Psychiatric disorders and drug and alcohol use disorders commonly co-occur. A growing literature has documented the epidemiology and effects on the course of illness of comorbid psychiatric and substance use disorders (SUDs). Advances in treatment of co-occurring illnesses have progressed more slowly. The current article reviews recent developments in the diagnosis and treatment of co-occurring psychiatric disorders and SUDs with particular focus on psychotic disorders, affective disorders, anxiety disorders, personality disorders, and attention-deficit/hyperactivity disorder. Current treatment options and implications for future research are highlighted.

Introduction
Recognition of the prevalence of co-occurring substance use disorders (SUDs) with other psychiatric disorders has grown tremendously over the past 20 years. As awareness of prevalence has increased, the number of studies focusing on various aspects of comorbidity also has increased. These include studies focused on etiologic connections, diagnostic difficulties, consequences, and treatments for individuals with comorbid SUDs and other psychiatric disorders. In this review, we focus on a number of studies published in the last several years that address important issues in the area of comorbidity.

Epidemiology
SUDs and other psychiatric disorders frequently co-occur, with prevalence estimates reported as high as 60% in earlier studies such as the Epidemiological Catchment Area (ECA) study and National Comorbidity Survey (NCS) [1,2]. In the last several years, two large epidemiologic studies, the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC) and the National Comorbidity Survey Replication (NCS-R), have sought to replicate and extend these findings.

The NESARC study reported that 22% of individuals with any mood disorder and 19% of individuals with any anxiety disorder had a co-occurring drug use disorder, with greater comorbidity among women than men [3]. As in both the NCS and ECA studies, comorbidity rates were highest for individuals with bipolar disorder as compared with any other Axis I disorder, with lifetime rates of alcohol and drug use disorders of 58% and 38%, respectively. Diagnoses of panic disorder and social phobia also conferred considerable risk for co-occurring SUD, with 12-month odds ratios of 3.7 and 8.3 for alcohol and other drug dependence, respectively, in panic disorder and 2.3 and 4.6 for alcohol and other drug dependence, respectively, in social phobia.

Similarly, the NCS-R validated the findings of earlier epidemiologic studies and demonstrated that a small number of individuals account for a majority of comorbidity. In particular, more than three fourths of NCS-R diagnoses were given to individuals comorbid for two or more disorders, whereas individuals with three or more disorders accounted for more than one half of diagnoses [4]. Additionally, severity of illness was associated with comorbidity, as a greater percentage of disorders were classified as serious among individuals with three or more diagnoses.

The NCS-R includes a follow-up survey of a subgroup of individuals in the original NCS study. This subgroup contains individuals aged 15 to 24 years at baseline and who participated in follow-up interviews.
a decade later. These interviews were conducted in an
attempt to determine the extent to which baseline psy-
chiatric disorders predict subsequent transitions to SUDs,
and baseline SUDs predict transitions to psychiatric dis-
orders. Most previous research on temporal priority in
comorbidity has relied on retrospective self-report con-
cerning relative age of onset of disorders in cross-sectional
surveys. This study will be particularly valuable in
promoting more in-depth exploration of temporal rela-
tionships involving onset, progression, and recovery from
psychiatric disorders and SUDs.

Psychotic Disorders
The NCS-R has reported alarmingly high rates of comor-
bidity SUDs in individuals with nonaffective psychotic
disorders. The lifetime prevalence rate for any SUD
among psychotic individuals was 27%, with a 12-month
odds ratio of 22 for drug dependence [5]. Data from the
large, multicenter Clinical Antipsychotic Trials of Inter-
vention Effectiveness study found that approximately
60% of the sample used substances, with 37% meeting
current criteria for an SUD [6]. Clearly, this comorbidity
is highly prevalent and deserving of a dedicated focus in
terms of treatment.

