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Rethinking Withdrawal Management: Expanding the Use of Outpatient Settings

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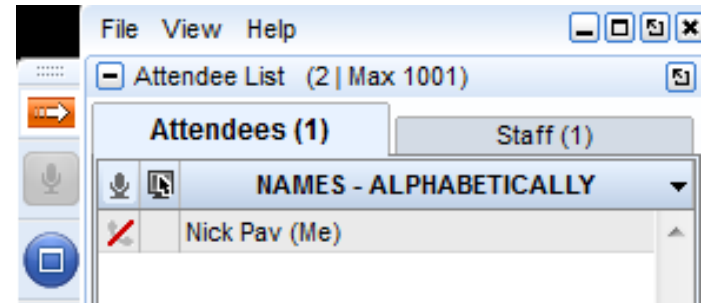
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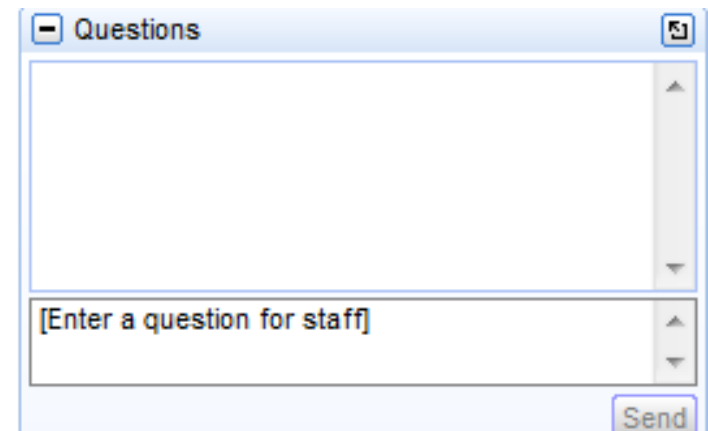
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Disclosures

- I have no conflicts to disclose.

Target Audience

- The overarching goal of PCSS is to train a diverse range of healthcare professionals in the safe and effective prescribing of opioid medications for the treatment of pain, as well as the treatment of substance use disorders, particularly opioid use disorders, with medication-assisted treatments.

Educational Objectives

At the conclusion of this activity participants should be able to:

- Review traditional withdrawal management protocols in an outpatient setting;
- Assess the importance of simultaneous participation in psychosocial treatment services;
- Contrast the increased transition into ongoing care compared to inpatient withdrawal management.

Outline

- Introduction
- Clinical Context
- Medication Protocols
- Concluding Comments

Introduction

Why Outpatient?

- Increased likelihood, compared to inpatient withdrawal management, that patients will continue in long term follow up treatment for their substance use disorder

My Perspective

- 1973. Looking for an outpatient alternative to traditional 28-day Minnesota model alcohol rehabilitation
- Patient population: commercially insured adults working in blue and white collar jobs
- First intensive outpatient treatment program (IOP)
- Subset of patients required withdrawal management
 - Patients more likely to continue into IOP if WM was done as outpatient

Contrasting Acceptance: IOP Versus Outpatient WM

- IOP has become widely established as a mainstream level of care for the rehabilitation of substance use disorders as well as other diagnostic groups
- Outpatient WM is still under-available
 - Despite being a well-established procedure for mild to moderate severity
 - 1975: American Journal of Psychiatry article
 - Entrenched resistance regarding higher severity end of the spectrum

Clinical Context

How to Predict Withdrawal Severity?

- Variability between patients and with a given patient
- Withdrawal syndrome evolves rapidly
- Balance the importance of staying ahead of symptoms with avoiding over-medicating

Tracking Treatment Progress

- CIWA-Ar (Clinical Institute Withdrawal Assessment for Alcohol–Revised)
 - Most commonly used but many alternatives
 - Routinely mis-applied to level of care decisions
 - The problem with scores >15
- Anxiety and restlessness are the best parameter
- Tendency of clinicians to overly focus on elevated blood pressure, which can be caused by chronic heavy alcohol intake and takes weeks or months to decline

Withdrawal Discomfort Experience: A Simple Guide for Making Medication Decisions

- “What number would you put your withdrawal discomfort now? If zero equals feeling completely well and ten equals the worst withdrawal you have ever had?” - Goal is zero to one

