Prescribing Challenges in Dual Diagnostic Patients

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Disclaimer

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Objectives

- Review of dual diagnosis as a concept
- Epidemiology and diagnostic stratification
- Current evidence pertaining to prescribing challenges

What is dual diagnosis?

- Term “dual diagnosis” (DD) introduced in 1995 by World Health Organization

- It indicates concomitance of substance use disorder and a psychiatric condition, also known as “Co-occurring disorders.”

Challenges with DD

- DD complicates the psychopathological clinical status:
  - Leading to higher heterogeneity
  - Complicates diagnostic framing
  - Makes it difficult to treat
  - Creates labeling of “difficult patients”
    - Poor overall compliance with therapies
    - High drop out rates of treatment
    - High hospitalization rates

REVIEW OPEN

Global research challenges and opportunities for mental health and substance-use disorders

Florence Baingana[1], Mustafa al'Absi[2], Anne E. Becker[3] & Beverly Pringle[4]

The research agenda for global mental health and substance-use disorders has been largely driven by the exigencies of high health burdens and associated unmet needs in low- and middle-income countries. Implementation research focused on context-driven adaptation and innovation in service delivery has begun to yield promising results that are improving the quality of, and access to, care in low-resource settings. Importantly, these efforts have also resulted in the development and augmentation of local, in-country research capacities. Given the complex interplay between mental health and substance-use disorders, medical conditions, and biological and social vulnerabilities, a revitalized research agenda must encompass both local variation and global commonalities in the impact of adversities, multi-morbidities and their consequences across the life course. We recommend priorities for research — as well as guiding principles for context-driven, intersectoral, integrative approaches — that will advance knowledge and answer the most pressing local and global mental health questions and needs, while also promoting a health equity agenda and extending the quality, reach and impact of scientific enquiry.

Nature 527, S172–S177 (19 November 2015), DOI: 10.1038/nature16032

- Major gaps in understanding epidemiology
- SUD has major impacts on the neurobehavioral and neurodevelopmental functions
- Epidemiology influenced in low middle income countries:
  - Poverty
  - Malnutrition
  - Political conflicts
  - Overall poor health

Association between alcohol and substance use disorders and all-cause and cause-specific mortality in schizophrenia, bipolar disorder, and unipolar depression: a nationwide, prospective, register-based study

Carsten Hjorthøj, Marie Louise Drivsholm Østergaard, Michael Eriksen Benros, Nanna Gilliam Toftdahl, Annette Erlangsen, Jon Trærup Andersen, Merete Nordentoft

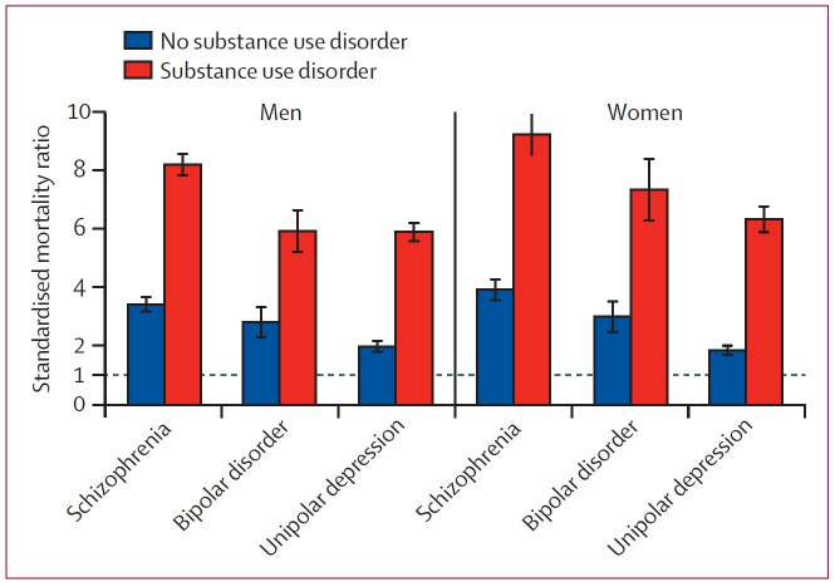


Figure: **Standardised mortality ratio for the period 1990–2012 in people with schizophrenia, bipolar disorder, or depression, with and without substance use disorder**
Error bars show 95% CI.

