DE-PRESCRIBING BENZOS, 2019

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DISCLOSURE/INVOLVEMENT

- DUR CMS Board Member (Community Representative)
- Presbyterian Health Insurance P&T Member (Community Representative)
- Nothing additional to disclose

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OBJECTIVES

- Identify new CMS Benzo Guidelines for use with or without concurrent opioid therapy
- Relate how these new Guidelines will affect current practice
- Describe the health care provider role in the implementation of Guidelines
- Identify case based scenarios where new Guidelines may affect patient care and resolve as necessary

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THE WHY BEHIND NEW GUIDELINES

- In 2017,alprazolam was the #1 prescription medication involved in overdose death in New Mexico
- Diazepam and clonazepam were amongst the top 10 prescription drugs involved in overdose death in New Mexico
- BZDs are the most widely prescribed psychotropic med for long term use (6 wks or more) despite lack of clinical evidence for long term efficacy
- Risk of overdose death increases with BZDs, CNS depressants, opioids, and alcohol (i.e."trinity" opioid, BZD, and barbiturate)
- In 2016, FDA issued boxed warning to limit quantity of BZDs and monitor for respiratory depression symptoms
- In 2016, CDC guidelines recommend avoiding use of BZDs with opioids

NM DOH bureau of vital records and health stat. data
https://www.fda.gov/Drugs/DrugSafety/ucm518473.htm
https://www.cdc.gov/drugoverdose/pdf/Guidelines_Factsheet-a.pdf

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PRESCRIPTIONS IN THE US

- 2013, 48 million alprazolam prescriptions dispensed
- Trending downwards in New Mexico (pdf)
- There are 4 conditions/disorders that have clinical evidence to support BZD use
  - Panic Disorder; Generalized Anxiety Disorder; Social Anxiety Disorder; Insomnia
    - Used in short durations (2-4 wks)
    - Used as 2nd line treatments (SSRIs or SNRIs are 1st line)
    - Co-prescribed with 1st line to allow for immediate relief while 1st line takes effect
    - Insomnia use should be short duration due to tolerance causing ineffectiveness
- British National Formulary advises "BZDs are indicated for short term relief of anxiety that is severe, disabling or subjecting the individual to unacceptable distress…"

Guina and Merrill 2018

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REDUCTION OF INAPPROPRIATE BENZODIAZEPINE PRESCRIPTIONS AMONG OLDER ADULTS THROUGH DIRECT PATIENT EDUCATION

THE EMPOWER CLUSTER RANDOMIZED TRIAL

- A total of 261 participants (86%) completed the 6-month follow-up
- Of the recipients in the intervention group, 62% initiated conversation about benzodiazepine therapy cessation with a physician and/or pharmacist
- At 6 months, 27% of the intervention group had discontinued benzodiazepine use compared with 5% of the control group
- Dose reduction occurred in an additional 11% (95%CI, 6%-16%)
- In multivariate sub-analyses, age greater than 80 years, sex, duration of use, indication for use, dose, previous attempt to taper, and concomitant polypharmacy (10 drugs or more per day) did not have a significant interaction effect with benzodiazepine therapy discontinuation

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TRUE OR FALSE

- There is no evidence/indication to use a BZD for PTSD?
  - True, according to the guidelines Published Dec, 2018
- BZDs can increase the incidence of developing PTSD and interfere with effective treatment
  - True, according to the guidelines Published Dec, 2018
- The Dept of Defense states it is acceptable to use BZDs when treating PTSD
  - False, according to the guidelines Published Dec, 2018
- Overlap of substance abuse disorders in PTSD patients create increased risk in use of BZDs
  - True, according to the guidelines Published Dec, 2018

Guina and Merrill 2018
US Dept of Veterans Affairs 2014

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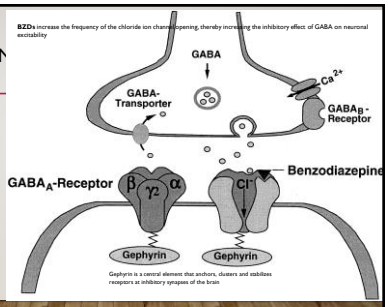
BZD DEPENDEN

