Comprehensive Continuous Integrated System of Care (CCISC)

Psychopharmacology Practice Guidelines for Individuals with Co-occurring Psychiatric and Substance Use Disorders (COD)

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Developed by

Kenneth Minkoff, MD
Clinical Assistant Professor of Psychiatry, Harvard Medical School
Senior Systems Consultant, ZiaLogic

With invaluable assistance from
Terry Schwartz, MD, Jeff Rowe, MD, and other members of the Psychopharmacology Committee of the San Diego County CCISC Project

Based on the psychopharmacology guidelines in
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©2005 Kenneth Minkoff, MD
100 Powdermill Road, #319
Acton, MA 01720
KMinkov@apl.com
www.kenminkoff.com
Background

Individuals with co-occurring psychiatric and substance disorders (COD) represent a challenging population associated with poorer outcomes and higher costs in multiple domains. In addition, the prevalence of comorbidity is sufficiently high that we can say that comorbidity is an expectation, not an exception throughout the system of care. Consequently, individuals with cod cannot be adequately served with only a few specialized programs; rather, the expectation of comorbidity must be addressed throughout the system of care. The Comprehensive Continuous Integrated System of Care (CCISC) (Minkoff & Cline, 2004) is a model for system design which permits any system to address this problem in an organized manner within the context of existing resources. The basic premise of this model is that all programs become dual diagnosis programs meeting minimal standards of Dual Diagnosis Capability, and all clinician (including psychopharmacology prescribers) become dual diagnosis clinicians meeting minimal standards of dual diagnosis competency, but each program and each clinician has a different job. The job of each program is based first on what it is already designed to be doing, and the people with cod who are already being seen, but the goal is to organize the infrastructure of the program to routinely provide matched services to those individuals within the context of the program design, which in turn defines specific clinical practices for clinicians working within that setting, that define their competency requirements. The service matching in this model is based on a set of evidence-based principles in the context of an integrated philosophic model that makes sense from the perspective of mental health and addiction treatment. These principles in turn have been utilized to develop practice guidelines that define the process of assessment and treatment matching at the clinical level, and outline the “job” of each program in the system as well.

The most recent version of the comprehensive CCISC practice guidelines were developed by Kenneth Minkoff, MD in 2001, based on work of a consensus panel that led to a SAMHSA report in 1998 entitled: “Individuals with Co-occurring disorders in Managed Care Systems: Standards of Care, Practice Guidelines, Workforce Competencies, and Training Curricula” (Minkoff, 1998). The 2001 updated version of the practice guideline section of the report is being utilized by the Behavioral Health Recovery Management Project in the State of Illinois, and is available on line at www.bhrm.org. The current document is an update of the psychopharmacology section of that document. The need for this document is based on the recognition that although there are psychopharmacology guidelines that have been developed for the treatment of individuals with a variety of mental illnesses OR substance disorders, most practitioners have neither training, or experience, in an organized approach to the individuals who have various combinations of mental health and substance conditions who commonly present in clinical practice, particularly in public sector settings.

General Principles

The seven general principles of CCISC are designed to provide a welcoming, accessible, integrated, continuous, and comprehensive system of care to patients with CODs. These principles, and their application to psychopharmacology, are listed below:

1. Dual Diagnosis is an expectation, not an exception.
All psychiatrists need to develop comfort with the likelihood that any patient requiring psychopharmacologic evaluation may also have a substance use disorder, and be able to incorporate this expectation into every clinical contact, beginning with assessment, and continuing throughout the treatment process. Consequently, it is necessary to have an organized evidence based approach to assessment and treatment of individuals who present with co-occurring conditions of any type. In addition, given the expected complexity of many patients with co-occurring disorders, it is helpful to routinely organize access to peer consultation (defined below) as a valuable way for prescribers to obtain help and guidance when treating patients with unusual or complicated clinical situations.

2. Successful treatment is based on empathic, hopeful, integrated and continuing relationships.

Successful psychopharmacology is not an absolute science governed by the application of rigid rules. Rather, it is best performed in the context of an empathic, hopeful relationship, which integrates ongoing attention to both psychiatric and substance use issues. Emphasis needs to be placed on an initial integrated (both mental health and substance use) evaluation and continuous re-evaluation of diagnoses and treatment response.

Practitioners of psychopharmacology in mental health settings should not underestimate the importance of ongoing inquiry regarding co-occurring substance use, continued encouragement of healthy decision making regarding substance use, and support to other caregivers who are engaged with the patient and his or her family in addressing these issues.

