Funding Org.	Year When Study First Received Funding	Study Title	Principal Investigator	Abstract
AFSP	2008	A National Study of Ethnic Differences in Suicidal Ideation and Attempts	Carlos Blanco	The aim of the study is to identify high-risk groups among Hispanics that can form the basis for the development of targeted treatment and prevention interventions. The study will involve the analysis of the largest and most complete dataset on the study of psychiatric disorders in the U.S. general population. First, we will examine how many Hispanics and non-Hispanics have suicidal ideations or attempt suicide at least once in their life, and what variables predict suicidal ideation and attempts. Then, we will examine which aspects of the Hispanics culture may have protective effects against suicidal ideation and attempts and how they could help guide the development of culturally appropriate treatment and prevention interventions. A better understanding of the risk factors (possibly including low-rates of treatment-seeking among Hispanics) and protective factors will help develop treatment and preventive interventions for this underserved minority group.
AFSP	2008	Risk factors for suicidal behaviors in a nationally-representative sample of adolescents: do they vary by subgroups?	Martie Thompson	The proposed research will identify key risk factors for predicting suicidal behaviors one and five years later in a nationally representative sample of US adolescents and determine if these risk factors operate similarly among certain subgroups. The proposed study will analyze data from the National Longitudinal Survey of Adolescent Health (Add Health), a prospective, population-based data set that contains measures for many variables that research indicates predict suicidal behavior. We will test the unique and combined roles of various risk factors in predicting suicidal behavior, and determine if and how these associations vary by gender, race, recent family history of suicidal behavior, and recent friend history of suicidal behavior. This proposal is consistent with AFSP's mission of funding studies that will identify the relative importance of different risk factors, and is responsive to the IOM (2002) report that nationally-representative, prospective studies are needed. These findings will guide suicide prevention because they will elucidate which risk factors uniquely predict suicidal behavior among different subgroups one and five years later. Further, because these findings will demonstrate prospective associations in a nationally-representative sample of US youth, they are widely applicable.
AFSP	2009	Explaining the sexual orientation disparity in adolescent suicide risk	Stephen Russell	This study seeks to explain the sexual orientation disparity in suicide ideation and suicide attempts among U.S. adolescents through the examination of risk and protective factors that characterize the important contexts of adolescents' lives: individual emotional and behavioral health and risk, family and peer relations and the school environment. The study involves secondary analysis of data from the National Longitudinal Study of Adolescent Health ("Add Health"), a nationally representative, longitudinal study of over 13,000 adolescents in the United States. The data source is strategic for this study because it is the only U.S. population-representative data that includes sexual orientation and suicidality, as well as information about the important contexts that shape adolescent development. The results of this study will identify factors for suicide in adolescence and young adulthood that are particularly salient based on adolescent same-sex sexual orientation. The study will offer the possibility for the development of holistic suicide prevention and intervention efforts designed to address the unique needs of same-sex oriented youth and young adults through the identification of risk and protective factors within specific contexts of their lives (individual adolescents, families, peers, or schools).
AFSP	2009	Determining the effects of early alcohol use on suicide attempts in early adolescence through young adulthood	Monica Swahn	This study will investigate the impact of early alcohol use on suicide attempt, and the factors tbat may influencethe link between alcohol use and suicide attempts, in a nationally representative study of adolescents and young adults. The study involves secondary data analyses of the National Longitudinal Study of Adolescent Health which is a database that will permit analyses to examine the impact of early alcohol me among both adolescents and yound adults since the study has fallowed participants over time. Analyses will examine the role of early alcohol use (prior to age 13) in suicide attemps as well as identify factors that may reduce or increase the impact of alcohol use on suicide attempts across adolescence and young adulthood. If the analyses show that early alcobol use is a consistent predictor of suicide attempts across adolescence and young adulthood, additional efforts to delay and deter alcohol use as a strategy for also preventing suicide attempts is waranted from both a policy and a clinical perspective. In particular, providing guidelincs for pediatricians and other primary care providers that promote proactlve identification of youth at risk for early alcohol initiation may be an effective suicide prevention strategy because clinicians may be the first to treat at-risk adolescents and may be more experienced and confident in screening youth for substance abuse than they are for suicidal behaviors.
AFSP	2009	Suicide risk and the Danish criminal justice system: a nested case-control study	Roger Webb	To compare relative risk of suicide among a broad range of people dealt with by the Danish Criminal Justice System with the general population suicide risk. We will analyze linked Danish national registers for the period 1981 to 2006. These large registers, which are unavailable in the US or any other country, provide a unique resource for conducting truly population-based investigations of all criminal convictions, all psychiatric inpatients admissions and all deaths by suicide and other causes nationally. We will use standard epidemiologic analytic methods to estimate the relative risk of suicide in various forensic groups versus the general population suicide risk, and assess the how severe mental illness and key demographic and psychosocial factors modify suicide risk in the forensic population. Novel findings will include accurate and precise estimation of sex-specific relative risks in the various groups dealt with by the Danish Criminal Justice System. By identifying subgroups within the wider forensic population with higher (or lower) suicide risk, our anticipated findings will guide researchers, clinicians and service planners, and also inform the appropriate targeting of resources and the development of specific suicide prevention strategies for this high-risk population.
AFSP	2009	Factors Promoting Good Adult Functioning in Adolescents with Suicidal Ideation: A Pilot Study	Helen Reinherz	This proposed research is one of the first utilizing a community sample to identify familial, environmental, and individual characteristics at ages 18, 21, and 26 leading to good functioning at age 30 among a group of youth who expressed suicidal thoughts at age 15 with the goal of informing the design of prevention programs for suicide and other negative outcomes. The study utilizes a unique 8 wave data set collected over 30 years from a single aged-cohort of almost 400 youth and their families. Moving beyond our prior work on risk factors for suicidal behavior1 and its long-term aftermath,2 the proposed study will focus on adolescents with suicidal thoughts who have achieved good levels of functioning at age 30. The protective influences of familial, environmental, and individual factors at particular developmental periods will be examined for the insights they may provide for both treatment and policy. It is anticipated that this prospective study of adolescents with suicidal thoughts who progressed to healthy adult functioning will provide critical information that can be tested further in studies using larger and more diverse samples. The findings of this pilot study examining the relative potency of specific types of modifiable protective factors over time may lead to more targeted interventions designed for specific age groups as well as guide prevention policies and enhance screening for suicidal thoughts and behaviors.3
AFSP	2009	A prospective study of the relationship between non-suicidal self-injury and suicidal behavior in a college population	Janis Whitlock	To longitudinally investigate the relationship between non-suicidal self-injury and suicidal ideation, plan, gesture, and attempt in a college sample drawn from 6 universities. This study will permit longitudinal follow-up of 1,647 students from 6 universities who provided detailed information on prevalence, risk and protective factors for both suicidal behavior and non-suicidal self-injury. Wave II data collection is currently underway and is dedicated to examining the temporal relationship between NSSI and suicidality. AFSP funds will be used to extend the study by adding wave III and wave IV collection so that we can better mediation, trajectories, and non-linear patterns. Understanding the temporal relationship between NSSI and suicidal behavior will illuminate the extent to which NSSI serves as a harbinger of later suicidal behavior and, thus, as an important target for early targeted intervention - in community and clinical settings. Understanding the extent to which NSSI directly contributes to later development of suicidality, independent of common risk factors, is particularly important because finding direct effects would suggest that early intervention is warranted, even in cases which appear to have low clinical relevance.

AFSP	2009	Suicide clusters across the globe: Geospatial trends from America, Ireland, and New Zealand	Gregory Larkin	The aims of this study are to conduct an observational epidemiological investigation of the prevalence and trends in cluster suicides in three countries (Ireland, New Zealand and selected states of the United States) using geospatial statistical techniques, and, if significant clusters are detected using this method, to determine their characteristics and the extent to which cluster hot spots can be explained by known or suspected risk factors including demographic factors (age, gender, race/ethnicity, sexual orientation, socioeconomic status, urbanicity/rurality), mental health factors (psychopathology, substance abuse, previous suicide attempts), institutional settings (schools, colleges, hospitals), meso-level epiphenomena (social deprivation, social fragmentation, social capital), and macro-level contextual influences, income inequality, economic restructuring, population density, availability and lethality of suicide methods, overall suicide rate and media coverage of proband cases). Geo-spatial, temporal, and cyber-linked suicide clusters will be studied among selected states of the united states (including rural areas and regions with high population of native Americans and Alaskan Americans. The geographic areas to be studied include selected states of the United States including rural areas and regions with high populations of Native Americans or Alaskan Natives in which there are reportedly high numbers of suicide clusters), and both Ireland and New Zealand, two countries that share similar population sizes (four million), similar mixes of urban and rural townships, similar longitudinal data registries, and similarly high rates of suicide clusters reported in the media. Initially, spatial scan and time series statistics will be used to analyze geospatially-linked mortality data from publicly available records provided by the national ministries of health and statistics in New Zealand and Ireland and by the National Violent Death Reporting System (NVDRS) and related data sources in the US in order to examine the incidence of suicide clusters in the five-year period 2001/2-2005/6 and time trends in selected geographic areas from 1984-2006. For clusters identified by these methods we will use available data to: describe the profiles of the clusters and of the decedents; explore whether it is possible to explain the clusters by individual risk factors such as gender, age, race/ethnicity, socioeconomic status, urbanicity/rurality, and explore, by using area-level data, whether the aggregation of (socially and economically) vulnerable people prior to the occurrence of a suicide may facilitate the development of a cluster. There is increasing concern about allegedly rising numbers of suicide clusters, particularly in rural areas and in youth; however, there has been remarkably little study of this phenomenon to inform community and professional responses to emerging or suspected clusters. We anticipate that our study will provide an evidence base for developing cluster prevention and interruption strategies as part of national/state suicide prevention programs, specifically by estimating the prevalence of clusters, describing the characteristics of decedents in clusters, exploring current trends, and identifying at-risk sites and populations which require specialized prevention efforts.
AFSP	2010	Development of a brief psychological autopsy instrument to improve the accuracy of injury death reporting in China	Mingjun Jiang	This study will identify 1) the primary causes for missing and misclassified suicide deaths in Sichuan, China, and 2) based on this information, develop and pilot a brief psychological autopsy questionnaire that will be used by the personnel who complete death certificates to improve the accuracy and reliability of their classification of injury deaths. The study will involved two components: 1) a situation analysis of the current death reporting system for injury deaths (including suicides) and 2) a pilot test of a revised method of determining the cause of injury deaths that is developed based on the results of the situational analysis,. For Aim 1, we will conduct in-depth interviews about current problems in China?s death registration system with 20 expert informants from different administrative levels and 12 focus groups with relevant stakeholders in Sichuan Province (physicians, 2 groups of village health workers, judges, coroners, policemen, officers from the Chinese Centers for Disease Control, public health officials, media representatives, 2 groups of relatives of persons who have died of suicide, and relatives of persons who died of other injuries). For Aim 2, qualitative assessments of the transcripts from the focus groups along with retrospective evaluation of the death records of 100 suicides and 100 deaths by other types of injuries will be used to develop a revised method of determining the cause of injury death that includes the use of a draft version of a brief psychological autopsy questionnaire to be administered by the individual who completes the death certificate; this revised method will be pilot tested in four rural and two urban communities in Sichuan, a geographically and socially diverse province in Southwest China. This proposed AFSP-funded Pilot Project will identify the primary causes of missing and misclassified injury deaths in China, information that can be used to adjust unreliable official rates of suicide and, thus, provide a more accurate picture of the pattern of suicides in the country. The study will pilot test a method for reducing the problem of missing and misclassified suicide deaths that will be revised and rigorously assessed in a future large-scale study and subsequently employed in future studies of the effectiveness of different suicide prevention strategies.
AFSP	2010	Suicide rates and misclassification of suicides in Hui, Tibetan, and Han in Qinghai Province of China	Liang Zhou	Aims of this study are to examine the differences of the suicide rates and to explore the level and sources of misclassification of suicides among Hui, Tibetan, and Han ethnic groups. Suicide and unintentional death surveillance system will be established in six counties in Qinghai province of China which include more than 200,000 people for each of the three ethnic groups. Investigators will use telephone screening interview to collect information of all deaths originally coded as unintentional, due to mental disorders, and undetermined, and then reclassify them as suicides or others. Detailed psychological autopsy study will be carried out in probably misclassified cases to clarify manner of deaths, and to describe levels and sources of misclassification of suicide in the three ethnicity community. The proposed project will provide reliable data on suicide rates in the Hui, Tibetan, and Han ethnic groups and, thus, will make it possible to assess differences in rates between the three groups while adjusting for the potential confounding of socioeconomic status and geographic location. These data will help us in the understanding of suicide behavior in different religious context, thus, will help us to develop different suicide prevention strategies in different ethnic and religious communities.
AFSP	2008	Urocortin 3 in Dorsolateral Prefrontal Cortex of Depressed Suicides	Garth Bissette	We will determine whether urocortin 3 protein, the major endogenous brain ligand for the type 2 corticotropin releasing factor receptor, is increased in concentrations in the dorsolateral prefrontal cortex of subjects dying of suicide with depressive symptoms at the time of death. We will micropunch frozen sections of post mortem brain dorsolateral prefrontal cortex and measure the amount of urocortin 3 protein by sensitive and specific radioimmunoassay. Subjects dying of suicide with and without antidepressant drugs that were assessed for depressive symptoms at the time of death by psychiatric autopsy will be compared to age- and sex-matched controls dying of sudden death. We expect that we will find urocortin 3 protein levels to be increased in the depressed subjects relative to the non-depressed controls and this will indicate that stress circuits in a major executive control center of the brain are active during depression that leads to suicide. If urocortin 3 is elevated in the dorsolateral prefrontal cortex of subjects with depressive symptoms at the time of suicide then a drug that blocks the type 2 CRF receptors may be useful in preventing part of the inpulsivity or hopelessness that contribute to suicide attempts. Such a drug might also function as an antidepressant.
AFSP	2008	Cortisol Reactivity in the Prediction of Suicide Attempts in Borderline Personality Disorder	Eric Fertuck	The key aim of this study is to investigate if cortisol (a stress hormone) changes in reaction to social stress can predict whether or not individuals with this borderline personality disorder have made are suicide attempters. This study will involve the administration of a standardized procedure that creates a moderate amount of social stress to individuals at high risk for suicide and to healthy comparison individuals. We will evaluate change in cortisol before, during, and after the stress, and compare our groups on cortisol changes. Finally, we will use this measure of stress reactivity to attempt to distinguish individuals who have made a suicide attempt from non-attempters, and to identify if cortisol reactivity differentiates the types of environmental ?triggers? to suicide attempts. Identifying more specific and readily assessable environmental and biological indicators of stress reactivity, and how they may differentially predict vulnerability to suicide, should help prevention and treatment efforts for suicidal individuals such as many of those with borderline personality disorder. Our study of social stress cortisol reactivity and environmental ?triggers? to predict suicide attempts in borderline personality disorder has the potential to contribute substantially to this effort.
AFSP	2008	The Temporal Association between Substance Use and Suicidality among Adolescents with Bipolar Disorders	Benjamin Goldstein	To characterize the nature and timing of substance use and suicidality in a high-risk sample of adolescents with bipolar disorders. This study will involve careful detailed assessment of substance use and suicidality in a sample of thirty adolescents (ages 12-18 years) with bipolar disorders. Adolescents diagnosed with bipolar disorders will be recruited from a specialty outpatient clinic if they have made a suicide attempt or had suicidal intentions/plans in the past year, and if they have become intoxicated with alcohol or used illicit drugs in the past year. Subjects will complete in-person assessment of overall psychiatric symptoms and status every three months, as well as telephone-administered measures of suicidality and substance use at monthly intervals through 9 months of follow-up. The anticipated findings of this pilot study will yield an estimate of the duration of the hazard period associated with acute substance use among high-risk adolescents with bipolar disorders and a history of suicidality. These findings will inform future applications for a large-scale study employing similar methodology, which will in turn inform research on risk assessment as well as targeted psychosocial and pharmacologic interventions.

AFSP	2008	A prospective study of suicidal ideation, suicide attempts, and completed suicide in body dismorphic disorder	Katherine Phillips	The primary aim of this study is to examine the following in 192 individuals with body dysmorphic disorder (BOD): 1) the rate and characteristics of suicidal ideation; 2) the rate and characteristics of suicide attempts; 3) the rate of completed suicide; 4) the relationship between severity of current suicidality, current BOD symptoms, and current depressive symptoms; and 5) predictors of suicidal ideation and suicide attempts. This study will involve 192 individuals who have participated in a prospective, longitudinal, observational follow-up interview study of the course and clinical features of body dysmorphic disorder who have already had annual interviews for up to 4 years of follow-up. These individuals will be recontacted and re-interviewed to obtain new information on suicidal ideation and suicide attempts. We will also determine the rate of completed suicide in this sample by searching the Social Security Death Index and other databases and by obtaining death certificates. Body dysmorphic disorder is a severe and relatively common illness that appears to be associated with high rates of suicidal ideation, suicide attempts, and completed suicide, although available data are very limited. By obtaining new and unique data on suicidality in BOD, this study: I) will raise clinician awareness of the importance of identifying body dysmorphic disorder, monitoring these patients' suicidality, and focusing treatment on suicide prevention; and 2) by better characterizing suicidal ideation and attempts, this study will lay essential groundwork for the future development of a much-needed treatment for highly suicidal patients with body dysmorphic disorder.
AFSP	2009	Genetic variation in glutamate receptor subunits may contribute to suicidal ideation susceptibility in pregnancy	Alicia Smith	This study will examine if differences in genetic structure or expression of genes relevant for glutamate-mediated neurotransmission, previously implicated in suicidal ideation (SI), contribute to the risk of developing SI during the perinatal period, which is a common clinical problem. Glutamate-mediated neurotransmission is altered during pregnancy and, almost 30% of pregnant women with psychiatric illness experience SI. To examine if variations in glutamate-mediated neurotransmission contribute to the high rate of SI in women with psychiatric illness during the perinatal period, we will examine gene expression profiles of two glutamate receptor subunits during the pre-conception period, each trimester of pregnancy and postpartum to test if expression patterns of these genes are more common in those who develop SI. We will then determine if the frequency of genetic polymorphisms in these genes are more common in women who experience SI than those who do not and whether the polymorphisms can be associated with patterns of gene expression. This study will confirm previous findings and further characterize of role of genes needed for glutamate-mediated neurotransmission in SI. The potential contribution of these genes to SI is a valuable lead for understanding the causes of SI and developing a risk model for suicidal behavior.
AFSP	2009	The Impact of RNA editing on suicide risk	Monsheel Sodhi	The key aim of this study is to investigate the diagnostic and molecular specificity of RNA editing in suicide, and to determine the influence of genetic variation on this process. The study will comprise statistically powerful investigations of postmortem brain tissue, from 369 subjects, including controls and subjects with schizophrenia, bipolar depression or major depression; of the subjects with psychiatric disorders, 38 % are suicide cases. The aims of this investigation are to determine: whether the influences of 5-HT2C RNA editing on suicide risk are specific to a diagnostic group; if there is a generalized increase in RNA editing activity in dorsolateral prefrontal cortex due to altered activity of the ADAR enzymes or if the RNA editing changes observed in suicide are specific to the 5-HT2C transcript; genetic variation which may be influencing the RNA editing process in suicide. The current proposal aims to identify pathophysiological mechanisms by which suicidality could arise. Better understanding of this dysfunctional neurochemistry will facilitate the development of improved prediction and treatment of the underlying problem.
AFSP	2009	Genome-wide association study of attempted suicide	Virginia Willour	Our goal is to compare the genomes of 1000 cases with a history of attempted suicide to the genomes of 2000 controls to identify genetic variation associated with an increased risk of suicidal behavior. Genetic studies of suicidal behavior in families with bipolar disorder, major depression, and alcohol dependence all provide strong evidence that there are genetic risk factors for suicidal behavior. Our goal is to compare the genomes of 1000 cases with a history of attempted suicide to the genomes of 2000 controls to identify genetic variation associated with an increased risk of suicidal behavior. We will use this whole genome comparison to identify the top 3-5 suicidal behavior candidate genes to be studied in depth, with the goal of finding genetic variation that can eventually be used to identify subjects at increased risk for attempting suicide. Identifying genetic risk factors associated with suicidal behavior is an essential component of any suicide prevention program. It would allow for the identification of individuals at higher risk for suicidal behavior, would provide new therapeutic targets, and would facilitate the identification of the medications that increase or decrease suicidal behavior in individuals with this risk factor.
AFSP	2009	Dissecting serotonergic influences on impulsivity and aggression	Luis Pennanen	The key aim of the study is to use mouse molecular genetic approaches to elucidate the contributions of a specific neurotransmitter receptor, the serotonin 2C receptor, in regulating impulsive and aggressive behaviors. To determine whether complete loss of serotonin 2C receptor function leads to impulsive and/or aggressive behav- iors, mice lacking functional serotonin 2C receptors will be assessed in specific behavioral tasks for impulsivity and aggression. Moreover, I will analyze the underlying neural mechanisms causing impulsive and/or aggressive behav- iors in mice lacking functional serotonin 2C receptors. In a second aim, I will ask specifically which brain regions are important for impulsivity and aggression by genetically inactivating serotonin 2C receptors subpopulations in these target regions. Loss of behavioral inhibition leading to impulsive and aggressive behaviors is a key factor for suicidal behavior, and this is modulated by the serotonin system. Elucidation of the underlying mechanisms using a sensible model system for impulsivity/aggression could lead to new insights into the complex serotonergic modulation of both normal and pathological brain function, including suicide.
AFSP	2009	Investigating Glial cell line-Derived Neurotrophic Factor (GDNF) in the amygdala of suicide victims	Naguib Mechawar	This postmortem study in suicide completers is aimed at studying cells using the growth and survival factor Glial cell line-Derived Neurotrophic Factor (GDNF) in the amygdala, a brain region previously involved in major depression. The distributions of GDNF, its main receptor (GFR?1) and the GDNF-sensitive dopaminergic innervation will be analyzed in postmortem amygdalae from depressed suicide victims and age-matched controls. Qualitative as well as quantitative aspects of these distributions will be described. To complement this morphological data with a neurochemical correlate, GDNF levels in amygdalar tissues will be also be measured using a highly sensitive assay. Alterations documented in limbic regions of depressed and suicide brains are hypothesized to result from dysregulations in neurotrophin signaling. By providing the first comparative data on GDNF transmission in relation with dopaminergic afferents in the amygdala of depressed suicides and control subjects, this pilot study will pave the way to new research avenues in the neurobiology of suicide.
AFSP	2009	Childhood trauma and suicidal behaviors: the role of the hypothalamic-pituitary-adrenal (HPA) axis in mediating risk	Holly Wilcox	To study the role of Hypothalamic-Pituitary-Adrenal (HPA) axis dysfunction in mediating risk for suicidal behaviors among those exposed to childhood trauma. The potential pathway from childhood trauma to suicidal behaviors will be studied by assessing whether: I) childhood trauma increases risk for HPA axis dysfunction and 2) whether HPA axis dysfunction increases risk for suicidal behaviors via increasing impulsive aggression. The aforementioned associations will be analyzed among offspring of adults enrolled in the Baltimore site of GenRED and GenRED II (Genetics of Recurrent Early-Onset Major Depressive Disorder). Elements of the proposed pathway to suicidal behavior will be elucidated and should constitute potential preventive and therapeutic targets.
AFSP	2009	A prospective study of completed suicide in a large bipolar I disorder sample	William Coryell	To identify clinically important risk factors for suicide in bipolar I disorder and to collect data necessary for genetic association studies of completed suicide. The investigators will collect the names and birthdates of individuals with bipolar I disorder identified in five successive waves conducted by the NIMH Genetics Initiative Bipolar Group. These will be submitted to a National Death Index search to identify those who bave died and their causes of death. This outcome information will be added to the central data file and used to test hypotheses concerning relative risk factors for suicide in bipolar I disorder. Nearly all of the research into risk factors for suicide in the affective disorders has been conducted using groups that either mixed unipolar and bipolar subjects, or that were confined to major depressive disorder subjects. Recent evidence that the risk factors for suicide differ across groups with MDD, bipolar II, and bipolar I disorders indicates that the identification of risk factors peculiar to bipolar I disorder will better inform clinicians in their decisions regarding surveillance and intervention.
AFSP	2011	Investigation of inheritance patterns of polymorphisms in genes regulating the hypothalamic-pituitary-adrenal (HPA axis), in relation to suicidal behavior and its endophenotypes	Danuta Wasserman	To help us better understand the underlying vulnerability towards suicidality at the level of individual variation in the genes involved in regulation of the stress-modulating ?HPA-axis?, with the goal to increase and improve the options available for suicide prevention. Specific (combinations of) genetic variants in genes regulating one of the major stress-responsive neurosystems, the HPA axis, explain in part why certain individuals are susceptible towards performing suicidal acts (as well as displaying the endophenotypes thereof), in addition to, or by interaction with, the exposure to certain adverse life experiences. Identification of novel and verification of previously indicated genetic components of suicidality, holds the promise of delivering significant explanations as to why certain individuals are at risk for suicidality, as well as being seemingly necessary for the future improvement of current population-based interventions and clinical risk-assessement, as well as for construction of reliable diagnostic and treatment tools, respectively, having increased sensitivity and specificity for the suicidality aspect of the individual. Investigation of the predictive risk-assessment potential of the (combinations of) identified genetic variants for identifying suicidal individuals in the clinic, as well as using the novel genetic parameters in the design and analysis of outcomes of various public health interventions performed against suicide in the general population. More detailed studies of the neurobiological mechanism(s) involved with these variants, on the impact on intermediate (endo)phenotypes of suicidal behavior, opening the possibility for better causal understanding and increasing the possibilities in treatments by using drugs.

AFSP	2008	White Matter Integrity and Suicide Risk: Histologic Evaluation of Potential DTI Targets	Andrew Dwork	Our goal is to study autopsy brains in order to localize abnormalities that could be identified on magnetic resonance imaging (MRI) of live patients to assess suicide risk. We will use uniform random sampling to conduct histological analyses of myelin integrity and microglial activation in frontal white matter from autopsy brains that we have already collected from 27 suicide cases and 27 nonsuicide cases matched for diagnosis, age, sex, and medication history. The data will allow us to identify and to localize subtle variations in white matter integrity that may be associated with suicide. We will also examine whether such abnormalities are associated with a history of aggressiveness or violent behavior, characteristics that have been associated with suicide and that may be associated with abnormalities in prefrontal white matter. White matter abnormalities can be recognized in live subjects with high sensitivity by diffusion weighted MRI and magnetization transfer MRI. Finding a white matter abnormality that is associated with suicide could allow the use of MRI to help assess suicide risk in individuals, so that close observation and other intense preventive efforts could be directed towards those individuals for whom they are most needed.
AFSP	2008	Cognitive and biological responses to social stimuli as longitudinal predictors of adolescent girls' suicidality	Mitchell Prinstein	To understand how specific biological and social-cognitive responses to interpersonal stress may be associated with a greater likelihood of future suicidal ideation and behavior among adolescent girls. This study offers a rare opportunity to examine adolescent girls' responses to interpersonal stimuli using a lab? based, experimental paradigm, and a longitudinal design. Adolescent girls will be asked to participate in an established interpersonal stressor during a videotaped lab-based visit, and to complete measures of suicidality at four time points (baseline, 3, 6, and 9 months later). Measures of HPA Axis functioning and vagal tone/suppression will be obtained to measure biological responses, and videotapes will be analyzed and coded to measure social-cognitive responses. Past research has identified stressor domains (i.e., school, family, peers) associated with suicidality, but little research has addressed how or why these stressors lead to adolescents' decisions to engage in suicidal behavior. By examining both social-cognitive and biological responses to interpersonal stimuli, this study offers an integrative model with direct implications for preventive interventions; it will be possible to more accurately identify adolescents at risk and to modify processes that mediate the link between stressful events and suicidal behavior.
AFSP	2008	Measuring Suicidality in Adolescent Major Depressive Disorder Using fMRI	Michael Stevens	The aim of this study is to use functional magnetic resonance imaging (fMRI) to describe differences in emotion-related neural activity between sub-groups of previously suicidal depressed adolescents who have different profiles of suicide attempt histories in order to replicate and extend previous adult results. The study will involve recruitment, standardized psychiatric evaluation, and fMRI assessment of 30 adolescents ages (12-19) with Major Depressive Disorder and history of suicide and a demographically matched control group of 15 healthy teens. The MDD sample will be split evenly between those who have a history of impulsive suicide behavior and those who do not We will compare groups on brain activity elicited by an emotion provocation paradigm that measures the function of neural systems which are theoretically relevant to MDD and known to function abnormally in MDD adults. This will be the first fMRI study to examine brain activity in suicidal teenagers. The findings will greatly increase our understanding of now differences in brain function may confer risk for specific types of suicidal behavior.
AFSP	2008	Cognitive correlates of suicidality in late-life depression: identifying targets for prevention and treatment	Katalin Szanto	In the proposed study we aim to explore what makes elderly, who have the highest suicide rate in the U.S., vulnerable to suicidal behavior. More specifically we will explore the thinking patterns of suicidal elderly. Based on existing literature and our own observations, we believe that suicidal elderly may be impaired in three domains of thinking: problem solving, decision making, and abilities needed for social interaction. We will study these in two groups of elderly - 60 suicidal depressed patients (who recently attempted suicide) and 60 depressed non-suicidal patients (no lifetime history of suicidal ideation or attempt). The study will involve specific neuropsychiatric and clinical evaluations in addition to comprehensive psychiatric, physical, and suicide assessments. The need for targeting suicidal behavior in this high risk group is highlighted, not only by the high rate of such behavior among this population, but also by the fact that in our previous study we found that suicidal depressed elderly had significantly lower treatment response rates than non-suicidal ones and needed twice as long time to get well even when they received state-of-art antidepressant treatment and interpersonal psychotherapy 1. Understanding specific abnormalities in thought patterns of suicidal elderly could facilitate better assessment and identification of vulnerable elderly and will help create new psychotherapeutic treatments.
AFSP	2009	Neurobiology of inhibitory control in late-life suicide	Alexandre Dombrovski	Suicide attempts are far more likely to result in death in the elderly than in younger people; a suicide attempt follows a decision which the rest of us see as unfortunate, and recent studies indicate flaws in suicide attempters' decision-making; using brain imaging, we will try to understand whether elderly with depression who have attempted suicide are impaired in their ability to use brain circuits involved in making decisions compared to similarly depressed elderly without past suicide attempts. After a careful assessment of their mental health and medical history, past suicidal behavior, and cognition, 40 elderly depressed participants (20 with past suicide attempts and 20 without past attempts or suicidal ideation) will undergo a non-invasive brain scan (functional magnetic resonance imaging, fl\1RI) as they make decisions guided by positive or negative feedback. We will examine whether elderly with past suicide attempts fail to flexibly adjust their decision-making and show altered activity of the brain circuit that is critical to decision-making (ventral prefrontal-striatal circuit). The two comparison groups will be similar on the severity of depression, burden of physical illness, and global cognitive impairment. Decision-making is not currently explicitly addressed by any psychotherapy or medication regimen for treating suicidal elderly, though some medications currently used in depression and Parkinson's disease affect neurotransmitter systems (e.g., dopamine and serotonin) involved in decision-making. This study could suggest not only the importance of decision-making mechanisms but what specific brain circuits to target in the development of new interventions for older people at risk for suicide.
AFSP	2009	Childhood traumatic stress and adolescent girls' suicidality: A longitudinal examination of psychophysiological mechanisms	Nicole Heilbron	The primary aim of this study is to examine how the psychobiological effects of childhood trauma may be associated with an increased risk of suicidality among adolescent girls. The proposed study offers an innovative methodology to examine physiological mechanisms believed to underlie associations between childhood trauma and suicidality. Measures of (1) fear-potentiated startle reactivity, a psychophysiological measure offear reactivity, and (2) prepulse inhibition of startle (PPI), a psychophysiological index of information processing, will be analyzed to examine stress reactivity and neurocognitive functioning. Participants will complete measures of childhood maltreatment, traumatic stress, and suicidality at the baseline assessment and at two additional time poi nts (3 and 6 months later). Although childhood trauma has been established as a robust predictor of suicidal ideation and suicide attempts, relatively few studies have explored how physiological adaptations to childhood traumatic stress may be related to adolescent suicidal behaviors. This longitudinal study will inform suicide prevention efforts by examining biological pathways between childhood trauma and suicidality, thus contributing to knowledge of suicide risk factors and highlighting possible targets for future prevention and intervention programs.
AFSP	2009	Bio-behavioral markers of affect regulation in teen suicide attempters vs non-suicidal self-injurers	Daniel Dickstein	The goal of our study is to identify how adolescents who have attempted suicide differ from those who engage in non-suicidal self-injury (such as cutting themselves) with respect to how they handle their emotions. We will study three groups of teens (ages 13-17years): (1) teens who have attempted suicide 2 or more times, but who do not engage in non-suicidal self-injury (cutting), (2) teens who cut/self-injure, but who have not attempted suicide, and (3) typically-developing teens without psychiatric illness. The reason to study multiple suicide attempters (MSAs) is because they are a more homogeneous, uniform group who are more likely to engage in future suicidal behavior compared to first-time attempters (Esposito 2003). To identify bio-behavioral markers that separate teen suicide attempters from those who cut themselves, we will measure: (a) psychological factors (including self- and parent ratings of suicidality and non-suicidal self-injury, psychiatric disorders and early life trauma/neglect, behavior problems including aggression, and substance use) and (b) performance on computerized behavioral games (including identification of facial emotions, cognitive function (e.g., decision-making, attention, executive function), response to interpersonal collaboration and conflict, and associations between oneself and suicidality). While many have theorized that problems of affect regulation underlie both teen suicide attempts and nonsuicidal self-injury (cutting), our study will be the first to objectively test these theories by using psychological assessments and computerized behavioral tasks, each tapping into an aspect of affect regulation, to identify biobehavioral markers of teen suicide and cutting. Such bio-behavioral markers of teen suicide and cutting identified by our study will contribute to suicide prevention by (1) improving what is known about the underlying neurobiology of teen suicide and cutting, and (2) providing critical preliminary data for future functional magnetic resonance imaging studies of teen suicide and self-cutting, and (3) resulting in improved identification and treatment of teens at risk for suicidal behavior by using such bio-behavioral markers to augment clinical history in the psychiatric care of teens, and thus in the future to prevent teen suicides.
AFSP	2009	Diffusion tensor imaging (DTI) studies of suicidal behavior	Emil Coccaro	The key aim of this study is to examine the structural integrity of white matter tracts in the brains of individuals who have a history of attempting suicide. Individuals with Borderline Personality Disorder (BPD) with and without a history of suicide attempts will be compared to healthy controls with Diffusion Tensor Imaging (DTI). This form of neuroimaging examines the integrity of white matter tracts and localizes differences in the integrity of white matter tracts among comparison groups. Demonstration of abnormalities in white matter tracts in individuals with histories of suicide attempts will highlight the role played by white matter integrity, as well as the nature of the neuronal circuits, that may be involved in suicide risk. Such work will enhance our understanding of neuronal pathways in individuals with histories of suicidal behavior.

