Priority Actions to Improve the Care of Persons with Co-occurring Substance Abuse and Other Mental Disorders: A Call to Action

Co-occurring diagnoses of substance abuse and mental disorders (e.g., schizophrenia, depression, or bipolar, anxiety, personality, conduct, or attention-deficit/hyperactivity disorders) are highly prevalent, often begin in youth, and place an immense burden on individuals, families, and society. Unchecked, co-occurring mental and substance use disorders represent a formula for troubled, unproductive, and foreshortened lives. Co-occurring mental and substance use disorders are associated with underachievement or failure at work and school, poor health, human immunodeficiency virus infection, hepatitis, difficulty fulfilling family responsibilities, abuse, violence, failed treatment attempts, incarceration, poverty, and homelessness (Drake and Wallach 2000; Drake et al 2001; Gonzalez and Rosenheck 2002; Mertens et al 2003). The risk of suicide is very high for persons with co-occurring mental and substance use disorders, especially for individuals with bipolar disorder (Dalton et al 2003; Kelly et al 2002) and those who are lesbian, gay, transgender, or bisexual (Botnick et al 2002; Lebson 2002; Wichstrom and Hegna 2003).

Though co-occurring mental and substance use disorders are common in general medical settings (Jones et al 2003; Mertens et al 2003) and community samples (Grant et al 2004; Kessler et al 1996; Regier et al 1990), they are endemic in specialty behavioral health care settings, the criminal justice system, and among the homeless (Gonzalez and Rosenheck 2002; Havassy et al 2004; Jordan et al 2002; North et al 2004; Reardon et al 2003; Swartz and Lurigio 1999; Whitbeck et al 2004). For example, in one study, 89% of adult male detainees with a lifetime history of serious mental illness (e.g., schizophrenia, bipolar disorder, major depression) or antisocial personality disorder had co-occurring substance use disorders, and 63% of those with a history of substance use disorder also had a serious mental illness (Swartz and Lurigio 1999). Co-occurring serious mental illness and substance use disorders also are highly prevalent among the homeless, with comorbidity rates of 43% reported in one large study (Gonzalez and Rosenheck 2002). Rates of co-occurring disorders among homeless and runaway teens are approximately six times that of the general adolescent population (Whitbeck et al 2004). Persons with co-occurring mental and substance use disorders, as a group, have a more persistent and severe illness course and are more refractive to treatment than those with only a single disorder. Stable remission of co-occurring mental and substance use disorders does indeed occur, but there are few data to guide therapy.

The rates and patterns of treatment for co-occurring mental and substance use disorders are far from ideal. Practice models featuring simultaneous, coordinated (i.e., integrated) treatment are promising (Drake et al 2004b), but the availability of integrated treatment programs is not widespread. In the early 1980s, 29% of adults with co-occurring mental and substance use disorders received some treatment in the health care sector, and an additional 8% received assistance from self-help organizations (Narrow et al 1993; Regier et al 1993). One decade later, the National Comorbidity Survey (NCS) found that approximately 40% of persons with co-occurring mental and substance use disorders were receiving some form of treatment (Kessler et al 1996). The NCS-Replication (NCS-R) (Kessler et al 2003), completed in 2002, 1 decade after the baseline NCS, asked explicitly about treatment focus. Preliminary NCS-R results suggest that of those being treated, approximately 25% were treated only for their mental disorder, and 25% received some form of treatment for both mental illness and substance abuse. Very few persons with co-occurring mental and substance use disorders are treated only for substance abuse (personal communication, R.C. Kessler, Ph.D., May 8, 2004). Thus, though treatment rates seem to be increasing, integrated treatment for both the mental disorder and the substance use disorder is not the norm.

Co-occurring mental and substance use disorders represent a legitimate public health crisis. Funding for both mental health and substance abuse care is shrinking and along with it, the availability of appropriately trained peer and professional personnel (McLellan and Meyers 2004; Renner 2004). Few in the health care system, including health care educators, state and federal governments, the pharmaceutical industry, and clinicians, have taken responsibility for research, training, insurance coverage, and integration of addiction care into medical/psychiatric services. The system truly is in chaos. Persons with co-occurring mental and substance use disorders are as deserving of accessible, effective, and fully insured care as those with other chronic illnesses, such as diabetes and hypertension. Immediate action is required to meet the needs of persons with co-occurring mental and substance use disorders and to intervene in those at greatest risk of developing mental illness and later substance abuse.

Process

The Depression and Bipolar Support Alliance (DBSA) is the nation's largest, illness-specific organization run by and for people living with depression or bipolar disorder. In November 2003, the DBSA convened a conference to address the unmet needs of substance use disorders in persons with depression or bipolar disorder. The prevalence and severity of substance use disorders that are comorbid with other mental illnesses was acknowledged; however, the DBSA conference focused on comorbid mood and substance use disorders. Unless otherwise specified, the term "substance use disorders" is used in this statement to include the full spectrum of abuse and dependence on alcohol, nicotine, and illegal and prescription drugs. Participants included 43 experts in psychiatry, psychology, addiction treatment, health care policy, primary care, adolescent health, epidemiology, and advocacy (Appendix 1). Presentations and deliberations from the conference and articles published in this special issue of *Biological Psychiatry* are reflected herein. Participants listened to presentations, debated workgroup reports, and provided input to interim versions of this statement. All authors approved the final version. The objectives of this statement are to assess available data, describe unmet needs, and outline priority clinical actions and research directions that are needed to improve treatment, access to care, and professional training. Recommendations for priority actions are evidence-based, when pos-

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sible; however, there is a remarkable lack of empirical data in this area. When data are available, they are often gleaned from heterogeneous populations that include patients with psychiatric diagnoses other than mood disorders. Thus, by necessity, the remaining priority action recommendations are based on the opinions and clinical experiences of the experts who participated in this conference. This statement reflects input from all participants.

Epidemiology

Alone, the prevalence of either mood disorders or substance use disorders is staggering. Major depressive and bipolar spectrum disorders occur during the lifetimes of 16.2% and 6.4% of Americans, respectively (Judd and Akiskal 2003; Kessler et al 2003). In 2002, substance dependence or abuse was estimated to occur in 22 million Americans (i.e., 9.4% of the U.S. population), including drug and alcohol dependence/abuse in 3.2 million (1.4%), drug dependence/abuse in 3.9 million (1.7%), and alcohol dependence/abuse in 14.9 million (6.4%). These data are similar to the findings of the National Epidemiologic Survey on Alcohol and Related Conditions (Grant et al 2004), which found 12-month prevalence rates of 2.0% for drug use disorders and 8.5% for alcohol use disorders. In addition, approximately 30 million Americans are addicted to nicotine (SAMHSA 2003).

Mental and substance use disorders are inherently intertwined, with comorbidity being the rule rather than the exception. As many as 7–10 million persons have co-occurring mental and substance use disorders, and up to 66% of addicts have one or more psychiatric diagnoses during their lifetimes (Kessler et al 1996). Substance use disorders are especially prevalent in persons with antisocial personality disorder, bipolar I disorder, and schizophrenia, of whom 84%, 61%, and 47%, respectively, either abuse or are dependent on substances (Regier et al 1990). One in four persons with major depression is a substance abuser (Kessler et al 2003). Compared with persons without mood disorders, bipolar I disorder (odds ratio [OR] 7.9), bipolar II disorder (OR 4.7), and major depression (OR 1.9) are associated with a greatly increased risk of substance abuse (Regier et al 1990). Women might be particularly vulnerable. When compared with the general population, women with bipolar disorder are seven times more likely to be alcoholics (OR 7.4) (Frye et al 2003).

