Summary and Conclusions

Effects of Medical Interventions on Suicidal Behavior

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Background: An international symposium evaluated current knowledge of the epidemiology, psychobiology, and effects of medical treatment on suicidal behavior. ***Method:*** Moderators summarized the main findings and conclusions of the participants on the basis of presentations and consensus statements at the meeting. ***Results:*** Despite striking advances in the medical treatment of mood disorders in the past half-century, rates of suicidal acts have changed little in the general population. Evidence of reduction of long-term rates of suicidal acts in specific at-risk populations remains very limited, particularly persons with major affective illnesses and other common, primary or comorbid psychiatric and substance use disorders. It is plausible that reduction of psychiatric morbidity should limit suicidal risk, but very little is known about specific effects of most psychiatric treatments or other interventions aimed at suicide prevention. An exception is substantial evidence of lower suicidal risk during long-term lithium treatment that was not equaled with carbamazepine. However, diagnosis and timely therapeutic interventions reach only a minority of psychiatrically ill persons at risk for suicide. ***Conclusion:*** Renewed efforts are strongly urged to: (1) improve public and professional awareness of risk factors for suicide, (2) enhance earlier access to appropriate clinical assessment and increasingly safe and effective treatments for affective and psychotic disorders, and (3) encourage and support research to clarify specific benefits and risks of medical treatments and social interventions aimed at preventing suicide.
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The preceding reports prepared by participants in the 1998 international symposium in Miami, Florida, on the effects of medical interventions on suicidal behavior summarize their contributions. These reports cover a broad range of presentations and discussions pertaining to the epidemiology and psychobiology of suicide, predictive or risk factors associated with suicidal behavior, and current knowledge concerning the effects of medical treatment on suicidal behavior. In addition to their presentations, participants discussed a series of conclusions to summarize current knowledge and guide future research on this important and unsolved international public health problem.

Conclusions and recommendations arising from the symposium fall into 3 categories: (1) clinical assessment of suicidal risk and guidelines for clinical and research reports pertaining to suicide; (2) effects of specific medical treatments on suicidal risks; and (3) recommendations for general and educational efforts aimed at reducing suicidal risks. These areas are addressed in the following sections. Findings and literature supporting the conclusions are provided in the preceding individual reports.

CLINICAL ASSESSMENT AND REPORTING ON SUICIDE

Recommendations concerning clinical assessment and reporting on suicidal behavior are summarized in Table 1. Research on suicide provides quite consistent support for the association of suicidal behavior with particular psychiatric disorders, though there is substantial quantitative variation among studies. Much of this variation probably reflects diagnostic variance and case selection, particularly in terms of illness severity, duration, and disability. Suicide is especially strongly associated with previous and current depressive illness, including both major depres-

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Table 1. Concluding Points About Medical Treatment and Suicide: Clinical Assessment and Reporting on Suicide