AFSP	2010	Dysfunction of prefrontal cortex, cognitive control and suicide risk in schizophrenia	Michael Minzenberg	The aim of this study is to determine if problems with a part of the brain called the prefrontal cortex, and associated inability to control one?s behavior (called cognitive control), is a determinant of suicide risk in patients with schizophrenia. This study will involve testing patients who are in the first year of schizophrenia with functional magnetic resonance imaging (fMRI) while they perform a task that measures cognitive control. We will also evaluate these patients with clinical measures of suicide risk, depression, impulsivity, and the characteristic symptoms of schizophrenia. We predict that these patients will show impaired activity in the frontal cortex of the brain, and related problems in the control of their behavior, which will be associated with the degree of suicide risk. The brain dysfunction that underlies the elevated suicide risk in schizophrenia patients remains uncertain, despite a wealth of knowledge concerning neural and psychological disturbances in this illness. Identification of how brain dysfunction relates to elevated suicide risk will be critical to the development of new treatments to minimize this risk.
AFSP	2010	Cognitive Control and Emotion Processing Markers of High-Intent Suicide Ideations in Adolescents	Fadi Maalouf	This study aims at investigating cognitive control of emotion processing, an important aspect of emotion regulation, in adolescents with high-intent suicide ideation as compared to non-suicidal and healthy adolescents using computerized behavioral tasks and self-report measures. We propose to recruit 30 adolescents with major depressive disorder and high-intent suicide ideation (defined as suicide ideation with a plan within the year preceding the assessment), 30 adolescents with no history of suicide ideation and 30 healthy controls. Subjects will be interviewed, given self-reports and administered computerized behavioral tasks to assess various aspects of cognitive control, emotion processing and the interface of the two. We aim at comparing performance of the three groups on these tasks and investigating whether they predict worsening of suicidal ideation or suicide attempt at a nine-month follow-up. This will be the first study to examine the cognitive and emotion processing profile in young high-intent suicide ideators and how it longitudinally predicts suicide attempts. The cognitive and emotion processing deficits, once identified in this population, may be targeted by future interventions to help prevent the potentially fatal outcome of a suicide attempt.
AFSP	2008	Impact of antidepressant discontinuation on risk of suicide attempt	Robert Valuck	This study will assess the risk of suicide attempt in relation to stages and duration of antidepressant treatment, focusing on discontinuation of therapy and its impact on risk. Data come from the largest patient-centric longitudinal integrated claims database of managed care enrollees in the U.S. from 1998-2006. From that national sample, we obtained an exceptional subsamp of all patients who ever attempted suicide by age and gender (approximately 20,000 individuals). We will identify stages of antidepressant treatment-pre-initiation, initiation, titration, maintenance, and discontinuation for patients who attempted suicide, focusing on the nature and timing of discontinuation relative to the risk of suicide attempt. Recent efforts to assess the impact of antidepressant use on risk of suicide attempt focused on antidepressant use in general terms (any vs. none), and suggested that longer treatment reduces risk. A gap remains in understanding the risk associated with the discontinuation of antidepressants, which promises targets for improved clinical practice to combat heightened risk for suicide attempt.
AFSP	2008	A Pilot Study of the Effect of Oxytocin on Self-Aggression	Royce Lee	This study aims to measure the effect of an acute dose of intranasal oxytocin on a laboratory model of selfaggressive behavior, and compare this with intranasal placebo administered in double blind, randomized fashion. Subjects in this study will be adult volunteers with a history of major depressive episode and history of suicide attempt. Subjects will be randomized to receive either placebo or oxytocin. Under controlled laboratory conditions, intranasal drug will be administered, followed by performance of the Self-Aggression Paradigm, a laboratory model of self-aggressive behavior. This study will provide vital preliminary data regarding a novel approach to pharmacological suicide prevention, under safe laboratory conditions. This could provide the first step towards the development of a rational pharmacological approach towards preventing suicide in patients identified to be clinically at high risk for suicide.
AFSP	2011	Paliperidone and lithium in the treatment of suicidality: treatment indication and epigenetic regulation	Richard Shelton	This study aims to identify an efficient pharmacotherapy for the acute management of suicidality and the epigenetic regulation associated with the treatment. The primary objective of this study is a clinical trial to compare the efficacies of antipsychotic paliperidone and the mood stabilizer lithium in the acute management of suicidality in patients with depression. In this 12-week study, subjects with diagnosis of major depressive disorder, currently experiencing severe depression with suicidality, will be treated with a SSRI antidepressant in addition to being randomized to paliperidone, lithium, or placebo. The secondary but equally important objective of this study is to begin to test the epigenetic regulation of paliperidone and lithium during treatment of suicidality. This study uses a combined clinical and translational approach to compare the efficacy of antipsychotic paliperidone and mood stabilizer lithium in the acute treatment of suicidality and to determine their effects in epigenetic regulation. Therefore, the study will directly contribute to suicide prevention as an immediate clinical need as well as new treatment development.
AFSP	2008	Feasibility of agency-wide training in community-based cognitive therapy for suicide attempters	Aaron Beck	The aims of this pilot study are 1) to conduct a preliminary investigation of the outcomes and sustainability of Cognitive Therapy (CT) for the prevention of suicide when administered with case management to suicide attempters in community mental health agencies, 2) to develop means of assessing outcomes using administrative data and assessment instruments that can be administered in community mental health settings, and 3) to assess the feasibility of an organization-level intervention to promote the dissemination and sustained adoption of CT in community settings. This exploratory study will 1) Compare the outcomes of the CT for suicide treatment package as implemented on an agency? wide basis to outcomes of prior efficacy and effectiveness studies using CT for suicide and 2) to examine outcomes of the implementation at the therapist and agency and level. Suicide attempters will begin CT within three days of their discharge from the hospital, and will also receive case management from city mental health agencies. Suicide attempters will begin CT within three days of their discharge from the hospital, and will also receive case management from city mental health agencies. Barriers to the implementation and sustained use of CT within the agency during a follow-up period will also be assessed. The findings will provide valuable information to inform a larger clinical trial that will use a research design that imposes fewer artificial elements upon the therapeutic process than prior outcome research, and will explore the use of administrative data to assess "real? world" treatment outcomes. The findings will also provide information that is essential to determining and addressing the barriers to the dissemination of cognitive therapy in community settings, which may ultimately lead to more widespread consumer access to CT for suicide prevention.
AFSP	2008	Suicidal patients seeking help at an emergency room: Pilot trial of a "next-day appointment" outpatient treatment	Katherine Comtois	The aim of this study is to improve care for patients following an emergency room admission for suicidal behavior, both to resolve their suicide ideation and prevent subsequent admissions to the emergency room and reduce primary care visits. This study evaluates a model of care, the Collaborative Assessment and Management of Suicidality (CAMS), developed by co-investigator David Jobes, Ph.D. This study first proposes to train community mental health clinicians to use the CAMS model with patients referred for next-day appointments following an admission to the emergency room for suicidal behavior. Then a pilot randomized controlled trial of CAMS + usual care for next-day appointments versus usual care alone will be conducted to evaluate CAMS? effectiveness in reducing suicidal ideation and subsequent emergency room admissions and medical visits. Recent studies have shown that patients admitted to an emergency room for suicidal behavior had an approximately 30-fold to 66-fold increase in risk of suicide when compared with the general population. It is critical that promising interventions such as CAMS are developed and evaluated to prevent suicide in this high-risk population.
AFSP	2008	Attachment-based family therapy for suicidal and depressed lesbian, gay and bisexual adolescents: a treatment development study	Gary Diamond	Revise the Attachment-Based Family Therapy (ABFT) manual so that it articulates specific clinical issues, therapeutic challenges and intervention strategies pertinent to working with lesbian, gay and bisexual suicidal and depressed adolescents. First, a treatment development team comprised of the originators of ABFT, experts on suicide among LGB youth and experts in counseling LGB youth, will conduct an initial revision of the ABFT treatment manual and accompanying adherence measure. These revisions will be based on the team's collective knowledge-base and clinical experience, the extant literature on counseling LGB youth, and the observation of videotaped sessions from prior ABFT cases with LGB suicidal and depressed youth. Then, we will conduct an open, pilot study during which we will treat 10 suicidal and depressed LGB teenagers using the revised ABFT-LGB manual in order to evaluate the feasibility and acceptability of the treatment, as well as fine-tune intervention strategies and measurement procedures. Lesbian, gay and bisexual adolescents are at increased risk for suicide. This study represents a first step in developing an empirically supported therapy for suicidal and depressed adolescents which is sensitive to the unique needs of, and effective with, sexual minority youth.
AFSP	2008	Exercise prevents negative behavioral effects of acute SSRIs: neurobiological mechanisms	Benjamin Greenwood	The purpose of the proposed studies is to determine the neurobiological mechanisms by which exercise prevents the negative behavioral effects (such as anxiety and cognitive deficits) produced by acute treatment with selective-serotonin reuptake inhibitors (SSRIs). Similar to the effects of acute SSRI administration in humans, a single systemic injection of an SSRI produces anxiety and learning deficits in a rat model; possibly by sensitizing a specific brain circuit involving serotonin neurons. The proposed studies will test the role of individual components of the proposed neural circuit in the behavioral effects of acute SSRI treatment. Additionally, we will determine if exercise prevents the anxiety and learning deficits produced by acute treatment with SSRIs by altering the effects of the SSRI on this same neural circuit. Results will shed light on the potential role of exercise as an adjunct therapy to SSRIs in order to ameliorate the deleterious behavioral effects present during the onset of pharmacotherapy for depression or anxiety; thereby increasing adherence to SSRIs and reducing the risk of suicide. Completion of the proposed studies will elucidate neurochemical mechanisms underlying the behavioral effects of SSRIs and exercise, thus leading to novel treatment strategies for reducing depression or suicide.

AFSP	2009	An adjunctive intervention to reduce suicide risk in patients with bipolar I depression	Lauren Weinstock	The aim of this study is to develop and evaluate the preliminary efficacy of an adjunctive intervention targeted toward the reduction of suicide risk in patients with bipolar I depression, tentatively named the Coping Long-Term with Attempted Suicide Program for Bipolar Disorder (CLASP-BD) ? an innovative, multi-modal intervention that integrates and administers cognitive-behavioral strategies and family support via telephone. Forty individuals with bipolar I depression, who have been hospitalized secondary to a suicide attempt, will be recruited to participate in the proposed study. Along with an identified significant other, patients will be randomized to receive either Treatment as Usual (TAU) or TAU + CLASP-BD over the 6-month period following hospital discharge. Assessments of suicidal ideation and behavior, as well as mood symptomatology and psychosocial functioning, will be conducted at hospitalization, 3 months postdischarge, and 6 months post-discharge. Results from the proposed study will contribute to the larger aim of suicide prevention by providing information regarding the preliminary efficacy of a novel treatment designed to target suicidal risk in a particularly high risk group of patients ? those with bipolar I depression. These data, if promising, will inform ongoing development of a suicide risk reduction program for bipolar disorder that can be readily implemented across a variety of clinical and community settings.
AFSP	2009	Examination of a relapse prevention task in preventing future suicide attempts	Megan Spokas	The proposed study will examine whether the successful completion of the relapse prevention task in the context of cognitive therapy for suicide prevention can predict which patients are likely to benefit from cognitive therapy in terms of their reduction of the subsequent reattempts. This could also help to identify those patients who, on the basis of inadequate completion of the task, are likely to reattempt, and thus, should receive more than the standard ten sessions of cognitive therapy. Previously recorded cognitive therapy sessions will be examined to assess if a relapse prevention task was completed and if so, the quality of the intervention will be rated. Analyses will examine whether the completion or quality of the relapse prevention task in the cognitive therapy relate to treatment outcomes throughout the 12 to 18 month follow-up period, specifically examining the incidence of suicide attempts, and ratings of suicidal ideation, depression, hopelessness, and problem-solving. Several aspects of the relapse prevention task, such as effective use of imagery, identification of key cognitions and behaviors related to the previous attempt, review of alternative adaptive coping skills, change in hopelessness, and decrease in negative affect, will be examined as they relate to outcome. Findings of the proposed study can inform suicide prevention efforts by identifying a relapse prevention task as useful component of cognitive therapy for reducing future suicide attempts among those who have recently attempted suicide. If completion of the task is associated with a reduction in future suicide attempts, certain aspects of the intervention may be identified as particularly related to positive outcomes, which can contribute to refining the intervention for use in various clinical contexts, including inpatient psychiatric units, group settings, and outpatient psychotherapy.
AFSP	2009	Development of a manual for patients with schizophrenia and suicidality	John Kasckow	The key aim of the study is to develop a recovery manual for patients with schizophrenia and suicidality, to administer this to patients and determine feasibility of use and degree of acceptance. The study will involve the design and development of a manual for patients with schizophrenia and suicidality utilizing advice from a panel of five experts in the fields of suicidality and schizophrenia. The manual will be distributed to 25 inpatients with schizophrenia and a history of suicide attempt and/or hospitalization for a suicide attempt. We will then administer a questionnaire to determine how useful the manual is for the patients. Future research will determine how this manual can serve as an enhancement to inpatient and outpatient treatment for patients with schizophrenia and suicidality. In addition, it should help lead to the development of a clinician m:l!lual for use by clinicians who treat this population of patients.
AFSP	2010	The relationship between positive mastery recollections and hopelessness in older adults	Sunil Bhar	The aims of the study are to develop and evaluate a one-session intervention for reducing hopelessness, a key risk factor for suicide, in older adults. Older adults with high levels of hopelessness will be randomized to two conditions: An intervention condition involving a personal history interview and mastery memory activation task, or to a control condition involving the personal history interview without the mastery memory activation task. The mastery memory activation task involves participants recollecting memories about their past successes at solving problems. Participants will complete self-report measures of hopelessness and problem-solving efficacy (a) before and after completing the intervention or control procedures, as well as (b) I month and 2 months following the procedures to determine the sustainability of effects related to the intervention. The study explores whether recalling past problem solving successes is feasible for older adults, and is associated with some improvement in their levels of hopelessness, a validated risk factor for suicide in older adults. By identifying the importance of such an intervention for reducing hopelessness in older adults, this study provides a platform for future research to investigate (a) the mechanisms of the outcomes associated with the intervention, (b) the long-term stability of these therapeutic outcomes and (c) the efficacy of various delivery options for the intervention (e.g., in primary care settings, as a component of a broader treatment approach for older patients at risk for suicide).
AFSP	2010	Safety Planning Intervention for Suicidal Individuals Who Contact Crisis Centers	Barbara Stanley	Crisis hotlines receive a significant proportion of their calls from suicidal individuals and, in fact, for many of these callers, this is the only intervention they receive either due to their unwillingness to seek treatment or the unavailability of treatment. Therefore, maximizing the clinical utility of the hotline calls is of utmost importance. This project, in collaboration with the National Suicide Prevention Lifeline, will develop and test a safety planning manual for use in crisis centers with calls from suicidal individuals. The study will develop and test the efficacy of a safety planning intervention for suicidal individuals on crisis hotlines. Through the collaboration with the National Suicide Prevention Lifeline (Dr. John Draper, Director), we will select two matched crisis centers to be part of this study, one center will implement the safety planning intervention and the other will serve as our control and will continue doing their calls as usual practice. Both centers will enroll participants in the trial and we will give our study measures at both sites. Efficacy will be evaluated in several ways: perceived utility of the safety planning mechanism by crisis workers and callers; whether or not the plan was used in times of distress; and reduction in suicidal behavior. If our findings are positive, this intervention has great potential to for immediate impact in the reduction of suicidality in a population that generally receives minimal treatment but is at high risk for committing suicide. When individuals are in suicidal crises, their ability to see other options diminishes substantially. If they have an already developed and rehearsed plan of what to do should they become suicidal, they may be more likely to survive suicidal crises. Training staff on the implementation of a safety planning process is a straightforward process and does not require significant investment in time and effort. Thus, this intervention holds promise as a cost effective and easily transportable intervention for an important point of intervention that has received little research attention.
AFSP	2010	Factors Associated with Suicide in Youth and Adults with Eating Disorders	Cynthia Bulik, PhD, FAED	Individuals with anorexia nervosa are over 50 times more likely to commit suicide than their age matched peers. Risk is elevated in other eating disorders as well. This investigation will link extensive diagnostic information obtained from the Swedish Twin Registry to the Swedish Cause of Death Register and Hospital Discharge Registry in order to explore prospectively and concurrently measured personality, environmental, and psychopathological factors associated with suicide attempts and completed suicide in individuals with eating disorders. The research plan is to prospectively identify assessed risk factors and correlates of suicide attempts and completed suicide in individuals with eating disorders. Analyses will focus on identifying genetic and environmental factors influencing liability to eating disorders and suicide in order to assist with identifying individuals who are most at risk. By enhancing our ability to identify individuals at risk, these results will provide guidelines for clinicians and families to enhance their assessment and detection of risk factors. Our unique ability to assess risk factors across age cohorts will also allow tailoring of any resultant recommendations by age.
AFSP	2010	An fMRI Study of Affect Arousal and Cognitive Control in Suicidal Subjects with Borderline Personality Disorder	Paul Soloff, MD	Suicidal patients are characterized by deficits in emotion regulation and executive cognitive function, increased vulnerability for impulsive and aggressive behaviors, structural and metabolic brain abnormalities in areas of prefrontal cortex. These deficits appear highly interrelated and may constitute a neurobiological diathesis to suicidal behavior independent of diagnoses. This study will use functional Magnetic Resonance Imaging (fMRI) in subjects with borderline personality disorder and histories of medically significant suicide attempts to define the neural basis by which affective arousal impairs executive cognitive functions and contributes to impulsive suicidal behavior. Twenty female borderline personality disorder subjects, 10 attempters and 10 non-attempters, will be compared to 10 control subjects on three fMRI cognitive performance tasks, each incorporating emotional stimuli (positive, negative or neutral faces or pictures). The cognitive tasks engage the function of brain regions previously shown to be structurally or metabolically abnormal in borderline personality disorder. We will assess the degree to which affective arousal impairs cognitive task performance, and compare patterns of neural activation reflecting excitation and inhibition in suicidal and non-suicidal borderline personality disorder subjects with healthy control subjects. This study will characterize the neurobiological basis of the borderline patientâ€™s failure of inhibitory control over emotion and behavior at times of affective stress and contrast subjects with medically significant suicide attempts with non-attempters and control subjects. Identification of dysfunctional brain networks using readily available fMRI techniques may provide a biological marker for patients at highest risk for impulsive suicidal.

AFSP	2011	GABA System Genes and Suicidal Behavior in Psychiatric Disorders	Clement Zai, PhD	The key objectives of the proposed study are to investigate DNA polymorphisms in genes associated with the GABA neurotransmitter system for association with suicidal behavior, and to determine the potential functional significance of these polymorphisms. The applicant hypothesizes that selected GABA system genes will be associated with suicide risk, that DNA resequencing of these genes will reveal novel variants that will determine gene expression levels, and that combination of variants may interact to contribute to risk variants for suicide. This research will genotype SNPs across several GABAergic related genes, including GAD, the GABA transporter and three GABA receptor subunits. These genes were chosen based on previous associations with mood disorders. In addition, targeted multiplexed resequencing of the 10 kb region upstream of each of the five selected candidate genes will be conducted to identify variants within regions of these genes that might contribute to changes in gene expression. Two samples consist of bipolar patients and a third schizophrenics. One bipolar population has 352 subjects with 86 attempters, the second has 450 subjects and 122 attempters and the schizophrenic population has 231 subjects with 81 attempters. There are postmortem brain tissue samples from Brodmanâ€™s area 46 (Stanley Foundation) from 41 schizophrenic subjects (10 suicide) and 44 bipolar subjects (22 suicide). In addition, the investigator plans access to additional schizophrenic, bipolar and depressed brain tissue from the Harvard Brain collection and the Stanley Foundation brain collection.
AFSP	2010	Neural Substrates of Emotion Dysregulation and Self-Harm in Suicide Attempters	Michael McCloskey, PhD	The study will investigate fMRI signals from borderline personality disorder females who will engage in tasks during the MRI designed to elicit emotional responses relating to self aggression and suicidal behavior. This work will provide the brain circuitry associated with the failure to regulate negative emotions and the initiation of self-harming behavior in a group of previously suicidal women with borderline personality disorder. While undergoing the fMRI scan the individuals will be subjected to emotionally evocative pictures and a stimulus emulating self-harm. The difference between suicidal and non-suicidal subjects in the limbic and cortical areas of brain activation will be compared to identify patterns of brain activation associated with suicide risk. This is an important investigation targeting core issues of the neurobiology of suicide. No one has done this before, thus highly innovative.
AFSP	2010	Prefrontal and Genetic Determinants of Suicidality in the Elderly with Cardiac Di	Arthur Simen, MD, PhD	Aging and medical illness are important risk factors for the development of suicide and suicidal behaviors and thinking. Suicide risk is higher among the elderly than any other age group. Aging is associated with multiple psychosocial and biological stressors including medical illness, as well as changes in cognitive function that is governed by the prefrontal cortex. Studies to date have established the importance of poor neurocognitive function and medical illness in increasing risk for suicide in the elderly, but the causal mechanism remains unclear. This research program will test for the individual differences in suicidal ideation in the elderly which are due in part to individual differences in cognitive function, and that adaptive coping and hopelessness mediate the relationship between cognitive function and suicidal ideation. The research will examine the individual differences in prefrontal cortex function which are largely determined by genetic variation in HCN1, a gene involved in determining prefrontal cortex function, will be related to prefrontal cortex performance at the time of the first assessments in patients and their spouses. Prefrontal cortex cognitive function will be assessed using the CANTABeclipse program, a very well characterized and standardized computerized neuropsychological test package. This research will be done on a particularly high risk population, elderly patients with acute coronary syndrome (ACS) and their spouses. This work will serve as the foundation of a translational research program examining the multifactorial etiology of suicidal ideation in the elderly.
AFSP	2010	Predicting Suicidal Behavior: Internal Consistency and Predictive Validity of the Suicide Trigger Scale	Igor Galynker, MD, PhD	Currently available tools have only modest predictive power for identifying individuals at the greatest risk for future suicide attempts. The goal of this project is to develop a scale to operationalize and measure a clinically identified emotional â€œtrigger stateâ€that puts individuals with suicidal ideation at increased risk of acting on these ideations. In patients who attempted suicide we have identified a clinical â€œtriggerâ€state (termed suicidal trigger state) which preceded the suicide attempt and is characterized by fear of entrapment, dread, confused thinking, pain or pressure in the head, and a sense of disconnection from reality. In our preliminary work we have developed the Suicide Trigger Scale (STS) to measure this state and have found that patients with higher scores on the STS are more likely to have had prior suicide attempts while those with low scores are more likely to have had only suicidal ideation. We now propose to further develop and refine the STS in order to determine its reliability in a high-risk patient population drawn from an emergency room setting and to establish its ability to predict future suicide attempts in this setting. This research is building on their early results with STS, further refining it into an instrument that can be used in office settings or in emergency rooms to directly identify patients who are at greatest risk of suicide and whose lives can be saved by timely intervention.
AFSP	2010	Development of a Treatment Protocol for Suicidal Latino/a Adolescents	Yovanska Duarte-Velez, PhD	Suicide is the third leading cause of death in 10 to 24-year-old Latinos/as in the U.S. and the third in 14 to 24-year-olds living in Puerto Rico. Research on suicidal behavior with Latino/a adolescents is very limited. Latino/a adolescents are at an increased risk for suicide relative to White youth and are the fastest growing ethnic minority in the U.S. Serious disparities in the delivery of mental health services to the Latino population have been evidenced. No culturally informed and evidence based treatment has been developed for suicidal Latino/a adolescents. The aim of the proposed study is to develop and pilot test a culturally competent treatment manual for suicidal Latino/a adolescents. Adaptations to a Cognitive Behavioral Therapy (CBT) treatment manual, previously utilized with depressed Latino/a adolescents will be made to address suicidal behavior. Initial adaptations and the development of new modules will be conducted based on previous studies. Adaptations will be based on quantitative and qualitative data from a clinical sample of adolescents with suicidal thoughts and depressive symptoms and outcomes from former studies with suicidal Latino/a adolescents, initial adaptations and the development of new modules will be conducted based on previous studies. In a second phase, the treatment protocol will be tested with twelve adolescents referred for suicidal behavior (suicide ideation or suicide attempts) to refine and assess the protocolâ€™s feasibility. This study represents an important step towards developing a treatment that could benefit Latinos/as in Puerto Rico and the U.S., because it will produce a bilingual culturally sensitive treatment protocol for suicidal adolescents.
AFSP	2010	Epidemiology of Undetermined Deaths: Prevalence and Patterns of Misclassified Suicides	Nathalie Huguet, PhD	Suicide is a major public health problem. In the U.S., over 34,000 decedents were classified as suicides; suicide statistics are not accurate and the â€œtrueâ€rate of suicide is unknown. Evidence suggests that suicide rates may be underestimated by as much as 30%. Many, if not most, deaths classified as undetermined are considered â€œhidden suicides.â€Many studies have demonstrated that certification of death, as undetermined, is not random. However, most of these studies relied exclusively on death certificate records limiting our understanding of the variations in death certification and of its impact on suicide rate estimates. The National Violent Death Reporting System (NVDRS) offers a unique opportunity to assess variations in death certification using characteristics other than the one available on the death certificate. The NVDRS provides a wide array of suicide risk factors and recent population data. The overall objective of this project is to assess the epidemiology of undetermined deaths and to estimate the rate of misclassified suicides. This study will describe decedents whose cause of death was classified as undetermined and compare them with suicide decedents using the NVDRS. The project will estimate the rate of suicides misclassified as undetermined deaths for specific subgroups of the population. This project will enhance our understanding of death certification and the potential impact of misclassification on suicide surveillance efforts. It is essential to delineate whether the variations in certifying decedents as undetermined deaths are random or socially patterned because the degree to which suicides are valid may differ in certain groups of the population which may result in less effective suicide preventions for these specific groups.
AFSP	2010	Evaluation of a Gatekeeper Training Program as Suicide Intervention Training for Medical Students	Shay-Lee Bolton, MSc	The main objective of the proposed study is to evaluate the efficacy of a gatekeeper training suicide intervention program, Applied Suicide Intervention Skills Training (ASIST), in improving medical studentsâ€™ knowledge about suicide intervention, impact of attitudes on someone at risk for suicide and competent use of intervention skills to recognize risk and intervene effectively compared to medical education as usual. Findings from previous studies have demonstrated a significant positive effect of gatekeeper training on suicide prevention attitudes, skills and knowledge. General studies in medical education reveal that students who have been able to practice, observe and receive feedback in small groups showed an improvement in skills and confidence over those who were given didactic teaching only. This research project will use a randomized-controlled trial design. Questionnaires and objective structured clinical examinations using simulated patients will be completed at three time points: 1) before training, 2) after training and 3) at one year following the training. Medical studentsâ€™ clinical skills in recognizing risk and intervening with simulated patients, as well as knowledge about suicide intervention and the impact of attitudes on someone at risk for suicide will be evaluated. The current research will indicate whether training in suicide intervention for medical students can increase their ability to detect a suicidal individual and intervene over training as usual. Such training could allow for more efficient detection and management of suicide risk in vulnerable patients, particularly in non-psychiatric settings.
AFSP	2010	Differential microRNA Expression in the Prefrontal Cortex of Suicides	Gustavo Turecki, MD, PhD	This state-of-the-art genomic study will identify Âµ RNA differences in prefrontal brain cortex of depressed suicides as compared to appropriate controls. Âµ RNAs are non-coding, small, single stranded, 21-base RNA transcripts that play an important role in the posttranscriptional regulation messengerRNA (mRNA) thus playing a major role in the regulation of a large number of genes, including those expressed in the brain. A global profiling of expression patterns of Âµ RNA levels in the orbital prefrontal cortex in 40 depressed suicide subjects and 40 psychiatrically normal controls will be done. The results of the global profiling analysis will be used for bioinformatics analysis to determine specific Âµ RNA targets for validation, subsequent investigation and functional characterization. This study will facilitate our understanding of molecular mechanisms associated with the regulation of brain gene activity and how these mechanisms could be related to major depression and suicide. Âµ RNA may, in fact, be an important regulating mechanism in the biological processes associated with suicide, and could lead to new biological markers, therapeutic targets and ultimately prevention.

AFSP	2010	Alcohol as an Acute Risk Factor for Suicide Attempts: A Case-Crossover Pilot Study	Courtney Bagge, PhD	Given the clinical and public health significance of suicide, there is considerable interest in identifying acute factors that increase the risk for suicide attempts. As such, the aim of the current research is to characterize the role of acute alcohol use within suicide attempts. It is well recognized that drinking often surrounds suicide attempts; approximately 40% of adult suicide attempters ingest alcohol prior to their attempt. However, the majority of research on drinking and suicide is descriptive in nature, and, thus, cannot speak to their relation. The aim of this study is to determine whether suicide attempters are more likely to drink on the day of their attempt compared to a day when they did not attempt suicide, taking into account other factors that vary from day-to-day. Eighty individuals presenting for medical evaluation after a suicide attempt will complete a battery of questionnaires and interviews assessing participants' experiences, substance use, and mood during the 48 hours prior to their suicide attempt. Analysis of this data will test the unique role of proximal alcohol use in suicide attempts. It is anticipated that the pilot study's results will help fill an important gap in our knowledge and inform suicide prevention efforts.
AFSP	2010	BDNF Promoter Methylation and Suicidal Behavior in Bipolar Disorder	John Strauss, MD, MSc	This research grant will investigate methylation patterns in the brain-derived neurotrophic factor (BDNF) gene. Published research has reported that the BDNF gene and its products have been associated with suicidal behavior. Several lines of evidence point to BDNF as a factor in mood disorders and specifically bipolar disorder illnesses, where there are greater percentages of suicides or attempts. Epigenetic factors may play a role and a mechanism for epigenetics is the modifications in gene expression that are controlled by heritable, but potentially reversible by changes in DNA methylation. Peripheral lymphocyte DNA methylation will be studied for genetic and epigenetic association with suicidal behavior. Two sources of variation at the BDNF locus will be analyzed: SNP variation (sequencing) and quantitative methylation using mass spectrometry. A subset of subjects of a genome-wide association study will be used for the lymphocyte samples. There will two sample groupings. Each will contain three separate subjects groups of 20 subjects each, for a total of 60 in both Sample I (bipolar depression with and without suicide attempts and matched health controls) and II (child-onset mood disorder bipolar depression prior to 17 years of age with and without suicide attempts and matched health controls). A deeper understanding of the genetic and neural substrates of behavior is essential for the next generation of preventive interventions, ranging from the role of biomarkers and endophenotypes in identifying those most in need of prevention to the longitudinal environmental sensitivity of neural systems.
AFSP	2010	Genetic and Clinical Predictors of Suicidal Behavior in Veterans Returning from Iraq and Afghanistan	Rachel Yehuda, PhD	Recently deployed combat veterans serving in Operation Iraqi Freedom (OIF) in Iraq or Operation Enduring Freedom (OEF) in Afghanistan appear to be at high risk for attempted and completed suicide, but have not been formally characterized from a clinical or genetic perspective. Identification of clinical and gene markers for suicidal behavior (in consideration of co morbid conditions such as PTSD and depression) in this group would contribute to efforts by the Department of Defense (DOD) and the Department of Veterans Affairs (VA) to more accurately identify persons at greater risk for suicide following combat trauma; this will help identify pathways that may be involved in suicide and, accordingly, the development of more effective strategies for prevention of suicide in this group at high risk population. The contribution of extreme stress experienced during deployment is thought to be a contributor to suicidal behavior raising the question of whether in combat veterans; there are additional markers of suicide other than those that have been associated with suicide in non-veterans (e.g., impulsivity, aggression). The study aim is to determine clinical and genetic/molecular risk factors for suicidal behavior in treatment-seeking combat veterans. The investigator will conduct a case control study of 120 treatment-seeking combat veterans expressing suicidal behavior (cases) compared to those who do not (controls). Half of the sample will have made a recent suicide attempt and cases will be matched to controls on age, gender, race/ethnicity and length of deployment. A single blood sample will be obtained in order to examine gene expression profiles using microarray analyses and quantitative polymerase chain reaction (qPCR) from RNA extracted from whole blood.
AFSP	2010	Investigation into the Role of Genes and Stress in Depression and Suicide Among Medical Interns	Srijan Sen, PhD, MD	The first aim of this study is to identify the factors involved in the development of suicide-related outcomes (SROs) and other mood symptoms among medical interns. A second is to investigate the interactions between genes and stress in the development of suicide. Medical internship is a time of high stress, characterized by sleep deprivation, extreme emotional situations and long work hours. This study will assess baseline psychiatric symptoms in subjects prior to the start of internship duties and then follow these subjects through the course of the intern year for the development of SROs and other depressive symptoms. DNA samples will be collected to investigate the interactions between specific genes and stress in the development of SROs. This project will contribute to suicide prevention by increasing the awareness among training physicians of the risk of SROs and depression, both for themselves and for their patients. It will also help us to understand the pathophysiology underlying suicide and mood disturbances in order to clarify the underlying biological mechanisms that will lead to better identification and treatment of at risk patients.
AFSP	2010	Emergency Mental Health Management Following Deliberate Self-Harm	Mark Olfson, MD, MPH	The primary goal of this study is to identify modifiable factors that promote emergency mental health services and follow-up outpatient mental health treatment for youth and adults who present to emergency departments with deliberate self-harm. Epidemiological analyses will be used to characterize naturally occurring variation in mental health assessments and follow-up mental health treatment of a national cohort of over 60,000 youth and adults treated in emergency departments for deliberate self-harm. This study will identify and characterize systems of care that promote timely mental health treatment of individuals who deliberately harm themselves focusing specifically on potentially lethal events. This knowledge will inform and enhance treatment interventions and policy reform aimed at improving mental health care for the large number of these high risk individuals who do not currently receive mental health services.
AFSP	2010	Number and Severity of Suicide Attempts: Relationship with Toxoplasma Gondii Antibodies	Teodor Postolache, MD	This preliminary case-control study is based on the hypothesis that Toxoplasma Gondii(the most common parasitic infection of the nervous system, which shifts between silent and micro-activated states) and the immune response that keeps the parasite in check may contribute to suicidal attempts in the presence of other vulnerabilities. The investigators preliminarily studies confirm an association between levels of antibodies to Toxoplasma and a history of attempting suicide in patients with recurrent mood disorders. In this current study bloods from healthy controls and patients with mental illness who either attempted or did not attempt suicide will be analyzed for Toxoplasma antibody levels. Considering the high prevalence and the neurotropism of Toxoplasma Gondii, confirming a role in predisposing or triggering suicidal attempts or exacerbating other suicide risk factors may have public health implications for treatment of mental illness and suicide prevention. Success in finding a connection between Toxoplasma Gondii infections and attempting suicide will lead to a focus on behavioral, cellular and molecular mechanisms underlying the connection; expand to suicide completion and modeling suicide risk factors in animals; and design intervention trials in animals and then humans.
AFSP	2010	Personality Disorders and Suicidal Behaviors: A Prospective Study of Associations	Emily B. Ansell, PhD	This research will test the prospective associations between anxious, personality disorders (PD, anxious and/or introverted personality phenotype, the "anxious" cluster C PDs, avoidant, obsessive-compulsive and dependent) and suicide-related outcomes (SROs; ideation, plans, attempts) and if the cumulative effect of multiple personality disorders is prospectively associated with suicide related outcomes. It will also examine the potential mediators and moderators of these relations that may explain conflicting research findings. Current research reports on anxious PDs have been mixed and at times contradictory, making it difficult to draw firm conclusions about associations with suicide risk. It is expected that the prospective associations between anxious PDs and suicidal behaviors will directly inform scientific understanding of suicidal behaviors as well as current risk assessment practices by identifying PDs beyond borderline PD and antisocial PD (cluster B PDs) associated with risk for suicidal behaviors. Moreover, findings on the mediators and moderators of these relations will be especially valuable because they will advance the understanding of why and for whom PDs are associated with suicidal thoughts and behavior -- information that will be directly and immediately useful for risk assessment and treatment development.
AFSP	2011	Global Expression Analysis of Patients with Treatment Emergent Suicidal Ideations	Falk Lohoff, MD	Suicidal thoughts emerging during antidepressant treatment, while controversial, have led to black box warnings and concern about suicide risk in patients treated for major depression. Yet, little is known about the mechanism by which antidepressants might provoke suicidal thinking, at least in vulnerable patients. This proposal aims to address this issue. If successful, the project could shed light on mechanisms and nominate peripheral biomarkers that could be used to identify patients at high risk. The main objective of the grant is to determine differences in baseline and serotonin-induced global gene expression in lymphoblastoid cell lines from major depressive subjects that developed treatment emergent suicide ideation (TESI) relative to major depressive subjects that did not develop suicide ideation. All patient recruitment has been completed from the STAR*D trial and clinical as well as lymphoblastoid cell lines are available. Gene expression will be evaluated in 22 patients with MDD+TESI and 22 patients without MDD+TESI. Subjects will be matched for severity based on the HAM-D baseline scores, and for age, gender and family history of suicide.
AFSP	2008	Case control study of the relative important of impulsive and aggressive personal	Michael Phillips, MD, MPH	The study aims to systematically assess the relative importance of impulsive and aggressive personality traits and triggering life events in both attempted and completed suicides in rural China. If a large proportion of completed and attempted suicides in rural China are, in fact, impulsive acts following acute interpersonal crises in persons without an underlying mental illness, suicide prevention strategies need to primarily focus on restricting access to the means of suicide on developing psychological resiliency and social interconnectedness, putting less emphasis on the traditional strategies of mental-health education and services. In rural China, where the rates of suicide are very high, it is essential to clarify this issue before expending limited social resources on suicide prevention efforts.

