referred to neurology for evaluation of dementia. Within months of tapering off clonazepam cognitive impairment reversed
2. Patient on clonazepam 1mg twice daily for 10 years for anxiety. Patient experienced significant irritability attributed to chronic neurological disorder. Clonazepam stopped abruptly due to prescription refill issue. Experienced acute and post-acute withdrawal and then irritability resolved within a few months.
3. Patient on lorazepam 1mg nightly for 5 years for sleep difficulty. Abruptly discontinued due to prescription being sent to the wrong pharmacy. Over a course of a few weeks, patient experienced acute insomnia, anxiety and agitation which led to a few ED visits. Primary care physician unwilling to continue prescription and said they needed to see a psychiatrist.



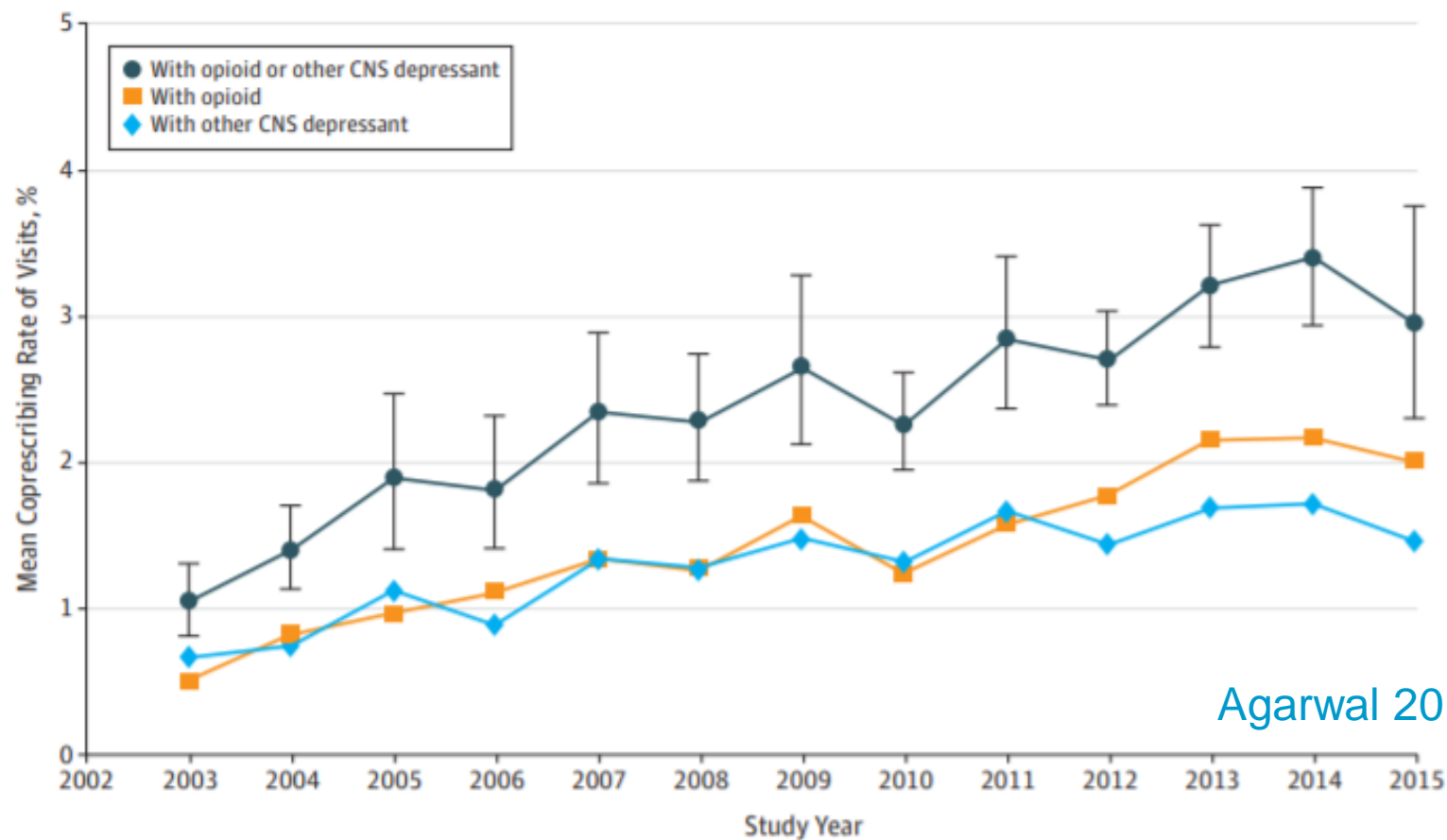
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# Deprescribing (Tapering)

- Depending on criteria used 58-100% experience withdrawal symptoms upon cessation after daily BZ use for >1 year (Rickels 1990)
- Studies report 10-44% of chronic BZ users experience moderate to severe protracted withdrawal symptoms upon cessation lasting months to years (Ashton 2004, Lugoboni 2014)
- Prescriber and the patient are on the same team: the patient's team!
- For the majority of patients it will be a marathon not a sprint. Proceed slowly and cautiously.
- For some patients risk of tapering > risk of continued BZ