3. Treatment must be individualized utilizing a structured approach to determine the best treatment. The national consensus “four quadrant” model for categorizing individuals with co-occurring disorders can be a first step to organizing treatment matching.

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This model divides individuals throughout a service system into four quadrants based on high and low severity of each disorder. Psychopharmacologic strategies may need to be adjusted based on type and level of severity of each illness in COD. In particular, individuals with high severity mental illness are more likely to be considered high priority mental health clients with Serious and Persistent Mental Illness (SPMI) and associated disability, who are a high priority for continuing engagement in psychopharmacologic treatment in the mental health system. Individuals with high severity substance use disorders generally are those with active substance dependence (addiction), as opposed to those with lower severity disorders, such as substance abuse. Pharmacologic strategies for either mental illness or substance use disorder may vary, depending on the severity of the mental illness and the diagnosis of dependence versus abuse (see below).

4. Case management and clinical care (in which we provide for individuals that which they cannot provide for themselves) must be properly balanced
with empathic detachment, opportunities for empowerment and choice, contracting, and contingent learning.

As most individuals cannot legally prescribe their own medication, the ability to receive medication for the treatment of CODs is a vital aspect of the integrated treatment relationship. Given that treatment involves learning, the psychopharmacologic treatment relationship needs to balance ongoing necessary continuity of care (see below) with opportunities for contingent learning (negotiation of type, quantity, and duration of treatment with any medication) without threat of loss of the treatment relationship. This contingent learning may require a “trial and error” process and several attempts before successful. Contingency plans are most effective in the context of a good therapeutic alliance.

5. When mental illness and substance use disorder co-exist, each disorder is “primary”, requiring integrated, properly matched, diagnosis specific treatment of adequate intensity.

Thus, in general, psychopharmacologic interventions are designed to maximize outcome of two primary disorders, as follows:

a. For diagnosed psychiatric illness, the individual receives the most clinically effective psychopharmacologic strategy available, regardless of the status of the comorbid substance disorder. (N.B. Special considerations apply for utilization of addictive or potentially addictive medications that may have psychiatric indications, such as benzodiazepines and stimulants. See below.)

b. For diagnosed substance disorder, appropriate psychopharmacologic strategies (e.g., disulfiram, naltrexone, opiate maintenance) are used as ancillary treatments to support a comprehensive program of recovery, regardless of the status of the comorbid psychiatric disorder (although taking into account the individual’s cognitive capacity and disability).

Within the application of the above rules, there is some evidence for improvement in certain addictive disorders reported with several medications that also have common psychiatric indications (e.g., SSRIs, bupropion, topiramate) (See below). Although there is little evidence to support selecting one medication for any combination as a “magic bullet”, the prescriber may want to consider the possible impact on a co-occurring substance use disorder when choosing medication for a psychiatric disorder.

6. Both serious mental illness and substance dependence disorders are primary biopsychosocial disorders that can be treated in the context of a “disease and recovery” model. Treatment must be matched to the phase of recovery (acute stabilization, engagement/motivational enhancement, active treatment/prolonged stabilization, rehabilitation/recovery) and stage of change or stage of treatment for each disorder.

Psychopharmacologic practice may vary depending on whether the individual is requiring acute stabilization (e.g., detoxification) versus relapse prevention or rehabilitation. In addition, within the psychopharmacologic relationship, individuals may be engaged in active treatment or prolonged stabilization of one disorder (usually mental illness), which may provide an opportunity for the prescriber to participate in provision of motivational strategies regarding other comorbid conditions.
7. There is no one correct approach (including psychopharmacologic approach) to individuals with co-occurring disorders. For each individual, clinical intervention must be matched according to the need for engagement in an integrated relationship, level of impairment or severity, specific diagnoses, phase of recovery and stage of change. This principle provides the framework for practice guidelines and treatment matching generally, including the application of the practice guidelines to psychopharmacologic practice.

Clinical Practice Guidelines

Utilizing the principles as a foundation, the following clinical practice guidelines can be developed. These guidelines include both specific recommended or suggested practices, as well as providing a suggested sequence for prioritization of clinical activities.

1. Welcoming: All psychopharmacologic practitioners should strive to welcome individuals with co-occurring disorders into treatment as a high risk, high priority population, and to engage them in empathic, hopeful, integrated and continuing treatment relationships in which outcomes of psychopharmacologic intervention can be optimally successful.

