ACCEPT

Addiction & Co-morbid Conditions: Enhancing Prevention & Therapeutics

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For attendance, purposes please text the following code: QODTES to 608-260-7097

Session Date: Friday, March 17, 2023

Didactic Topic and Presenter:
Helping People with SUD's and MH Disorders: Important Factors in Diagnosis and Treatment

Dean Krahn, MD
Content Experts:
Ritu Bhatnagar, MD; CRC; Sheila M. Weix, MSN, RN, CARN, Joesph Galey, CPS

- 12:15 PM: Attendance text-in – Introductions
- 12:25 PM: Case Presentation and Discussion
  - Presenter: Ezra Lyon, MD - *Associate Medical Director for Integrative Addiction Treatment, Family Medicine with Obstetrics, ThedaCare Physicians-Waupaca*
- 1 PM: Didactic Presentation
  - Presenter: Dean Krahn, MD
- 1:15 PM End of Session

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Interprofessional Continuing Education Partnership
UNIVERSITY OF WISCONSIN-MADISON
School of Medicine and Public Health
School of Nursing
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Project ECHO
University of Wisconsin

ECHO ACCEPT
Addiction & Co-morbid Conditions: Enhancing Prevention & Therapeutics
2022-2024
Helping People with SUD's and MH Disorders: Important Factors in Diagnosis and Treatment
3/17/23
Didactic Presenter: Dean Krahn, MD
Case Presenter: Ezra Lyon, MD

Provided by the University of Wisconsin–Madison Interprofessional Continuing Education Partnership (ICEP)

Intended Audience:

Nurses, Nurse Practitioners, Pharmacists, Physicians, Physician Assistants, Pharmacy Technicians, Psychologists, Social Workers, Patient/Caregivers, Students

Objectives:

As a result of this educational regularly scheduled series, learners as members of the healthcare team will be able to:

1. Analyze the rate of co-occurring substance use and mental health disorders found in studies of general and clinical populations.
2. Explain the mechanisms proposed in the etiology of these co-occurring states.
3. Identify people with the combinations of co-occurring disorders that are particularly important in the development of specific treatment plans.

implications

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Name	Role	Financial Relationship Disclosures	Discussion of Unlabeled/Unapproved uses of drugs/devices in presentation?	COI completion date
Randall Brown	RSS Chair	Usona Institute (Grant / Contract), multi-disciplinary association for psychedelic studies (Grant / Contract)	Yes	1/30/2023
Nada Rashid	RSS Coordinator	No relevant financial relationships to disclose	No	1/31/2023
Kathleen Maher	RSS Coordinator	No relevant financial relationships to disclose	No	1/30/2023
Ritu Bhatnagar	Planner	No relevant financial relationships to disclose	Yes	1/29/2023
Paul Hutson	Planner	No relevant financial relationships to disclose	Yes	1/28/2023
Susan Mindock	Planner	No relevant financial relationships to disclose	No	1/31/2023
Sheila Weix	Planner	No relevant financial relationships to disclose	No	2/3/2023
Kellene Eagen	Planner	No relevant financial relationships to disclose	No	1/27/2023
Joseph Galey	Planner	No relevant financial relationships to disclose	Yes	1/27/2023

Dean Krahn	Presenter	No relevant financial relationships to disclose	Yes	2/5/2023
Ezra Lyon	Presenter	No relevant financial relationships to disclose	Yes	3/10/2023

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Helping People With SUD's AND MH Disorders

Important Factors in Diagnosis and Treatment

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Overview

- How frequently do people experience co-occurring mental health and substance use disorders?
  - In the general population
  - In clinical populations
- How can we understand the mechanisms of co-occurrence of these disorders?
  - Neurobiological overlap
  - Common risk factors
  - Symptoms triggered by substance use, withdrawal, intoxication and symptoms which patients cope with via substance use
- How does this knowledge allow us to better evaluate and treat people who are experiencing these co-occurring disorders?
- Discussion of your experiences, hypotheses, questions with this group of people.