Large-scale epidemiologic studies have assessed the nature of comorbidity between mental and substance use disorders (Armstrong and Costello 2002; Kandel et al 2001; Kessler et al 1997; Merikangas et al 1998). With regard to mood disorders, the risk relationship is reciprocal, with mood disorders predicting increased risk of later substance abuse and vice versa. Although major depression and anxiety disorders moderately predict substance abuse, the predictive strength of bipolar, antisocial personality, conduct, and oppositional defiant disorders and attention-deficit/hyperactivity disorder is particularly strong. Multiple comorbidities are especially strong predictors, and persons with three or more psychiatric disorders are 14 times more likely to be drug dependent than persons without these diagnoses. Substance abuse also predicts the development of mental disorders, with drug dependence more strongly predicting first-onset mental illness than drug abuse. In addition, illegal drug abuse more strongly predicts first-onset mental disorders than abuse/dependence of legal substances (e.g., alcohol, narcotic analgesics). Drug or alcohol use/abuse tends to occur before the onset of mood disorders; however, bipolar, anxiety, and conduct disorders often predate alcohol or drug use disorders (Merikangas et al 1998; Kessler 2004).

There is a strong relationship between depression and nicotine use that is complex, possibly bidirectional, and not fully understood (Farrell et al 2001; Fergusson et al 2003). Smokers with a history of depression experience more severe withdrawal symptoms (Covey et al 1990) and have lower rates of smoking cessation (Glassman et al 1990; Smith et al 2003). A history of smoking increases the risk of major depression, but the risk seems to be the same for abstinent and nonabstinent persons (Kessler 2004). Abstinent smokers are at greater risk of recurrent depression than nonabstinent smokers (Glassman et al 2001). Current depression predisposes to the onset of daily smoking, as well as to the transition to nicotine dependence (Breslau et al 2004), which has implications for smoking prevention.

The clinical utility of psychiatric epidemiologic research lies in its potential to identify and evaluate causal factors that can be modified to facilitate primary and secondary preventive efforts (Kessler 2004). Most complex mental illnesses are characterized by an interaction between biological vulnerabilities and environmental factors. Longitudinal and cross-sectional epidemiologic evidence is emerging to suggest a significant interaction between environmental stressors and the neurobiology of mood and substance use disorders at the level of genetic mediators, neurochemical mechanisms, and neurocircuitry (Volkow 2004). Isolated studies demonstrate genetic variance in neurocircuitry and neurotransmitter systems that mediate vulnerability to depression and suicide (Caspi et al 2003), anxiety (Enoch et al 2003; Hariri et al 2002), antisocial personality (Caspi et al 2002), and stress response (Zubieta et al 2003), all of which are also associated with substance abuse.

Research Priorities

Participants summarized topics for psychiatric epidemiologic research in co-occurring mental and substance use disorders and outlined priority items for ongoing and future studies, as follows:

- Study shared susceptibility genes and behavioral phenotypes to document environmental potentiation of genetic vulnerability
  - Include mental health/substance abuse measures and blood sample collection in ongoing epidemiologic studies
  - Conduct longitudinal studies of childhood disorders and genetically relevant populations (e.g., twins, siblings)
  - Conduct post hoc genomic/proteomic analysis of samples from existing databanks
  - Define the molecular, cellular, and neurocircuitry mechanisms underlying genetic vulnerability to co-occurring mental and substance use disorders
- Identify developmental risk factors to better understand temporal development of comorbidity and to define vulnerability and resilience
  - Focus on understudied populations—children/adolescents; ethnic, sexual, and gender minorities; college students; elderly, homeless, incarcerated, and rural populations; persons with bipolar disorder, suicidal behavior
  - Study long-term effects of fetal drug/alcohol exposure on risk for later development of mood disorders

Treatment

Data from randomized, controlled studies that inform pharmacologic and psychotherapeutic treatment of co-occurring mood and substance use disorders are relatively scarce because this population is generally excluded from treatment studies (Drake et al 2004b; Weiss et al 2000); however, a literature on

treatment that is specifically designed for persons with co-occurring mood and substance use disorders is beginning to emerge (Carroll 2004; Nunes et al 2004).

Major Depression

With the exception of co-occurring depression and nicotine dependence, treatment of persons with co-occurring disorders is currently based on clinical consensus and studies in patients with either mood disorder or substance use disorder but not both. There is strong evidence for the efficacy of bupropion (Hughes et al 2004; Richmond and Zwar 2003) and nortriptyline (Hall et al 1998), but not the selective serotonin reuptake inhibitors (SSRIs) (Covey et al 2002; Hughes et al 2004), in the treatment of nicotine dependence in nondepressed and depressed persons. Cognitive behavioral therapy also is an effective and durable intervention for smokers with depression and alcohol dependence (Patten et al 1998).

The SSRIs, TCAs, and nefazodone have been studied in the treatment of co-occurring depression and alcoholism (Cornelius et al 1997; Hernandez-Avila 2004; Mason et al 1996; McGrath et al 1996; Moak et al 2003; Nunes et al 1993; Pettinati et al 2001; Roy 1998; Roy-Byrne et al 2000). There is moderate evidence of improvement in depressive symptoms, but a less consistent effect on drinking outcomes (Pettinati 2004). One controlled trial of older adults found no advantage of adding naltrexone to sertraline, and psychosocial support (Oslin 2004). Another study demonstrated that cognitive behavioral therapy alone improved mood and prolonged abstinence in depressed alcoholics (Brown et al 1997).

Evidence for the effect of antidepressants and behavioral therapies on affect in opiate dependence comes from studies of methadone-maintained opiate addicts, only some of which enrolled patients with a diagnosis of depression (Nunes et al 2004). Mood improvement has been demonstrated by some (Nunes et al 1998; Titievsky et al 1982; Woody et al 1975) but not all TCA studies (Batki et al 1987; Kleber et al 1983; Woody et al 1982). Adverse effects associated with the TCAs might limit acceptance of this form of treatment. Most SSRI studies have failed to show improvement in depressive symptoms (Carpenter et al 2004; Dean et al 2002; Gonzalez et al 2003; Petrakis et al 1998); however, a recently reported study showed that the combination of citalopram and cognitive behavioral therapy in intravenous drug users who adhered to treatment resulted in improved rates of remission (Stein et al 2004). Modest improvement in short-term drug use, but not long-term abstinence, was observed in one imipramine (Nunes et al 1998) and one sertraline trial (Carpenter et al 2004), the latter of which showed that support systems and absence of aversive circumstances were related to therapeutic response. This finding suggests the need for concurrent behavioral therapy for both depressive symptoms and abstinence outcomes.