- https://www.youtube.com/watch?v=42HudePhc8g
- Enhance action of GABA on receptors causing anxiolytic and sedative effects
- Various forms differ in ADME, active/inactive metabolites, duration of activity, etc.
  - Short acting: alprazolam, midazolam, triazolam
  - Intermediate acting: oxazepam, lorazepam, temazepam
  - Long acting diazepam, clonazepam, clorazepate, chlordiazepoxide, flurazepam
  - Z drugs: zaleplon, zolpidem, eszopiclone



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GOALS OF NEW BENZODIAZEPINE (BZD) GUIDELINES FOR NEW MEXICO

1) To provide recommendations on appropriate use of BZDs, including evidence based clinical indications & durations of use
2) To enhance understanding of risk of BZDs in the context of combination therapy, especially with other sedatives
3) To provide advice on how to identify/manage use, and how to safely discontinue BZDs when indicated

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NEW GUIDELINES AFFECTING CURRENT PRACTICE

BEFORE

- Before initiating BZD therapy:
  1) all sedatives should be prescribed by one provider only or coordination between two providers and encourage the patient to use one pharmacy
  2) Provider must counsel on risks of sedation/dependence and discuss strategy for taper after 6 wks of therapy & ensure risks are understood
  3) Non BZDs should be offered as first line medication
  4) PMP must be reviewed before writing a new script for BZD for more than 4 days, then every 3 months for ongoing prescriptions
  5) Consider using treatment contracts and periodic urine toxicology testing

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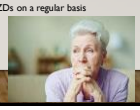
NEW GUIDELINES AFFECTING CURRENT PRACTICE

- Patients age 65 years and over:
  - BZDs and Z drugs are listed on the Beers criteria and should be avoided in elderly
  - This age group is:
    - A) vulnerable to adverse effects and metabolic rates decline with age
    - B) more susceptible to CNS depression and cognitive impairment
    - C) may develop state of confusion an ataxia leading to falls/hip fractures
    - D) may develop drug interactions with other medications
    - E) are at risk of permanent cognitive impairment when using high doses of BZDs on a regular basis



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NEW GUIDELINES AFFECTING CURRENT PRACTICE

- Long term use:
  - BZD or Z drugs are NOT recommended for long term use (longer than 6 weeks), unless exceptional circumstances (i.e. terminal illness)
  - Lack of evidence to support long term use for any mental health condition or insomnia
  - Physical dependence can occur in >12 wks of use, especially with higher doses and short acting formulations
- Multiple BZD concurrent use:
  - Lack of clinical evidence nor treatment guidelines to support using more than one form of BZD at a time

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NEW GUIDELINES AFFECTING CURRENT PRACTICE

- Treating patients on methadone/buprenorphine or opioids:
- One study found, 47% of patients in methadone treatment programs has a history of BZD use
- Another review found, 18%-50% in methadone treatment programs were dependent on BZDs
  - 1) Follow American Association for Tx of Opioid Dependence Guidelines (2018)
  - 2) Check PMP regularly as required by licensing Board (Methadone treatment program use not reported)
  - 3) Communication with treatment programs
  - 4) Educate patient on risks
  - 5) Make efforts to decrease/replace BZDs with safer treatments
  - 6) Develop safety plan
  - 7) Address BZD misuse if occurs

Chen et al 2011
Williams 2014

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NEW GUIDELINES AFFECTING CURRENT PRACTICE

- Management of chronic BZD/Z drug patients:
  - A) Use should be for no longer than 6 wks
  - B) Effort made to decrease and/or discontinue BZD after 6 wks
    - I) Conduct proper assessment to include accurate diagnosis, review 1st and 2nd line treatment information
    - II) Assess effectiveness with focus on functioning
    - III) Assess harms from the medication
  - C) Discontinuation should include repeated education, support counseling, cognitive behavioral therapies

