

Diagnosing comorbidity: concepts, criteria, and methods

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Background: The clinical and etiologic implications of comorbid psychiatric and substance-use disorders are relevant across countries and cultures. The DSM-IV now places greater emphasis on the clinical and research utility of the substance-induced disorders classification, and clarifies several important diagnostic issues specific to primary and substance-induced disorders. However, no research consensus exists over the core problem of identifying and differentiating the drug and alcohol intoxication and withdrawal symptoms that can mimic psychiatric symptoms in heavy drinkers and drug users.

Objective: To investigate how various diagnostic instruments have measured comorbid psychiatric and substance-use disorders and how each instrument operationalizes the DSM-IV classification.

Method: We review the evolution of the concept of comorbidity beginning with its formalization as the ‘primary–secondary’ distinction in the Feighner Criteria. We address the ‘organic–non-organic’ distinction found in the RDC, DSM-III, and DSM-III-R; and finally, review the ‘primary’ and ‘substance-induced’ categories of DSM-IV, DSM-IV-TR and ICD-10. We describe how these distinctions have been operationalized in widely used diagnostic instruments.

Conclusion: Further understanding of these classifications and the relationship of co-occurring psychiatric and substance disorders can be accomplished with the range of available measures, particularly the Psychiatric Research Interview for Substance and Mental Disorders (PRISM), which reliably utilizes and refines DSM-IV classification distinctions.

Introduction

Psychiatric and substance-use disorders are serious problems for the individuals who have them as well as for society as a whole. Unfortunately, the presence of one of these types of problems greatly increases the risk for the other. A high level of comorbidity between major psychiatric conditions and substance abuse in clinical samples was shown in the U.S. starting in the 1980s (1,23,45,6). Clinical samples in Europe also show high comorbidity, including those in Germany (7), Finland (8), Iceland (9), Switzerland (10), Italy (11), and the UK (12). Other areas of the world reflect the same pattern, including Iran (13), Pakistan (14), Taiwan (15,16), and Israel (17).

Comorbidity is also high in the general population in the U.S. (18–20), and in Europe, for example

in the Netherlands (21), England and Wales (22), Finland (23), and Norway (24). General population surveys conducted in other parts of the world also show high rates of comorbidity, including Taiwan (25), the United Arab Emirates (26), and Russia (27). Thus, the clinical and etiological implications of the comorbidity between psychiatric and substance-use disorders are relevant across countries and cultures.

Despite the importance of understanding relationship of psychiatric to substance disorders when comorbid, progress in this area has been slow. This is owing, in part, to measurement problems. Research on comorbidity is complicated by the fact that drug and alcohol intoxication and withdrawal symptoms can mimic psychiatric symptoms, without consensus on how to differentiate

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these symptoms in heavy drinkers and drug users. This problem was demonstrated in the mid-1980s by a study (28,29) that compared diagnoses from two widely used research diagnostic interviews on a series of alcoholic patients. The results showed that the diagnoses from the two instruments agreed poorly. Subsequently, a review (30) showed that even when the same diagnostic interview was administered, the procedures to differentiate psychiatric symptoms from intoxication and withdrawal symptoms varied widely from group to group.

This article reviews the evolution of the concept of comorbidity beginning with the 'primary–secondary' distinction first formalized in the Feighner Criteria, continuing with the 'organic–non-organic' distinction found in the Research Diagnostic Criteria (RDC) (31), DSM-III (32), and DSM-III-R (33), and finally in the 'primary' and 'substance-induced', categories of DSM-IV (34), DSM-IV-TR (35), and ICD-10 (36). After reviewing these concepts, we then describe how they have been operationalized in widely used diagnostic instruments. We end with recent examples of research illustrating what can be gained by fully utilizing and refining the distinctions in DSM-IV.

