

Intervention Research With Persons at High Risk for Suicidality: Safety and Ethical Considerations

Jane L. Pearson, Ph.D.; Barbara Stanley, Ph.D.; Cheryl A. King, Ph.D.; and Celia B. Fisher, Ph.D.

There is a critical need for studies designed to reduce suicidality. Individuals at high risk for suicidality deserve safe and effective treatments, just as do other individuals with mental disorders who do not experience suicidality. Points for consideration regarding safety and monitoring procedures are offered to help researchers who conduct treatment trials with individuals who have mental disorders and investigators specifically interested in developing treatments to reduce suicidality. Issues such as study design, increased monitoring and supervision, research clinician competencies, and liability concerns are addressed. Points to consider in planning an intervention trial, a checklist of informed consent issues, and a list of relevant active federal regulations are provided.

(*J Clin Psychiatry* 2001;62[suppl 25]:17-26)

Individuals at high risk for suicidality (significant suicidal ideation or intent, a suicide attempt, or completed suicide) deserve to receive safe, well-tested, effective treatments, just as do other individuals with mental disorders who do not experience suicidality. In 1998, approximately 30,000 people died by suicide in the United States, making suicide the eighth leading cause of death in the United States.¹ The age-adjusted suicide rate for that year was 10.4 per 100,000.¹ The incidence of attempted suicide is estimated to range from 0.2 to 2.2 per 100, with the higher rate reflective of younger age groups.² Despite the public health and personal burden associated with suicide ideation, attempts, and deaths, the empirically validated knowledge base of effective approaches to reducing suicidality is limited.

Clinical wisdom has little empirical substantiation when it comes to intervention with persons at high risk for suicidality. Only a few interventions, including community crisis hotlines,³ "no-suicide contracts,"⁴ and acute hospitalization,⁵ have been evaluated, and, of those, there has been little or no evidence to support their effectiveness in reducing suicide risk over time. One reason for the paucity of empirical evidence on suicidal behaviors, particularly completed and attempted suicide, is that they are relatively rare phenomena, and few studies have been able to recruit sufficient numbers of patients to ensure sufficient statistical power to determine the efficacy of interventions.

A second reason for limited empirical evidence for treatments to reduce suicidality is that it is often assumed that if treatments are effective for nonsuicidal persons with certain mental disorders, such treatments should be effective in reducing suicidal behavior among persons with the particular disorder. There is little evidence in support of this assumption. Third, perceived liability risks, inadequate training in monitoring and treating suicidal crises, and empirically unsupported assumptions that potential risks exceed the possible benefits of treatment have led to exclusion of persons with a history of suicide attempts or perceived to be at high risk for future suicide from clinical trials for most mental disorders. Although the National Institute of Mental Health (NIMH) and the American Foundation for Suicide Prevention have recently funded a number of interventions focused on reducing suicidal behaviors (for funded abstracts, see reference 6), perceived liability risks and burdens to investigators and/or sponsors of research continue to limit research efforts in this area.

From the National Institute of Mental Health, Rockville, Md. (Dr. Pearson); Columbia University, New York, N.Y. (Dr. Stanley); the University of Michigan, Ann Arbor (Dr. King); and Fordham University, Bronx, N.Y. (Dr. Fisher).

This article is based on a report prepared under National Institute of Mental Health Contract Numbers 263-MD-004930 (Dr. Stanley), 263-MD-004928 (Dr. King), and 263-MD-004929 (Dr. Fisher). Jane L. Pearson, Ph.D., Project Officer. Available at <http://www.nimh.nih.gov/research/highrisksuicide.cfm>.

Presented at the symposium "Suicide Prevention Intervention," which was held October 24, 2000, in Boston, Mass., and supported through an unrestricted educational grant from Solvay Pharmaceuticals.

The views presented here are those of the authors and do not necessarily represent those of the National Institute of Mental Health or the U.S. Department of Health and Human Services.

Reprint requests to: Jane L. Pearson, Ph.D., Division of Services and Intervention Research, National Institute of Mental Health, 6001 Executive Blvd., Room 7160 MSC 9635, Bethesda, MD 20892.

The purpose of this article is to highlight the critical need for studies designed to reduce suicidality and to suggest possible safety and monitoring procedures to ensure that safety and ethical concerns are adequately addressed. These suggestions are not intended to be consensus or enforceable guidelines for researchers or to reflect the policy of any agency on human research protections. Rather, the article offers points for consideration to help researchers who conduct treatment trials with individuals with mental disorders and investigators specifically interested in developing treatments to reduce suicidality to safely and effectively meet the needs of individuals who become suicidal during the trial. This article is based on the report "Issues to Consider in Intervention Research With Persons at High Risk for Suicidality,"⁷ which was developed by NIMH and experts in suicide research and ethics and addressed issues primarily concerned with adult research participants.

NATIONAL AND FEDERAL INITIATIVES

To understand why the critical need for effective treatments is receiving attention now, it may be useful to consider the current context of national and federal initiatives. In October 1998, the Centers for Disease Control and Prevention, the Substance Abuse and Mental Health Services Administration, and the Health Resources and Services Administration expanded a regional meeting on suicide prevention into the first national meeting focusing on suicide prevention goals at the request of the Suicide Prevention Advocacy Network. At that meeting, a panel received hundreds of recommendations for needed suicide prevention efforts, and these were summarized into a set of draft goals for a national suicide prevention strategy. The Surgeon General, Dr. David Satcher, further developed these goals and issued the Surgeon General's "Call to Action to Prevent Suicide"⁸ in July 1999. Later that year, the Surgeon General's report on mental health⁹ was issued, which more fully developed the nation's understanding of mental disorders and the increased risk for suicide among those with mental disorders. On May 2, 2001, the Surgeon General launched the National Strategy for Suicide Prevention,¹⁰ which builds on these prior efforts to mobilize the nation into acting on objectives and goals aimed at reducing suicide, including the development and testing of treatments to reduce suicidality.

