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Review Article

Substance use Disorders and Co-Occurring Psychiatric Disorders: Pharmacotherapeutic Challenges and Integrated Clinical Management- Comprehensive Narrative Review

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ABSTRACT

Substance use disorders (SUDs) commonly occur with psychiatric disorders and can make diagnosis and treatment more difficult. Poor adherence, drug interactions, adverse effects, polypharmacy, and relapse are common challenges. This review discusses the pharmacological management of alcohol, opioid, stimulant, cannabis, and nicotine use disorders in patients with depression, bipolar disorder, schizophrenia, anxiety, and ADHD. Pharmacotherapy is well established for alcohol and opioid use disorders, while treatment options for stimulant and cannabis use disorders are more limited. Safe treatment requires careful monitoring of drug interactions, organ function, adverse effects, and medication adherence. Clinical pharmacists can support medication reviews, patient counselling, adherence monitoring, and adverse drug reaction management. An integrated approach combining pharmacotherapy, psychosocial care, and harm reduction is important for improving patient outcomes.

INTRODUCTION

Substance use disorders constitute a major clinical and public health challenge and frequently occur alongside psychiatric disorders. Co-occurring disorders are described using terms such as dual diagnosis, concurrent disorders, and co-occurring mental health and substance use disorders. The clinical relationship is complex because

psychiatric symptoms can precede substance use, emerge during intoxication or withdrawal, develop as a consequence of prolonged exposure, or occur independently in a person who already has an SUD.^{1, 2, 3}

No single mechanism adequately explains this association. Shared genetic and neurobiological vulnerability, reward-system dysfunction,

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impulsivity, stress sensitivity, environmental adversity, trauma, and social determinants may contribute to the development or persistence of both psychiatric illness and SUD. The self-medication hypothesis may explain substance use reported by some individuals, but it should not be assumed to explain every co-occurring presentation. Longitudinal assessment is, therefore, essential.⁴

Co-occurring disorders are associated with substantial treatment complexity. Patients may experience recurrent substance use, psychiatric relapse, impaired functioning, medication non-adherence, medical comorbidity, hospitalization, and an increased risk of premature mortality. In schizophrenia, comorbid SUD is associated with major clinical-management difficulties, including poor physical health, adherence problems, relapse, and fragmented service delivery.⁵

Pharmacotherapy may involve the simultaneous use of antidepressants, antipsychotics, mood stabilizers, medications for addiction treatment, analgesics, sedatives, and drugs for physical comorbidities. Such combinations may increase the risk of pharmacodynamic and pharmacokinetic interactions, additive sedation, respiratory depression, QT prolongation, metabolic complications, hepatotoxicity, renal toxicity, and medication-related harm. Medication review is consequently an important component of integrated care.^{10, 11, 13}

This narrative review critically examines pharmacotherapeutic approaches and practical management issues in major SUDs co-occurring with psychiatric disorders, with particular emphasis on medication selection, safety, adherence, interactions, monitoring, integrated treatment, harm reduction, and the role of clinical pharmacists.

2. LITERATURE SEARCH AND REVIEW APPROACH

This narrative review was based on the literature identified through PubMed/MEDLINE and relevant clinical guidelines. We prioritized systematic reviews, meta-analyses, clinical trials, guidelines, and recent relevant reviews. Key terms included "substance use disorder," "psychiatric disorders," "dual diagnosis," "pharmacotherapy," "drug interactions," "integrated treatment," and "harm reduction."

The relevant literature on SUDs and co-occurring psychiatric disorders was reviewed, with emphasis on pharmacological treatment, safety, monitoring, adherence, and integrated care. The findings were synthesized narratively, with attention to the strengths and limitations of the available evidence. As this was a narrative review, no formal meta-analysis or risk-of-bias assessment was performed.