Two Outpatient Settings

- **Office Based**
 - ASAM Level 1-WM: Ambulatory Withdrawal Management without Extended On-Site Monitoring
- **Structured Program Based**
 - ASAM Level 2-WM: Ambulatory Withdrawal Management with Extended On-Site Monitoring

Risk Rating and Care Level: Alcohol or Sedative/Hypnotics

Risk Rating	Symptoms	Level of Care
1. Mild	Mild anxiety, sweating, insomnia	Office Based
2. Moderate	Moderate anxiety, fine tremor	Program Based
3. Significant	Significant anxiety, gross tremor	Program Based or Residential
4. Severe	Clouded sensorium, visual hallucinations, seizure	Hospital

Risk Rating and Care Level: Opioids

Risk Rating	Symptoms	Level of Care
1. Mild	Mild anxiety, yawning, rhinorrhea	Office Based
2. Moderate	Moderate anxiety, restlessness, body aches, abdominal cramps	Program Based
3. Significant	Significant anxiety, vomiting, diarrhea, tremor	Program Based or Residential
4. Severe	Agitation, debilitating vomiting and diarrhea	Hospital

Medication Protocols

Medication Overview

- Alcohol and Sedative/Hypnotics
 - Withdrawal management
 - Relapse prevention
- Opioids
 - Withdrawal management
 - Relapse prevention

General Strategy

- Minimize waiting time for initiating WM
 - Have patient present in early withdrawal
- Medicate aggressively: hourly observation for first 4 to 6 hours to achieve patient comfort as rapidly as possible while avoiding over-sedation
 - Creates foundation for therapeutic relationship
 - Allows rapid transition into psychosocial treatment

Alcohol Withdrawal Management Protocols Covered Today

- Standard Symptom Triggered Benzodiazepine
- Alternative Non-Benzodiazepine
- Hybrid of Standard and Alternative

Use Long Acting Benzodiazepines

- **Chlordiazepoxide** 50 mg = Diazepam 20 mg
- Can be used even if liver enzymes are moderately elevated

Why to Avoid Shorter Acting Agents, e.g. Lorazepam

- Less reduction of agitation
- When tapering, multiple daily doses are necessary
- Rebound withdrawal symptoms
 - Relapses back to alcohol are triggered
- Use only when patient
 - Is in liver failure
 - Is unable to take oral medication due to vomiting
 - Switch to longer acting as soon as possible

Symptom Triggered Chlordiazepoxide Taper

- **First day**: 50 mg hourly until withdrawal discomfort is 0 to 1 (usually 50 to 300 mg)
- **First night**: 50 mg at bedtime
 - Repeat hourly x 2 until asleep
- **Second day**: 50 mg x 1 – 2 in A.M.
- **Second night**: 50 mg at bedtime
 - Repeat in one hour if not asleep
- **Third night**: 50 mg at bedtime if needed

Why Avoid Benzodiazepines Entirely?

- Addictive potential
- Using GABA agent in a down-regulated system requires very large doses
- Motor impairment, ataxia
- Sedation and cognitive changes interfere with psychosocial interventions
- Potential for delirium
- Limited effectiveness for delirium tremens

Alternative Agent: Anticonvulsants

- Options: gabapentin, carbamazepine, valproate
- Act on hyperactive glutamatergic system
- Effective for mild to moderate withdrawal severity
- Useful for extended use to reduce post-acute withdrawal symptoms
- Problem: not adequate alone for severe withdrawal

Disordered Neurotransmitters

- Down-regulated
 - GABA
- Up-regulated
 - Glutamatergic/NDMA
 - Dopaminergic
 - Noradrenergic

Symptoms of Noradrenergic Hyperactivity

- Anxiety
- Agitation
- Tremor
- Tachycardia
- Elevated blood pressure

Expanded Non-Benzodiazepine Protocol for All Severity Levels

- Based on correcting:
 - Adrenergic hyperactivity (“adrenergic storm”)
 - Up-regulated glutamatergic system
- Add alpha-2 adrenergic agonist
 - Clonidine
 - Positive: patch available
 - Negative: hypotension, unpleasant sedation
 - Guanfacine
 - More specific activation of alpha-2 adrenergic receptor
 - Less hypotension and sedation

