

Suicide Ideation or Behavior Among Research Participants

University of Kentucky Office of Research Integrity

Guidance for Investigators and IRB Members

This set of recommendations includes guidance on medical and non-medical research with participants who may exhibit suicidal ideation or behaviors. This guidance extends to participants who might have suicidal ideas, intentions, a history of attempts, or non-lethal attempts.

FIDUCIARY DUTIES: Researcher vs. Clinician

Suicidal ideation and behaviors, perhaps more than most behavioral health problems, provoke need for urgent response. For some studies, there is a potential overlap between clinical and research functions and ethical duties. It is important to clarify the relationships between researchers and participants versus clinicians and patients, so that participant expectations are accurate.

Research duty

Researchers have a *duty to protect*, that is, their fiduciary duty is to conduct research in which risk of harm or discomfort is “minimal” and in a reasonable or favorable ratio to the potential benefits. Efforts must be made to minimize and mitigate potential risks. In some instances, researchers also try to provide benefit to participants either directly or in terms of appeals to participants’ altruism in advancing science. The research duty is not a duty to protect a person from the various effects of disorder or from life experiences that occur outside what occurs in the study.

Clinical duty

By contrast, treatment providers (i.e., clinicians) have a *duty to care and a duty to treat*. This includes a fiduciary duty to care for persons’ health and wellbeing. In the case of suicidal ideation or behavior, this means clinical providers have a duty to fully assess, treat (either directly by treating persons or by referral to appropriate entities), and meet health/behavioral health care needs that can prevent suicidal actions.

FDA approved studies

This distinction between research and clinical ethical duties and obligations is less clear in FDA approved studies of investigational drugs where clinical practices are tightly woven into research. Careful examination of FDA guidelines should be considered in developing FDA clinical trials.

RISK CATEGORIZATION

Research which focuses directly on suicide ideation or behavior, treatment for suicidal thoughts, or populations with high likelihood for suicide, need careful analysis to determine risk category (e.g., \leq minimal risk; potential benefit). The population’s situation does not necessarily define the research risk category; rather, the risk-benefit

assessment is based on the research exposures. That is, the study's risk classification should consider the risk of research method upon participants' conditions when suicidal ideation or behavior is thought to be likely.

ETHICAL PRINCIPLES AND CONCERNS -

The three main Belmont ethical principles of respect for persons, beneficence, and justice shed light on how participants with suicidal ideation or behavior might be approached. These principles are generally applied in both clinical medicine and in scientific research.

Respect for Persons

Respect for persons' autonomy means treating them as rational agents who voluntarily and knowingly make an informed decision. Some investigators may question whether individuals with a suicidality can be considered as "rational" agents; however, research has shown that individuals who have attempted suicide can be cognitively capable of autonomously consenting and choosing involvement in research (Waliski, et al, 2015).

An independent assessment of decisional capacity using IRB-recommended screening instruments is recommended when there is reason to believe that decisional capacity might be limited or impaired (see ORI Form T). In some cases, a legally authorized representative is engaged for formal consent process. However, even in these cases, engagement of participants in consent process is recommended in lieu of assent processes. Implementing consent process enhancements to improve understanding may enable an autonomous decision or at least allow meaningful participation in shared decision-making or proxy consent.

Beneficence

The ethical duty to minimize risks to participants involves protecting participants from harm or discomfort that might be caused by the research. In some cases, unintentional harm or discomfort to the participant may be unavoidable, however, investigators must assess the probability and magnitude of risks in the context of a primary interest in betterment of human conditions.

There is a lay belief that merely asking about suicidality in more detail will have the effect of increasing suicidal risk. Empirical research is counter to this misconception (Cha, et al, 2016; DeCou & Schumann, 2017; Gould, et al., 2005; Dazzi et al., 2014). Regardless, research focused on involving suicidal participants may need additional vigilance to monitor participants' thoughts and emotions throughout the study. Study designs with surrogate outcome measures or protocol allowances for rescue or add-on treatments enable inclusion of populations with high suicide incidence.

Justice

There is also the concern regarding the ethical principle of justice, which implies complete fairness in how participants are recruited and exposed to research procedures. Excluding participants solely because of suicidal ideation or behavior may not be ethically justified. Broad scale exclusion in clinical trials leaves this population unrepresented with a void in generalizable knowledge related to the condition or study

treatment. Similar to federally defined vulnerable populations, participants with suicidal ideation or behavior should not be unnecessarily excluded without scientific justification. They should, however, be provided with safeguards or special protections to enable inclusion.