The SSRIs and TCAs have been studied in depressed cocaine abusers (Rounsaville 2004), with moderate evidence for a positive effect on mood from some (Carroll et al 1995; Nunes et al 1995, 2000; Oliveto et al 2003) but not all (Schmitz et al 2001) studies. Post hoc subgroup analyses suggest a more robust antidepressant effect is achieved by persons with higher baseline depression scores (Carroll et al 1995; Nunes et al 1995). Although antidepressants might have a modest effect on cocaine abuse (Nunes et al 1995; Oliveto et al 2003), cognitive behavioral therapy (Carroll et al 1995) and modified motivational therapy (Daley et al 1998) have been shown to improve addiction outcome compared with standard care (Kosten et al 2003).

Bipolar Disorder

There are few data to guide the treatment of persons with co-occurring bipolar and substance use disorders (Drake et al 2004; Kosten and Kosten 2004; Levin and Hennessy 2004), which is especially unfortunate given the high rates of substance abuse in this population (Frye et al 2003; Kessler 2004; Merikangas et al 1998; Regier et al 1990). Even more so than with depression, treatment of co-occurring bipolar and substance use disorders often is based on anecdotal experience and guidelines intended for persons without co-occurring disorders (American Psychiatric Association 2002). Given the relative scarcity of controlled trials, the use of mood stabilizers, such as lithium, valproic acid, carbamazepine, and lamotrigine, is the mainstay of treatment in this population.

Encouraging data are beginning to be reported from randomized, controlled trials, however. One controlled trial of valproate in bipolar alcoholics demonstrated a reduction in the number of heavy drinking days (Le Fauve et al 2004). In another report of a small sample of substance-abusing adolescents with bipolar disorder, lithium was superior to placebo on measures of psychiatric symptoms and on reduction in the number of positive urine drug screens (Geller et al 1998). A third controlled trial evaluated the use of carbamazepine in cocaine-dependent adults with or without affective disorder. Though the cohort with affective disorder in this study included patients without bipolar spectrum disorders, carbamazepine was associated with fewer positive urine drug screens and days of cocaine use among those with affective disorder (Brady et al 2002). Novel therapies, such as anticonvulsants (Brady et al 1995; Brown et al 2003; Johnson et al 2003), atypical antipsychotics (Brown et al 2002), and mood stabilizers (Calabrese et al 2001; Nunes et al 1990), offer promise but have not been evaluated in randomized, controlled trials.

Behavioral interventions have been shown in controlled trials to enhance treatment adherence, improve coping skills, and increase awareness for relapse symptoms in bipolar disorder (Gonzalez-Pinto et al 2004; Otto et al 2003; Zaretsky 2003) or substance abuse (Fuller and Hiller-Sturmhofel 1999; Hennessy et al 2003; Woody 2003) but rarely in co-occurring bipolar and substance use disorders (Weiss et al 2000). Motivational interviewing seems to be a promising technique to reduce recidivism (Dunn 2003; Martino et al 2002; Swanson et al 1999) that warrants further study. The findings of two psychotherapy studies suggest that integrated treatment approaches, in which both the bipolar and substance use disorders are addressed simultaneously, might improve measures of mood, mania, abstinence, and other quality-of-life outcomes (Drake et al 2004b; Weiss et al 2000).

Priority Actions to Improve Treatment

- Screen for substance abuse and bipolar and other mood disorders in schools, universities, primary care/psychiatry, women's clinics, homeless shelters, jails
- Rule out bipolarity and substance abuse in persons with personal and/or family histories of substance abuse, mood disorders, childhood adversity, cultural or environmental stressors, or suicidality
- Engage in risk management for substance abuse and suicidality in persons with bipolar disorder
- Treat co-occurring mood and substance use disorders aggressively and simultaneously (i.e., integrated approach). Treating one disorder without addressing the other is insufficient
- Include psychosocial modalities, such as cognitive behavioral therapy, motivational interviewing, trained peer-sup-

port strategies (Fricks 2004; Sabin and Daniels 2003), and 12-step programs, into treatment plans
- Develop integrated treatment plans that consolidate remission, prevent relapse, and facilitate full return to function
- Take responsibility for ongoing care of substance-abusing patients
  - Seek out qualified referrals and maintain effective follow-up
  - Take a long-term view, where symptom improvement is just the beginning. Stable remission and a return to functionality are the goals of treatment.

Research Priorities
- Design and test simple screening tools for complex co-occurring disorders
- Develop practice models to facilitate treatment initiation, appropriate referral, and effective follow-up for patients who screen positive for mood disorders and substance abuse
- Collect data to inform treatment decisions
  - Gain consensus on randomized, controlled trial design (e.g., simple combination trials; stepped-care; sequential randomization)
  - Include patients with co-occurring mood and substance use disorders, including understudied populations, in treatment studies funded by the National Institutes of Health (NIH) and the pharmaceutical industry
  - Focus on medication, psychosocial, and self-help modalities with proven efficacy in primary disorders
  - Identify biomarkers for treatment response and nonresponse

Access to Care

Access to care for persons with co-occurring mental and substance use disorders is limited at best, especially for adolescents and young adults at high risk for incident illness. Barriers to care are significant and multidimensional (Hayes et al 2003). Logistic issues that hinder access to care include a diminishing number of substance abuse clinics serving a growing population and a segregated system in which patients must negotiate access to separate substance abuse and mental health services (Grella and Gilmore 2002; McLellan and Meyers 2004). Funding mechanisms are not sufficiently flexible to allow for shared resources between the two health care sectors, which often compete for the same scarce funds. Treatment of co-occurring mental and substance use disorders, when available, is costly and constrained by rigid managed care review requirements and limited or nonexistent insurance coverage. Language and other cultural barriers often make obtaining and continuing in treatment difficult. Stigma regarding mental and substance use disorders, which contributes to embarrassment, denial, fear of discrimination, and distrust of medications or counseling, also blocks access to care (McLellan and Meyers 2004; SAMHSA 2002).

The addiction treatment sector is shrinking and in disarray. A recent survey of 175 government-owned or privately owned for-profit or nonprofit alcohol/drug abuse programs found that within a 16-month period, 15% had closed, and an additional 29% were reorganized under a different agency. Ongoing problems faced by substance abuse treatment facilities include substantial staffing turnover, shortage of full-time health care professionals, few treatment options other than group counseling, lack of standardized admission assessment tools, and archaic information technology, all of which undermine the ability of the system to treat serious, complex illnesses (McLellan et al 2003). The growing scarcity of addiction services results in patients being shuttled to other marginally effective and costly avenues of care, such as emergency departments, shelters, or jails.

There was consensus among the experts at the conference that integrated treatment for co-occurring mental and substance use disorders should be the standard of care, particularly for nonresponding or severely ill patients. Though effectiveness and economic viability of integrated services has been demonstrated (Drake et al 1998, 2004a, 2004b; Gonzales and Insel 2004; Grella and Gilmore 2002; Judd et al 2003; Katz 1999; Minkoff and Regner 1999; Tobin et al 2001; Weisner et al 2001; Weiss et al 2000), widespread implementation is in its infancy (Drake and Wallach 2000). A four-quadrant continuity-of-care model has been proposed that provides a framework for conceptualizing consultation, collaboration, and integration of services (NASMHPD/NASADAD 1999). According to this model, persons with serious mental illness and addiction should receive fully integrated treatment in specialty mental health care settings. Minor depression in the context of addiction might be best treated in the substance abuse sector. Persons with episodic substance use in the context of serious and persistent psychiatric illness would be best served by the mental health sector; however, a working system for referral and collaboration between point-of-contact (e.g., emergency departments, primary care) and substance abuse and mental health specialists must be in place for integrated treatment to function properly. When resources are available, inclusion of mental health personnel on the staff of substance abuse treatment programs is an excellent means of achieving integration.