AFSP	2013	Mindfulness-Based Cognitive Therapy + Safety Planning for Suicidal Behavior: A Treatment Development Study	Megan Chesin, PhD	There are currently few evidence-based treatments for individuals with suicidal behavior. Barriers to mental health treatment, such as the stigma associated with engaging in psychotherapy and the cost of treatment, prevent a large proportion of suicidal individuals from receiving available, effective treatment. Dr. Chesin will use her postdoctoral fellowship to develop a treatment that adapts Mindfulness-Based Cognitive Therapy (MBCT) + Safety Planning Intervention (SPI) for individuals with recent suicidal behavior and current suicidal ideation. She will assess treatment feasibility, acceptability, safety, and preliminary effectiveness. In Phase I, a manual combining MBCT+SPI will be developed after feedback from the targeted population and from one of the developers of MBCT. In this phase, eight individuals will be enrolled and provided with the new adapted treatment. In Phase II, two pilot trials will be conducted with eight individuals in each trial. It is hypothesized that participants will show reductions in suicidal ideation, hopelessness, and depression over the course of treatment. An exploratory aim is to examine which components of the treatment are most effective. If this intervention is found to be effective, acceptable, and feasible, a randomized controlled trial will be Dr. Chesin's next step towards preventing suicide.
AFSP	2012	White Matter Integrity and Suicide Attempt History	Doreen Olvet, PhD	The fibers in the brain's white matter serve as information networks for sending messages throughout the brain. Their structure and functioning may relate to impulsiveness, as well as to suicide intent and lethality in people who have made a suicide attempt. Dr. Olvet will use an imaging technique called Diffusion Tensor Imaging (DTI) to discover how the structural integrity of white matter cells in the brain differs among three groups of participants: depressed individuals who have made a suicide attempt, depressed individuals who have not attempted suicide, and individuals with no psychiatric history. Dr. Olvet expects to find that individuals with a history of suicide attempts will have less white matter integrity than those who have not attempted suicide. She will also attempt to identify specific paths, or tracts, that might play a role in suicidal behavior.
AFSP	2012	Life Stress and Affect Regulation in Multiple and First Time Adolescent Suicide Attempters	Richard Liu, PhD	Given that a previous suicide attempt is the best predictor of future suicidal attempts, Dr. Liu will interview adolescents who are hospitalized for a suicide attempt and compare those with previous suicide attempts to those who have made only one attempt. He hypothesizes that, prior to their most recent attempt, adolescents with multiple attempts will 1) have experienced lower levels of precipitating life stress outside of their control (e.g., death of a family member); 2) have experienced higher levels of life stress that are in part influenced by their behavior (e.g., fight with parents); 3) have greater difficulty managing their emotions; and 4) have a greater likelihood of having a combination of both life stress and difficulties in managing emotion.
AFSP	2012	Feasibility of an Online Intervention for Population-Based Suicide Prevention	Ursula Whiteside, PhD	The goal of this fellowship project is to develop online treatment modules for three of the active ingredients in Dialectical Behavior Therapy (DBT): Mindfulness, Opposite Action, and Mindfulness of Current Emotion. Dr. Whiteside will use an online delivery model by email because this approach is suitable for the large numbers of at-risk patients identifiable in healthcare settings. Online delivery models are scalable and can be provided securely, inexpensively, and utilizing existing systems in healthcare. She will develop a brief online DBT skills intervention and will test it in patients, adapt it, and retest it across the training period with 30 patients. The intervention will supplement usual care among high-risk patients identified via depression scales collected at outpatient primary care and mental health visits. The intervention content will be drawn from research involving DBT skills interventions. The project will involve ongoing refinement of the interventions based on qualitative/formative feedback from patients and consultation with suicide intervention experts.
AFSP	2011	Functional Analyses of Differential DNA Methylation in Frontal Cortex of Suicide Completers	Gilles Maussion, PhD	DNA methylation is the normal process through which genes are turned on or turned off during the early stages of development. Dr. Maussion will use his fellowship to study the methylation of a specific gene, the TrkB receptor, a gene that has been found to be related to suicide by his mentor, Dr. Turecki. TrkB plays a critical role in the development of the nerves, synapses, and the messaging system of the brain. In his study, Dr. Maussion will characterize the TrkB receptor gene DNA sequence in the frontal cortex of the brain by studying 40 men who had major depression and died by suicide and comparing them with a group of 40 men who did not have major depression and died of other causes. He will also examine the expression of the TrkB receptor gene in other parts of the brain in comparison with the frontal cortex. He expects to find that variations in methylation impact the expression of TrkB and partially account for the lower levels found in suicide.
AFSP	2012	A Pilot Study of Suicide Assessment in Rural Adults	Kelly Cukrowicz, PhD	Suicide in rural areas has not received significant attention in the research literature, even though some studies indicate that suicide rates are higher among adults and older adults in rural areas than in urban areas. The aims of this study are (1) to establish the feasibility of assessing suicide risk in rural communities with limited access to referral care; (2) to determine a preliminary estimate of the prevalence of suicide ideation, self-injury, and history of suicide attempts in these rural communities; and (3) to examine the effectiveness and acceptability of safety and referral plans for individuals whose responses indicate elevated suicide risk. Participants will be adults aged 40 and older residing in Cochran or Parmer Counties in West Texas. This pilot study will provide necessary data for a future study of risk factors associated with suicide ideation and suicidal behavior in rural locales.
AFSP	2012	Person-Specific Modeling of Suicidal Ideation in Sexual Minority Youth	Katerina Sinclair, PhD, MAS	While many factors have been identified that are associated with suicidal ideation and behavior, it is difficult to predict what factors are functioning to produce such behavior in a particular individual. The goal of Dr. Sinclair's study is to develop a method to predict changes in the severity of suicidal ideation and depression in an individual over time. She is particularly focused on sexual-minority youth and the application of Joiner's model of suicide. Her primary aim is to demonstrate that following individuals intensively over time will allow for the identification of factors that increase and decrease suicidal ideation and behavior. Using this novel approach, she hypothesizes that: (1) individual models will predict changes in suicidal ideation more effectively than population models; (2) factors that affect suicidal ideation will be specific to each youth and their impact will change over time; and (3) individual models will successfully identify protective factors and interventions that reduce suicidal ideation over time in each youth. In order to test this, three to five youth who report high levels of suicidal ideation will be recruited from a larger, multisite, longitudinal study of suicidal ideation in LGBT youth. Each participant will complete a 120-day daily assessment using a battery of instruments that assess suicidal ideation and depression, stressful experiences, coping skills, and treatment received. She will examine and compare the patterns identified for each youth to understand suicidal ideation and behavior.
AFSP	2012	Familial Risk for Suicide and Self-Injury: Testing Theories in Multigenerational Pedigrees	Sheila Crowell, PhD	Completed suicide is relatively infrequent and large samples are needed for informative family genetic studies of suicide. Because of this, the first recommendation in the Institute of Medicine's report on suicide was for the National Institutes of Health (NIH) to "develop and support a national network of suicide research Population Laboratories devoted to interdisciplinary research on suicide and suicide prevention across the life cycle." The University of Utah houses the Utah Population Database (UPDB), a unique database that contains linked, de-identified medical, census, birth/death, marriage/divorce, driver's license, and demographic records on over seven million individuals dating from 1750 to the present. The goal of this pilot study is to lay the foundation for a sustained research program of population-level suicide research. Dr. Crowell's study has two primary aims: (1) to construct high risk family trees or pedigrees of families with multiple suicides, and (2) to examine the relative risk for suicide and intentional, non-fatal self-injury within those family trees in comparison with families without suicidal behavior. She hypothesizes that rates of suicide and self-injury will be elevated within high-risk pedigrees relative to case-matched controls. The establishment of this database will provide a national resource that can be linked with other public databases for studying suicide and suicidal behavior.
AFSP	2012	Medical Students' Suicide Risk Assessment Proficiency after Interaction with a Virtual Patient in Crisis	Adriana Foster, MD	It has been demonstrated that educating physicians to assess for suicidal ideation and behavior, and then to treat accordingly, has reduced suicidal behavior. Dr. Foster's randomized clinical trial seeks to demonstrate that virtual patients (VP) can be used to teach medical students to assess and treat people with suicidal ideation and behavior more effectively than simply observing a physician interviewing a patient. VPs are computerized, web-based patients with whom medical students can interact by asking questions and eliciting answers. In this study, the experimental group examines a VP named Denise who has bipolar disorder and soon makes a suicide attempt. The medical student uses virtual technology to interview the patient, and subsequently to interview her husband after she makes a suicide attempt. Throughout the process, the student receives feedback and a transcript is available for later review. The control group watches a film of a professional interviewing a standard patient about suicidal ideation, suicide attempts, and family history of suicidal behavior. Finally, students from both groups complete an online survey to provide information about their demographics and experience with mental illness. Later, the medical students interview a live patient and their skill is assessed. The two groups are compared, and the hypothesis is that those who had interactive experience with the VP will have better skills with real patients than those who watched an interview.
AFSP	2011	Surviving Prostate Cancer but Succumbing to Suicide: Do Poor Health Outcomes Explain the Increased Risk?	Christopher Recklitis, PhD, MPH	Men with prostate cancer are two to four times more likely to die by suicide compared with men who have never had prostate cancer. While the statistics clearly show this higher rate, little is known about what aspects of the cancer or health outcomes contribute to later suicide. Dr. Recklitis intends to determine whether physical health issues like pain, incontinence, and sexual problems following cancer treatment contribute to a cancer survivor's suicidal ideation. The study involves a survey mailed to former patients of the Dana-Farber Cancer Institute to assess patients' physical and mental health as well as suicidal ideation. It is expected that 500 men will participate. Dr. Recklitis's study will be one of the first studies of suicidal ideation after prostate cancer to focus on the role of the patient's health after treatment.

AFSP	2012	Suicide Onset Following Antidepressant Initiation	Robert Penfold, PhD	There is conflicting evidence concerning the effects of antidepressant medications on the risk of suicide attempts. It is unknown whether antidepressant treatment exacerbates suicidal ideation or behavior in people previously reporting those thoughts, or whether individuals with no history of suicidal ideation spontaneously develop these thoughts after exposure to antidepressants. Dr. Penfold's study population will include approximately 148,000 individuals undergoing depression treatment at Group Health Cooperative between July 2006 and June 2012 for whom baseline (pre-treatment) and follow-up Patient Health Questionnaire (PHQ-9) scores were available The goal is to examine the risk for new or increased suicidal ideation and suicide attempts associated with antidepressant treatment among individuals 13 to 84 years old. He will compare those who just began antidepressant treatment with individuals in ongoing treatment for depression. He will also compare the risk of increased suicidal ideation and attempts in individuals who (1) use antidepressants only, (2) attend psychotherapy only, and (3) use both psychotherapy and antidepressant medications together. A unique aspect of the study is the application of sophisticated statistical techniques (Marginal Structural Models) to routinely collected patient medical record data.
AFSP	2012	Multilingual Assessment of Suicidal Ideation and Behavior on the Internet	Yan Leykin, PhD	Mood disorders, such as major depression, are the most common precursor of suicide attempts and suicide. Depressed individuals often go online to find information about their disorder, as well as to find help for their symptoms. Many choose to turn to the Internet instead of connecting to trained professionals, for reasons that may range from lack of access to standard treatment to unwillingness to engage with providers because of stigma or other sociocultural factors. Given that many individuals who attempt or seriously contemplate suicide are neverseen by qualified mental health professionals, it is imperative to study their needs and experiences in the medium of their choice—the Internet. Dr. Leykin will recruit 1400 English-, Spanish-, Chinese-, and Russian-speaking participants worldwide. Participants will complete a depression screening instrument and receive feedback on their results in their language. All participants will be invited to participate in a follow-up study. Participants consenting to the follow-up study will complete a more extensive survey, which will include the Suicidal Behaviors Questionnaire, a comprehensive questionnaire on suicidal ideation and behavior, and will be offered personalized feedback based on their responses. Individuals exhibiting suicidal ideation will be directed to resources in their language. Results of the study will help in the creation of targeted outreach and psychoeducation programs that encourage individuals to seek care.
AFSP	2013	Brief Sleep Intervention for Suicide in Bipolar Disorder	Louisa Sylvia, PhD	It is estimated that 25% to 65% of individuals with bipolar disorder (BD) attempt suicide, and that 4% to 19% of individuals with BD eventually die by suicide. Sleep disturbance is a primary indicator and causal symptom of mood episodes, and recently has been found to be associated with higher rates of suicidal ideation and behavior. Dr. Sylvia will use a non-invasive innovative home sleep monitoring device called the Embla to characterize sleep profiles in adult outpatients with BD, and will use the findings to examine the association of sleep with suicidal ideation and behavior in this population. Fifty-five patients who have experienced suicidal ideation or a recent suicide attempt and sleep disturbance will participate in a one month treatment. Participants will wear the Embla device for Week 1, participate in a brief sleep intervention for suicide during Weeks 2 and 3, and then wear the Embla device for one more week in Week 4. The intervention consists of two 60-minute sessions using a manualized form of cognitive-behavioral therapy to reduce sleep disturbance. Patients will continue treatment as usual with minimum medication changes during the study. Dr. Sylvia hypothesizes that from pre- to post-intervention, individuals will report less sleep disturbance as well as decreased suicidal ideation and behaviors. If effective, the treatment will ultimately be available for clinical use.
AFSP	2012	Suicidal Ideation in Older Prisoners: The Role of Functional Disability	Lisa Barry, PhD, MPH	Suicide is the leading cause of death among prisoners. Trends show that suicide rates increase with age, and the fastest-growing prison population is age 50 and older, indicating a risk of increasing suicide rates in our prisons. Among the elderly, disability in acts of daily living (ADLs), such as bathing and dressing, is associated with suicidal ideation above and beyond other known risk factors such as a previous suicide attempt or depression. In prison, in addition to the typical ADLs, prisoners engage in prison-specific ADLs (PADLs), like being able to drop to the floor, walk to meals, hear instructions, or get up onto a bunk bed. Dr. Barry will administer interviews and questionnaires to 190 prisoners in three Connecticut prisons to examine the role of PADLs as well as other ADLs and known risk factors for suicidal ideation and behavior. These risk factors include psychiatric and medical illness, depression, social support, history of alcohol or drug use problems, prison sentence, and type of offense. If PADLs are indeed contributing to suicidal ideation, there may be easy remedies to help reduce suicidal ideation.
AFSP	2011	Smoking and Suicide: Changes in State Tobacco Policies as Natural Experiments	Richard Grucza, PhD, MPE	While smoking and suicide are strongly related, the nature and direction of that relationship is unclear: We don't know whether smoking increases the risk for suicide or whether it serves as "self-medication"for individuals already at risk. Using several population-based data sets, Dr. Grucza aims to determine whether policies at the state level intended to lower the smoking rate, such as taxes on cigarettes or limiting access for youth, are related to changes in suicide rates. Residents in states with anti-smoking policies will be compared with residents in states without such policies. Dr. Grucza will also study the impact of smoking policies by examining the suicide rates of policy-holding states before and after the policy was implemented. These natural experiments may help to increase our understanding of the relationship between smoking and suicide.
AFSP	2012	Fatal Decisions: Behavioral Economic Study of Decsion Pathways to Suicidal Behavior in the Second Half of Life	Katalin Szanto, MD	It is difficult to understand the thinking of someone who attempts or dies by suicide. Some people seem to act impulsively while others seem engaged in premeditated and deliberate suicidal behavior. Both types of thinking can be deadly. Dr. Szanto will investigate decision profiles associated with a predilection to deliberate (planned attempts with high medical lethality) versus impulsive (less premeditated attempts often causing less medical damage) suicide attempt. Decision-making abilities will be assessed at four complementary levels: 1) behavioral (decision-making in the laboratory); 2) cognitive (decision making problems); 3) self-report (of problem-solving, impulsivity, and interpersonal reactivity); and 4) real-life (history of poor decisions). The study will enroll and assess 90 individuals ages 40 to 60, including deliberate and impulsive suicide attempters, depressed individuals without suicide attempts, and non-psychiatric controls. Dr. Szanto hypothesizes that she will find an association between the type of attempt that was made and the pattern of performance and responses obtained on the decision-making measures. These varying patterns may help us to understand different pathways to suicide attempts.
AFSP	2011	The Consequences of Bereavement by Suicide	Annette Erlangsen, PhD	When people experience grief, their health may worsen. Dr. Erlangsen is investigating the effect of bereavement after a suicide loss on physical and mental health using the Danish Register Data, a registry of all medical and psychiatric contacts as well as medication prescriptions issued to all individuals living in Denmark from 1981 to 2008. She will use 29 years of records to determine whether those who have lost someone to suicide differ from the general public in their use of medical and psychiatric resources after the loss. She will use the registry to examine the effects of specific demographic characteristics and previous physical and mental health factors in relation to any changes identified. The results are expected to increase our understanding of the medical and psychiatric impact of bereavement following a suicide.
AFSP	2011	Meta-Analysis of Case-Control Psychological Autopsy Studies of Suicide	Kenneth Conner, PsyD, MPH	Dr. Conner will analyze various case-control psychological autopsy studies that compare individuals who died by suicide with those who died by other causes in order to update and improve the current databases on suicide risk. The project will look at the suicide risk associated with common mental disorders and stressful life events, and will re-examine the roles that age, sex, and regional differences play with regard to those risks. Dr. Conner hypothesizes that depressive disorders confer greater suicide risk than do substance use disorders. He also hypothesizes that interpersonal life events confer greater suicide risk than do other types of stressful life events, and that depression and alcohol/drug use disorders confer the highest suicide risk among women and older individuals.
AFSP	2011	A Functional Magnetic Imaging Study in First-Degree Relatives of Suicide Completers	Fabrice Jollant	Studying the family members of individuals who died by suicide helps us understand more about genetic vulnerability for risk factors for suicide by comparing them with individuals with a family history of depression and no suicide and those with no family history of either depression or suicide. Dr. Jollant will use the brain imaging technique known as fMRI to discover whether cognitive and emotional vulnerability traits are shared within families. During brain imaging, participants will be asked to respond to faces expressing various emotions including anger, sadness, and happiness, and they will also perform the Iowa Gambling Task that measures an individual's thinking flexibility and impulse control. Dr. Jollant expects that family members of those who died by suicide will perform differently on these two tasks and evidence differences in brain function.
AFSP	2013	Feasibility and Efficacy of a DBT Skills "App" for Suicidal Individuals with BPD	Shireen Rizvi, PhD	Borderline Personality Disorder (BPD) is characterized by problems with emotional regulation and behavioral control frequently exhibited in the form of suicidal behaviors. Dialectical Behavior Therapy (DBT) is an effective treatment for BPD with co-occurring suicidal behaviors. The "DBT Coach"is a mobile technology application (app) that provides immediate, interactive coaching in DBT skills via smartphone to individuals when they need it. Dr. Rizvi is conducting a clinic-based study of the use of DBT Coach when integrated into a six-month standard outpatient DBT program for 15 individuals with BPD and chronic suicidal ideation and behavior. She is evaluating the safety, acceptability, and clinical outcomes of DBT Coach. Participants will be assessed at baseline, mid-treatment, post-treatment, and three month follow-up. She hypothesizes that individuals will report a decrease in distress and suicidal urges as a result of in vivo skills coaching by the DBT Coach, and that the frequency of use will be related to changes in suicidal behaviors, non-suicidal self-injurious behaviors, suicide ideation, urges to self-injure, depression, psychological distress, and treatment satisfaction. She suggests that the addition of the DBT Coach will have a positive effect on treatment by increasing the use of skills taught during individual and group therapies.

AFSP	2012	Randomized, Double-Blind Ketamine Augmentation in Chronically Suicidal, Treatment	Cristina Cusin, MD	A novel approach to the treatment of acute suicide risk has involved the use of ketamine, an anesthetic that seems to have an immediate impact on reducing depression and suicidal ideation. The proposed study involves three phases to examine an innovative administration method that may prolong the positive effects of ketamine. Phase (1) is a two-week, prospective, open-label continuation of current medications; Phase (2) a three-week, double-blind, randomized treatment with IV ketamine or a placebo for a total of six infusions in a controlled setting under the supervision of an experienced anesthesiologist; and Phase (3) a prospective follow-up for three months, with visits every two weeks. If augmentation with intravenous ketamine is found to be safe, effective, and well-tolerated, it can become a novel therapeutic tool in the outpatient or inpatient setting to help those patients who are affected by severe treatment-resistant major depression and suicidal ideation.
AFSP	2011	The Neural Circuitry of Suicidality in Adolescent Depression	Hilary Blumberg, MD	Dr. Blumberg will use a brain scanning technique known as functional magnetic resonance imaging (fMRI) to identify differences between the brain circuitry of depressed adolescents who have made a suicide attempt and depressed adolescents who have not attempted suicide. Both groups will be asked to perform certain tasks while brain images are taken. In addition, the adolescents will complete an interview, perform behavioral tasks, and complete questionnaires relating to suicidal ideation and behavior, aggression, and impulsiveness. Dr. Blumberg will also measure the density of brain fibers, known as white matter. She is testing the hypothesis that adolescents with major depression and a history of suicide attempts show a decrease in regulation and structural integrity of the brain circuitry of the frontal cortex, the part of the brain responsible for emotion and impulse control.
AFSP	2012	Modeling 5-HT1A Receptor Transduction Pathways in Suicide	Thomas Franke, MD, PhD	Chronic stress has been found to affect the biochemistry of the brain. Some types of changes are in the serotonin system and have been identified in postmortem brain studies of depressed individuals who have died by suicide. Akt is one such serotonin related brain chemical. Dr. Franke will use his grant to try to recreate, in genetically modified mice, the brain changes in the Akt protein that have been found in post-mortem studies of depressed suicide victims. He will use a behavioral model of depression in mice that is based on a chronic stress model. He will test the importance and relevance of brain and behavioral changes to depression and suicide, as well as to resilience and resistance, when confronted with chronic stress.
AFSP	2011	microRNAs in Postmortem Brain of Suicide Subjects	Yogesh Dwivedi, PhD	The hypothesis to be tested is that a subset of microRNAs (µRNAs) will show alterations in the brain of suicides and will be a part of the pathogenesis of suicide by targeting genes that regulate normal brain function. µRNAs are single stranded non-coding RNAs that are post-translational regulators. An individual µRNA can interact with several mRNAs and thus may regulate the expression of a family of functionally related genes. Each µRNA may silence hundreds of mRNAs. The study of µRNAs is a very new research area. There is emerging evidence that µRNAs contribute to risk of neuropsychiatric disorders, and that these brain disorders exhibit altered µRNA expression; more recently, it was shown that antidepressants regulate the expression of µRNAs in rat brain. Proteins such as CREB and BDNF, that are down-regulated in suicide, both are regulated and targeted by certain µRNAs. Therefore, µRNAs are likely to interact with known pathways involved in pathogenesis of neuropsychiatric diseases. This investigator will: test whether expression of µRNAs is altered in prefrontal cortex of suicide subjects; test whether the nucleotide sequences of µRNAs are specifically altered in suicide brain, by carrying out high through put deep sequencing; and identify predicted targets of altered µRNAs and examine whether mRNA levels of some of the predicted targets are altered in suicides. This proposed study will be performed in postmortem brain samples obtained from adult suicide subjects and matched non-psychiatric controls.
AFSP	2012	The Electronic Intervention for Suicidality (EIS): A Novel Adjunctive Treatment for Suicide risk	Michael Armey, PhD	Imagine an individualized approach to suicidal ideation where a person who is struggling can use the internet and a smartphone to help him or her through a difficult moment. Dr. Armey is working to develop an acceptable and feasible add-on to interventions for suicidal ideation using a combination of internet-based interactive educational modules and adaptive, smartphone-delivered, interventions. His study is aimed at refining the Electronic Intervention for Suicidality (EIS) treatment manual, software, and website. Treatment development involves a two-wave assessment of the intervention program. A small sample of adults who recently attempted suicide will participate after their discharge from the hospital. They will use the interactive internet modules and smartphone interventions to provide feedback to the researcher regarding suicidal ideation, urges, and hospitalization. Feasibility and acceptability of the interventions will be assessed and the program will be improved as a result of this process. Electronic aids may provide a suitable approach to engaging and helping people who have suicidal ideation and a history of suicide attempt.
AFSP	2011	Objective Sleep and Suicide in General Population Sample of Youth	Ravi Singareddy, MD	Substantial evidence indicates that sleep disturbances such as insomnia, hypersomnia, and nightmares increase the risk of suicidal behaviors. Dr. Singareddy aims to determine the association among suicidal ideation, suicidal attempts. and sleep disturbances in 500 adolescents. He will record specific aspects of sleep in a sleep laboratory, including sleep efficiency, sleep latency, REM latency, poor subjective sleep, nightmares, and hypersomnia or oversleeping. He hypothesizes that adolescents experiencing suicidal ideation or history of a suicide attempt will also have measurable sleep problems. Further, he expects the severity of suicidal ideation to increase when sleep disturbances are accompanied by difficulties in attention and concentration, impulsiveness, and increased risk-taking behaviors.
AFSP	2011	Ketamine for Rapid Reduction of Suicidal Ideation and Suicide Risk in Hospitalized Patients	James Murrough, MD	Strong suicidal ideation is a medical emergency, and hospitals urgently need to identify fast-acting interventions that will help reduce imminent suicide risk. Ketamine may be one example of such a rapid intervention. Dr. Murrough will test the use of low doses of ketamine administered by IV for patients admitted to a psychiatric hospital for clinically significant suicidal ideation and elevated risk for suicide and examine its feasibility and tolerability. He will measure patients' psychiatric and suicide symptoms at the time of admission and then again at 4 and 24 hours after treatment with ketamine. Dr. Murrough's hypothesis is that ketamine will prove effective at rapidly reducing suicidal ideation. Further follow-ups to assess for safety and efficacy will be administered daily during hospitalization and weekly during the month following hospitalization, ending with one final assessment 6 months after the ketamine treatment.
AFSP	2011	Copy Number Variation in Suicide	Carl Ernst, PhD	Dr. Ernst is working to identify genetic risk factors for suicide by studying changes in gene structures known as copy number variations (CNV). DNA or gene structures vary from person to person as genes copy themselves. Over time, imperfections in this process, known as "disruptions," can lead to large losses or increases in DNA. CNVs have been shown to be important, although uncommon, sources of risk for some psychiatric disorders. Dr. Ernst will examine the relationship between CNVs and suicide risk among individuals with bipolar and unipolar depression by comparing individuals with a history of suicide attempts and individuals without a history of a suicide attempt. His hypothesis is that those with a history of a suicide attempt will carry CNVs with 1) more disrupted genes; 2) larger disruptions; and 3) more possible problems in the way the genes are interpreted in the brain. In addition, he will examine whether CNV disruptions found in people who have made suicide attempts are also found in people who died by suicide. The mentorship goal is to develop skills to understand the genetic risk for suicide, with an emphasis on the association between CNVs and suicide.
AFSP	2011	Lethal Means Restriction for Suicide Prevention: Beliefs and Behaviors of Emergency Department Providers	Marian Betz, MD, MPH	Emergency department (ED) staff often possess attitudes toward suicide that limit their ability or willingness to ask about suicidal ideation and suicide attempts. This Young Investigator Grant tests two hypotheses. The first is that many providers are skeptical that suicide can be prevented. The second is that few staff members ask about access to lethal means, such as firearms, even when they know someone is thinking about suicide or has made a recent suicide attempt. The project also measures whether attitudes change after ED professionals participate in a training program designed to teach them to screen for suicide risk. Finally, ED nurses will be trained to conduct a brief intervention for patients with suicidal behavior that includes asking about access to lethal methods such as firearms. After the training, attitudes and beliefs will be assessed a third time.
AFSP	2012	The Acquired Capability for Suicide: A Mechanism Underlying the Gender Disparity in Suicide Rates	Phillip Smith, PhD	Does the way in which boys and men are socialized play a role in their increased suicide rate over that of women and girls? Dr. Smith hypothesizes that the greater exposure of men to life events involving physical pain, and to fear such as violence, injury, and trauma, will reduce their fear of death and increase their tolerance for pain. Decreased fear of death and increased pain tolerance combine to produce an acquired capability for suicide. One hundred men seen in a hospital psychiatric emergency room or admitted to inpatient psychiatric facilities will be interviewed and asked to complete questionnaires about their experiences, acquired capability for suicide, and suicidal ideation and attempts. Dr. Smith theorizes that men who adhere to traditional male gender norms involving restricted emotional expression, and those who report greater suicidal ideation in the presence of greater acquired capability for suicide, will be more likely to report a recent suicide attempt. These characteristics might help explain why men complete suicide four times as often as women.
AFSP	2011	A Test of the Interpersonal-Psychological Theory of Suicide in Prison Inmates	Jon Mandracchia, PhD	The Interpersonal-Psychological Theory of Suicide suggests that a person who feels more disconnected and burdensome, has less fear of death, and has an increased pain tolerance is at higher risk for suicide. These factors may contribute to current suicidal ideation above and beyond the contributions of depression, hopelessness, past suicidal ideation, history of suicide attempt, psychopathy, criminal thinking and criminal behavior. Dr. Mandracchia will administer questionnaires to inmates in the Mississippi Department of Corrections and analyze the relative contributions of these factors to suicidal ideation to test this theory. He hypothesizes that inmates reporting less connectedness and more burdensomeness will report more suicidal ideation. An additional hypothesis is that people who report less concern for others (psychopathy) will be less likely to feel like a burden.

AFSP	2012	Self-Harm & Suicide Attempt Risk: Evaluation of an Intervention for Youths with Self-Harm Behavior	Jennifer Hughes, PhD	Clinicians need more information about the links between non-suicidal self-injury (NSSI) and suicidal behavior, and effective interventions for addressing NSSI in adolescents. Dr. Hughes will use an intervention for adolescent suicide attempters called the Safe Alternatives for Teens and Youth (SAFETY), adapting it specifically for youth presenting with NSSI. She will test the adapted SAFETY intervention by randomly assigning 30 treatment-seeking youth with significant self-harm behavior to receive Enhanced Treatment As Usual (Enhanced TAU) vs. SAFETY. Youth and families in the SAFETY group will receive weekly intervention sessions for three months. The SAFETY intervention aims to reduce the risk of suicide attempts by targeting individual and environmental risk and protective factors using a cognitive behavioral approach. Youth and families in the Enhanced TAU group will receive one intervention session targeted at enhancing safety, reducing self-harm and suicide risk, and highlighting the importance of outpatient treatment to address NSSI and any psychiatric symptoms. They will also receive monthly check-ins to encourage linkage to community care. Outcomes will be assessed at three and six months. Dr. Hughes predicts that the SAFETY intervention will be feasible, tolerable, acceptable, and safe. In addition, she predicts that the rate of repeat NSSI will be lower in the SAFETY group compared with the Enhanced TAU group at the three-month assessment.
AFSP	2012	Optical Brain Imaging Predictors of Treatment Response to Dialectical Behaviour Therapy for Non-Suicidal Self-Injury in Borderline Personality Disorder	Anthony Ruocco, PhD	The reduction of non-suicidal self-injury (NSSI) is a key target of Dialectical Behavior Therapy (DBT) for patients with borderline personality disorder (BPD). The identification of biological indicators of treatment response for NSSI in BPD is an important unmet need that has significant ramifications for optimizing treatments to reduce NSSI among these patients. Impulsivity has been identified as an essential feature of BPD that places patients at an increased risk for NSSI and suicide completion. Neuroimaging studies of impulse control, or response inhibition, implicate the ventrolateral prefrontal cortex (VLPFC) of the brain as a critical behavioral control center for BPD patients, who show reduced activation of this region under conditions of response inhibition; that is, not acting when identifying a stimulus. Activation of the VLPFC may thus serve as a promising biological indicator of treatment-associated changes in NSSI for patients with BPD. Dr. Ruocco will evaluate activation of the VLPFC on tests of response inhibition as a possible predictor of treatment response in this high-risk group. Thirty-one outpatients with BPD and NSSI from the Centre for Addiction and Mental Health in Toronto, Canada, will be evaluated prior to and after completing six months of DBT, Patients will complete tests of response inhibition (go/no-go and stop-signal tasks) while functional activation of the VLPFC is monitored using near-infrared spectroscopy. He will test whether VLPFC activation is associated with NSSI outcome measures. This research has the potential to identify biological markers that could predict which BPD patients may be most responsive to a psychological treatment aimed at reducing NSSI.
AFSP	2012	Posttraumatic Stress Disorder and Suicide Among Massachusetts Veterans	Jaimie Gradus, DSc, MPH	The rate of suicide among military veterans has been found to be higher than in the general population. Post-traumatic stress disorder (PTSD) has been associated with suicide and nonfatal suicidal acts by some researchers but not others, depending on their methodology. Dr. Gradus will use data from the VA hospital system in Massachusetts from 2000 to 2007, including data available from approximately 18,000 veterans with PTSD and 90,000 without PTSD, to examine the association between suicide and nonfatal suicidal acts in veterans with PTSD. She hypothesizes that: (1) the rate of suicidal behavior (suicide attempts and suicides) among veterans diagnosed with PTSD will be higher than the rate of suicidal behavior among VA patients without PTSD, and (2) the rate of suicidal behavior among veterans with PTSD and depression will be greater than for those with either a PTSD or depression diagnosis alone. She will examine the role of demographic characteristics, psychiatric diagnosis, and treatment to help clarify the relationship between PTSD and suicidal behavior in veterans who are treated in the VA hospital in Massachusetts.
AFSP	2012	Identifying Risk Factors and Intervention Methods to Prevent Suicide in Pediatric Bipolar Disorder	Sally Weinstein, PhD	Pediatric bipolar disorder (PBD) is an illness characterized by episodic mood disturbance and psychosocial impairment, and suicidal ideation and behavior at rates that exceed any other childhood disorders. Dr. Weinstein is developing a targeted suicide prevention intervention for this population. She will add 30 youth age 7 to 13 and a focus on suicidal ideation and behavior to an ongoing, NIH-funded, randomized clinical trial examining psychosocial treatment for PBD. The manualized psychotherapy for PBD is a one month Child- and Family-Focused Cognitive Behavioral Therapy (CFF-CBT). She hypothesizes that (1) higher rates of suicidal events will be associated with family dysfunction, child cognitive risk, and affective vulnerability (rapid mood shifts); (2) youth receiving CFF-CBT will experience a moderate, but not complete, reduction in suicidal events that will be greater than that of the control group; and (3) treatment-related changes will relate to changes in the number of suicidal events. Youth and parents will be assessed pre- and post-treatment and at six month following treatment. Data will be used to identify family, child, and affective risk factors associated with suicidal ideation and behavior. Findings will be used to develop a targeted suicidal-event reduction (SURE) intervention module designed to optimize suicide prevention in PBD.
AFSP	2011	Identification of Neurophysiological Markers of Suicidal Behavior and Impulsivity in Bipolar Disorder	Masoud Kamali, MD	The aims of this study are to compare neurophysiological measures of response inhibition in two groups of 20 bipolar subjects with and without a lifetime history of suicide attempts, and a group of 20 unaffected controls to identify a marker for suicidal behavior and to correlate that marker to other clinical measures of impulsivity. It is hypothesized that bipolar patients with a history of suicidality will exhibit deficits in a response inhibition task as indicated by smaller amplitude and delayed latency in two event relate brain potential (ERP) components (P300 & N200). The patient groups are to be matched by drug class of active medication. Patient subjects will be drawn from an existing pool of subjects participating in an ongoing high surveillance-intensity follow-up study. ERP deficits will reflect impaired impulse control and correlate with suicidal behavior and other clinical measures of impaired impulse control. This project hopes to identify markers of response inhibition in patients with a history of suicidality with the intention of better prediction of suicidal behavior in the future.
AHRQ	2011	Screening for Suicide Risk in Primary Care	Elizabeth O'Connor	Background: In the United States, the annual burden of suicide is substantial, accounting for almost 37,000 deaths and an estimated 1.4 million years of potential life lost in recent years. Purpose: To systematically review evidence for the accuracy of suicide risk screening instruments, the efficacy and safety of screening for suicide risk, and the efficacy and safety of treatments to prevent suicide. Conclusions: Suicide screening is of high national importance. It is very difficult, however, to predict who will die from suicide, and there are many inherent difficulties in establishing the effectiveness of treatment to reduce suicide and suicide attempts. Limited evidence suggests that primary care-feasible screening instruments may be able to identify adults at increased risk of suicide, and psychotherapy targeting suicide prevention can be an effective treatment in adults. Evidence was more limited in older adults and adolescents; additional research is urgently needed.
BBRF	2013	Identification and Characterization of Transcriptional Regulators Mediating the Relationship Between Early Childhood Adversity and Development of Psychopathology Later in Life	Laura Marie Fiori	Mental illnesses are debilitating and often chronic conditions whose development and pathology result from the interaction of a variety of clinical, social, genetic, and environmental factors. In recent years, the importance of early life stressors in the development of psychiatric disorders has become increasingly recognized. Numerous efforts are currently being undertaken to identify the biological mechanisms by which the early environment can interact with the genome to produce long-term neurobiological alterations. One method by which this is believed to occur is through the epigenetic process known as DNA methylation, which can occur at specific sites in the DNA, and yield stable changes to gene expression. The aim of the present study is to investigate the functional relationship between gene expression and specific DNA methylation marks which have been found to be associated with early childhood adversity and the development of psychopathology later in life. To this end, we will first use reporter gene assays to assess the effects of DNA methylation at these sites on gene expression. We will then use a combination of bioinformatics, electromobility shift assays, and yeast one-hybrid assays, to identify transcription factors whose binding abilities at these sites are affected by the presence of DNA methylation. Subsequently, reporter gene assays will be used to confirm transcription factor binding and examine their effects on gene expression in vitro. Finally, chromatin immunoprecipitation assays will allow us to confirm the existence of transcription factor-DNA complexes in cell culture, as well as to identify the presence of specific post-translational histone modifications: another important epigenetic process which has been implicated in mental illness. Overall, these studies will allow us to elucidate specific molecular mechanisms by which epigenetic changes which occur early in development are capable of yielding long-term changes to gene expression. Ultimately, these processes represent novel targets for both early diagnosis and psychopharmacological treatment of mental disorders.
BBRF	2013	Genetic Contribution to Suicidal Behaviors	Molly Adrian	Both hypothalamic-pituitary-adrenal (HPA) axis dysregulation and childhood adversity shape individual responses to stress and are associated with increased risk for suicidal behaviors. The aim of this proposal is to examine how 4 single nucleotide polymorphisms (SNPs) affect suicidal behaviors. First, utilizing Bayesian statistical models, we will explore if in the context of chronic family adversity 4 SNPs directing HPA axis activity have an appreciable influence on suicidal behaviors during adolescence. Next, we will examine if intermediate individual characteristics (i.e., endophenotypes) of emotion regulation, hopelessness, and impulsive-aggression, mediate the effects of genetic contributions to the HPA axis onto suicidal behaviors. We hypothesize that SNPs associated with the HPA dysregulation will influence hopelessness, which will subsequently impact suicidal ideation. Additionally, we hypothesize that SNPs will impact emotion regulation and impulsive-aggression traits, which will then directly affect suicide attempts.