STUDY TYPES

The varied examples of research that could include participants with suicidal ideation or behaviors can be classified into five broad research types including:

1. Studies where suicide is a direct focus of the study or is a highly likely finding;
2. Studies assessing suicide treatments, including clinical outcomes assessments and clinical trials where the researchers may also be clinical providers;
3. Studies where suicide is not a direct research focus, but where the incidence of suicidal ideation or behavior is highly likely due to participant characteristics;
4. Studies where suicidality is totally an incidental finding; and
5. Studies that involve low risk, anonymous surveys on suicide among the general public or anonymous surveys with persons who have been exposed to suicide (e.g., having family members or being friends of someone who dies by suicide, including even medical or mental health service providers).

The following provides considerations and suggestions for each category.

1. STUDIES WITH A DIRECT FOCUS ON, (BUT NOT TREATMENT FOR), SUICIDALITY.

- Given that these studies are directly focused on the characteristics or manifestation of suicidal ideation or behaviors, it is likely that participants would be recruited from clinical populations where some degree of suicidality has been manifest. Ideally, researchers who are not a part of the treatment team would do the recruitment. However, if the researcher is also a member of the treatment team, he/she should employ methods to prevent undue influence and any misperception that treatment might be influenced by research participation.
- When suicide is the direct object of study (either among persons with suicidal ideation or behavior or among persons close to those who are or have been suicidal), the research team should provide a range of ancillary intervention supports such that ready hand-off referrals can be made to participants who become acutely suicidal and whose management requires services outside the scope of the study. The referral should be what is known as a 'warm hand-off' meaning that there is a direct, person-to-person referral of the suicidal participant to the treatment provider with the participant present or involved, not just giving participants a list of possible contacts.

- Since research in this category does not involve treatment, researchers are encouraged to avoid standard of care clinical interview approaches that could elicit expectations that clinical care will be provided, rather than a research data being collected.

The consent should:

- disclose procedures (e.g., survey questions; interview procedures) which could trigger a negative emotional or psychological response involving suicidality;
- include criteria for referral for clinical care; and
- Indicate the planned referral procedure (e.g., referral where direct contact is made by the researcher and the provider with participants involved in the process.

Example Studies:

- Studies of characteristics of adolescents with suicidal ideation or behaviors who were admitted to a drug abuse program;
- Studies of differences in suicidal thinking among men and women admitted to an inpatient psychiatric unit;
- Examination of the history of treatment episodes among adults admitted to a psychiatric unit with suicidal thoughts.

2. STUDIES WITH FOCUS ON SUICIDALITY TREATMENT INCLUDING CLINICAL OUTCOMES ASSESSMENT OR RESEARCH INTERVENTIONS

A. Clinical Treatment Outcome Studies (without random assignment or novel experimental interventions):

- As with the first group of studies above, it is likely that participants would be recruited from clinical populations where some degree of suicidality has already been assessed. Ideally, researchers who are not a part of the treatment team would do the recruitment. However, if the researcher is also a member of the treatment team, he/she should employ methods to prevent undue influence and any misperception that treatment might be influenced by research participation.
- The risks of participation most likely only involve inadvertent data breaches or misuse of data. These studies are generally minimal risk studies because the research design is observational in nature.
- The consent process should clearly state that the research is examining participant experiences with interventions. The consent should explain the research component but make it clear that the research is separate from clinical care

Example Studies without random assignment:

- Studies of the effects on treatment outcome among those who select family-based interventions versus those who do not;
- Studies of the differences in treatment effectiveness among males and females in treatment; and,
- Studies that examine whether trauma experiences affect treatment readiness and treatment outcomes.

B. Clinical Treatment Outcome Studies with random assignment, including Clinical Trials:

1. Research Design and Informed Consent:

- Again, the assumption is that most participants would have already been assessed as potentially suicidal by a clinical provider and that recruitment would come from a clinical setting. Some investigators are also providing clinical services and they should be aware of the distinct boundaries between their two roles when examining suicide interventions.
- Research examining the effects of suicide interventions, including clinical trials, comparisons to “treatment as usual (TAU)” or manipulation of treatment variables (e.g., exposure or assignment) carries research rather than clinical objectives. Thus, the imposition of research design carries with it a duty to minimize risks due to the research, but not duties of care in the clinical sense.
- While these studies have clinical interventions that are secondary to the research duties, suicidal crises might require discontinuation of participants in research in order to focus on their clinical needs. Having criteria for removing participants from the study, may be critical to shifting the ethical burden out of research and into clinically driven ethical duties. **The protocol should describe criteria for removing participants from the study and the procedure for referral (even if the referral is to the same person who has been performing a research role.** Most medical studies include provisions for removing participants from studies when clinical conditions either become severe or involve factors outside the specific focus of the research and that might confound findings. Suicide studies would be no different from these medical studies.
- Given that participants have a diagnosis, special attention might be needed to explain randomization and blinding. Suicidality is often characterized by decisional ambiguity and inability to focus on things other than those that are central to the crisis. Thus, the consent process might need to give careful explanation of such concepts. The federal Office for Human Research Protections provides educational videos on randomization for potential research participants.