2. Access: Because of the importance of engaging individuals in treatment as quickly as possible, and because (as will be noted below) initial diagnostic evaluation is based significantly upon historical data, **there should be no arbitrary length of sobriety requirement for access to comorbid psychiatric evaluation.** Initial evaluations should only require that the client be able to carry on a reasonable conversation, and not require that alcohol or drug levels be below any arbitrary figure. Referral for psychopharmacologic evaluation should occur as quickly as possible (based on triage of acuity and dangerous risk factors). Maintaining existing non-addictive psychotropic medication during detoxification and early recovery is strongly recommended as substance abuse increases the risk of destabilization of the mental illness.

3. Safety: The first priority in the evaluation process is to maintain safety, both for the patient and the treatment staff. Psychopharmacologic intervention can be vital in this effort. In situations involving acutely dangerous behavior, it may be necessary to utilize antipsychotics and other sedatives (including benzodiazepines) to establish behavioral control. In acute withdrawal situations requiring medical detoxification, use of detoxification medications for addicted psychiatric patients is no different than for patients with addiction only.

4. Integrated Assessment (ILSA): Assessment and diagnosis of individuals with CODs is based on a process of **integrated longitudinal strength based assessment (ILSA)** (See Center for Substance Abuse Treatment, Treatment Improvement Protocol #42, 2005), which begins as soon as the patient is welcomed into care, immediate safety established, and the capacity to obtain a history (from...
client or collaterals) is present. This process incorporates a careful chronological
description of both disorders; including emphasis on onset, interactions, effects of
treatment, and contributions to stability and relapse of either disorder. As with all
psychiatric disorders, obtaining information from family members and collateral
caregivers can be extremely helpful. Particular attention to assessing previous
periods of sobriety or limited use for presence of psychiatric symptoms, and history
of medication responses with or without sobriety can be useful.

Diagnosis of persistent psychiatric disorders in patients with COD can be
difficult given the overlap of symptoms with substance use disorders. Information
about the presence of symptoms and need for continued psychiatric treatment
either prior to onset of substance use disorder, or during periods of abstinence or
low substance use of 30 days or longer can be vital in making a meaningful
psychiatric diagnosis. These periods of time can occur at ANY TIME in the
patient's history after the onset of illness, and do not have to be current.

Diagnostic and treatment decisions regarding psychiatric illness are ideally
made when the comorbid substance disorder is stabilized, ideally for 30 days or
longer. Nonetheless, thorough assessment (as described above) can provide
reliable indications for diagnosis and immediate initiation or continuation of
psychopharmacologic treatment, even for individuals who are actively using.
This is particularly true for individuals with more serious and persistent mental
illness and more severe symptomatology, regardless of diagnosis.

Diagnostic and treatment decisions regarding substance disorder are best made
when the comorbid psychiatric disorder is at baseline. Nonetheless, thorough
assessment can provide reliable information about the course and severity of
substance disorder, even for an individual whose mental illness is destabilized, and
can provide reliable indications for diagnosis and immediate initiation or
continuation of psychopharmacologic treatment (e.g., opiate maintenance).

Finally, integrated assessment during periods of stabilization may also provide
evidence that justify rescinding a previously made diagnosis, and carefully
discontinuing medication that may seem to have no further indication, either
because the condition for which treatment was initiated has completely resolved
(e.g., substance induced psychosis), or because further evaluation indicates that
justification for the diagnosis no longer exists.

5. Continuity: Provision of necessary non-addictive medication for treatment
of psychotic illness and other known serious mental illness must be initiated or
maintained regardless of continuing substance use. Individuals whose substance
use appears to be significantly risky warrant closer monitoring or supervision,
NOT treatment discontinuation. Peer consultation is indicated for cases in which
the treating psychiatrist is considering medication discontinuation due to ongoing
substance use for an individual with known or probable serious and persistent mental
illness, including persistent substance induced disorders.

In patients with active substance dependence or substance dependent patients in
early recovery, non-addictive medication for any psychiatric disorders may be initiated
or maintained, provided reasonable historical evidence for the value/need for the
medication is present.

Over time, within the context of a continuing psychopharmacologic relationship,
continuing re-evaluation of diagnosis and psychopharmacologic regimes is
recommended, both to insure appropriate continuity of stabilizing medication for
established disorders, as well as to insure discontinuation of medication for disorders
that have resolved, discontinuation of medication that is not effective, and cautious
discontinuation of treatment for disorders whose diagnosis appears to be no longer
supported (while maintaining awareness that there is always a risk of recurrence in
discontinuing medication, even for asymptomatic individuals).