There are distinct disincentives to providing integrated care. Insurance regulations encourage overdiagnosis of psychiatric illness and minimize diagnosis of substance use disorders. Additionally, the stigma of substance abuse even within the mental health care sector and the desire for secrecy among patients (or among parents of young patients) might lead to reluctance about entering treatment. These problems can be expected to worsen if state systems adopt parity legislation for mental health but not substance use. Additionally, the gap in quality and availability of care between advantaged and disadvantaged persons is large and seems to be widening.

Priority Actions to Improve Access to Care
- Take responsibility for persons with co-occurring mental and substance use disorders. Health care professionals must routinely screen for mental illness and substance abuse, refer to appropriately trained medical/mental health specialists when necessary, and monitor patients to ensure that they receive and adhere to treatment
- Integrate addiction services into psychiatric and general medical treatment settings
- Seek out and consult health care providers and self-help programs with experience and success in addressing co-occurring mental and substance use disorders (Appendix 2)
- Focus on stable remission (i.e., full recovery) rather than symptom reduction as the primary treatment goal. Recovery-based care includes returning to work, achieving a meaningful life in the community, and personal satisfaction with treatment outcome
- Adopt successful elements of trained peer-support practice models with proven reimbursement strategies (Fricks 2004; Sabin and Daniels 2003)
- Enhance the desirability of treatment programs to increase retention rates in prisons and other settings. Explore novel

methods to attract and retain patients (e.g., harm-reduction models) and funding opportunities to reward providers for promoting a recovery system that meets the needs of those served
- Ensure aftercare treatment for persons with co-occurring mental and substance use disorders upon release from prison or jail
- Advocate for increased funding and insurance parity for integrated treatment programs
- Maintain personal privacy with regard to diagnoses

Research Priorities

- Document economic burden of co-occurring mental and substance use disorders, including rates of health care resource use, criminalization, and suicide
- Conduct outcome studies of integrated clinical practice models and "best practice" models
- Develop treatment programs that increase retention rates in prisons and other settings (e.g., harm-reduction and abstinence models)
- Evaluate effectiveness and viability of trained peer-support programs

Training for Health Care Professionals

There is a severe shortage of psychiatrists, psychologists, nurses, social workers, and others with training in addiction treatment, and even fewer have expertise in co-occurring mental and substance use disorders (Brems et al 2002; Renner 2004; SAMHSA 2002). The historical divide between addiction treatment and the fields of medicine and psychiatry (Drake et al 2001) contributes to this situation. Medical school and residency curricula are weak, owing to the combined lack of faculty who are addiction specialists and high-quality clinical rotations. Most physicians, including psychiatrists, know very little about addiction treatment. The field of medicine has failed to properly train residents in substance abuse diagnosis, prevention, and treatment (Renner 2004). Training typically focuses on acute management rather than long-term outcome. Economic factors also contribute to the shortage of trained personnel. Lack of parity has translated into inadequate reimbursement for treating patients with co-occurring mental and substance use disorders. Treatment programs with low and inconsistent levels of funding preclude adequate salary and compensation packages for staff, which when coupled with the escalating burden of educational debt and liability insurance, is a significant disincentive for entering the field of addiction treatment.

Priority Actions to Increase Professional Training

- Expand training programs
  - Develop long-term co-occurring mental and substance use disorders treatment and training units in outpatient and inpatient settings staffed by trained clinicians with teaching credentials
  - Integrate suicide prevention, basic science of addiction, and addiction treatment into medical school and residency curricula and other health care training programs
  - Create partnerships among government, industry, foundations, advocacy groups, and health care organizations to support training and establish basic levels of competency for health care professionals who provide integrated services
- Develop programs to train educators
  - Advocate for government incentive programs to train specialists who will supervise students in treating patients with co-occurring mental and substance use disorders
  - Increase funding to support faculty and infrastructure in addiction psychiatry and addiction treatment programs
  - Use existing NIH grant mechanisms (e.g., K awards, R25 education grants) to help young investigators launch their careers
- Design tools to facilitate training of health care providers
  - Establish monitoring systems to evaluate training outcomes and update programs
  - Develop databases of didactic training systems, best practices, and health care courses
  - Design modular training workshops, available on the Internet
- Provide real incentives to enter the fields of addiction treatment and addiction psychiatry
  - Fund awards, fellowships, and NIH grants for medical students/residents and other health care professionals
  - Facilitate loan forgiveness programs for health care professionals in training who commit several years to treating co-occurring mental and substance use disorders in the public sector
  - Improve salaries and working conditions of substance abuse treatment staff

Conclusions

The needs of persons with co-occurring mental and substance use disorders must be addressed immediately, and long-range planning should be undertaken to improve treatment, access to care, parity, and professional training. There was overwhelming consensus among the experts at the conference that integrated treatment for co-occurring mental and substance use disorders must be recognized as the standard of care, particularly for non-responding or severely ill patients. This was perhaps the strongest statement made by the participants as a group. In addition, participants agreed on the following:

- Co-occurring mental and substance use disorders are highly prevalent
- The precise burden of co-occurring mental and substance use disorders is not known
- Persons with co-occurring mental and substance use disorders are as deserving of accessible, effective, simultaneous care as are those with other disabling, chronic illnesses
- Medication, psychosocial, and self-help modalities are available that show promise of effectiveness, but data to inform treatment are relatively scarce
- There is a severe shortage of trained clinicians and services

The different elements of the health care system, including legislative bodies, governmental agencies, health care educators, pharmaceutical industry, and health care professionals, have not taken adequate responsibility for the care of patients with co-occurring mental and substance use disorders. The following organizations need to address and correct the many barriers to treatment and rehabilitation:

- Congress should:
  - Pass parity legislation mandating full coverage for co-occurring mental and substance use disorders treatment
  - Increase research funding that is commensurate with the economic and societal burden of co-occurring mental and substance use disorders

- Governmental agencies (e.g., SAMHSA) should:
  - Expand community block grants to develop and sustain integrated treatment programs
  - Conduct effective and broad-reaching public education campaigns that reach teens, elders, and others
- The National Institute of Mental Health, National Institute on Alcohol Abuse and Alcoholism, and the National Institute on Drug Abuse should:
  - Increase interinstitute collaboration on research projects
  - Create infrastructures that facilitate basic and clinical research
  - Integrate networks to optimize clinical trials
- Health care educators, including medical schools, residencies, and continuing education programs, must bolster the quality and quantity of education about co-occurring mental and substance use disorders to increase the number of qualified professionals
- Pharmaceutical manufacturers should increase efforts to bring antiaddiction therapies to market and include persons with co-occurring mental and substance use disorders in ongoing and future studies
- Professional societies, such as the American Academy of Addiction Psychiatry, American Medical Association, American Psychiatric Association, American Psychological Association, American Society of Addiction Medicine, American College of Physicians, American Academy of Family Physicians, International Association of Psychosocial Rehabilitation Services, National Association of Social Workers, and others, should increase efforts to educate physicians and other professionals and promote prevention, treatment, and access to care for persons with co-occurring mental and substance use disorders
- Advocacy organizations should join with the DBSA and others in addressing the needs of persons with co-occurring mental and substance use disorders.