- There are two major recurring studies of appropriate groups that allow estimates of prevalence of substance use and MH disorders in the US population
  - NESARC and NSDUH
  - NSDUH revealed that in 2018
    - 57.8 million Americans (>18) had a mental disorder and/or SUD
    - 47.6 million (19.1% of Americans over 18) had MH disorder
    - 19.3 million (7.8%) had SUD (of these, 38% had DUD, 74.5% had AUD, and 13% had both AUD and DUD
    - 3.7% of Americans had both SUD and MH Disorder (ie 9.2 million)

- NESARC in 2012-2013 revealed that:
  - 9.9% of adult Americans have lifetime history of DUD and 3.9% have a 12-month history of DUD and 29% have lifetime history of AUD with 13.9% having a 12-month history of AUD.
  - Significant associations of 12-month DUD with several types of MH disorder were found. 12-month DUD was significantly associated with increased rates of Major Depression, dysthymia, bipolar I, PTSD, and antisocial, borderline, and schizotypal personality disorders. Strongest relationships were with bipolar, PTSD, and the personality disorders. Lifetime DUD was also related to GAD, panic, and social phobia.
  - 12 month and lifetime AUD was related most strongly to other SUD's, MDD, bipolar I, and antisocial and borderline personality disorders. DUD's were by far the most strongly related to AUD, while PTSD, antisocial PD, and borderline PD were the most strongly related MH disorders to AUD.

- If one looks at the rate of SUD's in people identified as having a MH disorder, these are the findings:
  - For people with any mood disorder, the ECA revealed a 32% prevalence of a co-occurring SUD
  - But those with a lifetime hx of Major Depression had 16.5% rate of AUD and an 18% rate of DUD (about 25% overall SUD) but those with bipolar d/o had a 56% prevalence of SUD
    - In the National Comorbidity Study, data shows that people with depression were twice as likely to have SUD compared to those without depression, while those people with bipolar disorder were 7X as likely to have an SUD than those w/o bipolar.
    - Note, however, that if one is looking at people presenting for treatment for AUD, you will find a 20-67% rate of depression and a 6-8% with bipolar. Somewhat higher rates of these disorders for those seeking tx for stim d/o's
- Much like mood disorders, there are specific anxiety disorders that are more highly connected to addiction (eg social anxiety, PTSD (not really an anxiety d/o but can present that way))

- The problem of perspective on these co-occurrences that depends on what kind of clinic setting you work in
  - If you are part of a psychiatric setting, will get more co-occurring disorders
  - If you are part of a long-standing addiction program with hx of being reliant on 12 step treatment, might get less (depending on lots of related variables)
  - ETC!!! Need to learn your own clinical population

- Both MH disorders and Substance Use Disorders involve abnormalities in function of prefrontal cortex, amygdala, and ventral and dorsal basal ganglia.
  - In SUD, see changes in reward systems and "habit" systems in the basal ganglia; see interactions of the stress/anxiety system involving amygdala and use of substances/withdrawal from substances; see changes in prefrontal cortex leading to increased impulsivity and inability to regulate use of substances
  - In MH disorders, see changes in ability to experience pleasure/reward (ie anhedonia) related to basal ganglia dysfunction; see interactions mediated by amygdala between mood/thinking and stress; and see changes in prefrontal cortex leading to difficulty in thinking and in regulating behavior
  - So, it would be surprising if there wasn't co-occurrence and interactions

- Similar genetic and environmental risk factors
  - ACE's
  - Other trauma
  - Social determinants of disorders
  - Genetic vulnerability

- Clinical hints re: treatment
  - Thorough history taking from person who is using drugs and others who know that person is critical
    - Need to understand longitudinal relationships of the clinical syndromes
    - Need to recognize syndromes induced by repeated withdrawals or intoxications
    - Need to identify comorbid MH problems that occur when the person has had a verified extended sobriety or that occurred prior to use/misuse of substances.

- Need to identify disorders that require specific treatment not likely to respond to the “one-size, one-type fits all SSRI”
  - Bipolar might well get worse over time with SSRI even though an early initial response might look very good
  - Social anxiety disorder requires specific psychotherapy and might not require meds at all
  - PTSD clearly requires specific expert psychotherapy in addition to medications and addiction treatment (? Role of prazosin, SSRI’s, etc)
  - ADHD: treatment often helpful but brings up the process of using somewhat “addictive” meds in tx of addiction
    - Important to note that studies support the use of stimulants for people misusing cocaine who have ADHD—but it is hard work and requires lots of education of patient and all other concerned parties in family/friend group

- Treatment must be integrated, not sequential
  - Telling people with PTSD who have often been using substances to cope with aspects of PTSD that they need to stop using for X amount of time prior to getting tx for PTSD is often a reason for treatment drop-out.
    - Might need to be creative in how to work on both issues at once
  - CBT approaches can be worked into the treatment plan of nearly every person with co-occurring disorders as there are forms of CBT for problems with mood, anxiety, alcohol, other substances. Using these skills across problems and across other parts of one's life can be a real boon to recovery/success in life.