As these national and federal efforts were evolving, recent reviews by U.S. and U.K. researchers found surprisingly limited research focused on testing the efficacy and effectiveness of treatments aimed at reducing suicidality.¹¹⁻¹³ The majority of these studies have focused on reducing suicide attempts among adults. However, some have examined the reduction of serious suicide ideation and intent, as well as suicide attempts and completion, particularly in adolescent samples. Of the 20 or so studies

designed to specifically reduce suicide attempts, several had positive outcomes. For those studies that did not have positive findings, it is impossible to know if the treatments were ineffective or still hold promise because the studies did not have sufficient statistical power to detect significant differences, especially for suicide attempts and completions. Studies focusing on reducing suicidality often face such challenges due to the low base rate of suicide attempts and completions and the small number of individuals examined. The number of studies primarily focused on the treatment of disorders that have also examined changes in suicidality or rates of suicide deaths as part of broader outcome assessments is also limited. This may be because study participants who were at high risk for suicidality were excluded from these trials. However, some treatment studies not specifically designed to reduce suicidal behavior have found that certain medications may be useful in reducing suicidal behavior for persons with depression, bipolar illness, or schizophrenia.¹⁴⁻¹⁷

The striking lack of empirically based interventions to reduce suicidality comes at an interesting time in NIMH research developments. NIMH has been expanding its research portfolio to include more representative samples in clinical trials and to develop assessments of longer-term functional outcomes. This expansion translates into broader inclusion criteria that allow for more comorbid conditions and often more severe levels of illness.¹⁸ Such efforts are likely to increase the numbers of research participants who have been, or will become, suicidal. Yet few protocols have been tested and proved effective in reducing suicidality. Increased requirements for data and safety monitoring for clinical trials¹⁹ require that investigators consider the likely risk of adverse events such as suicide attempts and completions and develop risk management procedures to minimize such events. However, currently, safety approaches are limited by challenges in predicting imminent risk, as well as by few effective treatments for reducing suicidality.

FACTORS ASSOCIATED WITH INCREASED RISK FOR SUICIDAL BEHAVIOR

While there has been increasing evidence for various risk factors for suicidal behavior for a number of subgroups, the precision of researchers' abilities to adequately predict who will complete suicide and when remains limited.²⁰ Most research examining "risk factors" associated with suicide is based on postdictive correlational studies.²¹ Psychological autopsy studies of adults who have died by suicide indicate that mental and/or substance abuse disorders, including personality disorders, were present in at least 90% of decedents. Among young and middle-aged adults, previous suicide attempts, impulsive or aggressive tendencies, and stressful life events involving losses in financial, work, or social areas are common

risk factors, while for older adults, a late onset of depression is most common.²² Common risk factors in youth include prior suicide attempt, symptoms of a mood disorder, substance abuse that is frequently comorbid with a mood disorder,²³ parental depression,²⁴ and stressful life events.²⁵ With regard to risk for suicide attempts, risk factors for suicide completion, as well as comorbid personality disorders, particularly cluster B disorders (borderline, antisocial, histrionic), have been suggested.²⁶ Risk factors for attempted suicide among youth include the same risk factors for completed suicide in youth, as well as a history of physical and sexual abuse.^{27,28} Homosexuality has also been shown to be correlated with suicide attempts among youth.²⁹ Within groups of individuals with certain mental disorders, more specific risk factors may be present. Risk factors are also assumed to be cumulative with regard to increased risk for suicidality.

This knowledge base forms the foundation for approaches to risk assessment in clinical research trials. Assessment of risk for suicidality is an ongoing process, since suicidal risk may fluctuate with changes in the participant's life situation, course of comorbid mental health problems, or reactions to psychosocial or psychopharmacologic treatments. Some populations are more likely to have repeated suicidal ideation or behavior at frequent intervals.²¹ Factors should also be considered with regard to their long-term (e.g., family history of suicide, history of early sexual abuse) or more proximal (e.g., recent loss) contributions to risk. As described below, it is important to estimate, plan to treat, and inform study participants of these assessments and procedures.

STUDY DESIGN CONSIDERATIONS

As investigators consider various treatment designs for their interventions to reduce suicidality, they must also consider how to balance the risks and benefits to the research participant in the design. For studies focused on reducing suicidality among research participants *per se*, the choice of comparator is critical. Because of the lack of validated treatment approaches, no one comparison condition stands out as a "gold standard" that must be used. While several active treatments could be compared, many treatments aimed at reducing suicidality will be initially compared with the standard of care in the community, with the addition of increased monitoring of suicidality in the control or comparison groups. Increased monitoring, as described later in this article, may offer a level of enhanced care, and, in that sense, community standards of treatment plus monitoring could be considered an enhanced treatment. Although enhanced treatment as usual as a comparison condition could be criticized for lacking standardization within and across studies, the lack of empirically supported interventions for suicidal persons may justify this design approach.