3. RELATIONSHIP BETWEEN SUBSTANCE USE DISORDERS AND PSYCHIATRIC DISORDERS

3.1 Shared vulnerability

SUDs and psychiatric disorders share multiple biological and psychosocial pathways. Alterations in reward processing, executive control, stress response, impulsivity, motivation, and dopaminergic and glutamatergic signalling may increase vulnerability to both conditions. Shared vulnerability does not imply that one disorder necessarily causes the other; rather, the two conditions may arise through partially overlapping mechanisms.^{1, 4}

3.2 Self-medication and reinforcement

Some individuals reported using alcohol, cannabis, opioids, stimulants, or sedative substances to reduce anxiety, insomnia, dysphoria,



emotional distress, or other symptoms. Short-term subjective relief may reinforce the repeated use of these substances. With continued exposure, tolerance, withdrawal, social consequences, and neuroadaptation can worsen functional outcomes. Therefore, clinical assessment should explore the reasons for use without assuming that self-medication is the sole explanation.^{4, 6}

3.3 Substance-induced psychiatric symptoms

Differentiating an independent psychiatric disorder from substance-induced symptoms is central to diagnosis. Stimulant intoxication can produce agitation, paranoia, anxiety, and psychosis, while withdrawal can produce fatigue, dysphoria, anxiety, insomnia, and depressive symptoms. Alcohol withdrawal may present with anxiety, agitation, perceptual disturbances, seizures, or delirium. These presentations may overlap with primary psychiatric disorders and require an assessment of timing, duration, previous episodes, periods of abstinence, collateral information, and longitudinal course.^{6, 14}

3.4 Diagnostic implications

Diagnostic formulation should document the psychiatric diagnosis, substance involved, pattern and severity of use, temporal relationship between substance exposure and symptoms, withdrawal history, current medications, previous treatment response, and relevant medical comorbidities. Reassessment after stabilization may be necessary when intoxication or withdrawal obscures the underlying psychiatric condition.⁶

4. CLINICAL BURDEN OF CO-OCCURRING DISORDERS

Co-occurring SUD and psychiatric illness can produce a more complicated clinical course than either condition alone. Common problems include

poor adherence, recurrent substance use, psychiatric relapse, hospitalization, impaired social and occupational functioning, medical comorbidity, and increased mortality. Fragmentation between addiction and mental health services may further reduce continuity of care.⁷

Integrated care is increasingly emphasized because the two conditions influence one another and may require coordinated pharmacological and psychosocial interventions. Recent umbrella-review evidence found substantial heterogeneity across studies but generally supports the feasibility and potential value of coordinated treatment, while also emphasizing that the evidence is not sufficiently uniform to identify a single universally superior integrated intervention.^{8, 9}

Polysubstance use also increases clinical complexity. Patients may use alcohol together with opioids, benzodiazepines, stimulants, cannabis, or nicotine. Such combinations can complicate diagnosis, increase overdose or cardiovascular risk, and alter medication selection. Treatment plans should therefore be based on the complete substance-use pattern rather than a single primary substance.^{7, 13, 14}

5. ALCOHOL USE DISORDER AND PSYCHIATRIC COMORBIDITY

AUD is one of the SUDs for which pharmacotherapy has the strongest evidence. A large systematic review and meta-analysis conducted in 2023 evaluated 118 trials involving more than 20,000 participants and supported clinically meaningful benefits for several pharmacotherapies, particularly oral naltrexone and acamprosate.¹⁰

5.1 Naltrexone



Naltrexone is an opioid receptor antagonist used to reduce alcohol consumption and the risk of heavy drinking. Oral naltrexone has evidence supporting a reduction in return to heavy drinking and may be useful when a reduction in drinking is an appropriate treatment goal. Before initiation, clinicians should assess recent opioid exposure because naltrexone can precipitate withdrawal in opioid-dependent individuals and blocks opioid analgesia. Hepatic considerations and adherence should also be assessed.^{10, 11}