- In summary,
  - Co-occurring disorders (SUD + MH) are frequent and all people involved in treatment of people who have problems due to substance use should be able to recognize and arrange or provide integrated treatment for these disorders
  - Some MH disorders are more tightly connected to problems with SUD than others and require greater specificity in treatment planning.
  - People seeking treatment often don't "want" to have multiple diagnoses, but one must become adept at creating hope through the appropriate treatment of all the problems, not just some.
- Thanks/comments and questions???

- References:

- Nunes, EV & Weiss R. Co-occurring Addiction and Affective Disorders in Principles of Addiction Medicine 4th edition, Ch. 84, pages 1151-1181, 2009 (with additional material from Dr Nunes' talk on Antidepressant and Antianxiety Pharmacotherapy with Co-Occurring SUD in the Advanced Addiction Psychopharmacology course 2021
- NESARC data: Grant BF, et al. Epidemiology of DSM-5 Drug Use Disorder: Results from the National Epidemiological Survey on Alcohol and Related Conditions-III; JAMA Psychiatry.2016; 73(1):39-47 and Grant BF, et al. Epidemiology of DSM-5 Alcohol Use Disorder: Results from the National Epidemiological Survey on Alcohol and Related Conditions III, 2016

- References (continued)
- Quello SB et al., Mood Disorders and Substance Use Disorder: A Complex Comorbidities. SciPract Perspective 2005 Dec; 3(1):13-21
- Smith JP et al., Anxiety and Substance Use Disorders: A Review. Psychiatric Times. 2008 October; 25(10):19-23
- Brady KT, Post-traumatic Stress Disorder and Comorbidity:Recognizing the Many Faces of PTSD. J Clin Psychiatry 1997; 58(suppl 9); 12-15
- Zulauf CA et al., The Complicated Relationship Between Attention Deficity/Hyperactivity Disorder and SUD's. Curr Psychiatry Rep. 2014 March; 16(3): 436.

Conclusions

DSM-5 Substance Use Disorder ("Addiction")

- Tolerance
- Withdrawal

} **Physical Dependence ≠ Use Disorder**

- Larger amts/longer periods than intended
- Persistent desire/failed attempts to quit/control use
- Much time obtaining/using/recovering
- Important activities sacrificed
- Continued use despite known adverse effects
- Failure to fulfill major obligations
- Recurrent hazardous use
- Craving
- Ongoing use despite interpersonal problems

2–3 = mild
4–5 = moderate
≥ 6 = severe

Project ECHO®
University of Wisconsin

Phenibut Withdrawal

Ezra Lyon MD

Family Medicine with Obstetrics, ThedaCare-Waupaca

Associate Medical Director for Integrative Addiction Treatment, ThedaCare

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Project ECHO University of Wisconsin

Case Introduction

- JM is a 33 y/o woman with opioid use disorder, anxiety, depression, history of hep C who has been using phenibut for 2 years for anxiety and has been unable to stop due to withdrawals.

- What is the best way to treat patients with a phenibut use disorder?

Medical & Behavioral Health Diagnosis:	Current Medications:
• Opioid use disorder, in sustained remission, on buprenorphine since 7/2021 • Major depression, recurrent, in remission • Generalized anxiety disorder • Panic disorder with agoraphobia • Insomnia • Neuropathic pain of the left leg, 2/2 mononeuropathy of L deep peroneal nerve from overdose 2018 • History of hepatitis C x 2, with sustained virologic response • History of rhabdomyolysis	• Buprenorphine tablets 4-8 mg daily (prescribed 8-12 mg) • Gabapentin 600 mg TID PRN for anxiety and neuropathic pain, taking every 4 days • Paroxetine 30 mg daily, taking every 4 days • Zolpidem 5 mg nightly PRN • Etonogestrel (Nexplanon) implant