Risk-benefit considerations will be different for studies in which suicidal participants will be enrolled, but in which suicidality is not the focus of treatment. In these studies, treatment comparison conditions will most likely involve approaches designed to address the illness, as well as adequate measurement of suicidality, and could include components of treatment or risk management protocols aimed at reducing suicidality. For these studies, there are quite likely a number of alternative, active treatments for mental disorders to consider as comparison conditions beyond treatment as usual. Such studies may also involve adequate assessment of suicidality and then participant removal from the trial if the treatment or risk management is not adequate for the disorder or conditions of interest. However, the consequences of censoring (excluding the distribution of participants who are suicidal) should be considered in these types of designs.

For studies aimed at reducing suicide risk *per se*, as well as studies focused on treating suicidality as part of an intervention focused on a mental or substance abuse disorder, investigators should consider whether increased monitoring of suicidality in all arms of the study may work to reduce the power to detect effects of the active treatment. Much of the early intervention research on reducing suicidality had inadequate statistical power to detect differences among treatment groups. To justify enrolling participants in treatment trials that may increase their level of risk, trial designs must be scientifically sound in order to produce meaningful results; otherwise, benefits based on improved knowledge about these issues cannot reasonably be expected. Thus, investigators must find the balance between safety and statistical power as they consider designs.

Treatment trial protocols with participants who are or may become suicidal should include provisions for managing serious suicide attempts or the expression of clear suicide intent and for facilitating greater intensity of care when indicated, such as day treatment/partial hospitalization or inpatient hospitalization. Increased intensity of care is likely to be a part of the treatment protocol in studies focused on reducing suicidality *per se*. For studies focused on treating mental or substance abuse disorders in which suicidality is expected to be less frequent, a risk management protocol appropriate for the expected frequency of suicidality should be operationalized. In working with their institutional review board (IRB) and data and safety monitoring board (DSMB), investigators should describe how likely serious attempts are to occur and how frequent inpatient hospitalization may be and specify protocols for managing serious attempts and referring participants to inpatient settings. Since an emergency department visit or hospitalization does not guarantee that suicidal behavior will be avoided, investigators need to discuss with their IRBs and DSMBs how serious suicide attempts will be managed (e.g., individualized treatment in either an

inpatient hospital or intensive outpatient setting) and/or by whom. In some instances, such as a treatment-as-usual condition, the clinical research team will not be primary care providers and may not be able to control all aspects of treatment.

MONITORING AND RISK MANAGEMENT PROTOCOLS

All trials that explicitly recruit suicidal persons should establish a risk management protocol or strategy prior to initiating recruitment into the study. "Risk management protocol" describes the steps to be taken with life-threatening situations or with significant deterioration in clinical status.³⁰ The risk management protocol identifies the signs, symptoms, or conditions indicative of meaningful change in risk, establishes procedures for the documentation of this change, and presents decision rules or algorithms for crisis intervention. "Meaningful change in risk" will depend on the study. When the individual's status reaches a level of unanticipated deterioration, it could result in the study participant's removal from the study. Criteria for withdrawal from the study should be explicit and specified as much as possible in advance, including plans for additional or alternative treatment. Withdrawal of patients may or may not need to be reported as "unanticipated problems" or an adverse event, depending on the study (see reference 31 for National Institutes of Health [NIH] policy on reporting adverse events; see reference 19 for policy relevant to single-site trials).

While empirically validated instruments can aid in the judgment of risk status, the decision to shift into a risk management protocol is best left to the clinical judgment offered by adequately trained and experienced clinicians. The operationalization of this approach and its inclusion for review by the IRB, scientific review, and review by the DSMB can help develop some guideposts for the field with regard to risk management. Risk management protocols could include use of multiple thresholds in screening and monitoring. If these measures are administered by persons with little clinical experience, supervision should be established to assure timely and appropriate action. Beyond screening, the next level of risk evaluation should include the systematic recording of clinicians' concerns. Review of existing research can assist researchers in deciding the detection/specification area of assessment, as well as more in-depth assessment of suicidality or such protective factors as reasons for living (see the NIMH Web site for reviews of measures of suicidal behavior in youth, adults, and older adults³²). Investigators may also wish to consider other approaches to additional safeguards (see reference 33).

With regard to a risk management protocol for persons who become suicidal, Linehan²¹ has proposed detailed steps for assessing and treating suicidal behavior. Clini-

cians should identify and reduce the study participant's access to means of suicide and determine whether the individual can be left alone or requires monitoring until further evaluation takes place. When appropriate, family members should be informed of the need for monitoring and the urgency of limiting access to any means of suicide (firearm, medications). Additional steps to maintain or increase contact and treatment and support intensity when suicide risk is imminent and high may also be warranted.

Clinicians often develop a "no-suicide contract" or some form of agreement with the high-risk individual as a trusting agreement intended to prevent impulsive acts in the short run. Although there is no empirical evidence that such signed contracts reduce risk for suicidal behavior or, for that matter, reduce liability risk for providers, such agreements may help an individual develop a commitment to staying alive and provide some focus and structure during a chaotic time. Useful components of a contract that are consistent with recommended treatments for suicidal patients include (1) providing the opportunity for both research participant and therapist to commit to actions that decrease suicidality and not being ambivalent about this goal; (2) defining the thoughts and behaviors that precede suicidal behaviors, as well as defining the suicidal thoughts and behaviors themselves, which may help the research participant and his or her support network to better monitor downward trends; (3) identifying possible steps to take to reduce these thoughts and behaviors; and (4) informing the research participant and his/her support network how to access crisis care, including the treating professional. Some groups using cognitive-behavioral approaches in treatment have recommended that, along with the steps described above, therapists consider with the patients likely scenarios of when suicide risk will increase again and rehearse strategies and develop alternative reactions and behaviors that are more appropriate and effective than becoming suicidal (reference 26 and A. T. Beck, M.D., and G. K. Brown, Ph.D., unpublished manuscript, 1999).