A number of studies have suggested preferential use
of atypical antipsychotics rather than conventional agents
because they have fewer side effects that might compro-
mise compliance, more effectively treat negative symptoms
of schizophrenia, and may decrease craving for substances
[7]. Although some investigators have reported poor
outcomes and/or worsening substance use with typical anti-
psychotic agents [8], others have not supported this finding
[9]. Clozapine is the most-studied agent in this population.
In a recent study [10], dually diagnosed schizophrenic indi-
viduals were studied prospectively for 10 years in order to
examine differential relapse rates with antipsychotic medi-
cations. Individuals prescribed clozapine were significantly
less likely to relapse to substance use than those who
were prescribed other antipsychotic agents (8% vs 40%,
P = 0.003). However, there is at least one published report
of increased cocaine serum levels in individuals treated
with clozapine [11]. Evidence supporting the use of other
atypical antipsychotics is growing. Smelson et al. [12]
found that olanzapine significantly reduced the energy
subscale ratings on the Voris Cocaine Craving Scale in
a controlled study of cue-elicited craving in 31 individu-
als with schizophrenia and cocaine dependence. Posthoc
analysis of data from a randomized treatment trial dem-
onstrated that dually diagnosed schizophrenic individuals
with olanzapine had a significantly longer time to
treatment discontinuation as compared with those treated
with risperidone or typical antipsychotics [12]. In contrast,
Sayers et al. [13] found lower cocaine craving with haloper-
idol as compared with olanzapine in a similar population,
and others have reported that individuals with first-episode
schizophrenia-related psychosis and an alcohol use disor-
der (AUD) were less likely to respond to olanzapine than
those without an AUD. Another randomized controlled
trial assessing olanzapine versus risperidone in the treat-
ment of early psychosis and cannabis use found a greater
reduction in cannabis use in the olanzapine group, but
no between-group differences in craving, subjective well
being, or psychopathology [14].

There are limited data to support the use of other
atypical antipsychotic agents. One 12-week, open-label
trial found improved substance use and psychiatric out-
comes with quetiapine [15], although preliminary reports
of intranasal quetiapine abuse may limit its utility in sub-
stance-abusing patients [16]. Aripiprazole was reported to
reduce alcohol and cocaine craving, as well as to result
in fewer positive urine toxicology screens in a small,
open-label trial of schizophrenic individuals with cocaine
dependency [17]; similar findings have been reported
with aripiprazole in bipolar and schizoaffective disorders
with co-occurring substance use [18]. Our group recently
completed a small, open-label trial of aripiprazole for
individuals with co-occurring SUDs and schizophrenia,
schizoaffective disorder, or bipolar disorder and found
improvements in both psychiatric and substance use
outcomes (McRae et al., Unpublished data). Treatment
with the long-acting injectable form of risperidone led
to improved substance use and psychiatric outcomes, as
well as better treatment compliance, as compared with
substance-using schizophrenic individuals treated with
long-acting injectable zuclopenthixol [19]. Finally, Stuyt
et al. [8] conducted a retrospective study of dually diag-
nosed individuals enrolled in a 90-day inpatient treatment
program evaluating differential antipsychotic effective-
ness. Patients prescribed risperidone and ziprasidone
stayed in treatment for a longer duration than those
prescribed olanzapine or typical neuroleptics. The same
pattern was true for successful program completion, with
88% and 64% of the risperidone and ziprasidone groups,
respectively, completing treatment, as compared with
33% and 40%, respectively, of the olanzapine and typical
neuroleptic groups. Further research with more rigorous
methodology is needed.

Topiramate augmentation of antipsychotic treatment
has been reported effective in reducing alcohol use in a
schizophrenic individual in another case report [20].
Whereas initial reports suggested that disulfiram must be
used with caution because it may increase central levels of
dopamine by blocking dopamine β-hydroxylase and exac-
erbate psychosis, recent studies have safely investigated its
use in severe mental illness and alcoholism. A prospec-
tive study evaluating disulfiram and naltrexone alone
and in combination versus placebo in alcohol-dependent
individuals with psychotic spectrum disorders revealed
improved alcohol outcomes with active medication but no
between-group differences among the active medication
groups [21••]. Another study also found improved alcohol