Opioid Use

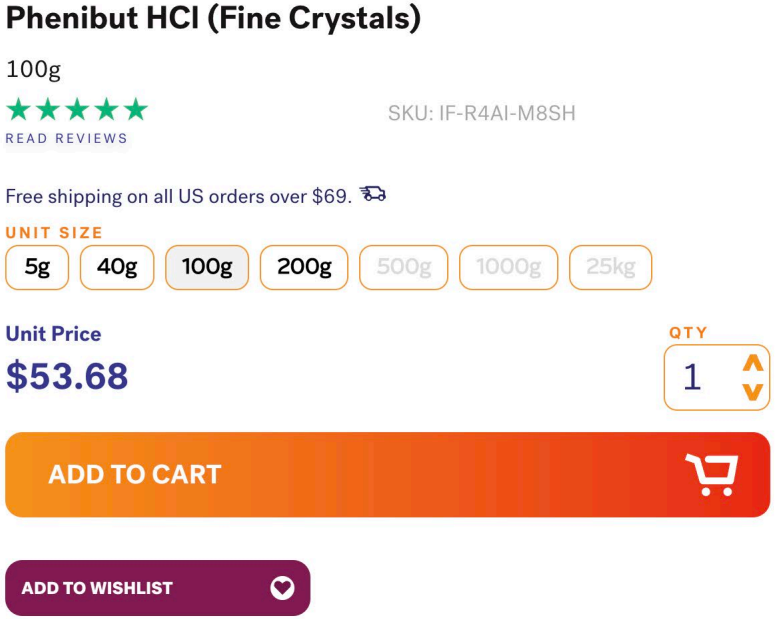
- History: Started using opioids after a car accident at age 19 in 2008. Used heroin daily from 2013 until her first overdose in 2016 and then for 3-6 months at a time since then until starting drug court in 2020 and buprenorphine in 2021.
- Consequences of Substance Use:
  - Social/occupational/educational: incarcerated
  - Physical (including evidence of tolerance/withdrawal): overdosed x 3, hospitalized for rhabdomyolysis and L foot drop from L deep peroneal neuropathy after overdose in 2018
- Past treatments: IM naltrexone

Phenibut Use

- History: Started buying phenibut powder online in 2020 to help with anxiety. Taking 1-2 scoops (1-2 g) daily.
- Consequences of Substance Use:
  - Social/occupational/educational: None except when withdrawing. Phenibut helps with the anxiety of working with co-workers.
  - Physical (including evidence of tolerance/withdrawal):
  - Has tried to cut down or stop multiple times but has withdrawal symptoms after 2 days. First has severe anxiety then tremors and agitation. Lights were harsh, noises were loud and frightening and she would feel a sense of impending doom. Has tried taking paroxetine or gabapentin to help with the withdrawal. Gabapentin helps a little but she goes back to taking phenibut after 3-4 days.
  - Took 2 weeks off between leaving a factory job and starting as a CNA at a local nursing home to quit phenibut. Tried to quit twice during the 2 weeks but could not so called me for assistance.
- Past treatments: self-treatment with gabapentin or paroxetine

Phenibut

- GABA agonist (beta-phenyl-GABA) developed in the 1960s in the Soviet Union as an anxiolytic and sedative
- Prescribed in former Soviet Union (Russia, Belarus, Kazakhstan)
- Not regulated in the United States but easily available online



Phenibut

HOME / CALM & STRESS RELIEF / PHENIBUT HCL (FINE CRYSTALS) - F

PRODUCT DESCRIPTION —

Phenibut is a chemical compound that is not approved for food, drug, or veterinary uses by any US regulatory agency and is not considered a dietary supplement by any regulatory bodies nor by supplement industry language. Phenibut is a zwitterionic acid" or '

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Phenibut pharmacology

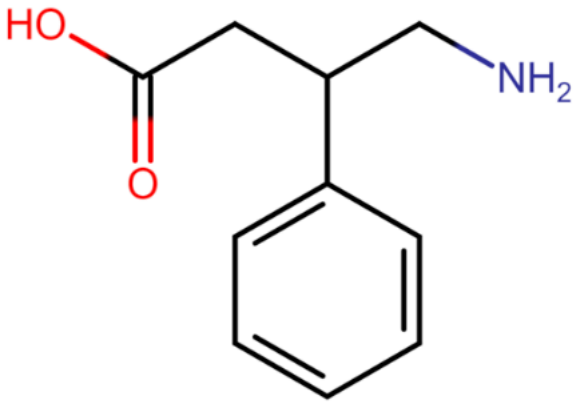
- $GABA_B$ full agonist
- $\alpha_2\delta$-subunit of voltage-dependent calcium channel agonist (gabapentioid)