DD Outcomes

ALCOHOLISM: CLINICAL AND EXPERIMENTAL RESEARCH

Vol. 31, No. 4
April 2007

Treatments for Patients With Dual Diagnosis: A Review

Quyen Q. Tiet and Brent Mausbach

- No single treatment identified as efficacious for both SUD and mental illness

- However, important conclusions:
  - ✓ Existing psychiatric treatments work well for DD patients
  - ✓ Existing SUD treatments work equally well for DD patients
  - ✓ Integrated treatment outcomes are still unclear due to lack of clear outcomes data

DD Outcomes

Effectiveness of Treatment for Substance Abuse and Dependence for Dual Diagnosis Patients: A Model of Treatment Factors Associated with One-Year Outcomes*

FRANZ MOGGI, PH.D.,† PAIGE CROSBY OUIMETTE, PH.D., JOHN W. FINNEY, PH.D., AND RUDOLF H. MOOS, PH.D.

Program Evaluation and Resource Center and HSR&D Center for Health Care Evaluation, Veterans Affairs Palo Alto Health Care System & Stanford University Medical Center, Palo Alto, California

- Participants in a naturalistic multisite study of VA treatment programs for SUD
- Examined a model of treatment with focus on 5 variables:
  - Social background
  - Intake functioning
  - DD treatment orientation
  - Patients change on proximal outcomes
  - Aftercare participation
- Studied 981 male DD patients at the VA

Study outcomes

- Important findings:
  - DD patients more likely to be abstinent, employed, and free of significant psychiatric symptoms, than prior to treatment
  - At 1 year follow-up:
    - 39% abstinent
    - 68% no significant psychiatric symptoms
    - 29% employed
  - Programs with practical orientation, active participation, and liberal use of psychotropic medications:
    - Higher reduction of psychiatric symptoms
    - Being employed
    - Longer program tenures

Diagnostic Stratification

Substance/Medication-Induced Depressive Disorder

Diagnostic Criteria

A. A prominent and persistent disturbance in mood that predominates in the clinical picture and is characterized by depressed mood or markedly diminished interest or pleasure in all, or almost all, activities.

B. There is evidence from the history, physical examination, or laboratory findings of both (1) and (2):

1. The symptoms in Criterion A developed during or soon after substance intoxication or withdrawal or after exposure to or withdrawal from a medication.

2. The involved substance/medication is capable of producing the symptoms in Criterion A.

C. The disturbance is not better explained by a depressive disorder that is not substance/medication-induced. Such evidence of an independent depressive disorder could include the following:

The symptoms preceded the onset of the substance/medication use; the symptoms persist for a substantial period of time (e.g., about 1 month) after the cessation of acute withdrawal or severe intoxication; or there is other evidence suggesting the existence of an independent non-substance/medication-induced depressive disorder (e.g., a history of recurrent non-substance/medication-related episodes).

D. The disturbance does not occur exclusively during the course of a delirium.

E. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Note: This diagnosis should be made instead of a diagnosis of substance intoxication or substance withdrawal only when the symptoms in Criterion A predominate in the clinical picture and when they are sufficiently severe to warrant clinical attention.

Substance/Medication-Induced Anxiety Disorder

Diagnostic Criteria

A. Panic attacks or anxiety is predominant in the clinical picture.

B. There is evidence from the history, physical examination, or laboratory findings of both (1) and (2):

1. The symptoms in Criterion A developed during or soon after substance intoxication or withdrawal or after exposure to or withdrawal from a medication.