5.2 Acamprosate

Acamprosate is primarily used to support the maintenance of abstinence after alcohol cessation. It is particularly relevant when maintaining abstinence is the treatment goal and when hepatic considerations make an alternative to hepatically metabolized medication desirable. Renal function is important because acamprosate is renally eliminated; severe renal impairment is a contraindication, and dose adjustment may be required with moderate impairment.¹⁰

5.3 Disulfiram

Disulfiram inhibits aldehyde dehydrogenase and produces an aversive reaction when alcohol is ingested. Its effectiveness is strongly influenced by adherence and supervision. It may be considered in carefully selected, motivated patients when abstinence is the treatment objective and contraindications have been excluded. Hepatic and cardiovascular considerations should be reviewed carefully.¹⁰

5.4 Other and off-label pharmacotherapies

Topiramate, gabapentin, baclofen, and other agents have been studied for the treatment of AUD. Evidence differs in magnitude and certainty among agents, and several agents are used off-

label. Therefore, treatment selection should consider treatment goals, psychiatric comorbidities, renal and hepatic function, seizure risk, sedation, misuse potential, concurrent medications, and patient preference.¹²

5.5 Psychiatric comorbidity considerations

When AUD co-occurs with depression, bipolar disorder, anxiety, or psychotic illness, treatment should not be limited to reducing alcohol consumption. Psychiatric symptoms require independent assessment and treatment. Sedating medications should be used cautiously, especially when alcohol use continues, and medication reconciliation should be performed to identify potentially hazardous combinations.^{4, 8}

6. OPIOID USE DISORDER AND PSYCHIATRIC COMORBIDITY

OD is another SUD for which effective medications have been established. Current evidence-based treatment options include methadone, buprenorphine, and naltrexone. Contemporary guidelines emphasize that withdrawal management alone is not equivalent to ongoing treatment for OD and that medications for OD should be incorporated when clinically indicated.^{11, 13}

6.1 Methadone

Methadone is a full opioid agonist that suppresses withdrawal symptoms and reduces opioid cravings. Important safety considerations include sedation, respiratory depression, drug accumulation, drug interactions, and QT-interval prolongation. These concerns are particularly important when methadone is combined with sedating psychotropics, benzodiazepines, alcohol, or other CNS depressants.^{11, 13}

6.2 Buprenorphine



Buprenorphine is a partial opioid agonist and an established medication for OUD. Its pharmacological profile provides effective suppression of withdrawal and craving with a ceiling effect on respiratory depression relative to full agonists, although clinically important respiratory depression can still occur, particularly with other CNS depressants. Selection and initiation should follow current clinical guidance.^{11, 13}

6.3 Naltrexone

Naltrexone can be considered for appropriately selected opioid-free patients who prefer an antagonist approach or for those for whom agonist treatment is unsuitable. Adequate opioid-free status must be established before administration to avoid precipitating withdrawal. The choice of medication should incorporate treatment goals, prior response, adherence, access, medical comorbidity, and patient preference.^{11, 13}

6.4 Psychiatric comorbidity

Patients with OUD and depression, anxiety, psychotic, or bipolar disorders require simultaneous psychiatric assessment. Untreated psychiatric symptoms can interfere with retention and recovery, while intoxication and withdrawal can mimic or worsen psychiatric symptoms. Co-prescription of sedatives requires particular caution. Medication reviews should specifically identify benzodiazepines, gabapentinoids, sedating antipsychotics, alcohol exposure, and other CNS depressants.^{5, 13}

7. STIMULANT USE DISORDER

Unlike AUD and OUD, stimulant use disorder does not have an equally established medication treatment. The 2024 ASAM/AAAP clinical practice guideline identifies contingency

management as a key evidence-based treatment approach and allows consideration of selected off-label pharmacotherapies in specific clinical circumstances.^{14, 15}

7.1 Intoxication and withdrawal

Acute stimulant intoxication can cause agitation, paranoia, hypertension, tachycardia, hyperthermia, seizures, and cardiovascular complications. These presentations may require urgent medical management. Withdrawal symptoms can include fatigue, dysphoria, anxiety, insomnia, increased appetite, and anhedonia. Psychiatric symptoms should be assessed during both intoxication and withdrawal and should not be automatically attributed to a primary psychiatric disorder.¹⁴