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American Psychiatric Association (2002): *Practice Guideline for the Treatment of Patients with Bipolar Disorder* (revision). Arlington, Virginia: American Psychiatric Association.

Armstrong TD, Costello EJ (2002): Community studies on adolescent substance use, abuse, or dependence and psychiatric comorbidity. *J Consult Clin Psychol* 70:1224–1239.

Batki S, Wheeler S, Jones R, Sorensen J, Brennan K (1987): Doxepin treatment of depressed opiate addicts undergoing methadone detoxification. National Institute on Drug Abuse Research Monograph. NIH Pub. No. 61-12192. Washington, DC: Supt. of Docs, US Government Printing Office 81–292.

Botnick MR, Heath KV, Cornelisse PG, Strathdee SA, Martindale SL, Hogg RS (2002): Correlates of suicide attempts in an open cohort of young men who have sex with men. *Can J Public Health* 93:59–62.

Brady KT, Sonne SC, Malcolm RJ, Randall CL, Dansky BS, Simpson K, et al (2002): Carbamazepine in the treatment of cocaine dependence: Subtyping by affective disorder. *Exp Clin Psychopharmacol* 10:276–285.

Brady KT, Sonne SC, Anton R, Ballenger JC (1995): Valproate in the treatment of acute bipolar affective episodes complicated by substance abuse: A pilot study. *J Clin Psychiatry* 56:118–121.

Brems C, Johnson ME, Bowers L, Lauver B, Mongeau VA (2002): Comorbidity training needs at a state psychiatric hospital. *Adm Policy Ment Health* 30:109–120.

Breslau N, Novak SP, Kessler RC (2004): Psychiatric disorders and stages of smoking. *Biol Psychiatry* 55:69–76.

Brown ES, Nejtek VA, Perantie DC, Orsulak PJ, Bobadilla L (2003): Lamotrigine in patients with bipolar disorder and cocaine dependence. *J Clin Psychiatry* 64:197–201.

Brown ES, Nejtek VA, Perantie DC, Bobadilla L (2002): Quetiapine in bipolar disorder and cocaine dependence. *Bipolar Disord* 4:406–411.

Brown RA, Evans DM, Miller IW, Burgess ES, Mueller TI (1997): Cognitive-behavioral treatment for depression in alcoholism. *J Consult Clin Psychol* 65:715–726.

Calabrese JR, Shelton MD, Bowden CL, Rapport DJ, Suppes T, Shirley ER, et al (2001): Bipolar rapid cycling: Focus on depression as its hallmark. *J Clin Psychiatry* 62(suppl 14):34–41.

Carpenter KM, Brooks AC, Vosburg SK, Nunes EV (2004): The effect of sertraline and environmental context on treating depression and illicit substance use among methadone maintained opiate dependent patients: A controlled clinical trial. *Drug Alcohol Depend* 74:123–134.

Carroll KM (2004): Behavioral therapies for co-occurring substance use and mood disorders. *Biol Psychiatry* 56:778–784.

Carroll KM, Nich C, Rounsaville BJ (1995): Differential symptom reduction in depressed cocaine abusers treated with psychotherapy and pharmacotherapy. *J Nerv Ment Dis* 183:251–259.

Caspi A, McClay J, Moffitt TE, Mill J, Martin J, Craig IW, et al (2002): Role of genotype in the cycle of violence in maltreated children. *Science* 297: 851–854.

Caspi A, Sugden K, Moffitt TE, Taylor A, Craig IW, Harrington H, et al (2003): Influence of life stress on depression: Moderation by a polymorphism in the 5-HTT gene. *Science* 301:386–389.

Cornelius JR, Salloum IM, Ehler JG, Jarrett PJ, Cornelius MD, Perel JM, et al (1997): Fluoxetine in depressed alcoholics. A double-blind, placebo-controlled trial. *Arch Gen Psychiatry* 54:700–705.

Covey LS, Glassman AH, Stetner F, Rivelli S, Stage K (2002): A randomized trial of sertraline as a cessation aid for smokers with a history of major depression. *Am J Psychiatry* 159:1731–1747.

Covey LS, Glassman AH, Stetner F (1990): Depression and depressive symptoms in smoking cessation. *Compr Psychiatry* 31:350–354.

Daley DC, Salloum IM, Zuckoff A, Kirisci L, Thase ME (1998): Increasing treatment adherence among outpatients with depression and cocaine dependence: Results of a pilot study. *Am J Psychiatry* 155:1611–1613.

Dalton EJ, Cate-Carter TD, Mundo E, Parikh SV, Kennedy JL (2003): Suicide risk in bipolar patients: The role of co-morbid substance use disorders. *Bipolar Disord* 5:58–61.

Dean AJ, Bell J, Mascord DJ, Parker G, Christie MJ (2002): A randomised, controlled trial of fluoxetine in methadone maintenance patients with depressive symptoms. *J Affect Disord* 72:85–90.

Drake RE, Essock SM, Shaner A, Carey KB, Minkoff K, Kola L, et al (2001): Implementing dual diagnosis services for clients with severe mental illness. *Psychiatr Serv* 52:469–476.

Drake RE, Mercer-McFadden C, Mueser KT, McHugo GJ, Bond GR (1998): Review of integrated mental health and substance abuse treatment for patients with dual disorders. *Schizophr Bull* 24:589–608.

Drake RE, Mueser KT, Brunette MF, McHugo GJ (2004a): A review of treatments for persons with severe mental illness and co-occurring substance use disorders. *Psych Rehab J* 27:360–374.

Drake RE, Wallach MA (2000): Dual diagnosis: 15 years of progress. *Psychiatr Serv* 51:1126–1129.

Drake RE, Xie H, McHugo GJ, Shumway M (2004b): Three-year outcomes of long-term patients with co-occurring and bipolar and substance use disorders. *Biol Psychiatry* 56:749–756.

Dunn C (2003): Brief motivational interviewing interventions targeting substance abuse in the acute care medical setting. *Semin Clin Neuropsychiatry* 8:188–196.

Enoch MA, Xu K, Ferro E, Harris CR, Goldman D (2003): Genetic origins of anxiety in women: A role for a functional catechol-O-methyltransferase polymorphism. *Psychiatr Genet* 13:33–41.

Farrell M, Howes S, Bebbington P, Brugha T, Jenkins R, Lewis G, et al (2001): Nicotine, alcohol and drug dependence and psychiatric comorbidity. Results of a national household survey. *Br J Psychiatry* 179:432–437.

Fergusson DM, Goodwin RD, Horwood LJ (2003): Major depression and cigarette smoking: Results of a 21-year longitudinal study. *Psychol Med* 33:1357–1367.