1. Most cases of suicide involve an ongoing, and typically treatable, psychiatric disorder—in perhaps half of cases, a major mood disorder, alone or complicated by comorbid abuse of alcohol or other substances.
2. Reasonably well-established risk factors for suicide include current severe depression (particularly early in the course of illness), previous or family history of depression or suicide attempts, abuse of alcohol or other substances, psychosis, agitation, severe anxiety, insomnia, male sex, advanced age (particularly in association with medical illness) and perhaps youth, lack or loss of social supports, incarceration, recent loss, personal crisis or cause for shame, and lack of active and sustained psychiatric treatment.
3. Refinement of predictive assessments for suicide requires better definition of relevant psychological states (which include agitation, anger, guilt, anxiety, and a drive to act, as well as depressive despair) and consideration of quantifying risk, such as by number, severity, duration, or clustering of factors.
4. Additional studies are required to specify suicidal risks in specific groups defined by such factors as sex, age, ethnicity, psychiatric and medical diagnoses, treatment setting, and social environment.
5. Further clarification is required of impressions that suicidal risk rises with changes in clinical state or treatment, particularly in new episodes of depression or psychosis, soon after hospital discharge, or following discontinuation of ongoing treatment, and with residual symptoms during recovery from an episode of acute illness.
6. Clarification of the timing of suicidal risk is needed to pursue observations that suicidal acts often occur early in affective or psychotic illness, but also continue over many years in many persons, particularly at times of recurrences of episodic, and notably depressive, illness. Since suicidal risk typically arises long before clinical assessment and establishment of sustained treatment, earlier assessment and protective intervention are required.
7. Studies and research reports should define and specify levels of severity of suicidal behavior (thoughts, plans, minor self-injury, life-threatening attempts, and fatalities).
8. Current concepts of major depression are excessively broad, include a range of suicidal risks, and require modification to guide assessment of suicidal risk.
9. Assessment for suicide risk is an ongoing, individualized clinical process, and risks of violent behavior should be a routine component of psychiatric assessment procedures and records.
10. Comprehensive assessments of patients, as well as reports of studies, should report information on past suicidal history (including lethality, number, and types of acts), age at onset of illness and suicidality and time at risk; psychiatric and major medical diagnoses; family history of mood and substance use disorders and suicidal acts; history and current abuse of alcohol and drugs; type, dose, and duration of treatments given; and estimates of acceptance and adherence to treatments.
11. Increased efforts are needed to facilitate early access and maintenance in treatment of men and women, their more equal representation in studies of suicide and in "psychological autopsies," in all of which women now predominate.
12. Further study is required to test emerging associations of disturbed functional status of central serotonergic mechanisms with aggression and suicide.

sion and the depressive or mixed (dysphoric-agitated) phases of bipolar manic-depressive disorders. Schizophrenia and other psychotic syndromes and certain personality disorders as well are associated with increased suicidal rates. A role of psychic tension or severe anxiety, perhaps independent of specific diagnosis, also is a strongly suspected contributing or triggering factor. Abuse of alcohol, heroin, stimulants, possibly other substances, and particularly syndromes of polysubstance abuse—independently or as comorbid factors in primary psychiatric illnesses—increase suicidal risk, especially in the young.

In addition to specific psychiatric disorders and a past history of suicide attempts, certain personality disorders or traits, as well as sociodemographic, psychological and medical conditions and life circumstances, were identified as probable risk factors for suicide. These include male sex, youth or advanced age, absence of social supports, unemployment, separation or other recent loss, incarceration or other personal crisis or circumstances leading to shame, impulsive and rigid traits, as well as a lack of active and sustained treatment for psychiatric illness or the recent interruption of such treatment. Suicide rates also have been reported to vary with the season of the year.

Several areas of suicide prediction were identified as requiring further study. These include better definition and clarification of the contributions to suicidal risk of clinically suspected personality traits (e.g., impulsivity, rigid inflexibility) and affective states (e.g., agitation, anger, anxiety, and a drive to action, as well as depressive despair). Prediction may also be improved by quantifying risk, such as by the number, severity, duration, or clustering of individual factors. Additional studies also are required to clarify suicidal risks in specific groups defined by sex, age, ethnicity, psychiatric and medical diagnoses, and social environment. Another matter of concern is that current concepts and diagnostic criteria for some disorders, and particularly major depression, are very broad, include a wide range of suicidal risks, and require modification or additional specification to guide clinical assessment of suicidal risk. Further study is also required to evaluate compelling associations of diminished functional status of central serotonergic mechanisms with aggression and suicide, and suggestive associations of suicidality with genetically based relatively low activity of tryptophan hydroxylase, which controls serotonin synthesis.

Relationships of suicidal risk to the long-term course of psychiatric illnesses, in particular, need further clarification. Findings reviewed at the symposium indicate relatively high rates of suicidal behavior early in affective or psychotic illness, but also continued risk over many years, particularly in the absence of long-term treatment. Suicidal risk probably increases with recurring episodes of depression or psychosis, soon after hospital discharge, and with residual symptoms during recovery from an episode of acute illness, as well as shortly after discontinuation of ongoing treatment. However, the relative importance of such events and their timing require further quantification and refinement for effective clinical application as predictive or modifiable risk factors for suicide. A specific finding of public health concern is that suicidal risk typically arises long before clinical assessment and sustained treatment are established in many psychiatric disorders and may vary with diagnosis, sex, and age. This potentially

lethal latency calls for earlier assessment and protective intervention.