BBRF	2013	The Development of a Longitudinal Endophenotype for Aggressive and Impulsive Suicidal Behavior	Rashelle Jean Musci	With recent release of the 2012 National Strategy for Suicide Prevention (NSSP), suicidality has come to the forefront as a major public health concern. With suicide being the 10th leading cause of death, it is essential for developers of prevention and intervention programs to know and understand the etiology of suicidal behavior, and more specifically, understand how biology may play a role in the development of such behaviors. Previous work has attempted to identify direct links between genetic variation and suicide behavior. These analyses have resulted in a number of conflicting results. Due to this, researchers have begun to explore the use of endophenotypes to replace the traditional outcome in genetic analyses. An endophenotype is a term developed in the genetic epidemiology to compile behavioral phenotypes that have a clear genetic origin. An endophenotype associated with suicidal behavior is one characterized by high levels of aggression and impulsivity, the genetic origins of which have not yet been explored in an African American population. The current study aims to first estimate the longitudinal endophenotype of aggression and impulsivity as it relates to suicidality. Further, this study explores the relationship between the established longitudinal endophenotype and selected gene systems. These gene systems will be chosen based on previous literature as well as results from existing, publically available datasets. We hypothesize that genes within the serotonergic system will be significantly related to the aggressive/impulsive suicide phenotype because of previous findings linking suicide attempts, aggression and impulsivity. These aims will be accomplished using an existing dataset from the Center for Prevention Research. This longitudinal preventive intervention began in 1993 with 799 primarily African American first-graders from the Baltimore City Public Schools. Data collection has continued yearly, with blood or saliva samples collected during the 19-21 year follow-up. Measures of aggressive and impulsive behavior were collected from parents, teachers and peers of the participants. Suicidal behavior was collected from participants annually with a self-report measure. DNA was collected via blood or saliva and genotyped using a genome wide Affymetrix 6.0 microarray. All genotypic data required passing quality control in order to be used in any analyses.
BBRF	2013	Improving the Prediction of Suicide in a High-Risk Emergency Department Cohort	James Michael Bolton	This research study will be conducted by Dr. James Bolton, an Assistant Professor of Psychiatry, Psychology, and Community Health Sciences at the University of Manitoba in Canada. The goal of this study is to improve the prediction of suicide in people who go to emergency departments with mental health concerns. This will help doctors and other care providers identify people who are at risk of taking their own life, which to date has been very difficult to predict. Knowing who is at risk for suicide is a research priority in medicine and public health. Suicide is the 10th leading cause of death in the United States, with 100 people taking their own life every day. One of the main problems in the battle against suicide is that it is very hard to know who will die by suicide in the future. If these people can be identified in advance, they have a chance to receive potentially lifesaving treatments. Dr. Bolton will accomplish the goal of improving suicide prediction with a series of exciting studies that use new techniques to better understand suicide risk. Using a state-of-the-art database, he will follow a large group of people who attended emergency departments, and clarify which characteristics of these people increase their risk of suicide. One of the projects of the study will test whether a scale can predict suicide in the future ? this scale was designed to predict suicide risk, and is widely used, but has never been tested. Together, these studies will greatly improve the understanding of suicide, and will help doctors, nurses, and other treatment staff who see suicidal people in the emergency department. These studies will lead to the creation of new tools that are better able to detect people at risk for suicide. Ultimately, Dr. Bolton?s study will help reduce the rate of suicide, which is a national health care priority in the United States and around the world.
BBRF	2013	Ketamine vs Midazolam: Testing Rapid Relief of Suicide Risk in Bipolar Disorder	Michael Grunebaum	Suicide and suicide attempts cost an estimated $33 billion annually in the U.S. and immeasurable pain and suffering. Most suicidal behavior is associated with a depressive disorder, and persons suffering from bipolar disorder are at particularly high risk. Unfortunately, there is an absence of antisuicidal treatment of demonstrable efficacy for patients with bipolar disorder. The evidence base is severely limited because suicidal patients are excluded from most clinical trials. Several recent studies, including two in bipolar disorder, show rapid improvement in suicidal ideation, in as little as one hour, in depressed patients after intravenous infusion of sub-anesthetic ketamine, a commonly used anesthetic. However, neither study in bipolar disorder sought to specifically enroll suicidal patients and neither used state of the art measures of suicidal thoughts, a key precursor to suicidal behavior. We are currently conducting an NIMH-funded clinical trial in suicidal, unipolar depressed patients to test random assignment to intravenous infusion of ketamine or midazolam control followed by open continuation treatment. In this grant application, we propose an add-on, pilot feasibility study to include a sample of patients with bipolar disorder. The primary goal is to test ketamine?s potential antisuicidal effects versus midazolam, a similarly sedative control medication not known to reduce suicidal thoughts. Exploratory aims include analysis of neurocognitive correlates as well as systematic, state of the art assessment of suicidal ideation and behavior during follow-up. Adding a bipolar disorder sample to our unipolar depression study would extend potential impact to a population of crucial public health importance, and leverage the opportunity of an ongoing clinical trial. Establishing the feasibility of this ketamine vs. midazolam study in suicidal patients with bipolar disorder would support conducting a more definitive trial that could change clinical care in bipolar disorder.
BBRF	2013	Preventing Firearms Violence and Suicide Among Adults with Serious Mental Illness: Bringing Evidence to Public Policy Reform	Jeffrey Swanson	The proposed research project will: (1) examine the prevalence and correlates of firearms?related suicide and other?directed violence in a sample of approximately 23,000 adults with schizophrenia, bipolar disorder, or major depression who received services in Florida?s public behavioral healthcare system between 2002 and 2012; (2) examine the prevalence and correlates of gun?disqualifying mental health adjudications, criminal disqualification from firearms, and the overlap between these categories of prohibited persons; (3) describe patterns of psychiatric hospitalization and (Medicaid?funded) outpatient mental health services utilization in this cohort and evaluate the effectiveness of services? pharmacological and other behavioral health treatment?specifically in preventing firearms suicide and other violence; (4) describe patterns of historic and current criminal justice involvement in the cohort? arrests and incarcerations?and evaluate their effects on access to firearms and risk of gun violence and suicide; and (5) evaluate the effectiveness of federal and state gun laws, as implemented in Florida through the NICS, to identify mentally ill individuals prohibited from purchasing firearms and to prevent gun?related suicide and other violence in these individuals. The study will use a quasi?experimental design with multivariable statistical analysis of a longitudinal database of matched records of mental health treatment, criminal justice involvement, and deaths in Florida over 10 years. The findings will be used to inform the development of targeted interventions, services, and public policies?such as more accurate screening and reporting of gun?disqualifying records to NICS?designed to effectively reduce firearms injury and mortality in persons with mental illness. The proposed study will address evidence gaps at a time when behavioral science may have a unique opportunity for public impact in the design and implementation of new approaches to reduce gun violence.
BBRF	2013	Remediating Decision-Making Deficits in Depressed Subjects at High Risk for Suici	Marcelo T. Berlim	Marcelo T. Berlim, M.D., M.Sc., of McGill University, will use repetitive transcranial magnetic stimulation (rTMS), a safe, noninvasive method of stimulating brain activity, in an effort to relieve symptoms in depressed patients at high risk for suicide. Sixty patients, age 18 to 60, with a current major depressive episode of at least moderate intensity and a lifetime history of at least one serious suicide attempt, will be enrolled in the study. The hope is that the trial will provide a better understanding of the neurobiological basis of a well-known predisposing factor for suicidal behavior, namely decision-making deficits, and that high-frequency rTMS can improve those deficits, thus reducing suicide risk.
BBRF	2008	Patterns and Trajectories of Suicide Attempters in Terms of the Utilization of He	Johanne Renaud	Johanne Renaud, M.D., M.Sc., of Douglas Mental Health University Institute/McGill University, seeks to identify unmet needs and trajectories of utilization of services in the last 12 months in the lives of 85 suicide attempters, all under 25, with respect to the type of services used, frequency and collaboration to the services. Dr. Renaud will also compare unmet needs and trajectories of utilization to a sample of suicide completers and population controls. This design will lead to formal recommendations for mental health service delivery in order to better differentiate suicide attempters with suicide completers, and ultimately to support and improve mental health care services and prevent youth suicide.
BBRF	2013	Suicide and Obesity a Curious Association	Zainab Samaan, M.D.	Zainab Samaan, M.D., of McMaster University, Canada, is interested in probing the association, if any, between obesity and the risk of suicide in an individual. It is known that obesity is associated with depression, and depression is in turn a risk factor for suicide; yet obesity has been cited as a 'protective' or mitigating factor in suicide risk. Samaan hypothesizes this is explained by high levels of cholesterol in the blood. Obesity is associated with high levels of cholesterol, and cholesterol is an important substance in the brain. 60% of our brains are made of lipids including cholesterol that is essential for normal brain function such as transmission of brain cells signals. Some studies also show that low cholesterol might be associated with suicide and low serotonin levels. The current project will investigate the association between suicide attempts and obesity (using body mass index or BMI as the measure of obesity) and test if this association holds up when one controls for the presence of confounding variables such as psychiatric diagnosis, medical illness and life style factors such as diet and physical activity. The team also plans to test the association between cholesterol blood level and suicide attempts and for the effect of cholesterol on the relation between obesity and suicide.
BBRF	2008	Inpatient Post Admission Cognitive Therapy (PACT) for the Prevention of Suicide A	Marjan G. Holloway	Marjan G. Holloway, Ph.D., of Uniformed Services University (USUHS), proposes an adaptation of Beck and colleagues cognitive therapy suicide protocol for implementation, feasibility, and pilot testing at an inpatient psychiatry setting for specific delivery to military service members and their family members with a recent suicide attempt. Suicide attempt behavior is one of the most powerful risk factors for repeat suicide behavior as well as eventual death by suicide. Delivering a brief and possibly potent psychotherapeutic intervention (PACT) during a patient's inpatient hospitalization aims to directly target individuals at high risk for future suicide behavior, i.e., young adult, mostly males with a recent suicide attempt, under direct stress of a military career. The timing of the intervention, more specifically its implementation immediately following a suicide-related hospitalization may be an important factor in preventing subsequent suicide behavior and bypassing the challenges involved in patient compliance and connecting suicidal individuals to community aftercare.

BBRF	2008	Lithium Therapy and Attempted Suicide in Youth Bipolar Affective Disorder	Brady G. Case	Brady G. Case, M.D., of New York University School of Medicine, will utilize a case control method with national Medicaid administrative claims data to compare risk of suicide attempt in youth treated with lithium versus not treated with lithium after inpatient hospitalization for bipolar affective disorder. Suicide attempts are serious adverse outcomes of bipolar illness in youth, and treatment of high-risk bipolar children and adolescents is a common and difficult challenge for mental health providers. Evaluating the potential of promising interventions to prevent suicide attempts in this population is a pressing task, and results of the proposed study may guide treatments and enhance outcomes of pediatric bipolar disorder.
BBRF	2009	The neuropeptide galanin and its receptors	Tomas Hakfelt	Tomas Hakfelt, M.D., Ph.D., of Karolinska Institute, is studying several neuropeptide receptors, including those of galanin, which represent targets for development of a new class of antidepressant drugs. Neuropeptides represent the largest group of messenger molecules in the brain, almost always representing co-transmitters. They act via 7-transmembrane, G-protein coupled receptors (GPCRs) and are potential targets for drug development. The focus in this project is on galanin and its three receptors, GalR1-R3. In rat, galanin is coexpressed in the noradrenaline (NA) neurons in the locus coeruleus (LC) and in the serotonin neurons in the dorsal raphe nucleus (DRN). A number of animal studies suggest that a galanin antagonist could have an antidepressant effect, a theory strongly supported by the recent demonstration that small-molecule GalR3 antagonists have antidepressant and anxiolytic action in several rat models. The question to be addressed in this study is the extent to which the galanin system shown in rodents also exists in the human brain, and whether promising results with galanin antagonists in animal models might apply in humans.
BBRF	2011	Risk Factors for Completed Suicide in the Israeli Military	Gadi Lubin	Gadi Lubin, M.D., of the Chaim Sheba Medical Center, Tel Aviv University, will study risk factors for suicide, utilizing data generated by the Israeli Defense Force (IDF) from 260 soldiers, aged 18 and 21, who committed suicide during militaryservice between 1997 and 2008. Data regarding psychiatric disorders, personality disorders, use of drugs and alcohol, previous psychiatric treatment, nonspecific signs of distress such as sleep or appetite disturbances and physical illness will be scrutinized as will treatment by physicians and mental health professionals and behavior changes preceding the suicide. The study will also utilize data from the pre-recruitment screening, which includes IQ, behavioral and personality traits, medical and psychiatric diagnoses.
BBRF	2011	Neurobiological Predictors of Suicide in Bipolar Disorder	Alison Gilbert	Alison Gilbert, Ph.D., of Zucker Hillside Hospital, Feinstein Institute for Medical Research,North Shore-Long Island Jewish Health System, wants to uncover the underlying biology linking impulsivity, cognition and suicidal behavior in people with bipolar disorder. She proposes to use a neuroimaging method called diffusion tensor imaging to take pictures of the white matter, tracts that connect various brain regions to one another, and compare the images from a group of bipolar patients who have made an unambiguous suicide attempt with a group of bipolar patients who have never attempted suicide. She hypothesizes that there will be reduced integrity in the white matter in the orbitofrontal cortex of the brain in those who have attempted suicide versus those who have not. The goal of the trial is to find reliable biological markers to predict which patients may pose the greatest suicide risk.
BBRF	2010	Interaction between the Glutamatergic and Serotonergic Systems in Suicide in Mood	Adolfo Sequeira	Adolfo Sequeira, Ph.D., of the University of California, Irvine, proposes that understanding the gene expression changes associated with suicide in mood disorder subjects should improve suicide intervention and prevention efforts. He wants to study whether and how key genes affecting glutamate and serotonin receptors are implicated in mood disorders and suicide. He will be part of a team focusing on gene expression three regions, the dorsolateral prefrontal cortex (DLPFC), the amygdala and the nucleus accumbens. In order to explore the specific involvement of those genes in suicide and/or mood disorders, a cohort of mood disorder patients and a cohort of normal controls will be utilized. The ultimate goal is a specific brain-biological signature of suicidal behavior and of mood disorders.
BBRF	2008	Suicidality in Major Psychoses: Methylation Analysis Based on Genomic Imprinting	Vincenzo De Luca	Vincenzo De Luca, M.D., of Centre for Addiction and Mental Health/University of Toronto, aims to identify genetic (polymorphism) and epigenetic (gene methylation) predictors of increased suicide risk in psychiatric patients with chronic mental illness (the most common diagnoses include schizophrenia and bipolar disorder). Suicide has been noted to be familial in many cases, and subjects with schizophrenia and bipolar disorder have a high rate of suicide attempts. The genetic risk markers for suicide that this study could, in the future, identify persons at risk and thus facilitate preventive measures such as counseling, family education, and early treatment intervention for these individuals. Furthermore, the identified genes may reveal new neurobiological mechanisms in suicide that may be used as targets for development of novel medications to prevent suicide.
BBRF	2013	Genetics of Suicidal Behaviour: Genome-wide Association Study and Targeted Research	Clement C. Zai, Ph.D.	Clement C. Zai, Ph.D., of the Centre for Addiction and Mental Health at the University of Toronto, is studying possible genetic linkages with suicidal behavior. He notes that suicides tend to run in families, and that 90% of victims suffered at least one psychiatric disorder. His team seeks to identify identifying novel DNA variants across the human genome in archival samples of chronic schizophrenia/bipolar disorder patients (sample size>1,000), and then compare the frequency distributions of the genotypes and alleles of these polymorphisms between patients with and without lifetime history of suicidal attempts. By sequencing of regions around significant DNA variants Zai will provide extensive information at the DNA level that could identify novel variants for further study. The ultimate aim of the research is to generate information that would permit screening of people at risk.
CDC	2008	Prospective Risk and Protective Factors for Suicide and co-occurring Risk Behavio	Manfred Van Dulmen	Suicide is the 3rd leading cause of death among adolescents and young adults aged 10-24 years (CDC, 2008). Despite a long period of declining rates of suicide among youth, suicide rates are twice as high as those in the 1950s and a recent study identified the first increase among adolescents in more than a decade (CDC, 2007). Previous studies have identified theoretically grounded and empirically validated risk and protective factors for suicide among adolescents and young adults (Borowsky et al., 2001, Bridge, Goldstein & Brent 2006, van Heeringen 2001). However, relatively few studies have attempted to explicitly compare the influence of specific risk and protective factors across samples of youth in different contexts and with different risk exposures. By considering the relationship between risk characteristics and socioenvironmental context, the results of the current project have direct implications for the development of targeted prevention and intervention efforts designed to reduce adolescent and young adult suicide. The long-term goal of the proposed study is to reduce rates of suicide by directly informing suicide prevention and intervention efforts by identifying differences in theoretically informed risk and protective factors across diverse samples of adolescents and young adults. The current project will use data from four prospective longitudinal studies (National Longitudinal Study of Adolescent Health, NICHD Study of Early Child Care and Youth Development, National Study of Child and Adolescent Well-Being, Behavioral Health/Juvenile Justice Project) to achieve the specific aims. These four data sources include information from more than 25,000 individuals on risk and protective factors for suicide from childhood through young adulthood. The overall objective of this study is in accordance with several national-level objectives related to decreasing suicide prevalence, including: the Surgeon General's Call to Action to Prevent Suicide (Enhance research to understand risk and protective factors, their interaction, and their effects on suicide and suicidal behaviors) "Healthy People 2010" (reduce the suicide rate among 10-14 year old and 15-19 old youth), and the National Center for Injury Prevention and Control's research priorities in preventing suicidal behavior (priority E: Clarify the influence of contextual forces on suicidal behavior and priority F: Clarify the impact of individual level factors on suicidal behavior). The study will achieve its aims through a comprehensive examination of existing data to better understand the risks for suicidal behavior across socio-environmental contexts. This inter-disciplinary and collaborative project involves three research institutions and is led by a uniquely and highly qualified research team guided by an oversight committee comprised of distinguished and renowned suicide scholars. The project is uniquely positioned to provide cost-effective and useful new findings that will directly inform efforts to reduce injuries and deaths from suicides. Because the proposal relies on existing data, analyses can be conducted quickly and findings can be disseminated rapidly to inform the prevention community and have an impact on suicide prevention within the next 3-5 years. The long-term goal of this study will be achieved by addressing three specific research aims: Aim I. Investigate whether risk and protective factors for suicidal behavior are unique in predicting suicidal behavior versus predicting co-occurring behavior problems. Recent empirical evidence indicates that protective and risk factors associated with suicide overlap with those predicting youth violence (Lubell & Vetter, 2006). Because these factors may overlap in predicting risk behaviors co-occurring with suicide, it is important to investigate the unique role of contextual factors and individual characteristics in the development of suicidal behavior versus other high risk behaviors such as violence perpetr

CDC	2008	Developmental Pathways to Dating Violence and Suicidal Behavior: The Healthy Teen	Pamela Orpinas	The goal of Healthy Teens is to increase scientific understanding of different levels of risk and protective factors that influence the developmental pathways (i.e., patterns of continuity or patterns of change over time) that children and young adolescents follow from 6th through 12th grade, in relation to dating violence and suicidal thoughts and behaviors. Healthy Teens differs from much of the extant research literature in that it: a) is a longitudinal study of a large sample (cohort of approximately 700 students); b) uses multiple methods (student surveys, teacher ratings, archival data on academic achievement and discipline, focus groups, and interviews; c) includes two samples of students (random and high risk); d) evaluates a large number of violence related constructs and behaviors, including risk and protective factors at multiple levels of an ecological framework; and e) includes students who dropped out of school. The unique, comprehensive design of Healthy Teens will serve to enhance our comprehension of the development of dating violence and its interrelation with suicidal thoughts and behaviors and, thus, provide a firm foundation to enhance prevention strategies. Objectives: Specific objectives are to: a) evaluate developmental trajectories from middle to high school in relation to dating and dating violence victimization and perpetration and its interrelation to suicidal thoughts and behaviors; b) evaluate the risk and protective factors that influence these developmental trajectories; and c) explore the context and meaning of dating violence from students' perspectives. Study Design: Healthy Teens is a mixed method study that began when students were in the 6th grade; they are currently in the 11th grade. This study proposes to complete one more year of data collection (12th grade—Year 1) so that that there will be complete, comprehensive data set of this cohort from middle through high school. Data analyses will be conducted during Years 1, 2 and 3 of the proposed study. This study will employ the same data collection strategies used since students were in the 6th grade, that is: a) student self-reported assessments; b) teacher behavioral ratings of students (BASC); and c) archival data. Additionally, individual interviews will be conducted with a purposeful, maximum variation sample of students who have been victims and/or perpetrators of dating violence. Setting: Healthy Teens researchers will work cooperatively with school administration and staff to collect data in the schools, as in years past. When this is not possible (e.g., student who has dropped out of school), data will be collected in students' homes or another convenient location (e.g., public library). Participants: Healthy Teens has followed a cohort of approximately 700 students (currently in the 11th grade) in eight Northeast Georgia high schools. When students were in the 6th grade (9 middle schools), two types of samples were recruited: a random sample and a high risk for aggression sample. The random sample (676 students) represented the student population of each school; the high risk sample (213 students) consisted of students who were considered by their teachers to be aggressive and influential with peers. A small number of students (107) in the random sample were also selected for the high risk sample. Outcome Measures: All students have completed questions on dating violence norms, dating, and dating violence behaviors; high school students have completed questions related to feelings of sadness and hopelessness and suicidal thoughts and attempts. In addition, all students have completed an array of measures of risk and protective factors at the individual, family, peer, and school levels. Census data on individual neighborhood characteristics are also available.
CDC	2010	Etiology of suicidal behavior during adolescence and emerging adulthood	Kenneth Conner	This 3-year project "etiology of suicidal behavior during adolescence and emerging adulthood" is in response to the Centers for Disease Control and Prevention RFA-CE-10-005 "Research Grants for Preventing Violence - and Violence Related Injury" that calls for "etiologic research" on suicidal behavior. Our primary research objective is to identify variables that decrease risk for suicide attempts in young people ages 12 to 25. We will examine three types of variables that decrease risk: 1) "promotive" factors that decrease risk directly, that is they show a direct, inverse relationship to SA; 2) "protective" factors that serve as a buffer against risk by moderating (lowering) the potency of risk factors; 3) variables that are both promotive and protective. Informed by a social connectedness framework, we will focus on promotive and protective effects of connectedness to peers, school, parents, and family. We will also examine promotive and protective effects of social capital, a measure of the connectedness within a community. Finally, we will investigate whether or not the promotive and/or protective effects of connectedness to parents, etc. assessed during adolescence endure into emerging adulthood. To accomplish these goals, we will analyze two large prospective datasets of adolescents and emerging adults assessed for the Collaborative Study on the Genetics of Alcoholism (COGA). We will also analyze measures of social capital derived through external data sources (e.g., Area Resource File). In Aim 1, we will test an etiological model of risk for suicidal behavior in youth. In Aim 2, we will examine the potentially promotive effects and protective effects of connections with peers, school, parents, and family. Protective effects will be examined by testing moderators of the risk factors confirmed in the Aim 1 analyses. In Aim 3, we will examine the promotive and protective effects of social capital. We will perform the analyses primarily using mixed effects models and structural equation models. The project will be carried out by an experienced multi-disciplinary research team. Results will be disseminated through peer-reviewed research papers, conference presentations, and twice-yearly suicide prevention meetings held in New York State (dissemination conferences) where non-technical presentations will be made to general audiences. PUBLIC HEALTH RELEVANCE: While most studies of suicidal behavior focus on risk factors, the goal of this project is to identify variables that decrease risk for suicide attempt during adolescence (ages 12 to 17) and emerging adulthood (ages 18 to 25), a time in the life course when the prevalence of suicide attempts peak and represents the most potent risk factor for eventual suicide. Informed by a social connections framework for suicide research and prevention, we will study the extent to which connectedness to peers, school, parent, and family lowers risk for a suicide attempt and whether or not the risk-lowering effects of these connections endures into emerging adulthood. We will also examine whether or not social capital, a measure of connectedness within a community, serves to lower adolescents and emerging adults risk for making a suicide attempt, with implications for developing strategies to strengthen young peoples' connections with others in order to prevent suicidal behavior.
CDC	2012	STAT-ED Suicidal Teens Accessing Treatment after an Emergency Department Visit	JACQUELINE GRUPP-PHELAN	While many young patients at risk for suicide present to the emergency department (ED) following suicide attempts or in situations of extreme suicidal crises, other patients at risk for suicide go unrecognized, and therefore untreated, in the ED. Once discharged, 30% of suicidal adolescents return to the ED with another crisis within six months of the sentinel event. Currently, no evidence-based standards exist for appropriate screening and post-screening interventions in order to improve outcomes for patients presenting in EDs who are at elevated risk for suicidal behavior. This two-site R01 application tests the effectiveness of a brief treatment engagement intervention termed Suicidal Teens Accessing Treatment after an ED Visit (STAT-ED) for adolescents seeking treatment in the ED for non-psychiatric concerns but identified via systematic screening as being at risk for suicide. In this unique 3-year proposal, investigators from two institutions (Cincinnati Children's Hospital Medical Center [CCHMC] and Nationwide Children's Hospital [NCH]) will recruit and randomize 160 adolescents (80 per site) to (a) the STAT-ED intervention or (b) enhanced usual care (EUC) as a comparison condition. EUC consists of a brief consultation and a mental health referral. The STAT-ED intervention targets family engagement, problem solving, assistance with referral and limited case management during the transition from the ED to outpatient care with the goal of maximizing the initiation of mental health treatment and aftercare among youth screening positive for previously unrecognized suicide risk. The application builds on a pilot study in which STAT-ED was well- accepted by patients, families, and clinicians and was more effective than EUC. We now propose to test the STAT-ED intervention against EUC in a larger, more diverse sample from two geographically separate, urban pediatric EDs serving broad populations (Cincinnati and Columbus, Ohio). A second aim is to compare the effectiveness of STAT-ED and EUC in reducing suicidal ideation and depression symptoms after ED discharge. The rationale is that by using the pediatric ED to identify and treat unrecognized suicide risk, adolescents will be less likely to overuse ED services in the future, have a better quality of life and ultimately have a reduced risk of morbidity and mortality. If successful, it will provide a brif and sustainable intervention that can be implemented across diverse pediatric ED settings. This study will contribute to the mission of the CDC by improving our capacity to identify "best practices" for screening, assessing, and implementing practical suicide prevention interventions in the pediatric ED setting. PUBLIC HEALTH RELEVANCE: Public Health Relevance. By providing a brief treatment engagement intervention to youth identified by ED staff as being at elevated risk for suicide, the study will be the first to test whether outpatient mental health care uptake and treatment attendance can be improved without undue burden on the work flow and resources of the pediatric ED setting.
CDC	2008	Psychiatric Services Following Adolescent Suicide Attempt	Jeffrey Bridge	The proposed study is a 1-year naturalistic, longitudinal follow-up investigation of a consecutive sample of 75 adolescents aged 13 - 19 who present to a university-based psychiatric hospital following a suicide attempt. At intake, subjects will be assessed with respect to demographic characteristics; presenting symptoms and diagnoses; psychosocial risk factors for suicide, past and intercurrent psychiatric treatment; characteristics of the suicidal episode; and prior history of suicidal behavior. Subjects will be followed up at 3 months to learn whether service factors occurring during the emergency management of the adolescents, and in the peri- and post-hospital periods, are associated with increased risks of repeated suicide attempt, return to the emergency department (ED), and re-hospitalization during follow-up, controlling for other risk factors. A secondary goal is to identify factors occurring during hospitalization that are associated with poor outcome.

CDC	2012	Creating and Testing a Suicide Prevention Curriculum for Domestic Violence Crisis	Catherine Cerulli	Depression is a devastating public health concern which leads to decreased life expectancy and reduced quality of life. Untreated, depression can lead to hopelessness and increased morbidity and mortality. IPV is also a public health problem affecting 44% of women and 30% of men over their lifetime. Among IPV victims, depression is the leading comorbid disease and most often untreated. Building on findings from the Principal Investigator's K01 Career Development Award (K01MH075965; C. Cerulli, PI, 3/1/06-2/28/11), this study deploys suicide prevention training to IPV hotline counselors, who victims often seek advice to change their lives. We will train IPV hotline workers at the National Domestic Violence Hotline (NDVH) agency located in Austin, Texas. The hotline receives over 20,000 calls per month. Given preliminary studies, it is likely that almost one-third of those callers have STB. The study's goal is to improve IPV hotline workers ability to listen for STB and refer IPV victims for mental health care. This study, based on community-based participatory research principles (CBPR), capitalizes on an already existing relationship IPV victims have with their advocates by providing IPV hotline counselors to the opportunity to help modify a suicide prevention curriculum for use on an IPV hotline and offer ongoing feedback. Aim 1 tailors a currently established IPV-STB curriculum for use with crisis hotlines. Aim 2 examines IPV hotline counselors' acceptability of an IPV-STB curriculum. Aim 3 estimates the impact of the IPV-STB curriculum on IPV hotline counselors' knowledge, attitudes and skills regarding suicide prevention immediately post-curriculum delivery, 3 and 6-months. Lastly, Aim 4 examines whether baseline measures (knowledge, attitudes and skills) and attendee characteristics (race, age, gender and tenure with the agency) moderate attendee skills at 6 months. The proposed study will forward implementation science generally, through investigation of training methods for IPV hotline counselors, and adoption of the suicide prevention strategies specifically through careful measurement of trainee characteristics, knowledge, attitudes, skills and fidelity. The results of this innovative study could provide the necessary empirical foundation for IPV advocates to become frontline suicide prevention experts with a population they have acces to, and relationships with: untreated IPV victims.
CDC	2012	Structure, Policy, and Suicide Variability across Communities	Robert Bossarte	This ICRC-S small research project proposes to begin systematically laying the foundation for a new generation of studies that will study context as an essential domain for better understanding suicide as a social phenomenon, not solely as an adverse clinical-medical epiphenonenon of primary psychiatric disorders. The need for improved understanding of variability in suicide rates has been widely recognized in sociological and public health literature; the proposed project addresses multiple NCIPC research priorities, including an examination of societal- and community-level factors associated with increased rates of suicide, consideration of individual-level risk and protective factors other than those related to mental health on suicidal behavior, and identification of community-specific attributes. As a final objective, this proposal will seek to obtain measures of state-level policies related to domestic violence and to identify associations between these policies and variability in rates of suicide. Ultimately we to use our overall findings to inform how innovative programs and policies can be developed or modified for use among diverse communities and culturally distinct populations.
CDC	2010	Links to Enhancing Teens' Connectedness (LET'S CONNECT)	Cheryl King	Suicidal behavior is highly prevalent among adolescents in the United States and associated with substantial morbidity. Moreover, suicidal behavior is a primary risk factor for suicide, which is the third leading cause of death for this age group. Despite the public health significance of suicidal behavior and suicide, few evidence-based prevention strategies have been developed for adolescents and even fewer have focused on preventing the initial occurrence of suicidal behavior. In response to RFA- CE-10-006 "Prevention of Suicidal Behavior through the Enhancement of Connectedness," this application proposes to rigorously assess the effectiveness of Links to Enhancing Teens' Connectedness (LET'S CONNECT) in a randomized controlled prevention trial. LET'S CONNECT was designed for adolescents who are at elevated risk for suicidal behavior due to low interpersonal connectedness, a recent history of bullying others, and/or a recent history of being bullied. It teams the adolescent with an adolescent-nominated "natural" mentor and a community mentor to actively facilitate and support the adolescent's engagement with community organizations and activities. Specific aims are to determine if adolescents in the LET's CONNECT condition relative to adolescents in the control condition (community resource information only): (1) report greater improvement in individual connectedness and community connectedness, and (2) are less likely to engage in suicidal behavior. PUBLIC HEALTH RELEVANCE: Despite the high prevalence of suicidal behavior among adolescents and the too frequent tragedy of suicide, few evidence-based suicide prevention strategies have been developed. This application proposes to rigorously assess the effectiveness of the Links to Enhancing Teens' Connectedness (LET'S CONNECT). This strategy was designed to enhance family and community connectedness and to prevent the onset of suicidal behavior in adolescents who are at elevated risk due to a history of victimization or exposure to interpersonal violence.
CDC	2010	The Senior Connection	Yeates Conwell	There is a pressing need for interventions that reduce risk for suicide in later life. Older adults in the U.S. have the highest rate of suicide and are the fastest growing segment of the population. We can anticipate a large rise in the number of older adults who die by suicide in coming decades. This application is in response to RFA-CE-10-006. Consistent with the CDC's key strategy of reducing suicide by promoting connectedness, our long-term goal is to reduce late life suicide-related morbidity and mortality by leveraging the resources and expertise of the aging services provider network (ASPN) to address unmet social needs of community-dwelling older adults. Our objectives with this proposal are (1) to examine whether linking socially disconnected seniors with peer supports through the Retired and Senior Volunteer Program (RSVP) is effective in reducing risk for suicide, and (2) to test an hypothesized mechanism for the association of social disconnectedness and suicidal ideation and behavior informed by the Interpersonal Theory of Suicide. We will recruit 400 primary care patients (200 men and 200 women) over age 60 years who endorse feeling lonely and/or as if they are a burden on others. They will be randomly assigned to either of two conditions. Those assigned to The Senior Connection (TSC) will either be paired with a peer companion or, if they prefer and are eligible, be trained and placed as a peer companion for others by RSVP. The comparison group will receive no further intervention ("care-as-usual" [CAU]). Subjects will be followed for up to 24 months with repeated in-home (baseline, 12, and 24 months) and telephone assessments (3, 6, and 18 months). The study has four specific aims: (1) To compare the impact of TSC and CAU on social connectedness of older adult primary care patients; (2) to compare the effectiveness of TSC and CAU in reducing factors associated with proximal risk for suicidal behavior; (3) to determine if changes in measures of older adults' social connectedness mediate the relationship between social connectedness and suicide risk; and (4) is to examine whether responsiveness to the intervention differs by gender. PUBLIC HEALTH RELEVANCE: The Retired and Senior Volunteer Program (RSVP) is offered in communities nationwide by social service agencies that are dedicated to maintaining the independence and quality of life of older adults. Their expertise and resources are well suited to the reduction of suicide risk in later life. If RSVP is shown to be effective in reducing suicidal ideation and increasing connectedness, it will be easily disseminated across the aging services provider network as a means to prevent suicide among seniors at risk.
CDC	2008	Epidemiology of Intimate Partner Homicide-Suicide in Los Angeles County	Billie Weiss	This study is an extension of an earlier UCLA study, Incidence and Patterns of Intimate Partner Homicide, which assembled data from the Los Angeles County Coroner for 59 cases during the years 1994-1997. This was formerly a seed project which is now a small project. Data have now been collected through 2004, with a total of over 200 cases. Three local agencies have collaborated with us on this study: the Los Angeles County Department of the Coroner, the Los Angeles Police Department, and the Los Angeles Office of the Bureau of Alcohol, Tobacco and Firearms (ATF). Initial case ascertainment was made using the California Master Mortality File and coroner data. First, all suicides of males age 15 or older were identified in the Master file. Each suicide was identified in the Coroners database to determine if it was associated with a homicide. Homicide records were physically examined to confirm that the death was associated with a suicide. After case identification, corresponding records of the law enforcement agencies were identified using first and last name of decedent, and date of incident. Where information on a weapon identified at the scene was found additional information was sought from law enforcement and ATF. Data were abstracted from paper records by undergraduate and graduate public health students.

