Report on the Developmental Epidemiology of Comorbid Psychiatric and Substance Use Disorders

E. Jane Costello
Tonya D. Armstrong
Alaattin Erkanli

Presented to the National Institute on Drug Abuse
April 2000

Center for Developmental Epidemiology
Department of Psychiatry and Behavioral Sciences
Duke University Medical Center
Box 3454 DUMC
Durham NC 27710

Table of Contents

Abstract

STUDY 1.

Aim. To review the published literature that could provide information on the development, extent, and predictors of psychiatric comorbidity with substance use and abuse in children and adolescents. **Method.** From a review of 141 published papers, 21 were identified that could contribute to a meta-analysis of the extent of comorbidity with three disruptive behavior disorders (DBDs): conduct disorder (CD), oppositional defiant disorder (ODD), and attention deficit hyperactivity disorder (ADHD), and with depression and anxiety. **Results.** Comorbidity was highest with the DBDs and lowest with anxiety. Controlling for comorbidity among psychiatric disorders reduced the odds ratios but maintained their relative ranking. Odds ratios for comorbidity with substance abuse/dependence were higher than those for any use. The excess risk associated with abuse/dependence compared with any use was highest for ADHD and depression, lowest for CD. Sex was the only correlate available for meta-analytic review of causes and correlates. For both abuse/dependence and any use, the odds ratios for comorbidity were higher in girls than boys, significantly so for CD and anxiety. **Conclusions.** While psychiatric comorbidity with drug abuse is high, varying by diagnosis, published data are lacking on correlates, risk factors, temporal ordering, and treatment.

STUDY 2.

Aim. To review the information available in existing data sets that could contribute to a more detailed examination of correlates and risk factors of psychiatric comorbidity with substance use and abuse, and of the temporal relationships between psychiatric disorders and drug abuse. **Methods.** We identified 65 potentially useful data sets, and sent out a questionnaire to the Principal Investigators. **Results.** Sixteen data sets met the minimal requirements of representative sampling, psychiatric diagnoses, data on drug abuse, and information on timing. Most were panel studies with repeated assessments of participants. Data are available on over 17,000 youth, providing some 84,000 person-observations over time. Of these, 50 percent are female, about 3,500 (11,000 person-observations) are African American, 2,700 (6,000 person-observations) are Hispanic, and 450 (2,000 person-observations) are American Indian. The age ranges of the studies cover the period from birth through age 26. **Conclusions.** Given modern methods of data analysis, and the impressive resource represented by the data sets available, there is a real opportunity to advance understanding of the predictors and timing of psychiatric comorbidity with drug abuse, using existing data.

INTRODUCTION

In this report we present an overview of the data available to estimate the co-occurrence of psychiatric disorders with drug use, abuse, and dependence in childhood and adolescence. We provide this as background to the discussion of the impact of childhood interventions on subsequent drug use.

In order for childhood interventions to have an effect on subsequent drug abuse, they need to affect risk factors for later drug use. In these analyses we concentrate on psychiatric disorders of childhood and adolescence as potential risk factors for later drug abuse. The policy question is where it makes most sense to target early interventions. For example, if depression and drug abuse co-occur in childhood, an intervention program could have an effect on future drug abuse by reducing current drug use, or by ameliorating current depression, or both. A program targeting only childhood drug use might have little effect on children put at risk for future drug abuse primarily by their history of depression, while a program targeting only childhood depression might have little effect on youth put at risk by early drug use. If childhood depression and drug use co-occur, it would be helpful for program planners to know how often, whether the risk is the same across the population, or is higher in some groups, and how depression affects the risk of later drug abuse as children move into adolescence and early adulthood. The same is true of other psychiatric disorders of childhood.

The first question, then, is how often drug use and abuse co-occur with psychiatric disorders. Second, one would like to know whether co-occurrence is more common with some disorders than with others, and conversely, whether some forms of drug abuse are more likely than others to be comorbid with specific psychiatric disorders. Third, are some groups of children (boys or girls, younger or older children, White or minority groups, poor or nonpoor, urban or rural) more at risk than others of co-occurring psychiatric disorders and drug abuse? Fourth, understanding the temporal sequencing of psychiatric disorders and drug abuse would help in planning interventions. In particular, it would be helpful to know how a disorder that co-occurs with drug abuse in childhood or adolescence affects later risk of drug abuse. With this information available, it might be possible to estimate the attributable risk, or the proportion of later drug abuse that would be prevented by intervening with one risk factor (e.g., early depression) rather than another (e.g., early drug use). This kind of calculation is often useful to policy planners making cost-/efficiency-based choices among programs.

In this report we review the data relevant to the first and second questions: the co-occurrence of specific psychiatric disorders with drug use and abuse/dependence in children and adolescents. We present a meta-analysis of comorbidity with five different groups of psychiatric disorders based on the published literature. Questions 3 and 4 cannot yet be answered from the published literature, but in the second part of this report we provide an overview of existing data sets that have the potential to provide answers to some of these questions.

PART 1. REVIEW OF PUBLISHED DATA AND META-ANALYSIS

METHODS

Method of selecting studies for inclusion in the review

Articles appropriate for the review were selected by several methods. First, literature searches were conducted in PsycINFO, Medline, and Web of Science using combinations of the keywords "adolescent," "adolescence," "drug or substance," "use or abuse," and "psychiatric comorbidity." The search was limited to articles in the English language. Literature that focused on parental drug abuse as a predictor of adolescent drug abuse were excluded, as were manuscripts from Dissertation Abstracts International. Second, the bibliographies of these articles were examined for the purpose of yielding additional articles. Third, the in-house reference library of the Center for Developmental Epidemiology was searched. Finally, advisors to the Center were asked for references that might be appropriate for our purposes. One hundred forty-one papers were found that contained all the keywords or were found through the other methods described. The list can be found in appendix A.

Selection criteria for meta-analysis

Two criteria had to be met before papers were included in the list for meta-analysis: community-based sampling and formal psychiatric diagnostic procedures. We had hoped to include only studies that contained information on the temporal ordering or risk and protective factors, but too few met this criterion, so it was dropped.

1. Community-based samples

Information about psychiatric disorders that co-occur with substance use or abuse comes from two main sources: clinical studies and studies using representative population-based samples. This meta-analysis is based on the latter. While clinic-based studies of comorbidity can be valuable for suggesting developmental pathways, causal patterns, or likely interventions, they cannot be used as sources of information about the extent of comorbidity, its distribution in different groups, or attributable risk. The reasons are that:

1. People with two illnesses are more likely to seek treatment than people with either one of those illnesses separately (Berkson, 1946). This means that a clinic-based sample is likely to have a higher proportion of comorbid people in it than does the general population, and so one cannot use them to estimate the size of the problem.
2. Some combinations of disorders may bring people into treatment settings more often than others. For example, youth with substance abuse disorder and conduct disorder might be referred to clinics in higher proportions than youth with substance abuse disorder and an anxiety disorder. This would give clinicians the impression that comorbidity with conduct disorder is very common and comorbidity with anxiety very rare. This may or may not be true, but the point cannot be established from clinic samples.

3. Clinic cases may or may not be more severely affected with either of the comorbid conditions than community cases. Alternatively, comorbid cases may seek clinical treatment even though they have less severe symptoms of one or other disease than most community cases.
4. The temporal ordering of comorbidity may or may not be the same in clinical as in community cases.
5. Comorbidity seen in clinic cases may or may not be precipitated by the same risk factors as those that precipitate cases in the general population. These potential differences can be checked empirically for diseases where almost all cases get into treatment. However, in the case of drug abuse there is very strong evidence that this is not so. We also know that many people with psychiatric disorders never receive treatment. For these reasons we cannot assume that the patterns of association and risk seen in clinic samples mirror those seen in the population.
6. What appear to be risk factors for one or other disorder may in fact be predictors of treatment referral. For example, it might appear from a clinic study that poverty was associated with one or more disorders, where in fact stiff managed care regulations restricted access to treatment for children from privately insured families, while Medicaid regulations were more generous. This could mean that only children on Medicaid had much chance of getting treatment, and so poor children were overrepresented in the clinic sample.

For all these reasons, the scientific study of prevalence, incidence, development, and risk for comorbidity cannot rely solely on clinic-based samples.

Among community-based samples, one would of course like to use only those that employed appropriate (random or stratified random) sampling of representative population samples. These are hard to find. Many studies of adolescent drug use and abuse, for example, have relied on school samples, which tend to miss children who are absent or have dropped out—often a high-risk group. However, we have included studies using school-based samples to increase the number suitable for analysis.

2. Formal diagnostic rules and procedures

This meta-analysis includes studies that use structured interviewer-based or respondent-based interviews and formal scoring algorithms or best-estimate diagnostic procedures to generate psychiatric diagnoses using one of the recent taxonomies: ICD-9 or ICD-10, DSM-III, DSM-III-R, or DSM-IV. Three exceptions to this criterion that were included because authors made an attempt to generate diagnostic-like symptom clusters from survey questionnaires were the Ontario study (Offord et al., 1987), the National Household Survey of Drugs and Alcohol (SAMHSA, 1993), and the Middle Adolescent Vulnerability Study (Windle & Davies, 1999). Five diagnostic groupings were available for analysis of comorbidity in a large enough number of studies: conduct disorder (CD), oppositional defiant disorder (ODD), attention deficit hyperactivity disorder (ADHD), depressive disorders, and anxiety disorders.

When it came to drug abuse and dependence the requirement of a formal diagnosis was somewhat relaxed. The DSM-IV rules for dependence rely heavily on physical or work-related incapacities that most adolescents have not had time or been in a position to experience. In this meta-

analysis we have taken researchers' definitions of abuse and dependence at face value, even if they do not demonstrate that they are using strict adult diagnostic criteria.

We have where possible distinguished between any use and abuse/dependence. However, it is important to note that the studies that report "any use" often do not report abuse/dependence separately; thus, the rates for any use usually *include* those for the nested category of abuse/dependence. Too few studies were available with the necessary information for us to model psychiatric comorbidity with specific drugs.

Comorbidity is used differently in different studies (Angold, Costello, & Erkanli, 1999), to refer to everything from concurrent co-occurrence of two disorders at the time of interview to their both having been diagnosed at some time during the lifetime of the individual. Because there were so few papers that met even basic criteria for inclusion in the analysis, we chose to include papers across the entire spectrum, from lifetime to concurrent comorbidity.

3. Risk factors and correlates

We had hoped to include only studies that could advance our understanding of risk factors for comorbidity, but there were not enough studies to make this possible. The tables and figures present the data for both sexes combined and separately, but the available data did not permit analysis at any more fine-grained level. There are not enough studies for separate analyses by race/ethnicity, or even by age.

Analytic method

In combining information from multiple studies we used random-effects hierarchical Bayesian regression models to account for study-to-study variability. Specifically, we assumed that the estimated log-odds ratios obtained from available studies were distributed normally and independently with each study having its own unknown mean, and a variance equal to the (estimated) variance of the log-odds ratios in each sample. This constituted the first level of the hierarchy. At the second level, the unknown means of study effects (i.e., the "true" log-odds ratios) were assumed to be independently and identically distributed with a normal distribution having a common (unknown) population mean and (unknown) variance. At the third and final level these common population parameters were given independent noninformative priors. Posterior computations were then performed using Gibbs sampling.

Among the available studies, that is, the studies that provided estimates of odds ratios and their standard errors, two only published the estimated odds ratios. So before applying the hierarchical model described above we imputed the unknown standard errors by imposing a statistical model on them: they are independently distributed as Gamma with unknown scale and shape parameters α and β, respectively. Once again assuming a Bayesian model, we treated these parameters as random having independent uniform prior distributions between 0 and 100. These values were uninformative so the prior distributions had no influence on the imputed values of unknown standard errors.

Assuming that any missing data were missing at random, these unknown standard errors were simulated from their posterior predictive distributions, and the arithmetic means of the simulated values

were treated as imputed values, which in turn replaced the missing values in the data set needed to run the hierarchical model as discussed above.

All the necessary computations for imputing the unknown standard errors and estimating the combined (population) estimates of the odds ratios for each substance use group, each male-female group, and the overall population estimates were performed using the latest version of the Bayesian software WinBUGS1.3, which implements a Markov chain Monte Carlo approach based on the Gibbs sampler. Documentation and more information on the technical background to Gibbs sampling and other related issues are available at http://www.mrc-bsu.cam.ac.uk/bugs. During these computations, we used 1,000 simulations to initialize the posterior distributions (burn-in time), and 10,000 iterations for convergence. More details including the WinBUGS codes used for these analyses can be obtained from Dr. Erkanli at al@psych.mc.duke.edu.

Conditional comorbidity estimates

The analyses described above were applied to each comorbidity pair, e,g., substance use/depression, independent of other comorbidity pairs. In other words, the estimates of odds-ratio for one pair was not adjusted for the other pairs. We know that in reality the estimated odds-ratios obtained from each study were correlated across comorbidity pairs (Angold et al., 1999). However, most published papers did not provide cross-tabulations between substance use and all the other diagnoses considered simultaneously, so there was no way of knowing the true correlation between any comorbidity pair and another. In the absence of this information, the best we could do was to use a statistical model to try to recover these correlations, adjusting the population odds ratios for other pairs of comorbid diagnoses. We used an extension of the model we described above. At the first level, estimated log-odds ratios from each data set and for each comorbidity pair were assumed to be statistically independent conditional on unknown mean and variance equal to the (estimated) variance of the log-odds ratios in each study and comorbidity pair. At the second level, the unknown log-odds ratios were assumed to be independently distributed with a normal distribution having a common (unknown) population mean and (unknown) variance, for each comorbidity pair. At the third and final level these common population parameters were given dependent priors, using a slightly modified version of the conditional auto-regressive (CAR) model of Besag (1974). These priors, in effect, induced correlations between the population estimates of the log-odds ratios for each comorbidity pair. Computations were again performed using Gibbs sampling in WinBUGS1.3.

RESULTS

Articles included in the meta-analysis

Twenty-one of the 141 articles evaluated met the basic criteria for inclusion in the meta-analysis. Articles were excluded if they did not meet the criteria for population-based, community studies (n=34), were reviews or conceptual papers (n=28), provided insufficient comorbidity data (n=24), included adults ages 20 or older in the sample in such a way that they could not be excluded for analytic purposes (n=19), did not provide lifetime or current prevalence rates (n=10), or provided data only on comorbid use,

abuse, or dependence regarding one specific substance (n=5). Appendix B provides a summary of the studies used in the analyses. Appendix C summarizes the results from each individual study in both tabular and descriptive form. Table 1 lists the eight studies that provided only information on comorbidity with any substance use, including abuse or dependence. Table 2 lists studies that provided information on abuse or dependence.

The tables of comorbidity findings presented in this paper show that (1) not many studies have published the data needed to assess comorbidity with substance abuse, and (2) the estimates generated from these studies show wide variability. It is easy to see why this happens. Apart from all the issues of different diagnostic methods and scoring algorithms, estimates of comorbidity are likely to be small and therefore unstable when derived from small samples. As an example, if we were to assume that the population base rate of drug abuse in adolescents was 2 percent and that of major depressive disorder 2 percent (Costello et al., 1996), then the two would co-occur by chance four times in 1,000 observations. If they co-occured twice as often as expected by chance there would still only be eight cases in 1,000 observations. Given the uncertainties of measurement, a single study with 1,000 subjects could easily overestimate or underestimate the "real" association. Combining estimates from different studies using the methods described above enabled us to provide much more stable estimates than most individual studies can offer.

Results of meta-analysis

Figure 1 provides a general picture, showing the extent of comorbidity with the five diagnostic groupings, for any use, abuse, or dependence, for both boys and girls together. Results are presented in the form of odds ratios with their standard errors. An odds ratio of one indicates that the comorbid condition Y is equally likely to occur in persons with the index condition X and in those without X. An odds ratio of 2 indicates that Y is twice as likely in those with X as it is in those without X. The rule of thumb is that an odds ratio whose 95-percent confidence interval (CI) does not include 1 is "statistically significant." In general, an odds ratio of two or more is statistically significant. There are no standard procedures for statistically comparing two odds ratios derived from the modeling procedures described above. However, it is reasonable to assume that in the figures in this report two odds ratios are "significantly" different if one odds ratio is outside the 95-percent CI of the other (i.e., in the figures the CI bar on the odds ratio bar for one type of comorbidity does not overlap the top of the odds ratio bar for the other type of comorbidity).

Figure 1 shows that the extent of comorbidity varied widely from one type of psychiatric disorder to another. The extent of comorbidity with anxiety disorders was low (OR 1.9, 95% CI 1.4-2.2), while that for disruptive behavior disorders (DBDs: conduct disorder, oppositional defiant disorder, attention deficit hyperactivity disorder) was high (ORs 5.6-6.9), and not significantly different from one DBD to the other. The odds ratio for comorbidity with depression (OR 4.2, 95% CI 2.9-6.1) fell between those for anxiety (OR 1.9 95% CI 1.4-2.2) and ADHD (5.6, 95% CI 3.2-8.6). It was significantly higher than that for anxiety, and lower than those for CD and ODD, but not significantly lower than that for ADHD.