Diagnostic concepts in research on comorbidity

'Primary' and 'secondary'

The primary–secondary distinction has been used to imply cause and effect between substance abuse and co-occurring disorders (for example, delusions 'secondary' to cocaine intoxication). In a more specific sense (37), primary–secondary has also been defined by age at lifetime onset of the disorders. In this system, while the secondary condition can run concurrently with the previously existing primary disorder, this is not required. The Feighner primary–secondary distinction has face validity in suggesting that the first disorder is independent of subsequent disorders. However, it does not distinguish whether the 'secondary' disorder is independent of the first or how the disorders may be related. Psychiatric disorders tend to have characteristic ages of onset, with conduct disorder and attention deficit disorder (ADD) beginning in childhood, alcohol and drug abuse beginning in early to mid-adolescence, and mood, anxiety, and psychotic disorders beginning in late adolescence and adulthood. Thus, based on ordinary natural history, conduct/antisocial personality disorder and ADD are usually chronologically primary while mood, anxiety,

and psychotic disorders are chronologically secondary, regardless of the nature of the relationships between the primary and secondary disorders.

'Organic' and 'non-organic'

Between 1978 and 1993, three sets of diagnostic criteria were used: the RDC, DSM-III and DSM-III-R. These classification systems operationalized the differentiation of psychiatric symptoms from drug and alcohol effects similarly, ascribing symptoms to 'organic' or 'non-organic' etiology. Subjects 'in whom organic factors may play a significant role in the development of the psychiatric disturbance' (31) are excluded from assessment using the RDC. However, specific criteria for distinguishing organic from non-organic disorders are not provided, leaving the differentiation process unclear. As alcohol and drug abuse increased among patients with psychiatric disorders, this lack of specificity became increasingly problematic. DSM-III and DSM-III-R operationalized 'organic' etiology similarly. A psychiatric syndrome is considered 'non-organic' if 'it cannot be established that an organic factor initiated and maintained the disturbance'. (33). As in RDC, specific criteria for this decision were not provided, leaving room for discrepant approaches (30).

'Primary', 'substance-induced', and 'expected effects'

DSM-IV introduced important new concepts for differentiating between psychiatric and substance-use disorders. These were 'primary' and 'substance-induced' psychiatric disorders, and the 'expected effects' of intoxication and withdrawal. DSM-IV and DSM-IV-Text Revision provide more specific guidelines for making this differentiation. A 'primary' disorder is diagnosed if 'the symptoms are not due to the direct physiological effects of a substance'. In order to classify a disorder as 'substance-induced', a primary classification must first be ruled out. There are four conditions under which an episode that co-occurs with substance intoxication or withdrawal can be considered primary: (1) symptoms 'are substantially in excess of what would be expected given the type or amount of the substance used or the duration of use'; (2) a history of non-substance-related episodes; (3) the onset of symptoms precedes the onset of the substance use; and (4) the symptoms persist for a substantial period of time (i.e. at least a month) after the cessation of intoxication or acute withdrawal (35; pp.342,409). If neither

‘primary’ nor ‘substance-induced’ criteria are met, then the syndrome is considered to represent intoxication or withdrawal effects of alcohol or drugs (35; pp.342,409).

In DSM-IV and DSM-IV-TR, the older notion of chronological primary disorder is expanded in an important way. This is because a diagnosis can be made *after* the onset of a substance-use disorder if it occurs during a period of abstinence. Furthermore, through inclusion of a substance-induced category, DSM-IV recognizes that psychiatric syndromes may have clinical importance even though they co-occur with heavy alcohol or drug use. To assist in diagnosis and in training (an important function of a nosological system), DSM-IV-TR provides a table of diagnoses associated with different classes of substances (35; pp.193).

ICD-10

The American Psychiatric Association coordinated efforts with the World Health Organization in their preparation of ICD-10, Chapter V, ‘Mental and Behavioral Disorders’, to provide an international classification system that is as compatible as possible with DSM-IV (35; pp.883). The ICD-10 Diagnostic Criteria for Research (38) provides specified criteria to differentiate primary disorders and disorders resulting from psychoactive substance use, but only for psychotic disorders. As in DSM-IV, ICD-10 excludes psychotic episodes attributed to psychoactive substance use from a primary classification. In ICD-10, psychotic disorders can be attributed to psychoactive substance use under three conditions: (1) the onset of symptoms must occur during or within 2 weeks of substance use; (2) the psychotic symptoms must persist for more than 48 h; and (3) the duration of the disorder must not exceed 6 months. A psychotic disorder attributed to psychoactive substance use can be specified as predominantly depressive or predominantly manic. However, unlike DSM-IV, ICD-10 does not provide a separate psychoactive substance-related category for any other type of psychiatric disorder. By definition, ICD-10 ‘organic mental disorder’ excludes alcohol or other psychoactive substance-related disorders. ICD-10 organic mood disorder and organic delusional disorder cannot be used to diagnose episodes co-occurring with heavy psychoactive substance use. Thus, the DSM-IV concept of symptoms that are greater than the expected effects of intoxication and withdrawal is not included in ICD-10.