INCREASED MONITORING AND SUPERVISION

The frequency of clinical monitoring of suicidality is determined by the level and frequency of risk of research participants. Some people are suicidal only sporadically. Others may be persistently suicidal. Provision for planned, routine monitoring for meaningful clinical change is a necessary step to ensure early identification of distress and appropriate crisis intervention.

The quality of data gathered on suicidal states needs to be monitored and evaluated in a timely manner by appropriately trained and supervised personnel in consultation with those treating the research participants. Enhanced monitoring can also address other safety aspects of treatment trials with persons at high risk for suicidal behavior,

including treatment side effects, lack of treatment response, or an increase in related symptoms. NIMH has recently requested that intervention studies provide a plan for oversight and monitoring to ensure the safety of participants and the validity and integrity of the data.³⁴ Studies focused on reducing suicidality per se are strongly urged to establish a DSMB that reports to NIMH and the investigator's IRB as a way of increasing safety through monitoring. In the case of multisite trials, the DSMB can serve as the central point for reporting adverse events.³⁵

Based on the study population, the investigators should estimate the frequency and level of severity of suicidality for which reports of events may be provided and obtain advice from their IRB and DSMB for type and frequency of reporting. For example, if the rate of self-harming behavior is anticipated to be high, and treatment protocols are designed to manage such high rates, a periodic report may be sufficient to keep the IRB and NIMH informed. It is critical that the clinical research staff have sufficient expertise and experience with high-risk study participants to balance the risk of false-positive reporting of adverse effects (e.g., ideation without an imminent suicide plan), yet maintain a conservative and safe approach to monitoring and reporting. Incorporating measures with sufficient validity and specificity in protocols and follow-up procedures to further determine risk, along with the clinical judgment of experienced and competent staff, can minimize false-positive reports of adverse events. It is the responsibility of the investigators to know the adverse events reporting requirements for their state and/or institution, as well as follow-up procedures. For example, some institutions request that clinical researchers not directly involved in the trial be consulted with regard to retaining or withdrawing a study participant from the study when an adverse event occurs. See reference 31 for NIH policy regarding the reporting of adverse events.

RESEARCH CLINICIAN COMPETENCIES

Initial review groups assess whether investigators and their research teams have the clinical training, capacity, and expertise to perform the scientific work of the study. In research involving suicidal patients, this assessment may include a description of the relevant qualifications of supervisory personnel as well as those who will be working directly with study participants who are likely to become suicidal. Prior to initiating the treatment protocol, individuals potentially treating persons at risk for suicidal behavior need to be adequately trained and conversant in both the approaches and steps to take when a research participant reports having suicidal thoughts and/or is planning to engage in suicidal behavior. Research teams should be able to minimize their ambivalence, fear, or confusion about gathering information about and acting on treatment plans to reduce or prevent suicidality.

Investigators should have plans in place for evaluating, treating, and/or referring of individuals who are in a suicidal crisis or other emergency. These plans include considering how to manage or refer potential research participants, just as any competent practitioner should, if imminent risk for suicidal behavior is detected during study recruitment prior to consent.³⁶ Voluntary or involuntary inpatient hospitalization requires knowledge of insurance plans, state laws, professional access to facilities, and procedures. All professionals involved in the treatment study should be well versed in the circumstances in which such steps are to be taken and understand the legal ramifications of these actions for individual participants, such as breaking confidentiality and involuntary commitment, and the potential involvement of other agencies and entities (e.g., protective services). Research participants and, if appropriate, family members need to be informed of these potential actions and consequences.

In the event of a suicide by a research participant, investigators should follow their institution or treatment facility policies on critical incident or sentinel event review, staff debriefing, and procedures for informing family members, as well as provide clinical referrals to family members. Investigators are also encouraged to have in place plans for helping staff review and debrief on the events and interactions pertaining to the study participant to address distress among research team members.

LEGAL RISKS TO INVESTIGATORS AND INSTITUTIONS CONDUCTING RESEARCH WITH PERSONS AT HIGH RISK FOR SUICIDAL BEHAVIOR

Practitioners have suggested a number of ways to conduct treatment with suicidal patients to reduce liability claims.^{37,38} Many of these recommendations include adequate suicide risk assessment, monitoring, and documentation and informing family members of the status of the suicidal patient. However, case law to guide clinical researchers with regard to their liability in studies involving suicidal study participants is limited. In reviews of case law pertaining to clinicians treating suicidal patients, an acceptable standard of care requires an initial and periodic evaluation of suicide potential for all patients seen in clinical practice.^{37,39,40} If the diagnosis, treatment, and surveillance of a patient is seen as adequate, the practice of care is usually considered of sound judgment and the clinician is typically not found liable. Practitioners are responsible for assessing risk for suicide and implementing a treatment plan to reduce or eliminate the risk. Assessment for elevated risk is not the same as prediction.⁴¹ The courts typically recognize that the prediction of suicide is fraught with uncertainty and that if providers were considered completely responsible for patients' suicidal behaviors, no health care provider would risk liability exposure to treat such patients, denying suicidal persons necessary

treatment. The majority of decisions against practitioners in malpractice related to suicide deaths involve cases concerning inpatients; hospitals and institutions appear to be held to a higher standard of care since they are assumed to have greater control over the patient environment. Courts have held practitioners or hospitals culpable in the following situations: when a practitioner failed to investigate previous psychiatric history and current mental state, when a treatment plan has been overlooked or a practitioner has neglected evidence of suicidal tendencies, when a patient has been inadequately supervised, and when a patient is released from a hospital while acutely suicidal. Liability is less likely to be found when a patient denies suicidal intent.