2. The involved substance/medication is capable of producing the symptoms in Criterion A.

C. The disturbance is not better explained by an anxiety disorder that is not substance/medication-induced. Such evidence of an independent anxiety disorder could include the following:

The symptoms precede the onset of the substance/medication use; the symptoms persist for a substantial period of time (e.g., about 1 month) after the cessation of acute withdrawal or severe intoxication; or there is other evidence suggesting the existence of an independent non-substance/medication-induced anxiety disorder (e.g., a history of recurrent non-substance/medication-related episodes).

D. The disturbance does not occur exclusively during the course of a delirium.

E. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Note: This diagnosis should be made instead of a diagnosis of substance intoxication or substance withdrawal only when the symptoms in Criterion A predominate in the clinical picture and they are sufficiently severe to warrant clinical attention.

Specific DD Challenges and Recommendations

Alcohol use related DD epidemiology

- Approximately 50% of AUD patients have some co-morbid psychiatric disorder

- Predominant psychiatric disorders in AUD include:

  -Affective disorders (about 13.4% of AUD patients vs 7.5% in gen pop)

  -Major depressive disorder (about 32.5% of DD patients vs 11.2% AUD only)

  -Anxiety disorders (**33% with AUD** and 28% with other drug use)

  -Cluster B or C personality traits

Prescribing suggestions in AUD patients with DD

- Rossinfonte's study shows SSRIs in AUD work to reduce craving and relapse frequency
- Carbamazepine appears to be helpful in withdrawal from alcohol in mild or moderate use
- ABEAD (Brazilian Association for alcohol studies) recommends restrictive benzodiazepine use in AUD patients

CANMAT (Canadian Network of Mood and anxiety treatment)

- <u>Recommendations:</u>
  - -Quetiapine can help in bipolar patients with AUD
  - -Topiramate and Gabapentin can be used in patients with AUD
  - -Minimal benefit from Li treatment in AUD r/t poor tolerability
  - -Mirtazapine preferred over TCA due to better efficacy

AUD and antidepressants

- Escitalopram
  - Shown to reduce depressive symptoms by ~50% in AUD patients (in monotherapy)
  - Appears more effective for late-onset depression (age>30)
  - Combination with acamprosate appears more effective with:
    - Marked improvement in depressive symptoms*
    - Reduced weekly and monthly alcohol consumption*
  - Combination with aripiprazole showed improvement in symptoms and cravings

*Did not achieve statistical significance due to exiguous sample

AUD and antidepressants

- Citalopram
  - No differences in affective symptoms or alcohol consumption
- Sertraline
  - Reduce depressive symptoms and alcohol use in combination with CBT
  - Higher rates of abstinence when in combination with naltrexone

AUD and antidepressants

- <u>Mirtazapine</u>
  - Significant improvement in anxiety and depressive symptoms
  - Reduction in cravings and alcohol compulsiveness
  - Marked reduction in weekly alcohol consumption (34 → 13 alcohol upw*)
  - 2-year follow up showed similar responses
  - Also has evidence that it can reduce social anxiety in AUD patients

*upw = units per week

AUD and antidepressants

- Venlafaxine
  - Effective in reducing depressive symptoms in AUD patients
  - Recent controlled trial did not show difference in anxiety in combination with CBT as compared to CBT alone

Mood stabilizers and AUD

- Lithium
  - Showed no particular efficacy in AUD patients
  - No significant differences noted in depressive patients as compared to placebo
  - Studies in Bipolar I or II patients with AUD or cannabis use, showed reduction in weekly urine drug screen positives in Lithium group

Mood stabilizers and AUD

- Valproate
  - Valproate w/ Lithium appeared superior to Lithium w/ placebo in reducing:
    - Heavy drinking days
    - Lower amounts of daily alcohol use
  - Valproate group also showed lower GGT blood levels
  - Study length was 24 weeks