CDC	2008	Risk and Protective Factors for Partner Abuse, Child Maltreatment & Suicidality	Amy M. Smith Slep	Partner abuse, child abuse and neglect, and suicidal behavior are costly occurrences in American society, in terms of both human suffering and economics. Healthy People 2010 targets all three problems for reduction. However, brevention of each of these areas is hampered by inadequate knowledge about the relative relations of risk and protective factors to the problems. The purpose of this project is to use a large (over 100,000 respondents), representative archival sample from 83 communities to provide effect sizes of risk factors at various levels (i.e., individual, family, work, and community), to test hypotheses about the buffering effects of protective factors, and use these results to create exploratory models of risk and resilience for these problems. The archival data set contains detailed assessments of suicidality, partner and child physical assaults and their impacts, partner and child emotional assaults and their impacts, and child neglectful omissions. We will test the effect sizes of risk factors using correlations, the buffering effects of protective factors using correlations and backward stepwise logistic and linear regressions, and overall models using structural equation modeling. We will use statistical packages that can appropriately estimate standard errors in a complex data set collected at 83 communities. Prevention science is guided by a five stage, recursive research cycle: (1) defining the problem and measuring its prevalence; (2) establishing risk and protective factor relations with the problem; (3) efficacy trials; (4) effectiveness trials; and (5) dissemination trials (Mrazek & Haggerty, 1994). Large gaps remain in the risk factor literature on all forms of partner abuse and child maltreatment (Slep & Heyman, 2001); very little is known at all about putative protective factor relations. Because this knowledge provides the bedrock on which to build effective prevention activities, reaching the Healthy People 2010 objectives is unlikely without improvements. This project is unique and innovative because (a) it is large enough to have very high power and low standard errors in its estimations of risk and protective factor effect sizes and additive effects; (b) it will examine risk and protective relations for injury as well as lower level behaviors (e.g., assault); (c) it will test these relations for partner and child physical abuse, partner and child emotional abuse, child neglectful omissions (lack of supervision and exposure to physical hazards), and suicidality; (d) it will examine risk and protective factors for comorbid conditions; and (e) it is large enough to examine these relations for children in different age groups.
CDC	2009	Evaluating Population-Based Approaches to Suicide Prevention through Systematic R	Carolyn DiGuiseppi	Suicide is the most common cause of violent death in the US, and the eleventh leading cause of all deaths. The identification of biological, psychological, and socio-environmental risk factors has prompted many disciplines to develop interventions to prevent suicide. National government objectives include identifying and evaluating the effectiveness of suicide prevention programs. Comprehensive identification of studies in the field of suicide prevention is difficult because of the range of disciplines involved, the publication of many studies as government or other internal reports, and the international body of literature on suicide prevention programs. This proposal aims to comprehensively identify and disseminate controlled evaluations of suicide prevention programs, and use the identified studies to conduct two systematic reviews of suicide prevention strategies targeting the high-risk or general population. A sensitive search strategy will be systematically developed and applied to multiple databases that span disciplines relevant to suicide prevention. Results will be screened to identify controlled evaluations of suicide prevention. Unpublished and international literature will be identified by searching gray literature databases, hand-searching conference proceedings, and contacting organizations and experts. Studies identified as eligible will be transmitted to the Cochrane Injuries Group for inclusion in their specialized register and, where applicable, publication in the Cochrane Central Register of Controlled Trials. Systematic reviews of selected population-based suicide prevention strategies will be performed according to the Cochrane Collaboration's guidelines. Results will be combined quantitatively when possible. Reviews will be published in the Cochrane Library. By making a broader domain of evaluation studies publicly accessible, and by conducting systematic reviews of population-based suicide prevention strategies, this project will contribute to the available evidence base for policy makers and health and other professionals to make appropriate decisions about implementation of effective interventions. Public Health Relevance: Since many people who commit suicide never seek treatment, it is necessary to find effective interventions that target the general population. This project will search for high-quality studies of suicide prevention programs, then evaluate the studies of two population-based suicide prevention programs to determine whether they are effective. Results will help public health professionals decide which suicide prevention programs to use.
DoD	2012	Suicide Bereavement in Military and their Families	Julie Cerel	Aim (1) Measure lifetime exposure to suicidal behavior among a representative US veteran population sample; Hypothesis 1a: more than half of veterans will report lifetime exposure to suicide attempts and/or deaths Hypothesis 1b: more than a third of the veteran population will report lifetime exposure to suicide deaths. Aim (2) Explore factors that influence adverse affects and resilience within veterans exposed to suicide death compared to veterans who experienced a sudden traumatic death of a coworker during their military career. Hypothesis 2a: identification as a survivor of suicide will be related to adverse effects including suicidal behavior, prolonged grief and posttraumatic stress disorder (PTSD) which will be similar to individuals who experienced a sudden traumatic death of a coworker during their military career. Hypothesis 2b: demographic variables and kinship relationship to the decedent will not predict adverse effects but self-perceived closeness to the decedent and variables related to the acquired capability and perceived burdensomeness will be related to adverse effects. Aim (3) Explore psychiatric outcomes and variables related to resilience in a sample of adult children, parents and spouses of recent active duty military and veterans who died by suicide
DoD	2011	Suicide in the Active Duty Army 2000-2009	Owen Hill	Objective: The purpose of this study is to identify risk factors for suicide and suicide attempts in the US Army Soldier population, and to provide evidence to guide unit commanders and medical personnel as to identifying high risk Soldiers who should be targets for preventive intervention. Hypotheses Being Tested: Yearly completed suicide rates in Active Duty Army Soldiers are on an increasing trend from 2000-2009. Yearly attempted suicide rates in Active Duty Army Soldiers are on an increasing trend from 2000-2009. Soldiers who have committed suicide have a profile of unique occupational and demographic characteristics that set them apart from Soldiers who do not commit or attempt suicide. Soldiers who have attempted suicide have a profile of unique occupational and demographic characteristics that is significantly different from comparison Soldiers.
DoD	2009	Usability and Utility of a Virtual Hope Box (VHB) for Reducing Suicidal Ideation	Nigel Bush	Our overall objective in the proposed study is to conduct a proof of concept development and evaluation of a virtual hope-box (VHB) smartphone app to supplement in-person clinical therapy for service members with suicide ideation or behavior. We propose to develop and test the VHB app in two phases: Phase 1: an initial prototype development followed by usability testing of the prototype to inform refinement of the app interface, functioning and content and; Phase 2: a proof of concept pilot comparing acceptability and utility of the VHB with a conventional ?physical? Hope Box (PHB) in clinical practice. We hypothesize that the VHB will demonstrate high usability (e.g., easy to learn, efficient and convenient to use) with clinical outpatients, that patients will use the VHB more than a PHB, and that the VHB will demonstrate high patient acceptability and satisfaction. We also hypothesize that users will prefer the convenience, easy utility, content richness, and hip-pocket portability of the VHB to the more static, cumbersome, and immobile PHB.
DoD	2009	Military Continuity Project (Caring Texts)	Catherine Comtois	Our overall objective in the proposed study is to conduct a randomized controlled trial with military Service Members to determine whether or not the addition of a Continuity Contact via Texts (CCVT) intervention to treatment as usual (TAU) results in reductions in suicidal ideation and behavior over the year following identification of suicide ideation or behavior. To accomplish this objective we will randomize 800 Service Members who report suicidal ideation or behavior to receive CCVT+TAU or TAU alone. We have two specific aims and related hypotheses. Aim 1: To determine if the addition of 12 months of CCVT+TAU results in lower rates of suicidal ideation and behavior relative to TAU alone. Hypothesis 1a: Participants assigned to CCTV + TAU compared to TAU alone will experience reduced suicidal ideation at 12-month follow-up. Hypothesis 1b: Over the 12 months post-study enrollment, a smaller proportion of participants assigned to CCVT+TAU vs. TAU alone will have suicide risk incidents (i.e., those requiring medical evacuation or hospital admission. Hypothesis 1c: Over the 12 months post-study enrollment, CCVT+TAU vs. TAU alone will have fewer total number of suicide risk incidents requiring medical evacuation or hospital admission. Aim 2: To test two proposed mechanisms of action of CCVT outcome: 1) reduced ?thwarted belongingness? and 2) increased engagement in behavioral health services. Hypothesis 2a: The effect of CCVT compared to treatment as usual alone will be mediated by reductions in ?thwarted belongingness? from pre to post-study. Hypothesis 2b: The effect of CCVT compared to treatment as usual alone will be mediated by increased use of outpatient behavioral health services in the CCVT condition.
DoD	2011	Study to Examine Psychological Processes in Suicidal Ideation and Behavior (STEPPS)	Rory O'Connor	Suicide and attempted suicide are major public health concerns across the globe. Suicide is the second leading cause of death in the military, indeed the military suicide rate is now higher than that in the civilian population. Despite the scale of the problem, until recently there has been a paucity of studies investigating integrative theoretical models to understand why people take their own lives. Therefore, the focus of the present program of basic scientific research is to advance our understanding of suicidal ideation and behavior by empirically testing two theoretical models of suicidal behavior (Integrated Motivational?Volitional Model of Suicidal Behavior, IMV; O?Connor, 2011 and Interpersonal?Psychological Theory of Suicide, IPT; Joiner, 2005) to determine the key factors which underpin suicide risk. Objective/Hypothesis: This research program will address two broad aims: (1) To advance our understanding of the basic psychological processes associated with suicidal ideation and behavior and (2) To further test two theoretical models of suicidal ideation and behavior (i.e., the IMV and IPT). There will be 8 specific research questions associated with these aims, including: (i) how do personality and individual differences variables relate to suicidal ideation and behavior; (ii) what is the nature of the relationship between defeat, entrapment, belongingness and burdensomeness and; (iii) do the central components of the IMV and IPT predict suicidal ideation over time?

DoD	2008	The Association Between Suicide and OEF/OIF Deployment History	Mark Reger	The proposed research project will address Topic Area 5 by developing a database in collaboration with other federal agencies to provide population-based estimates of the rates of suicide among service members with and without a history of deployment to OIF/OEF, and nondeployed veterans from the beginning of OIF/OEF forward. Our specific aims are: 1) To compare suicide rates among non-veterans (general population) and service members/veterans with and without a history of deployment in support of OIF/OEF. 2) To determine whether active duty and veteran National Guard members and Reservists with a history of OIF/OEF deployment are at increased risk of suicide compared to postdeployed service members/veterans from the active component and non-veterans. 3) To examine the relationship between suicide rates and rates of deaths of undetermined intent among non-veterans and service members/veterans with and without a history of deployment in support of OIF/OEF. 4) To transition the valuable database created to conduct the proposed study to the DCoE for additional analyses to maximize the benefits of this seminal effort.
DoD	2009	Romantic Relationship Satisfaction and Self-Directed Violence in Veterans	Amanda Stoeckel	Social stressors have been implicated in self-directed violence in returning service men and women Acquisition of additional information on psychosocial stressors that may be associated with self-directed violence is needed in order to develop improved intervention strategies. We hypothesize that Veterans with a history of self-directed violence will report lower romantic relationship satisfaction compared to Veterans without a history of self-directed violence It is also hypothesized that there may be a discrepancy between the self-report ratings of Veterans and that of their spouses/partners, which may be associated with the presence of self-directed violence among Veterans.
DoD	2009	U.S. Army-National Institute of Mental Health Study to assess Risk and Resilience in Service Members (Army STARRS)	Bob Ursano	TThis proposal is submitted in response to RFA-MH-09-140 by an interdisciplinary team from four institutions: the Uniformed Services University of the Health Sciences (USUHS), Harvard Medical School (HMS), the University of Michigan (UM), and Columbia University (CU), The team has unparalleled expertise in research on military mental health (USUHS), general population psychiatric epidemiology (HMS), large-scale epidemiological data collection (UM), and neurobiological-clinical research on suicidal behaviors (CU). We propose a multi-phase epidemiological study that considers diverse psychosocial and neurobiological risk and protective factors for suicidal behaviors and secondary outcomes in order to make evidence-based recommendations for implementation of Army suicide prevention interventions. An enriched version of the Army Suicide Event Report (ASER) system will be developed to define the primary outcomes incorporating information from the DoD Medical Mortality Registry (MMR) and Total Army Injury and Health Outcomes Database (TAIHOD). Our study design will include both a retrospective case-control component for quickefficient hypothesis testing and a prospective survey component to predict subsequent suicidal behaviors and secondary outcomes (onset, persistence, worsening of DSM-IV disorders, suicide ideation, suicide plans). We will also use data from the ongoing Pre- and Post-Deployment Health Reassessment Program (PDHRP) surveys as secondary outcomes. The case-control survey will study soldiers who made nonfatal attempts and relatives of soldiers who committed suicide in a psychological autopsy framework. Parallel data will be collected from carefully matched controls. Blood samples and, in the case of nonfatal attempters and their controls, saliva samples will be collected to allow neurobiological risk and protective factors to be studied. The survey component will include active duty personnel across all phases of Army service. Survey reports will be link to subsequent ASER records and PDHRP reports to study prospective associations of predictors with suicidal behaviors and secondary outcomes. A number of innovative measurement, design and analysis features will be used to increase chances of discovering effective intervention possibilities.
DoD	2013	Neuroimaging Correlates of Suicide Risk	Deborah Yurgelun-Todd	Brain changes have been implicated in self-directed violence in returning service men and women. Additional information on neurobiologic changes that may be associated with risk for self-directed violence is needed in order to develop improved intervention and treatment strategies. We hypothesize that Veterans with a history of self-directed violence as evaluated by MSRC gold standard assessments will show significant differences in frontal frontal imaging endpoints. We also hypothesize that significant associations will be present between MR indices and measures of suicidal ideation, suicide intent and suicidal and non-suicidal self-injury.
DoD	2011	Evaluation of Suicidality, Cognitions and Pain Experience (ESCAPE): Implications for CBT in Military Populations	Kathryn Kanzler	Cognitive behavioral therapy (CBT) is a term for empirically-supported treatments addressing myriad complaints including suicidality, chronic pain and PTSD. Evidence demonstrates that individuals experiencing the steadily-growing problem of chronic pain are at increased risk for suicidal ideation/attempts. Research evaluating cognitive mechanisms underlying this phenomenon (including fear-avoidance, perceived burdensomeness, pain acceptance, and pain catastrophizing) is sparse. No available studies have confirmed/explained the role of these processes in suicide risk among pain sufferers for whom these cognitions may be particularly prevalent. These factors will be examined with consideration of trauma-related symptoms, based on limited evidence suggesting trauma (a growing problem for service members deployed for OIF/OEF) can further increase suicide risk. If cognitive and trauma variables play a significant explanatory role in suicide risk among pain sufferers, then examining these mechanisms is a crucial first step in identifying effective CBT treatments for the at-risk pain population. We hypothesize that cognitive variables associated with chronic pain will predict suicide risk presence/intensity and that the beneficial impact of social support (another CBT intervention target) for suicide risk will be mediated by these cognitive constructs. Participants will be recruited from three clinics at a MTF in the Southwestern US and asked to complete an anonymous battery assessing pain, suicidality and the cognitive variables above. egression analyses will be conducted to determine significant mechanisms. The overall aim of this basic research study is to inform CBT clinicians through advancing understanding of cognitive mechanisms impacting suicidality in military pain sufferers.
DoD	2013	A Taxometric Investigation of Suicide	Jill Holm-Denoma & Tracy Witte	Problem: It is not currently known if suicide risk is a categorical or dimensional phenomenon. This may explain why current suicide risk assessment procedures have limited predictive validity. Hypothesis: Military personnel at ?high risk? for suicide are qualitatively distinct from those at ?low risk? for suicide. Military Relevance : As suicide rates among military personnel continue to rise, effectively determining how to classify suicide risk is critical. Valid classification impacts: Assessment of suicide risk; Allocation of suicide prevention programs; Allocation of research resources
DoD	2013	A Novel Approach to Identifying Behavioral & Neural Markers of Active Suicidal Ideation	Beeta Homaifar & Melissa Amick	Study will assess the cognitive and neural vulnerabilities through which actively suicidal OEF/OIF/OND Veterans become overtaxed during a novel experimental task that induces emotional and cognitive stress. The authors hypothesize that during a working memory task with induced cognitive and emotional stress, we will demonstrate the 1) cognitive, 2) functional, and 3) structural changes in the frontal lobes and amygdala that are markers unique to SI. Identifying markers of clinically significant SI will improve military suicide prevention programs by focusing interventions to address cognitive and neural vulnerabilities. These markers can serve as objective outcome measures to determine intervention efficacy.

DoD	2008	Optimizing Screening and Risk Assessment for Suicide Risk in the U.S. Military	Thomas Joiner	Suicide is a leading cause of death in the general population (National Insititute for Mental Health, 2008), and it is the second most common cause of death in the United States Armed forces (Ritchie, Keppler, a& Rothberg, 2003). In fact, in recent years the suicide rate of military service members and veterans has been quickly rising, which has sparked a pressing interest in better ways to treat and assess this phenomenon in milatary personnel (Lorge, 2008). For instance, one study found that the most common type of traumatic death suffered during armed forces training was suicide (Scoville, Gardner, & Potter, 2004). Employing the most up-to-date measurement technologies and theoretical approaches to risk assessment may represent a key component in allaying this worrisome mental health trend in the military. Objective/Hypothesis: In a sample of several thousand army recruiters - a group with documented high risk for suicidal behavior - we will administer an innovative and highly promising battery of measures (agitation, insomnia, suicidal ideation, implicit associations, suicide-specific hopelessness, perceived burdensomeness, low belonging, and fearlessness), and use them to predict suicide-related outcomes over eighteen months in a high-risk military sample, recruiters. Importantly, we have gained access to this sample, and administration of all measures is feasible in the relevant setting. Scores from the measures, as well as data from existing, status quo risk assessment, will be entered into regression equations simultaneously, which will reveal which particular measure - or set of measures - is optimally predictive of outcomes. Classification statistics (e.g., sensitivity, specificity, postive predictive value, negative predictive vale) will be used to inform how best to implement the resulting battery and to evaluate how well it might do overall. As the explicit aim of this proposal is to compare very promising risk factor assessment approaches to each other, we make no specific predictions about which measure(s) will perform best. An advantage of the project and the research team is that most approaches have a "partisan advocat" on the team (e.g., Joiner for interpersonal-psychological variables; Rudd for suicide-specific hopelessness; Nock for implicit associations). This is advantageous because it ensures a fair test, and any potential allegiance effects are negated. Study Design: Except for two weeks each year, over 100 recuriters per week attend the Army Recruiters Course (ARC) at The Recruiting and Retention School (RRS) on Fort Jackson, South Carolina, During their orientation to the ARC, recruiters complete a number of surveys and assessment instruments, such as a post deployment survey and a personality inventory. The results from these instruments are downloaded and reviewed by the RRS recruiter coaches and the Behavioral Health Consultant to identify those who may need behavioral health care and/or other services. Thus, the infrastructure for the proposed project is up and running in the project's setting; our project would thus seamlessly integrate with existing infrastructure, in that we would add our brief battery to the exisiting protocol. We will use elements of our battery to predict suicide-related outcomes over time; these outcomes will be tracked using the exisiting electronic infrastructure. We will use the indices in our battery as predictors of our suicide-related dependent varieables, which, in order of specificity, are suicide attempts, non-suicidal self-injury, episodes of suicidal ideation, episodes of depression, and mental health visits. For each of these DV's, we will examint the number of occurrences and time to first occurrence, over the course of approximately eighteen months; time to first occurrence is an index of interst because it may illuminate predictors' temporal parameters (e.g., near-term vx. longer-term prediction). The project will utilize existing electronic infrastrucure to track these variables. As illustrated in our Preliminary Studies section, our team has already begun tracking these outcomes in the proposed setting.
DoD	2010	Assessment of Cognitive Functioning as it relates to Risk for Suicide in Veterans with HIV/AIDS	Gina Signoracci	In the last several decades the occurrence of with human immunodeficiency virus (HIV) among military personnel has risen to pandemic proportions. Cognitive and/or psychiatric impairments are frequently present among those with HIV and acquired immune deficiency syndrome (AIDS) and those with HIV/AIDS have been shown to be at higher risk for self-directed violence. Primary Hypotheses: Among Veterans with HIV/AIDS: 1) cognitive impairment (composite score of neuropsychological measures) is associated with greater suicidal ideation (SI) as measured by the Beck Scale for Suicide Ideation (BSS); and 2) current psychiatric distress as measured by the Outcome Questionnaire-45 (OQ-45) is associated with greater SI as measured by the BSS. Military Relevance: Results of this study are expected to benefit Departments of Defense (DoD) and VA policy makers and providers regarding the utility of assessing cognitive and/or psychological deficits secondary to HIV, in particular, as they relate to suicide risk.
DoD	2010	Development and Validation of a Theory Based Screening Process for Suicide Risk	Steve Vannoy	Suicide and suicide related behavior are a substantial source of medical morbidity and mortality in the general population and in the armed services (WISQARS, 2007). Recent reports indicate that suicide rates in the military may have surpassed rates in the general population and are significantly greater in postdeployment personnel (Kang & Bullman, 2008; Kuehn, 2009). Identifying risk for suicide is a critical task for prevention efforts. Efficient methods for identifying acute risk for suicide are hampered by limited tools that have predictive validity. Development of such tools is in-turn hampered by variety of methodological challenges, most of which can be addressed by adequate sample size. Standard operating procedures related to routine health screening of all personnel returning from deployment (i.e. the Post Deployment Health Assessment and Re-Assessment, PDHA/PDHRA) have the potential to assist suicide prevention efforts. What is currently unknown at this time is an optimal method for identifying at-risk individuals. The development of an empirically supported screening mechanism will directly assist suicide prevention efforts. Objective/Hypotheses: The ultimate objective of this study is to assist in increasing the capacity of military based health services to accurately identify persons at risk for suicide. To do so we will characterize and evaluate the ability of a proposed suicide screening instrument and associated clinical decision making algorithm to accurately identify at-risk individuals and provide appropriate treatment recommendations. Furthermore we will evaluate key theoretical questions related to distinguishing who is at most risk for actual suicide. We will achieve this objective through three specific objectives. Objective 1: Characterize response rates on a proposed suicide screener that assesses the domains of imminent danger to self, acute suicide related behavior, acute indicators of distress, common stressors ? all evidence based constructs related to suicide. Analyses 1: We will compute descriptive statistics and compare and contrast with two separate data sources: 1) the PDHA/PDHRA captures recent suicide ideation via clinician inquiry, this data can be directly linked to our screener for individual-level comparisons; 2) our anonymous mail-in survey will capture acute indicators, passive, and active suicide ideation at a group level allowing population comparisons on these constructs. Objective 2: Characterize the performance of a proposed clinical decision making algorithm for accurately categorizing mental health treatment recommendations for respondents. Analyses 2: We will compare treatment recommendations from the clinical decision making algorithm against the standard PDHA/PDHRA process as well as in-depth clinical interviews on a sub-sample. We will compute the sensitivity, specificity, positive predictive value along with inter-rater reliability. We will also compute inter-rater congruency between the PDHA/PDHRA and screener. Objective 3: Increase clinically relevant knowledge regarding the ability to distinguish who is at highest risk for suicide (i.e., enhance specificity and positive predictive value). Compare results of the screening and clinical interview against predictions based on Interpersonal Theory of Suicide (IPTS) (Joiner, 2005). Hypotheses 3: Participant levels of perceived burdensomeness and thwarted belongingness will be positively correlated with the number and intensity of suicide risk indicators (resolved plans/preparation, history of multiple attempts, suicide desire, axis-I disorder, axis-II disorder, life stressors, social isolation). Acquired capacity for suicide will be significantly and positively associated with recent suicide ideation above and beyond the following traditional risk factors. Furthermore, the IPTS constructs will be confirmed in large sample factor analyses.
DoD	2012	Toward a Gold Standard for Suicide Risk Assessment for Military Personnel	Peter Gutierrez; Thomas Joiner	Specific Aims: The proposed study will pit several psychometrically sound suicide risk assessment measures against one another, to determine which tool or combination of tools optimally assesses the likelihood of future suicide-related indices over a three month period, in a large sample of military personnel seeking services from or referred to inpatient psychiatry, outpatient behavioral health, or the emergency department because of suicide risk concern. We will also test whether a simple self-report measure performs as well or better than more comprehensive interview-based assessment approaches and if there is a benefit to combining the two assessment methods. If funded, this project will be initiated in the second year of a projected 5-year award for the MSRC. As such, the study is designed with a three year timeline to optimize recruitment and data collection efforts. The risk assessment measures are: 1) Columbia-Suicide Severity Rating Scale (C-SSRS; Posner et al., 2011); 2) Self-Harm Behavior Questionnaire (SHBQ; Gutierrez, Osman, Barrios, & Kopper, 2001); 3) Suicidal Behaviors Questionnaire-Revised (SBQ-R; Osman, Bagge, Gutierrez, Konick, Kopper, & Barrios, 2001). These measures were selected because of their existing data regarding reliability and validity when used in clinical settings, broad-spectrum coverage of the suicidal behavior domain, and promise of predictive validity. Hypothesis: Because no research has evaluated the ability of existing measures to assess the likelihood of suicidal behavior in the future, no specific hypotheses are being made regarding the measures selected for this study. Instead, our intention is to determine which of the selected measures has the best combination of positive and negative predictive power.
DoD	2013	Identifying factors associated with future suicidal self-directed violence within a sample of Mississippi National Guard personnel	Michael Anestis	Problem: Prominent models of suicide risk tested primarily on civilians and prior suicidal self-directed violence. Prior work relies heavily upon single method/self-report methodology and assumes risk is similar across time. Current risk assessments struggle to identify future attempters. Hypothesis: Emerging models of risk (e.g., IPTS, elevated distress tolerance) will significantly predict past and future suicidal behavior. Military Relevance: Results based specifically on military sample and include potential methods to overcome barriers of self-report data

DoD	2012	Behaviorally Assessing Suicide Risk	Sean Barnes	Problem: Prediction of suicidal behavior remains tenuous and relies almost entirely on patient self-report. This is problematic when suicidality is transient or patients are motivated to conceal intentions. Primary Hypothesis: Higher scores on a behavioral test (the suicide implicit association test; IAT) will be associated with significantly greater odds of having made a suicide attempt in the past week. Secondary Hypothesis: Higher scores on the IAT will be associated with greater odds of making a suicide attempt in the next 6 months. Military Relevance: Service members may be especially motivated to minimize or deny suicidality in order to avoid loss of status and other negative repercussions. The IAT may eventually provide a more accurate assessment of suicide risk in military personnel by reducing the potential for response bias.
DoD	2013	Warning Signs for Suicide Attempts	Courtney Bagge & Ken Conner	Problem: Warning Signs (WS) define when at acute risk for suicidal behavior; Identification of WS are key to prevention efforts; Minimal a priori research or controlled data on WS Aims: Identify WS for suicide attempts in veterans and civilians. Categories of WS: behavioral, affective, and cognitive. Specific Hypothesis (based on preliminary studies): WS include: rage/anger, anxiety, hopelessness, acute use of alcohol, interpersonal negative life events. Military Relevance: Novel controlled study of WS in military population; Military suicide prevention trainings largely focus on warning signs (DoD Task Force Report, 2010); Warning signs are widely disseminated (e.g., VA pocket cards)
DoD	2013	New Approaches to the Measurement of Suicide-Related Cognition	Matthew Nock	Problem: Suicide is among the leading causes of death among Soldiers and Veterans. Methods are needed to better identify who is at risk for, and to decrease the likelihood of, suicidal behavior. Hypotheses: (a) Suicidal individuals will show biases in cognitive processes related to their experience of the past, present, and future; (b) measures of these cognitive biases will predict suicidal behavior; and (c) modifications of this cognitive biases will decrease suicidal behavior. Military Relevance: The results of this study will significantly advance the understanding of suicidal behavior among Veterans, and may yield new tools for prediction and intervention.
DoD	2008	Brief Cognitive Therapy for Military Populations	David Rudd	The research gap in the treatment of suicidality is considerable, particularly with military populations, including those returning from deployment in support of OIF/OEF. Only one randomized clinical trial targeting suicidality has been conducted with a military sample (Rudd et al., 1996). Due to these circumstances, researching the trajectory and psychotherapeutic treatment of suicidality among military personnel has become increasing critical. When focusing specifically on methodologically sound studies of treatments that have effectively reduced suicide attempts, Cognitive-Behavior Therapy (CBT) emerges as the dominant psychotherapy. CBT embodies several elements, techniques and interventions that supporting research suggests are effective in treating suicidality, including: a theoretical model that is easily explained to patients (specifically, learning about the relationships between cognitions, emotions, and behavioral responses); a manual-driven approach with treatment fidelity checks; and a focus on treatment compliance, targeting identifiable skills, and assuming personal responsibility. Brief Cognitive-Behavior Therapy (B-CBT) includes all of the aforementioned, empirically supported treatment components of CBT. B-CBT is a 12-session modification of a previously tested and empirically supported approach to treating suicidality (Rudd et al., 1996; Rudd, Joiner, & Rajab, 2004). This study will be conducted at Fort Carson, targeting 150 participants. Participants will be recruited from the appropriate clinical facilities, including the outpatient clinic, emergency room, and inpatient facility. Those agreeing to participate will be randomly assigned to one of two conditions, B-CBT (experimental condition) or treatment as usual (control condition). Treatment as usual is simply the existing outpatient treatment currently available at Fort Carson. Participants will be assessed with clinician administered interviews as well as self report scales at intake as well as 1,3,6,12,18, and 24 months. Although time-limited treatment of suicidality is the primary target of the project, additional elements will be explored including prospective investigation of suicide risk factors and warning signs, as well as development of a centralized software assessment/management tracking system for high-risk suicidal individuals. This study design is firmly grounded in empirical support and has great potential to further our understanding of the development and treatment of suicidality in the military population.
DoD	2009	A Behavioral Sleep Intervention for the Prevention of Suicidal Behaviors in Military Veterans: A Randomized Controlled Trial	Rebecca Bernert	The Overarching Aim of this proposal is to develop and test a brief sleep intervention to prevent suicidal behaviors among OEF/OIF veterans in a randomized controlled trial. Suicide represents a public health problem for which efficacious interventions are either few in number, unacceptable to patients (i.e., based on retention rates), or inaccessible to those most in need. Evidence suggests that disturbed sleep confers elevated risk for suicidal behaviors. Controlling for depression, this effect has been replicated across diverse populations (civilian, military), designs (longitudinal, cross-sectional), assessments (objective, subjective sleep), and outcomes (suicide ideation, suicide). Preliminary evidence additionally suggests that modifying this factor therapeutically impacts suicidal risk. Use of a non-mental health intervention, targeting a physical symptom of depression that is amenable to treatment and highly prevalent among veterans, may thus be an effective strategy to enhance clinical detection and improve access to care.
DoD	2008	High Risk Suicidal Behavior in Veterans-assessment of Predictors and Efficacy of Dialectical Behavior Therapy	Marianne Goodman	Background: Suicide is the second leading cause of death in active duty military personnel (CDC, 2005), with evidence of increased suicide risk particularly among soldiers serving in Iraq and Afghanistan (Allen et al. 2005; Hill et al. 2006; Kuehn 2009). Despite this pressing problem, there exist very few treatment studies that empirically evaluate efficacy to prevent suicide in military or civilian populations. One psychosocial treatment approach that has been shown empirically to decrease suicidal behavior is Dialectical Behavior Therapy (DBT), although studies of DBT and suicidal behavior have been limited to patients with borderline personality disorder. The current proposal aims to examine the efficacy of DBT in reducing suicidal behavior more broadly in a diagnostically heterogeneous group of veterans with high risk (HR) suicidal behavior. Objective/Hypothesis: The purpose of this study is to examine the efficacy of a 6 month treatment with standard DBT compared to treatment as usual (TAU) in veterans recently discharged from an acute psychiatric inpatient stay with high risk suicidal behavior. We hypothesize that DBT will be better than TAU in decreasing suicidal events. We will also compare high-risk and low-risk suicidal veterans in interpersonal functioning and resilience, in an effort to identify intermediate symptoms that are closely associated with suicidal behavior. Specific Aims: Aim 1: To examine the efficacy of a 6 month treatment with standard DBT compared to TAU in 120 veterans recently discharged from an acute psychiatric inpatient stay with HR suicidal behavior. The primary treatment outcome will be a quantification of suicidal events. Aim 2: To recruit veterans recently discharged from an acute psychiatric inpatient stay with HR suicidal behavior and compare 150 veterans with HR suicidal behavior to 150 veterans without such behavior (LR) in symptom domains focusing on interpersonal functioning and resiliency. Aim 3: To explore the effect of DBT on the candidate intermediate symptoms of interpersonal functioning and resiliency associated with HR suicidal behavior. Study Design: We will conduct a randomized control trial comparing 6 month of standard DBT (weekly individual sessions, skills training group and telephone coaching as needed) to TAU in 120 veterans recently discharged from an acute psychiatric inpatient stay with high risk suicidal behavior. Our primary outcome measure will include suicidal events, as assessed by the Columbia Suicide Severity Rating Scale. Secondary outcomes will include suicidal ideation, parasuicidal events, treatment compliance, depressed mood and hopelessness. We will also compare high-risk and low-risk suicidal veterans in interpersonal functioning and resiliency at baseline in order to identify intermediate symptoms that are closely associated with HR suicidal behavior, and will explore the effect of DBT vs. TAU on these symptom domains. Subjects randomized to TAU vs. DBT will continue to receive standard psychopharmacology and case management services from their clinic providers, and will be followed with a battery of assessments at month 6, 12 and 18. Relevance: Since 2005, over 35% of recent military suicides occurred in the post-deployment time period, and 50% of these events occurred greater than one year post-deployment (Alvarez 2009). These statistics suggest that recently discharged military personnel remain at risk for completed suicide and justify suicide prevention treatment efforts at this phase of service. Due to the escalating problem of suicidal behavior in soldiers returning from Iraq, the VA has identified suicide prevention as a key part of its mission and is instituting prevention efforts on a systemwide basis. Each VA hospital now employs a Suicide Prevention Coordinator, maintains a HR suicide list with increased monitoring of identified at-risk individuals and mandates yearly suicide training for employees. However, in spite of increased identification and monitoring of these at-risk veterans, there exist few empirically supported treatments for suicide prevention in post-deployment military personnel. This project aims to test whether DBT, one of the few psychosocial treatments with proven efficacy in diminishing suicidal behavior in individuals with personality disorder, can be applied to veterans irrespective of personality diagnosis. If this intervention is successful, DBT programs could be implemented in outpatient clinics in active military, veteran and civilian settings.