Clinical researchers conducting intervention trials with suicidal study participants should consult their institution and/or facilities where the research will be conducted to determine possible recommendations for type and amount of professional liability insurance to be maintained for the research team members.

SUMMARY

There is a critical need for adequately designed intervention studies to reduce suicidality. We hope that the suggestions for employing safety and monitoring procedures described here can assist investigators, as well as enhance the safety of the research participants. As more evidence-based treatments become available, we hope that this discussion will be updated and further refined to point to more safe and effective ways of managing and reducing suicidality. We also hope that someday in the near future the evidence base will be sufficient so that it will be necessary to justify why individuals at high risk for suicidality are being *excluded* from trials, rather than providing justification for their inclusion. Individuals at high risk for suicidality deserve safe and effective treatments, just as do other individuals with mental disorders who do not experience suicidality.

RESOURCES

This final section includes checklists that clinical researchers may find useful in developing study designs and consent forms and further information on NIH policies.

Points to Consider in Planning an Intervention Trial With Suicidal Study Participants

1. Identify specific inclusion criteria and their measurement with regard to suicidality. Examples include high levels of suicidal ideation as measured by a valid self-report scale and history of a near-lethal suicide attempt as rated by an interview and lethality scale. Exclusion criteria, including those relevant to suicidality, should also be specified.

2. Describe procedures in the protocol for managing increases in suicidality and how research staff are trained and available to provide such clinical management.
3. Identify the range of symptomatic and behavioral factors with which withdrawal from the treatment trial should be considered, such as increased suicidality, increased related symptoms, lack of treatment response, and treatment side effects; the procedures for determining if withdrawal is warranted and for withdrawing a participant if withdrawal is judged to be appropriate; and what alternative treatment or referral will be offered.
4. Consider and establish criteria for hospitalization, where the hospitalization should take place, and procedures within the hospital that provide additional safety.
5. Have a procedure for emergency coverage that is clearly understood by the clinical research staff, study participants, and families, if appropriate. Consider providing a written document describing this coverage.
6. As part of the consent process, consider having explicit discussion with relevant family members, guardians, or friends that includes the risks inherent when study participants are suicidal (risk of death, side effects of treatments), the procedures for handling increases in suicidality, the criteria for withdrawal from the study, the risks and benefits of the treatment and control conditions offered, and the limits of confidentiality. Investigators may want to consider having family members, guardians, or friends as participants in the research study. Family members' or friends' roles in the treatment should be clear and understood by both the study participant and family members.
7. Consider and identify the limits to confidentiality with respect to suicidality, as well as other circumstances. Communicate these limits to the study participants; in particular, inform them that confidentiality will not be maintained if there is imminent risk. Any additional limits to confidentiality for minors should be clear to them and their parents or guardians.
8. Consider the possible impact of suicidality and other emotional states on the study participants' capacity to give informed consent. Develop additional procedures to ensure protection of study participants' rights, if needed.
9. Determine whether additional safeguards are needed to ensure the safety of the study participants. These include safeguards available to individual study participants, such as study participant advocates, or those relevant to the overall conduct of the study, such as a DSMB.

10. Consider situations in which a trial would be terminated prematurely. A DSMB may independently review the progress of the trial and relevant safety concerns and address “stopping rules.”

Checklist of Informed Consent Issues

For actively suicidal participants in treatment trials, it is particularly important to convey foreseeable risks and reasonably expected benefits, alternatives to study participation such as individualized treatment available outside the study, and the limits of confidentiality. Because there has been so little systematic investigation of effective treatments for reducing suicidal behavior, the description of the risks and benefits of research on this topic is relatively straightforward, compared with that of studies in which a number of effective treatments exist. Most clinical trials that test treatments aimed at reducing suicidal behavior will reflect the research evidence and inform participants that there are no treatments proved to effectively reduce suicidal behavior per se. However, investigators should consider informing potential participants what might be standard practice for treating their condition (if there is one). For example, if adult patients with depression and suicidality are usually treated with a selective serotonin reuptake inhibitor and/or psychotherapy, then potential participants should be informed about this, even though such a combination has not been proved to be successful in reducing suicidal behavior. Best estimates of success rates for depression treatment should be conveyed, along with information about suicide risk associated with untreated depression.

Increased monitoring will also influence the likelihood that other parties may be informed of study protocols and actions, as in the case of withdrawing an individual from a trial and referring him or her to a clinician who is not a part of the research team or notifying family members when increased monitoring is needed. Reporting adverse events to an IRB or DSMB may also require identification of participants and their family members. The possibility that family members, outside clinicians, and monitoring entities (IRB, DSMB) may have access to study protocols should be noted in the consent document. Informing research participants and their families that this level of oversight is taking place may also be reassuring to them and improve recruitment and retention. Asking permission of participants to contact and inform a third party of their research participation and solicit input from them is an important way of increasing monitoring. Information for participants and designated third parties on how to obtain assistance in emergencies should be provided. For example, a small, user-friendly contact card containing this information could supplement similar information on a consent form.