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PROVIDER ROLE IN THE IMPLEMENTATION OF GUIDELINES

- Guidelines clearly state to avoid BZD or use with great caution in:
  1) Active/history of substance abuse
  2) Pregnancy/risk of pregnancy
  3) Treatment with opioids for chronic pain/opioid use disorder
  4) Mental health problems that may be aggravated by BZDs
     1) Fibromyalgia, traumatic brain injury, developmental disability, chronic fatigue syndrome, somatization disorders, depression, bipolar (except for urgent sedation in acute mania), attention deficit disorders, kleptomania, other impulse disorders
  5) Borderline personality disorders
  6) Cardiopulmonary disorders
     1) Asthma, sleep apnea, COPD, CHF, etc.

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PROVIDER ROLE IN THE IMPLEMENTATION OF GUIDELINES IN ASSESSING DRUG RELATED BEHAVIOR

- I) Being more interested in BZDs (especially short acting) than in other meds or aspects of treatment
- 2) Taking doses larger than those prescribed or increasing dosage without consultation
- 3) Insisting that higher doses are needed
- 4) Resisting urine drug screens or referrals to specialists and other aspects of treatment
- 5) Resisting changes to non BZD therapy
- 6) Repeated losing meds/scripts or seeking early refills

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PROVIDER ROLE IN THE IMPLEMENTATION OF GUIDELINES IN ASSESSING DRUG RELATED BEHAVIOR

- 7) Making multiple phone calls about prescriptions
- 8) Attempting unscheduled visits, typically after office hours
- 9) Appearing sedated
- 10) Misusing alcohol or illicit drugs
- 11) Showing deteriorating functioning and beginning to experiencing adverse effects from meds
- 12) Injecting (track marks) or snorting oral formulations
- 13) Obtaining medications illegally (unlicensed pharmacists, street dealers, forged scripts)

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THE WHY BEHIND THE SLOW TAPER OF BZDS

- Withdrawal symptoms (tremors, seizures, delirium, anxiety, restlessness, irritability, agitation, insomnia, muscle tension, weakness, aches/pains, blurred vision, tachycardia, nausea, sweating, runny nose, hypersensitivities, psychosis, hallucinations, paranoid delusions, and tinnitus) lasting <2 wks
- Education, support, and psychotherapy may be helpful in withdrawal symptoms
- Slow tapers minimize withdrawal symptoms
- Some medications may offer comfort to the withdrawal symptoms above including:
  - Carbamazepine, propranolol, clonidine, and analgesics

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TAPERING BZD GUIDELINE RECOMMENDATIONS

- 1) Based on assessment, have appropriate replacement treatment in place for primary behavioral health diagnosis
- 2) Provide as needed, or refer for supportive psychotherapy during taper process
- 3) Educate and share a clear plan for the taper
- 4) Reduction of 25% every 2-3 wks, with if needed, slower decrease (12.5%) for the last 2 wks
- 5) Offer "rescue" dose, one dose per day to use at their discretion, providing reassurance and sense of control
- 6) Higher potency patients/short acting BZD patients slower taper may be needed or switching to long acting BZD during taper may be needed to ease withdrawal
- 7) Discontinuation of Z drugs is less studied than discontinuation of BZDs, but same approach is recommended

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DIAZEPAM MG EQUIVALENT (DME) TABLE

	Brand Name	Half Life	Dose equivalent to 5mg diazepam
Alprazolam	Xanax	12-15 hours	0.25-0.5mg
Chloridiazepoxide	Librium	5-30 hours	15mg
Clonazepam	Klonopin	18-50 hours	0.25-0.5mg
Diazepam	Valium	20-80 hours	5mg
Lorazepam	Ativan	10-20 hours	0.5-1mg
Temazepam	Restoril	3.5-18.5 hours	10mg
Triazolam	Halcion	1.5-5.5 hours	0.25mg

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DIAZEPAM MG EQUIVALENT (DME) TABLE

	Brand Name	Half Life	Dose equivalent to 5mg diazepam
Z Drugs			
Eszopiclone	Lunesta	6-9 hours	2mg
Zaleplon	Sonata	1 hour	10mg
Zolpidem	Ambien	1.4-4.5 hours	10mg

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CHECKLIST (A SUMMARY OF THE GUIDELINES DISCUSSED TODAY)

- HANDOUT FOR YOUR EASE OF USE

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GO OR NO GO!