Comorbidity with any substance use and with substance abuse/dependence

Some of the studies available for analysis presented rates of any substance use, a category that included abuse and dependence. Others provided data for abuse/dependence only, or for the two categories separately. We wanted to use the data to test the hypothesis that comorbidity was more likely in cases of abuse/dependence than in cases of use. Our ability to do so was limited by the fact that many studies reporting any use include in that category abuse/dependence. From the data sets available it was not possible generate odds ratios for use *alone*. We divided the data sets into 13 that provided information on comorbidity with substance abuse and/or dependence, and 8 that provided information on any use, abuse, or dependence.

Figure 2 shows the odds ratios associated with abuse/dependence (grey bars) and any use (white bars). Comparing figure 2 with figure 1, we see that the rank ordering of odds ratios for comorbidity with the various diagnostic categories remained the same for both substance abuse/dependence and any use, although the smaller number of studies in each group led to wider confidence intervals. In the studies of abuse/dependence, the odds ratios for comorbidity with the DBDs were not significantly different from one another, but were significantly higher than the odds ratios for comorbidity with depression or anxiety; the latter two were not significantly different. In the case of any use, the odds ratios for comorbidity with CD and ODD were not significantly different, but they were higher than that for ADHD, which was higher than that for depression, while depression was in turn higher than anxiety. The odds ratio for comorbidity between any use and anxiety was not itself much above the level that might be seen by chance alone (OR 1.6, 95% CI 1.3-2.1).

For every diagnosis except CD, the odds of a comorbid psychiatric condition was significantly higher for adolescents with abuse/dependence than for those with any use. The difference was most extreme for ADHD, where abuse/dependence involved a 2.5-fold increase of risk compared with any use, followed by anxiety and depression (twofold increase of risk). The increase was lowest for conduct disorder, where the increase in risk was only around 20 percent, and ODD, where it was 45 percent.

In summary, the meta-analysis showed a stable pattern of high comorbidity with DBDs, low comorbidity with anxiety disorders, and intermediate comorbidity with depression. It is worth noting that even at the lowest level, substance use/abuse/dependence was associated with a doubling of the likelihood of an anxiety disorder, while the risk of a DBD increased six- to eight-fold. However, these analyses do not permit us to draw any conclusions about the temporal ordering or causal relationship between one disorder and the other, only that the association between them greatly exceeds what would be expected by chance alone.

Effects of comorbidity among other diagnoses

If the comorbid conditions were themselves comorbid, this could affect the estimates shown in figures 1 and 2.

Figure 3 presents the results after attempting to model other forms of comorbidity in the data. It is immediately clear that (1) the rates of comorbidity maintained the same ordering as before, with higher

comorbidity with DBDs and lower comorbidity with emotional disorders, but (2) the odds ratios were very much lower than they were for the simple two-way comorbidity. Only two were greater than 2: comorbidity with CD and ODD. In the case of depression and anxiety comorbidity was around 1; that is, substance abuse was no more likely in the presence of the other diagnosis than in its absence. The 95-percent confidence intervals were very wide, reflecting the extreme conservatism of the model and the small number of data sets available. In no case did the confidence interval exclude 1, an indication that the odds ratios were not significantly different from 1.

Given our limited ability to model the conditional comorbidities in the available data, the rest of these analyses are based on the two-way analyses, uncorrected for comorbidity among other diagnoses. It is, however, important to bear in mind that the relationship between drug abuse and any of the psychiatric disorders is likely to be influenced by comorbidity among the latter.

Correlates of and risk factors for comorbidity

We might get closer to understanding the causes of comorbidity if we could establish clear associations with putative risk factors. The published literature provides almost no data to make a meta-analytic review possible at this level. Sex was the only variable on which information was available in all studies.

Comorbidity in boys and girls

Figures 4 and 5 show the odds ratios associated with abuse/dependence (figure 4) and any use (figure 5) by sex. Figure 4 shows that for abuse/dependence the odds ratios were higher for girls than for boys, for every diagnosis, although in the case of depression the difference was very slight. The higher odds ratios for girls' comorbidity were statistically significant for CD and anxiety.

Figure 5 shows a similar pattern for any use. Girls who used alcohol or drugs were at greater risk of comorbidity than boys, for every type of disorder except depression; the difference was statistically significant for CD and anxiety. Thus the pattern of sex differences in comorbidity was similar for both types of substance use.

Figures 6 and 7 look at the question another way, comparing the odds ratios associated with any use versus abuse/dependence within sex. These figures show that although, as seen in figures 4 and 5, the odds ratios were lower for boys than for girls, the increase in risk associated with abuse/dependence relative to any use was similar across the sexes. Thus, the increase in risk associated with abuse/dependence compared with any use was highly significant for every diagnostic group except for anxiety, where comorbidity was actually slightly higher (though not significantly so) with any use than with abuse. A comparison of the size of the difference in odds ratios between users and abusers shows that for both boys and girls it was highest for ADHD (a 2.5-fold increase in risk for with abuse/dependence compared with any use) and depression (2.4-fold increase in risk). CD showed the smallest difference in risk between users and abusers: a 40-percent excess risk for girls, and a 60-percent excess risk for boys.

In summary, patterns of comorbidity were similar for boys and girls, but more extreme in girls. Substance-using girls were at higher risk than boys for every type of comorbidity except for that with

depression. Although DBDs are less common in girls than in boys, the higher odds ratios for girls imply that when they do occur, they are more likely to be associated with other harmful behaviors, such as drug abuse. In both sexes, for every diagnosis except anxiety comorbidity was higher in association with abuse/dependence than with any use, an effect that was strongest for ADHD and depression and weakest for conduct disorder.

Other risk factors

Although individual studies discuss other risk factors (see appendix C), too few studies provide data on any one factor for meta-analysis to be possible. This is not to say that the data were not collected, only that they have not yet been published in a form that makes aggregation feasible. Thus we could draw no general conclusions from the published literature on the association between different diagnostic comorbidities and, for instance, age, race/ethnicity, poverty, family history, early development, or (most importantly for this meeting) the effects of treatment. Nor could meta-analysis help with teasing out the temporal ordering of different disorders because of a lack of published data to address this question.

DISCUSSION

This analysis of published studies makes it absolutely clear that adolescents who use or abuse substances are significantly more likely than other youth to have one or more of the five major groups of psychiatric disorder. The risk ranges from twofold for anxiety disorders to sevenfold for CD. The risk of comorbidity is higher for girls than for boys for everything except depression. Controlling for comorbidity among psychiatric diagnosis the pattern is similar, although the odds ratios are lower. However, with so few studies the confidence intervals are very wide.

It is important to emphasize that these findings are based on cross-sectional (correlational) analyses. Few published studies provide the data needed to examine temporal relationships, and no attempt has been made to do so here. Without this dimension, we cannot talk about *cause* or *prediction*; even the word *risk* carries etiologic implications that the data cannot support. These analyses merely confirm that when substance use or abuse is present, other psychiatric diagnoses are present to a degree not expected by chance alone.

The data contain two hints of causal explanations, although these are very weak. First, the higher comorbidities associated with abuse/dependence than with any use, for every psychiatric diagnosis except anxiety, suggest a dose-response relationship, which is one step on the path to establishing causality (Robins & Guze, 1970). Second, the fact that girls, who are less likely to have DBDs (Loeber & Keenan, 1994), are more likely to use or abuse substances if they do have a DBD raises the possibility of a causal arrow from DBDs to substance use/abuse rather than vice versa. However, we have also to account for the fact that girls are both more likely to have anxiety disorders (Costello & Angold, 1995) and more likely to show comorbidity.

It is important to bear in mind the limitations of these analyses. Apart from those already discussed, there are many reasons why comorbidity itself could be the result of methodologic artifacts

rather than a real phenomenon (Angold et al., 1999). Also, a meta-analysis can only be as good as the data that go into it, and even stretching our criteria to the limits there were many problems with the data; in particular, the construction of DSM diagnoses from instruments not designed for that purpose. We could stratify by sex but by no other variable. The number of psychiatric diagnoses was limited, and these had to be grouped into what may be misleading categories. For example, analysis of the Great Smoky Mountains data set showed no association between substance use or abuse/dependence and anxiety disorders as a group, controlling for other psychiatric comorbidities (Costello, Erkanli, Federman, & Angold, 1999). However, further analysis showed that separation anxiety reduced the likelihood of alcohol use, and increased the age at first use, whereas generalized anxiety disorder increased the risk of alcohol use and lowered the age at first use (Kaplow, Curran, & Costello, 2000). This suggests the importance of being able to look at the association of substance abuse with different psychiatric disorders separately. One would also want to examine the association of different psychiatric disorders with specific substances (alcohol, cannabis, etc.). Further, investigation of the association between substance abuse, psychiatric comorbidity, and mental health service use is desirable but not possible given the limits of the studies included in the meta-analysis. Finally, it would be fascinating to be able to use the power of Markov chain Monte Carlo modeling to examine the temporal relations among disorders.

None of these is possible using published papers. Comorbidity with psychiatric disorder has seldom been the focus of publications from the data sets we used for the meta-analysis. But for longitudinal psychiatric epidemiologic surveys a great deal of information has to be collected that is usually not published in scientific papers. For example, a study has to collect detailed information on a wide range of drugs that adolescents might use, even to publish a simple analysis of "drug abuse." The detailed information that lies behind the single published figure may never appear in print. The literature on child psychopathology contains reports from several large studies of adolescent substance abuse with representative samples, careful, consistent methods of data collection and data aggregation, and at least some information about co-occurring psychiatric disorders. Several are panel studies with repeated assessments of the same participants over years or even decades. This raised for us the question of whether these data sets could potentially yield more than they have so far on psychiatric comorbidity with drug abuse. Recent advances in data transfer, computing speed, and statistical methods raise the possibility of exploiting this wealth of information. In the next section we report on a preliminary exploration of what is "out there" to address the question of psychiatric comorbidity as a risk for later drug abuse.

PART 2. DATA SETS FOR FURTHER STUDY

INTRODUCTION

The basic information required for the study of comorbidity is not difficult to collect, and any study that collects information on more than one diagnosis has already done so. What the researchers may not have done, however, is publish their data in a form that makes the calculation of comorbidity rates possible. These are laid out in detail elsewhere (Angold et al., 1999), but basically consist of (1) the base

rates of disorders X and Y; (2) the prevalence of X|Y and X|not-Y; (3) the prevalence of Y|X and Y|not-X. Thus, a simple 2x2 table provides the data needed. However, most researchers, while having the data readily available to construct such tables, have seen no reason to publish them in this form.

At a more complex level, one needs to account for other comorbidities in examining the one of interest. Thus, one needs to account for comorbidities among psychiatric disorders in examining comorbidity of psychiatric disorders and substance use/abuse/dependence. This requires that the data are laid out in the form of a multiplex table of the kind needed to calculate, for example, a Mantel-Haenzsel chi-square. Once again, researchers have the data necessary for this purpose; they just don't normally present them in this format. Similarly, to examine risk factors and correlates of various types of comorbidity, one needs the basic 2x2 tables broken out by age, sex, race/ethnicity, poverty, etc., and possibly by all of these simultaneously. Problems with working from the published data increase when studies use complex sampling designs rather than simple random sampling, or both. It then becomes difficult to combine reports unless the relevant variance estimates are also available. Many studies also have the potential to examine comorbidity longitudinally using repeated data waves. Meta-analysis of longitudinal data is more complex, but still possible given the power of recent analytic software.

In this section we (1) review the data sets that have potential for this activity, (2) suggest some key questions that could be addressed, and (3) suggest an approach to answering these questions.

METHODS

Sources of information

The three main sources of information about potentially useful data sets were (1) the National Institutes of Health's database of currently and previously funded grants (Computer Retrieval of Information on Scientific Projects [CRISP]), (2) the literature review described earlier, and (3) personal contact with researchers, especially those in other countries. The Principal Investigator (PI) of each study was identified and an e-mail address sought for each one. Over 60 studies were identified that might possibly be able to provide relevant data.

Type of information

The goal was to collect information to answer three kinds of questions about each data set: (a) Does it meet the basic requirement for comorbidity analyses?, (b) If so, what are the characteristics of the data set relevant to these core requirements (sample size, etc.)?, and (c) Does the data set have other characteristics that would make it valuable for additional analyses (e.g., repeated measures, risk and protective factors)?

The basic requirements were those discussed earlier; we were mainly interested in representative population samples, with reliably collected DSM or ICD diagnoses, and enough information to permit a determination of any substance use, substance abuse, and substance dependence, separately for alcohol, tobacco, and other drugs. Beyond these basic data, we were interested in knowing what other information might be available across several data sets. We were also interested in the potential for analyses using (1) longitudinal data, (2) different race/ethnic groups, (3) a range of putative risk and

protective factors, (4) information on treatment for drug abuse or psychiatric disorders, and on the effectiveness of treatment, and (5) a range of "real world" outcomes, such as school dropout, arrest, incarceration, unwanted pregnancy, or suicide. However, these were not criteria for inclusion in the list of useful studies, but rather additional information for exploring what kinds of analysis might be possible.

Procedure

A form (appendix D) was sent out as an e-mail attachment to everyone on the list of PIs. Responses were collected in a summary chart.

RESULTS

Table 3 presents a summary of the potentially usable data sets on which information has been collected so far. This is an ongoing project; as new studies reach an analyzable stage they can be added to the list. At this point we can say that at least 16 studies, collecting information on at least 17,000 children and adolescents, contain the minimum necessary data (psychiatric diagnoses, substance use and abuse, onset dates, demographic and risk factor data). What is even more important for NIDA's purposes is that most of these are panel studies, with repeated assessments of the same subjects. This provides the opportunity to examine the timing and precipitators of the onset of drug use, and progressions from use to abuse, *prospectively*, in large, ethnically diverse samples of children and adolescents.

All the studies include approximately equal numbers of male and female subjects. Several studies contain sizable samples of minority participants. There are more then 3,500 African American youth contributing over 11,000 person-observations, and 2,600 Hispanic participants contributing some 6,000 person-observations. However, data on American Indians (N = 450, person-observations $\tilde{=}$ 2,000), Asians, and other minorities in the United States are sparse.

All the data sets contain information on a range of correlates and risk factors such as age, sex, school performance, urban/rural residence, family income, family structure and functioning, and neighborhood and community resources, although not all studies contain all the variables. A few provide information on service use for drug and mental health problems.

DISCUSSION

Data to examine the development of drug abuse comorbidity *have already been collected* on some 17,000 children and adolescents. With repeated assessments in many studies these data sets provide over 84,000 person-observations. At a very rough estimate, the dozen usable data sets have cost Federal and other agencies at least $60 million over the years since the early 1970s, when the first of these studies began. However, few of them have used their data to address the specific question that NIDA wants answered (exceptions are Costello et al., 1999; Newman, Silva, & Stanton, 1996). Additionally, the *combined* strength of this resource has certainly not been exploited to address this issue.

There are different methods of using data from multiple sources. Meta-analyses of the type used in the first part of this report are one approach. A second is for researchers to carry out cooperative projects, in which they agree to carry out parallel studies using common sets of variables (e.g., Costello,

1998 #11041]. A third approach is to combine the relevant variables from each study into a common data set. Programs for data analysis are much more flexible than was the case even a few years ago, and any or all of these approaches might be feasible, depending on the questions to be answered. Inevitably, problems would arise and considerable expertise would be needed to use any of these approaches.

Clearly there are many questions that further analysis of existing data will not answer. The core question of this conference—the impact of early treatment on later drug abuse—needs answering in new studies with different designs. But it would be helpful to be able to base those new studies on a firm foundation of knowledge about prevalence, comorbidity, and development.

REFERENCES

American Psychiatric Association (1994). *Diagnostic and Statistical Manual of Mental Disorders Fourth Edition (DSM-IV)*. Washington, DC: American Psychiatric Press, Inc.

Angold, A., & Costello, E. J. (1995). The Child and Adolescent Psychiatric Assessment (CAPA). *Psychological Medicine, 25,* 739-753.

Angold, A., Costello, E. J., & Erkanli, A. (1999). Comorbidity. *Journal of Child Psychology and Psychiatry, 40,* 57-87.

Berkson, J. (1946). Limitations of the application of fourfold table analysis to hospital data. *Biometrics Bulletin, 2,* 47-52.

Costello, A. J., Edelbrock, C., Kalas, R., Kessler, M. D., & Klaric, S. H. (1982). *The National Institute of Mental Health Diagnostic Interview Schedule for Children (DISC)*. Rockville, MD: National Institute of Mental Health.

Costello, E. J., & Angold, A. (1995). Epidemiology. In J. March (Eds.), *Anxiety Disorders in Children and Adolescents* (pp. 109-124). New York, NY: Guilford Press.

Costello, E. J., Angold, A., Burns, B. J., Stangl, D. K., Tweed, D. L., Erkanli, A., & Worthman, C. M. (1996). The Great Smoky Mountains Study of Youth: Goals, designs, methods, and the prevalence of DSM-III-R disorders. *Archives of General Psychiatry, 53,* 1129-1136.

Costello, E. J., Erkanli, A., Federman, E., & Angold, A. (1999). Development of psychiatric comorbidity with substance abuse in adolescents: Effects of timing and sex. *Journal of Clinical Child Psychology, 28,* 298-311.

Kaplow, J. B., Curran, P. J., & Costello, E. J. (2001). The prospective relation between dimensions of anxiety and the initiation of adolescent alcohol use. *Journal of Clinical Child Psychology, 30*, 316-326.