Investigators are encouraged to develop an informed consent process that is thorough, yet understandable. See

reference 42 for an example of a simplified sample consent form recommended in NIH cancer treatment trials. The following checklist suggests specific issues that investigators may want to consider addressing in obtaining consent for intervention studies involving study participants at high risk for suicidality. Each of the categories listed below is usually contained in consent forms for research. Indicated under each category are issues that may be specific to research with suicidal persons. Format and content for consent forms will vary across institutions.

1. Purpose. This section should succinctly describe the main purpose of the study and why it is necessary to include people at risk for suicidality. The hypotheses of the study should be clearly stated, including whether certain interventions are expected to reduce suicidality.

2. Research participants. This section should describe the characteristics of the research participants, including age range, possible clinical characteristics (e.g., a mental disorder with increased risk for suicidality, a recent suicide attempt), or the service setting that characterizes why they are being sought (e.g., consecutive patients seen in an emergency department for a suicide attempt). Investigators may consider describing particular inclusion and exclusion criteria in this section. For example, if potential research participants are likely to be imminently suicidal at enrollment, investigators may wish to indicate that a number of factors will be used as part of an initial evaluation to determine whether enrollment in the study is appropriate at that time.

3. Free choice to join or to terminate participation. This issue can be complicated when potential research participants are psychiatric inpatients, as might be the case if a protocol involves enrolling persons who are actively suicidal or patients who have recently attempted suicide. Although it is likely that such persons will be found in inpatient units and psychiatric emergency departments, it is important to be able to justify that persons in the unit/department are an appropriate sample and not just a convenient sample. While being in a locked unit does not necessarily preclude a voluntary choice to refuse or agree to participate in research, extra care should be taken to ensure that recruitment is not tainted by coercion or undue inducement. IRBs will want to assure that potential research participants understand that their current status and their receipt of appropriate treatment do not depend on research participation and that there is no loss of benefits for nonparticipation. Similarly, if research participants have been involuntarily committed to treatment due to their imminent suicidal or homicidal status, voluntary choice with regard to research participation and access to treatment must be clarified. Many IRBs will not allow involuntarily committed patients to participate. Other IRBs may invoke subpart C of the Code of Federal Regulations, Title 45, Part 46, Protection of Human Subjects,⁴³ for prisoners, to provide additional protections.

4. Study protocol and explanation of procedures. Any special assessment procedures for suicidality risk, as well as procedures that may be followed in emergency situations, should be described.

5. Alternative treatments. For studies focused on reducing suicidality per se, most alternative treatments will be limited with regard to their known effectiveness for decreasing suicidality. Investigators may want to indicate that the best way of treating suicidality is not known, although treatments that are routinely used may be effective. For studies focused on treating mental or substance abuse disorders and associated suicidality, alternative treatments that have shown effectiveness in the treatment of the disorder that are relevant to the study population should be described as such.

6. Follow-up care. For study participants perceived to be at increased risk for suicidality at the end of the study, appropriate referrals should be provided to the study participant and family members, if appropriate. Study participants should be informed that, in the case of imminent suicidality, research staff may need to limit confidentiality in order to obtain appropriate care for the individual.

7. Risks, discomforts, and inconveniences of the research and measures to be taken to minimize them. Statements about steps that will be taken to monitor suicide risks, as well as the possible use of risk management procedures, should be described. Risks associated with the treatments provided should be articulated (e.g., side effects of medications). The consequences of ineffective treatment, such as continued risk for suicidality, continuing depression, and negative effects on social, educational, or work outcomes, should be described.

8. Withdrawal from the study. The anticipated risks and benefits of being withdrawn from the study, whether initiated by the investigator or initiated by the participant, should be considered and discussed with the IRB. Investigators should describe what will happen if the participant wishes to withdraw from the study. Participants should be informed of steps that will be taken to determine if they are at high risk for suicidal behavior and what treatment or referral will be provided if needed. Potential limits to confidentiality at the time of the study participant's withdrawal should be explained. Consent statements should note that the investigators may need to withdraw the participant from the study and the criteria for doing so. These may include withdrawal from the intervention trial due to increased suicidality, increased related symptoms, lack of treatment response, or treatment side effects. Alternative treatments or referrals to be offered should be specified.

9. Measures to preserve confidentiality of the information collected, privacy of the subject, and limits to confidentiality. Identify the limits to confidentiality with respect to suicidality, as well as other circumstances, such as referral to appropriate care when the research participant wishes to withdraw from the study, or if the investiga-

tors withdraw a participant from the study. Investigators and research participants may want to jointly develop procedures for contacting third parties under various circumstances to maintain confidentiality as well as safety (e.g., contact a family member before contacting law enforcement). Such limitations of confidentiality should be clear to both the participant and research team. Investigators may also wish to emphasize that confidentiality will not be maintained if the participant is in imminent risk. Any additional limits to confidentiality for minors should be clear to them and their parents or guardians.

10. Expected direct benefits to the research subjects. The anticipated direct benefits of treatment and monitoring in reducing suicidality can be described in this section. The possibility that the study participant will not benefit from the treatments studied should also be stated.