6. Consultation for Prescribers: It is highly recommended that every system
establish a mechanism for expert and/or peer consultation to assist both
psychopharmacology prescribers and other members of the treatment team in
making decisions regarding challenging patients. Consultation provides a
framework for obtaining clinical support, as well as for reviewing clinical decision
making from a risk management standpoint. Furthermore, work with people who have
CODs can be both frustrating and very rewarding, and the peer consultation process
can be a vehicle for both recognizing special effort by clinicians, as well as to support
the clinical team when dealing with particularly challenging cases. Examples of
appropriate cases for expert or peer consultation include (but are not limited to):

1. Continuation of treatment with benzodiazepines (beyond
detoxification) in patients with known substance
dependence.
2. Discontinuation of psychiatric medications for a substance
using patient with a serious, persistent psychiatric illness.
3. Unilateral termination of clinical care for any patient with
CODs

7. Psychopharmacological Treatment Strategies

A. General principles: In patients with psychotic presentations, with or
without active substance dependence, initiation of treatment for psychosis is
generally urgent. In patients with known active substance dependence and non-
psychotic presentations, it is recommended to utilize the integrated longitudinal
assessment process to determine the probability of a treatable mental health
diagnosis before medication is initiated. It can be very difficult to make an
accurate diagnosis and effectively monitor treatment without this first step. It is
understood that all diagnoses are “presumptive” and subject to change as new
information becomes available. If there is uncertainty about diagnosis after
reasonable history taking, evidence for initial efforts to discontinue substance use
may need to occur prior to initiation of psychopharmacology, in order to establish a
framework for further diagnostic evaluation. However, for high risk patients,
with or without psychosis, developing a treatment relationship is a priority,
and there should not be an arbitrary length of time required before treatment
initiation takes place, nor should absolute diagnostic certainty be required.
Individuals with reasonable probability of a treatable disorder can be treated

Psychotropic medications, particularly for anxiety and mood disorders, should
be clearly directed to the treatment of known or probable psychiatric disorders, not
to medicate feelings. It is important to communicate to patients with addiction
that successful treatment of a comorbid anxiety or mood disorder with medication
is not intended to remove normal painful feelings (such as normal anxiety or
depressed feelings). The medication is meant to help the patient feel his or her
painful feelings accurately, and to facilitate the process of developing healthy
capacities to cope with those feelings without using substances. If psychotropic
medications are used for mental illness in individuals with addiction, or if medication is used in the treatment of the addiction itself, the following precepts may be helpful to communicate to the patient:

“The use of medication for either type of disorder does not imply that it is no longer necessary for the patient to focus on the importance of his/her own work in recovery from addiction. Consequently, utilizing medication to help treat addiction should always be considered as an ancillary tool to a full addiction recovery program.”

Addicts in early recovery have great difficulty regulating medication; fixed dose regimes, not PRN’s, are recommended in the treatment of mood and anxiety disorders.

Just as in individuals with single disorders, and perhaps more so, it is important to engage patients with co-occurring disorders as much as possible in understanding the nature of the illness or illnesses for which they are being treated, and to participating in partnership with prescribers in determining the best course of treatment. For this reason, most established medication algorithms (e.g. TMAP) and practice guidelines recommend that medication education and peer support regarding understanding the risks and benefits of medication use are incorporated into standard treatment practice. This is certainly true for individuals with co-occurring disorders, for whom information provided by peers may be particularly helpful in making good choices and decisions regarding both taking medication and reduction or elimination of substance use.

B. Diagnosis specific psychopharmacological treatment for mental illness

1. Psychotic Disorders: Use the best psychotropic agent available for the condition. Improving psychotic or negative symptoms may promote substance recovery. This includes treatment of substance-induced psychoses, as well as psychosis associated with conventional psychiatric disorders.

   a. Atypical neuroleptics: Consider olanzapine, risperidone, quetiapine, aripiprazole, ziprasidone or clozapine. In addition, it is well documented that clozapine has a direct effect on reducing substance use in this population, beyond any improvement in psychotic symptoms, and therefore may be specifically indicated for selected patients.

   b. Typical neuroleptics: Consider use in adjunct to the atypicals, especially in situations of acute agitation, unresolved psychosis, and acute decompensation

   c. Many individuals with cod will benefit from depot antipsychotic medications. Both typical and atypical neuroleptics (e.g., risperidone) are available in depot form. There have not been specific studies about the utilization of depot risperidone in individuals with co-occurring substance use disorder, but there is no apparent contraindication to its use.