Kessler, R. C., McGonagle, K. A., Zhao, S., Nelson, C. B., Hughes, M., Eshleman, S., Wittchen, H. U., & Kendler, K. S. (1994). Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States: Results from the National Comorbidity Study. *Archives of General Psychiatry, 51,* 8-19.

Loeber, R., & Keenan, K. (1994). Interaction between conduct disorder and its comorbid conditions: Effects of age and gender. *Clinical Psychology Review, 14,* 497-523.

Newman, D. L., Silva, P. A., & Stanton, W. R. (1996). Psychiatric disorder in a birth cohort of young adults: Prevalence, comorbidity, clinical significance, and new case incidence from ages 11 to 21. *Journal of Consulting and Clinical Psychology, 64,* 552-562.

Offord, D. R., Boyle, M. H., Szatmari, P., Rae-Grant, N. I., Links, P. S., Cadman, D. T., Byles, J. A., Crawford, J. W., Blum, H. M., Cyrne, C., Thomas, H., & Woodward, C. A. (1987). Ontario child health study: I. Methodology. *Archives of General Psychiatry, 44,* 826-831.

Robins, E., & Guze, S. B. (1970). Establishment of diagnostic validity in psychiatric illness: Its application to schizophrenia. *American Journal of Psychiatry, 126,* 107-111.

SAMHSA (1993). *National Household Survey on Drug Abuse: Population Estimates 1992*. Rockville, MD: U.S. Department of Health and Human Services.

Windle, M., & Davies, P. T. (1999). Depression and heavy alcohol use among adolescents: Concurrent and prospective relations. *Development and Psychopathology, 11,* 823-844.

APPENDIX A: BIBLIOGRAPHY OF ARTICLES REVIEWED FOR META-ANALYSIS

Anderson, J. C., Williams, S., McGee, R., & Silva, P. A. (1987). DSM-III disorders in preadolescent children: Prevalence in a large sample from the general population. *Archives of General Psychiatry, 44,* 69-77.

Andreasson, S., Allebeck, P., Brandt, L., & Romelsjo, A. (1992). Antecedents and covariates of high alcohol consumption in young men. *Alcoholism: Clinical and Experimental Research, 16,* 708-713.

Angold, A., & Costello, E. J. (1993). Depressive comorbidity in children and adolescents: Empirical, theoretical, and methodological issues. *American Journal of Psychiatry, 150,* 1779-1791.

Angold, A., Costello, E. J., & Erkanli, A. (1999). Comorbidity. *Journal of Child Psychology and Psychiatry, 40,* 57-87.

Anthony, J. C., & Petronis, K. R. (1995). Early-onset drug use and risk of later drug problems. *Drug and Alcohol Dependence, 40,* 9-15.

Anthony, J. C., Warner, L. A., & Kessler, R. C. (1994). Comparative epidemiology of dependence on tobacco, alcohol, controlled substances, and inhalants: Basic findings from the National Comorbidity Survey. *Experimental and Clinical Psychopharmacology, 2,* 244-268.

Barkley, R. A. (1990). The adolescent outcome of hyperactive children diagnosed by research criteria: I. An 8-year prospective follow-up study. *Journal of the American Academy of Child and Adolescent Psychiatry, 29,* 546-557.

Beitchman, J. H., Douglas, L., Wilson, B., Johnson, C., Young, A., Atkinson, L., Escobar, M., & Taback, N. (1999). Adolescent substance use disorders: Findings from a 14-year follow-up of speech/language-impaired and control children. *Journal of Clinical Child Psychology, 28,* 312-321.

Biederman, J., Faraone, S. V., & Kiely, K. (1996). Comorbidity in outcome of attention-deficit/hyperactivity disorder. In L. T. Hechtman (Ed.), *Do They Grow Out of It? Long-term Outcomes of Childhood Disorders* (pp. 39-75). Washington, DC: American Psychiatric Press.

Biederman, J., Wilens, T., Mick, E., Faraone, S., Weber, W., Curtis, S., Thornell, A., Pfister, K., Jetton, J., & Sorlano, J. (1997). Is ADHD a risk factor for psychoactive substance use disorders? Findings from a Four-Year Prospective Follow-up Study. *Journal of the American Academy of Child and Adolescent Psychiatry, 36,* 21-29.

Bird, H. R., Gould, M. S., & Staghezza, B. M. (1993). Patterns of diagnostic comorbidity in a community sample of children aged 9 through 16 years. *Journal of the American Academy of Child and Adolescent Psychiatry, 32,* 361-368.

Boyle, M. H., & Offord, D. R. (1991). Psychiatric disorder and substance use in adolescence. *Canadian Journal of Psychiatry, 36,* 699-705.

Boyle, M. H., Offord, D. R., Racine, Y. A., Szatmari, P., Fleming, J. E., & Links, P. S. (1992). Predicting substance use in late adolescence: Results from the Ontario Child Health Study Follow-up. *American Journal of Psychiatry, 149,* 761-767.

Brook, J. S., Whiteman, M., Finch, S., & Cohen, P. (1995). Aggression, intrapsychic distress, and drug use: Antecedent and intervening processes. *Journal of the American Academy of Child and Adolescent Psychiatry, 34,* 1076-1084.

Brook, J. S., Cohen, P., & Brook, D. W. (1998). Longitudinal study of co-occurring psychiatric disorders and substance use. *Journal of the American Academy of Child and Adolescent Psychiatry, 37,* 322-330.

Brook, J. S., Whiteman, M. M., & Finch, S. (1992). Childhood aggression, adolescent delinquency, and drug use: A longitudinal study. *Journal of Genetic Psychology, 153,* 369-384.

Brown, J. H., & Horowitz, J. E. (1993). Deviance and deviants: Why adolescent substance use prevention programs do not work. *Evaluation Review, 17,* 529-555.

Brown, S. A., Mott, M. A., & Stewart, M. A. (1992). Adolescent alcohol and drug abuse. In C. E. Walker & M. C. Roberts (Eds.), *The Handbook of Clinical Child Psychology* (pp. 677-693). New York: Wiley.

Bry, B. H., McKeon, P., & Pandina, R. J. (1982). Extent of drug use as a function of number of risk factors. *Journal of Abnormal Psychology, 91,* 273-279.

Bukstein, O. G., Brent, D. A., & Kaminer, Y. (1989). Comorbidity of substance abuse and other psychiatric disorders in adolescents. *American Journal of Psychiatry, 146,* 1131-1141.

Bukstein, O. G., Glancy, L. J., & Kaminer, Y. (1992). Patterns of affective comorbidity in a clinical population of dually diagnosed adolescent substance abusers. *Journal of the American Academy of Child and Adolescent Psychiatry, 31,* 1041-1045.

Cadoret, R. J., Troughton, E., O'Gorman, T. W., & Heywood, E. (1986). An adoption study of genetic and environmental factors in drug abuse. *Archives of General Psychiatry, 43,* 1131-1136.

Cadoret, R. J., Yates, W. R., Troughton, E., Woodworth, G., & Stewart, M. A. (1995). Adoption study demonstrating two genetic pathways to drug abuse. *Archives of General Psychiatry, 52,* 42-52.

Capaldi, D. M. (1992). Co-occurrence of conduct problems and depressive symptoms in early adolescent boys: II. A 2-year follow-up at grade 8. *Development and Psychopathology, 4,* 125-144.

Caron, C., & Rutter, M. (1991). Comorbidity in child psychopathology: Concepts, issues and research strategies. *Journal of Child Psychology and Psychiatry, 32,* 1063-1080.

Caton, C. L. M., Gralnick, A., Bender, S., & Simon, R. (1989). Young chronic patients and substance abuse. *Hospital and Community Psychiatry, 40,* 1037-1040.

Chassin, L., Curran, P. J., Husson, A. M., & Colder, C. R. (1996). The relation of parent alcoholism to adolescent substance use: A longitudinal follow-up study. *Journal of Abnormal Psychology, 105,* 70-80.

Chassin, L., Pillow, D. R., Curran, P. J., Molina, B. S. G., & Barrera, M., Jr. (1993). Relation of parental alcoholism to early adolescent substance use: A test of three mediating mechanisms. *Journal of Abnormal Psychology, 102,* 3-19.

Chassin, L., Pitts, S. C., DeLucia, C., & Todd, M. (1999). A longitudinal study of children of alcoholics: Predicting young adult substance use disorders, anxiety, and depression. *Journal of Abnormal Psychology, 108,* 106-119.

Chassin, L., Rogosch, F., & Barrera, M. (1991). Substance use and symptomatology among adolescent children of alcoholics. *Journal of Abnormal Psychology, 100,* 449-463.

Chatlos, J. C. (1997). Substance use and abuse and the impact on academic difficulties. *Child and Adolescent Psychiatric Clinics of North America, 6,* 545-568.

Chong, M.-Y., Chan, K.-W., & Cheng, A. T. A. (1999). Substance use disorders among adolescents in Taiwan: Prevalence, sociodemographic correlates and psychiatric co-morbidity. *Psychological Medicine, 29,* 1387-1396.

Christie, K. A., Burke, J. D., Regier, D. A., Rae, D. S., Boyd, J. H., & Locke, B. Z. (1988). Epidemiologic evidence for early onset of mental disorders and higher risk of drug abuse in young adults. *American Journal of Psychiatry, 145,* 971-975.

Cicchetti, D., & Rogosch, F. A. (1999). Psychopathology as risk for adolescent substance use disorders: A developmental psychopathology perspective. *Journal of Clinical Child Psychology, 28,* 355-365.

Clark, D. B., & Neighbors, B. (1996). Adolescent substance abuse and internalizing disorders. *Child and Adolescent Psychiatric Clinics of North America, 5,* 45-57.

Clark, D. B., Parker, A. M., & Lynch, K. G. (1999). Psychopathology and substance-related problems during early adolescence: A survival analysis. *Journal of Clinical Child Psychology, 28,* 333-341.

Clark, D. B., Pollock, N., Bukstein, O. G., Mezzich, A. C., Bromberger, J. T., & Donovan, J. E. (1997). Gender and comorbid psychopathology in adolescents with alcohol dependence. *Journal of the American Academy of Child and Adolescent Psychiatry, 36,* 1195-1203.

Clark, D. B., Smith, M. G., Neighbors, B. D., Skerlec, L. M., & Randall, R. (1994). Anxiety disorders in adolescence: Characteristics, prevalence, and comorbidities. *Clinical Psychology Review, 14,* 113-137.

Cohen, P., Cohen, J., & Brook, J. (1993a). An epidemiological study of disorders in late childhood and adolescence: 2. Persistence of disorders. *Journal of Child Psychology and Psychiatry, 34,* 869-877.

Cohen, P., Cohen, J., Kasen, S., Velez, C. N., Hartmark, C., Johnson, J., Rojas, M., Brook, J., & Streuning, E. L. (1993b). An epidemiological study of disorders in late childhood and adolescence: 1. Age- and gender-specific prevalence. *Journal of Child Psychology and Psychiatry and Allied Disciplines, 34,* 851-867.

Costello, E. J., Angold, A., Burns, B. J., Erkanli, A., Stangl, D. K., & Tweed, D. L. (1996a). The Great Smoky Mountains Study of Youth: Functional impairment and severe emotional disturbance. *Archives of General Psychiatry, 53,* 1137-1143.

Costello, E. J., Angold, A., Burns, B. J., Stangl, D. K., Tweed, D. L., Erkanli, A., & Worthman, C. M. (1996b). The Great Smoky Mountains Study of Youth: Goals, designs, methods, and the prevalence of DSM-III-R disorders. *Archives of General Psychiatry, 53,* 1129-1136.

Costello, E. J., Erkanli, A., Federman, E., & Angold, A. (1999a). Development of psychiatric comorbidity with substance abuse in adolescents: Effects of timing and sex. *Journal of Clinical Child Psychology, 28,* 298-311.

Costello, E. J., Farmer, E. M. Z., & Angold, A. (1999b). Same place, different children: White and American Indian children in the Appalachian Mountains. In P. Cohen, L. Robins, & C. Slomkowski (Eds.), *Where and When: Historical and Geographical Aspects of Psychopathology* (pp. 279-298). NJ: Lawrence Erlbaum Associates.

Crowley, T. J., & Riggs, P. D. (1995). Adolescent substance use disorder with conduct disorder and comorbid conditions. In E. Rahdert & D. Czechowicz (Eds.), *NIDA Research Monograph* (pp. 49-111). Rockville, MD: National Institutes of Health.

DeMilio, L. (1989). Psychiatric syndromes in adolescent substance abusers. *American Journal of Psychiatry, 146,* 1212-1214.

Deykin, E. Y., Buka, S. L., & Zeena, T. H. (1992). Depressive illness among chemically dependent adolescents. *American Journal of Psychiatry, 149,* 1341-1347.

Deykin, E. Y., Levy, J. C., & Wells, V. (1987). Adolescent depression, alcohol and drug abuse. *American Journal of Public Health, 77,* 178-181.

Disney, E. R., Elkins, I. J., McGue, M., & Iacono, W. G. (1999). Effects of ADHD, conduct disorder, and gender on substance use and abuse in adolescence. *American Journal of Psychiatry, 156,* 1515-1521.

Eisen, S. V., Youngman, D. J., Grob, M. C., & Dill, D. L. (1992). Alcohol, drugs, and psychiatric disorders: A current view of hospitalized adolescents. *Journal of Adolescent Research, 7,2* 250-265.

Famularo, R., Kinscherff, R., & Fenton, T. (1992). Parental substance abuse and the nature of child maltreatment. *Child Abuse and Neglect, 16,* 475-483.

Federman, E. B., Costello, E. J., Angold, A., Farmer, E. M. Z., & Erkanli, A. (1997). Development of substance use and psychiatric comorbidity in an epidemiologic study of white and American Indian young adolescents: The Great Smoky Mountains Study. *Drug and Alcohol Dependence, 44,* 69-78.

Feehan, M., McGee, R., Raja, S. N., & Williams, S. M. (1994). DSM-III-R Disorders in New Zealand 18-year-olds. *Australian and New Zealand Journal of Psychiatry, 28,* 87-99.

Fergusson, D. M., Horwood, L. J., & Lynskey, M. T. (1993a). Prevalence and comorbidity of DSM-III-R diagnoses in a birth cohort of 15 year olds. *Journal of the American Academy of Child and Adolescent Psychiatry, 32,* 1127-1134.

Fergusson, D. M., Lynskey, M. T., & Horwood, L. J. (1993b). Conduct problems and attention deficit behaviour in middle childhood and cannabis use by age 15. *Australian and New Zealand Journal of Psychiatry, 27,* 673-682.

Gabel, S., & Shindledecker, R. (1991). Aggressive behavior in youth: Characteristics, outcome, and psychiatric diagnoses. *Journal of the American Academy of Child and Adolescent Psychiatry, 30,* 982-988.

Gilvarry, E. (1999). Substance use and misuse by children and adolescents. *Current Opinion in Psychiatry, 12,* 409-413.

Glantz, M. D. (1992). A developmental psychopathology model of drug abuse vulnerability. In M. Glantz & R. Pickens (Eds.), *Vulnerability to Drug Abuse* (pp. 389-418). Washington, DC: American Psychological Association.

Grant, B. F., & Harford, T. C. (1995). Comorbidity between DSM-IV alcohol use disorders and major depression: Results of a national survey. *Drug and Alcohol Dependence, 39,* 197-206.

Greenbaum, P. E., Foster-Johnson, L., & Petrila, A. (1996). Co-occurring addictive and mental disorders among adolescents: Prevalence research and future directions. *American Journal of Orthopsychiatry, 66,* 52-60.

Greenbaum, P. E., Prange, M. E., Friedman, R. M., & Silver, S. E. (1991). Substance abuse prevalence and comorbidity with other psychiatric disorders among adolescents with severe emotional disturbances. *Journal of the American Academy of Child and Adolescent Psychiatry, 30,* 575-583.

Greene, R. W., Biederman, J., Faraone, S. V., Sienna, M., & Garcia-Jetton, J. (1997). Adolescent outcome of ADHD boys with social disability: Results from a four-year longitidinal follow-up study. *Journal of Consulting and Clinical Psychology, 65,* 758-767.

Groves, J. B., Batey, S. R., & Wright, H. H. (1986). Psychoactive-drug use among adolescents with psychiatric disorders. *American Journal of Hospital Pharmacy, 43,* 1714-1718.

Guzder, J., Paris, J., Zelkowitz, P., & Marchessault, K. (1996). Risk factors for borderline pathology in children. *Journal of the American Academy of Child and Adolescent Psychiatry, 35,* 26-33.

Hawkins, J. D., Catalano, R. F., & Miller, J. Y. (1992). Risk and protective factors for alcohol and other drug problems in adolescence and early adulthood: Implications for substance abuse prevention. *Psychological Bulletin, 112,* 64-105.

Henry, B., Feehan, M., McGee, R., Stanton, W., Moffitt, T. E., & Silva, P. (1993). The importance of conduct problems and depressive symptoms in predicting adolescent substance use. *Journal of Abnormal Child Psychology, 21,* 469-480.

Horner, B., & Scheibe, K. E. (1997). Prevalence and implications of attention-deficit hyperactivity disorder among adolescents in treatment for substance abuse. *Journal of the American Academy of Child and Adolescent Psychiatry, 36,* 30-36.

Huizinga, D. H., Menard, S., & Elliott, D. S. (1989). Delinquency and drug use: Temporal and developmental patterns. *Justice Quarterly, 6,* 419-455.