11. Expected indirect benefits to others. The type of information from the study expected to improve understanding of effective interventions for suicidal persons is stated here. The likelihood that the improved understanding will guide the clinical practice of mental health professionals and inform further research on interventions to reduce suicidality can also be described.

12. Management of any physical injury. Persons who are research participants and who attempt suicide may incur physical injury. The institution's plans for provision of acute treatment related to suicidal behavior injury, injury related to the study treatment, and injury unrelated to suicide intent or study treatments should be clarified. Availability (or lack thereof) of long-term treatment or other compensation should also be noted in the consent document.

13. Payments to the subject for participating in the study. Payments should not be considered a benefit to be balanced against research risks. It is important for investigators to avoid undue inducement to be in a study with an inactive treatment in which the participant may be asked to delay the opportunity to receive individualized treatment. Reasonable payments can be considered for participant time, but payment should not be the only reason for participation.

14. Costs to the subject or subject's health insurance carrier resulting from participation in the study. Investigators should be aware of research participants' insurance carrier policies with regard to coverage for treatments of suicidal behavior. Participants should know whether their insurance will be billed and how this may affect future coverage.

15. How to learn more about the study or raise concerns, and whom to ask.

16. Documentation of consent. If family members or other designated third parties are not directly involved in the intervention study, investigators may want to consider obtaining permission from participants to share information included with consent documents, such as whom to contact, and how, in the face of an emergency or crisis situation.

Active Federal Regulations and Policies for Support of Human Research

These regulations and policies include, but are not limited to, the following:

- Office of Human Research Protection
<http://ohrp.osophs.dhhs.gov>
- Code of Federal Regulations, Title 45, Part 46, Protection of Human Subjects
<http://ohrp.osophs.dhhs.gov/humansubjects/guidance/45cfr46.htm>
- Data and Safety Monitoring for Phase I and Phase II Trials
<http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html>
- Guidance on Reporting Adverse Events
<http://grants.nih.gov/grants/guide/notice-files/not99-107.html>
- Interim Research Involving Individuals With Questionable Capacity to Consent: Points to Consider
<http://grants.nih.gov/grants/policy/questionablecapacity.htm>
- NIMH Policy on Data and Safety Monitoring in Clinical Trials
<http://www.nimh.nih.gov/researchsafetymonitoring.cfm>

Disclosure of off-label usage: The authors have determined that, to the best of their knowledge, no investigational information about pharmaceutical agents has been presented in this article that is outside U.S. Food and Drug Administration–approved labeling.