As can be seen from the descriptions, the DSM-IV concept of ‘primary’ and ‘substance-induced’ syndromes and the ICD-10 concept of ‘psychotic

disorders due to psychoactive substance use’ (38) support the notion that a psychiatric disorder warranting clinical attention can co-occur with heavy substance use. However, these categories continue to present diagnostic challenges. Differential diagnosis of categories of depression, anxiety, and psychosis often hinges on interpretation of the term ‘in excess’ of the ‘expected’ effects of substance use, including patients with chronic substance use beginning at an early age. These expected effects are not clearly defined by either system and are thus left to clinical judgment.

Structured diagnostic instruments

Several diagnostic instruments have been widely used in studies of psychiatric and substance comorbidity. Table 1 summarizes basic features of each with respect to differentiating primary from substance-induced disorders and describes the way each instrument operationalizes the intoxication and withdrawal ‘expected effects concept’.

SCID-IV

The Structured Clinical Interview for DSM-IV-TR Axis I Disorders (SCID-I, research version) (39) is a semistructured interview designed for use by experienced clinicians. Standard initial questions are provided, and the interviewer may re-word questions, if necessary, to clarify an item.

The differentiation of ‘primary’ and ‘substance-induced’ disorder is made on a syndromal level in the SCID. The interviewer assesses about substance etiology in a two-step process, as exemplified in the section on depression. In the SCID Depression module, relevant DSM criteria and a list of ‘etiological substances’ (39) are provided. A probe follows on whether the subject was drinking or using street drugs before the episode. Based on the subject’s response, the interviewer decides if there is a possibility of ruling out a diagnosis of primary depression. If so, the interviewer skips to a series of probes about the temporal relationship of the mood symptoms and substance use and if the mood symptoms were greater than the expected effects of the substance used.

Because the SCID relies on the interviewer’s clinical judgment, the SCID assessment of substance etiology can be problematic. First, the probe on whether the subject used substances to a relevant extent will often yield information that is open to interpretation. Second, the ‘primary’ vs. ‘substance-induced’ differentiation is established on a syndromal level. The SCID does not provide

Table 1. Features of psychiatric diagnostic interviews used to assess comorbidity of substance use and other psychiatric disorders

Instrument	Diagnostic criteria used	Psychometric testing of interview	Approach to comorbidity	Notable features
SSAGA (45,46)	DSM-III-R (DSM-IV and ICD-10 items can be extracted)	2 test-retest reliability studies; 1 validity study.	Ages at onset and offset of alcoholism and comorbid disorders organized into timelines. The comorbid disorder is classified as 'independent', 'completely co-occurring', or a mixture.	Structured interview developed for a multisite genetic linkage study of alcoholism (COGA). Available in seven languages.
SCAN 2.1 (47,51,52)	DSM-IV, ICD-10	Multiple reliability and validity studies in treatment and community samples.	Clinician codes an Attributional Rating Scale, for symptoms that match the Glossary definition (e.g. psychoactive substances). decision to assign attribution to a psychoactive substance.	Developed by WHO for cross-cultural studies. No guidelines provided for the Available in thirteen languages. Semi-structured interview designed to be administered by psychiatrists and clinical psychologists. Clinical phenomena are coded based on definitions provided in a 'Glossary'. Developed by WHO for cross-cultural studies.
CIDI 2.1 (54,55)	DSM-IV, ICD-10	Multiple reliability and validity studies in treatment and community samples.	Standardized Probe Flow Chart ascertains organic etiology based on MD diagnosis or subject's attribution. If organic etiology is attributed to all occurrences of a symptom, it is not considered of psychiatric relevance.	Structured interview designed to be administered by lay interviewers Available in thirteen languages. Standardized Probe Flow Chart. Depressed mood assessed for organic etiology before evaluation of other depressive symptoms.
SCID-IV (39,40,44)	DSM-IV	Multiple reliability and validity studies in substance treatment samples.	Comorbid depression rated per DSM-IV 'primary', 'substance-induced', or 'expected effects' of substance use.	Separate module for 'substance-induced' provided. Differentiation of primary and substance-induced disorders is on a syndromal level. Middle column provides DSM-IV criteria and guidelines to assess organicity.
PRISM 6.0 (57–59)	DSM-IV	2 test-retest reliability studies of substance abusers.	Within depression and psychosis, organic etiology assessed on a symptom-by-symptom level. Symptoms are 'primary', 'substance-induced', or the 'expected effects' of intoxication or withdrawal.	Structured interview designed to be administered by clinicians and lay interviewers with sufficient training. Substance sections precede psychiatric sections so information on substance use is available to assess comorbidity. Middle column provides DSM-IV criteria and specific guidelines to assess substance etiology. Differentiation of primary and substance-induced disorders is on a symptom level. Structured probes assess temporal relationship of symptoms and substance use. Psychiatric symptom that mimic substance use symptoms are assessed using a substance-using baseline.