Iacono, W. G., Carlson, S. R., Taylor, J., Elkins, I. J., & McGue, M. (1999). Behavioral disinhibition and the development of substance-use disorders: Findings from the Minnesota Twin Family Study. *Development and Psychopathology, 11,* 869-900.

Jessor, R. (1993). Successful adolescent development among youth in high-risk settings. American *Psychologist, 48,2,* 117-126.

Johnson, R. J., & Kaplan, H. B. (1990). Stability of psychological symptoms: Drug use consequences and intervening processes. *Journal of Health and Social Behavior, 31,* 277-291.

Johnston, L. D., O'Malley, P. M., & Bachman, J. G. (1987). Psychotherapeutic, licit, and illicit use of drugs among adolescents. *Journal of Adolescent Health Care, 8,* 36-51.

Johnston, L. D., O'Malley, P. M., & Eveland, L. K. (1978). Drugs and delinquency: A search for causal connections. In D. B. Kandel (Ed.). *Longitudinal Research on Drug Use: Empirical Findings and Methodological Issues* (pp. 132-156). Washington, D.C.: Hemisphere.

Kandel, D. B. (1978). Convergences in prospective longitudinal surveys of drug use in normal populations. In D. B. Kandel (Eds.), *Longitudinal Research on Drug Use: Empirical Findings and Methodological Issues* (pp. 3-38). Washington, DC: Hemisphere Publishing Corporation.

Kandel, D. B., Johnson, J. G., Bird, H. R., Canino, G., Goodman, S. H., Lahey, B. B., Regier, D. A., & Schwab-Stone, M. (1997). Psychiatric disorders associated with substance use among children and adolescents: Findings from the Methods for the Epidemiology of Child and Adolesdent Mental Disorders (MECA) study. *Journal of Abnormal Child Psychology, 25,* 121-132.

Kandel, D. B., Johnson, J. G., Bird, H. R., Weissman, M. M., Goodman, S. H., Lahey, B. B., Regier, D. A., & Schwab-Stone, M. E. (1999). Psychiatric comorbidity among adolescents with substance use disorders: Findings from the MECA study. *Journal of the American Academy of Child and Adolescent Psychiatry, 38,* 693-699.

Kandel, D. B., Kessler, R. C., & Margulies, R. Z. (1978). Antecedents of adolescents' initiation into the stages of drug use: A developmental analysis. In D. B. Kandel (Ed.). *Longitudinal Research on Drug Use: Empirical Findings and Methodological Issues* (pp. 73-100). Washington, DC: Hemisphere-Wiley.

Kashani, J. H., Beck, N. C., Hoeper, E. W., Fallahi, C., Corcoran, C. M., Mcallister, J. A., Rosenberg, T. K., & Reid, J. C. (1987). Psychiatric disorders in a community sample of adolescents. *American Journal of Psychiatry, 144,* 584-589.

Kellam, S. G., Brown, C. H., Rubin, B. R., & Ensminger, M. E. (1983). Paths leading to teenage psychiatric symptoms and substance use: Developmental epidemiological studies in Woodlawn.

In S. B. Guzé, F. J. Earls, & J. E. Barrett (Eds.), *Childhood Psychopathology and Development* (pp. 17-51). New York: Raven Press.

Kessler, R. C. (1991). *Comorbidity of Substance Use Disorders and Other Psychiatric Disorders: An ADAMHA Report on Prevalence, Etiology, Implications for Prevention, Course of Illness and Research*. Institute for Social Research, Department of Sociology, University of Michigan.

Kessler, R. C., Crum, R. M., Warner, L. A., Nelson, C. B., Schulenberg, J., & Anthony, J. C. (1997). Lifetime co-occurrence of DSM-III-R alcohol abuse and dependence with other psychiatric disorders in the national comorbidity survey. *Archives of General Psychiatry, 54,* 313-321.

Kessler, R. C., Nelson, C. B., McGonagle, K. A., Edlund, M. J., Frank, R. G., & Leaf, P. J. (1996). The epidemiology of co-occurring addictive and mental disorders: Implications for prevention and service utilization. *American Journal of Orthopsychiatry, 66,* 17-31.

Kingsbury, S., Hawton, K., Steinhardt, K., & James, A. (1999). Do adolescents who take overdoses have specific psychological characteristics? A comparative study with psychiatric and community controls. *Journal of the American Academy of Child and Adolescent Psychiatry, 38,* 1125-1131.

Kratzer, L., & Hodgins, S. (1997). Adult outcomes of child conduct problems: A cohort study. *Journal of Abnormal Child Psychology, 25,* 65-81.

Lewinsohn, P. M., Gotlib, I. H., & Seeley, J. R. (1995a). Adolescent psychopathology: IV. Specificity of psychosocial risk factors for depression and substance abuse in older adolescents. *Journal of the American Academy of Child and Adolescent Psychiatry, 34,* 1221-1229.

Lewinsohn, P. M., Hops, H., Roberts, R. E., Seeley, J. R., & Andrews, J. A. (1993). Adolescent psychopathology: I. Prevalence and incidence of depression and other DSM-III-R disorders in high school students. *Journal of Abnormal Psychology, 102,* 133-144.

Lewinsohn, P. M., Rohde, P., & Seeley, J. R. (1995b). Adolescent psychopathology: III. The clinical consequences of comorbidity. *Journal of the American Academy of Child and Adolescent Psychiatry, 34,* 510-519.

Loeber, R., Green, S. M., Keenan, K., & Lahey, B. B. (1995). Which boys will fare worse? Early predictors of the onset of conduct disorder in a six-year longitudinal study. *Journal of the American Academy of Child and Adolescent Psychiatry, 34,* 499-509.

Loeber, R., & Keenan, K. (1994). Interaction between conduct disorder and its comorbid conditions: Effects of age and gender. *Clinical Psychology Review, 14,* 497-523.

Loeber, R., Stouthamer-Loeber, M., & White, H. R. (1999). Developmental aspects of delinquency and internalizing problems and their association with persistent juvenile substance use between ages 7 and 18. *Journal of Clinical Child Psychology, 28,* 322-332.

Mannuzza, S., Klein, R. G., Bessler, A., Malloy, P., & LaPadula, M. (1998). Adult psychiatric status of hyperactive boys grown up. *American Journal of Psychiatry, 155,* 493-498.

Mannuzza, S., Klein, R. G., Bonagura, N., Malloy, P., Giampino, T. L., & Addalli, K. A. (1991). Hyperactive boys almost grown up. V. Replication of psychiatric status. *Archives of General Psychiatry, 48,* 77-83.

McDowell, D. M., Levin, F. R., & Nunes, E. V. (1999). Dissociative identity disorder and substance abuse: The forgotten relationship. *Journal of Psychoactive Drugs, 31,* 71-83.

McGee, R., Feehan, M., Williams, S., Partridge, F., Silva, P. A., & Kelly, J. (1990). DSM-III disorders in a large sample of adolescents. *Journal of the American Academy of Child and Adolescent Psychiatry, 29,* 611-619.

Merikangas, K. R., Angst, J., Eaton, W., Canino, G., Rubio-Stipec, M., Wacker, H., Wittchen, H.-U., Andrade, L., Essau, C., Whitaker, A., Kraemer, H., Robins, L. N., & Kupfer, D. J. (1996). Comorbidity and boundaries of affective disorders with anxiety disorders and substance misuse: Results of an international task force. *British Journal of Psychiatry, 168,* 58-67.

Merikangas, K. R., Mehta, R. L., Molnar, B. E., Walters, E. E., Swendsen, J. D., Aguilar-Gaziola, S., Bijl, R., Borges, G., Caraveo-Anduaga, J. J., Dewit, D. J., Kolody, B., Vega, W. A., Wittchen, H.-U., & Kessler, R. C. (1998a). Comorbidity of substance use disorders with mood and anxiety disorders: Results of the international consortium in psychiatric epidemiology. *Addictive Behaviors, 23,* 893-907.

Merikangas, K. R., Swendsen, J. D., Preisig, M. A., & Chazan, R. Z. (1998b). Psychopathology and temperament in parents and offspring: Results of a family study. *Journal of Affective Disorders, 51,* 63-74.

Mezzich, A. C., Moss, H., Tarter, R. E., Wolfenstein, M., Hsieh, Y.-C., & Mauss, R. (1994). Gender differences in the pattern and progression of substance use in conduct-disordered adolescents. *American Journal on Addictions, 3,* 289-295.

Milberger, S., Biederman, J., Faraone, S. V., Wilens, T., & Chu, M. P. (1997). Associations between ADHD and psychoactive substance use disorders. Findings from a longitudinal study of high-risk siblings of ADHD children. A*merican Journal on Addictions, 6,* 318-329.

Milin, R. P. (1996). Comorbidity of substance abuse and psychotic disorders. *Adolescent Substance Abuse and Dual Disorders, 5,* 111-121.

Miller-Johnson, S., Lochman, J., Coie, J., Terry, R., & Hyman, C. (1998). Comorbidity of conduct and depressive problems at sixth grade: Substance use outcomes across adolescence. *Journal of Abnormal Child Psychology, 26,* 221-232.

Monopolis, S. J., Brooner, R. K., Jadwisiak, R. M., March, E., & Schmidt, C. W., Jr. (1991). Preliminary report on psychiatric comorbidity in adolescent substance abusers. *NIDA Research Monograph, 105,* 293-294.

Nelson, C. B., & Wittchen, H.-U. (1998). DSM-IV alcohol disorders in a general population sample of adolescents and young adults. *Addiction, 93,* 1065-1077.

Newcomb, M. D., & Bentler, P. M. (1988). Impact of adolescent drug use and social support on problems of young adults: A longitudinal study. *Journal of Abnormal Psychology, 97,* 64-75.

Newcomb, M. D., Bentler, P. M., & Fahy, B. (1987). Cocaine use and psychpathology: Associations among young adults. *International Journal of Addictions, 22,* 1167-1188.

Newcomb, M. D., Maddahian, E., & Bentler, P. M. (1986). Risk factors for drug use among adolescents: Concurrent and longitudinal analyses. *American Journal of Public Health, 76,* 525-531.

Novins, D. K., Duclos, C. W., Martin, C., Jewett, C. S., & Manson, S. M. (1999). Utilization of alcohol, drug, and mental health treatment services among American Indian adolescent detainees. *Journal of the American Academy of Child and Adolescent Psychiatry, 38,* 1102-1108.

Offord, D. R., Boyle, M. H., Szatmari, P., Rae-Grant, N. I., Links, P. S., Cadman, D. T., Byles, J. A., Crawford, J. W., Munroe-Blum, H., Byrne, C., Thomas, H., & Woodward, C. A. (1987). Ontario child health study: II. Six-month prevalence of disorder and rates of service utilization. *Archives of General Psychiatry, 44,* 832-836.

Pedersen, W., & Skrondal, A. (1999). Ecstasy and new patterns of drug use: A normal population study. *Addiction, 94,* 1695-1706.

Perkonigg, A., Lieb, R., & Wittchen, H.-U. (1998). Prevalence of use, abuse and dependence of illicit drugs among adolescents and young adults in a community sample. *European Addiction Research, 4,* 58-66.

Pervova, I. (1999). Delinquency in Russian children and adolescents. *Behavioral Disorders, 25,* 52-55.

Pettinati, H. M., Pierce, J. D., Jr., Belden, P. P., & Meyers, K. (1999). The relationship of Axis II personality disorders to other known predictors of addiction treatment outcome. *American Journal on Addictions, 8,* 136-147.

Randall, J., Henggeler, S. W., Pickrel, S. G., & Brondino, M. J. (1999). Psychiatric comorbidity and the 16-month trajectory of substance-abusing and substance-dependent juvenile offenders. *Journal of the American Academy of Child and Adolescent Psychiatry, 38,* 1118-1124.

Rao, U., Ryan, N. D., Dahl, R. E., Birmaher, B., Rao, R., Williamson, D. E., & Perel, J. M. (1999). Factors associated with the development of substance use disorder in depressed adolescents. *Journal of the American Academy of Child and Adolescent Psychiatry, 38,* 1109-1117.

Raymond, N. C., Coleman, E., Ohlerking, F., Christenson, G. A., & Miner, M. (1999). Psychiatric comorbidity in pedophilic sex offenders. *American Journal of Psychiatry, 156,* 786-788.

Riggs, P. D., Mikulich, S. K., Whitmore, E. A., & Crowley, T. J. (1999). Relationship of ADHD, depression, and non-tobacco substance use disorders to nicotine dependence in substance-dependent delinquents. *Drug and Alcohol Dependence, 54,* 195-205.

Robins, L. N., & Przybeck, T. R. (1985). *Age of Onset of Drug Use as a Factor in Drug and Other Disorders*. Rockville, MD: National Institute of Drug Abuse Research.

Roehrich, H., & Gold, M. S. (1986). Diagnosis of substance abuse in an adolescent psychiatric population. *International Journal of Psychiatry in Medicine, 18,* 137-143.

Rohde, P., Lewinsohn, P. M., & Seeley, J. R. (1991). Comorbidity of unipolar depression: II. Comorbidity with other mental disorders in adolescents and adults. *Journal of Abnormal Psychology, 100,* 214-222.

Rohde, P., Lewinsohn, P. M., & Seeley, J. R. (1996). Psychiatric comorbidity with problematic alcohol use in high school students. *Journal of the American Academy of Child and Adolescent Psychiatry, 35,* 101-109.

Rounds-Bryant, J. L., Kristiansen, P. L., Fairbank, J. A., & Hubbard, R. L. (1998). Substance use, mental disorders, abuse, and crime: Gender comparisons among a national sample of adolescent drug treatment clients. *Journal of Child and Adolescent Substance Abuse, 7,* 19-34.

Rounsaville, B. J., Kranzler, H. R., Ball, S., Tennen, H., Poling, J., & Triffleman, E. (1998). Personality disorders in substance abusers: Relation to substance use. *Journal of Nervous and Mental Disease, 186,* 87-95.

SAMHSA (1996). *Mental Health Estimates from the 1994 National Household Survey on Drug Abuse*. Rockville, MD: Office of Applied Studies.

SAMHSA (1993). *National Household Survey on Drug Abuse: Population Estimates 1992.* Rockville, MD: U.S. Department of Health and Human Services.

SAMHSA (1999). *The Relationship Between Mental Health and Substance Abuse Among Adolescents.* Rockville, MD: U. S. Department of Health and Human Services.

Shedler, J., & Block, J. (1990). Adolescent drug use and psychological health: A longitudinal inquiry. *American Psychologist, 45,* 612-630.

Simonoff, E., Pickles, A., Meyer, J. M., Silberg, J. L., Maes, H. H., Loeber, R., Rutter, M., Hewitt, J. K., & Eaves, L. J. (1997). The Virginia Twin Study of adolescent behavioral development: Influences of age, sex and impairment on rates of disorder. *Archives of General Psychiatry, 54,* 801-808.

Sullivan, T. N., & Farrell, A. D. (1999). Identification and impact of risk and protective factors for drug use among urban African American adolescents. *Journal of Clinical Child Psychology, 28,* 122-136.

Sussman, S., Dent, C. W., Stacy, A. W., Burciaga, C., Raynor, A., Turner, G. E., Charlin, V., Craig, S., Hansen, W. B., Burton, D., & Flay, B. R. (1990). Peer-group association and adolescent tobacco use. *Journal of Abnormal Psychology, 99,* 349-352.

Van Kammen, W. B., Loeber, R., & Stouthamer-Loeber, M. (1991). Substance use and its relationship to conduct problems and delinquency in young boys. *Journal of Youth and Adolescence, 20,* 399-413.

Walter, H. J., Vaughan, R. D., & Cohall, A. T. (1993). Comparison of three theoretical models of substance use among urban minority high school students. *Journal of the American Academy of Child and Adolescent Psychiatry, 32,* 975-981.

Weinberg, N. Z. (1997). Cognitive and behavioral deficits in children associated with parental alcohol use. *Journal of the American Academy of Child and Adolescent Psychiatry, 36,* 1177-1186.

Weinberg, N. Z., & Glantz, M. D. (1999). Child psychopathology risk factors for drug abuse: Overview. *Journal of Clinical Child Psychology, 28,* 290-297.

Weinberg, N. Z., Rahdert, E., Colliver, J. D., & Glantz, M. D. (1998). Adolescent substance abuse: A review of the past 10 years. *Journal of the American Academy of Child and Adolescent Psychiatry, 37,* 252-261.

Whitmore, E. A., Mikulich, S. K., Thompson, L. L., Riggs, P. D., Aarons, G. A., & Crowley, T. J. (1997). Influences on adolescent substance dependence: Conduct disorder, depression, attention deficit hyperactivity disorder, and gender. *Drug and Alcohol Dependence, 47,* 87-97.

Wilens, T. E., & Biederman, J. (1993). Psychopathology in preadolescent children at high risk for substance abuse: A review of the literature. *Harvard Review of Psychiatry, 1,* 207-218.

Wilens, T. E., Biederman, J., Mick, E., Faraone, S. V., & Spencer, T. (1997). Attention deficit hyperactivity disorder (ADHD) is associated with early onset of substance use disorders. *Journal of Nervous and Mental Disease, 185,* 475-482.

Windle, M. (1990). A longitudinal study of antisocial behaviors in early adolescence as predictors of late adolescent substance use: Gender and ethnic group differences. *Journal of Abnormal Psychology, 99,* 86-91.