Fricks L (2004): Why are we here?A patient's perspective on living with an untreated dual diagnosis. *Biol Psychiatry* 56:726–727.

Frye MA, Altshuler LL, McElroy SL, Suppes T, Keck PE, Denicoff K, et al (2003): Gender differences in prevalence, risk, and clinical correlates of alcoholism comorbidity in bipolar disorder. *Am J Psychiatry* 160:883–889.

Fuller RK, Hiller-Sturmhofel S (1999): Alcoholism treatment in the United States. An overview. *Alcohol Res Health* 23:69–77.

Geller B, Cooper TB, Sun K, Zimerman B, Frazier J, Williams M, et al (1998): Double-blind and placebo-controlled study of lithium for adolescent bipolar disorders with secondary substance dependency. *J Am Acad Child Adolesc Psychiatry* 37:171–178.

Glassman AH, Covey LS, Stetner F, Rivelli S (2001): Smoking cessation and the course of major depression: A follow-up study. *Lancet* 357:1929–1932.

Glassman AH, Helzer JE, Covey LS, Cottler LB, Stetner F, Tipp JE, et al (1990): Smoking, smoking cessation, and major depression. *JAMA* 264:1583–1584.

Gonzales JJ, Insel TR (2004): The conundrum of co-occurring mental and substance use disorders: Opportunities for research. *Biol Psychiatry* 56: 723–725.

Gonzalez G, Feingold A, Oliveto A, Gonsai K, Kosten TR (2003): Comorbid major depressive disorder as a prognostic factor in cocaine-abusing buprenorphine-maintained patients treated with desipramine and contingency management. *Am J Drug Alcohol Abuse* 29:497–514.

Gonzalez G, Rosenheck RA (2002): Outcomes and service use among homeless persons with serious mental illness and substance abuse. *Psychiatr Serv* 53:437–446.

Gonzalez-Pinto A, Gonzalez C, Enjuto S, Fernandez De Corres B, Lopez P, Palomo J, et al (2004): Psychoeducation and cognitive-behavioral therapy in bipolar disorder: An update. *Acta Psychiatr Scand* 109:83–90.

Grant BF, Stinson FS, Dawson DA, Chou SP, Ruan WJ, Pickering RP (2004): Co-occurrence of 12-month alcohol and drug use disorders and personality disorders in the United States. *Arch Gen Psychiatry* 61:361–368.

Grella CE, Gilmore J (2002): Improving service delivery to the dually diagnosed in Los Angeles County. *J Subst Abuse Treat* 23:115–122.

Hall SM, Reus VI, Munoz RF, Sees KL, Humfleet G, Hartz DT, et al (1998): Nortriptyline and cognitive-behavioral therapy in the treatment of cigarette smoking. *Arch Gen Psychiatry* 55:683–690.

Hariri AR, Mattay VS, Tessitore A, Kolachana B, Fera F, Goldman D, et al (2002): Serotonin transporter genetic variation and the response of the human amygdala. *Science* 297:400–403.

Havassy BE, Alvidrez J, Owen KK (2004): Comparisons of patients with comorbid psychiatric and substance use disorders: Implications for treatment and service delivery. *Am J Psychiatry* 161:139–145.

Hayes RA, Andrews N, Baron-Jeffrey M (2003): Service enhancement to a dual-diagnosis population: Mental illness/substance abuse (MISA). *Qual Manag Health Care* 12:133–150.

Hennessy GO, De Menil V, Weiss RD (2003): Psychosocial treatments for cocaine dependence. *Curr Psychiatry Rep* 5:362–364.

Hernandez-Avila CA, Modesto-Lowe V, Feinn R, Kranzler HR (2004): Nefazodone treatment of comorbid alcohol dependence and major depression. *Alcohol Clin Exp Res* 28:433–440.

Hughes JR, Stead LF, Lancaster T (2004): Antidepressants for smoking cessation (Cochrane Review). *The Cochrane Library*. Chichester, UK: John Wiley & Sons, Ltd., issue 4.

Johnson BA, Ait-Daoud N, Bowden CL, DiClemente CC, Roache JD, Lawson K, et al (2003): Oral topiramate for treatment of alcohol dependence: a randomized controlled trial. *Lancet* 361:1677–1685.

Jones EM, Knutson D, Haines D (2003): Common problems in patients recovering from chemical dependency. *Am Fam Physician* 68:1971–1978.

Jordan BK, Federman EB, Burns BJ, Schlenger WE, Fairbank JA, Caddell JM (2002): Lifetime use of mental health and substance abuse treatment services by incarcerated women felons. *Psychiatr Serv* 53:317–325.

Judd LL, Akiskal HS (2003): The prevalence and disability of bipolar spectrum disorders in the US population: Re-analysis of the ECA database taking into account subthreshold cases. *J Affect Disord* 73:123–131.

Judd PH, Thomas N, Schwartz T, Outcalt A, Hough R (2003): A dual diagnosis demonstration project: Treatment outcomes and cost analysis. *J Psychoactive Drugs* 35(suppl 1):181–192.

Kandel DB, Huang FY, Davies M (2001): Comorbidity between patterns of substance use dependence and psychiatric syndromes. *Drug Alcohol Depend* 64:233–241.

Katz RI (1999): The Addiction Treatment Unit: A dual diagnosis program at the California Medical Facility—a descriptive report. *J Psychoactive Drugs* 31:41–46.

Kelly TM, Cornelius JR, Lynch KG (2002): Psychiatric and substance use disorders as risk factors for attempted suicide among adolescents: a case control study. *Suicide Life Threat Behav* 32:301–312.

Kessler RC (2004): The epidemiology of dual diagnosis. *Biol Psychiatry* 56: 730–737.

Kessler RC, Berglund P, Demler O, Jin R, Koretz D, Merikangas KR, et al (2003): The epidemiology of major depressive disorder. Results from the National Comorbidity Survey Replication (NCS-R). *JAMA* 289:3095–3105.

Kessler RC, Crum RM, Warner LA, Nelson CB, Schulenberg J, Anthony JC (1997): Lifetime co-occurrence of DSM-III-R alcohol abuse and dependence with other psychiatric disorders in the National Comorbidity Survey. *Arch Gen Psychiatry* 54:313–321.

Kessler RC, Nelson CB, McGonagle KA, Edlund MJ, Frank RG, Leaf PJ (1996): The epidemiology of co-occurring addictive and mental disorders: Implications for prevention and service utilization. *Am J Orthopsychiatry* 66:17–31.

Kleber HD, Weissman MM, Rounsaville BJ, Wilber CH, Prusoff BA, Riordan CE (1983): Imipramine as treatment for depression in addicts. *Arch Gen Psychiatry* 40:649–653.

Kosten TR, Kosten TA (2004): New medication strategies for comorbid substance use and bipolar affective disorders. *Biol Psychiatry* 56:771–777.

Kosten T, Oliveto A, Feingold A, Poling J, Sevarino K, McCance-Katz E, et al (2003): Desipramine and contingency management for cocaine and opiate dependence in buprenorphine maintained patients. *Drug Alcohol Depend* 70:315–325.

Lebson M (2002): Suicide among homosexual youth. *J Homosex* 42:107–117.