specific guidelines for differentiating whether specific symptoms are greater than the expected effects of intoxication or withdrawal. Finally, probes to assess the temporal relationship of the episode and substance use are unstructured, potentially leading to vague or inaccurate information.

A reliability study of an earlier version of the SCID (40) included 50 subjects from a substance abuse treatment facility. Kappas for substance dependence were excellent (e.g. .70 and better). However, for many comorbid diagnoses they were poor to fair (e.g. .30–.59). In another sample of substance-abusing subjects drawn from

several sites, the reliability of current psychotic disorders and current mood disorders was only fair (psychotic disorders $\kappa = .49$, mood disorders $\kappa = .42$) (41). An independent test–retest study of the SCID in a sample of 173 substance abusers found poor reliability for most psychiatric diagnoses (42). Disagreement over the ‘substance-induced’ rule-out items was found to contribute to poor reliability. In a study that evaluated whether structured interviews increase validity of psychiatric diagnosis among substance abusers (43), 100 patients were diagnosed without a structured interview by clinicians and by research technicians using the SCID. Comparisons of the two diagnoses showed that structured instruments could increase diagnostic validity of substance-use disorders, but comorbid psychiatric diagnoses showed generally poor validity regardless of the method. These studies support the conclusion that the diagnosis of comorbid psychiatric disorders requires either clinical expertise or use of a diagnostic instrument specifically designed for that purpose (44).

SSAGA

The Semi-Structured Assessment for the Genetics of Alcoholism (SSAGA) (45) was developed for the Collaborative Study on the Genetics of Alcoholism (COGA), a National Institute on Alcohol Abuse and Alcoholism (NIAAA) multisite genetic linkage study of alcoholism. It is designed to be administered by non-clinicians with review by a clinician. Current and lifetime diagnoses are assessed. Administration time is 45 minutes to 4 hours (with longer duration among individuals who report extensive physical, psychological, or social manifestations of alcohol abuse or dependence). Differentiation of independent and substance induced disorders is based on relative chronology and is reminiscent of the pre-DSM-IV ‘primary–secondary’ method of classification. For example, comorbid depression and alcoholism are evaluated by organizing ages at onset and offset of both disorders, abstinent periods, etc., onto a time-line, and then classifying depression as ‘independent’, ‘completely co-occurring’, or some mixture of the two.

SSAGA reliability has been investigated in two test–retest reliability studies (45). Subjects in both studies were recruited from chemical dependency units, general in-patient or out-patient units, and ‘normal’ groups (variously defined). In the ‘within-center’ study ($n = 154$), two raters in the same site interviewed the subject. In the ‘cross-center’ study ($n = 84$), raters from site A conducted the test