Mood stabilizers and AUD

- Topiramate
  - Shows significant efficacy in reduction of cravings and other AUD related indices
  - Also reduces post-traumatic hyperarousal in patients with PTSD & AUD

Mood stabilizers and AUD

- Gabapentin
  - Shows significant improvement in sleep related outcomes in AUD patients
  - An open study shows higher effectiveness of gabapentin vs trazodone in patients with AUD and insomnia
  - A 2019 review shows significant reduction of cravings, improves rates of abstinence, delays return to heavy drinking days, and treats acute alcohol withdrawal
  - More effective as adjunctive treatment vs monotherapy
  - NO BENEFIT was seen for OCD, PTSD, or depressive symptoms in SUD

BENZODIAZEPINES and SUBSTANCE USE DISORDERS

- **Common themes**
  - Benzodiazepine use has been controversial in AUD treatment
  - Continue to remain mainstay for management of alcohol withdrawal
  - Most common reason for benzodiazepine use in DD is for anxiety disorders

- **IS IT SAFE TO USE BENZODIAZEPINES IN PATIENTS WITH SUD?**

NO camp!

- General consensus among most providers to restrict benzodiazepine use in SUD patients

- <u>Stats:</u>
  - Per 2016 NSDUH data, around 30 million people use benzos
  - About 0.5 million met criteria for benzodiazepine use disorder
  - About 30% of opioid OD deaths involved benzodiazepines, and
  - About 77% of benzodiazepine OD deaths involved opioids (2010)

  - Benzodiazepine misuse is also highly prevalent in AUD patients (~30%)
  - Very high prevalence of patients co-using benzodiazepines with other substances (**100%** of patients in this study)