- Criteria and procedures for removal from the study should be described in the consent form along with assurances that treatment will not be adversely affected by removal or withdrawing from research.
- If the researcher plans to offer both treatment and research procedures, the consent process and form should carefully describe the dual functions. FDA provides guidance on design of trials to test safety and efficacy of short-term treatment in FDA-regulated research (i.e., treatment of a depressive episode) and maintenance (relapse prevention).

2. Food and Drug Administration (FDA) -Regulated Clinical Trials

As noted above, the Food and Drug Administration has issued guidelines that somewhat bridge clinical and research duties in cases involving suicidal ideation or behaviors. The FDA encourages inclusion of patients with Major Depressive Disorder (MDD) who have a history of suicidal thoughts or suicide attempts in clinical trials designed to assess efficacy of antidepressant drugs. (FDA 2018) As long as sponsors have appropriate safety protocols and monitoring in place, inclusion allows data that is generalizable to patients with depression.

FDA also provides guidance on safety monitoring and standardized assessment and reporting of adverse events. The agency recommends prospective assessment for select clinical trials in order to provide standardized, timely and complete data for determining causality of events occurring during a trial. (FDA 2012) The following summarizes the [FDA guidelines](#) for evaluating treatment-emergent suicidal ideation and behavior.

- To better standardize reporting, FDA has adopted an 11-category instrument that leads to classification of suicidal risk status. It includes five levels of suicidal ideation, five levels of suicidal behavior, and the category self-injurious behavior, no suicidal intent. This distinguishes and classifies events previously labeled as suicide attempts that did not meet the criteria for such a designation. The Columbia-Suicide Severity Rating Scale (C-SSRS) or an equivalent instrument may be used.

General Recommendations:

- Administer screening questions at baseline and each visit (1-2 minutes)
- Full interview as indicated by positive findings (10 minutes)
- May warrant repeat assessment after dosing has ended for drugs with long half-lives.
- Formal training of raters

Scope of FDA-regulated Trials:

- Indicated for outpatient and inpatient clinical trials involving investigational drugs being developed for any psychiatric indication, antiepileptic drugs and other neurologic drugs with central nervous system (CNS) activity.
- Includes multiple-dose phase 1 trials involving healthy volunteers.
- May also be warranted for trials of investigational drugs that are pharmacologically similar to those above.

Population Considerations:

- May not be indicated for trials involving patients with significant cognitive impairment or critically ill populations
- May be used in children or adolescent patients of sufficient maturity and no cognitive impairment.

Example FDA-regulated Studies:

- A study comparing antidepressant medication plus individual psychotherapy versus antidepressant medication plus family-based therapy;
- A study that examines differences in outcome between non-manualized treatment plus medication versus a specifically suicide-focused manualized intervention plus medications;
- A study that examines differences in suicidal thinking outcomes among participants receiving trauma-informed medication interventions versus treatment as usual;
- A study examining differences in symptom reduction using a novel atypical antipsychotic medication plus a new SSRI.

3. STUDIES THAT FOCUS ON PARTICIPANTS WITH POTENTIAL SUICIDALITY (EXCLUDING FDA-REGULATED CLINICAL-TRIALS)

Non-FDA regulated studies of participants with characteristics that suggest a likely potential for suicidal ideation or behaviors, include participants with depression, schizophrenia, bipolar disorder, or substance use disorders.

- Studies with these populations must make provision for treatment referrals for participants who become acutely suicidal. In studies of this kind, merely providing national hotline numbers to participants is inadequate.
- **The majority of these studies should include “warm handoffs,” meaning referrals directly into a provider system or to a specific provider professional. This provides assurance that the referral is made, taken, and accepted.**
- A passive referral process may be adequate for less critical situations where assurance of contact with clinical care is less pressing.

The consent should:

- Disclose procedures (e.g., survey questions; interview procedures) which could trigger a negative emotional or psychological response involving suicidality;
- Include criteria for referral for clinical care; and
- Indicate the planned referral procedure(s),
 - A ‘warm handoff’ referral where direct contact is made by the researcher and the provider with participants involved in the process; and/or
 - In less critical situations where assurance of contact with clinical care is less pressing, a ‘passive referral’ which consists of giving participants names and contact information that can be used by participants to make their own referrals to clinical care.