7.2 Pharmacotherapy evidence

Evidence for pharmacotherapy is less definitive than that for AUD or OUD. Off-label medications may be considered in selected patients after assessing the substance used, psychiatric comorbidity, cardiovascular risk, medication interactions, and strength of available evidence. Pharmacotherapy should not be considered an established universal standard for stimulant use disorder. Ongoing research continues to address pharmacological options, the implementation of contingency management, stimulant-induced psychosis, and harm reduction.^{14, 15}

8. CANNABIS USE DISORDER

Cannabis use disorder represents another major pharmacotherapeutic evidence gap. No medication currently has universally accepted standard-of-care status for CUD. A 2024 systematic review identified a heterogeneous evidence base and continued emphasis on psychosocial treatment approaches.¹⁶



Management should address the pattern and severity of cannabis use, withdrawal symptoms, motivation to reduce or stop use, and co-occurring psychiatric illnesses. The relationship between cannabis exposure and psychotic symptoms warrants particular attention in patients vulnerable to psychotic disorders. Integrated treatment should address both cannabis use and the psychiatric disorder rather than treating them as unrelated conditions.^{5, 16}

8.1 Pharmacological approaches under investigation

Several pharmacological strategies have been investigated; however, inconsistent efficacy, small trials, heterogeneous populations, and limited replication prevent the designation of routine medication treatment. Investigational findings should therefore be distinguished from established clinical practice.¹⁶

9. NICOTINE USE DISORDER AND PSYCHIATRIC COMORBIDITY

Nicotine use disorder is highly relevant to psychiatric practice, particularly in schizophrenia-spectrum disorders, where smoking prevalence is high and cessation may be difficult. Smoking contributes to cardiovascular and cancer risk and can also affect the metabolism of some psychotropic medications through tobacco-smoke-induced enzyme effects.^{17, 18}

9.1 Nicotine replacement therapy

Nicotine replacement therapy can reduce withdrawal symptoms and support smoking cessation. In psychiatric populations, it may be used alone or in combination with behavioural support. Monitoring should focus on adherence, withdrawal, continued smoking, and the overall cardiovascular status.^{17, 18}

9.2 Varenicline

Varenicline is a partial agonist at $\alpha 4\beta 2$ nicotinic acetylcholine receptors and is an effective smoking cessation medication. Evidence from people with schizophrenia-spectrum disorders supports pharmacological smoking cessation treatment, including varenicline, without evidence that these treatments worsen psychiatric symptoms overall. Nausea is a common adverse effect.^{17, 18}

9.3 Bupropion

Bupropion sustained release is another established smoking cessation option that has been studied in schizophrenia-spectrum populations. It should be considered in relation to seizure risk, drug interactions, psychiatric history, and concomitant antidepressant therapy. The overall treatment plan should include behavioral support and monitoring.^{17, 18}

10. DEPRESSION AND SUBSTANCE USE DISORDERS

Depressive symptoms are common in patients with SUD, but clinicians should distinguish an independent depressive disorder from symptoms caused or amplified by intoxication, withdrawal, sleep disruption, psychosocial consequences, or chronic substance exposure. Timing, persistence during abstinence, previous depressive episodes, family history, and symptom characteristics can help refine the diagnosis.⁶

Antidepressants may benefit selected patients with an independent depressive disorder, but they should not be considered substitutes for direct treatment of SUD. Treatment choice should consider overdose toxicity, adherence, interactions, seizure risk, hepatic or renal function, and the possibility of activation or mood switching in patients with bipolar-spectrum illness.^{4, 8}



Integrated behavioural approaches may provide additional benefits. Recent evidence on integrated treatment for common mental health disorders and SUD shows improvements across several outcomes; however, substantial heterogeneity remains between interventions and populations.^{8, 9}