Windle, M., & Davies, P. T. (1999). Depression and heavy alcohol use among adolescents: concurrent and prospective relations. *Development and Psychopathology, 11,* 823-844.

Windle, M., & Windle, R. C. (1993). The continuity of behavioral expression among disinhibited and inhibited childhood subtypes. *Clinical Psychology Review, 13,* 741-761.

Zeitlin, H. (1999). Psychiatric comorbidity with substance misuse in children and teenagers. *Drug and Alcohol Dependence, 55,* 225-234.

APPENDIX B: SUMMARY OF THE STUDIES USED IN THE META-ANALYSIS

Beitchman et al. (1999) studied a one-in-three random sample of all 5-year-old English-speaking kindergarten children in Ontario, Canada. They administered a multistage speech and language screening procedure that resulted in 284 participants at time 1 and 258 participants at time 2 (age 19; 6.4 percent lost to followup, 2.1 percent refused, 0.7 percent died). At age 19, psychiatric status and Substance abuse/dependence for the 12-month period preceding the interview date were measured using the University of Michigan modification of the Composite International Diagnostic Interview (UM-CIDI; American Psychiatric Association, 1994; Kessler et al., 1994) using DSM-III-R criteria. Additionally, functional impairment was measured using the Global Assessment of Functioning (GAF). More than 90 percent of the sample identified themselves as "Caucasian."

Boyle and Offord (1991) used data from the Ontario Child Health Study (OCHS), a cross-sectional community study investigating the epidemiology of childhood psychiatric disorder and adolescent substance use (SU). The study targeted all children between the ages of 12 and 16 with a household residence in Ontario between January and February of 1983. The sampling frame was based on the 1981 Canada Census. Data on CD, ADD, and emotional problems were collected from 1,265 (97 percent) adolescents and their parents (female head of household) using structured, self-administered questionnaires, while data on SU (use of tobacco, alcohol, cannabis, and hard drugs) were collected from adolescents only. Diagnoses were made according to DSM-III criteria and referred to the preceding 6-month period.

In a longitudinal study of comorbid psychiatric disorder and SU, **Brook, Cohen, & Brook (1998)** followed a random sample of families with children ages 1-10 in two counties of upstate New York in 1975. The current study reflects data from 698 (72-percent retention) children who were followed prospectively into adulthood at timepoints in 1983, 1986, and 1992. No significant group differences were noted with regard to retention/attrition rates. Ninety-two percent of the sample was White. Information from mothers and adolescents on psychiatric diagnoses and SU (of tobacco, alcohol, cannabis, and illicit drugs) and substance abuse/dependence was collected using the Diagnostic Interview for Children Version 1 (DISC-1; Costello, Edelbrock, Kalas, Kessler, & Klaric, 1982), with computer algorithms based on DSM-III-R criteria. Additionally, adolescents completed a paper-and-pencil assessment of SU.

Cross-sectional data from the Project on Adolescent Substance Use Disorders in Taiwan (PAST) were reported by **Chong, Chan, and Cheng (1999).** The PAST is a 3-year longitudinal survey of 774 (99.2 percent participation) 9th-graders (411 males and 363 females) from rural, urban, and suburban schools that assesses the prevalence of substance use disorders (SUDs) and psychiatric comorbidity. Substance abuse/dependence (e.g., alcohol, cigarettes, betel, prescribed and illicit drugs) was measured using a brief questionnaire, and psychiatric status was assessed using the Chinese version of the Kiddie Epidemiologic Version of the Schedule for Affective Disorders and Schizophrenia (K-SADS-E; Puig-Antich, 1978) using DSM-III-R criteria.

The Great Smoky Mountains Study (GSMS; **Costello et al., 1999**) is a longitudinal study of the development of SU, substance abuse/dependence (tobacco, alcohol, cannabis, and other illicit drugs), and psychiatric disorder within a sample of 1,420 (80-95 percent retention) 9-, 11-, and 13-year-olds followed since 1993. Adolescents and their parents recruited from a predominantly rural area in western North Carolina were interviewed separately using the Child and Adolescent Psychiatric Assessment (CAPA; Angold & Costello, 1995), with diagnoses based on DSM-III-R and DSM-IV psychiatric symptoms occurring during the previous 3 months. In terms of ethnic diversity, American Indians were oversampled and thus represented 25 percent of the entire sample; African Americans comprised less than 10 percent of the sample, and Hispanics comprised less than 1 percent of the sample.

Deykin, Levy, and Wells (1987) interviewed 424 (271 females, 153 males; 42 percent participation) college students aged 16 to 19 in the Boston area as part of a cross-sectional study designed to identify the manifestations and correlates of adolescent major depressive disorder (MDD). Data on lifetime prevalence of MDD and alcohol or drug abuse were collected from participants using the Diagnostic Interview Schedule (DIS; Robins, Helzer, Croughan, & Ratcliff, 1981) based on DSM-III criteria. The sample was predominantly White (94 percent) and upper class (based on Hollingshead classification of paternal occupation).

Disney, Elkins, McGue, & Iacono (1999) reported data from the Minnesota Twin Family Study, a longitudinal study of genetic and environmental factors influencing the development of substance abuse and associated psychological disorders. All twins born in the State of Minnesota were identified by public birth records. A sample of 626 reared-together twin pairs (674 girls, 578 boys; 83 percent participation of eligible families) at age 17 and their mothers were interviewed separately regarding ADHD, CD, and substance disorder symptoms (use, abuse, or dependence of tobacco, alcohol, or cannabis) using the Diagnostic Interview for Children and Adolescents-Revised (DICA-R; Reich & Weiner, 1988), an additional structured interview, the substance abuse module from the CIDI, and a computer-administered SU and abuse questionnaire. Diagnoses were based on DSM-III-R criteria. Ninety-eight percent of respondents were White.

Fergusson and colleagues (1993a, 1993b) reported on data from the Christchurch Health and Development Study (CHDS), a longitudinal study of a birth cohort of 1,265 children born in the Christchurch urban region during mid-1977. From this sample, 875 (69.2 percent overall, 78.7 percent of all cohort members alive and resident in New Zealand) children at age 15 were assessed for psychiatric disturbance and SU (tobacco, alcohol, cannabis, and illicit drugs) using the DISC (based on DSM-III-R criteria), portions of the DIS, the Self-Report Early Delinquency (SRED) scale (Moffitt & Silva, 1988), survey questions regarding substance abuse behaviors, and the Rutgers Alcohol Problems Index (White & Labouvie, 1989). In addition to these measures, mothers of each adolescent also completed the Revised Behavior Problems Checklist (RBPC; Quay & Petersen, 1987).

Another birth cohort from New Zealand was studied by **Henry et al. (1991)** as part of the Dunedin Multidisciplinary Health and Development Study. This longitudinal study of 1,037 children born in

Dunedin between April 1972 and March 1973 and living in the province of Otago at the onset of the study has been followed every 2 years since 1975. Data collected when the respondents were ages 11 (n=752, 72.5 percent; 355 females, 397 males) and 15 (n=956, 92.2 percent; 464 females, 492 males) assessed depressive symptomatology, conduct problems, and SU (alcohol, cannabis, glue, and other drugs) using the DISC-Child Version (DSM-III criteria) and the SRED.

In a cross-sectional study occurring between April 1990 and June 1991, **Feehan, McGee, Raja, and Williams (1994)** assessed the same New Zealander participants at age 18 (n=930, 454 females, 476 males; 91 percent participation of survivors) using the DIS (DSM-III-R criteria), the Denver Youth Survey Youth Interview Schedule (Huizinga, 1989), and the Health Services Utilization questionnaire (Shapiro, 1984). Eight hundred thirty of the participants also had data from "significant-other" informants. Diagnoses were made on the basis of DSM-III-R symptoms in the last 12 months as well as a disturbance in life functioning (as indicated by interference in daily functioning, help seeking, or police contact). Data were also collected on economic disadvantage, social competence, self-perceived physical health status, self-medication, and suicidal ideation. In terms of the ethnic origin of the participants, 93 percent identified themselves as "European," 3 percent as "New Zealand Maori," and 4 percent as "other."

Kandel and colleagues (1997, 1999) reported findings from the Methods for the Epidemiology of Child and Adolescent Mental Disorders (MECA) study, a cross-sectional study of 1,285 (604 females, 681 males) children and adolescents ages 9 to 18 investigating the extent of substance abuse/dependence (of cigarettes, alcohol, and illicit drugs) and other psychiatric disorders among adolescents in the general population. Probability samples were drawn from four geographic regions of the United States in 1992: Connecticut, Georgia, New York, and Puerto Rico. Non-White samples ranged from 22-37 percent, except in Puerto Rico, where the sample was 100 percent Hispanic. Adult caretakers were also interviewed in 77 percent of the households. Psychiatric symptoms during the prior 6 months were assessed using computer-assisted parent and child versions of the DISC-2.3 (DSM-III-R criteria), and functional impairment was assessed using the Service Utilization and Risk Factors Interview (SURF; Goodman et al., 1994) and a lay interview version (Bird, 1996 #10810) of the Children's Global Assessment Scale (CGAS; Shaffer et al., 1983). A study examining adolescent SUDs and comorbid psychiatric disorders used a subsample of 401 adolescents (190 females, 211 males) ages 14 to 17. Puerto Rican adolescents were excluded from this study given significantly lower rates of SU compared to the adolescents from the three other samples.

In an investigation of the prevalence, incidence, and comorbidity for affective, SU (alcohol and other psychoactive substance use, abuse, and dependence disorders using DSM-III-R and DSM-IV criteria), and other psychiatric disorders in adolescents ages 14 to 18, **Lewinsohn, Rohde, and colleagues (1991, 1993, 1995, 1996)** report findings from the Oregon Adolescent Depression Project (OADP). The OADP is a large-scale, community-based epidemiological survey with a prospective, longitudinal design. The population was drawn from the high schools of two urban communities and three rural communities in west central Oregon. Each adolescent was assessed at two timepoints

(approximately 1 year apart) using the K-SADS (combined features of both the Epidemiologic and Present Episode Versions), the Hamilton Rating Scale for Depression (Hamilton, 1960), the Center for Epidemiologic Studies-Depression Scale (CES-D; Radloff, 1977), the Beck Depression Inventory (BDI; Beck, Ward, Mendelson, Mock, & Erbaugh, 1961), and the LIFE (Shapiro & Keller, 1979) interview, an instrument that yields information about the longitudinal course of all DSM disorders. Three cohorts were recruited in 1987, 1988, and 1989, consisting of 352, 864, and 494 students, respectively. The sample size at time 1 was 1,709 adolescents, and 1,507 adolescents at time 2 (overall participation rate was 61 percent). At time 1, 91.1 percent of the sample was White. Lewinsohn, Rohde, et al. (1995) additionally assessed mental health treatment utilization, global adjustment of functioning, history of suicide attempts, elevated physical symptoms, academic problems, and conflict with parents. Rohde et al. (1991) included a sample of 2,060 adults selected from three separate longitudinal studies.

Substance Abuse and Mental Health Services Administration (SAMHSA; 1996) reported estimates on psychosocial problems and SU from the 1994 National Household Survey on Drug Abuse (NHSDA) from a nationally representative sample of 21,773 adolescents ages 12 to 17. This cross-sectional study assessed the extent of emotional and behavioral problems during the prior 6 months using the Youth Self-Report (YSR; Achenbach, 1991) and any use of cigarettes, cannabis, illicit drugs, or "binge" alchohol use in the last 30 days. Blacks and Hispanics were oversampled and represented 26.5 percent of the sample. **SAMHSA (1999)** used data from the 1994-1996 NHSDA among 13,831 adolescents ages 12 to 17 and assessed 30-day use of cigarettes, alcohol, illicit drugs, as well as alcohol or illicit drug dependence (DSM-IV criteria). Data from the older adolescents (ages 16 to 17) were used for the purposes of this meta-analysis.

Windle and Windle (1993) studied 1,067 (519 males, 548 females; 74 percent participation) from the Middle Adolescent Vulnerability Study (MAVS), a study of vulnerability factors and adolescent SU that incorporates a four-wave longitudinal design. This study represented data from suburban high school juniors and seniors on the cross-sectional, retrospective portion of the MAVS collected at time 4. Two percent of the sample was non-White. The Retrospective Childhood Problems (RETROPROB; Windle, 1993) scale and a delinquency measure were used to measure symptoms of ADHD, ODD, CD, and avoidant personality disorder (DSM-III-R criteria). The CES-D was used to measure depressive symptoms. SU was measured with questions regarding alcohol use, onset of drinking behavior, and other SU (cigarettes, cannabis, and nonprescribed hard drugs) during the last 30 days and last 6 months. **Windle and Davies (1999)** examined relationships between depression and heavy alcohol use focusing on the second and fourth timepoints (separated by 1 year) of the same data set with 1,094 adolescents (533 males, 561 females; retention above 90 percent). Surveys on depression (CES-D), alcohol consumption (Quantity-Frequency Index; Armor & Polich, 1982), childhood problems (RETROPROB), and other variables were administered to the adolescents in their high school settings.

APPENDIX C: SUMMARY OF THE RESULTS OF THE STUDIES USED IN THE ANALYSES

Results from individual studies

Comorbidity of substance use and CD/ODD. Henry et al. (1993) discovered a strong association between conduct problems at age 15 and use of multiple substances. They found no evidence for an association between conduct disorder and later SU after controlling for depressive symptomatology. Boyle & Offord (1991) demonstrated that adolescent SU was strongly associated with CD. Additionally, they found that parent report of CD symptoms produced no significant predictive value beyond adolescent self-report of CD symptoms. They concluded from their data that CD precedes rather than follows the onset of SU. Brook et al. (1998) reported that adolescent SU was associated with higher rates of CD over extended periods. However, they found no evidence that CD has an influence on later drug use when earlier drug use is accounted for. Specifically, SU activity following the onset of SU does not appreciably affect later drug use, although earlier psychopathology may. Disney et al. (1999) found evidence for an association between CD and early onset of substance problems in both males and females, particularly among those adolescents exhibiting delinquent behaviors after age 15. Data from Lewinsohn, Rohde, et al. (1995) indicated that males and females receiving diagnoses of both CD and ODD revealed the highest levels of delinquent behavior and comorbid SU, with or without the additional diagnosis of ADHD.

Fergusson, Lynskey, and Horwood (1993) reported that conduct problems at all ages were significantly related to early cannabis use. These authors found that CD was related to the development of social adjustment and conformity problems. Risk factors associated with higher rates of CD included lower socioeconomic status, higher parental conflict, less nurturing and more punitive parenting, and instability in the parent structure of the family. They concluded that their data suggested that cannabis use often operates as a covert symptom for CD among adolescents.

With respect to substance abuse/dependence criteria, Chong, Chen, & Chang (1999) reported prevalence rates of 45-91 percent for CD among adolescents with SUDs, but no CD diagnoses among adolescents without SUDs. In terms of additional comorbidities, 60 percent of adolescents with ADHD and SUD also had a diagnosis of CD. Fifty percent of adolescents with SUD and depression also met criteria for CD. Lewinsohn, Hops, et al. (1993) reported significant rates of adolescent SUDs with any disorder, particularly disruptive behavior disorders (DBDs). In fact, they reported that SUDs were third highest in prevalence after MDD and anxiety disorders. In their paper on clinical consequences, Lewinsohn, Rohde, et al. (1995) reported that psychiatric comorbidity had the least impact on SUDs; that is, adolescents with SUD and a comorbid psychiatric condition were less likely to receive mental health treatment compared to adolescents with two or more comorbid psychiatric conditions, neither of which was SUD. Adolescents with a DBD and SUD were significantly more likely to experience serious academic problems.

Comorbidity of substance use and ADHD. Disney et al. (1999) concluded from their data that a diagnosis of ADHD has little effect on SU outcomes in males or females independent of the effects of CD.

However, they provided evidence for a possible effect of ADHD on nicotine dependence. SAMHSA (1999) reported that attentional problems, along with social problems and delinquent behavior, best predicted SU. In terms of findings on substance abuse/dependence, Windle and Windle (1993) demonstrated that adolescents were at increased risk for SUDs when an externalizing disorder such as ADHD occurs with a comorbid internalizing disorder.

Comorbidity of substance use and depression. Kandel et al. (1997) reported that use of illicit substances during the past year was associated with increased risk for mood disorders. Boyle and Offord (1991) also found that emotional disorders were related to SU (with the exception of cannabis use). In fact, parent report of emotional disorder was a more significant predictor for SU than adolescent self-report of emotional disorder. Their data revealed findings of subjective turmoil based on the degree of SU and of associations between depression and cigarette smoking. Similarly, Brook et al. (1998) reported that adolescent cigarette smoking was associated with later depression. With regard to timing of comorbidity, Brook et al. found no evidence that depression has an influence on later SU after the onset of SU. They further noted that early SU is associated with later psychiatric disorder, especially depression. While Deykin, Levy, and Wells (1987) showed that the onset of depression as well as other psychiatric disorders preceded the development of SUD, Costello et al. (1999) demonstrated that the onset of psychiatric disorder preceded the onset of SU except with respect to depression, which tended to occur 1 year after the onset of alcohol use and 2 years after the onset of cigarette use. Notably, 79 percent of substance abusers from Deykin et al.'s study developed an additional psychiatric disorder following the SUD diagnosis. Windle & Davies reported that the prevalence of comorbid depression and heavy drinking was similar across gender groups. Between 24 and 27 percent of depressed adolescents met criteria for a lifetime alcohol or other SUD, and 23 to 27 percent of heavy drinkers also met criteria for depression. Furthermore, adolescents with depression and comorbid heavy drinking had the highest levels of childhood externalizing as well as avoidance problems, temperamentally inflexible, lowest levels of family support, highest levels of stressful life events, high levels of SU and delinquency, and the lowest GPA.