DoD	2010	Post Admission Cognitive Therapy (PACT) for the Inpatient Treatment of Military Personnel with Suicidal Behaviors: A Multi-Site Randomized Controlled Trial	Marjan Holloway	Background: Suicide remains a serious national public health problem and has become a leading cause of death in the United States military. To date, there is no evidence-based civilian or military inpatient interventions aimed at the reduction of suicide behavior. Our proposal addresses this important gap and aims to evaluate an innovative suicide intervention, Post Admission Cognitive Therapy (PACT). Left untreated, severe suicide ideation and/or suicide attempts that require psychiatric hospitalization may place an individual at a lifetime risk for increased psychopathology, subsequent suicide behavior, and death. Objective: The broad objective is to implement and empirically evaluate the efficacy of a cognitive behavioral intervention program, titled, Post Admission Cognitive Therapy (PACT), for military service members and beneficiaries admitted for inpatient care due to severe suicide ideation and/or a recent suicide attempt. Specific Aims: To evaluate the efficacy of PACT plus Enhanced Usual Care (EUC) versus EUC for the prevention of suicide in psychiatrically hospitalized military personnel and beneficiaries at follow-up (1, 3, 6, and 12-month) on (1) incidence of repeat suicide attempt(s) and number of days until a repeat suicide attempt (primary outcomes), and (2) psychiatric symptoms (depression, trauma, sleep, suicide ideation), repeat number of psychiatric hospitalization(s), linkage to specialty care, attitudes toward seeking help for mental health issues, and subsequent mental health service utilization) (secondary outcomes). We expect that adults in the PACT+EUC (experimental) condition compared to those in the EUC (control) condition will show favorable outcomes on both primary and secondary measures. Study Design: The research design is a multi-site, single-blind, randomized controlled trial (RCT). A total of 218 individuals who are over the age of 18, able to communicate in English and willing to provide informed consent will be recruited from the inpatient psychiatric units at the Walter Reed Army Medical Center and the Naval Medical Center Portsmouth. Participants will be randomized into one of two conditions: (1) [Post Admission Cognitive Therapy (PACT) + Enhanced Usual Care (EUC)] or (2) Enhanced Usual Care (EUC). Individuals randomized into PACT+EUC will participate in the study assessments, receive six 60-90 minute individual face-to-face PACT psychotherapy sessions provided during their inpatient stay, up to a maximum of four 60-minute phone PACT booster sessions during the 3 months post hospital discharge, and case management services for 12 months. Individuals randomized into the control condition (EUC) will not receive the study intervention; they will receive the usual care provided in the inpatient setting, participate in study assessments, and receive case management services for 12 months. Patients in both conditions will be assessed on the dependent measures at baseline and at 1-, 3-, 6-, and 12-month follow-up intervals. Relevance: Delivering a brief and possibly potent psychotherapeutic intervention during a psychiatric inpatient hospitalization followed by an aftercare component aims to directly target individuals at high risk for future suicide behavior, specifically young, psychiatrically hospitalized adults under the direct stress of a military career. The development and empirical validation of an inpatient cognitive behavioral treatment is a significant endeavor in our national as well as Department of Defense (DoD) suicide prevention efforts. If Post Admission Cognitive Therapy is found to be efficacious, the intervention can be subsequently disseminated to inpatient settings as the standard of care for military personnel and beneficiaries admitted for suicide-related events.
DoD	2011	Intranasal Delivery of Biodegradable Neuropeptide Nanoparticls in the Treatment of Combat Related Physical and Psychological CNS Co-Morbidities	Michael Kubek	Background: Suicide and suicide risk among combat soldiers has been an alarming unabated problem in the military for much of the conflicts in Iraq and Afghanistan. Presently we have no rapidly acting anti-suicidal drug in clinical use. Importantly, clinical reports demonstrated Thyrotropin-releasing hormone (TRH, Protirelin), a brain-derived neuropeptide, to have rapid onset efficacy against suicidal ideation and severe depression, but its effectiveness was limited because of a short duration of action and required high doses delivered either intrathecally or intravenously. This central nervous system (CNS) delivery problem is due to rapid TRH metabolism in nearly all tissue compartments as well as difficulty in penetrating the blood brain barrier. Thus, if CNS uptake and bioavailability could be enhanced for TRH using a non-invasive approach, it seems reasonable that this adaptation could mitigate the issue of diminished effectiveness and duration of TRH action so it could be used successfully against suicide risk and other combat-related CNS disorders.
DoD	2012	Reduction in Suicide Risk: A Double-Blind, Placebo-Controlled Trial of Omega-3 Fatty Acid Supplementation among Military Veterans	Bernadette Marriott	Background: Effective interventions that reduce the risk for suicide and diminish mental illnesses that amplify risk for suicide, are a high priority within the US Military. Omega-3 fats are essential to brain function, must be obtained in the diet, and research indicates may be effective as treatments for suicide risk factors. Objective/Hypothesis: Determine if compliance with 4 gm/d of omega-3 fats, reduces risk of New Episodes of Significant Suicidal Risk (NESSRs), and mental illness risks for suicide among US Military Veterans with enhanced risk for suicidal behaviors. Low levels of omega-3's are associated increase risk of suicide among US military personnel. A pilot intervention among suicide attempters reduced risk of suicidal thining and depression by 50%. Study Aims: Primary 1) Assess efficacy for reduction in NESSRs (defined as suicides, attempts, inpatient hospitalization or emergence of new significant symptoms). Secondary. 2) Assess reduction in self and performance ratgings of suicide risk and symptoms of significant depression, anxiety and PTSD. 3) A sub-study will assess reduction in alcohol misuse. 4) Neuropsychological/fMRI paradigms will evaluate neurophysiological bases of efficacy. Study design: Enrollment of a veteran population with enhanced risk for NESSRs after screening for recent suicide risk factors. Monthly visits will evaluate a stratified randomization to omega-3 fats or placebo in smoothie juice boxes containnng riboflavin for 6 months, in double blinde design, without interference with ongoing psychiatric care. Compliance assessment achieved by blood fatty acids and urine UV fluorescence. Relevance: Positive findings can be readily translated to suicide risk prevention and mental health programs among the US Military, veterans and the public by multiple delivery mechanisms including food enhancement.
DoD	2012	Randomized Controlled Trial to Decrease Suicidal Thinking in a Military Emergency Department	Robert McLay	Background: Patients presenting with acute depression and/or acute suicidality have few immediate treatment options to alleviate their suffering aside from psychiatric hospitalization for safety assurance, observation, and psychiatric intervention (psychotherapy and/or pharmacotherapy). Preliminary data from a study by Larkin et al at Yale showed evidence to support a promising novel treatment modality with rapid effects and sustained relief of depressive symptoms and suicidal ideation for up to 10 days post infusion through the use of a single sub-anesthetic rapid intravenous bolus dose of ketamine (0.2-mg/kg) administered in the acute Emergency Department setting. Of their 15 patients, 14 had complete remission of suicidal ideations within 40 minutes and a marked improvement in their depressive symptoms. Additionally, of the 14 patients with complete remission of suicidal ideation at 40 minutes, 13 had sustained remission of these thoughts at a 10 day follow-up assessment. No lasting side effects were noted in the research population beyond 40 minutes post-infusion. A pilot study at Naval Medical Center San Diego replicated these findings, and performed a randomized controlled trial of the same intervention in 18 participants. Preliminary findings indicate a rapid relief from suicidal thinking with improvements that persist to the point of psychiatric discharge and beyond. Other research supports the use of ketamine as an effective, safe, rapid, treatment of depression, but the majority of these studies included only a treatment-resistant depression population. Objective/Hypothesis: It is hypothesized that a rapid infusion of ketamine will result in rapid decrease in suicidal thinking as measured on the Beck Scale of Suicidal ideation, and that this decrease will be significantly greater than any change seen with a placebo infusion. It is further proposed that such changes will last out to at least two weeks post treatment. Specific Aims: This study will test if an infusion of ketamine can acutely lower suicidal thinking in a military emergency setting.
DoD	2009	Development and Evaluation of a Brief, Suicide Prevention Intervention Reducing Anxiety Sensitivity	Norman (Brad) Schmidt	Hypotheses: 1. Cognitive Anxiety Sensitivity Treatment (CAST) will reduce overall AS and Cognitive AS in military, veteran and other relevant samples (e.g., individuals with PTSD). 2. CAST will reduce suicidal ideation and risk for suicidal behaviors. 3. CAST will have a positive impact on other adverse outcomes associated with elevated AS including PTSD and substance use. 4. CAST will impact emotional TBI sequelae. Technical Objectives: 1. Cognitive Anxiety Sensitivity Treatment (CAST) will reduce overall AS and Cognitive AS in military, veteran and other relevant samples (e.g., individuals with PTSD). This research objective will allow us to determine whether a brief psychoeducational program can effectively reduce a known risk factor for psychopathology. 2. CAST will reduce suicidal ideation and risk for suicidal behaviors. This research objective will help answer the question of whether reductions in cognitive risk factors will result in decreases in suicidal ideation and other relevant behaviors such as suicide attempts. 3. CAST will have a positive impact on other adverse outcomes associated with elevated AS including PTSD and substance use. This research objective will help determine whether reductions in cognitive risk will lead to reductions in symptoms relevant to PTSD and substance use. 4. CAST will impact emotional TBI sequelae. This research objective will help us to determine whether reductions in risk may lead to less impairing emotional symptoms associated with TBI.
DoD	2013	Home-Based Mental Health Evaluation to Assist Suicidal Veterans with the Transition from Inpatient to Outpatient Setting	Bridget Matarazzo	Problem: Research indicates that the time period when Veterans are at the highest risk to die by suicide is following psychiatric hospitalization. Low rates of treatment engagement have been associated with further increased risk. Primary Hypothesis: Veterans receiving HOME will be significantly more likely to engage in treatment 3 months post-discharge. Secondary Hypotheses: Veterans receiving HOME will engage in treatment in a shorter amount of time, attend more appointments and report lower suicidal ideation. Military Relevance: HOME addresses the military problem of suicide through a novel, nontraditional, culturally-relevant means of service delivery.

DoD	2013	Development and Evaluation of a Brief, Suicide Prevention Intervention Targeting Anxiety and Mood Vulnerabilities	Norman (Brad) Schmidt	How do we Mitigate Risk for a Complex, Multifaceted Problem (Suicide) in the context of a Complex, Multifaceted Organization (Military)? Hypothesis: Efficient, Computer-based Risk Reduction can significant reduce Anxiety and Mood-Related Risks Hypothesis: Reduction in Risks will Diminish Risk for Suicide Outcomes Objectives: (1) Develop Novel Interventions for Suicide Risk Factors (Belongingness/Burdensomeness) (2) Develop Cognitive Bias Modification Augmentation for Risk Reduction (3) Evaluate Singular and Combined Effects of Anxiety and Mood Risk Reduction in an RCT (4) Identify Biomarkers of Suicidality
DoD	2009	Brief Intervention for Short-Term Suicide Risk Reduction in Military Populations: Reasons for Living (RFL) Intervention	Craig Bryan	Study Aims: To identify the most effective interventions for reducing the risk of suicide attempt among active duty Soldiers presenting to clinical facilities for behavioral health emergencies. To identify potential mechanisms of change for suicide-focused interventions among active duty Soldiers. Approach: Randomized controlled trial randomizing 360 Soldiers to one of three interventions: treatment as usual (TAU), crisis response plan (CRP), or crisis response plan with reasons for living enhancement (CRP+RFL), with follow-up occurring over the course of 6 months
DoD	2008	A Brief Intervention to Reduce Suicide Risk in Military Service Members and Veterans (SAFE-MIL/SAFE-VET)	Marjan Holloway	Background: Recently, the Army Suicide Event Reporting (ASER) and the Total Army Injury and Health Outcomes Database (TAIHOD) systems have indicated increasing rates of suicide among Active Army, Guard, and Reserve units over the last several years. Additionally, research has indicated that veterans are more than twice as likely to kill themselves as compared to the general population. There are limited evidence-based suicide prevention interventions that have been developed for military personnel and veterans who are experiencing suicide ideation or who have made a suicide attempt. Objective/Hypothesis: The objective of this study is adapt and evaluate a brief, readily accessible, and personalized intervention, safety planning, that will reduce suicide risk in military and veteran populations in three ways by: (1) evaluating suicide risk using a structured assessment measure; (2) enhancing suicide-related coping strategies; and (3) increasing acceptability and initiation of appropriate mental health and substance use treatments. This proposal is unique in that the intervention, safety planning, will be evaluated in both military and VA settings, with the aim of disseminating related educational materials to both military and VA patients and providers. Specific Aims: To evaluate the efficacy of the safety planning intervention on suicide ideation, suicide-related coping, and attitudes toward help seeking for hospitalized military personnel at high suicide risk. To evaluate the effectiveness of the safety planning intervention on suicide attempts, suicide ideation, attendance of outpatient mental health and substance abuse interventions, and suicide-related coping for veterans at high suicide risk in emergency department (ED) settings. Study Design: Two separate, but related projects will be conducted to compare the study intervention with enhanced usual care conditions on suicide-related outcomes. In Project 1, the safety plan intervention will be specifically adapted for military service members who are at high risk for suicide. A randomized controlled trial will be conducted to determine the efficacy of the safety planning intervention for hospitalized military personnel at the Walter Reed Army Medical Center. Outcomes include suicide ideation, suicide-related coping, and attitudes toward help seeking at discharge and 1-month post discharge. In Project 2, a quasi-experimental design will be used to examine the effectiveness of the safety plan intervention for veterans at high suicide risk at VA ED. Outcomes include suicide attempts, suicide ideation, and suicide-related coping at 1, 3, and 6 months following the index ED visit as well as attendance at an outpatient mental health or substance abuse treatment appointment within 30 days post the index ED visit. Relevance: If the safety plan intervention is determined to be effective, then this intervention may be widely and quickly disseminated in the DoD and VA settings through publications and presentations using in a variety of multi-media platforms. The ultimate goal of the safety plan dissemination initiative is to provide clinicians and other professionals who work with high risk military service members and veterans with a brief, easily administered intervention that is designed to mitigate suicide risk.
DoD	2010	Suicide Risk Assessments within Suicide-Specific Group Therapy Treatment for Veterans: A Pilot Study	Lori Johnson	Problem: Suicidality in veterans. Overall Hypothesis: Enhancing an already established group therapy for veterans with suicidality by adding formalized suicide assessment will improve outcomes for participants. Military Relevance: Potential to improve (clinically and scientifically) in cost effective ways, treatment options for suicidality that have shown initial benefits to veterans? functioning
DoD	2013	An RCT to Test the Effectiveness of a Virtual Hope Box Smartphone App in Enhancing Veteran's Coping with Suicidal Ideation	Nigel Bush	The Virtual Hope Box (VHB) applies personal smartphone technology to supplement and enhance efficacious treatments for suicide behaviors. High risk veterans using a VHB smartphone app will demonstrate reductions in 1) severity of suicidal ideation 2) ability to cope with stressors and 3) increases in perceived reasons for living, both pre-post and compared to Tx as Usual (TAU). Service members (SMs) and veterans already are high users of personal smartphones. A successful study will demonstrate the clinical effectiveness of a convenient, portable tool to support SMs and veterans at risk of suicidal behavior
DoD	2013	Longitudinal Assessment of Physical Activity and Suicide Risk	Collin Davidson	Background: Psychosocial interventions for people at risk for suicide have demonstrated reductions in suicide risk. Decreasing overall rates of suicide may hinge on the development of interventions that are cost effective, easily accessible, and target at less acute risk. Hypothesis: We hypothesize that the level of physical activity, operationalized by average daily minutes of objective physical activity, will be negatively associated with level of suicidal ideation reported during ecological momentary assessments (EMA). Also, the relationship between physical activity and suicidal ideation will be mediated by self-reported depression and disturbed sleep. The level of self-reported over-exercise will be positively associated with the level of acquired capability for suicide, after controlling for age and gender. Finally, the relationship between exercise and suicidal ideation will be curvilinear. Specific Aims: This study aims to prospectively examine the relationship between physical activity and suicidal ideation in Veterans. Study Design: Forty-five Veterans will be recruited to participate in self-report assessments on their mental health, physical activity, and sleep quality. They will also be provided an ActiGraph ActiSleep device to objectively measure sleep disturbance and physical activity. Relevance: Active duty military and Veterans have been exposed to physical activity as part of their military training and may be more willing to participate in physical activity as an intervention. Physical activity is an effective treatment for depression, PTSD, and sleep disturbances, which are common in military populations and have been linked to suicidal ideation. A physical activity intervention is less stigmatizing that traditional treatment options.
DoD	2009	Window to Hope	Lisa Brenner	Window To Hope (WtoH): There are increased rates of suicide among US military service members. Significant rates of service members are sustaining TBIs while serving in Operation Enduring Freedom/Operation Iraqi Freedom. There is a paucity of evidence-based treatments addressing psychological distress among those with moderate to severe TBI. Primary Hypothesis: Participants receiving the WtoH treatment will report a significant post-treatment reduction in hopelessness. Secondary Hypotheses: Participants receiving the WtoH treatment will report a significant post-treatment reduction in suicidal ideation and depression. Additional Research Questions: 1) Can PST-SP be successfully implemented at a VA Medical Center (VAMC)? ; 2) Will PST-SP demonstrate positive implementation outcomes?; and 3) Does PST-SP reduce hopelessness among Veterans with a history of moderate to severe TBI?; Military Relevance: WtoH and PST-SP target the intersection of two of the most pressing health problems facing our service members: suicide and TBI.
DoD	2013	Controlled evaluation of a computerized anger-reduction treatment for suicide prevention	Jesse Cougle	Problematic anger is associated substance abuse, relationship difficulties, and suicide risk Anger may contribute to suicidality via thwarted belongingness and perceived burdensomeness (Hawkins et al., in prep). In a study of Iraq-Afghanistan combat veterans, anger was the most commonly reported problem experienced since homecoming, occurring in 57% of the sample (Sayer et al., 2010). An internet-based anger treatment may reduce suicide risk in military personnel

DoD	2013	Intervening to Reduce Suicide Risk in Veterans with Substance Use Disorders	Mark Ilgen	Background: Reducing suicide risk among active duty soldiers and Veterans is a national priority. Because substance use disorders (SUDs) are key risk factors for both fatal and non-fatal suicidal behaviors. SUD treatment program staff are in frequent contact with high-risk individuals. However, no data exist on the efficacy of suicide-specific interventions conducted in SUD treamtent. The proposed research study addresses this gap by testing the efficacy of a targetd intervention designed to reduce suicide risk in Veterans treated for SUDs. Objective: The primary objective of this study is to evaluate the impact of a Cognitive Behavioral Therapy (CBT) intervention compared to a Supportive Psycho-education Control (SPC) condition on subsequent suicidal thoughts and behaviors in Veterans with SUDs. Specific Aims: To compare CBT and SPC delivered kin VA intesnive SUD treatment programs for; (1) Reducing the frequency and intesity of suicidal thoughts at 1-,2-,3 -, 6- and 12-month follow-up; and (2) Decreasing the likelihood of suicide attempts(s) at 1-,3-,6-, and 12-month follow-up. Study Design: The proposed project is a fully-powered multi-site randomized controlled trial of the CBT intervention versus the SPC condition fo r300 suicidal Veterans seen in Veterans Helath Administration (VHA) intensive outpatient SUD treatment programs. Relevance: The evaluation of strategies to reduce suicide among former members of the US armed forces is of high public helath sifnigicance. testing an intervention for use with suicidal Veterans seen in intensive outpatient SUD treatment programs has the potential to sifnificanly improve functioning and well-being., and decrase teh substantial loss of life in Veterans with SUDs due to suicide.
DoD	2008	Blister Packaging Medication to Increase Treatment Adherence and Clinical Response: Impact on Suicide-related Morbidity and Mortality	Peter Gutierrez	To determine if patients receiving their VA prescribed medications in blister packages rather than pill vials will be more adherent with treatment. To determine if those in the blister pack condition experience better clinical outcomes than the dispense as usual condition. To determine if those in the blister packaging condition experience fewer incident of self-directed violence, particularly by prescription medication overdose than those in the dispense as usual condition. It is hypothesized that patients in the blister pack condition will be more adherent, have better clinical outcomes, and fewer overdoses than those in the dispense as usual condition.
DoD	2012	Management of Suicide-Related Events during Deployment	Barbara Stanley	Background: Recent data indicate that suicide in the Army is highest during deployment. There is limited research information about how suicides, suicide attempts, other suicide-related behaviors and suicide-related evacuations are handled in deployed settings. To date, there are no standardized and systematic procedures within the Army for the handling of suicide-related evacuations, suicide-related behaviors, and suicide deaths that occur during deployment. Objective/Hypothesis: The broad objective of this project is to provide military leaders, military behavioral health providers and chaplains with targeted, practical, and scientifically-informed guidelines and decision aids on how to respond to suicide-related events during the deployment. Specific Aims: The aims of this project are as follows: (1) To qualitatively and quantitatively determine, using guided interviews, focus groups and questionnaires, the type and range of decisions made by behavioral healthcare providers, chaplains, and leaders to address suicide-related events that occur during deployment, the process for making these decisions and the lessons learned; (2) To assess, from the perspective of affected Service Members, how suicide-related events were managed and what could be improved; (3) To develop guidelines and decision aids for use in deployed settings when suicide-related events occur. Study Design: The study will be conducted in three stages. Stage 1 consists of interviews and focus groups with previously deployed behavioral health providers, chaplains, and unit leaders as well as Service Members with documented suicide-related events during their deployment. The purpose of Stage 1 is to characterize the most common types of decisions made during deployment pertaining to suicide-related evacuations, suicide-related behaviors, and suicide deaths as well as the possible impact of others. In Stage 2, we will conduct a web-based survey of behavioral health providers, chaplains, and leaders in order to: (1) determine the types of decisions made in relation to suiciderelated evacuations, suicide-related behaviors, and suicide deaths; (2) identify the methods of decision making for each subgroup in relation to suicide-related evacuations, suicide-related behaviors, and suicide deaths; and (3) summarize lessons learned from the outcomes of these decisions. In Stage 3, the qualitative and quantitative data will be synthesized and reported to the Expert Advisory Panel in order to develop guidelines and decision aids for use by providers, leaders and chaplains. Relevance: In recent years, suicide and suicide-related behaviors have increased in deployed active duty military personnel, Reserve and National Guard personnel, civilian contractors, and in Veterans. Given the existing demands and pressures associated with deployment and the public health significance of suicide in deployed settings, military helping professionals and leadership must receive evidence-informed guidance and training on how to best address high risk suicide-related crises and events during their deployment.
DoD	2010	A Randomized clinical trial of the Collaborative assessment and management of Suicidality vs. Enhanced Care as Usual for Suicidal soldiers (CAMS)	David Jobes	Apparent increases in suicidal behaviors and death by suicide among active duty service members has gained considerable attention from the media, members of Congress, and the Department of Defense, particularly because it appears that active duty males now carry?for the first time in known history?a completed suicide risk that is greater than comparable male cohorts in the general population. This is striking because military service has been historically correlated with decreases in suicide risk among Soldiers. The proposed study is a randomized clinical trial designed to implement a novel way of working with suicidal patients, using the ?Collaborative Assessment and Management of Suicidality? approach (CAMS), to determine if it is more effective than ?Enhanced Treatment as Usual? (E-TAU) in reducing suicidal ideation and behavior for suicidal Soldiers. Additionally, the study examines if CAMS is more effective at reducing symptoms and psychological distress and increasing overall functioning and resiliency
DoD	2012	Increasing Treatment Seeking Among At-Risk Service Members Returning from Warzones	Tracy Stecker	Background: Reducing suicide is a national priority and an urgent concern within the Department of Defense and the Department of Veterans Affairs. Indeed, rates of suicide among active duty service members have increased dramatically since 2005, and there is great concern that elevated risk will carry over following discharge from active service. The goal of the proposed study is to improve initiation of behavioral health (i.e., mental health, substance use) treatment services among untreated, at-risk U.S. military service members. The goal to facilitate behavioral health treatment is consistent with recommendations provided in reports by the Department of Defense, U.S. Army, U.S. Surgeon General, and the Institute of Medicine. Objective/Hypothesis: Test the effectiveness of the intervention on attitudes toward behavioral health treatment among at-risk service members. Hypothesis 1a: Participants receiving the cognitive-behavioral (CB) intervention will have significant increases in positive attitudes about treatment at 1-month follow-up compared to controls. Hypothesis 1b: Participants receiving the CB intervention will have significant increases in the intention to initiate behavioral health treatment compared to controls. Test the effectiveness of the intervention on the initiation of and adherence to behavioral health treatment. Hypothesis 2a: Participants receiving the CB intervention will be more likely to initiate behavioral health treatment than participants in control group during 6-month follow-up. Hypothesis 2b: Participants receiving the CB intervention will attend more behavioral health treatment sessions than participants in the control group over 6-month follow-up.
DoD	2010	Caring Letters for Military Suicide Prevention: A Randomized Controlled Trial	David Luxton	Psychiatric inpatients are at high risk for suicide, especially shortly after treatment discharge. Several studies have examined the effects of sending brief, personalized expressions of care and reminders of treatmtnavailability to discharged inpatients. These "caring Letters" are one of the only suicide prevention interventions to reduce sucide mortality in a randomized contrlled trial (RCT). Objective/Hypothesis: The primary hypothesis is that the frequency of sucide after hospital admission wil be lower among participants in the Caring Letters condition compared to those in the usual care condition. We also predict tha tthe frequency of repeated hopitalization for sucide behaciors will be lower for the Caring Letters group and that the time to a repeated self-injury will be greater for the Caring Letters group compared to th eusual care group. Specific Aims: The primary aim is to conduct an RCT that compares a Caring Letters intervention to usual care to prevent suicide. The proposal also aims to examine hospitalization rates for suicide behaviors and time to a suicide behaviro requireing hospitalization. Study Design: Psychiatric inpatients (N=4,730) wil be recruited from six major DoD and VA medical centers and randomized to either a Caring Letters condition or Usual Care (no letters). Personalized caring letters will be emailed to the intervention group on a set schedule with decreasing frequency for two years after discharge. Relevance: Despite the intense interest in suicide prevention in the DoD, the Caring Letters intervention, one of the only suicide prevntion interventions with any initial empicial support, remains untested and unuse din the DoD. Postivie study results would provide senior leaders key information about an inexpensive suicide prevention approach that may actually impact suicide rates in the Dod.

DoD/DARPA	2011	Medical Informative and Analytics Toolkit (MINAT); NeuroAnalysis	Michael Crystal	MINAT is a novel combination of natural language processing, voice stress analysis and data-driven machine learning for extracting DSM-IV-derived constructs for PTSD, depression, and suicidality from text and voice data. The system analyzes incoming data in real-time and extracts rich linguistic and acoustic features, which include word use and sentence statistics, sentiment words, domain phrases derived from annotator rationales, as well as a combination of lexical, voice-acoustic and interaction features. MINAT then uses state-of-the-art statistical classifiers to provide an assessment of the person?s psychological state across DSM-IV constructs of affect, behavior, trauma exposure, cognition and domains of impairment. In addition, MINAT provides contextual evidence to support the detected distress indicators. Finally, MINAT triages individuals based on their risk to harm themselves or others. MINAT leverages a combination of verbal and non-verbal cues, and social and non-social activities for an accurate assessment of psychological status. In its ultimate realization, MINAT would greatly improve quality, richness (e.g. relevant contextual evidence) and timeliness of information available to medical professionals in both clinical and non-clinical settings. NeuroAnalysis effort is developing a hardwaresoftware system for detecting PTSD and stress indicators from the analysis of multisensor data. The system relies on structured delivery of audio-visual stimuli to elicit affective physiological responses. As part of this effort, our team is identifying combinations of modalities, sensors, and stimulus genre that elicit the most informative responses for PTSD and stress prediction. An important objective of the effort is development of machine learning and signal processing algorithms that identify and leverage multi-modal patterns for the detection of PTSD and stress indicators. Our team brings together Advanced Brain Monitoring?s (ABM) wireless EEG sensing capabilities, Intific?s platform for rapid development of immersive experiences, and BBN?s expertise in the application of multi-modal processing and machine learning techniques. The resulting system uses a combination of positive, negative, neutral, and subject trauma-specific stimuli, along with questionnaires to elicit responses that distinguish healthy subjects, those at risk for PTSD, and those with high stress levels. The system synchronously records responses to these stimuli from multiple neuro-physiological modalities including Electrocardiography (EEG), Electroencephalography (EEG), Galvanic Skin Response (GSR), audio (spoken answers to questions), video, and head motion sensors. Ultimately, the system extracts statistical featuresfrom these data and uses a machine learning engine to estimate risk of PTSD and predict stress indicators.
DoD/DARPA	2011	MultiSense and SimSensei	Albert Rizzo; Louis-Philippe Morency	Multisense automatically tracks and analyzes in realtime facial expressions, body posture, acoustic features, linguistic patterns and higher level behavior descriptors (e.g., attention and fidgeting). Multi-Sense infers from these signals and behaviors, indicators of psychological distress that directly inform the virtual human. SimSensei is a virtual human platform specifically designed for healthcare support and is based on the 10+ years of expertise at ICT with virtual human research and development. The platform enables an engaging face-to-face interaction where the virtual human automatically reacts to the perceived user state and intent, through its own speech and gestures. Development of MultiSense continues as initial analyses suggest that patterns in smiles, gaze, head position, rate and patterns of speaking, voice quality and voice emotion correlate with psychological distress. These behaviors are being further grouped into indicators of variability, latency, agitation, affect and engagement, which would form the key meta-indicators of the system.
DoD/DARPA	2010	Independent Evaluation and Assessment of Developer DCAPS Tools	Roy Stripling	For Detection and Computational Analysis of Psychological Signals (DCAPS), CRESST serves as the developerindependent evaluator. To carry out these evaluations, CRESST seeks to recruit veteran volunteers from the greater Los Angeles area, which is home to an estimated 328,000 veterans. CRESST relies on professional clinicians trained to conduct diagnostic psychological evaluations to provide ground truth on the psychological condition of each volunteer. These ground truth assessments would be compared at the symptom level with the assessments produced by the DCAPS tools. Symptom-level data from these tools would be used to generate collective symptom- and condition-level assessments that are compared to the clinicians? assessments, using a method known as latent variable analysis. CRESST rounds out the evaluation by assessing each tool for usability, cost-effectiveness, and user acceptability. Besides the tool-by-tool evaluation against developer claims, CRESST?s effort seeks to develop a ?behavioral calculus? capable of identifying relationships among sources of evidence and psychological constructs. It also seeks to develop an evaluation testbed implementing the behavioral calculus with interfaces to DCAPS tool outputs.
DoD/MC	2011	Psychological Autopsy Study	Lanny (Alan) Berman	Interview family, friends and others knowledgeable about Marines who died by suicide from 2010 through 2012 to learn more about the person and the events leading up to his or her death. This process is called ?psychological autopsy.? To identify ?lessons learned? for prevention of the potential next case; Analyze data collected to identify suicide risk factors or trends unique to Marines; Develop a working model of Marines who could potentially be at risk for suicidal behaviors; Identify ways to improve Corps data collection.
DoD/MC	2011	Marine Resiliency Study II	Dewleen Baker	Project 1 - extends MRS I beyond the original 3- & 6-month post-deployment assessments to better understand and track the biological markers found in PTSD and TBI; Project 2 - Pre-post deployment study to identify additional predictors of mental health vulnerability and resiliency, conducted in coordination with Army STARRS to more accurately identify risk and resilience factors and identify predictors of suicide risk; Project 3 - In collaboration with Army STARRS, test the feasibility of specific experimental designs such as targeted prevention, treatment protocols, and the use of new technology to identify biomarkers.
DoD/MC	2012	Family Member Survivor Study	Keith Aronson	Understand the impact of Marine Corps suicide on the surviving spouse and family as well as to ascertain the spouse and family current level of resilience, functioning, and well-being at 1, 2, and 3 years post-suicide; Examine individual, family, and community-related factors that predict resilience, and well-being of Marine Corps families after Marine suicides; Determine the needs of Marine Corps spouses and families that have survived a suicide of a Marine; Identify potential signs of suicide risk among Marines who completed suicides in 2008, 2009 and 2010.
DoD/MC	2012	Accessions and Behavioral Health Risk Factors Study	Michael Boivin	Predict suicides, suicide attempts and ideations by selected demographic, accession, and service related factors, including deployment, length of service and military occupation; Determine if there is an association between suicidal behavior and AFQT, mental health disqualifications, psychiatric morbidity or medical and moral waivers; Determine if the above stated associations differ among suicide completers, attempters and ideators.
DoD/MC	2012	Qualitative Study on Suicide Attempts	Adam Walsh	To learn from Marines how the Marine Corps can improve its suicide prevention activities; to obtain contextual information about the events, conditions, and processes leading up to and surrounding Marine suicide attempts
DOT/FRA	2008	Countermeasures to Reduce Suicides on Railway Rights-of-Way: Phase III	Michael Martino	The scope of the overall project, for which this amendment provides additional funding, is for a 5 year phased study, including a detailed prevalence assessment and causal analysis of rail-related suicides representative of the U.S. railroad industry. Appropriate and cost-effective prevention countermeasures will be developed and scaled for implementation in one or more selected pilot projects, where feasible. The objectives of the research to be undertaken with this project are to: 1) Determine the prevalence of and underlying causal factors for rail-related suicides. The purpose of the prevalence assessment is to better understand the scope of suicides and attempted suicides on railroad property, which will support the development of effective prevention strategies. Accurate documentation of the true extent of the problem will also provide an important baseline measure to help monitor rail suicide trends and help determine the effectiveness of prevention strategies; and 2) Develop effective measures to reduce the incidence of suicide along railway rights of way (including crossings).
DOT/FRA	2010	Countermeasures to Reduce Suicides on Railway Rights-of-Way: Phase IV Continuation	Michael Martino	The current grant provides funding for year 4 of a 5 year phased study. The period of performance for the current grant shall be approximately 12 months, beginning August 2010 and ending October 31, 2011. The scope of the overall project includes a detailed prevalence assessment and causal analysis of rail-related suicides representative of the U.S. railroad industry. Appropriate and cost-effective prevention countermeasures will be developed and scaled for implementation in one or more selected pilot projects, where feasible. Accurate documentation of the true extent of suicides that occur on railway rights-of-ways will provide an important baseline to assist in the monitoring of rail suicide trends and help determine the effectiveness of prevention strategies. The objectives of the research to be undertaken with this project are to: 1) Determine the prevalence of and underlying causal factors for rail-related suicides. The purpose of the prevalence assessment is to better understand the scope of suicides and attempted suicides on railroad property, which will support the development of effective prevention strategies; and 2) Develop effective measures to reduce the incidence of suicide along railway rights of way (including crossings).
DOT/FRA	2010	Countermeasures to Reduce Suicides on Railway Rights-of-Way: Phase V Continuation	Michael Martino	The current grant provides funding for year 5 of a 5 year phased study. The scope of the work proposed for the additional funding will include the finalization of the Prevalence, Causal Analysis, and Railroad Recommendations draft reports, based on already collected data. Additionally, this additional funding will include a report of any preliminary indications of the effectiveness of suicide prevention signs near railroad rights-of-way, as well as a report or outline of an implementation plan for at least one countermeasure pilot study as determined most feasible for implementation in the Recommendations report. All deliverables produced during this grant phase will be completed according to FRA standards. Accurate documentation of the true extent of suicides that occur on railway rights-of-ways will provide an important baseline to assist in the monitoring of rail suicide trends and help determine the effectiveness of prevention strategies. The objectives of the research to be undertaken with this project are to: 1) Determine the prevalence of and underlying causal factors for rail-related suicides. The purpose of the prevalence assessment is to better understand the scope of suicides and attempted suicides on railroad property, which will support the development of effective prevention strategies; and 2) Identify potential measures to reduce the incidence of suicide along railway rights of way (including crossings).

DOT/FRA	2012	Evaluate Effectiveness of Current Trespasser Countermeasures	Stephanie Chase/Scott Gabree	Volpe center is involved in multiple tasks on suicide on the railroad right of way. Countermeasures. More information is needed regarding the effectiveness of countermeasures implemented to reduce trespasser incidents on the railroad right-of-way. Numerous countermeasure efforts have been implemented across the country including the use of signage at railway stations. To evaluate the effectiveness of countermeasure strategies, such as signage, we would work with railroads that have implemented such countermeasures in the past to track incident rates on their railroads before and after the implementation of these countermeasures. We would work with local law enforcement to see if there were any noticeable changes in railroad right-of-way incidents following the implementation of such countermeasures. This effort will also be coordinated with a GIS mapping study to track the number of trespass/suicide incidents over the years before and after the implementation of a countermeasure. In addition to working with the railroads, we would also review the media attention given to trespasser deaths on the railroad to investigate the media's potential role in affecting railroad right-of-way incidents. By analyzing similar groupings of incidents (e.g. data collected in the mapping tool) and the type of media attention they received, we would hope to better understand the potential influence of the media on events of this nature. The knowledge gathered from this initial investigation of railway systems will also help to develop a research plan for similar efforts with high-speed rail.
NIH	2011	China-Rochester Suicide Research Training Program (CRSRT)	CAINE, ERIC	DESCRIPTION (provided by applicant): This D43 NCD-LIFESPAN application is entitled the China-Rochester Suicide Research Training Program (CRSRT). It is built upon the International Clinical, Operational and Health Services Research Training Award ("ICOHRTA") program that has been funded since 2001 (D43TW005814). The current proposal is written in response to PAR-10-257 for a Chronic, Non-Communicable Diseases and Disorders Across the Lifespan: Fogarty International Research Training Award (NCD-LIFESPAN). Suicide is a major public health problem in China. It is the fifth leading cause of death overall, and the leading cause of death for individuals in the 15- 34 year old age range. It has a national rate of approximately 23 deaths per 100,000; during 1995-1999, approximately 287,000 died by suicide. In response, we now are systematically growing the CRSRT to encompass multiple complementary settings that serve to diversify the academic breath and geographical distribution of our initiatives, increase our committed mentors, and widen the pool of applicants. Our high rate of positive outcomes during the past decade reinforces the rewarding nature of our high-intensity mentoring strategy. The CRSRT involves the Center for the Study and Prevention of Suicide (CSPS) of the University of Rochester Medical Center (URMC), and six key collaborators in China who bring a diversity of skills and leadership to our growing collaborative efforts, with centers in Beijing, Shanghai, Chengdu, and Changsha. Our proposal reflects an ongoing, self-scrutinizing process that has informed our efforts to: 1) build training and research infrastructure, focusing primarily on public health and population-oriented research and prevention efforts; 2) identify and train excellent future scientists; and 3) develop new research findings that will inform efforts to prevent suicide in China during the coming decades. The CRSRT involves a year of intensive training in the CSPS, followed by two further years of mentored research in China. We provide trainees with the skills to emerge as independent investigators through intensive one-to-one mentoring and engagement in a variety of peer-oriented training experiences. We will continue to systematically evaluate the effectiveness of our recruiting, training, and research efforts. PUBLIC HEALTH RELEVANCE: Suicide is a major public health problem in China: It is the fifth leading cause of death overall and the leading cause of death for individuals in the 15-34 year old age range. The China-Rochester Suicide Research Training Program (CRSRT) includes the URMC Center for the Study and Prevention of Suicide and six complementary centers in China, and provides intensive mentoring and engagement in peer-oriented experiences to develop the skills needed to emerge as independent investigators.
NIH	2011	China-Rochester Suicide Research Training Program (CRSRT)	CAINE, ERIC	This D43 NCD-LIFESPAN application is entitled the China-Rochester Suicide Research Training Program (CRSRT). It is built upon the International Clinical, Operational and Health Services Research Training Award ("ICOHRTA") program that has been funded since 2001 (D43TW005814). The current proposal is written in response to PAR-10-257 for a Chronic, Non-Communicable Diseases and Disorders Across the Lifespan: Fogarty International Research Training Award (NCD-LIFESPAN). Suicide is a major public health problem in China. It is the fifth leading cause of death overall, and the leading cause of death for individuals in the 15-34 year old age range. It has a national rate of approximately 23 deaths per 100,000; during 1995-1999, approximately 287,000 died by suicide. In response, we now are systematically growing the CRSRT to encompass multiple complementary settings that serve to diversify the academic breath and geographical distribution of our initiatives, increase our committed mentors, and widen the pool of applicants. Our high rate of positive outcomes during the past decade reinforces the rewarding nature of our high-intensity mentoring strategy. The CRSRT involves the Center for the Study and Prevention of Suicide (CSPS) of the University of Rochester Medical Center (URMC), and six key collaborators in China who bring a diversity of skills and leadership to our growing collaborative efforts, with centers in Beijing, Shanghai, Chengdu, and Changsha. Our proposal reflects an ongoing, self-scrutinizing process that has informed our efforts to: 1) build training and research infrastructure, focusing primarily on public health and population-oriented research and prevention efforts; 2) identify and train excellent future scientists; and 3) develop new research findings that will inform efforts to prevent suicide in China during the coming decades. The CRSRT involves a year of intensive training in the CSPS, followed by two further years of mentored research in China. We provide trainees with the skills to emerge as independent investigators through intensive one-to-one mentoring and engagement in a variety of peer-oriented training experiences. We will continue to systematically evaluate the effectiveness of our recruiting, training, and research efforts.
NIH	2011	China-Rochester Suicide Research Training Program (CRSRT)	CAINE, ERIC	This D43 NCD-LIFESPAN application is entitled the China-Rochester Suicide Research Training Program (CRSRT). It is built upon the International Clinical, Operational and Health Services Research Training Award ("ICOHRTA") program that has been funded since 2001 (D43TW005814). The current proposal is written in response to PAR-10-257 for a Chronic, Non-Communicable Diseases and Disorders Across the Lifespan: Fogarty International Research Training Award (NCD-LIFESPAN). Suicide is a major public health problem in China. It is the fifth leading cause of death overall, and the leading cause of death for individuals in the 15-34 year old age range. It has a national rate of approximately 23 deaths per 100,000; during 1995-1999, approximately 287,000 died by suicide. In response, we now are systematically growing the CRSRT to encompass multiple complementary settings that serve to diversify the academic breath and geographical distribution of our initiatives, increase our committed mentors, and widen the pool of applicants. Our high rate of positive outcomes during the past decade reinforces the rewarding nature of our high-intensity mentoring strategy. The CRSRT involves the Center for the Study and Prevention of Suicide (CSPS) of the University of Rochester Medical Center (URMC), and six key collaborators in China who bring a diversity of skills and leadership to our growing collaborative efforts, with centers in Beijing, Shanghai, Chengdu, and Changsha. Our proposal reflects an ongoing, self-scrutinizing process that has informed our efforts to: 1) build training and research infrastructure, focusing primarily on public health and population-oriented research and prevention efforts; 2) identify and train excellent future scientists; and 3) develop new research findings that will inform efforts to prevent suicide in China during the coming decades. The CRSRT involves a year of intensive training in the CSPS, followed by two further years of mentored research in China. We provide trainees with the skills to emerge as independent investigators through intensive one-to-one mentoring and engagement in a variety of peer-oriented training experiences. We will continue to systematically evaluate the effectiveness of our recruiting, training, and research efforts.
NIH	2009	Suicidal Ideation, Social Networks, HIV and Drug Oversdose: A Methodological F	Kuramoto, Satoko	DESCRIPTION (provided by applicant): The goal of this research is to examine the relationships between social networks, suicidal ideation, non- fatal drug overdose and HIV risk behavior among adults over 18 years of age who use illicit drugs. Illicit drug users are at especially high risk for suicide, drug overdose and HIV/AIDS. Research has shown that suicidal ideation is a significant precursor for attempt and death by suicide. Starting with the work of Emile Durkheim, several studies have noted the influence of social integration and social support on risk for suicide. However, less attention has been paid to the interpersonal network structure that provides mechanisms through which integration and support operate and influence suicidal ideation. Prospective epidemiologic research will be conducted among individuals recruited from communities in the Baltimore area who inject drugs and/or use crack. The study will first compare social network structures of individuals who report suicidal ideation with those who do not at baseline. The extent to which psychological distress mediates the relationship between the change in social network structures and suicidal ideation will then be determined using structural equation modeling of baseline and 6th month data. With growing awareness of the link between mental health and behavior, there is a greater need to understand causal relationships between these constructs to inform the development of preventive interventions and enhance treatment efforts within this population. However, the current literature on suicidal risk and drug overdose is discrepant. Many speculate the association is due to some common factors. The use of baseline, 6th month, and 12th month surveys and propensity score matching is a more robust method to disentangle the relationships than conventional method of analysis. In addition, most studies on HIV and suicide has focused on how HIV infection increases risk for suicide. Whether suicidal ideation also changes the propensity of individuals to engage in behaviors that place them at risk for HIV is important but has been understudied. Using advanced statistical methods, the proposed study provides a novel approach to examine the impact of suicidal ideation on non-fatal drug overdose and HIV risk behavior. The study will also help generalize the findings to illicit drug users in the community setting. This proposed study has signficant public health potential to inform intervention strategies to reduce suicidal ideation, drug overdose and HIV transmission. The findings will help health professionals to better characterize individuals at risk for suicide and suicide attempt. In addition, this study will inform if targeting suicidal ideation may also decrease the individual's risk for drug overdose and HIV infection.