11. BIPOLAR DISORDER AND SUBSTANCE USE DISORDERS

SUD is common in bipolar disorder and may be associated with greater mood instability, impulsivity, treatment nonadherence, relapse, hospitalization, and functional impairment. Diagnosis can be difficult because intoxication and withdrawal may mimic manic, mixed, or depressive symptoms.^{20, 21}

11.1 Mood stabilizers

Lithium, valproate, lamotrigine, and selected antipsychotics may be used according to the phase and characteristics of bipolar illness. Lithium requires monitoring of renal function, thyroid function, hydration, serum concentrations, and clinically relevant interactions. Valproate requires hepatic and haematological monitoring and should be prescribed with attention to reproductive and other safety considerations. Lamotrigine is primarily relevant to depressive polarity and maintenance strategies rather than acute mania.²¹

Evidence specifically addressing pharmacotherapy for bipolar disorder with SUD remains limited. A systematic review identified a small and heterogeneous evidence base, with valproate and lamotrigine showing potential usefulness in selected outcomes, but many studies had small samples or open-label designs.²⁰

11.2 Integrated management

Psychiatric stabilization and SUD treatment should be coordinated with each other. Integrated psychosocial approaches may be particularly useful, and treatment plans should include relapse prevention, adherence support, sleep stabilization, and monitoring of medication-related adverse effects. Recent reviews continue to emphasize the limited certainty of the evidence and the need for larger randomized trials.^{21, 22}

12. SCHIZOPHRENIA AND SUBSTANCE USE DISORDERS

Schizophrenia with comorbid SUD is one of the most clinically challenging dual-diagnosis populations. Important problems include poor physical health, medication nonadherence, recurrent relapse, hospitalization, and increased mortality. Recent expert guidance emphasizes the need for coordinated management and individualized treatment planning.⁵

12.1 Antipsychotic treatment

Antipsychotic treatment remains central to the management of schizophrenia. Medication selection should consider previous response, adverse effects, metabolic risk, adherence, substance-use pattern, patient preference, and feasibility of monitoring. Long-acting injectable antipsychotics may be considered when adherence is a major concern, provided that the selected medication is clinically appropriate.⁵

12.2 Clozapine

Clozapine is indicated for treatment-resistant schizophrenia and has attracted interest because some studies have reported reductions in substance use among patients with schizophrenia and comorbid SUD. Systematic review evidence suggests potentially favourable outcomes, particularly for alcohol-related and polysubstance



outcomes, but much of the evidence is observational or of low-to-moderate quality. Therefore, any reduction in substance use should be regarded as a potential additional benefit rather than a primary anti-addiction indication.^{23, 24}

12.3 Smoking and antipsychotic pharmacokinetics

Changes in tobacco smoking can alter exposure to antipsychotics metabolized through CYP1A2, particularly clozapine and olanzapine. Therefore, smoking cessation can increase the concentrations, whereas resumption can reduce exposure. Clinical monitoring and dose reassessment may be necessary if smoking status changes.^{5, 17}

13. ANXIETY DISORDERS AND SUD

Anxiety symptoms may represent an independent anxiety disorder, intoxication, withdrawal, trauma-related distress, or a combination of factors affecting the patient. Benzodiazepines require particular caution because of tolerance, dependence, misuse, and additive CNS depressant effects, especially when opioids or alcohol are involved.^{6, 19}

For persistent anxiety disorders, SSRIs, SNRIs, psychological interventions, and integrated behavioral treatments may be considered in appropriately selected patients. A 2023 meta-analysis of integrated behavioral treatments found small-to-moderate improvements in both anxiety and substance-use outcomes compared with SUD treatment alone.¹⁹

14. ADHD AND SUBSTANCE USE DISORDERS

ADHD and SUD may coexist and create challenges involving impulsivity, adherence, diversion, and medication misuse. An expert consensus statement recommends that ADHD

should not be left untreated due to co-occurring SUD. Instead, clinicians should assess the severity and stability of substance use, risk of diversion, formulation, adherence, and treatment response.²⁵