2. Major Depression: The relative safety profile of SSRI’s (and to a somewhat lesser extend SNRI’s such as venlafaxine), other newer generation antidepressants and possibly buproprion (though higher seizure risk must be
considered) make their use reasonable (risk-benefit assessment) in the treatment of individuals with CODs. SSRI’s have been demonstrated to be associated with lower alcohol use in a subset of alcohol dependent patients, with or without depression. The use of tricyclic antidepressants (TCAs) and MAO inhibitors (MAOIs) can be more difficult and possibly more dangerous in the COD population if there is a risk of active substance use.

3. **Bipolar Disorder**: Use the best mood stabilizer or combination of mood stabilizers that match the needs of the patient. Be aware that rapid cycling and mixed states may be more common, hence consider valproate, oxycarbamazepine, carbamazepine or olanzapine (and other atypicals), in patients who may have these variants.

4. **ADHD**: Initial treatment recommendations, in early sobriety, have included buproprion. Recently, atomoxetine has been available, and may be a reasonable first choice, though there have not been specific studies in co-occurring populations. In both adolescents and adults, there is clear evidence that if stimulant medications are necessary to stabilize ADHD, then these medications can be used safely, once addiction is adequately stabilized and/or the patient is properly monitored, and will be associated with better outcomes for both ADHD and substance use disorder.

5. **Anxiety disorders**: Consider SSRIs, venlafaxine, buspirone, clonidine and possibly mood stabilizers such as valproate, carbamazepine, oxycarbamazepine, gabapentin, and topiramate, as well as atypical neuroleptics. There is evidence of effectiveness of topiramate for nightmares and flashbacks associated with PTSD.

For patients with known substance dependence (active or remitted), the continuation of prescriptions for benzodiazepines, addictive pain medications, or non-specific sedative/hypnotics is not recommended, with or without comorbid psychiatric disorder. On the other hand, medications with addiction potential should not be withheld for carefully selected patients with well-established abstinence who demonstrates specific beneficial responses to them without signs of misuse, merely because of a history of addiction. However, consideration of continuing prescription of potentially addictive medications for consumers with diagnosed substance dependence, is an indication for both (a) careful discussion of risks and benefits with the patient (and, where indicated, the family) and (b) documentation of expert consultation or peer review.

**Sleep disturbances** are common in mental illness as well as substance use disorders in early recovery. Use of non-addictive sedating medications (e.g., trazodone) may be used with a careful risk benefit assessment.

**C. Psychopharmacologic Strategies in the Treatment of Substance Use Disorders**

There is an increasing repertoire of medications available to treat substance use disorders, including medications that appear to directly interrupt the core brain
processes associated with lack of control of use. All of these medications have demonstrated effectiveness in populations who may also have psychiatric disorders, including severe mental illnesses.

1. Disulfiram
   A. Disulfiram interferes with the metabolism of alcohol via alcohol dehydrogenase, so that individuals who use alcohol will get ill to varying degrees when taking this medication. This can be a valuable tool in assisting individuals to resist impulsive drinking, but generally must be combined with additional recovery programming and/or positive contingencies. Disulfiram should NOT be used to coerce sobriety in any patient.
   B. As a dopamine beta-hydroxylase inhibitor, disulfiram occasionally will exacerbate psychosis, necessitating adjustment of antipsychotic medication.
   C. As a dopamine beta-hydroxylase inhibitor, disulfiram has also been found to reduce cocaine craving and cocaine usage in some studies.

2. Opiate maintenance treatment
   A. Methadone and LAAM are well established treatments for opiate dependence, and have been found to be successful in individuals with a wide range of psychiatric comorbidity, in the context of methadone treatment programs. Methadone dosing is now informed by the capacity to measure trough levels. The prescriber must be aware that there are enzymatic interactions that affect the interaction of methadone with various psychotropics, the details of which are beyond the scope of these guidelines, but which should be reviewed when such combinations are being initiated.
   B. Buprenorphine has been more recently introduced for opiate maintenance, does not require participation in a formal “program”, like methadone, and can be provided in office based settings by physicians who have addiction specialization and/or who have had eight hours of training. Oral buprenorphine is provided combined with naloxone to prevent diversion for parenteral use. It is a mixed m-opiate receptor agonist () and a k-receptor antagonist, that appears to be easier to utilize, with fewer side effects, and less severe abuse or withdrawal risk, than methadone. Although not well studied in the co-occurring disordered population, all indications in the literature indicate that it is effective. Again, there are a range of interactions that may occur with enzymes that metabolize psychotropic medication, that need to be reviewed when initiating treatment.