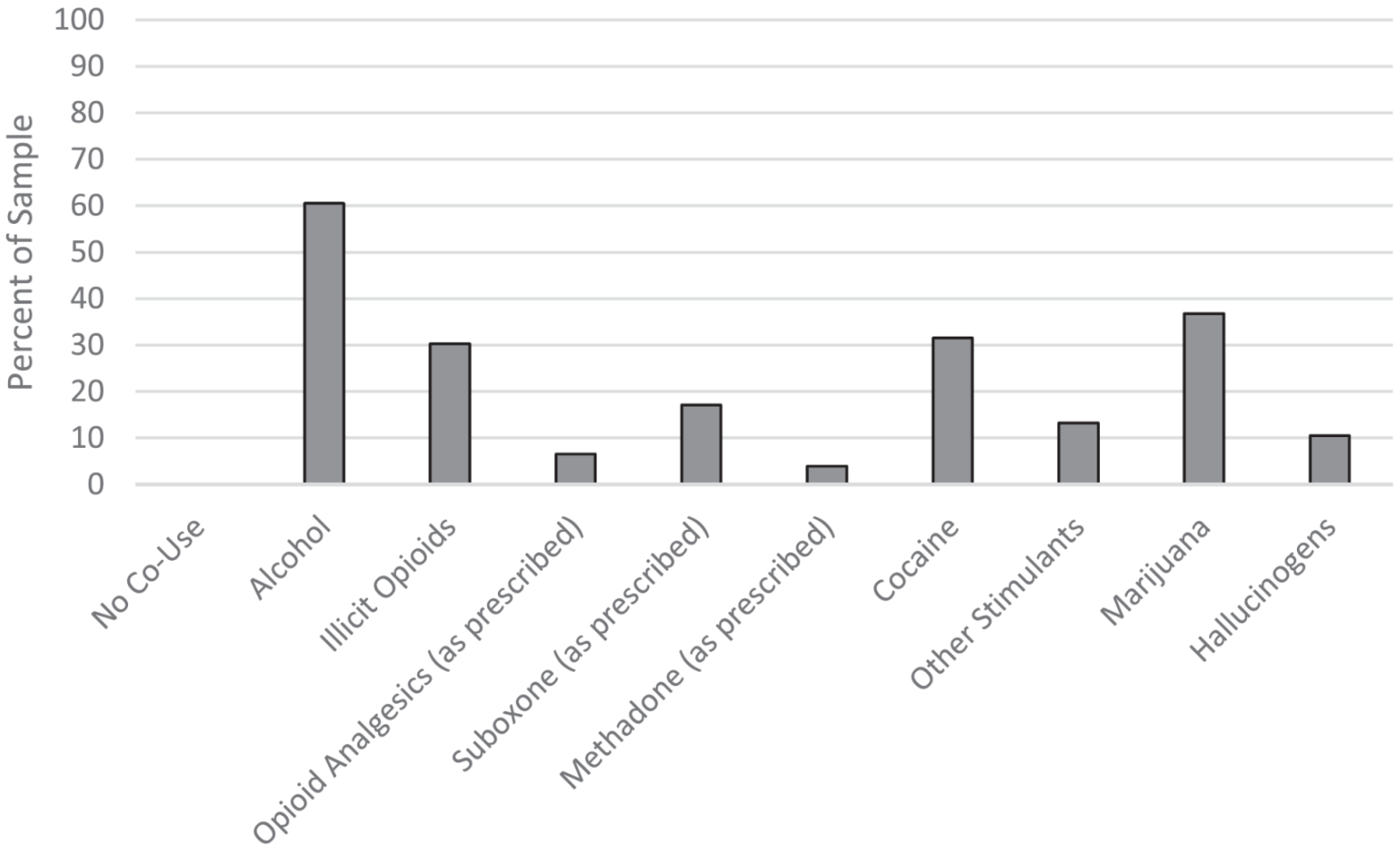
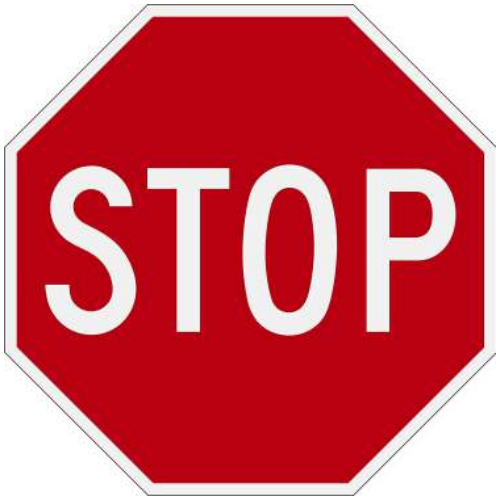


Fig. 1. Past-year co-use of benzodiazepines and other substances ($n = 55$).