interview at site B, and raters from site B conducted the test interview at site A. For the re-test, raters switched location. Within-center kappas were all in good range for substance dependence (.70 for stimulants, .90 for cocaine). Kappa for lifetime major depression (excluding organic explanations) was fair (.65). In the cross-center study, all kappas were .70 or greater for all substance-dependence disorders. Kappa for lifetime major depression (excluding organic explanations) was good (.74). A validity study of the SSAGA was conducted (46) by comparing SSAGA diagnoses to the Schedule for Clinical Assessment in Neuropsychiatry (SCAN) diagnoses (see later) in 80 subjects prescreened to ensure inclusion of subjects with different types of psychopathology. Kappas for cocaine, stimulant, and opiate dependence were high (greater than .70). Kappa for major depression (time-frame unspecified) was .70. Kappa for alcohol dependence (time-frame unspecified) was acceptable (.63), while kappas for sedative and cannabis dependence were lower (.48 and .53, respectively). Because the time-frame for major depression was not specified in this study, the interpretation of the level of agreement between the two instruments is not altogether clear.

SCAN and CIDI

In a joint project with the National Institutes of Health (NIH), the World Health Organization (WHO) developed two instruments to assess a broad range of mental disorders: the Schedule for Clinical Assessment in Neuropsychiatry (SCAN) and the Composite International Diagnostic Interview (CIDI) (47). The CIDI is based on the Diagnostic Interview Schedule (DIS), an instrument developed by the National Institute of Mental Health for the Epidemiologic Catchment Area (ECA) study (48–50). Both the SCAN and CIDI are available in many languages, have been field-tested in different countries, and are found to be generally acceptable across cultures and settings (47).

SCAN

The Schedule for Clinical Assessment in Neuropsychiatry (SCAN) is a set of instruments for assessing a range of clinical phenomena. A core instrument of the SCAN is the Present State Examination (PSE-10). The PSE covers ‘present state’, the month before the examination, and ‘lifetime before’. Present State Examination ratings are coded on score sheets and a computer program generates ICD-10 and DSM-IV diagnoses based

on these ratings. The PSE is a semistructured clinical examination in which the interviewer uses clinical judgement to ascribe specified definitions to clinical phenomena using the SCAN Glossary. The Glossary is a list of definitions of clinical symptoms and experiences (47). The psychiatrist or psychologist ‘cross-examines’ the subject (51), matches responses to a description in the Glossary, and then decides if a symptom is present, and if so, how severe. Once the subject’s report of a symptom is matched to a Glossary definition, the clinician can code an attributional rating scale for the item. Alcohol and other psychoactive substances are among the available attribution choices along with ‘known primary intracranial process’, non-psychiatric medication, and toxins. The decision to assign attribution to a psychoactive substance rests on the clinician’s judgement based on information gleaned from the ‘cross examination’. The SCAN does not provide specific guidelines for differentiating substance-related and independent disorders. The interviewer can, based on clinical judgement, depart from the words and order of questions. Considerable training is necessary to use this instrument.

Silverstone (52) studied the validity of current DSM-III-R diagnoses using the SCAN by combining the SCAN and the Schedule for Affective Disorders and Schizophrenia (SADS) (53) into one interview and comparing the results. Twenty-nine consecutive admissions to an in-patient psychiatric unit and 31 consecutive out-patient attendees were included in the study. While the results showed high correlations between SCAN and SADS diagnoses (52), only four subjects had a substance-use diagnosis. Therefore, data are limited on the SCAN reliability or validity of psychiatric diagnosis in substance abusers.

CIDI

The Composite International Diagnostic Interview (CIDI) is a fully structured interview designed for survey interviewers (54). Questions are read as written, without interpretation (54). For the ‘primary–substance-induced’ differentiation, the CIDI relies largely on the subject’s opinion. The DSM-IV concept of ‘expected effects’ of intoxication or withdrawal vs. symptoms greater than these effects is not addressed in the CIDI. The CIDI generates ICD-10 and DSM-IV diagnoses.