3. Naltrexone
   A. Opiate dependence: Naltrexone is a relatively long acting opiate blocker that can be effective given three times weekly for opiate dependence, particularly when combined with significant contingencies to support adherence.
   B. Alcohol dependence: Naltrexone has been demonstrated to be effective in reducing alcohol use through reducing craving and loss of control, presumably by affecting endogenous opiate pathways that are involved in the development of the brain disorder of alcohol dependence. Naltrexone has been
demonstrated to be effective in individuals with schizophrenia and other mental illnesses in preliminary studies.

4. Acamprosate: Available in Europe for several years, acamprosate has recently been approved in the US. It reduces alcohol usage through an impact on endogenous GABA pathways. The combination of acamprosate plus naltrexone is reportedly more effective than either alone.

5. Bupropion for nicotine dependence appears to have an effect on reward pathways associated with nicotine use. Nicotine replacement for nicotine dependence, including nicotine patch, gum, and more recently, nasal spray, which most closely mimics the effects of smoking in nicotine delivery. Bupropion and nicotine replacement combined tend to result in better outcomes than either alone.

6. Topiramate for alcohol dependence (one study) has some potential value through its effect on GABA receptors.

7. Desipramine for cocaine craving has yielded very inconsistent findings.

8. Dopaminergic agents for cocaine craving have also yielded inconsistent findings, with risk of exacerbation of psychosis.

9. Serotonergic agents (e.g., SSRIs) have been found in some studies to have a beneficial effect in reducing alcohol use in non-depressed alcoholics, particularly in certain subtypes of alcohol dependence.

D. General Strategies for Managing Interactive Effects of Substance Use on Psychiatric Symptoms and Interventions

The effects of various substances on psychiatric presentations and on psychiatric treatment are quite variable. Discussion of the effects of each type of substance on psychiatric symptoms and medications are described in most textbooks, and are beyond the scope of these guidelines. The prescriber should always keep in mind that the best way to evaluate the effect of a particular pattern of substance use on a particular client is to get a good history from that client and collaterals. Further, although there are unquestionably unpredictable risks that may be attached to continuing substance use in individuals receiving psychiatric care, the risks of poor outcome associated with NOT TREATING a known mental illness appear to significantly outweigh the risks of continuing treatment in an individual who is continuing to use substances. Individuals who engage in particularly risky behavior should be monitored more closely, not discontinued from necessary psychiatric or medical treatment.

E. Special Stage Specific Strategies

1. **Motivational Interventions:** In clinical situations where the psychiatric diagnosis and/or severity of substance disorder are unclear, psychotropic medications may be initiated if there is a reasonable indication, and used as part of a strategy to facilitate engagement in treatment and the creation of contingency contracts to promote abstinence.

2. **Contingency Management Interventions:** Within the context of a psychopharmacologic relationship where necessary medication is provided, interventions that may be considered
optional or discretionary can be linked to incremental progress in addressing substance use disorders. In addition, in individuals receiving benzodiazepines, emergence of substance use can be addressed by creating contingency plans that allow the individual to maintain benzodiazepine dosage only if abstinence is maintained. Slow reduction of dosage can offer multiple opportunities for the patient to regain the original dosage by re-establishing abstinence. Evidence of severe overuse or overdosage with benzodiazepines, however, is usually an indication for discontinuation, often in a hospital setting.

8. Continuing Evaluation and Re-evaluation

It is important not to expect that diagnostic certainty can be obtained at the beginning of treatment. Individuals may begin on medication for a presumed diagnosis during periods of substance use, and once they have stopped using the presumed diagnosis may appear to clear up, necessitating the discontinuation of medication. Conversely, once individuals stop using, psychiatric disorders may emerge or worsen, requiring the initiation of medication. It is important to maintain an open minded stance, and to consider all possibilities. Each patient must be considered as an individual, and continuity of care provides an opportunity to become increasingly more accurate about diagnosis and treatment over time.