Hybrid Protocol

- Day 1: Symptom triggered benzodiazepine protocol
 - Occasionally extend to Day 2 for severe anxiety
- Day 2 and thereafter:
 - Gabapentin 300 mg T.I.D.
 - Adjust dose up or down as needed
 - Maintain for 6 to 12 months
- Add alpha-2 adrenergic agonist if history of hallucinations
 - Guanfacine 2 to 3 mg/day

Disulfiram (Antabuse): General

- Blocks breakdown of alcohol, causing build up of acetaldehyde
- Removes expectation of pleasurable response to alcohol
 - Inserts delay in impulsive decision to drink
- Effective in early recovery only if administration is supervised
 - Superior to outcomes of naltrexone and acamprosate, which can be added
- Spectrum of acceptance by patients

Disulfiram (Antabuse): Prescribing

- Give first dose as soon as BAC = 0
- Daily dose: standard is 250 mg
 - Absorption and sensitivity to reaction vary
 - Use 125 mg (half tab) to reduce side effects and eliminate reaction to inadvertent alcohol contact
 - Increase dose if no reaction to alcohol intake
- Common side effects
 - Allergic rash
 - Mild rash responds to dose reduction
 - Allergic hepatitis
 - LFT testing after 4 weeks to detect ALT > AST

Alcohol and Naltrexone

- Naltrexone reduces euphoric response to alcohol by blocking mu opioid receptor
- Naltrexone reduces alcohol craving by unknown mechanism
 - Does not reduce opioid craving
- Formulations
 - Oral tablet
 - Extended release IM injection

Sedative/Hypnotics

- Stabilize for 2 days on equivalent dose of phenobarbital or benzodiazepine
- Gradual taper over 4 to 8 weeks
 - Decrease by 30 mg phenobarbital or equivalent every week
 - Adjust speed according to patient response
 - Taper may be slower toward the end

Choices of Medication

- Phenobarbital
 - Allows urine tracking of relapse
 - Useful for double addiction to alcohol and high potency benzodiazepine
- Clonazepam
 - Better for high potency benzos
- Chlordiazepoxide
 - Better for low potency benzos

30 mg Phenobarbital Equivalents

Alprazolam (Xanax)	1 mg
Chlordiazepoxide (Librium)	25 mg
Clonazepam (Klonopin)	1 mg
Diazepam (Valium)	10 mg
Lorazepam (Ativan)	2 mg
Oxazepam (Serax)	30 mg
Butalbital (Fiorinal)	50 mg
Zolpidem (Ambien)	20 mg

Benzodiazepine Withdrawal Management Concerns

- Frequently can only achieve less than complete patient comfort
 - Danger of plateau instead of taper
- Watch for co-occurring anxiety disorder that may require treatment

Combination: Alcohol and Sedative/Hypnotics

- Decide: simultaneous versus deferring sedative/hypnotics
 - Assess whether underlying anxiety disorder requires treatment
 - Assess whether trauma disorder would be destabilized
- Decide whether to use benzodiazepine or phenobarbital
- For withdrawal from sedative/hypnotics, extend taper over 4 to 8 weeks
 - More extended taper may be appropriate

Buprenorphine Protocol

- Mild withdrawal symptoms must be present to avoid precipitated withdrawal
 - Transition from methadone: reduce to 30 mg/day and wait 48 to 72 hours
 - Recent problems with heroin + “fentalogues”
 - Tramadol: up to 400 mg/day for 24 to 48 hours.
- 4 mg every 60 – 90 minutes until symptoms remit
 - Lower initial dose (2 mg) when no recent use
- Daily range: 8 to 24 mg
 - 12 mg is dose that blocks ability to get high from other opioids
- Can taper over 1 to 4 weeks but longer-term stabilization for months is preferable
 - High rate of relapse if use is short-term

Combination: Alcohol and Opioids

- Buprenorphine has a “ceiling effect” that prevents severe respiratory depression
 - Ceiling is gradually lifted by benzodiazepines
- Using benzodiazepines together with buprenorphine is not contraindicated but should be done with caution

Addicted Pain Patients

- Buprenorphine is an ideal medication
- Legitimate pain syndrome does not require DEA “X waiver” for prescriber
- Must divide into 3 to 4 doses/day
 - Analgesic effect is shorter
- May require up to 32 mg/day
 - Ceiling effect analgesia is higher
 - Insurance may not cover