Long-acting stimulant formulations may reduce some misuse and diversion concerns compared with immediate-release formulations, although the risk is not eliminated. Non-stimulant options may be considered in selected circumstances. Treatment decisions should be individualized and accompanied by monitoring. A 2024 systematic review highlights the need to monitor stimulant medication misuse and adverse outcomes in dual-diagnosis populations.^{25, 26}

15. MAJOR PHARMACOTHERAPEUTIC CHALLENGES

15.1 Polypharmacy

Polypharmacy increases the possibility of drug–drug interactions, therapeutic duplication, additive adverse effects, and adherence difficulties. Medication reconciliation should be performed at treatment initiation, transitions of care, hospitalization, and major changes in psychiatric or substance-use treatment.³¹

15.2 CNS and respiratory depression

Combining opioids with benzodiazepines, alcohol, sedating antipsychotics, sedating antidepressants, or other CNS depressants can increase sedation and respiratory depression risk. Risk assessment should include prescribed medicines as well as non-prescribed substances.¹³

15.3 QT-interval prolongation

Methadone and several other psychotropic medications can prolong the QT interval. When multiple QT-prolonging agents are used, medication review, correction of modifiable risk



factors, and ECG monitoring should be considered according to clinical circumstances.¹³

15.4 Hepatic impairment

Alcohol-associated liver disease and other hepatic conditions can alter drug metabolism and increase susceptibility to drug toxicity. Liver function should be considered when selecting and monitoring medications such as naltrexone, valproate, and other hepatically metabolized drugs.^{10, 21}

15.5 Renal impairment

Renal function is particularly important for lithium and acamprosate. Renal impairment may require

dose adjustment, increased monitoring, or avoidance depending on the medication and severity of the dysfunction.^{10, 21}

15.6 Medication adherence

Adherence difficulties may arise from cognitive symptoms, unstable housing, intoxication, psychiatric relapse, adverse effects, complex regimens, and limited access to care. Simplified regimens, long-acting formulations when appropriate, medication counselling, reminders, family or caregiver involvement when acceptable, and structured follow-up may support continuity.^{29, 31}

Table 1. Pharmacotherapeutic Options for Major Substance Use Disorders

Disorder	Medication/ Approach	Primary role	Important precautions	Evidence status
AUD	Naltrexone	Reduce heavy drinking/ consumption	Opioid exposure; hepatic considerations	Established
AUD	Acamprosate	Maintain abstinence	Renal impairment	Established
AUD	Disulfiram	Support abstinence in selected patients	Adherence; hepatic/ cardiovascular considerations	Established in selected patients
ODD	Methadone	Maintenance treatment	Respiratory depression; QT prolongation; interactions	Established
ODD	Buprenorphine	Maintenance treatment	Sedation/ interactions; initiation considerations	Established
ODD	Naltrexone	Opioid antagonist treatment	Must be opioid-free; adherence	Established in selected patients
StUD	Contingency management	Core treatment approach	Implementation/ access	Evidence-supported standard
StUD	Off-label pharmacotherapies	Selected patients	Evidence remains limited/ heterogeneous	Not a universal standard
CUD	Psychosocial interventions	Reduce use/ relapse	Engagement and retention	Core approach
Nicotine	Varenicline/ NRT/ Bupropion	Smoking cessation	Drug-specific contraindications/interactions	Established

16. INTEGRATED CLINICAL MANAGEMENT

Integrated management means that psychiatric illness and SUD are assessed and addressed within a coordinated treatment plan rather than being treated as separate conditions. Contemporary

evidence suggests the potential benefits of coordinated approaches, although the literature is heterogeneous and does not support a single intervention as being universally superior.^{8, 9, 27, 28}

16.1 Initial assessment



- Establish psychiatric diagnosis and assess current symptom severity.
- The substances used, frequency, route, quantity, duration, and recent changes were identified.
- Intoxication and withdrawal risks were assessed.
- Review prescribed, over-the-counter, and non-prescribed medications.
- Assess medical comorbidities, renal and hepatic function, and relevant laboratory parameters of the patients.
- Assess adherence, previous treatment response, adverse effects, and barriers to care.
- Assess suicide, overdose, violence, and other immediate safety risks when clinically indicated.