Phenibut and analogues at biological targets[16]

Compound	$\alpha_2\delta$	$GABA_B$
Phenibut	ND	177
(*R*)-Phenibut	23	92
(*S*)-Phenibut	39	>1,000
Baclofen	156	6
Gabapentin	0.05	>1,000
Values are K_i (μM) in rat brain.		

Zvejniece et al. 2015, table from Wikipedia

Phenibut pharmacology



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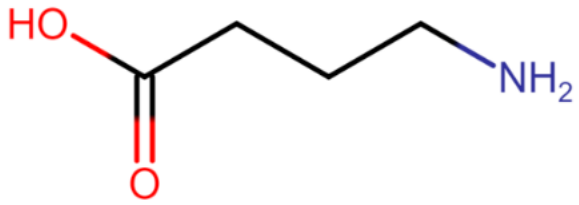
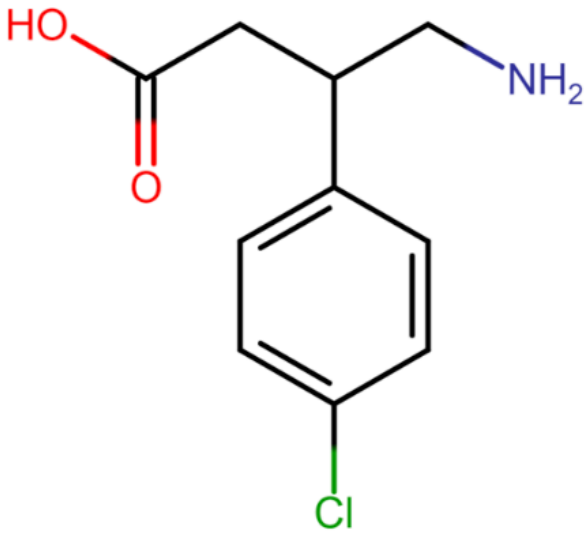
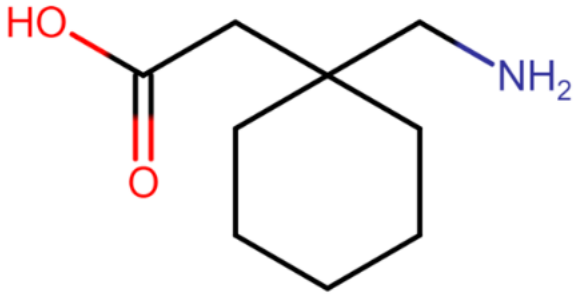


GABA



Baclofen



Gabapentin

Figures from Wikipedia

Social History:	Family History:
• Social Factors/History: Lives with her boyfriend in a supportive relationship. History of intimate partner violence in past. Worked as a CNA and then in a window factory. One son, age 8, who lives with patient's mother. • Education/Literacy: Finished high school and CNA program • Income source: Work. Not currently employed	• Brother with anxiety • Father with hypertension • Cancer, heart disease and multiple sclerosis in grandparents • No other history of substance use disorders

Patient strengths & protective factors:	Risk factors:
• Supportive home life and current relationship • Supportive family • Opioid use disorder in sustained remission • Established in primary care medical home • Depression and pain well controlled	• Poorly treated anxiety with strong component of social anxiety • History of opioid use disorder and chronic neuropathic pain from peroneal neuropathy • Between jobs • No health insurance – had stopped Medicaid due to a misunderstanding when switching from buprenorphine-naloxone to buprenorphine

Labs

- None
- Last urine drug screen 8/2022 positive only for buprenorphine

Patient Goals & Motivations for Treatment

- To be off phenibut “because it’s controlling my life”
- Better control of anxiety so she can leave the house and go to work

Proposed Diagnoses

- Phenibut use disorder, moderate
  - Meets 5 of the DSM-V criteria: tolerance, withdrawal, cravings, persistent desire to stop use, use for longer period than intended
  - No clear effect on employment, relationships or physical health
  - Positive effects of phenibut on anxiety, mood and pain
- Generalized anxiety disorder
- Panic disorder with agoraphobia
- Social anxiety disorder