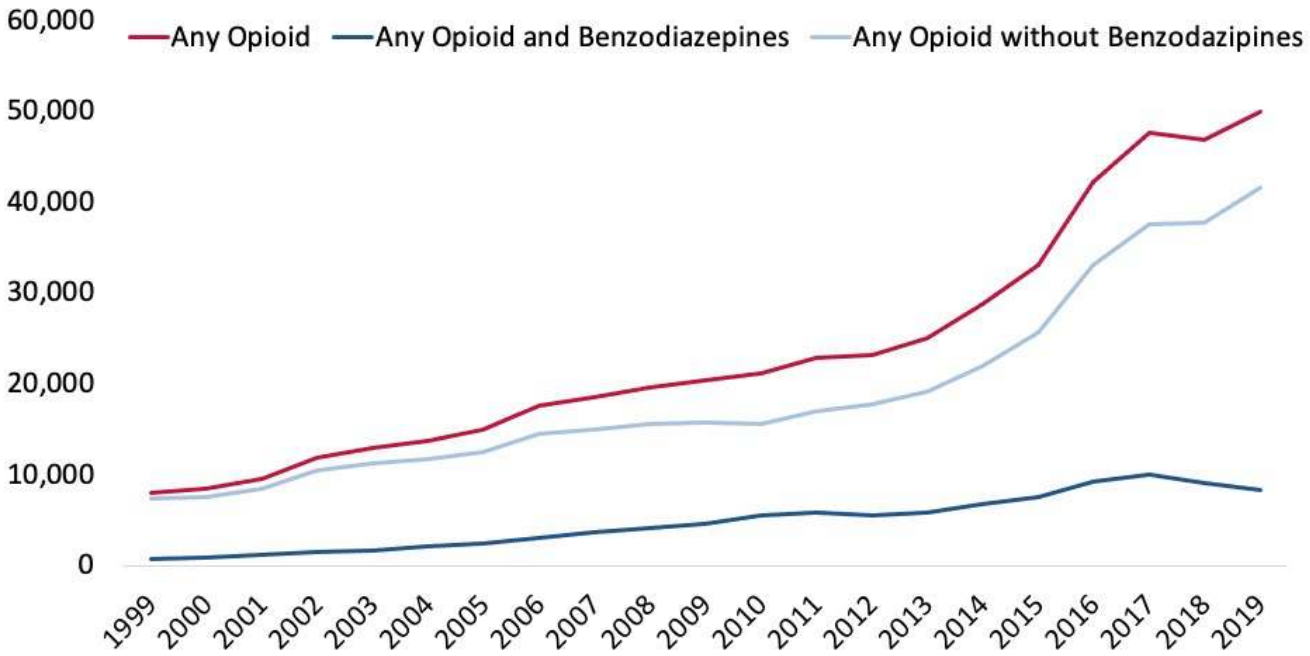
McHugh RK et al. Benzodiazepine misuse in adults with alcohol use disorder: Prevalence, motives and patterns of use. J Subst Abuse Treat. 2020 Oct;117:108061. doi: 10.1016/j.jsat.2020.108061. Epub 2020 Jun 22. PMID: 32811622; PMCID: PMC7438601.

Benzodiazepines and Opioids

- Benzos known to cause respiratory depression while taking in concert with CNS depressants (opioids)
- Benzodiazepines commonly involved in opioid overdoses
- In addition, benzos increase risks of OD deaths in patients using opioid analgesics by up to 4-fold, as compared to using opioids alone



National Drug Overdose Deaths Involving Opioids, by Benzodiazepine* Involvement, Number Among All Ages, 1999-2019



*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.

YES CAMP!

- Anxiety considered as a major public health issue, and when not treated can lead to significant reduction in quality of life and psychosocial functioning

- Recall significant co-morbidity with SUD making it a top DD challenge

Psychotherapy and Psychosomatics

Psychother Psychosom 2013;82:355–362
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Efficacy and Tolerability of Benzodiazepines versus Antidepressants in Anxiety Disorders: A Systematic Review and Meta-Analysis

Emanuela Offidani[a] Jenny Guidi[a] Elena Tomba[a] Giovanni Andrea Fava[a, b]

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[b] Department of Psychiatry, State University of New York at Buffalo, Buffalo, N.Y., USA

- Benzodiazepines better tolerated than TCAs in reducing panic attacks
- Benzodiazepines were comparable or better than SSRIs and SNRIs in reducing anxiety parameters
- "*The change in the prescribing pattern favoring newer AD over BDZ in the treatment of anxiety disorders has occurred without supporting evidence.*"

Published in final edited form as:
Am J Drug Alcohol Abuse. 2016 September ; 42(5): 490–499. doi:10.3109/00952990.2016.1168430.