Le Fauve CE, Litten RZ, Randall CL, Moak DH, Salloum IM, Green AI (2004): Pharmacological treatment of alcohol abuse/dependence with psychiatric comorbidity. *Alcohol Clin Exp Res* 28:302–312.

Levin FR, Hennessy G (2004): Bipolar disorder and substance abuse. *Biol Psychiatry* 56:738–748.

Martino S, Carroll K, Kostas D, Perkins J, Rounsaville B (2002): Dual diagnosis motivational interviewing: A modification of motivational interviewing for substance-abusing patients with psychotic disorders. *J Subst Abuse Treat* 23:297–308.

Mason BJ, Kocsis JH, Ritvo EC, Cutler RB (1996): A double-blind, placebo-controlled trial of desipramine for primary alcohol dependence stratified on the presence or absence of major depression. *JAMA* 275:761–767.

McGrath PJ, Nunes EV, Stewart JW, Goldman D, Agosti V, Ocepek-Welikson K, et al (1996): Imipramine treatment of alcoholics with primary depression: A placebo-controlled clinical trial. *Arch Gen Psychiatry* 53:232–240.

McLellan AT, Carise D, Kleber HD (2003): Can the national addiction treatment infrastructure support the public's demand for quality care? *J Subst Abuse Treat* 25:117–121.

McLellan AT, Meyers K (2004): Contemporary addiction treatment: A review of systems problems for adults and adolescents. *Biol Psychiatry* 56:764–770.

Merikangas KR, Mehta RL, Molnar BE, Walters EE, Swendsen JD, Aguilar-Gaziola S, et al (1998): Comorbidity of substance use disorders with mood and anxiety disorders: Results of the International Consortium in Psychiatric Epidemiology. *Addict Behav* 23:893–907.

Mertens JR, Lu YW, Parthasarathy S, Moore C, Weisner CM (2003): Medical and psychiatric conditions of alcohol and drug treatment patients in an HMO. Comparison with matched controls. *Arch Gen Psychiatry* 163:2511–2517.

Minkoff K, Regner J (1999): Innovations in integrated dual diagnosis treatment in public managed care: The Choate dual diagnosis case rate program. *J Psychoactive Drugs* 31:3–12.

Moak DH, Anton RF, Latham PK, Voronin KE, Waid RL, Durazo-Arvizu R (2003): Sertraline and cognitive behavioral therapy for depressed alcoholics: Results of a placebo-controlled trial. *J Clin Psychopharmacol* 23: 553–562.

Narrow WE, Regier DA, Rae DS, Manderscheid RW, Locke BZ (1993): Use of services by persons with mental and addictive disorders. Findings from the National Institute of Mental Health Epidemiologic Catchment Area Program. *Arch Gen Psychiatry* 50:95–107.

NASMHPD/NASADAD (National Association of State Mental Health Program Directors/National Association of State Alcohol and Drug Abuse Directors) (1999): *National Dialogue on Co-occurring Mental Health and Substance Abuse Disorders*. Alexandria, Virginia and Washington, DC: NASMHPD/NASADAD.

North CS, Eyrich KM, Pollio DE, Spitznagel EL (2004): Are rates of psychiatric disorders in the homeless population changing? *Am J Public Health* 94: 103–108.

Nunes EV, McDowell D, Rothenberg J, Seracini AM, Kleber H (2000): Desipramine treatment for cocaine-dependent patients with depression. Paper presented at the Committee on Problems of Drug Dependence; San Juan, Puerto Rico; June 19, 2000.

Nunes EV, McGrath PJ, Quitkin FM, Ocepek-Welikson K, Stewart JW, Koenig T (1995): Imipramine treatment of cocaine abuse: Possible boundaries of efficacy. *Drug Alcohol Depend* 39:185–195.

Nunes EV, McGrath PJ, Quitkin FM, Stewart JP, Harrison W, Tricamo E, et al (1993): Imipramine treatment of alcoholism with comorbid depression. *Am J Psychiatry* 150:963–965.

Nunes EV, McGrath PJ, Wager S, Quitkin FM (1990): Lithium treatment for cocaine abusers with bipolar spectrum disorders. *Am J Psychiatry* 147: 655–657.

Nunes EV, Quitkin FM, Donovan SJ, Deliyannides D, Ocepek-Welikson K, Koenig T, et al (1998): Imipramine treatment of opiate-dependent patients with depressive disorders. A placebo-controlled trial. *Arch Gen Psychiatry* 55:153–160.

Nunes EV, Sullivan MA, Levin FR (2004): Treatment of depression in patients with opiate dependence. *Biol Psychiatry* 56:793–802.

Oliveto A, Gonsai K, Poling J (2003): Clinical efficacy of sertraline augmented with bupropion in depressed, recently-abstinent cocaine abusers. Paper presented at the Committee on Problems of Drug Dependence; Miami, Florida; June 17, 2003.

Oslin DW (in press): The treatment of late life depression complicated by alcohol dependence. *Am J Geriatr Psychiatry*.

Otto MW, Reilly-Harrington N, Sachs GS (2003): Psychoeducational and cognitive-behavioral strategies in the management of bipolar disorder. *J Affect Disord* 73:171–181.

Patten CA, Martin JE, Myers MG, Calfas KJ, Williams CD (1998): Effectiveness of cognitive-behavioral therapy for smokers with histories of alcohol dependence and depression. *J Stud Alcohol* 59:327–335.

Petrakis I, Carroll KM, Nich C, Gordon L, Kosten T, Rounsaville B (1998): Fluoxetine treatment of depressive disorders in methadone-maintained opioid addicts. *Drug Alcohol Depend* 50:221–226.

Pettinati HM (2004): Antidepressant treatment of co-occurring depression and alcohol dependence. *Biol Psychiatry* 56:785–792.

Pettinati HM, Volpicelli JR, Luck G, Kranzler HR, Rukstalis MR, Cnaan A (2001): Double–blind clinical trial of sertraline treatment for alcohol dependence. *J Clin Psychopharmacol* 21:143–153.

Reardon ML, Burns AB, Preist R, Sachs-Ericsson N, Lang AR (2003): Alcohol use and other psychiatric disorders in the formerly homeless and never homeless: Prevalence, age of onset, comorbidity, temporal sequencing, and service utilization. *Subst Use Misuse* 38:601–644.

Regier DA, Farmer ME, Rea DS, Locke BZ, Keith SJ, Judd LL, et al (1990): Comorbidity of mental disorders with alcohol and other drug abuse: Results from the epidemiologic catchment area study. *JAMA* 264:2511–2518.

Regier DA, Narrow WE, Rae DS, Manderscheid RW, Locke BZ, Goodwin FK (1993): The de facto US mental and addictive disorders service system. Epidemiologic catchment area prospective 1-year prevalence rates of disorders and services. *Arch Gen Psychiatry* 50:85–94.

Renner JA Jr (2004): How to train residents to identify and treat dual-diagnosis patients. *Biol Psychiatry* 56:810–816.

Richmond R, Zwar N (2003): Review of bupropion for smoking cessation. *Drug Alcohol Rev* 22:203–220.

Rounsaville BJ (2004): Treatment of cocaine dependence and depression. *Biol Psychiatry* 56:803–809.