NIH	2008	Emotional and Behavioral Dysregulation in Borderline Personality Disorder	Selby, Edward	DESCRIPTION (provided by applicant): Borderline personality disorder (BPD) is a severe disorder in which individuals often engage in extreme behaviors such as self-injury, impulsive behaviors, substance abuse and suicidal behavior. Individuals with BPD symptoms utilize the health care system (e.g., visits to physicians, emergeny rooms, and hosptializations) at alarmingly high rates (Hueston, Mainous, & Schilling, 1996) and are at extremely high risk for death by suicide. This makes BPD a significant pulic health concern. Although successful treatments have been developed for BPD (Dialectical Behavior Therapy; Linehan, 1993), little attention has been given to understanding the underlying causes and functional aspects of the maladaptive behaviors seen in BPD, valuble information for the treatment of this disorder. Linehan's (1993) theoretical model of BPD asserts that individuals with BPD have significant problems with emotion dysregulation in that they 1) have a heightened sensitivity to emotional stimuli, 2) experience emotions as extremely intense, and 3) they have a slow return to emotional baseline. Research also suggests that the maladaptive behaviors of individuals with BPD may serve the common purpose of emotion regulation. Recent findings in the field of emotion science provide evidence that rumination (a form of cognitive emotion dysregulation) may account for the emotion dysregulation seen in BPD. Rumination is defined as focusing attention and thoughts on the causes and consequences of emotionally relevant stimuli. Consequently, rumination has been shown to magnify and perpetuate negative affect; intense negative affect, in turn, may result in increased attention to emotionally relevant stimuli - potentially resulting in a cycle that causes a "cascade" of intense emotions (Selby et al., in press). The proposed studies will examine the role of cognitive emotion dysregulation (defined as high levels of rumination) in BPD, as well as examine the role that maladaptive behaviors (including suicidal behaviors) have in interfering with rumination. Study 1 will examine the role of rumination in BPD with an induced rumination on negative affect procedure. A subsequent pain tolerance test with a cold-pressor will provide a proxy for self-injury, and information about the distracting quality of pain. The second study will examine the contextual and ruminative features surrounding behavioral dysregulation in BPD with an Ecological Momentary Assessment protocol. PUBLIC HEALTH RELEVANCE: This study will examine if real-time rumination and interpersonal problems tend to precede behavioral dysregulation in the daily life of BPD individuals, through the use of palm pilots. This study will also specifically examine if an interaction between rumination and interpersonal problems is associated with NSSI in individuals with BPD.
NIH	2009	Anorexia Nervosa and Suicidal Behaviors	Smith, April	DESCRIPTION (provided by applicant): The guiding hypothesis for the proposed research is that extreme atypical beliefs about beauty are cognitive risk factors for suicidal behavior and symptoms of anorexia (AN). There is accruing evidence that some people see death or "excessively thin" (to be described as "emaciation") as beautiful (e.g. Young, Sweeting, & West; Norris, Boydell, Pinhas, & Katzman, 2003), and this association may make them more likely to die by suicide or develop AN, respectively. Joiner's (2005) interpersonal-psychological theory of suicide holds that three conditions must be met before a person will die by suicide: thwarted belongingness, perceived burdensomeness, and the acquired capability for suicide (operationalized as fearlessness about death). Believing death to be beautiful may increase one's acquired capability for suicide by making one more fearless about death. In the case of AN, believing that an emaciated body ideal is more beautiful than a thin body ideal may motivate individuals to severely and unwaveringly restrict in order to achieve this beauty standard. Study 1 will provide initial estimates of the prevalence of the beliefs "death is beautiful" and "emaciation is beautiful" in young adults. It will also provide estimates of the association of these beliefs to levels of fearlessness about death and eating disorder symptoms, respectively. Through the employment of a lexical decision task, the second study will investigate whether people with AN symptoms associate emaciation with beauty more readily than non-eating disordered people. Utilizing a similar design, the third study will examine whether people with high levels of acquired capability for suicide are more likely to associate death with beauty than people with low levels of acquired capability for suicide. These studies will also begin to examine the link between AN and death by suicide. There is a pressing need for more research examining these outcomes as an average of 30,000 people die by suicide every year (Centers for Disease Control [CDC], 2004), and anorexia nervosa (AN) is the most deadly psychological disease (Thompsen, McCoy, & Williams, 2001). By clarifying the nature of the thoughts that some people with an acquired capability for suicide or symptoms of AN have, we will be better able to design prevention and treatment procedures.
NIH	2009	Neural Substrates of Emotion Dysregulation and Self Injury	Derbidge, Christina	DESCRIPTION (provided by applicant): Self-inflicted injury (SII) in adolescents is a significant risk factor for later suicide and psychopathology in adulthood, and may be a developmental precursor of borderline personality disorder (BPD). Consistent with Linehan's biosocial theory of BPD, recent research among self-injuring adolescents suggests that they are emotionally dysregulated and that SII functions to regulate their intensely negative affect. Neuroanatomical models of emotion regulation circuitry, derived from extensive neuroimaging research, implicate ventral portions of the prefrontal cortex (PFC), the amygdala, the anterior cingulate cortex (ACC), and their interconnections. Though functional neuroimaging research on emotion regulation has burgeoned in recent years, very little imaging research has been conducted in samples selected specifically for SII, and no functional imaging studies have been conducted with at risk adolescents. Nevertheless, studies conducted with adults with BPD suggest that some of the same brain regions implicated in emotion regulation are altered. In the proposed research, functional magnetic resonance imaging will be used to examine neural correlates of emotional processing in adolescent girls who engage in SII, relative to depressed and normally developing adolescent girls. The paradigm, which includes passive viewing of negative emotion faces, is well established and has been used successfully and commonly with adults with BPD and MDD. PUBLIC HEALTH RELEVANCE: This research may lead to improved understanding the neural bases and etiology of SII in adolescents and may ultimately lead to improvements in diagnostic specificity, intervention targets, and prediction of treatment response. This research is consistent with the strategy for suicide prevention presented by the U.S. Department of Health and Human Services (DHHS) in 2001.
NIH	2011	Early Stress and Suicidal Behavior	Class, Quetzal	DESCRIPTION (provided by applicant): Suicidal behavior places a staggering burden on individuals, families, and society. Although previous research has identified numerous risk factors for suicidal behavior, research that can draw strong causal inferences about such risk factors is needed for the most effective prevention of suicidal behavior. Several genetically-informed, Swedish population registries will be merged to form an unprecedented dataset of every individual born in Sweden from 1973 to 1996 (NH2,100,000) that is large enough to investigate the relatively rare, yet costly suicidal behavior. Early risk factors to be examined include maternal stress exposure pregestation, prenatally, and during the first 4 years of postnatal life. Stress is defined as the death or hospitalization of a first degree relative or partner of the mother. Suicidal behavior outcomes include definite and uncertain suicide attempts, suicide completions and accidental deaths. First, Cox Proportional Survival Analyses will be employed to examine the association between timing of stress exposure and suicidal behavior. Measures of early offspring, family, and community- level risks (e.g. parental age and socioeconomic status) will be included as covariates. Identifying periods of early development that are at heightened vulnerability would provide useful information for the support or rejection of different etiological hypotheses of suicide. Second, alternative hypotheses of the statistical associations will be tested. We will examine how early stress exposure covaries with other known risk factors for suicidal behavior, including maternal and paternal suicidal behavior. Further, because the dataset includes information on the biological relatedness of each individual with all of their family, the current project will also utilize powerful family-based, quasi-experimental methods to account for alternative causal hypotheses. In particular, the sibling comparison design, by examining differentially exposed siblings, will provide increased control of unmeasured background factors (both environmental and genetic) that may influence the association between early maternal stress and offspring suicidality. Third, the potential mediating effects of adverse birth outcomes, such as preterm birth and low birth weight, will be examined to further clarify the relations between early stress exposure and later suicidal behavior. The training plan will support instruction in advanced quasi- experimental and epidemiological methods, education in translational research and theory including animal studies of early stress, and hands-on clinical work with relevant populations. Findings from the current project will provide information to improve prevention programs and increase our understanding of the etiology of suicidal behavior. PUBLIC HEALTH RELEVANCE: Suicide reduction is a public health priority, but the effective prevention of suicidal behavior requires the identification of risk factors that are causally linked to suicidal behaviors. Previous research has been unable to draw strong causal inferences regarding risk factors because of empirical restrictions and limited data. In order to improve prevention programs and our understanding of the etiology of suicidal behavior, the current proposal uses novel analytical and methodological approaches to understand early risk factors for suicidal behavior in a study of every individual in Sweden from 1973 to 1996 (NH2,100,000).

NIH	2011	Brief Skills Training Intervention for Suicidal Individuals	Ward-Ciesielski, Erin	DESCRIPTION (provided by applicant): A significant percentage of individuals who die by suicide do not seek mental health services in the time preceding their death. This population is underserved and it is unclear what barriers keep them from seeking treatment. In order to begin a line of research aimed at addressing this high-risk population, this proposal rests on the hypothesis that suicidal individuals who do not seek treatment prior to attempting suicide experience the same psychopathological difficulties as suicidal individuals who do seek treatment - namely, severe emotion dysregulation. However, these non-treatment-seekers will likely require more creative recruitment strategies and briefer interventions than treatment-seeking individuals. As such, this application proposes to use wide-reaching recruitment efforts throughout the community to locate and enroll individuals who are suicidal but not seeking treatment. Further, there is a paucity of empirical support for interventions targeting suicidal individuals. Dialectical Behavior Therapy (DBT) is one of the few treatments that have been demonstrated to be effective with a suicidal population and is the only treatment whose effectiveness has been replicated. Previous research has suggested that an abbreviated version of the skills that are taught in DBT skills training have effectively reduced emotion dysregulation (i.e., depression and anxiety) in problem drinkers and the format of the proposed intervention is derived from this evidence-based emotion dysregulation intervention. As such, the proposed research is a randomized, controlled pilot trial of a very brief, one-time, skills-based intervention targeting difficulties in emotion regulation and distress tolerance. This research aims to evaluate the safety of the intervention, the feasibility of the research methods (including the appropriateness of the relaxation training control condition), and to preliminarily estimate the immediate (one week) and long-term (one and three month) changes resulting from the DBT Brief Skills Intervention (DBT-BSI) relative to a relaxation training control on the primary outcomes of suicide ideation and emotion dysregulation as well as a number of secondary outcomes. These results will inform the design of a subsequent full-scale randomized controlled trial of the DBT-BSI. PUBLIC HEALTH RELEVANCE: A significant percentage of individuals who die by suicide do not seek mental health treatment in the time preceding their death. Presumed barriers to treatment-seeking include a lack of appropriately broad advertising strategies and insufficient brief effective interventions targeting suicidal behaviors. This research aims to use wide-reaching recruitment strategies to reach non-treatment-seeking suicidal individuals and to preliminarily evaluate the effectiveness of a brief, one-time, skills-based intervention for this population.
NIH	2012	Suicide Behavior in College Students and Peers' Response	Garcia-Williams, Amanda	DESCRIPTION (provided by applicant): Suicide is a significant public health problem among American college students.1-4 Suicidal college students tend not to seek help in their time of crisis, and when they do seek help they overwhelmingly turn to peers (i.e., friends, roommates, intimate partners).1,5,6 Peers respond in different ways, such as talking with the suicidal peer alone, telling a trusted adult (such as a teacher or resident advisor), advising the peer to seek help, or ignoring the situation.1,5,7 There is currently little understanding of how college students experience a suicidal peer or the factors that predict prosocial helping behavior toward a suicidal peer. This mixed-methods study will use a prosocial helping behavior model to overcome this limitation and will meet the following two research aims: (1) qualitatively understand how undergraduate college students experience a suicidal peer and (2) quantitatively identifying the factors that predict helping behavior toward a suicidal peer. Qualitative interviews will be conducted among college students with prior experience with a suicidal peer and quantitative surveys will be administered to college students regardless of prior experience. In both qualitative and quantitative arms of this study situational, bystander, victim, arousal, decisional balance and behavioral characteristics will be explored. PUBLIC HEALTH RELEVANCE: This study meets Healthy People 2020's call for a reduction in the national suicide rate and number of suicide attempts among adolescents8 because the factors found to predict prosocial helping behavior among college students towards suicidal peers could be targeted in preexisting and widely used gatekeeper suicide prevention training.9 This could then result in more college students acting as prosocial bystanders who encourage their suicidal peers to seek, which could reduce attempted and completed suicides within this at-risk population.
NIH	2013	Computerized Intervention for Anxiety Sensitivity Cognitive Concerns	Capron, Daniel	DESCRIPTION (provided by applicant): Death by suicide in the US is currently at its highest rate in 15 years. Emerging evidence indicates that one component of anxiety sensitivity (AS), specifically cognitive concerns (ASCC) is a risk factor for elevated suicidality. ASCC refers to fear of arousal leading to mental incapacitation. ASCC is associated with suicidal ideation (SI) in a wide variety of populations including patients with post-traumatic stress disorder, air force cadets, and cigarette smokers. A separate line of study has revealed that AS is malleable through cognitive-behavioral interventions. Moreover, these effects can be achieved through brief computerized interventions and the benefits appear to be maintained over several years. However, current AS reduction protocols focus almost exclusively on the physical concerns facet of AS (i.e., arousal leading to physical catastrophe). There are several reasons why ASCC may represent a distinct construct from physical AS and thus warrant a specific intervention. First, ASCC are most closely associated with depression, whereas, AS physical concerns are more associated with anxiety conditions such as panic disorder. Second, individuals with elevated ASCC show elevated SI, whereas individuals with elevated AS physical concerns show reduced SI. Therefore, the effects of previous AS interventions may not be relevant to reducing SI and a targeted ASCC intervention is needed. The proposed study was designed to provide incremental training to the PI in psychophysiological assessment [specifically electroencephalogram/event related potential (EEG/ERP)], suicidology, and designing/executing a clinical trial. Learning EEG will allow for multilevel assessment in line with NIMH's Research Domain Criteria (RDoC) initiative and suicide is an urgent major public health burden. In the proposed study, approximately 60 individuals with elevated ASCC and SI will be randomized to receive either a recently developed one-session active ASCC intervention or a healthy living control intervention. The first specific aim of the project is to determine if ASCC can be reduced among a sample with elevated SI via this brief ASCC intervention. The next specific aim is to examine if high and low ASCC individuals show differential fear-specific event related potentials (ERP) to an emotional stroop task featuring ASCC threatening phrases using EEG measurement. To address this specific aim we will also recruit 15 individuals with absent/minimal ASCC. A related aim is to assess if the computerized intervention leads to reduced AN380 and P1 ERPs post-intervention (which have shown to differentiate high versus low AS individuals in previous work). The third aim is to determine whether this intervention leads to reduction in SI over time (one and four month follow ups). The final aim is to determine if reductions in ASCC mediate reductions in SI. By examining a brief treatment for ASCC in a sample with elevated SI, this study will provide critical knowledge regarding how to quickly and effectively reduce ASCC and potentially prevent/ameliorate SI.
NIH	2013	Shame as a Risk Factor for Severe and Costly Outcomes in Body Dysmorphic Disorder	Weingarden, Hilary	DESCRIPTION (provided by applicant): Body dysmorphic disorder (BDD) is a severe mental illness associated with extremely negative consequences. Most notably, the degree of unemployment, social dysfunction, comorbid major depressive disorder, and suicidality appear higher in BDD than in most other psychological disorders, including related disorders like obsessive compulsive disorder (OCD). Together, these outcomes produce substantial psychological and economic costs to the individual, as well as significant economic costs to society, making BDD a serious public health concern. Surprisingly, scant research has studied risk factors that may help to explain these elevated negative outcomes in BDD, as compared to other disorders. The present study addresses this gap by testing shame as a central risk factor for more severe outcomes in those with BDD vs. healthy individuals and individuals with OCD. Clinical anecdotes discuss shame as a central, destructive emotion in BDD, and broader emotions research links shame to each of the negative outcomes that are elevated among those with BDD. However, no scientific research has investigated the degree of shame in BDD vs. healthy individuals or those with related disorders (e.g., OCD), nor is there research examining how shame relates to the severe outcomes in BDD. Aim 1 is to conduct the first empirical evaluation of general shame as a central, robust risk factor accounting for more severe outcomes (i.e., social and occupational impairment, depression, suicidality) in BDD vs. healthy control participants and participants with OCD. Additionally, information about the specific nature of shame within BDD has important clinical implications. In particular, body shame appears central and nearly universal to BDD. Thus, it may be that, beyond the more universal experience of body shame in BDD, it is individuals with elevated general shame who are at greatest risk for the most severe negative outcomes in BDD. Aim 2 is, thus, to evaluate whether general shame is a stronger risk factor than body shame for the negative outcomes documented within BDD. Participants will be recruited for the three groups (BDD, OCD comparison, healthy control) through advertisements posted on online BDD, OCD, or non-mental health related forums, support groups, and clinic websites. Participants will provide self-report data through a secure online website. To verify the well-established self-report screening measures, a randomly selected subsample from each group will be called to complete a diagnostic interview via phone. An Internet-based approach was chosen because of the severe avoidance and impairment in BDD, the primary group of interest (e.g., 30% may be housebound). Thus, samples recruited from clinics or research labs would likely be biased, with less severe outcomes and shame. In keeping with NIMH Strategic Objective 2.3, the overarching goal of this project is to identify shame as a malleable and robust risk factor for serious and costly outcomes in BDD, a disorder of high public health concern. This information has the potential to provide new targets for BDD treatment and to minimize the painful and costly consequences that BDD sufferers currently experience.

NIH	2012	Behavioral and Physiological Predictors of Suicidal Behavior in Adolescents	Glenn, Catherine	DESCRIPTION (provided by applicant): The proposed research and training plan aims to advance our understanding of risk markers for suicidal behavior in adolescents, and to equip the applicant with the skills necessary to carry out independent longitudinal research in the areas of developmental psychopathology and suicide. There is an urgent need to identify ways to reduce rates of suicide among adolescents, and an important first step is to establish risk markers - or predictors - of suicide in this age group. The goal of the proposed research is to identify multipl behavioral and biological (psychophysiological) risk markers for suicidal behavior in adolescents. Importantly, these goals are also consistent with the National Institute of Mental Health (NIMH) Strategic Plan, which highlights the need for identifying biological and behavioral markers associated with clinically relevant problems. This goal will be achieved through the following specific aims: Aim 1. To examine the relation between two behavioral tasks for suicide (i.e., death/suicide IAT and suicide Stroop test) and suicidal behavior in adolescents. Aim 2. To examine the relation between reduced fear responding during suicide-related stimuli (psychophysiological measure) and suicidal behavior in adolescents. Aim 3. To examine additive and interactive associations between behavioral and psychophysiological predictors of suicidal behavior in adolescents. This work has the potential to better identify those adolescents at greatest suicide risk, who are in critical need of intervention. In line with state f the art methods used to diagnose physical conditions, this line of research aims ultimately to identify a short battery of tests that can be used to objectively assess risk for suicide in adolescents. These measures are ideal because they are brief, easily administered and scored, and thus could feasibly be used in an emergency department or inpatient setting to inform decisions about adolescents' admission and discharge from hospital care. Therefore, this program of research has the potential to significantly advance clinical science and to modernize the way the field assesses risk for suicidal behavior. The training plan in this application extends the applicant's previous research and clinical experiences in the following areas: developmental psychopathology, suicide, and longitudinal research design and analysis. In order to achieve these goals, the applicant has carefully assembled a team of sponsors and consultants to guide and support this project. Dr. Matthew Nock (sponsor) has expertise in suicide research and adolescent psychopathology. Dr. Ronald Dahl (consultant) is an expert in adolescent brain and pubertal development, as well as in early interventions. Finally, Dr. Terry Blumenthal has expertise in the startle reflex methodology - the physiological measure chosen for this project. In sum, the F32 training will advance the applicant's knowledge and expertise in three new areas and provide the foundation for a career as an independent clinical scientist. PUBLIC HEALTH RELEVANCE: Suicide is the third leading cause of death among youth ages 10 to 24 years, and alarmingly, the rates of suicide among this age group appear to be increasing. Although there is a critical need to identify adolescents at greatest risk for suicide, predicting suicidal behavior has proven difficult, and current strategies are insufficient. The goa of the current proposal is to identify behavioral and biological risk markers for suicidal behavior in adolescents in order to better detect those adolescents at greatest suicide risk, who are in urgent need of intervention.
NIH	2011	The Neurobiology of Self Appraisals and Social Cognition in Depressed Adolescents	Mendoza Quevedo, Karina	DESCRIPTION (provided by applicant): The goal of the proposed study is to study the neural basis of aspects of self and social cognition - negative self appraisals and elevated attention to negative emotional social signals - that are highly relevant to understanding the development of adolescent depressive disorders. Persistently negative self appraisal and elevated attention to negative emotional social signals, (e.g. negative facial expressions) are key processes that denote risk for depressive disorders across the lifespan. These processes are particularly relevant to understanding risk for depression in adolescence, because this is a period during which there is rapid transformation in self appraisals and interpersonal social functioning as part of the key developmental task of forming a positive and coherent self representation. Suboptimal resolution of this developmental task is linked to onset and recurrence of depressive disorders and risks for suicide in adolescence. Therefore, understanding the neural basis of negative self appraisals and attention to negative facial expressions in adolescent depression will provide valuable insights into specific neural mechanisms of depression during this vulnerable developmental period to guide intervention strategies. Furthermore, this research will also help identify objective, neurobiological markers of adolescent depressive disorders that can be used in the future to detect those adolescents who may be most at risk of future depression or who are on a trajectory to a recurrent course of the illness.
NIH	2009	Molecular characterization of a corticolimbic network in depression	SIBILLE, ETIENNE	DESCRIPTION (provided by applicant): Despite the substantial personal and economic burden of mood disorders, understanding the pathological and molecular features of these disorders remains a considerable challenge in psychiatric research. Dysregulated serotonergic and stress pathways appear to be contributing factors in major depression; however, it is likely that numerous other unidentified risk factors exist. Here we propose to investigate the molecular pathology of major depression, using a combined approach of microarray experiments, bioinformatic analysis and anatomical characterization of results. Our central hypothesis states that the biological liability to major depression is reflected in a persistent molecular pathology that is detectable in the postmortem human brain and that affects a cortico-limbic network, whose dysfunction might specifically cause, or at least correlate with, the affective component of depression. Hence, based on microanatomical and functional studies, we will concentrate on two densely interconnected brain areas within this cortical- limbic network of mood regulation: i) the amygdala (AMY), as a brain region that is crucial to the integration and expression of emotions, and ii) the anterior cingulate cortex (ACC), as depression-related functional and morphological changes have been consistently reported in this brain area. As microanatomical studies suggest a glial depression-related pathology in these two brain areas, we will apply novel analytical approaches to separately assess the contribution of altered glial or neuronal functions within the gray matter in correlation with major depression. Together, results from this research proposal could reveal either a general pathway that is common among all depressed subjects and/or specific pathways that may differ as a function of sex and family history of major depression, two factors that are associated with different phenotypic features of depression. The characterization of patterns of nuclei (AMY) and laminar (ACC) changes for selected genes will provide anatomical information to generate network-based hypotheses on the molecular pathology of depression. PUBLIC HEALTH RELEVANCE: The overall goal will be to assess causality of altered biological pathways or cellular mechanisms in the pathophysiology of major depression, as an essential step in identifying potential leads for novel therapeutic intervention in major depression.
NIH	2008	Neuroimaging of Fatty Acids in Major Depression	SUBLETTE, M	DESCRIPTION (provided by applicant): The applicant is seeking to become an independent investigator focusing on the role of dietary essential polyunsaturated fatty acids (PUFAs) in the neurobiology of mood disorders and suicide, using positron emission tomography (PET). PROJECT DESIGN: Background.- PUFAs are implicated in mood disorders: 1) Low plasma levels of omega-3 PUFAs and higher ratios of omega-6 to omega-3 PUFAs have been found among depressed patients, and our pilot study suggests these indices predict suicide attempts. 2) Double-blinded, placebo-controlled studies have found that adding omega-3 fatty acids (fish oil) to standard treatment of depression improves outcomes in Major Depressive and Bipolar Disorders. 3) We find that similar brain regions have low glucose uptake among suicide attempters and in depressed patients with low fatty acids. Hypothesis: A functional imbalance between omega-3 and omega-6 PUFAs contributes to depression and suicidality. The objective is to clarify relationships between plasma PUFA levels, clinical characteristics, including suicide risk, and regional cerebral rates of glucose metabolism (rCMRglu) in Major Depressive Disorder. Aim1. In regions of interest (ROIs), test the following hypotheses: a) Lower rCMRglu correlates with lower plasma PUFAs in depressed subjects b). rCMRglu are lower in suicide attempters vs. non-attempters. Aim 2. Perform voxel-level analyses on rCMRglu and plasma PUFA levels in: a) Depressed subjects vs. healthy volunteers, b) Depressed subjects with and without suicide attempt history. Aim 3. Perform voxel-level analyses of effects of augmentation treatment with fish oil on rCMRglu, plasma PUFA levels, symptom severity, and the relationships between them. Aim 4. Characterize the effects offish oil on plasma PUFAs and clinical status: a) Test the hypothesis that plasma levels of DMA will be lower in depressed subjects than healthy volunteers, and lower in suicide attempters than nonattempters. b) Assess overall clinical status and severity of individual symptoms. Methods: Thirty subjects with Major Depressive Disorder (half with history of suicide attempt) not responding to treatment and 15 healthy volunteers will have quantitative PET scanning with [18F]FDG before and after adjunctive treatment for 4-6 weeks with fish oil. We will perform group comparisons of rCMRglu in ROIs and use statistical parametric mapping at the voxel level to generate difference and correlational maps. TRAINING: The candidate proposes to undertake specialized studies in neuroimaging methodologies, statistics, and lipid biochemistry. PUBLIC HEALTH RELEVANCE: Major Depressive Disorder and suicide are major public health problems worldwide. This study is expected to contribute to understanding the neurobiology of depression and may provide new information relevant to treatment with dietary fatty acids.

NIH	2012	Tech-Based Depression and Anxiety Treatment for Youth in High Risk Environments	Burns, Michelle	The PIï¿½s career goal is to become an independent investigator developing and evaluating novel interventions for underserved, vulnerable youth with anxiety and depressive disorders. This proposal outlines a plan to achieve this goal, through culmination of the training and research plans into an extremely competitive R01 proposal. The training plan takes full advantage of the candidateï¿½s strong institutional support and environment at Northwestern Universityï¿½s Feinberg School of Medicine, as well as relations with the broader community of researchers working with youth in high risk social environments. Training will include multidisciplinary mentorship, coursework, conferences, seminars, systematic professional interactions, readings, collaboration with a youth advisory board, and a mentored publication plan. Training goals necessary to the PIï¿½s career goal involve growth in: 1) intervention development and evaluation; 2) adolescent psychology; 3) cultural issues pertinent to vulnerable youth; and 4) general career development. This plan builds on the PIï¿½s background in clinical psychology, which has focused on technology-based treatments for depression and anxiety, contextual models of mental health disparities, implications of co-occurring psychiatric disorders on treatment outcomes, and cognitive behavioral therapy (CBT). In this K08, the PI will extend her work to include youth, increasing the impact of her research through earlier intervention. The long-term goal of the research is to open a new avenue to culturally competent care by: 1) applying treatment principles efficacious in general populations to unique concerns of underserved youth facing multiple risks to their physical and mental health; 2) developing a mobile treatment that provides real-time, context-specific intervention; and 3) extending population-level care, via Internet and mobile phone technologies, to youth unable to access existing services. To this end, the research plan will: 1) identify context-specific risk factors for anxiety and depressive symptoms in vulnerable youth; 2) identify treatment targets accordingly; and 3) develop an engaging, accessible intervention tailored to vulnerable adolescents with Major Depressive Disorder (MDD) and Generalized Anxiety Disorder (GAD). The intervention, delivered via an advanced mobile phone application, the Internet, and brief telephone support, will be grounded in validated CBT techniques and more recent advances in transdiagnostic CBT. Research aims will be achieved via: 1) Study 1, analysis of an existing longitudinal, epidemiological dataset to identify context-specific social stressors that predict increased anxiety and depressive symptoms, and cognitive mechanisms by which the social stressors impact anxiety and depression; 2) Study 2, development, usability testing, and a subsequent feasibility trial of a new, transdiagnostic Internet and mobile phone intervention teaching CBT skills to vulnerable adolescents with MDD and GAD, and applying these skills to targets identified from Study 1; and 3) Study 3, a pilot randomized controlled trial (RCT) comparing the intervention to an attention control. Studies 2 and 3 will provide preliminary data for an R01 proposing a larger RCT.
NIH	2008	Behavioral treatment for alcohol dependent women with co-occurring depression	GAMBLE, STEPHANIE	DESCRIPTION (provided by applicant): This Mentored Patient-Oriented Research Career Development Award (K23) will serve as the foundation for a career devoted to developing and testing novel therapeutic interventions for women diagnosed with alcohol dependence and co-occurring major depression (AD-MD). AD-MD is a serious and common public health problem, yet one that is largely unaddressed. Among alcohol dependent patients, co-occurring depression is associated with poorer treatment outcomes, increased risk for relapse, worse long-term social and functional adjustment, and higher probability of dire outcomes such as suicide. Treatment research on AD-MD women is needed to inform effective practice. This K23 is devoted to enhancing the research development of the Candidate and to initially testing the applicability of Interpersonal Psychotherapy for alcohol dependent women with major depression (IPT-ADMD). The proposed education plan provides targeted coursework, training, and supervision to prepare the Candidate as an independent investigator of therapeutic interventions for AD-MD women. Mentored career development and research activities are designed to develop the Candidate's expertise in: 1) the measurement and classification of alcohol dependence and major depression, 2) interventions relevant for AD-MD women and 3) clinical trials methodologies. The goal of the proposed research project is to refine and test a behavioral intervention that addresses women's co-occurring alcohol dependence and depression within a cohesive interpersonal frame. In Phase 1 of the project, IPT-ADMD will be piloted with 15 AD-MD women enrolled in a* MICA (mentally-ill chemical abusers) group treatment program. Findings from Phase 1 will be used to refine the treatment, assessment, and therapist training procedures. In Phase 2, a randomized controlled trial with 60 AD-MD women will be conducted 1) to determine IPT-ADMD's feasibility and acceptability as an adjunct to standard MICA group treatment, and 2) to assess the comparative effects of IPT-ADMD to treatment-as usual individual therapy (TAU-IT). Compared to TAD-IT, IPT-ADMD is hypothesized to lead to greater reductions in women's drinking frequency, drinking intensity, and depressive symptoms, and to improved interpersonal functioning. Results will lay the foundation for a career-long program of interventions research devoted to improving the lives of this important but underserved and understudied population.
NIH	2009	Mental Health Help-Seeking for Suicide Ideation on Attempts in Diverse Youth	SILENZIO, VINCENT	DESCRIPTION (provided by applicant): Vincent M. B. Silenzio, MD, MPH is an academic family medicine physician and medical ethnographer with experience in the clinical care of underserved populations and the application of Internet technology in teaching and research. He is a faculty member in the University of Rochester Center for the Study and Prevention of Suicide pursuing mental health services research in help-seeking behaviors among adolescents and young adults at risk for suicide. His career goal is to become a leading independent researcher in translational mental health services research in this population. The candidate's career development goals will be to expand his relevant knowledge and skills in the following areas through structured training experiences in: 1) mental health services research, 2) advanced statistical analysis, 3) advanced network analysis methods and computational modeling of complex adaptive networks, 4) research informatics and emerging Internet-based research applications, and 5) adolescent and young adult development in youth at risk for suicide. This will include structured graduate-level coursework, tutorials, ongoing seminars in these areas. The planned research activities and aims include using Internet-based approaches to access a heretofore highly-isolated population of youth at risk for suicide ideation and attempts. We will complete a web-based survey using respondent-driven sampling techniques within social networks of youth to study of mental health resource use among adolescents and young adults at increased risk of suicide ideation or attempts. We will examine differences in predictors of formal vs. informal and technology-based vs. face-to-face mental health help-seeking behaviors for suicide, and the interaction effects of mental health stigma, sexual orientation stigma, and social network measures of peer support on mental health help-seeking. PUBLIC HEALTH RELEVANCE: This study will add to our understanding effectors that influence help-seeking behavior in a population at high risk for suicide. This will deepen our understanding of the ecology of mental health help-seeking for suicide while advancing our appreciation of the role of emerging technologies such as the Internet in future mental health services research and service delivery.
NIH	2009	Functional Magnetic Resonance Imaging Markers of Early-Onset Suicide Attempt	PAN, LISA	DESCRIPTION (provided by applicant): The proposed application will provide the candidate with the needed expertise to establish an independent research career focusing on the investigation of the neurobiology suicide attempt in children and adolescents. The applicant is a child and adolescent psychiatrist who proposes to obtain multidisciplinary training from mentors in suicidology and functional neuroimaging, with a panel of experts in childhood neurobiology, child development, neuroimaging, and data analysis. We propose to use established methods in functional neuroimaging and neuroscience to characterize the neurobiology underlying early onset suicide attempt. We will assess these adolescents, and age-matched psychiatric controls and healthy controls with well-established neurocognitive tasks. We hypothesize that history of suicide attempt in adolescents will be associated with differences in patterns of neural activity compared with both psychiatric and healthy controls. The primary objective of this research project is to examine the neural circuitry underlying traitdependent abnormalities in cognitive and emotion processing in adolescents with depression with and without history of suicide attempt, by focusing on the following areas: emotional processing, cognitive control, and risky decision-making, that have been demonstrated to recruit ventral and dorsomedial prefrontal cortices and amygdala and ventral striatum, dorsal prefrontal cortical regions, and ventromedial and dorsomedial prefrontal cortices, respectively. Our study of the neural circuitry of adolescent suicide attempt is important in that it will help to more precisely define: 1) cognitive and affective processing abnormalities associated with suicidal behavior; 2) functional neurocircuitry related to these neurocognitive abnormalities; and, in turn, 3) the relationship between these abnormalities and onset and history of suicidal behavior. Increased understanding of these neural markers will have a significant impact upon the future targeting of treatment and prevention efforts to improve the long-term outcome of individuals with suicidal behavior. This is the first study of its kind in a pediatric population. The functional neuroimaging instruction, didactics, coursework, and clinical research training, sponsored by Mary Phillips, M.D., M.D. (Cantab), Director of the Functional Neuroimaging Program, and David Brent, M.D., Endowed Chair in Suicide Studies, will prepare the candidate to perform multidisciplinary cognitive neuroscience research in adolescent suicide prevention. PUBLIC HEALTH RELEVANCE: Identification of markers for suicide risk and increased understanding of the cognitive neuroscience of suicide attempt may have a significant impact upon the future design and monitoring of treatment and prevention efforts to prevent death and improve the long-term outcome of individuals with suicidal behavior. This is the first study of its kind in adolescents.