With respect to studies measuring substance abuse/dependence, Rohde et al. (1991) provided evidence for a high degree of comorbidity among depressed adolescents, with SUD being the most common comorbidity after eating disorders. They further found that adolescents diagnosed with depression and a comorbid psychiatric disorder were at greatest risk for suicide. Rohde et al. (1996) reported that depression was significantly associated with adolescent SUD, with over 80 percent of adolescents with alcohol SUD having a comorbid psychiatric disorder, 20 percent of which were internalizing disorders and 45 percent more were mixed internalizing and externalizing disorders.

Comorbidity of substance use and anxiety. Interestingly, virtually all findings of SU and comorbid anxiety involved cigarette use. Brook et al. (1998) found that adolescent cigarette smoking was associated with later anxiety. Anxiety problems were found to be associated with a later onset of cigarette smoking (Costello et al., 1999). According to Kandel et al. (1997), daily cigarette smoking was

associated with increased risk for anxiety disorders. Chong, Chan, and Cheng (1999) found that adolescents who were diagnosed with SUD and comorbid anxiety often demonstrated additional comorbidities, making it difficult to understand the nature of the individual diagnoses.

Comorbidity of substance use and other disorders. In their community sample, Beitchman et al. (1999) reported that individuals in the speech- and language-impaired group diagnosed with SUD demonstrated higher frequencies of Antisocial Personality Disorder (ASPD) than individuals in the control group diagnosed with a SUD (80 percent vs. 43.8 percent). For this sample, there was on average a 4- to 5-year gap between the onset of SU and the development of SUD. Fergusson et al. (1993) concluded that their data on cannabis use among New Zealand adolescents provides evidence of substantial continuities in antisocial behavior from middle childhood to adolescence. Brook et al. (1998) reported the finding that adolescent cigarette smoking was associated with later antisocial personality disorder. Windle and Windle (1993) reported that the avoidant personality subtype served as a protective factor against certain externalizing behaviors, which decreased the risk of developing SUD.

Rohde et al. (1996) found that bipolar disorder was the only psychiatric disorder not significantly associated with adolescent alcohol use group status. SAMHSA (1999) reported that elevated scores on the YSR's delinquent behavior subscale were among the best predictors of adolescent SU. The severity of behavioral problems was associated with an increased likelihood of SU as well as substance dependence.

Gender differences. Henry et al. (1993) found that, for males, the relationship between early conduct problems and SU was mediated by the effects of depressive symptoms. Conversely, the association between depressive symptoms and SU were mediated by the effects of conduct problems. Depressive symptoms predicted later SU in males, but there was a contemporaneous association between conduct problems and SU in females. Furthermore, females with conduct problems appeared to self-medicate, independent of their depressive symptomatology. Kandel et al. (1997) found that the use of illicit substances was significantly associated with DBDs in females only. Windle & Davies showed that depressed boys (33 to 37 percent) were more likely to meet criteria for heavy drinking compared to girls (16 to 18.5 percent). Conversely, heavy drinking girls (27 to 33 percent) were more likely than heavy drinking boys (18 to 20 percent) to meet criteria for depression.

Lewinsohn et al. (1995) reported that comorbid DBDs and SUDs were much more prevalent among males compared to females in their sample. Males were also more likely to experience academic problems associated with such comorbidity, while females were more likely to have reported elevated physical symptoms, to have attempted suicide, and to have received treatment. Additionally, they reported that 75 percent of adolescents with SUD and a comorbid anxiety disorder were females. Costello et al. (1999) also found that substance abuse/dependence was more common among males reporting depressive symptoms compared to males not reporting depressive symptoms, and more common among females diagnosed with a behavior disorder. Disney et al. (1999) reported that ADHD may put adolescent females at slightly higher risk for developing SUD.

Demographic differences. Kandel et al. (1999) concluded from their data that adolescents in the general population with a lifetime prevalence of SUD have as great a risk for psychiatric comorbidity as adults. Moreover, those adolescents with a current SUD have a greater risk than adults for psychiatric comorbidity. SAMHSA (1996) reported no significant differences in reported SU by race or ethnicity, although Whites were more likely to receive outpatient mental health treatment compared to Blacks and Hispanics. Chong et al. (1999) reported a higher prevalence of substance use disorders and comorbid depression among adolescents residing in rural households. These adolescents tended to reveal tobacco and betel abuse much more frequently than alcohol.

APPENDIX D: COPY OF FORM USED TO COLLECT INFORMATION ON POTENTIALLY USEFUL DATA SET

NIDA SUMMARY OF DATA SETS AVAILABLE TO EXAMINE THE DEVELOPMENT OF PSYCHIATRIC COMORBIDITY WITH DRUG ABUSE *Please provide as much information as you think would be helpful in compiling this summary.*
Name, e-mail, and telephone number of person completing the form
What do you call the study or data set? Who funded the data collection? NIH_____ Other _____
Who is the Principal Investigator or person responsible for the data set? *If this person is not yourself, please give e-mail and telephone number.*
When were the data collected? First year_____ Last year_____ Still continuing_____
This data set does not meet NIDA's requirements, for one or more of the following reasons: *Not a representative population sample_____* *No participants ever assessed when under 18_____* *Does not provide DSM or ICD psychiatric diagnoses_____* *Does not provide enough information to diagnose substance abuse or dependence_____* *Does not distinguish among substances_____* *Does not provide onset dates, or permit onsets to be calculated (e.g., over repeated waves of data)_____* *Other reasons (please explain)* Signed: Date:

Appendix D: Copy of form used to collect information on potentially useful data set (continued)

NIDA SUMMARY OF DATA SETS AVAILABLE TO EXAMINE THE DEVELOPMENT OF PSYCHIATRIC COMORBIDITY WITH DRUG ABUSE *Please provide as much information as you think would be helpful in compiling this summary.*
IF YOUR DATA COULD BE HELPFUL NIDA, PLEASE COMPLETE THE REST OF THIS FORM How old were the participants at the first wave? How many waves of data collection have there been? When were they? *(If regular, please state annual, biennial, etc. If irregular, give years.)* If the study is ongoing, how old were subjects at the last wave?
How many participants were there at the first wave? *(Participant=index child)* On how many of these do you have at least one wave of followup data?
What is the population that the sample represents? *(e.g., is it a random sample from a school, city, State, whole country?)*
What is the age range of the study to date? *(age of youngest at first wave to oldest at latest wave)*
What is the ratio males/females?
What are the race/ethnic groups represented, in what proportions?
Can you diagnose substance abuse/dependence on all participants?

Appendix D: Copy of form used to collect information on potentially useful data set (continued)

NIDA SUMMARY OF DATA SETS AVAILABLE TO EXAMINE THE DEVELOPMENT OF PSYCHIATRIC COMORBIDITY WITH DRUG ABUSE *Please provide as much information as you think would be helpful in compiling this summary.*

For which drugs can you diagnose abuse/dependence?

Snuff___ Chewing tobacco____ Cigarettes, cigars, pipes___ Any tobacco use____

Alcohol_____ Inhalants_____ Cannabis_____ Sedatives_____ Amphetamines_____ LSD_____ Cocaine_____ Crack_____

Psilocybins_____ "Club drugs"_____ Opioids_____ Steroids_____ Other_____

Any use_____ Any use excluding tobacco_____ Any use excluding tobacco and alcohol_____ Any use excluding tobacco, alcohol, and cannabis_____

Any abuse_____ Any abuse excluding tobacco_____ Any abuse excluding tobacco and alcohol_____ Any abuse excluding tobacco, alcohol, and cannabis_____

Any dependence_____ Any dependence excluding tobacco_____ Any dependence excluding tobacco and alcohol_____ Any dependence excluding tobacco, alcohol, and cannabis_____

Any abuse/dependence_____Any abuse/dependence excluding tobacco_____ Any abuse/dependence excluding tobacco and alcohol_____ Any abuse/dependence excluding tobacco, alcohol, and cannabis_____

Do you have onset dates for substance use_____ abuse_____ or dependence_____?

If so, do you have it for specific substances, or in general?

Do you have offset dates for substance use_____ abuse_____ or dependence_____?

Appendix D: Copy of form used to collect information on potentially useful data set (continued)

NIDA SUMMARY OF DATA SETS AVAILABLE TO EXAMINE THE DEVELOPMENT OF PSYCHIATRIC COMORBIDITY WITH DRUG ABUSE *Please provide as much information as you think would be helpful in compiling this summary.*

For which psychiatric disorders can you make diagnoses?
DSM-III_____ DSM-IIIR_____ DSM-IV_____ ICD-9_____ ICD-10_____
Unipolar depression_____ Bipolar depression_____ Any depression_____
Specific anxiety diagnoses_____ Any anxiety disorder_____ Any emotional disorder (*anxiety or depression)*_____
ADD/ADHD_____ Oppositional disorder/ODD_____Conduct disorder_____ Conduct or oppositional disorder_____
Behavioral disorder (*CD, ODD, or ADHD*)_____
Schizophrenia____ Other psychotic disorder_____ Any psychotic disorder_____ OCD_____ Tics/Tourette's _____
Bulimia_____ Anorexia nervosa_____ Any eating disorder_____
Antisocial personality disorder_____ Other Axis II disorders *(please specify)*_____
Other diagnoses (*please specify)*_____
Any Axis I diagnosis_____ Any Axis I or Axis II diagnosis_____

Do you have onset dates for psychiatric symptoms_____ or diagnoses_____?

If so, are these based on asking for onset dates or on inference from repeated assessments?

Do you have offset dates for symptoms_____ or diagnoses_____?

Can you generate the raw data for calculating odds ratios for comorbidity estimates (e.g., N with anxiety, N with anxiety and drug abuse, N without anxiety, N without anxiety with drug abuse)?

Is it possible from your data to determine whether, and which, diagnoses preceded or followed the onset of drug use, abuse, or dependence?

Is it possible from your data to examine risk and protective factors for onset of drug abuse/dependence in the presence of psychiatric comorbidity?

Appendix D: Copy of form used to collect information on potentially useful data set (continued)

NIDA SUMMARY OF DATA SETS AVAILABLE TO EXAMINE THE DEVELOPMENT OF PSYCHIATRIC COMORBIDITY WITH DRUG ABUSE *Please provide as much information as you think would be helpful in compiling this summary.*
Is it possible from your data to examine functional impairment in association with drug abuse/dependence, psychiatric disorder, and/or comorbidity?
Assuming that NIDA were able to provide funding for you to analyze your data set to examine the effects of psychiatric comorbidity on the development of drug abuse and dependence, are there any special considerations that would affect whether you were willing to take part in a collaborative venture of this sort?
Any other comments? Thank you very much

Please fax to Jane Costello at 919-687-4737, or send as an e-mail attachment to Jcostell@psych.mc.duke.edu

Table 1. Rates of substance and psychiatric comorbidity in community-based samples

Study	N	Age	Time frame	Pop rate of a (%)	Pop rate of b (%)	Rate of a in b(%)	Rate of a in not b (%)	Rate of b in a (%)	Rate of b in not a (%)	OR	CI
a=substance use, b=depression, in females											
2	1265	12 to 16	6 mo	9.3	13.6					2.67	
3	698	12 to 21	lifetime	27	0					1.3	1.0, 1.6
9	875	14 to 15	lifetime	9.8						n/a	
10	464	15	lifetime	21.6	9.1					2.98	n/a
11	604	9 to 18	6 mo	41.7	7.2			25	5.3	5.8	4.2, 6.4
17	2346	12 to 17	1 mo	n/a	14.5	16.6	6.4			2.8	2.3, 3.3
19	548	16 to 17	6 mo	8.4						n/a	
21	561	15 to 16	1 mo	11.5	18.9	4.3				0.3	0.1, 0.5
a=substance use, b=depression, in males											
2	1265	12 to 16	6 mo	6.9	4.9					2.67	
3	698	12 to 21	lifetime	27						1.3	1.0, 1.6
9	875	14 to 15	lifetime	9.8						n/a	
10	492	15	lifetime	19.1	7.3					1.38	
11	681	9 to 18	6 mo	41.7	7.2			23.3	4.8	6	4.3, 7.7
17	2352	12 to 17	1 mo		13.8	13.9	7.6			1.9	1.5, 2.3
19	519	16 to 17	6 mo	16.6						n/a	
21	533	15 to 16	1 mo	25.6	9.9	5.8				0.2	0.1, 0.3
a=substance use, b=anxiety, in females											
2	1265	12 to 16	6 mo	9.3	13.6					2.67	n/a
3	698	12 to 21	lifetime	27						1.3	1.0, 1.6
9	875	14 to 15	lifetime	9.8						n/a	

Table 1. Rates of substance and psychiatric comorbidity in community-based samples (continued)

Study	N	Age	Time frame	Pop rate of a (%)	Pop rate of b (%)	Rate of a in b(%)	Rate of a in not b (%)	Rate of b in a (%)	Rate of b in not a (%)	OR	CI
10	464	15	lifetime	21.6						n/a	
11	604	9 to 18	6 mo	41.7	13			33.3	11.4	6.7	5.3, 8.1
17	2346	12 to 17	1 mo		14.5	16.6	6.4			2.9	2.4, 3.4
19	548	16 to 17	6 mo	8.4						n/a	n/a
21	561	15 to 16	1 mo	11.5						n/a	
a=substance use, b=anxiety, in males											
2	1265	12 to 16	6 mo	6.9	4.9					2.7	n/a
3	698	12 to 21	lifetime	27						1.3	1.0, 1.6
9	875	14 to 15	lifetime	9.8						n/a	
10	492	15	lifetime	19.1						n/a	
11	681	9 to 18	6 mo	41.7	13			16.7	11.7	2.2	1.6, 2.8
17	2352	12 to 17	1 mo		13.8	13.9	7.6			1.9	1.5, 2.3
19	519	16 to 17	6 mo	16.6						n/a	
21	533	15 to 16	1 mo	25.6						n/a	
a=substance use, b=ADHD, in females											
2	1265	12 to 16	6 mo	9.3	3.3					0.6	n/a
3	698	12 to 21	lifetime	27						n/a	
9	875	14 to 15	lifetime	9.8	8.6	20				0.7	0.5, 0.9
10	464	15	lifetime	21.6						n/a	
11	604	9 to 18	6 mo	41.7	10.3			33.3	5.6	8.3	6.1, 10.5
17	2346	12 to 17	1 mo		21.7	21.1	4.2			6.8	5.7, 7.9
19	548	16 to 17	6 mo	8.4	6.4	18.8	7.4			2.9	1.5, 4.3
21	561	15 to 16	1 mo	11.5						n/a	

Table 1. Rates of substance and psychiatric comorbidity in community-based samples (continued)

Study	N	Age	Time frame	Pop rate of a (%)	Pop rate of b (%)	Rate of a in b(%)	Rate of a in not b (%)	Rate of b in a (%)	Rate of b in not a (%)	OR	CI
a=substance use, b=ADHD, in males											
2	1265	12 to 16	6 mo	6.9	7.3					0.6	n/a
3	698	12 to 21	lifetime	27						n/a	
9	875	14 to 15	lifetime	9.8	8.6	20				0.7	0.5, 0.9
10	492	15	lifetime	19.1						n/a	
11	681	9 to 18	6 mo	41.7	10.3			50	9.3	9.8	7.8, 11.8
17	2352	12 to 17	1 mo		15.8	21.4	6.1			4.2	3.8, 5.6
19	519	16 to 17	6 mo	16.6	6.4	10.7	13.4			0.8	0.5, 1.3
21	533	15 to 16	1 mo	25.6						n/a	
a=substance use, b=ODD, in females											
2	1265	12 to 16	6 mo	9.3						n/a	
3	698	12 to 21	lifetime	27						n/a	
9	875	14 to 15	lifetime	9.8	8.1	21.13				2.8	1.9, 3.7
10	464	15	lifetime	21.6						n/a	
11	604	9 to 18	6 mo	41.7	10.3			33.3	5.6	8.3	6.1, 10.5
17	2346	12 to 17	1 mo		21.7	21.1	4.2			6.1	5.1, 7.1
19	548	16 to 17	6 mo	8.4	5	26.7	7.4			4.6	2.5, 6.7
21	561	15 to 16	1 mo	11.5						n/a	
a=substance use, b=ODD, in males											
2	1265	12 to 16	6 mo	6.9						n/a	
3	698	12 to 21	lifetime	27						n/a	
9	875	14 to 15	lifetime	9.8	8.1	21.13				2.8	1.9, 3.7
10	492	15	lifetime	19.1						n/a	

Table 1. Rates of substance and psychiatric comorbidity in community-based samples (continued)

Study	N	Age	Time frame	Pop rate of a (%)	Pop rate of b (%)	Rate of a in b(%)	Rate of a in not b (%)	Rate of b in a (%)	Rate of b in not a (%)	OR	CI
11	681	9 to 18	6 mo	41.7	10.3			50	9.3	9.8	7.7, 11.9
17	2352	12 to 17	1 mo		15.8	21.4	6.1			4.2	3.6, 4.8
19	519	16 to 17	6 mo	16.6	5	30	13.4			2.8	1.6, 4.0
21	533	15 to 16	1 mo	25.6						n/a	
a=substance use, b=CD, in females											
2	1265	12 to 16	6 mo	9.3	4					20.3	n/a
3	698	12 to 21	lifetime	27						n/a	
9	875	14 to 15	lifetime	9.8	8.1	21.13				2.8	1.9, 3.7
10	464	15	lifetime	21.6	10.3					10.35	n/a
11	604	9 to 18	6 mo	41.7	10.3			33.3	5.6	8.3	6.1, 10.5
17	2346	12 to 17	1 mo		21.7	21.1	4.2			6.1	5.1, 7.1
19	548	16 to 17	6 mo	8.4	5	26.7	7.4			4.6	2.5, 6.7
21	561	15 to 16	1 mo	11.5						n/a	
a=substance use, b=CD, in males											
2	1265	12 to 16	6 mo	6.9	10.4					3.28	n/a
3	698	12 to 21	lifetime	27						n/a	
9	875	14 to 15	lifetime	9.8	8.1	21.13				2.8	1.9, 3.7
10	492	15	lifetime	19.1	6.9					12.69	n/a
11	681	9 to 18	6 mo	41.9	10.3			50	9.3	9.8	7.8, 11.8
17	2352	12 to 17	1 mo		15.8	21.4	6.1			4.2	3.6, 4.8
19	519	16 to 17	6 mo	16.6	5	30	13.4			2.8	1.6, 4.0
21	533	15 to 16	1 mo	25.6						n/a	

Note.