Co-administration of Disulfiram and Lorazepam in the Treatment of Alcohol Dependence and Co-occurring Anxiety Disorder: An Open-label Pilot Study

Michael P. Bogenschutz[a], **Snehal Bhatt**[b], **Juliane Bohan**[b], **Bellelizabeth Foster**[b], **Paul Romo**[b], **Claire E. Wilcox**[b], and **J. Scott Tonigan**[c]

- "*Explore the effects of coadministering lorazepam and disulfiram to alcohol dependent patients with anxiety disorder symptoms.*"
- 40 total participants and 24 weeks length of study
- Significant reduction in anxiety noted along with reduction of cravings
- No evidence of lorazepam misuse noted and no dose escalation was necessary
- **Conclusion**: lorazepam was safe for short-term use in combination with disulfiram for AUD

REVIEW

Understanding and Treating Comorbid Anxiety Disorders in Substance Users

Review and Future Directions

Kate Wolitzky-Taylor, PhD, Joachim T. Operskalski, BA, Richard Ries, MD, Michelle G. Craske, PhD, and Peter Roy-Byrne, MD

"*Several studies demonstrated that treating the comorbid anxiety disorder not only improved anxiety symptoms but had a positive impact on SUD outcomes.*"

"*Taken together, treating anxiety disorders in these populations improves anxiety symptoms, but the degree to which adjunctive anxiety treatment (***non-benzodiazepine***) improves substance use outcomes above and beyond the improvement found from typical addictions treatment remains unclear.*"

Reasons for Benzodiazepine Use Among Persons Seeking Opioid Detoxification

Michael D. Stein, M.D. [a,b,*], Mitika Kanabar, M.D., M.P.H. [c], Bradley J. Anderson, Ph.D. [a], Anna Lembke, M.D. [c], Genie L. Bailey, M.D. [b,d]

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[d] *Stanley Street Treatment and Resources, Inc., Fall River, MA 02720, USA*

- Study surveyed 176 people and asked about primary reasons for using benzodiazepines
- Most commonly used benzo was alprazolam (52%)
- Most commonly reported reason for use was “to manage anxiety” (43%)
- Only 27% reported “to a get a high” as reason to use
- Strong correlation between reason to use and how it was obtained ($p<.001$)
  - 48% obtained from the street, were more likely to use it for high
  - 23% who obtained from prescriber, were mostly using it for anxiety relief

Overall Recommendation for benzodiazepine use in DD

- Not all DD patients will be appropriate candidates

- If considering initiating benzodiazepines in DD:
  - Comprehensive assessment involving risk factors for misuse
  - Prior treatments for anxiety
  - Discussion of risks, benefits, and side effects

Overall Recommendation for benzodiazepine use in DD

- Once decision made it is appropriate to prescribe, then:
  - Follow a “universal precautions” approach
  - Comprehensive substance use history
  - Using controlled substances agreements or other treatment contracts
  - Using accountability measures such as drug screens, PMP monitoring, or even pill counting if needed
  - Consider adding non-benzodiazepine option as a long term measure and use benzodiazepines for PRN or abortive treatment

Treating acute pain in DD patients

- **Patient related concerns:**
  - Fear of pain not being taking seriously
  - Sense of discrimination and overall poor experience and mistrust
  - Fear of relapse on opioids if given pain medications PO, or even IV
  - Fear of withdrawal from MAT treatments such as methadone or buprenorphine

Treating acute pain in DD patients

- **Provider or Clinician related concerns:**
  - General lack of trust with patients with SUD history
  - Fear of pain overtreatment, such as leading to respiratory depression
  - Concern regarding patients leaving AMA if pain not managed
  - Fear that patient is fabricating pain to get opioids for "high"

Management of acute pain in MAT patients

Most common questions from clinicians:

1. **What do I do with the Suboxone (or methadone) during or after surgery for pain control?**

2. **Is it safe to even give opioid pain medications in these patients?**

3. **What is the length of prescription for opioids can I provide them at discharge (if any)?**

Pain management for methadone MAT patients

- Any provider can order methadone in an inpatient setting while patient is admitted for other medical reasons

- Important steps:
  - **Perform urine drug screen for confirmation**
  - **Contact patient's OTP for dose confirmation**