Roy A (1998): Placebo-controlled study of sertraline in depressed recently abstinent alcoholics. *Biol Psychiatry* 44:633–637.

Roy-Byrne PP, Pages KP, Russo JE, Jaffe C, Blume AW, Kingsley E, et al (2000): Nefazodone treatment of major depression in alcohol-dependent patients: A double-blind, placebo-controlled trial. *J Clin Psychopharmacol* 20:129–136.

Sabin JE, Daniels N (2003): Strengthening the consumer voice in managed care: VII. The Georgia Peer Specialist Program. *Psychiatr Serv* 54:497–498.

SAMHSA (Substance Abuse and Mental Health Services Administration) (2003): *Overview of Findings from the 2002 National Survey on Drug Use and Health* (Office of Applied Studies, NHSDA Series H-21, DHHS Publication No. SMA 03–3774). Rockville, Maryland: US Department of Health and Human Services.

SAMHSA (Substance Abuse and Mental Health Services Administration) (2002): *Report to Congress on the Prevention and Treatment of Co-occurring Substance Abuse Disorders and Mental Disorders*. Rockville, Maryland: US Department of Health and Human Services.

Schmitz JM, Averill P, Stotts AL, Moeller FG, Rhoades HM, Grabowski J (2001): Fluoxetine treatment of cocaine-dependent patients with major depressive disorder. *Drug Alcohol Depend* 63:207–214.

Smith SS, Jorenby DE, Leischow SJ, Nides MA, Rennard SI, Johnston JA, et al (2003): Targeting smokers at increased risk for relapse: Treating women and those with a history of depression. *Nicotine Tob Res* 5:99–109.

Stein MD, Solomon DA, Herman DS, Anthony JL, Ramsey SE, Anderson BJ, et al (2004): Pharmacotherapy plus psychotherapy for treatment of depression in active injection drug users. *Arch Gen Psychiatry* 61:152–159.

Swanson AJ, Pantalon MV, Cohen KR (1999): Motivational interviewing and treatment adherence among psychiatric and dually diagnosed patients. *J Nerv Ment Dis* 187:630–635.

Swartz JA, Lurigio AJ (1999): Psychiatric illness and comorbidity among adult male jail detainees in drug treatment. *Psychiatr Serv* 50:1628–1630.
Titievsky J, Seco G, Barranco M, Kyle EM (1982): Doxepin as adjunctive therapy for depressed methadone maintenance patients: a double-blind study. *J Clin Psychiatry* 43:454–456.
Tobin MJ, Matters B, Chen L, Smith R, Stuhlmiller C (2001): Improving clinical management for consumers with co-existing mental health and substance use disorders: An integrated approach. *Aust Health Rev* 24:118–124.
Volkow ND (2004): The reality of comorbidity: Depression and drug abuse. *Biol Psychiatry* 56:714–717.
Weisner C, Mertens J, Parthasarathy S, Moore C, Lu Y (2001): Integrating primary medical care with addiction treatment: A randomized controlled trial. *JAMA* 286:1715–1723.
Weiss RD, Griffin ML, Greenfield SF, Najavits LM, Wyner D, Soto JA, et al (2000): Group therapy for patients with bipolar disorder and substance dependence: Results of a pilot study. *J Clin Psychiatry* 61:361–367.
Wichstrom L, Hegna K (2003): Sexual orientation and suicide attempt: A longitudinal study of the general Norwegian adolescent population. *J Abnorm Psychol* 112:144–151.
Whitbeck LB, Johnson KD, Hoyt DR, Cauce AM (2004): Mental disorder and comorbidity among runaway and homeless adolescents. *J Adolesc Health* 35:132–140.
Woody GE (2003): Research findings on psychotherapy of addictive disorders. *Am J Addict* 12(suppl 2):S19–S26.
Woody GE, O'Brien CP, McLellan AT, Marcovici M, Evans BD (1982): The use of antidepressants with methadone in depressed maintenance patients. *Ann N Y Acad Sci* 398:120–127.
Woody GE, O'Brien CP, Rickels K (1975): Depression and anxiety in heroin addicts: A placebo-controlled study of doxepin in combination with methadone. *Am J Psychiatry* 132:447–450.
Zaretsky A (2003): Targeted psychosocial interventions for bipolar disorder. *Bipolar Disord* 5(suppl 2):80–87.
Zubieta J-K, Heitzeg MM, Smith YR, Bueller JA, Xu K, Xu Y, et al (2003): COMT va1158met genotype affects mu-opioid neurotransmitter responses to a pain stressor. *Science* 299:1240–1243.

Appendix 1. Conference Participants

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Workgroups:

Workgroup 1 (Epidemiology and Description of the Problem): Jon-Kar Zubieta, M.D., Ph.D. (workgroup leader); James C. Anthony, Ph.D.; Anna Rose Childress, Ph.D.; Wilson M. Compton, M.D., M.P.E.[†]; Ronald C. Kessler, Ph.D.; Darrel A. Regier, M.D., M.P.H.; Richard K. Ries, M.D.; Thomas Sklar-Blake

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[†]Government employees provided scientific and technical expertise only for the development of the scientific content of this statement. All other recommendations and conclusions do not necessarily represent either the personal views of the government employees or the agencies with which they are affiliated.

Appendix 2. Resources for Patients and Health Care Providers

Dual Diagnosis Resources

Dual Diagnosis Recovery Network (www.dualdiagnosis.org)

Double Trouble in Recovery (www.doubletroubleinrecovery.org)

Georgia Certified Peer Specialist Project (www.gacps.org)

Mental Health Resources

American Academy of Child and Adolescent Psychiatry (www.aacap.org)

American Association for Geriatric Psychiatry (www.aagpgpa.org)

American Psychiatric Association (www.psych.org)

American Psychological Association (www.apa.org)

CONTAC – Consumer Organization and Networking Technical Assistance Center (www.contac.org)

Depression and Bipolar Support Alliance (www.dbsalliance.org)

National Alliance for the Mentally Ill (www.nami.org)

National Institute on Mental Health (www.nimh.nih.gov)

National Mental Health Information Center (www.mentalhealth.org)

President's New Freedom Commission on Mental Health (www.mentalhealthcommission.gov)

Alcohol, Drug, and Tobacco Abuse Resources

Alcoholics Anonymous (www.alcoholics-anonymous.org)

Al-Anon Family Group Headquarters (www.al-anon-alateen.org)

American Academy of Addiction Psychiatry (www.aaap.org)

American Cancer Society (for smoking cessation; www.cancer.org)

American Heart Association (for smoking cessation; www.americanheart.org)

American Society of Addiction Medicine (www.asam.org)

Association for Medical Education and Research in Substance Abuse (www.amersa.org)

Cocaine Anonymous (www.ca.org)

Drug Addiction Treatment (www.drug-addiction.com)

Narcotics Anonymous (www.na.org)

National Institute on Drug Abuse (www.nida.nih.gov)

National Institute on Alcohol Abuse and Alcoholism (www.niaaa.nih.gov)

Parents – The Anti-Drug (www.theantidrug.com)

Substance Abuse and Mental Health Services Administration (www.samhsa.gov)