REFERENCES

1. Murphy SL. Deaths: Final Data for 1998. National Vital Statistics Report 48(11). Hyattsville, Md: National Center for Health Statistics; 2000
2. Moscicki EK. Epidemiology of suicide. In: Jacobs DG, ed. The Harvard Medical School Guide to Suicidal Assessment and Interventions. San Francisco, Calif: Jossey-Bass; 1999:40–71
3. Miller HL, Coombs DW, Leeper JD, et al. An analysis of the effects of suicide prevention facilities on suicide rates in the United States. *Am J Public Health* 1984;74:340–343
4. Kroll J. Use of no-suicide contracts by psychiatrists in Minnesota. *Am J Psychiatry* 2000;157:1684–1686
5. Waterhouse J, Platt S. General hospital admission in the management of parasuicide: a randomised controlled trial. *Br J Psychiatry* 1990;156:236–242
6. National Institute of Mental Health. Abstracts of currently funded research grants pertaining to suicidal behavior. Available at: <http://www.nimh.nih.gov/research/suiabs.cfm>
7. Pearson JL, Stanley B, King C, et al. Issues to consider in intervention research with persons at high risk for suicidality [National Institute of Mental Health Web site]. Jan 2001. Available at: <http://www.nimh.nih.gov/research/highrisk suicide.cfm>
8. Satcher D. Call to Action to Prevent Suicide. July 1999. Available at: <http://www.sg.gov/library/calltoaction/default.htm>
9. Satcher D. Mental Health: A Report of the Surgeon General. 1999. Available at: <http://www.surgeongeneral.gov/library/mentalhealth>
10. National Strategy for Suicide Prevention. May 2, 2001. Available at: <http://www.mentalhealth.org/suicideprevention/index.htm>
11. Hawton K, Arensman E, Townsend E, et al. Deliberate self-harm: systematic review of efficacy of psychosocial and pharmacological treatments in preventing repetition. *Br Med J* 1998;317:441–447
12. Linehan MM. Behavioral treatments of suicidal behaviors: definitional obfuscation and treatment outcomes. *Ann N Y Acad Sci* 1997;836:302–328
13. Rudd MD. Integrating science into the practice of clinical suicidology: a review of the psychotherapy literature and research agenda for the future. In: Maris RW, Cannelto SS, McIntosh JL, et al, eds. *Review of Suicidology*. New York, NY: Guilford Press; 2000:47–83
14. Baldessarini RJ, Tondo L, Hennen J. Effects of lithium treatment and its discontinuation on suicidal behavior in bipolar manic-depressive disorders. *J Clin Psychiatry* 1999;60(suppl 2):77–84
15. Beasley CM Jr, Dornseif BE, Bosomworth JC, et al. Fluoxetine and suicide: a meta-analysis of controlled trials of treatment for depression. *Br Med J* 1991;21:685–692
16. Letizia C, Kapik B, Flanders WD. Suicidal risk during controlled clinical investigations of fluvoxamine. *J Clin Psychiatry* 1996;57:415–421
17. Meltzer HY, Okalyli G. Reduction of suicidality during clozapine treatment of neuroleptic-resistant schizophrenia: impact on risk-benefit assessment. *Am J Psychiatry* 1995;152:183–190
18. Norquist G, Lebowitz B, Hyman S. Expanding the frontier of treatment research. *Prevention and Treatment* [serial online]. March 21, 1999;2:0001a. Available at: <http://journals.apa.org/prevention/volume2/pre0020001a.html>
19. National Institutes of Health. Further guidance on data and safety monitoring for phase I and phase II trials. June 5, 2000. Available at: <http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html>
20. Porkorny AD. Prediction of suicide in psychiatric patients. *Arch Gen Psychiatry* 1983;40:249–257
21. Linehan MM. Standard protocol for assessing and treating suicidal behaviors for patients in treatment. In: Jacobs DG, ed. *The Harvard Medical School Guide to Suicidal Assessment and Interventions*. San Francisco, Calif: Jossey-Bass; 1999:146–187
22. Conwell Y, Brent D. Suicide and aging. 1: patterns of psychiatric diagnosis. *Int Psychogeriatr* 1995;7:149–181
23. Schaffer D, Craft L. Methods of adolescent suicide prevention. *J Clin Psychiatry* 1999;60(suppl 2):70–74
24. Brent DA, Bridge J, Johnson BA, et al. Suicidal behavior runs in families: a controlled family study of adolescent suicide victims. *Arch Gen Psychiatry* 1996;53:1145–1152
25. Brent DA, Perper JA, Moritz G, et al. Stressful life events, psychopathology, and adolescent suicide: a case control study. *Suicide Life Threat Behav* 1993;23:179–187
26. Brent DA, Poling K. *Cognitive Therapy Treatment Manual for Depressed and Suicidal Youth*. Pittsburgh, Pa: University of Pittsburgh, Services for Teens at Risk (STAR-Center); 1997
27. Fergusson DM, Horwood LJ, Lynskey MT. Childhood sexual abuse and psychiatric disorder in young adulthood, 2: psychiatric outcomes of childhood sexual abuse. *J Am Acad Child Adolesc Psychiatry* 1996;35:1365–1374
28. Kaplan SJ, Pelcovitz D, Salzinger S, et al. Adolescent physical abuse and suicide attempts. *J Am Acad Child Adolesc Psychiatry* 1997;36:799–808
29. Fergusson DM, Horwood LJ, Beautrais AL. Is sexual orientation related to mental health problems and suicidality in young people? *Arch Gen Psychiatry* 1999;56:876–880
30. Brown GK, Bruce ML, Pearson JL. High-risk management guidelines for elderly suicidal patients in primary care settings. *Int J Geriatr Psychiatry* 2001;16:593–601
31. National Institutes of Health. Guidance on reporting adverse events to institutional review boards for NIH-supported multicenter clinical trials. June 11, 1999. Available at: <http://grants.nih.gov/grants/guide/notice-files/not99-107.html>
32. National Institute of Mental Health. Suicide Research Consortium. Available at: <http://www.nimh.nih.gov/research/suicide.htm>
33. National Institutes of Health. Research involving individuals with questionable capacity to consent: points to consider. Jan 5, 2001. Available at: <http://grants.nih.gov/grants/policy/questionablecapacity.htm>
34. National Institute of Mental Health. NIMH policy on data and safety monitoring in clinical trials. Available at: <http://www.nimh.nih.gov/research/safetymonitoring.cfm>
35. US Dept Health Human Services. Continuing review of DSMB-monitored clinical trials. May 22, 2000. Available at: <http://ohrp.osophs.dhhs.gov/humansubjects/guidance/dsmb.htm>
36. Kleespies PM, Deleppo JD, Gallagher PL, et al. Managing suicidal emergencies: recommendations for the practitioner. *Professional Psychology: Research and Practice* 1999;30:454–463

37. Bongar B, Berman AL, Maris R, et al. Risk Management With Suicidal Patients. New York, NY: Guilford Press; 1998
38. Guthiel TG. Liability issues and liability prevention in suicide. In: Jacobs DG, ed. The Harvard Medical School Guide to Suicidal Assessment and Interventions. San Francisco, Calif: Jossey-Bass; 1999:561–578
39. Bongar B. The Suicidal Patient: Clinical and Legal Standards of Care. Washington, DC: American Psychological Association; 1991
40. Packman WL, Harris EA. Legal issues and risk management in suicidal patients. In: Bongar B, Berman AL, Maris RW, et al, eds. Risk Management With Suicidal Patients. New York, NY: Guilford Press; 1998:150–186
41. Jobes DA, Berman AS. Suicide and malpractice liability: assessing and revising policies, procedures, and practice in outpatient settings. *Professional Psychology: Research and Practice* 1993;24:91–99
42. National Cancer Institute. Cancer trials: sample consent form. Available at: <http://cancertrials.nci.nih.gov/researchers/safeguards/consent/sample02.html>
43. US Dept Health Human Services. Human Subject Protection Regulations, Code of Federal Regulations, Title 45, Part 46, Protection of Human Subjects. Available at: <http://ohrp.osophs.dhhs.gov/humansubjects/guidance/45cfr46.htm>.

© Copyright 2001 Physicians Postgraduate Press, Inc.
One personal copy may be printed