- If unable to contact (weekends, OTP closed, or nights):
  - **Continue up to 20 mg per day for withdrawals safely**

Pain management for methadone MAT patients

- For acute pain management
  - »Continue baseline dosage for OUD and not considered pain management dose
  - »Use multi-modal pain management if possible
  - »Recommend only short acting scheduled opioids in addition to methadone dosage
  - »Monitor for QT-prolongation and cardiac arrhythmias

Pain management for buprenorphine MAT patients

- Providers in inpatient settings can order buprenorphine without a DATA-2000 waiver (x-waiver) if patient admitted for primary medical reasons

- Important first steps:
  - **Perform urine drug screen for confirmation**
  - **Look for metabolite nor-buprenorphine for confirmation**
  - **Contact buprenorphine provider if needed for dosage**
  - **Check PMP database for dosing and prescription fills**

Pain management for buprenorphine MAT patients

- **Option 1: (Recommended)**
  - Continue baseline dosage of buprenorphine
  - Divide in 2-3 daily dosage for better tolerance and pain relief
  - **Use full agonist opioids for added pain relief**
  - **Likely require higher doses of opioids to overcome receptor blockade**
  - **Preferable to use fentanyl, hydromorphone, or morphine**
  - **These more likely to displace buprenorphine for better analgesia**
  - Recommended length of full agonist treatment should not exceed 3-5 days
  - If patients require more than 5 days of full agonist pain control, consider **OPTION 2**

  - **P.S.** Pregnant women can continue buprenorphine during labor, including epidural or IV opioids. Can receive spinal or GA if needed.

Pain management for buprenorphine MAT patients

- **Option 2:**
  - Appropriate option for patients who might require slightly longer length of peri-operative pain management for more than 5 days post procedure
  - Discontinue buprenorphine around 72 hours prior to operative procedure
  - Use full agonist opioids for pain relief and withdrawals
  - Can consider non-opioid multi-modal analgesia if withdrawals are not a concern
  - **Does have a risk of leaving patient vulnerable to relapse**
  - **Need to restart buprenorphine as soon as possible after termination of full agonist opioid treatment**

Pain management for naltrexone MAT patients

- **If taking PO naltrexone:**
  - Might need to discontinue **at least 72 hours** prior to surgery
  - This will allow dissociation from the opioid receptors
  - Easy to overcome receptor blockade in this situation

- **If taking IM naltrexone:**
  - Much more complicated to manage acute pain
  - Using non-opioid approaches including regional anesthesia may be necessary
  - In some situations, high doses of opioids can overcome receptor blockade, however, patients will need very close monitoring for respiratory depression

ADHD and SUD concerns

ADHD Medication and Substance-Related Problems

Patrick D. Quinn, Ph.D., Zheng Chang, Ph.D., Kwan Hur, Ph.D., Robert D. Gibbons, Ph.D., Benjamin B. Lahey, Ph.D., Martin E. Rickert, Ph.D., Arvid Sjölander, Ph.D., Paul Lichtenstein, Ph.D., Henrik Larsson, Ph.D., Brian M. D'Onofrio, Ph.D.

- *"Substance use disorders contribute substantially to elevated mortality rates among patients with ADHD."*
- Prior research had suggested that there might be increase in sensitivity whereas exposure to stimulants can elevate the risk for future SUD issues.
- This study was a retrospective review of patients in MarketScan database from 2005 to 2014.
- Found no evidence that stimulant prescription led to increase risk of SUD, even in patients with pre-existing SUD.

Take Home Points

- Very important to treat underlying psychiatric concerns which can have trickle down benefits in improving substance use issues.
- When prescribing benzodiazepines, consider comprehensive evaluation and risk stratification.
- Consider benefits of harm reduction and reducing potential triggers for relapse (such as anxiety).
- Accountability measures can be helpful in reducing risks of prescribing controlled substances in DD patients

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Questions?

Thank you!