Table 1. Rates of substance and psychiatric comorbidity in community-based samples (continued)

Study	N	Age	Time frame	Pop rate of a (%)	Pop rate of b (%)	Rate of a in b(%)	Rate of a in not b (%)	Rate of b in a (%)	Rate of b in not a (%)	OR	CI
Study 2. Boyle & Offord, 1991											
Study 3. Brook, Cohen, & Brook, 1998											
Study 9. Fergusson, Lynskey, & Horwood, 1993											
Study 10. Henry, Feehan, McGee, Stanton, Moffitt, & Silva, 1993											
Study 11. Kandel, Johnson, Bird, Canino, Goodman, Lahey, Regier, & Schwab-Stone, 1997											
Study 17. Substance Abuse and Mental Health Services Administration, 1996											
Study 19. Windle & Windle, 1993											
Study 21. Windle & Davies, 1999											

ADHD = attention-deficit/hyperactivity disorder; CD = conduct disorder; CI = confidence interval; ODD = oppositional defiant disorder; OR = odds ratio

Table 2. Rates of substance abuse/dependence and psychiatric comorbidity in community-based samples

Study	N	Age	Time frame	Pop rate of a (%)	Pop rate of b (%)	Rate of a in b(%)	Rate of a in not b (%)	Rate of b in a (%)	Rate of b in not a (%)	OR	CI
a=substance abuse/dependence, b=depression, in females											
1	142	19	12 mo	12.4	8.5			18.8	7.1	3.1	1.0, 6.3
4	363	14 to 16	lifetime	10.5	6.9			11.1	4.8	2.5	0.8, 4.2
5	1420	9 to 16	3 mo	6.3		34.7	1.1			47.7	32.9, 62.5
6	271	16 to 19	lifetime	7.8	10.3	17.9	6.6	23.8	9.2	3.1	1.1, 5.1
7	674	17	12 mo	20.3						n/a	
8	961	15	6 mo	8.9	9.7					4.4	2.9, 5.9
12	190	14 to 17	6 mo	5.3	12.5			32	11.2	3.7	1.5, 5.9
13	810	15 to 19	lifetime	10	32.96	20.1	5.3	49.3	17.7	4.5	3.7, 5.3
14	1507	14 to 18	lifetime	9.8	22.7	22.8		52.7		4.6	3.5, 5.7
15	1507	14 to 18	lifetime	6.2	24.8			47.9	16.8	4.5	3.5, 5.5
16	1710	14 to 18	lifetime	8.3	20.3	19.9	5.4			4.4	3.6, 5.2
18	2326	16 to 17	1 mo	10.4	15.5		6.3	18.9		2.2	1.8, 2.6
20	454	18	12 mo	12.6	26.4	22.6	13.8	29	18.3	1.8	1.3, 2.3
a=substance abuse/dependence, b=depression, in males											
1	142	19	12 mo	12.4	8.5			18.8	7.1	3.1	1.0, 6.3
4	411	14 to 16	lifetime	10.5	6.9			11.1	4.8	2.5	0.8, 4.2
5	1420	9 to 16	3 mo	5.7		29.9	1.5			28	20.2, 35.8
6	271	16 to 19	lifetime	12.4, 12.4	4.6	28.6, 42.9	11.6, 11.0	10.5, 15.8	3.7, 3.0	6.1	0.2, 12.0
7	578	17	12 mo	22.8						n/a	
8	961	15	6 mo	6.5	3.4					4.4	2.9, 5.9
12	211	14 to 17	6 mo	7.1	12.5			32	11.2	3.7	1.5, 5.9

Table 2. Rates of substance abuse/dependence and psychiatric comorbidity in community-based samples (continued)

Study	N	Age	Time frame	Pop rate of a (%)	Pop rate of b (%)	Rate of a in b(%)	Rate of a in not b (%)	Rate of b in a (%)	Rate of b in not a (%)	OR	CI
13	698	15 to 19	lifetime	11.75	16.33	20.1	5.3	49.3	17.7	4.5	3.7, 5.3
14	1507	14 to 18	lifetime	9.8	22.7	22.8		52.7		4.6	3.5, 5.7
15	1507	14 to 18	lifetime	6.2	24.8			47.9	16.8	4.5	3.5, 5.5
16	1710	14 to 18	lifetime	8.3	20.3	19.9	5.4			4.4	3.6, 5.2
18	2181	16 to 17	1 mo	11	12		7.2	22.7		3.4	2.8, 4.0
20	476	18	12 mo	60.7	13.9	22.6	13.8	29	18.3	1.8	1.3, 2.3
a=substance abuse/dependence, b=anxiety, in females											
1	142	19	12 mo	12.4	8.1			33.3		10.4	3.5, 17.3
4	363	14 to 16	lifetime	10.5	4.4			7.4	3	3.2	1.0, 7.1
5	1420	9 to 16	3 mo	6.3		18.7	1.1			20	13.5. 26.5
6	271	16 to 19	lifetime	5.9, 7.8						n/a	
7	674	17	12 mo	20.3						n/a	
8	961	15	6 mo	8.9	18.6					2.4	1.7, 3.1
12	190	14 to 17	6 mo	5.3	16			20	15.7	1.5	0.5, 2.5
13	810	15 to 19	lifetime	10	12.35	15.3	7.6	16.2	8.1	2.2	1.4, 3.6
14	1507	14 to 18	lifetime	9.8	8.2	19.4		16.2		0.4	0.2, 0.6
15	1507	14 to 18	lifetime	6.2	8.2			27.1	9.2	3.7	2.8, 4.6
16	1710	14 to 18	lifetime	8.3	8.7					n/a	
18	2326	16 to 17	1 mo	10.4	15.5		6.3	18.9		3	2.4, 3.6
20	454	18	12 mo	12.6	37.9	15.5	15.6	27.6	27.8	3.3	2.5, 4.1
a=substance abuse/dependence, b=anxiety, in males											
1	142	19	12 mo	12.4	8.1			33.3		10.4	3.5, 17.3
4	411	14 to 16	lifetime	10.5	4.4			7.4	3	3.2	1.0, 7.1

Table 2. Rates of substance abuse/dependence and psychiatric comorbidity in community-based samples (continued)

Study	N	Age	Time frame	Pop rate of a (%)	Pop rate of b (%)	Rate of a in b(%)	Rate of a in not b (%)	Rate of b in a (%)	Rate of b in not a (%)	OR	CI
5	1420	9 to 16	3 mo	5.7		4.8	1.5			3.3	n/a
6	271	16 to 19	lifetime	12.4, 12.4						n/a	
7	578	17	12 mo	22.8						n/a	
8	961	15	6 mo	6.5	6.9					2.4	1.7, 3.1
12	211	14 to 17	6 mo	7.1	16			20	15.7	1.5	0.5, 2.5
13	698	15 to 19	lifetime	11.75	5.44	15.3	7.6	16.2	8.1	2.2	1.6, 2.8
14	1507	14 to 18	lifetime	9.8	8.2	19.4		16.2		2.5	1.9, 3.1
15	1507	14 to 18	lifetime	6.2	8.2			6.5	6.4	1	0.6, 1.4
16	1710	14 to 18	lifetime	8.3	8.7					n/a	
18	2181	16 to 17	1 mo	11	12		7.2	22.7		1.3	1.1, 1.5
20	476	18	12 mo	60.7	18.1	15.5	15.6	27.6	27.8	3.3	2.5, 4.1
a=substance abuse/dependence, b=ADHD, in females											
1	142	19	12 mo	12.4	8.5					n/a	
4	363	14 to 16	lifetime	10.5	5.2			12.3	1.8	5.4	0.2, 10.6
5	1420	9 to 16	3 mo	6.3		26.2	1.1			31.8	21.4, 42.2
6	271	16 to 19	lifetime							n/a	
7	674	17	12 mo	20.3	3.6	29.2	20	5.1	3.2	2.1	1.2, 3.0
8	961	15	6 mo	8.9	2.7					7	4.5, 9.5
12	190	14 to 17	6 mo	5.3	13.8			68	10.1	20.3	7.6, 33.0
13	810	15 to 19	lifetime	10	1.73	28.8	6.7	25.4	5.7	5.6	4.3, 6.9
14	1507	14 to 18	lifetime	9.8	6.2	35.1		22.3		5.9	4.5, 7.3
15	1507	14 to 18	lifetime	6.2	6.2			25.5	2.5	13.9	9.8, 18.0
16	1710	14 to 18	lifetime	8.3						n/a	

Table 2. Rates of substance abuse/dependence and psychiatric comorbidity in community-based samples (continued)

Study	N	Age	Time frame	Pop rate of a (%)	Pop rate of b (%)	Rate of a in b(%)	Rate of a in not b (%)	Rate of b in a (%)	Rate of b in not a (%)	OR	CI
18	2326	12 to 17	1 mo	10.4						n/a	
20	454	18	12 mo	12.6						n/a	
a=substance abuse/dependence, b=ADHD, in males											
1	142	19	12 mo	12.4						n/a	
4	411	14 to 16	lifetime	10.5	5.2			12.3	1.8	5.4	0.2, 10.6
5	1420	9 to 16	3 mo	5.7		11.3	1.5			8.4	5.4, 11.4
6	271	16 to 19	lifetime	12.4, 12.4						n/a	
7	578	17	12 mo	22.8	4.8	14.3	23.3	3	5.4	1.3	0.9, 1.7
8	961	15	6 mo	6.5	5.7					7	3.6, 13.7
12	211	14 to 17	6 mo	7.1	13.8			68	10.1	20.3	7.6, 33.0
13	698	15 to 19	lifetime	11.75	4.15	28.8	6.7	25.4	5.7	5.6	4.3, 6.9
14	1507	14 to 18	lifetime	9.8	6.2	35.1		22.3		5.9	4.5, 7.3
15	1507	14 to 18	lifetime	6.2	6.2			25.5	2.5	13.9	9.8, 18.0
16	1710	14 to 18	lifetime	8.3						n/a	
18	2181	16 to 17	1 mo	11						n/a	
20	476	18	12 mo	60.7						n/a	
a=substance abuse/dependence, b=ODD, in females											
1	142	19	12 mo	12.4						n/a	
4	363	14 to 16	lifetime	10.5	1.6			2.5	1.2	2.1	1.0, 6.3
5	1420	9 to 16	3 mo	6.3		26.2	1.1			31.8	21.7, 41.9
6	271	16 to 19	lifetime	5.9, 7.8						n/a	
7	674	17	12 mo	20.3						n/a	
8	961	15	6 mo	8.9	9.5					11.4	8.3, 14.5

Table 2. Rates of substance abuse/dependence and psychiatric comorbidity in community-based samples (continued)

Study	N	Age	Time frame	Pop rate of a (%)	Pop rate of b (%)	Rate of a in b(%)	Rate of a in not b (%)	Rate of b in a (%)	Rate of b in not a (%)	OR	CI
12	190	14 to 17	6 mo	5.3	13.8			68	10.1	20.3	7.6, 33.0
13	810	15 to 19	lifetime	10	1.6	28.8	6.7	25.4	5.7	5.6	4.3, 6.9
14	1507	14 to 18	lifetime	9.8	6.2	35.1		22.3		6	4.6, 7.4
15	1507	14 to 18	lifetime	6.2	6.2			25.5	2.5	13.9	9.8, 18.0
16	1710	14 to 18	lifetime	8.3	7.3					n/a	
18	2326	12 to 17	1 mo	10.4	21.5		4	25.5		3.3	2.7, 3.9
20	454	18	12 mo	12.6						n/a	
a=substance abuse/dependence, b=ODD, in males											
1	142	19	12 mo	12.4						n/a	
4	411	14 to 16	lifetime	10.5	1.6			2.5	1.2	2.1	1.0, 6.3
5	1420	9 to 16	3 mo	5.7		11.3	1.5			8.4	5.4, 11.4
6	271	16 to 19	lifetime	12.4, 12.4						n/a	
7	578	17	12 mo	22.8						n/a	
8	961	15	6 mo	6.5	12.2					11.4	8.3, 14.5
12	211	14 to 17	6 mo	7.1	13.8			68	10.1	20.3	7.6, 33.0
13	698	15 to 19	lifetime	11.75	2.58	28.8	6.7	25.4	5.7	5.6	4.3, 6.9
14	1507	14 to 18	lifetime	9.8	6.2	35.1		22.3		6	4.6, 7.4
15	1507	14 to 18	lifetime	6.2	6.2			25.5	2.5	13.9	9.8, 18.0
16	1710	14 to 18	lifetime	8.3	7.3					n/a	
18	2181	16 to 17	1 mo	11	14.4		5	26.2		4.8	4.0, 5.6
20	476	18	12 mo	60.7						n/a	
a=substance abuse/dependence, b=CD, in females											
1	142	19	12 mo	12.4						n/a	

Table 2. Rates of substance abuse/dependence and psychiatric comorbidity in community-based samples (continued)

Study	N	Age	Time frame	Pop rate of a (%)	Pop rate of b (%)	Rate of a in b(%)	Rate of a in not b (%)	Rate of b in a (%)	Rate of b in not a (%)	OR	CI
4	363	14 to 16	lifetime	10.5	14.5			44.4	0	9.5	
5	1420	9 to 16	3 mo	6.3		26.2	1.1			31.9	21.8, 42.0
6	271	16 to 19	lifetime	5.9, 7.8						n/a	
7	674	17	12 mo	20.3	11.9	52.5	16	30.7	7.1	5.8	4.3, 7.3
8	961	15	6 mo	8.9	9.5					11.4	8.3, 14.5
12	190	14 to 17	6 mo	5.3	13.8			68	10.1	20.3	7.6, 33.0
13	810	15 to 19	lifetime	10	1.6	28.8	6.7	25.4	5.7	5.6	4.3, 6.9
14	1507	14 to 18	lifetime	9.8	6.2	35.1		22.3		6	4.6, 7.4
15	1507	14 to 18	lifetime	6.2	6.2			25.5	2.5	13.9	9.8, 18.0
16	1710	14 to 18	lifetime	8.3	7.3					n/a	
18	2326	12 to 17	1 mo	10.4	21.5		4	25.5		13.9	9.8, 18.0
20	454	18	12 mo	12.6	2.2	60.8	13	21.4	2.5	10.6	3.6, 17.6
a=substance abuse/dependence, b=CD, in males											
1	142	19	12 mo							n/a	
4	411	14 to 16	lifetime	10.5	14.5			44.4	0	9.5	
5	1420	9 to 16	3 mo	5.7		11.3	1.5			8.4	5.4, 11.4
6	271	16 to 19	lifetime	12.4, 12.4						n/a	
7	578	17	12 mo	22.8	28.5	38.8	16.5	48.5	22.6	4.6	3.6, 5.6
8	961	15	6 mo	6.5	12.2					11.4	8.3, 14.5
12	211	14 to 17	6 mo	7.1	13.8			68	10.1	20.3	7.6, 33.0
13	698	15 to 19	lifetime	11.75	2.58	28.8	6.7	25.4	5.7	5.6	4.3, 6.9
14	1507	14 to 18	lifetime	9.8	6.2	35.1		22.3		6	4.6, 7.4
15	1507	14 to 18	lifetime	6.2	6.2			25.5	2.5	13.9	9.8, 18.0

Table 2. Rates of substance abuse/dependence and psychiatric comorbidity in community-based samples (continued)

Study	N	Age	Time frame	Pop rate of a (%)	Pop rate of b (%)	Rate of a in b(%)	Rate of a in not b (%)	Rate of b in a (%)	Rate of b in not a (%)	OR	CI
16	1710	14 to 18	lifetime	8.3	7.3					n/a	
18	2181	16 to 17	1 mo	11	14.4		5	26.2		4.8	4.0, 5.6
20	476	18	12 mo	60.7	8.6	60.8	13	21.4	2.5	10.5	6.8, 14.2

Note.