Finally, several recommendations were made for the assessment and reporting of suicidal behavior for clinical or research purposes. In general, assessment for suicidal risk is an ongoing and individualized clinical process. Risks of violent behavior should be routinely evaluated in psychiatric assessment procedures and records, to help prevent injuries and fatalities, and as a component of risk-management.

Comprehensive clinical assessments of patients, as well as informative reports of studies of suicide, ideally, should include: (1) information on past suicidal history, including number and types of acts; (2) specification of levels of intensity or severity of suicidal behaviors defined as thoughts, plans, minor self-injury, life-threatening attempts or fatalities, and need for hospitalization; (3) psychiatric and major medical diagnoses; (4) estimates of age at onset of relevant major illnesses, age at first suicidal behavior, and time at risk; (5) family history of mood, psychotic, and substance use disorders and of suicidal acts; (6) history and current abuse of alcohol and other substances, including prescribed medicines; (7) type, dose or intensity, and duration of medical and psychiatric treatments given; and (8) estimates of acceptance and adherence to recommended treatments.

EFFECTS OF TREATMENTS ON SUICIDE RISK

Conclusions from the symposium concerning treatment effects on suicidal behavior are summarized in Table 2. Improved recognition and timely clinical intervention into affective, psychotic, and other relevant psychiatric disorders should be a powerful means of limiting suicidal risk, particularly if long-term maintenance treatments are provided for recurrent or chronic disorders marked by depression and dysphoria. However, evidence of the effectiveness and safety of all proposed interventions—medical and social—aimed at suicide prevention is very limited, and effects of treatment urgently require further study. Such studies should consider that generalized conclusions about treatment effects can be limited by biases inherent in the selection of patient-subjects who are available for study and adhere to recommended treatments. Even with mood-altering and antipsychotic treatments proved to reduce or prevent symptoms and to improve functional status and quality of life, effects on suicide risk require specific demonstration and distinction from nonspecific benefits of emotional support and close follow-up.

There is substantial evidence that long-term lithium treatment is associated with reduced rates of suicide attempts and fatalities. There also are preliminary indications that carbamazepine may not yield results equivalent to results of lithium treatment for suicide in manic-depressive patients. Evidence about the long-term impact of antidepressants and ECT on suicidal behavior remains inconclusive, although suggestive findings with antidepressant treatment in major depression are emerging. Other treatments requiring clarification of their effects on suicide include anticonvulsants, antipsychotics, anxiolytics, and

Table 2. Concluding Points on Medical Treatment and Suicide: Effects of Treatments on Risk of Suicide