“Fentalogue” Adulterated Heroin

- New development: buprenorphine triggers precipitated withdrawal even when moderate withdrawal symptoms are present after 24 hours of abstinence
- Solution: “tramadol bridge”
 - Opioid agonist with lower receptor affinity than buprenorphine
 - Initially not scheduled, now Schedule IV
 - Allowable under CSA 72-hour exception

Kratom

- Derived from leaves of Southeast Asian shrub
- Active ingredient: mitragynine
- Used for centuries for pain and depression
- Weak mu-opioid receptor agonist
 - Affinity for many other many CNS receptors
- Attempts to ban by DEA blocked by arguments for a less addictive alternative to opioids
- Kratom Trade Association (www.kratomtrade.org)
- Kratom addiction effectively treated with buprenorphine

Non-Agonist Withdrawal Management

- Alpha-2 adrenergic agonists are the cornerstone
 - Reduce adrenergic hyperactivity in up-regulated locus coeruleus
 - Agents
 - Clonidine most common
 - Guanfacine has less hypotension and sedation
 - Lofexidine is newest addition
- Supportive medications for other symptoms
 - Anxiety: phenobarbital
 - Insomnia: sedating antidepressants, quetiapine
 - Nausea: ondansetron

Opioid Antagonist for Relapse Prevention: Naltrexone

- Oral
 - 24 hour effective duration
 - Extend to 72 hours by giving 150 mg
- Extended release parenteral lasts 30 days
 - Large volume requires gluteal intramuscular injection

Naltrexone Initiation

- Must allow opioid washout period of several days before beginning oral
 - Length of washout depends on opioid being used
 - Some protocols use early administration of .5 mg to 1 mg doses prepared by compounding pharmacist
- Easier if non-agonist medications is used for withdrawal management
- Precede parenteral with one week of oral

Naltrexone Benefits

- No psychoactive effect
- Blocks psychoactive effect of opioid agonists
- Philosophical preference by some patients, Narcotics Anonymous, and corrections officials

Closing Comments

Inpatient Withdrawal Management ...

- Was once the only setting for effective treatment
- Is still an essential setting for a subset of patients

The Overutilization of Inpatient Treatment

- Creates a fragmentation of the system of care
- Contributes to premature termination of treatment
- Leads to inadequate attention to the chronic aspect of substance use disorders and the importance of continuity of care
- Results in the repeated treatment of relapses at an acute level of care

Outpatient Withdrawal Management

- Is medically safe and effective for all but the most severe withdrawal syndromes
- Facilitates transition into ongoing psychosocial treatment
- Can help correct the current imbalance in the treatment system for substance use disorders

Conclusion

By creating enough structure to deliver the withdrawal management in the same setting in which longer term treatment will be delivered, continuity of care is maximized and the chronic nature of substance use disorders is more effectively addressed.

Thank you! Questions?

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PCSS Mentoring Program

- PCSS Mentor Program is designed to offer general information to clinicians about evidence-based clinical practices in prescribing medications for opioid addiction.
- PCSS Mentors are a national network of providers with expertise in addictions, pain, evidence-based treatment including medication-assisted treatment.
- 3-tiered approach allows every mentor/mentee relationship to be unique and catered to the specific needs of the mentee.
- No cost.

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- ✧ **Opioid Use Disorder Virtual Learning Collaborative (VLC)**
 - Play a role in expanding the availability of medical for addiction treatment options for opioid use disorders
 - Each collaborative runs for 12-weeks and is lead by an experienced faculty advisor
 - Participants watch pre-recorded webinars, call into office-hours, engage with a virtual community and complete an individual project
 - Participants will earn up to 12 Continuing Medical Education (CME) credits
 - Fill out our interest intake form at apapsy.ch/OpioidSTR
Contact Eunice Maize at emaize@psych.org for more information.



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- Instructions will be provided in an email sent to participants an hour after the live session
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- Recordings of today's webinar can be accessed at www.pcassNOW.org and education.psychiatry.org

Upcoming PCSS Webinar

Tracking Drug Use Patterns

Jane Maxwell, PhD
Addiction Research Institute Research
Professor, The University of Texas at
Austin Steve Hicks School of Social Work

Tuesday, March 19, 2019
12:00-1:00 PM EST





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