16.2 Coordinated treatment

Treatment should address SUD and psychiatric disorders in parallel when clinically appropriate. Depending on the clinical presentation, this may include medication for SUD, psychotropic medication, psychotherapy, motivational interventions, relapse prevention, family support, peer support, social interventions, and harm-reduction services.^{3, 30}

16.3 Continuity of care

Transitions between emergency departments, inpatient psychiatry, addiction services, primary care, and community care are high-risk periods for medication discrepancies and treatment interruptions. A shared medication list, clear follow-up plan, communication between services,

and patient education can help reduce fragmentation.^{2, 27}

17. ROLE OF THE CLINICAL PHARMACIST

Clinical pharmacists can contribute to integrated management through medication-related assessments and coordination. Their role is particularly relevant when patients receive multiple psychotropic agents, medications for addiction treatment, and drugs for treating medical comorbidities.

- Medication reconciliation at admission, discharge, and during care transitions.
- Identification and management of drug–drug and drug–disease interactions.
- Assessment of medication adherence and barriers to adherence.
- Monitoring for adverse drug reactions and medication-related problems.
- Review of hepatic, renal, metabolic, haematological, and other laboratory monitoring requirements.
- Support for therapeutic drug monitoring when clinically indicated.
- Patient and caregiver counselling on medication use, missed doses, interactions, and warning signs.
- Education on overdose prevention and naloxone access, where appropriate.
- Support for smoking cessation and assessment of changes in smoking status that may affect psychotropic exposure.



- Communication of medication recommendations to psychiatrists, addiction specialists, nurses, psychologists, and primary-care clinicians.
- Documentation and follow-up of medication-related outcomes.³¹

18. HARM REDUCTION

Harm reduction should complement, rather than replace, the evidence-based treatment. In OUD, overdose prevention and access to naloxone are important components of the care. Patients should be educated about the risks associated with combining opioids with alcohol, benzodiazepines, and other CNS depressants. For stimulant use, harm-reduction counselling should address cardiovascular risk, overheating, polysubstance exposure and recognition of acute toxicity. Harm-reduction interventions should be adapted to patients' circumstances and treatment goals.^{13, 14}

19. EVIDENCE GAPS AND FUTURE RESEARCH

Several important evidence gaps remain. Patients with complex psychiatric comorbidities and polysubstance use may be underrepresented in controlled treatment research, limiting generalizability to real-world dual-diagnosis populations. Evidence for the pharmacotherapy of stimulant and cannabis use disorders remains substantially less definitive than evidence for AUD and OUD.^{8, 9, 15, 16, 20, 24}

Additional research is needed on long-term treatment retention, relapse, quality of life, functional recovery, mortality and patient-reported outcomes. Comparative effectiveness studies should evaluate medication strategies in well-characterized psychiatric populations rather than

treating all dual-diagnosis patients as a single group.^{8, 9, 20, 24}

There is also a need for research in low- and middle-income settings, where service availability, medication access, stigma, and patterns of substance use may differ from those in high-income countries. Pharmacist-led medication-management interventions, digital adherence support, collaborative care, and integrated hospital-to-community models represent additional research priorities.^{9, 29, 31}

Future studies should report psychiatric diagnoses, substance type, polysubstance use, treatment setting, adherence, medical comorbidity, and relevant patient-centered outcomes. Longer follow-up is required to determine whether early improvements are sustained.^{8, 9}

20. CONCLUSION

Co-occurring SUD and psychiatric disorders represent a complex clinical population in which diagnosis, pharmacotherapy, adherence, safety monitoring, and continuity of care are closely interconnected. Pharmacological treatment is well established for AUD and OUD, while evidence for stimulant and cannabis use disorders remains limited. Nicotine dependence should be actively addressed, particularly in psychiatric populations in which smoking-related health risks are substantial.