1. Evidence of the effectiveness of all proposed interventions—medical, and particularly psychosocial—aimed at suicide prevention is very limited and urgently requires further study.
2. Improved recognition of and timely clinical intervention in depressive and psychotic disorders should be a powerful means of limiting suicidal risk, particularly if long-term maintenance treatments are provided for recurrent or chronic disorders.
3. Many contemporary psychiatric treatments reduce or prevent symptoms and improve functional status and quality of life, but their effects on suicide risk require specific demonstration.
4. There is consistent support for reduced risk of suicidal acts during lithium prophylaxis (possibly due to its antiaggressive and antiserotonergic actions), evidence that carbamazepine may not share this effect, and inconclusive evidence about the long-term impact of antidepressants or ECT (though ECT has a short-term antisuicidal action).
5. It remains to be proved whether lower suicidal rates found during lithium treatment in bipolar, and perhaps schizoaffective and unipolar disorder, generalize to its use in other clinical conditions.
6. Many treatments require clarification of their effects on suicide, including anticonvulsants, antipsychotics, anxiolytics, and specific types of antidepressants (e.g., those that sedate or activate), particularly newer agents, alone and in combination with other treatments.
7. Clinical impressions suggest that general, palliative, or supportive medical and psychosocial interventions limit suicidal risk, but the specific impact of particular interventions remains unknown.
8. Comparisons of specific treatments predicted to be antisuicidal and naturalistic comparisons with nonexperimentally determined untreated groups should be both ethical and informative.
9. Studies of treatments for affective, psychotic, and substance abuse disorders should consider effects on overall mortality as well as suicide.
10. Studies of treatment of depressed patients have typically excluded those known to be suicidal, bipolar, or psychotic—all of whom carry high suicidal risks.
11. Factors contributing to low levels of diagnosis (ca. $^1/_3$) and adequate treatment ($\leq {}^1/_4$ of those diagnosed) of persons with major mood disorders (possibly $^1/_{10}$–$^1/_{20}$, overall), as well as limited long-term adherence to treatment require definition and modification.
12. Moderate, individualized doses of medicines, and treatment based in specialized, expert settings may enhance treatment adherence and so contribute to long-term reduction of suicide risk.
13. Suicide risk may result from rapid changes in treatments, doses, or drug discontinuation, which often occur without consultation with a physician.
14. Studies of the biology of mood disorders and of aggressive behaviors and of the actions of mood-altering agents may lead to more rational development of novel treatments that reduce suicidality.
15. It is not clear to what extent effects of treatments associated with reduced suicidal risk are due to specific psychobiological effects, amelioration of psychiatric illness, or nonspecific but important effects of being in treatment or reflect selection biases in who accepts and remains in treatment.
16. Serotonin-enhancing agents should be evaluated for potential beneficial effects on suicidal and other aggressive behaviors and compared with mood-altering agents acting mainly on catecholaminergic or other neuromodulatory systems.
17. Agents that interact with protein kinases and other enzymes involved in the actions of neurotransmitters should be evaluated for benefits in suicidality.

specific types of antidepressants (e.g., those that sedate or activate, and those that potentiate the actions of serotonin or catecholamines). Such information would be especially valuable for newer agents, used alone or in combination with other treatments. It also remains to be proved whether the lower suicidal rates found during lithium treatment in bipolar I and II disorders generalize to other disorders, such as nonbipolar depression or psychotic disorders. Clinical experience suggests that palliative or supportive medical and psychosocial interventions may also limit suicidal risk, but the effects of specific nonpharmacologic interventions need to be demonstrated.

Comparisons of specific treatments predicted to reduce suicidal risk, as well as their naturalistic comparison with nonexperimentally determined but comparable untreated groups should be both ethical and informative, provided that nonspecific effects of being treated are also considered. Studies of treatments for mood disorders, specifically, should consider effects on overall mortality, including the impact of comorbid medical illness and substance abuse as well as suicide. Studies of treatment of depressed patients have typically excluded subjects with high suicidal risks, including those known to be suicidal or who have bipolar or psychotic forms of depression. Safe and ethical methods for including such patients in treatment trials are urgently needed. A specific caveat in their design is to avoid the probably dangerous impact of rapidly removing lithium on entry into a protocol involving an alternative treatment, with a subsequently elevated suicidal risk for at least several months thereafter. Moreover, treatment comparisons will require correction for potential dissimilarities in effectiveness against morbidity other than suicidal behavior, adherence to recommended treatment, and retention rates associated with dissimilar treatments.

Further efforts are required to enhance timely access to treatments that can limit morbidity associated with suicidal risk. For example, it is well documented that rates of case identification and engagement and retention in appropriate treatment remain remarkably limited in major affective disorders. Perhaps a third of cases of major depression are ever diagnosed, and of these, probably fewer than one quarter receive treatment considered adequate by even conservative contemporary standards for agent, dose, and duration. The potential pool of treatable depressed patients, for example, may be 10 or 20 times higher than is currently being reached. Moreover, many cases of bipolar disorders are undiagnosed, misdiagnosed (especially in the juvenile population), and inappropriately treated. The potential for increased access to treatment has clinical, suicide-preventive, medical-economic, and even pharmaceutical marketing implications. Factors contributing to low levels of diagnosis and adequate treatment, as well as conditions accounting for limited adherence to the long-term treatment appropriate to many psychiatric disorders, also require definition and modification.