Figure 3. Coprescribing Rate for Benzodiazepines With Opioids and Other Central Nervous System (CNS) Depressants

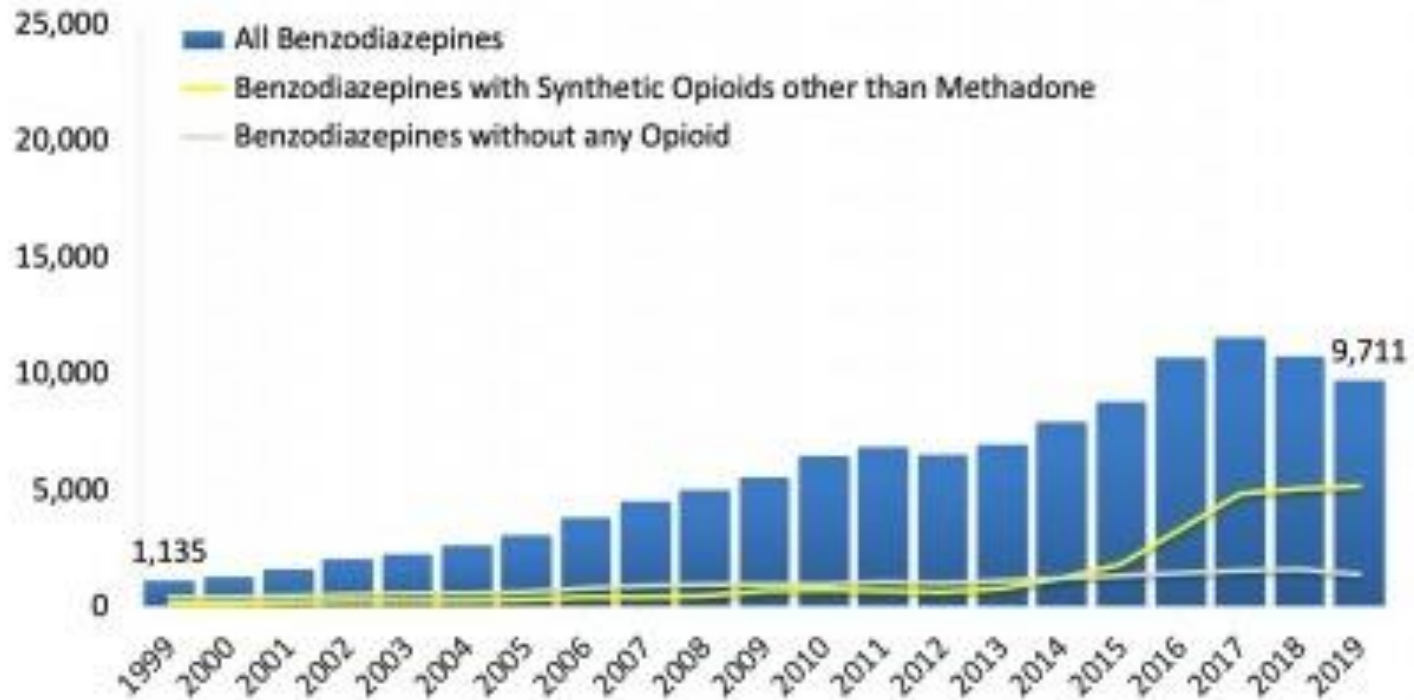


Agarwal 2019

35% of patients receiving a benzodiazepine script had a co-prescription for an opioid

# Overdose Deaths

**Figure 8. National Drug Overdose Deaths Involving Benzodiazepines\*, by Opioid Involvement, Number Among All Ages, 1999-2019**



NIDA 2021

\*Among deaths with drug overdose as the underlying cause, the benzodiazepine category was determined by the T402.2 ICD-10 multiple cause-of-death code. Source: Centers for Disease Control and Prevention, National Center for Health Statistics. Multiple Cause of Death 1999-2019 on CDC WONDER Online Database, released 12/2020.



# Overdose from BZ and Opioids

- Risk of opioid overdose increased five-fold during first 90 days of concurrent prescription with BZ (Hernandez 2018).
- 2016 FDA warns about serious risks and death when BZ and opioids combined
  - However, 2017 FDA urges caution withholding medication for addiction treatment (e.g. methadone and buprenorphine) due to BZ use
- If co-prescribed an opioid and a BZ, prescribe naloxone to patient and family/partner/roommate.
  - Opioid Safety and How to Use Naloxone  
<http://www.corxconsortium.org/wp-content/uploads/Naloxone-Brochure.pdf>

# Benzodiazepine Action Work Group Guidances

- Peer support
- Safe prescribing
  - Informed Consent
- Safe deprescribing



# Benzodiazepine Action Work Group

## Join Us!

- 1<sup>st</sup> Tuesday of the month 12pm-1pm
- Please contact us at [info@corxconsortium.org](mailto:info@corxconsortium.org) for more information or to volunteer to participate in the group's activities.
- 1 year: Peer Support Curriculum & Provider Education Curriculum
- 5 year: Funding and research for benzodiazepine deprescribing clinic



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# Resources & References



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# Q & A

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