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SCENARIO

- 80 y.o. male with a PMH of HTN presents to the clinic today with a chief complaint of anxiety. He is currently taking zolpidem 10mg QHS, lisinopril 40mg daily and aspirin 81mg daily. His score on the HAM-A is 19 (Moderate Anxiety) and his wife is concerned that his anxiety is affecting his quality of life. He has never received treatment for anxiety. He currently only sees one other provider.
- Is the Benzo a Go?

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NO GO!

- First line treatments haven't been tried/optimized:
  - SSRI, Buspirone, Etc.
  - Currently taking other CNS drug

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SCENARIO

- A 60 y.o. female presents to the clinic today with reports of multiple panic attacks over the past several months. Her PMH is significant for COPD, arthritis and diabetes. She is starting cognitive behavioral therapy soon but is worried that she will lose her job if she continues to have panic attacks. She has had an in-depth psychological work-up and has previously failed therapy with an SSRI and beta-blocker.
- Is the Benzo a Go?

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NO GO!

- COPD is a contraindication for Benzo therapy

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SCENARIO

- A 45 y.o. female presents to the clinic for a follow-up appointment after starting a benzodiazepine for social anxiety disorder. She began taking alprazolam 0.25mg TID and sertraline 25mg once daily about 6 weeks ago. She reports that she has been able to resume her ADL's and has now been excelling at work.
- Is the Benzo a Go?

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GO!

- Avoid abrupt discontinuation of benzodiazepines → Can lead to withdraw
- Decrease dose by 0.5mg every 3 days or as slow as 0.25mg per week

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2019 MEDICARE PART D OPIOID POLICIES; PHARMACIST ROLE

- 7 day supply limit for opioid naïve patients; provide info to the plan for override if patient has exclusion or is not opioid naïve (hard edit) (copays should be prorated)
- Opioid of 90 MME; provide info to the plan for override if prescriber has been consulted and patient is stable on therapy (soft edit)
- Opioid of 200 MME or more (hard edit); provide info to the plan for override if patient is stable on therapy
- **Concurrent opioid/BZD therapy (soft edit); conduct safety review and provide info to the plan for override if patient is stable on therapy**
- When an opioid safety edit cannot be resolved at the pharmacy, the pharmacist must give the patient a copy of the Medicare Prescription Drug Coverage and Your Rights document

https://www.primetherapeutics.com/content/dam/corporate/Documents/Resources/Pharmacists/MedicareResources/Additional/MedDRights.pdf

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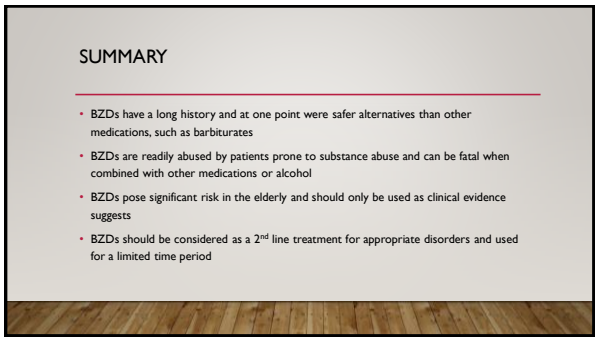
SUMMARY
• BZDs have a long history and at one point were safer alternatives than other medications, such as barbiturates
• BZDs are readily abused by patients prone to substance abuse and can be fatal when combined with other medications or alcohol
• BZDs pose significant risk in the elderly and should only be used as clinical evidence suggests
• BZDs should be considered as a 2nd line treatment for appropriate disorders and used for a limited time period

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