Acceptance of recommended treatments may be enhanced by use of moderate, individualized doses of medicines to optimize their tolerability, and a balanced application of pharmacologic, psychotherapeutic, and supportive treatments, including use of specialized settings with a high level of expertise. In turn, improved acceptance of long-term, comprehensive treatment should contribute to a reduction of suicide risk. Further efforts are required to identify and modify factors that limit acceptance and adherence to long-term treatment. Available research also indicates that discontinuities of long-term treatment can introduce risks that can exceed those associated with mere nontreatment. Notably, iatrogenic stressors contributing to affective morbidity and possibly to suicide risk include rapid changes in treatments or doses, as well as abrupt discontinuation of ongoing maintenance treatments of various types. Moreover, excessive use of antidepressants in patients with bipolar disorders may contribute to potentially dangerous emotional instability, rapid cycling, irritable moods, and aggression, although there is a lack of agreement about the level of risk involved and about possible differences in risk between specific types of antidepressants.

Symposium participants supported the principle that studies of the biology of mood disorders, aggressive behaviors, and the actions of mood-altering agents may lead to more rational development of novel treatments that reduce suicidality. Some noteworthy questions remain to be clarified. In particular, it is not clear to what extent treatments that may prove to diminish suicidal risk act through specific psychobiological mechanisms relevant to aggression and suicide, reflect effective and sustained amelioration of affective illness generally, or represent nonspecific benefits of sustained support and encouragement. Serotonin-enhancing agents should be evaluated for potential beneficial effects on suicidal and other aggressive behaviors, and compared with mood-altering agents acting mainly on catecholaminergic systems or cellular mechanisms that mediate the actions of various neurotransmitters and other neuromodulators.

Recent laboratory findings suggest that agents including valproic acid, which share interactions of lithium with protein kinases and other enzymes involved in mediating actions of neurotransmitters, should have priority in testing for antisuicidal benefits as well as mood-stabilizing actions. Agents with such potentially broad actions on ubiquitous cellular mechanisms might be made relatively specific for brain regions or cell types by targeting on specific isozymes.

RECOMMENDATIONS FOR GENERAL AND EDUCATIONAL EFFORTS

Recommendations from the Miami symposium about general efforts to limit suicidal risk and fatality rates are

summarized in Table 3. Public and even professional understanding of suicide as a common manifestation of psychiatric illness still appears to be far from universal, and suicide remains a matter of shame and secrecy for many persons. Suicidal acts are probably grossly underreported, and suicide is often unrecognized or not reported as a cause of death, including by acts of violence or "accidents." Patients and, ironically, many clinicians tend to avoid discussing suicide as a valid and treatable clinical problem. Accordingly, redoubled efforts are needed to increase awareness of physicians, mental health specialists, other professional colleagues, trainees, and the general public to encourage early recognition and timely treatment of depressive and psychotic illnesses arising independently or with medical illness, comorbid substance abuse disorders, and other psychiatric conditions, in order to limit suicide.

Effectiveness of clinical interventions may be enhanced through continuously refined and promulgated guidelines for assessing mood disorders and suicidal risk for physicians, other professionals, and the general public. However, standardized guidelines for the treatment and clinical management of depressed or suicidal patients can have benefits only if impersonal and routinized practice is avoided in dealing with a problem that suicidal persons may be reluctant to communicate. Vigorous efforts are required to increase recognition and appropriate psychiatric treatment of potentially suicidal patients, particularly those with depression with or without medical illness, who are commonly encountered first by primary care physicians. Assistance needed by primary care physicians includes practical guidelines for efficient assessment of suicidal risk, for recognizing clinical depression, and for seeking appropriate psychiatric assistance. Moreover, efficient access by primary care physicians and other professionals to psychiatric collaboration for the care of high-risk suicidal patients requires better administrative implementation and high priority for adequate financial support.

Additional steps that may enhance suicide prevention include improved training and professional backup for interventions aimed at suicide prevention, including illness screening and "hot-line" programs. Activities of survivor-support, advocacy, and political action groups seeking improved knowledge and treatment to prevent suicide also are strongly encouraged.