Standardized probes on a Probe Flow Chart (55) are used to ascertain a doctor’s attribution of organic etiology to depressed mood and loss of interest or pleasure. If no doctor was consulted,

probes are provided to elicit the subject’s opinion about whether the symptom was caused by alcohol, drugs or physical illness. Other symptoms associated with major depressive disorder (e.g. sleep disruption, appetite change) are not probed for attribution on a symptom-by-symptom level. As in the major depression section, the psychosis section includes attributional probes for individual symptoms (i.e. delusions and hallucinations). In the CIDI, symptoms attributed to alcohol, drugs, or physical illness are eliminated from consideration when making the psychiatric diagnoses (47). This symptom-level evaluation represents a departure from earlier procedures. Generally, the presence of substance-related factors is evaluated for an entire period of disorder once it has been established, rather than on a symptom-by-symptom basis before determining if any episode of the disorder has occurred. Importantly, we have been unable to find any psychometric studies of the CIDI examining Axis I psychiatric disorders within substance abuse samples. One study (56) explored the effects of sampling, diagnostic criteria and assessment procedures on the prevalence of DSM-III-R personality disorders within treated alcoholics. Antisocial and borderline personality disorder were assessed using the Personality Diagnostic Questionnaire Revised (PDQR) (Time 1, $n=459$; Time 2, $n=90$), and the International Personality Disorder Examination (IPDE) ($n=136$). Antisocial personality disorder was assessed using the CIDI ($n=587$). The prevalence rates varied greatly among assessment methods (PDQR, 52% vs. IPDE, 31%). With the CIDI, the prevalence of antisocial personality disorder varied across time-frames (from 3% to 18%) and across age groups (from 4% to 47%). Based on their findings, the authors suggested using a multimethod/multiple criteria assessment battery in place of a single instrument such as the CIDI.

PRISM (early development)

To address the diagnostic measurement problems in comorbidity research in heavy drinkers and drug users, the Psychiatric Research Interview for Substance and Mental Disorders (PRISM) (57,58) was developed. Several features were notable. These included placement of the alcohol and drug sections at the beginning of the PRISM (following the overview section), so that interviewers obtain the history of the subject’s substance use and the course of substance disorders before assessing psychiatric disorders. Also, the alcohol and drug use history utilized structured probes to improve consistency in the information obtained. Interviewer instructions and guidelines assisted in

evaluating symptoms and thus in differentiating ‘primary’ from ‘substance-related’ disorders. A test–retest study of the DSM-III-R PRISM (57) was conducted with 172 patients in dual-diagnosis or substance abuse settings. This study showed that the PRISM had substantially better reliability than other diagnostic instruments for diagnoses such as primary major depression ($\kappa = .86$ and $.66$ for current and lifetime diagnoses). Reliabilities for current and lifetime psychotic symptoms were also good to excellent ($\kappa = .63$ and $.79$ for current and lifetime). These findings indicated that structured probes and guidelines for specific symptoms to differentiate ‘primary’ from ‘substance-induced’ improved reliability in substance abusing samples.

Current DSM-IV PRISM

With publication of DSM-IV, the PRISM was modified to include the new category of substance-induced disorders. This included probes and guidelines to differentiate between ‘primary’ and ‘substance-induced’ symptoms and the ‘expected effects of intoxication and withdrawal’. PRISM Disorders diagnoses of ‘substance-induced disorder’ can be made for major depression, dysthymia, psychotic disorders, generalized anxiety disorder, and panic disorder. To systematize these diagnoses, the PRISM requires the same duration and number of symptoms as required for the corresponding DSM-IV primary disorder. In the major depression section, structured probes are provided to evaluate whether depressive symptoms are greater than the expected effects of intoxication and withdrawal. The subject’s own substance-using but non-depressed experience is used as a reference period (most often, a period of substance use immediately preceding onset of depressed mood). Symptoms during this reference period represent the subject’s expected intoxication/withdrawal effects. Symptoms that begin or become clearly worse only after the onset of depressed mood are counted toward a diagnosis of substance-induced Major Depressive Disorder (MDD). Only depressive symptoms cross-listed as DSM-IV intoxication/withdrawal symptoms for substances used by the patient are rated this way. For example, if the subject reports trouble concentrating during a period of heavy alcohol use with a worsening of the symptom with onset of depressed mood, the symptom is considered greater than the expected effect of alcohol intoxication and counted towards a diagnosis of alcohol-induced major depression. Conversely, trouble concentrating during a period of heavy alcohol use that did not get worse with the onset of depressed mood is consid-

ered an expected effect of alcohol intoxication. A separate code identifies depressive symptoms experienced during a period of low mood that are *not* greater than the expected effects of the substance used.