Treatment Plan

- Called UW Addiction Consultant Provider Hotline and got help from Dr. Salisbury-Afshar and Dr. Brown
- Decrease phenibut dose by ¼ every 2 days
- Start gabapentin 600 mg TID
- Start baclofen 10 mg TID (down from Dr. Brown's recommendation of 20 mg TID due to concern for sedation from patient and me)
- Self score withdrawal using Short Alcohol Withdrawal Scale (SAWS) and call if SAWS>12 to consider admission

SAWS

Short Alcohol Withdrawal Scale (SAWS)

Item	*None (0 points)*	*Mild (1 point)*	*Moderate (2 points)*	*Severe (3 points)*
Anxious				
Feeling confused				
Restless				
Miserable				
Problems with memory				
Tremor (shakes)				
Nausea				
Heart pounding				
Sleep disturbance				
Sweating				

Tool to assess the severity of alcohol withdrawal. Patients indicate how they have felt in the previous 24 hours. Mild withdrawal < 12 points; moderate to severe withdrawal ≥ 12 points.

Adapted with permission from Elholm B, Larsen K, Hornnes N, Zierau F, Becker U. A psychometric validation of the Short Alcohol Withdrawal Scale (SAWS). Alcohol Alcohol. 2010;45(4):362.

Treatment continued

- Office visit at 5 days: Cut back to ¾ of her phenibut dose. Somewhat in control and not in full panic mode. Good support from her mother.
- “I want to take my Paxil so bad because it’s been a couple of days but the thing is I can’t mix my Paxil with the phenibut [because] it literally makes my brain shake for hours on end, then I get the ringing in the ears and the pressure”
- Increase baclofen to 20 mg TID, buprenorphine to 12 mg daily
- Stop paroxetine (hadn’t taken in 3 days), start escitalopram 5 mg daily

Treatment continued

- Video visit at 8 days: Cut back to 1/4 of her phenibut dose.
- Withdrawals improved so stopped scoring her symptoms
- Didn't go up to baclofen 20 mg TID. After taking first dose of baclofen 20 mg, felt oversedated, fell asleep with a lit cigarette in her hand and burned holes in her sheets
- Tried to stop gabapentin but decided to continue it
- Hypnic jerks when going to sleep, patient stopped escitalopram and then restart 1 day later to help with paroxetine withdrawals
- Reapplied for BadgerCare

Treatment continued

- Video visit at 13 days: Off phenibut for 4 days.
- No withdrawals
- Went up to baclofen 15 mg TID and then 20 mg TID
- Doesn’t feel euphoria but doesn’t feel like “jumping out of her skin”
- Taking escitalopram 5 mg daily for the last 4 days.
- Threw away phenibut container while on the phone
- Plan to taper off baclofen by 15 mg per week (20 mg TID -> 15 mg TID -> 10 mg TID -> 5 mg TID -> stop)

Treatment continued

- Video visit at 25 days
- Severe worsening of anxiety with starting new job at Amazon warehouse
- Tapering off baclofen – on baclofen 5 mg TID
- Started PRN clonazepam 0.5 mg daily and PRN hydroxyzine
- Increase buprenorphine to 12 mg daily
- Continue gabapentin 600 mg TID

Treatment continued

- Video visit at 45 days
- Off baclofen
- Taking clonazepam 0.5 mg daily
- Continue gabapentin 600 mg TID
- Continue escitalopram 10 mg daily

Discussion:

- What is the best way to treat patients with a phenibut use disorder?

DSM-5 Substance Use Disorder ("Addiction")

- Tolerance
- Withdrawal

} **Physical Dependence ≠ Use Disorder**

- Larger amts/longer periods than intended
- Persistent desire/failed attempts to quit/control use
- Much time obtaining/using/recovering
- Important activities sacrificed
- Continued use despite known adverse effects
- Failure to fulfill major obligations
- Recurrent hazardous use
- Craving
- Ongoing use despite interpersonal problems

2-3 = mild
4-5 = moderate
≥ 6 = severe

By initialing here _____ you have acknowledged that Project ECHO case consultations do not create or otherwise establish a provider-patient relationship between any ECHO clinician and any patient whose case is being presented in a teleECHO clinic.