Example Studies:

- A qualitative study examining participants with schizophrenia and experiences with atypical antipsychotic medications;
- A study of participants’ lifetime experiences with the mental health care system;
- A study of participants’ co-occurring mental health problems associated with their substance use;
- A longitudinal study of domestic violence victims and their mental health consequences.

4. STUDIES UNRELATED TO SUICIDE THAT MIGHT HAVE INCIDENTAL FINDINGS OF SUICIDAL IDEATION OR BEHAVIORS

Any number of studies might encounter participants who exhibit suicidality. A questionnaire or health history might trigger a participant to report suicidality even if the research does not focus on or address suicidality. In these studies, suicidality might be best thought of as an incidental finding and reported as an unanticipated problem/adverse event. Nonetheless, the duty to protect and refer for care still exists.

- Researchers are advised to use a method that is commensurate with the severity or urgency of the situation. This could range from a “warm handoff” to a passive referral.
- Participants should generally be able to continue participation in the study if their suicidality does not require removal and the presence of suicidal symptoms does not interfere with research participation.

5. LOW RISK ANONYMOUS SURVEYS

In examining social factors relating to suicide, studies might use anonymous surveys in a variety of setting, including internet environments. These studies might include the

general population, persons who have had family members or friends with suicidal ideations or behaviors or who have a history of their own suicidal behavior but they do not identify persons and do not collect personally identifiable health information.

- Researchers in these studies are advised to give potential participants with specific information about what is and is not being examined in these surveys using a script if not a passive consent to participate.
- In-person participants should be given guidance on *how to* contact local resources for additional counseling or support should they feel the need to do so upon completing the surveys.
- For internet studies, researchers should provide a list of nationally available suicide information or help lines for those who wish more information upon completion of the surveys. For example, National Suicide Prevention Lifeline (1-800-273-8255) or Crisis Text Line (text start to 741-741) are the most commonly provided resources.
- With in-person surveys, investigators should offer participants national hotline numbers plus local suicide prevention information or counseling resources for those who wish to follow-through for more information or support upon completing the surveys.

Example Studies:

- Anonymous, web-based surveys of people's experiences with suicide among family members or friends;
- Focus groups among family members of people with non-lethal attempts, examining their reports on first responders; and,
- Anonymous web-based surveys among persons self-identified with non-lethal attempts examining their views on family support during crises.

CONCLUSION

The ethical conduct and level of safeguards for research participants who experience suicidal ideation or behaviors vary with the type of study and target population. Researchers who focus directly on the problems of suicide are encouraged to give careful thought to the separation of ethical duties between research and clinical care.

For other research types, investigators should consider and describe where applicable, criteria for removal and referral for clinical treatment, the extent and limitations of the clinical services provided as part of the study design, and the specific role that researchers have in the study.

The consent form and process should clarify these issues so that the expectations of researchers and participants align.

REFERENCES:

Cha, C.B., Glenn, J.J., Deming, C.a., D'Angelo, E.J., Hooley, J.M., Teachman, B.A., & Nock, M.K. (2016). *Psychological Assessment*. Advance online publication. <http://dx.doi.org/10.1037/pas0000280>

Dazzi, T., Gribble, R. Wessely, S. & fear, N. (2014). Does asking about suicide and related behaviors induce suicidal ideation? What is the evidence? *Psychological Medicine*, 44(16) 3361-3363. Doi: 10.1017/S0033291714001299.

DeCou, C.R. & Schumann, M.E. (2017). On the Iatrogenic Risk of Assessing Suicidality: A Meta-Analysis, *Suicide and Life-Threatening Behavior*. Retrieved from <https://doi.org/10.1111/sltb.12368>

Gould MS, Marrocco FA, Kleinman M, et al. Evaluating Iatrogenic Risk of Youth Suicide Screening Programs A Randomized Controlled Trial. *JAMA*. 2005;293(13):1635–1643. doi:10.1001/jama.293.13.1635

Major Depressive Disorder: Developing Drugs for Treatment, Food and Drug Administration, June 2018

<https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM611259.pdf>

Suicidal Ideation and Behavior: Prospective Assessment of Occurrence in Clinical Trials, Food and Drug Administration, August 2012

<https://www.fda.gov/downloads/drugs/guidances/ucm225130.pdf>

Waliski A, Townsend JC, Castro M, Doan R, MSW, et al. (2015) Navigating the Institutional Review Board System to Conduct Suicide Research. *Ann Public Health Res* 2(4): 1028. Also available at: <https://www.jscimedcentral.com/PublicHealth/publichealth-2-1028.pdf>