Pharmaceutical and insurance companies, as well as granting agencies, can help by supporting long-term studies of the clinical effectiveness and economic impact of various interventions. There is a particularly pressing need for support of studies of the effects of mood-altering and other psychotropic agents on suicidal behavior in patients with a broad range of severe, bipolar, and psychotic affective disorders at all phases of the life-cycle. Government can help by limiting access to alcohol and firearms or other potentially lethal means of suicide.

Table 3. Concluding Points on Medical Treatment and Suicide: Recommendations for General and Educational Efforts

1. There appears still to be limited public understanding of suicide as a manifestation of psychiatric illness, underreporting of suicidal acts or suicide as a cause of death, and avoidance of discussing suicide by patients and clinicians.
2. Redoubled efforts are needed to increase awareness of physicians, other professional colleagues, trainees, and the general public to encourage early recognition and timely treatment of depressive, psychotic, and substance abuse disorders in order to limit suicide.
3. Refinements are encouraged for guidelines for assessing mood disorders and suicidal risk for physicians, other professionals, and the general public.
4. Specific continued efforts are required to increase recognition and treatment of mood disorder patients, including those with medical illness, particularly by primary care physicians.
5. Guidelines for recognizing clinical depression, efficient assessment of suicidal risk factors, and seeking appropriate psychiatric assistance should be developed for primary care physicians.
6. Access to psychiatric backup by primary care physicians and other professionals for the care of high-risk suicidal patients requires better implementation.
7. Standardized guidelines for the treatment and clinical management of potentially suicidal patients can have benefits if impersonal and routine practice in dealing with a complex and often hidden problem is avoided.
8. Screening and public education programs are encouraged, with adequate training and professional backup for programs aimed at suicide prevention in the general population.
9. Activities of survivor-support, advocacy, and political action groups seeking improved knowledge and treatment to prevent suicide are encouraged.
10. Pharmaceutical and insurance companies and granting agencies can help by supporting long-term studies of the effectiveness of mood-altering and antipsychotic agents that include the broad range of affectively ill or psychotic patients and that address suicidality.
11. Medically based suicide prevention should include a chronic disease model as well as short-term interventions in acute crises, with improved access to stable, long-term care, in which economic and clinical system design factors are crucial.
12. Developing large national and international databases should contribute to studies of suicide and other critical events of rare incidence.
13. Suicide is a major public health problem. Efforts to assess the role of access and availability of highly lethal means of suicide, including firearms, as well as alcohol, are essential.

Medically based suicide prevention should include a chronic disease model as well as short-term interventions in acute crises, with improved access to stable, long-term care, in which economic and clinical system design factors and public support are crucial. Finally, large national and international databases should contribute to the study of suicide and other critical events of low incidence.

CONCLUSIONS

The participants in this symposium support the conclusion that international rates of suicidal behavior have changed little in the general population, or even among depressive and other specific clinical populations at increased suicidal risk. This conclusion stands in stark contrast to striking advances in the medical treatment of most psychiatric disorders in the past half century. A notable exception is the consistent evidence that long-

term maintenance treatment of manic-depressive patients with lithium is associated with markedly reduced risk of suicidal acts. It is not clear to what extent this association reflects specific effects to limit aggressive behavior, reduction of affective morbidity, or nonspecific but important benefits of sustained clinical care. Much less is known about the specific impact on suicidal behavior of other medical treatments commonly employed for the treatment of affective or psychotic disorders, or of other interventions aimed at suicide prevention. Moreover, diagnosis and appropriate and timely therapeutic interventions continue to reach only a minority of patients with disorders that account for a majority of suicides. Consensus conclusions from the symposium include the need to (1) improve both public and professional awareness of risk factors for suicide, (2) limit access to firearms and alcohol, (3) enhance access to appropriate clinical assessment and increasingly safe and effective treatments for mood and psychotic disorders, and (4) support additional research to clarify the specific benefits and risks of medical and social interventions aimed at preventing suicide.