The high prevalence of substance abuse among individuals with psychotic disorders (59) also requires the differentiation of independent psychotic symptoms from substance-induced psychotic symptoms. To address this distinction, the revised PRISM provides guidelines and probes in the psychosis section to assess the etiologic relationship of the psychotic symptom and the substance. For example, a prominent hallucination experienced during cocaine intoxication for which the subject lacks insight is coded with a designated code as greater than the expected effects of cocaine intoxication and counted towards a diagnosis of cocaine-induced psychotic disorder.

The revised PRISM also provides structured probes in those sections where a substance-induced diagnosis can be made, assessing the temporal relationship of psychiatric symptoms and substance abuse. Special attention was given to MDD, a source of considerable diagnostic controversy in earlier comorbidity research (60). By using the PRISM, three distinct types of MDD can be obtained, thus reflecting a refinement of DSM-IV. The first two types are both considered primary MDD in DSM-IV. These include ‘prior-onset’ MDD, defined to begin before the initial onset of substance disorders. This corresponds to the ‘primary’ diagnosis found in the Feighner criteria (37). An ‘abstinence’ primary MDD can also be diagnosed that occurs during periods of sustained abstinence or remission from substance-use disorders. The third type of MDD obtained from the PRISM is the ‘substance-induced’ MDD. This is an episode of MDD that occurs entirely during periods of substance use.

The DSM-IV version of the PRISM has recently been subjected to a rigorous test–retest reliability study ($n = 285$). Preliminary results show good to excellent reliability for PRISM DSM-IV primary and substance-induced depression diagnoses. For example, kappas for current and lifetime DSM-IV primary MDD are greater than $.70$, and kappas for the more difficult diagnoses of current and lifetime substance-induced MDD are greater than $.68$. The PRISM offered a solution to the problem of unreliable measurement of MDD in substance abusers, although the measure does take time to administer. The PRISM is now being used in several studies focusing on comorbidity, including single- and multisite studies in the U.S. and Europe. To increase the speed and ease of

PRISM administration, a computerized version is being prepared. The PRISM assesses 22 Axis I and two Axis II psychiatric disorders. As with most diagnostic interviews, an interviewer with clinical experience is better prepared to administer the PRISM, but with sufficient training non-clinicians can do an accurate assessment. Administration time ranges from 45 min to 2 h, depending on the level and complexity of the subject's psychopathology, and the interviewer's level of skill and experience.

Use of the DSM-IV primary option to differentiate between MDD occurring before the onset of substance dependence and MDD during extended periods of abstinence has facilitated comorbidity research on these two conditions. For example, a study of former drinkers in a large U.S. national survey showed that former drinkers with a past history of alcohol dependence were four-fold more likely to have current MDD than those without such a history (61). In addition, among patients who achieve stable remissions from substance dependence, PRISM data indicates that an episode of major depression poses a strong risk for relapse (62). Further, PRISM data on abstinence-MDD shows that this type of primary major depression predicts increased the lifetime number of suicide attempts (63). These findings support the importance of clinical attention to major depressive disorders, even when substance abuse patients appear successful because they have achieved stable periods of abstinence and recovery. Thus, the DSM-IV definitions and the new version of the PRISM are already serving useful purposes in clinical and epidemiologic research.

Conclusion

With the publication of DSM-IV, greater emphasis was placed on the clinical and research utility of the substance-induced disorders classification, as well as allowing primary disorders to be diagnosed during periods of abstinence or light substance use following remission of alcohol or drug dependence. The DSM-IV brought a number of very useful clarifications to the issues of diagnosing primary and substance-induced disorders. Now, further understanding of these classifications, and the relationship of co-occurring psychiatric and substance disorders in general, can be accomplished with the range of available measures, particularly the PRISM. Most diagnostic instruments assess the temporal relationship of co-occurring disorders to some degree, and consequently arrive at differential diagnosis. The SCID and the PRISM also operationalize the important concept of symptoms that are greater than the expected effects of

substance use. Finally, the PRISM evaluates symptoms of MDD on a symptom-by-symptom level allowing for the important differential diagnosis of prior onset MDD, abstinence MDD, and substance-induced MDD. Papers now being published with the DSM-IV improvements should represent the beginning of fruitful research leading to better prevention and intervention efforts.

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