Treatment should not routinely be postponed until SUD has resolved. Instead, psychiatric and substance-use conditions should be assessed and treated concurrently when clinically appropriate, with careful attention to substance-induced symptoms, medication interactions, organ function, adverse effects, adherence, and patient preferences. Integrated psychosocial care and



harm reduction can complement pharmacotherapy.

Clinical pharmacists can provide valuable support through medication reconciliation, interaction screening, adverse-effect monitoring, adherence assessment, counselling, laboratory monitoring, smoking cessation support, and multidisciplinary

communication. Future research should focus on severe psychiatric illness, polysubstance use, long-term outcomes, quality of life, treatment retention, and pharmacist-led interventions. A coordinated, patient-centered approach offers a practical framework for improving medication safety and continuity of care in dual-diagnosis populations.

Table 2. Psychiatric Disorder and SUD: Pharmacotherapeutic Considerations

Psychiatric condition	Key considerations	Medication issues	Monitoring focus
Depression	Differentiate primary vs substance-induced symptoms	SSRIs/SNRIs may be appropriate in selected patients; treat SUD directly	Mood response, adherence, suicidality, interactions
Bipolar disorder	Intoxication/ withdrawal may mimic mood episodes	Lithium, valproate, lamotrigine, antipsychotics according to presentation	Renal/thyroid function, hepatic/ hematologic safety, serum levels
Schizophrenia	High relapse/ adherence burden	Antipsychotics; LAIs when appropriate; clozapine for treatment resistance	Metabolic effects, adherence, smoking status, ANC for clozapine
Anxiety disorders	Withdrawal may mimic anxiety	SSRIs/SNRIs and psychotherapy; caution with benzodiazepines	Sedation, misuse risk, treatment response
ADHD	Impulsivity, diversion and misuse risk	Long-acting stimulants or non-stimulants in selected patients	Misuse/diversion, adherence, cardiovascular and psychiatric effects

Table 3. Major Pharmacotherapeutic Safety Concerns in Dual-Diagnosis Patients

Concern	Examples	Potential consequence	Clinical response
CNS/ respiratory depression	Opioids + benzodiazepines/ alcohol/ sedatives	Sedation, respiratory depression, overdose	Avoid/minimize risky combinations; monitor closely
QT prolongation	Methadone + QT-prolonging psychotropics	Arrhythmia risk	Medication review; ECG when indicated; correct modifiable factors
Hepatic impairment	AUD/liver disease + hepatically metabolized drugs	Accumulation/ toxicity	Assess liver function and treatment suitability
Renal impairment	Lithium, acamprosate	Accumulation/ toxicity	Renal monitoring and dose adjustment
Smoking-status change	Clozapine/ olanzapine	Altered drug exposure	Reassess concentration/clinical response after major changes
Polypharmacy	Multiple psychotropics + addiction medications	Interactions, adverse effects, adherence burden	Medication reconciliation and deprescribing where appropriate

Table 4. Clinical Pharmacist Contributions to Integrated Management

Domain	Pharmacist activity	Expected clinical value
Medication reconciliation	Identify discrepancies, duplication and omitted therapy	Improved medication safety
Interaction screening	Assess drug–drug and drug–disease interactions	Reduced preventable harm



Adherence	Assess barriers, simplify regimen and counsel	Improved continuity
Monitoring	Review laboratory and adverse-effect monitoring	Earlier detection of toxicity
Patient education	Explain medicines, risks, missed doses and warning signs	Improved understanding and self-management
Harm reduction	Support overdose-prevention education and naloxone access where appropriate	Reduced preventable harms
Smoking cessation	Support NRT/varenicline/bupropion use and monitor smoking-status changes	Improved tobacco treatment
Multidisciplinary care	Communicate medication recommendations and follow-up findings	More coordinated treatment

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