Study 1. Beitchman, Douglas, Wilson, Johnson, Young, Atkinson, Escobar, & Taback, 1999
Study 4. Chong, Chan, & Cheng, 1999
Study 5. Costello, Erkanli, Federman, & Angold, 1999
Study 6. Deykin, Levy, & Wells, 1987
Study 7. Disney, Elkins, McGue, & Iacono, 1999
Study 8. Fergusson, Horwood, & Lynskey, 1993
Study 12. Kandel, Johnson, Bird, Weissman, Goodman, Lahey, Regier, & Schwab-Stone, 1999
Study 13. Lewinsohn, Hops, Roberts, Seeley, & Andrews, 1995
Study 14. Lewinsohn, Rohde, & Seeley, 1995
Study 15. Rohde, Lewinsohn, & Seeley, 1996
Study 16. Rohde, Lewinsohn, & Seeley, 1991
Study 18. Substance Abuse and Mental Health Services Administration, 1999
Study 20. Feehan, McGee, Raja, & Williams, 1994
ADHD = attention-deficit/hyperactivity disorder; CD = conduct disorder; CI = confidence interval; ODD = oppositional defiant disorder; OR = odds ratio

Table 3. Studies that meet minimum criteria for further analysis Revised 4/4/2000

Current PI	Number of participants	# Waves	Age range of data	Sex ratio	Race/ethnic groups (AA= African American)	Timing?	Impair-ment?	Study Title and Comments
1. Terrie Moffitt	~1,037	11	birth-26	1:1	93% White 6% Maori			Dunedin Study. Birth cohort from New Zealand
2. Ron Kessler	479	1 (2nd coming)	15-17	1:1	74% White 15% AA			From National Comorbidity Survey. 10-year followup
3. Frederick Gibbons	~897	2	10-13	~1:1	91% AA	?		Family and Community Health Study (offshoot of Rand Conger's IYFP, studying rural AA families)
4. Rand Conger	~530	9-11	12-23	1:1	White			Iowa Youth and Families Project. Longitudinal study of rural families
5. Peter Lewinsohn	~1,500	3 (interview) 7 (questionnaire)	14-24	~1:1	91% White			Oregon Adolescent Depression Project
6.Helen Reinherz	~400	7	5-26	1:1	98% White			Youth in Boston
7. David Fergusson	~1,200	20	birth-24	1:1	87% White 12% Maori			Christchurch Study. Birth cohort from New Zealand
8. Hector Bird	777	1	4-16	1:1	Puerto Rican	?		Population sample, Puerto Rico Cross-sectional, no onset data, but wide age range
9. David Huizinga	~1,500	5	7-27	1:1	45% Hispanic 34% AA 12% White		? (drug use only)	Denver Youth Survey Depression, CD, ASPD only
10. Jane Costello	1,420	6	9-19	1:1	69% White 6% AA 25% American Indian			Great Smoky Mountains Study. Rural southeastern USA

Table 3. Studies that meet minimum criteria for further analysis Revised 4/4/2000, continued

Current PI	Number of participants	# Waves	Age range of data	Sex ratio	Race/ethnic groups (AA= African American)	Timing?	Impair-ment?	Study Title and Comments
11. Adrian Angold	921	1-3	9-18	1:1	55% AA 45% White			Caring for Children in the Community. Rural S-E USA
12. Rolf Loeber	503	15	7-20	Boys	50% AA 50% White			Pittsburgh Youth Study Focus on development of delinquency
13. Jan Beals	109	1 (2)	14-16	1:1	American Indian	?		Plains Indians study. Followup of 44% of 249 youth studied 6 years earlier.
14. Peter Jensen	1,285	1	9-17	1:1	52% White 15% AA 28% Hispanic 6% other			MECA Single wave at four sites including Puerto Rico
15. Peter Jensen	W1 500 W2 350	2	9-17	1:1	28% AA 59% White 7% Hispanic			Fort Meade Study Children on military base. Followup of 70% 1 year later
16. Robert Roberts	W1 4,208 W2 3,156	2	11-17	1:1	36% AA 36% White 27% Mexican American			Teen Health 2000 Random sample from two HMOs. Limited range of comorbid Dxs

Figure 1. Comorbidity with Substance Use/Abuse/Dependence:
Meta-Analysis of Published Studies (N=21)

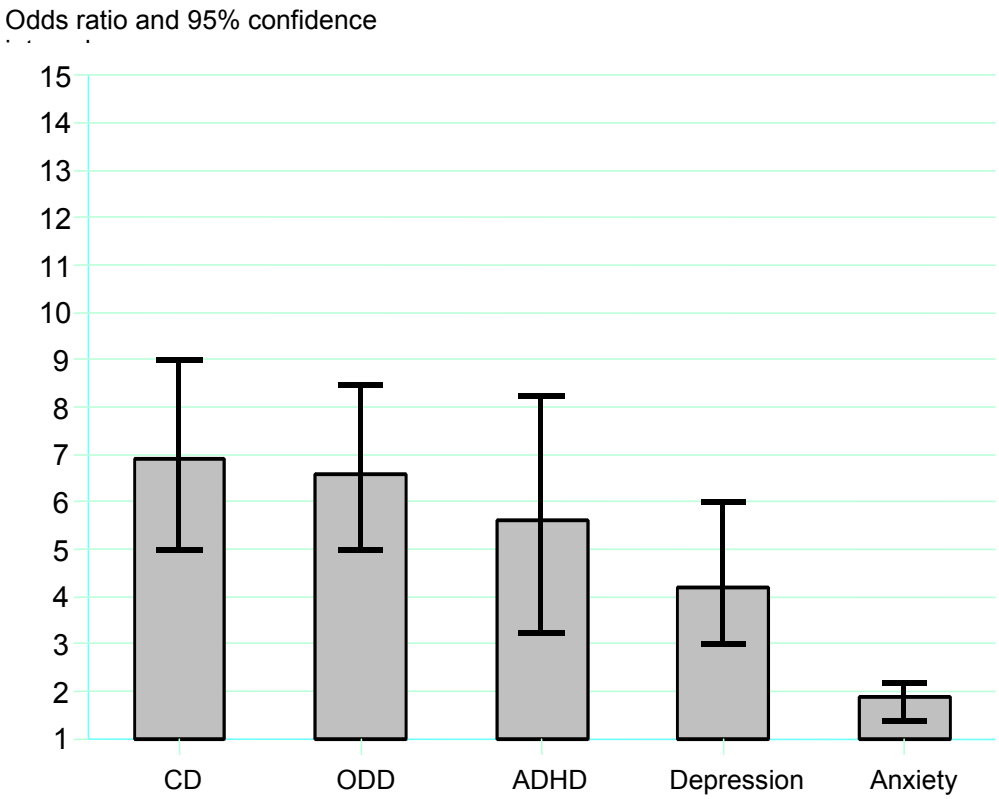

Figure 2. Comorbidity with Any Substance Use (N=8) and Substance Abuse/Dependence (N=13): Meta-Analysis of Published Studies

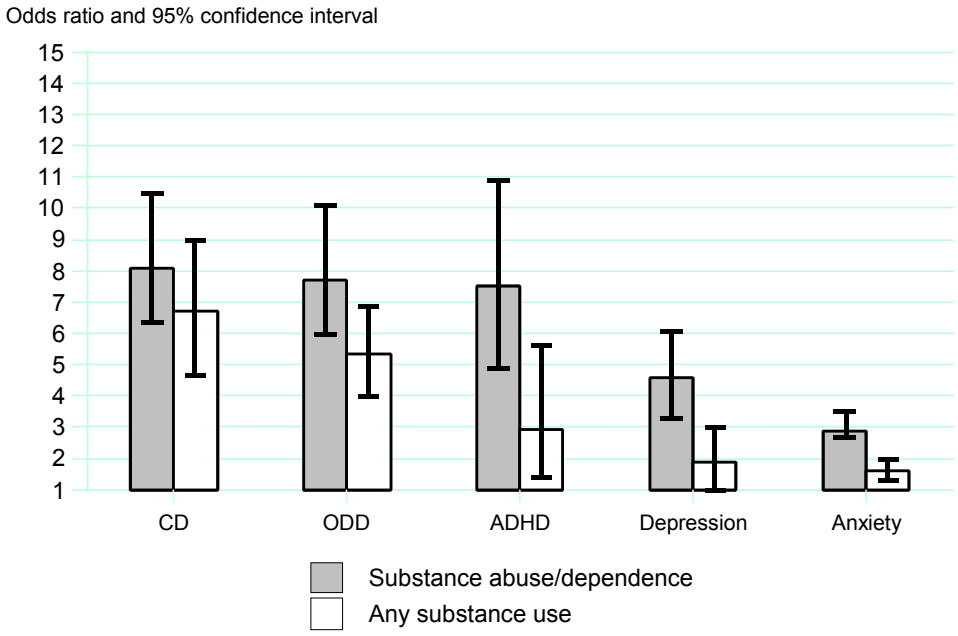

Figure 3. Comorbidity with Any Substance Use and Abuse/Dependence: Meta-Analysis of Published Studies Controlling for Other Comorbidity

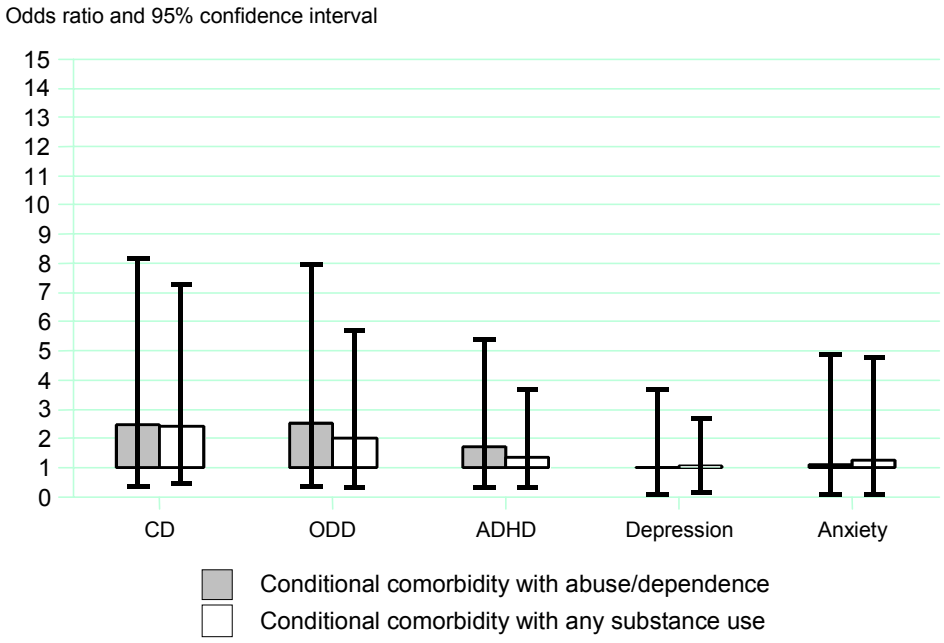

Figure 4. Comorbidity with Substance Abuse/Dependence (N=13):
Meta-Analysis of Published Studies, by Sex

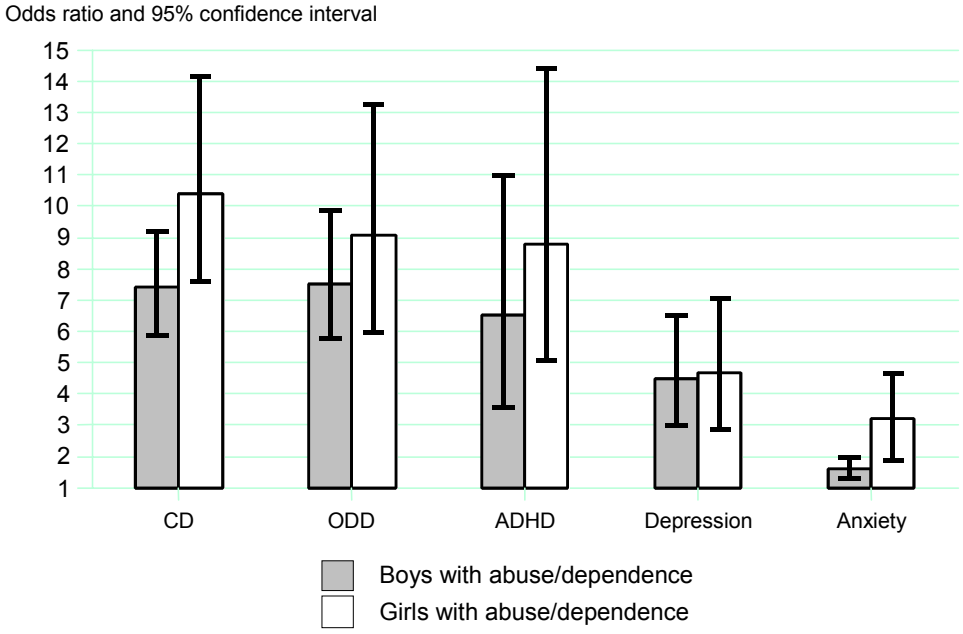

Figure 5. Comorbidity with Any Substance Use (N=8):
Meta-Analysis of Published Studies, by Sex

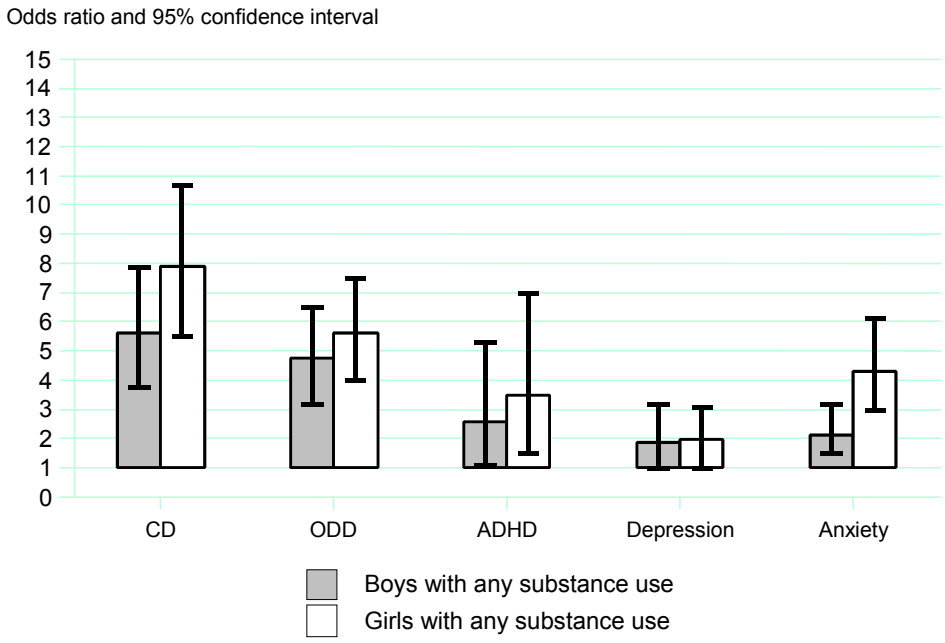

Figure 6. Comorbidity with Any Substance Use vs. Abuse/Dependence: Meta-Analysis of Published Studies (N=21): Girls

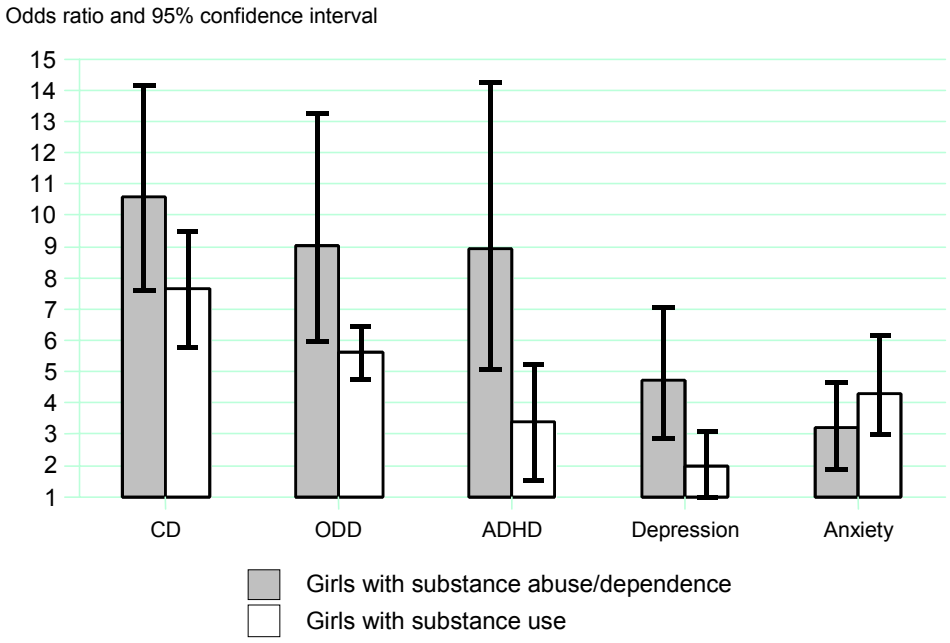

Figure 7. Comorbidity with Any Substance Use vs.Abuse/Dependence: Meta-Analysis of Published Studies (N=21): Boys