NIH	2009	Cognitive and Affective Neuroscience of Decision-Making in Late-Life Suicide	Dombrovski, Alexandre	DESCRIPTION (provided by applicant): Brain mechanisms of vulnerability to suicide in old age remain unclear, and very few researchers study the neurobiology of late-life'suicide. In particular, the field of suicide research lacks an understanding of how psychoiogicai and cognitive markers of suicidal risk (hopelessness, executive dyscontrol) relate to brain markers identified in post-mortem and imaging studies. The applicant - a geriatric psychiatrist with a clinical background in late-life suicide and in the treatment of late-life depression - views suicide as an outcome of an altered decision process, a view supported by preliminary behavioral and imaging data. Thus, the applicant's career goals are to apply advances in the basic neuroscience of decision-making to investigate the brain mechanisms of late-life suicide and, in the future, to identify intervention targets. This approach aims to bridge existing cognitive research on suicidal diathesis with basic and clinical neuroscience. This will be achieved through training in functional magnetic resonance imaging (fMRI; including computational model-based fMRI), in neurobiology of decision-making, and in using neuroscience models to identify intervention targets. An fMRI study of decision-making in elderly depressed suicide attempters focused on disruptions in the processing of value signals in the ventromedial and ventrolateral prefrontal cortex will serve as a vehicle for proposed training. Proposed training and research will be supported by the Advanced Center for Interventions and Services Research for Late-Life Mood Disorders directed by CF. Reynolds (mentor), G.J. Siegle's fMRI lab (co-mentor), and L. Clark's imaging lab (Cambridge, UK). Taking advantage of the neuroimaging resources at the University of Pittsburgh, H.J. Aizenstein will help the applicant to overcome challenges in MR imaging of the aging brain and M.L. Phillips will aid in refining the neural model and developing a life-span perspective on decision-making in suicide. K. Szanto will help the applicant sharpen clinical characterization and manage suicidal risk. An ROI geared towards identifying intervention targets should result from this work. PUBLIC HEALTH RELEVANCE (See instructions): Worldwide and in the US, the elderly have the highest suicide rate of all age groups - a public burden likely to increase as US population ages and access to firearms is legally upheld. Current prevention approaches are not selective, targeting mainly depression. Insight into brain mechanisms will help identify elderly at risk for suicide and develop neuroscience-based interventions.
NIH	2012	A Sleep-Oriented Intervention for Suicidal Behaviors	BERNERT, REBECCA	DESCRIPTION (provided by applicant): The overarching goal of this Mentored Patient-Oriented Research Career Development Award (K23) is to provide the Candidate with comprehensive training to facilitate her independence as an investigator within two distinct, but intersecting fields of study: sleep medicine and suicide prevention. Suicide is a complex, but preventable public health problem, for which research-tested interventions are scarce. Poor sleep has emerged as an empirically-established, modifiable suicide risk factor that is visible, amenable to treatment, and arguably less stigmatized compared to other risk factors. The current proposal will pursue rigorous evaluation of sleep as an intervention tool. It aims to develop a sleep-oriented intervention for suicidal behaviors. A programmatic line of research is proposed to endow the Candidate with critical methodological training in treatment development. Both education and research training plans will cultivate her independence as trialist and suicide preventionist. Using a multidisciplinary approach, the proposed education plan offers career development training across three general areas: (1) Randomized controlled trials (RCT) (design, conduct, analysis) using behavioral interventions, (2) Treatment development methods (manualizing, pilot-testing interventions) in sleep and suicide prevention, and (3) Emotion regulation research to evaluate underlying causal mechanisms, and potential intervention targets, in the study of sleep and suicide risk. Consultation, coursework, didactics, and applied trainings will enable the Candidate to acquire advanced conceptual, methodological, and biostatistical skills across specialty areas. Next, based on theoretical, empirical, and clinical rationale, the proposed research plan outlines two pilot studies to develop a new, sleep-based suicide intervention (SBSI). Development of a novel preventive intervention among this high-risk population is in accordance with several NIMH Strategic Plan Objectives. It will endow the Candidate with applied and explicit training in treatment development and RCT conduct. Study 1 will be a small, open-label pilot focused on SBSI development. SBSI will target sleep complaints known to present risk for suicide by integrating core components from three efficacious treatments: Cognitive behavioral therapy for insomnia (CBT-I) will address insomnia symptoms, social rhythms therapy (SRT) will address irregular sleep patterns, and imagery rehearsal treatment (IRT) will address residual nightmares. The protocol will be manualized, evaluated for feasibility, and revised based on focus groups, acceptance, and indications of response. Study 2 will be a randomized controlled pilot study. It will compare SBSI to an active control to evaluate feasibility, acceptance, retention, and preliminary indications of response. To promote the Candidate's career independence, results from these studies are expected to result in application for an R01 RCT in suicide prevention. PUBLIC HEALTH RELEVANCE: Suicide represents a global disease burden that, despite improvements in awareness and treatment, continues to account for more than half of all violent deaths worldwide. In this important research area, even modest symptom improvements may have great clinical significance when the potential outcome to be prevented is death. Given its target of a uniquely modifiable suicide risk factor, development of a novel sleep-based intervention for suicide has public health significance by addressing a gap in the literature wherein efficacious treatments are either few in number, unacceptable to patients (i.e., based on retention rates), or inaccessible to those most in need.
NIH	2013	Social Connections and Late Life Suicide	Van Orden, Kimberly	DESCRIPTION (provided by applicant): Older adults have higher rates of suicide than younger individuals in the U.S. (and most countries in the world) and the size of the older adult population will rise dramatically in the coming decades, making suicide in later life an issue of pressing public health concern. It is not known how to prevent suicide among older adults; empirical data indicating how to prevent suicide among this high-risk population are notably lacking. The Candidate's career development goal is to be a leading expert in the study of suicide and its prevention in older adults. Reaching that goal requires training in three domains of geriatric research (described below), as well as completion of a mentored research project that will produce substantive, foundational results (also described below). Primary care is a key site for late life suicide prevention: two-thirds or more of older adults who die by suicide are seen by primary-care physicians within a month of their deaths, and up to half within a week. Depressed older adults do not tend to seek specialty mental health treatment. For this reason, Training Objective 1 for this K23 proposal is to gain expertise interfacing with primary care as a site for both recruitment and implementation of innovative interventions with older adults at risk for suicide. It is also known that depression is a strong risk factor for late-life suicide, but te vast majority of depressed older adults do not die by suicide. Further, evidence is beginning to accumulate suggesting that targeting depression in older adults does not sufficiently lower suicide risk among older adults. For example, in the PROSPECT trial, a significant number of older adults remained suicidal at the end of the intervention. Thus, intervention studies targeting older adults at risk for suicide are needed; in particular, we need to understand how these interventions work to effectively implement and disseminate them. For this reason, Training Objective 2 is to gain expertise in the implementation of behavioral intervention protocols for older adults. Further, depressed older adults frequently present with cognitive impairment. Further, social functioning deficits are also associated with cognitive impairment. Thus, to properly characterize research samples and draw valid inferences from data, the candidate will need to know how to accurately assess cognitive decline. For this reason, Training Objective 3 is to gain knowledge of, and skills assessing, aging-related cognitive decline. The candidate's program of research will be informed by her training and experience as a clinical psychologist, in particular by theoretical and empirical evidence that she helped establish showing the central importance of social disconnectedness to suicide. With the long-term research goal of improving interventions for late-life suicide, the principal objective of the research proposed here is to examine whether increasing social connectedness -- the degree to which older adults feel connected to, and as if they contribute to, valued relationships -- is a mechanism by which behavioral interventions reduce risk for suicide. To achieve this objective, the candidate requires pilot data demonstrating that a manualized (thus replicable) behavioral intervention does, in fact, increase connectedness while adjusting for correlates of connectedness-depression and cognitive functioning. Despite the likelihood of this association, the question has simply not been comprehensively addressed. This study will recruit n = 100 adults aged 60 years from primary care who endorse both disconnectedness (i.e., feeling lonely and/or like a burden on others) and clinically significant depression. Subjects will be randomly assigned to a behavioral intervention targeting disconnectedness (i.e., Interpersonal Psychotherapy; IPT) or care-as-usual (CAU). At baseline, 3-month, and 6-month assessments, subjects will report on social connectedness, cognitive decline, and depression. The project's Research Aims are: Aim 1: To examine whether a manualized intervention (IPT) can increase connectedness among older adults. Aim 2: To examine whether an intervention targeting social functioning (IPT) also reduces late-life suicide risk. Aim 3: To examine increases in connectedness as a mechanism whereby IPT decreases depression. The resulting findings of this K23 project on depression and death ideation (i.e., indicators of suicide risk) will function as the basis for a larger R01-funded study powered to examine suicide ideation and behavior as outcomes. These findings will be coupled with the candidate's substantial pilot data supporting the link between disconnectedness and both suicide ideation/behavior and depression. Subsequent to this award, the candidate will build on the skills acquired in this period of mentored career development to contribute to the development and refinement of approaches to suicide prevention in later life.

NIH	2013	Mobile Phone Intervention to Prevent Youth Suicide in Rural Communities	Pisani, Anthony	DESCRIPTION (provided by applicant): Reducing youth suicide has been named as a national priority for more than a decade, yet rates of youth suicide and suicide attempts have not declined. Suicide is still the 3rd leading cause of death for ages 10 - 24, and suicide rates i rural communities are more than double the national average. The public health impact of commonly applied strategies, such as gatekeeper training, is limited by minimal communication between adolescents and adults, minimal help seeking by adolescents, and by problems with accessibility and acceptability of mental health services. These barriers are particularly relevant in rural and underserved communities, which have 2-10 times higher youth suicide rates and lower utilization of available services. School-based, population oriented strategies overcome some of these limitations, but existing programs have yet to harness mobile communication devices to reach adolescents with preventive interventions directly, even beyond the school context. Text messaging is low-cost, effective tool for changing health behaviors, and is emerging as a powerful public health tool for influencing adolescent risk behavior. My application would be the first extension of mobile devices into population-based suicide prevention. The K23 career development award will provide me with the education and experience I need to become an independent investigator focused on developing and testing mobile-mediated public health interventions to reduce youth suicide. This proposal has three career development goals: Goal 1. Intervention Development. Learn the principles and practices needed to develop a safe, engaging, and effective mobile-mediated mental health intervention to target suicide risk and protective processes for youth. Goal 2. Prevention Trial Design. Gain expertise and collaborators to select and sequence prevention trial designs and research methods that are suitable for testing flexible electronically-delivered interventions for youth. Gol 3. mHealth Knowledge. Gain scientific and technical knowledge to collaborate effectively with technical experts and to assess opportunities for mHealth technologies in youth suicide prevention. I developed a research project that provides a framework for meeting these career development goals. My research objective is to develop and test the effects of a suicide preventive intervention delivered to adolescents via mobile technology. To achieve this objective my project has three aims: Aim 1. Development. Develop a safe and engaging text messaging intervention (Text4Strength) to strengthen adolescent's emotion self-regulation skills and resources. Aim 2. Field Testing. Assess the usage, usability, participant perceptions, and system operation of Text4Strength by conducting a field test of with 43 adolescents, and revise the intervention as needed. Aim 3. Pilot RCT. Assess the promise of Text4Strength. Assess the impact of Text4Strength on key proximate targets examining: skills in monitoring emotions, reducing escalation, and using adult relational resources to maintain emotional equilibrium. Secondarily, I will explore the intervention's impact on psychological distress, depressive symptoms, anxiety symptoms, and suicide ideation. The career development plan anchored by this research project will give me the skills, experiences, collaborators, and technical infrastructure that I need to be a leading expert in applying mobile technology to prevent youth suicide in rural communities. By putting an option-rich intervention in the hands of youth in rural communities, the proposed research addresses NIMH priorities: Strategic Objective 3 to improve and personalize mental health interventions; Strategy 4.1 to test novel models and methods to bring mental health interventions to diverse groups, including rural communities.
NIH	2008	MidCareer Investigator Award: Suicidal Behaviors	GOLDSTON, DAVID	DESCRIPTION (provided by applicant): In this competing continuation application for a Mid-Career Investigator Award, David Goldston, Ph.D., requests support for mentoring of junior faculty and postdoctoral fellows, career development, and continued research in the area of adolescent suicidal behaviors. The initial K24 award, which was focused on treatment development and clinical trials, relapse prevention interventions, and treatment with substance abusing and dually diagnosed adolescents, ends in May 2008. As of March 2007, Dr. Goldston will have mentored 44 investigators from the level of doctoral student to junior faculty (including 9 minority investigators, and 28 investigators whose work focuses on suicidal behaviors and interventions). These investigators already have obtained 11 funded awards or grants from NIH and CDC, and have an additional 7 applications under review or in preparation for June 2007 submissions. As for his own research program, Dr. Goldston has continued with longitudinal research related to the course of suicidal behaviors, and expanded his research focus by developing an integrated relapse prevention intervention for substance abusing, depressed, and suicidal teens and their families. Therefore, Dr. Goldston has fulfilled the aims of increased mentoring and research development outlined in the original K24 application. For the next five years of the K24, a specific mentoring plan is described in which junior faculty and postdoctoral fellows will continue to be integrally involved with the candidate's program of research, develop their own independent research projects, and benefit from the proposed consultation during the K-24 period, particularly in the areas of suicidality and intervention research. In the career development plan, consultation and learning experiences are proposed in two primary areas: (1) intervention designs other than traditional randomized controlled trials (e.g., dynamic wait- list controlled trials; simple, pragmatic trials); and (2) factors that affect the outcomes and implementation of interventions for suicidal youths in community settings. The candidate's research during the K24 period (with opportunities for involvement of mentees) will include longitudinal studies of the course and impact of adolescent suicidal behavior; a collaborative efficacy trial of the intervention for suicidal, substance using youths, and a treatment development and effectiveness study of a community-based suicide prevention program collaboratively developed with the Ojibwe reservations in the upper Midwest.
NIH	2010	Adapting Dialectical Behavior Therapy for Children with Suicidality and/or Self-H	Perepletchikova, Francheska	DESCRIPTION (provided by applicant): Suicide and suicidal behaviors in youth are occurring at an epidemic rate. In the past 20 years death rates for suicide for youth 5 to 14 years of age have doubled. In 2005, suicide was the sixth leading cause of death in the USA for 5- to 14-year-olds and the third leading cause of death for 10- to 14-year-olds. The medical cost of suicide for Americans aged 0 to 20 approaches $1 billion a year. Although completed suicides are less frequent in childhood than in adolescence, the rate of 14.4 suicide attempts for every suicide in 10- to 11-year- olds indicates that suicide attempts are quite frequent in childhood. Further, suicidality is strongly associated with non-suicidal self-harm behaviors (e.g., cutting) as up to 40% of those who engage in self-harm report having suicidal ideations and up to 85% have attempted suicide at least once. Despite the urgent need, there are no empirically supported treatments, including psychosocial and pharmacological interventions, to address suicidality and self-harm behaviors in at risk children. The proposed research project will involve adapting Dialectical Behavior Therapy (DBT) for maltreated children (ages 7 to 12) with suicidality (ideations and attempts) and/or self-harm behaviors. DBT is an empirically supported intervention for adults with suicidality and self-harm behaviors, and is currently the only empirically supported intervention for suicidal adolescents. DBT engages patients in treatment and is cost effective, as clients receiving this treatment require fewer psychiatric hospitalizations and emergency room visits. Candidate: Dr. Perepletchikova received her Ph.D. in Clinical Psychology from Yale University. She has extensive clinical experience working with children and their families, expertise in treatment integrity of psychotherapy research, received intensive training in DBT, and has worked clinically with adults and adolescents using DBT model. Further, her preliminary studies support feasibility, acceptability and initial efficacy of DBT skills training for children. Training goals: 1) work closely with experts in the field of psychotherapy development research; 2) acquire knowledge in childhood maltreatment research and interventions, suicidality and self-harm behaviors, and interfacing with the child protective services system; 3) acquire expertise in conducting randomized clinical trials; 4) take courses in biostatistics and fundamentals of clinical trials; and 5) acquire knowledge on the neurobiological effects of trauma, and genetic and environmental predictors of risk and resiliency, to better understand the etiology of these symptoms in children. Research goals: 1) adapt established adult/adolescent DBT treatment manuals and treatment integrity measures for DBT for children; and 2) conduct a pilot randomized clinical trial comparing DBT for children with Treatment-As-Usual with maltreated children in state custody with suicidality and/or self- harm behaviors. The proposed training activities and research project will allow Dr. Perepletchikova to transition into an independent investigator with a specific focus on addressing the needs of maltreated children, including suicidality and self-harm behaviors. PUBLIC HEALTH RELEVANCE: Although suicidality and self-harm behaviors in children are currently on a rise, and are associated with increase in mortality and significant cost to society, there are no empirically supported interventions to address this problem. This research project will evaluate the efficacy of an intervention geared towards stabilization of children's self-control, reduction in suicidality, self-harm behaviors and other emotional and behavioral difficulties, helping caregivers manage severely affected children in the home environment, and reducing the need for higher level services (e.g., psychiatric hospitalizations) and, thus, associated economic burden. Given the impact of early onset psychopathology on development, the main objective of this intervention is to improve the life course trajectory of these vulnerable children.
NIH	2008	IMMUNE SYSTEM ACTIVATION IN ADOLESCENT SUICID	GABBAY, VILMA	This subproject is one of many research subprojects utilizing the resources provided by a Center grant funded by NIH/NCRR. The subproject and investigator (PI) may have received primary funding from another NIH source, and thus could be represented in other CRISP entries. The institution listed is for the Center, which is not necessarily the institution for the investigator. This protocol is designed to test the hypothesis that there is immune system activation in suicidally depressed adolescents, as reflected by higher Th1-type immunologic responses (cells and cytokines) than in non-suicidally depressed adolescents or age- and sex-matched controls. This is based on prior observations on the effect of serotonin and dopamine receptors and their dysfunction in depression and in the immune system. 20 suicide-attempt (within the past 10 days) adolescents will be recruited and compared to 20 depressed adolescents and 20 "normal" adolescents. The first aim is to measure a series of cytokines: IFNg, TNFa and IL-2 (Th1) vs IL-4 and IL-6. In addition, quantitation of intracellular cytokines will give an indication of Th1 or Th2 type cells in the peripheral blood following stimulation. All of the subjects will also undergo a series of standardized tests for depression. The patient groups will be as above, with exclusions for medication, infections, immunologic or hematologic disorders.

NIH	2008	SELF-HARM AND DRUG USE IN ADOLESCENTS	Dougherty, Donald	This subproject is one of many research subprojects utilizing the resources provided by a Center grant funded by NIH/NCRR. The subproject and investigator (PI) may have received primary funding from another NIH source, and thus could be represented in other CRISP entries. The institution listed is for the Center, which is not necessarily the institution for the investigator. While cross-sectional studies show that drug abuse, impulsivity, serotonin dysregulation, and stressful life events are associated with suicide, studies examining the specific relationships of these factors are limited. A NIDA-sponsored workgroup was formed to identify gaps in the literature and priorities for future research. Studies have typically related individual measures of impulsivity or serotonin (5-HT) markers to self reports of previous suicidal behaviors and drug abuse cross-sectionally, but they have not determined the predictive validity of these measures in determining future drug abuse and suicidal behaviors. Furthermore, the relationships between impulsive behavior and 5-HT, while often included in theoretical models of suicide, have not been firmly established. Also, how the combination of factors defined within these models affects the developmental trajectories of drug abuse and suicidal behaviors is unknown. The purpose of this longitudinal study is to examine the interrelationships among impulsivity, 5-HT, stressful life events, and the dual outcomes of drug use and different types of suicidality in high-risk adolescents. Our goal is to determine the direct and interactive contributions of these factors to the developmental trajectories of suicidal behavior and drug abuse.
NIH	2008	Depression Trials Network/Treatment Resistant MDD/Suicide Assessment/Combined M	No PI Identified	The results of the STAR*D trial prompted the next follow-on effectiveness trial study for the treatment of MDD, "Combining Medications to Enhance Depression Outcomes (CO-MED)." The CO-MED trial, supported by this contract modification, addresses the following specific questions regarding the use of combination medication therapy: 1) Do patients who receive combination medication therapy as initial treatment for the onset of a depressive episode recover (reach remission) faster than patients who receive the more traditional single medication therapy? 2) Are patients who receive treatment initially with combination medications more likely to reach remission? 3) Is the durability of remission (i.e., sustainable recovery) more likely in patients who receive combination rather than mono medication therapy? It is expected that the Contractor will implement and carry out all clinical trials with expert scientific leadership, careful guidance and attention to human subjects regulations and good clinical practice guidelines, and in a timely manner. Implementation will include but may not be limited to all of the following tasks: Obtain medication for the trial; Set up randomization procedures; Create and distribute assessment instruments and study management operations procedures; Establish study-wide communications, such as conference calls, investigator meetings, site coordinator meetings; Collect the assessment data; Transmit the assessment data to the data management center; Edit the data and establish a system of query resolution; Provide for the timely locking of the dataset so that statistical analyses may be conducted in a timely fashion; Prepare a public access database and appropriate documentation to meet standards and guidelines for data sharing; Write appropriate journal level scientific articles addressing the primary questions as well as secondary and other moderator and mediator questions as are appropriate. It is expected that the database will be made publicly available between one and two years after the database is locked.
NIH	2008	Dev. of a Suicide Prevention Training Curr f/Justice Sys Gatekeepers	No PI Identified	This proposal provides for an enhancement of the Phase I core curriculum to include information on specific sociodemographic groups (women, minorities, elders, juveniles), issues relevant to myriad legal practice settings (domestic violence), and those suicides which leave a wake of pain and suffering for communities and families, murder-suicides. Furthermore, the curriculum will address the ethical conflicts suicide and mental health awareness presents attorneys in their case deliberations. As such, the curriculum will target attorneys and administrative law clerks (as a secondary means of also reaching judges) and pretrial services staff in the criminal and civil court systems. The final curriculum will be packaged into both an instructor-led continuing legal education (CLE) program and a web-based CLE program. Since CLE credits are a requirement of all new and experienced attorneys in 41 states, including mandatory credits in the ethics and professionalism topic area in many states, this commercial mechanism has the potential to reach the target population through multiple modalities at a national level. Goals for participants in the Phase II curriculum include the ability to: Recognize the symptomatic and behavioral indicators of suicide risk; Accurately identify individuals "at-risk" for suicide based on this knowledge, applying behavioral and situational indicators to assist in making this determination; Make appropriate and judicious referrals to qualified mental health personnel for screening and assessment of those individuals identified as being "at-risk" for suicide; Understand the ethical issues present when confronted with possible suicide risk; Recognize additional needs and considerations when dealing with special situations such as domestic violence and murder-suicide. A rigorous research evaluation of the enhanced core curriculum and its modular components, including two Beta-1 and six Beta-2 national multi-site pilot tests, will be conducted. For both sets of tests, evaluation plans have been developed to assess the impact and effectiveness of the training, selection methodology, and diversity within the composition of training participants. In addition, the final curriculum will be integrated into existing curricula in law schools and a learning transfer evaluation at three test sites, similar to the Beta Test evaluation, will also be conducted. The law school implementation and evaluation is included as a method by which emerging professionals in the criminal and civil court systems may be targeted for early training prior to their entry into the court system. To build community capacity to further evaluate the effectiveness of such prevention efforts beyond the scope of the Phase II effort, this proposal also includes a community-based participatory research capacity strategy that piggy-backs on an already existing NIMH-funded initiative to enhance the quality and number of junior research faculty who focus on suicide. This R25 grant will dedicate two suicide research institutes to providing an opportunity for key community stakeholders to partner with academicians to assess the impact of suicide prevention in their communities across broad nontraditional mental health strategies. The proposed Phase II project is one that has the potential for having a significant national impact. The potential for this project to have a significant impact on public health is paramount, as is its potential to act as a vehicle for creating, facilitating and integrating successful community partnerships.
NIH	2010	Project 1: Mescalero	WILLIAMS, ROBERT	Behavioral health disparities among American Indian and Alaska Native youth are dramatic, particularly in terms of depression, suicide and post-traumatic stress disorder. The goal of this proposed community based participatory research (CBPR) project is to develop and pilot test elements of a public health prevention intervention model that is tailored to be culturally and socially appropriate for adolescents on the Mescalero Apache Tribal Reservation in New Mexico. We propose to partner with a Mescalero Mental Health Prevention and Intervention Task Force to (1) identify what serious MEB problems most need to be addressed (including, provisionally, depression, suicide risk, post-traumatic stress disorder, early symptoms of psychosis and coexisting substance abuse problems ; (2) broaden the focus of existing Mescalero prevention programs to focus on a larger array of serious MEB's; (3) review and adapt screening scales for depression, suicide risk, PTSD, and early symptoms of psychosis to insure their cultural and social appropriateness for youth on the Mescalero reservation; (4) similarly review and adapt measures of symptoms resulting from contemporary and historical trauma and of desirable life function outcomes; (5) review and adapt a multifamily group (MFG) prevention treatment model to ensure its cultural and social appropriateness for youth on the Mescalero reservation; (6) conduct a one-year pilot of the feasibility of the resulting public health model (outreach, identification, referral, screening and intervention) in the Mescalero Apache School Based Health Center (SBHC); and (6) conduct a three year evaluation of the model including; a process evaluation of its ability to reach, enroll and treat the target population, obtain acceptability in the community, maintain fidelity over time to the program model, its potential for sustainability and export; and, most importantly examine outcomes in terms of student satisfaction with treatment, MEB symptom levels, quality of life impairment and clinical assessment of improvement to develop some sense of the model's potential for reducing disparities in behavioral health.
NIH	2009	MONTANA INBRE II: A MULTIDISCIPLINARY RESEARCH NETWORK	HARMSEN, ALLEN	DESCRIPTION (provided by applicant): Montana INBRE established a multidisciplinary, statewide network with the goal of positioning Montana as a national leader in research on the pathogenesis of infectious diseases and on the increasing health issues related to the environment, while developing a Montana workforce to meet the biomedical research and economic development challenges of the future. Over the past four years, MT INBRE successfully created new biomedical research cultures at four of the state's baccalaureate institutions, established unique research and educational programs, built strong relationships with all seven of Montana's tribal colleges, and supported a student pipeline that will sustain biomedical research in Montana in the future. MT INBRE II builds on these successes with the goal of maintaining and further developing the Montana network and student pipeline, and taking advantage of this network to address the unique problems Montana faces in infectious disease, environmental health and, importantly, health disparities. INBRE II will support and mentor investigators from the baccalaureate and research universities to address these problems, and will build expertise and capabilities at the tribal colleges by supporting community-based participatory research (CBPR) projects designed to address health disparities on Montana Indian reservations. INBRE II has the long-term goal of utilizing its network to strengthen ties between tribal colleges and tribes and to make tribal colleges a conduit for tribal health research on the reservations. INBRE II will continue to build a statewide network of extremely diverse investigators, including individuals from research-intensive universities, teaching colleges, tribal colleges, and reservation-based community members to more effectively address the health problems of Montana.

NIH	2011	SMALL GRANT 4: SEROTONIN, IMPULSIVITY AND SUICIDE ATTEMPTS	BAGGE, COURTNEY	This subproject is one of many research subprojects utilizing the resources provided by a Center grant funded by NIH/NCRR. Primary support for the subproject and the subproject's principal investigator may have been provided by other sources, including other NIH sources. The Total Cost listed for the subproject likely represents the estimated amount of Center infrastructure utilized by the subproject, not direct funding provided by the NCRR grant to the subproject or subproject staff. Given the clinical and public health significance of suicide, there is considerable interest in identifying factors that are associated with the diathesis for suicide attempts. There are well-established links between impulsivity and suicide attempts, but the nature of these associations remain unclear. One reason for this may be due to the heterogeneous nature of the construct of impulsivity, and it is largely unknown which specific facets of impulsivity relate to suicide attempts. The propensity for impulsive behavior has also been consistently linked to biological mechanisms implicated in suicidal behavior. Examining genetic associations with facets of impulsivity may provide a clearer signal in the search for serotonergic genes associated with suicide attempts. The present proposal seeks to examine the inter-relations among serotonergic genes, facets of impulsivity, and suicide attempts. To achieve this research goal, we will employ a case-control design, recruiting 200 psychiatric inpatients (100 suicide attempters and 100 non-suicidal controls). The two-session assessment will comprise 1) a comprehensive assessment (Axis I and II diagnoses, history of suicide attempt and characteristics of attempt, and facets of impulsivity), and 2) a laboratory session where participants will complete five behavioral measures of impulsivity. At the end of the comprehensive assessment, a saliva sample will be collected in order to examine polymorphisms in serotonergic genes (Tryptophan Hydroxylase [TPH2], and 5HTT). This study will provide preliminary data on the magnitude of the relation between polymorphisms of serotonergic genes and facets of impulsivity on suicide attempt, as well as the effect of polymorphisms of serotonergic genes on facets of impulsivity. These preliminary data and effect sizes will be used to inform the development of a larger study. Of note, an important aspect of this research is that it will establish biological, self-reported, and laboratory-based measures of distinct impulsivity processes relating to suicide attempts, as well as a suicide attempt characteristics (violent attempts). Given the high cost of suicidality to individuals and to the health care system, gaining a fine-grained understanding of impulsivity-suicide attempt associations is a critical step in allowing us to refine our theoretical models, improve our assessment tools, and suggest better treatments for suicide attempts.
NIH	2009	CORE--Principal Research	MARTIRE, LYNN	Principal Research seeks to increase the number and availability of evidence-based interventions applicable to elderly persons at high risk for depression and its complications, to those with difficult to treat mood disorders seen within the specialty mental health sector, and to those seen in the primary care sector, in rehabilitation centers, and in nursing home and other long term care settings. Intervention studies will address the following themes: (1) preventing depression and suicide in elderly persons at high risk; and improving, preventing, or delaying cognitive and functional impairments in elderly with depression; (2) improving treatment for difficult to treat mood disorders in later life (e.g., bipolar disorders, psychotic depression, and unipolar major depression responding only partially to first line treatment); and (3) identifying and removing barriers to effective depression treatment in community clinical settings. Cutting across these themes is the Center objective (4) of using infrastructure support to enhance research-training opportunities in mental health and aging and in community-based participatory research. These themes capture our movement from efficacy to effectiveness research, to services, dissemination, and practice research, as mandated in the NIMH Council report, Bridgin.q Science and Service. To this end the bidirectional linkages between the Principal Research Core and the Research Network Development Core are of critical scientific importance.
NIH	2013	Clinical Evaluation Core	Oquendo, Maria	The Clinical Evaluation Core's (CEC) goals are: 1. Recruitment, Characterization and Retention of Human Subjects 2. Uniform Diagnostic Method and Clinical Assessment Battery Across All Projects Including Psychological Autopsies, 3. Methods Development. 4. Maintenance of Reliability among Clinical Staff. 5. Supervise Inpatient Study Phase and Conduct Outpatient Study Phase 6. Consultation to Investigators. The CEC identifies and recruits patients with MDE and post-mortem cases. Normal volunteers are recruited to provide normative values on measures used and to establish psychometric properties of measures in a nonpathological population. The CEC utilizes a core of clinical instruments covering major risk factor domains for suicidal behavior, and ensures uniformity of assessment domains and measures across the projects of the Conte Center. These assessments include Axis I and II diagnostic interviews, measures of state and trait-related risk factors, measures of suicidal behavior, demographic history, life events, social functioning, family psychiatric history. Assessments are performed at intake, at time of biological procedures, at discharge. CEC interacts extensively with other Cores and Projects in the Conte Center. The CEC conducts clinical evaluation, data collection and treatment for all Conte Center projects that include human subjects including the Clinical Project 5, PET Project 3, MRI Project 4 and Statistics Project 6. CEC works closely with the Data Management and Statistics Core (DMSC) staff to generate forms, data management procedures, and reliability statistics. CEC coordinates with the Brain Imaging Core (BIC) regarding subject recruitment, clinical interviewing, matching controls and monitoring drug washouts and subject flow through the brain imaging protocols. The CEC conducts assessments of the suicide victims whose brains are studied by the Postmortem Brain Studies Core (PMC). The CEC obtains blood, hair and saliva from subjects to be analyzed by the Neurobiology Laboratory Core (NLC). The CEC also interfaces with the Administrative Core to identify and recruit new staff and maintain a central database of CEC manuscripts. The CEC coordinates the diagnostic consensus conference for projects # 1 , 2 - 6 and maintains inter-rater reliability. CEC Faculty and staff are an experienced center structure as most have worked as a core for the past 10 years or longer.
NIH	2013	Neurobiology of Suicide: Childhood Adversity and Epigenetics	ARANGO, VICTORIA	Childhood adversity is associated with greater risk for adulthood depression (MDD), aggressive traits and suicide. The biological basis of this relationship is mostly unknown but for the interesting finding of DNA methylation/less expression of the glucocorticoid receptor (GR) gene in suicides reporting childhood adversity. Stress and suicide are also associated with fewer cells and dendritic shrinkage in prefrontal cortex (PFC) and hippocampus (HC). Smaller HC volume may constitute a risk factor for stress-related psychopathology. In MDD suicides we find lower serotonin transporter (5-HTT) and higher serotonin IA receptor (5-HTIA) binding in PFC and higher rate of childhood adverse events. We hypothesize that this neurobiological phenotype may result from genes, environment and epigenetic effects. We aim to determine whether 5-HT1A binding, BDNF, measures of the hypothalamus-pituitary-adrenocortical (HPA) axis and candidate gene expression and methylation levels, correlate with neuron and glia density or number in PFC and HC in 5 groups of age- and sex-matched MDD suicides and nonpsychiatric controls with and without reported childhood adversity (before 15y) and 12 non suicide MDDs, all with psychological autopsy and brain toxicology. We propose to measure: 1) neuronal and glial density in dorsal PFC (dPFC) and ACC and estimate total number in HC; 2) 5-HTT and 5-HTIA binding in dPFC and ACC and number of 5-HT1A-immunoreactive (IR) Axonal Initial Segments in the granule cell layer of the dentate gyrus (DG) of the HC and BDNF-IR neuron density or number in dPFC, ACC and BDNF-IR cell number in HC; 3) Determine the effect of childhood adversity on neuron number or density, and regional correlations with neuron number or density; 4) Determine the effect of childhood adversity on neuronal gene expression and methylation levels of 18 candidate genes in dPFC, ACC and HC in the same 5 groups as Aim 1. Exploratory aims will: 1) separate the effect of MDD from that of suicide or adversity on neuron, glia and BDNF-IR cell density, in dPFC and ACC, or number, in HC, comparing the suicide and non-suicide MDD groups; 2) test the relationship between lifetime aggression scores and childhood adversity, neuron and glia number or density, serotonin indices, HPA axis indices, gene expression and methylation.
NIH	2013	Animal Models of Suicide Relevant Intermediate Behavioral, Neurobiological and M	Champagne, Frances	The experience of childhood adversity in the form of neglect/abuse is a major risk factor for future suicidal behavior perhaps via long-term changes in molecular and neurobiological substrates of anxiety, depression, and impulsivity/aggression. The mechanistic links between childhood adversity, molecular/neurobiological pathways, and suicide risk have yet to be established. We propose to investigate key hypotheses regarding: 1) whether childhood adversity is a causal antecedent to suicide behavioral, neurobiological, and molecular phenotypes; 2) the time course of adversity-induced effects on gene expression and epigenetic variation within target gene clusters: 3) the degree of concordance between peripheral cell epigenetic marks and those present in the brain; and 4) explore reversal of such effects by "therapeutic" intervention. We propose to use mouse models as mice are especially well suited to mechanistic studies. Our experiments are designed to parallel the molecular and neurobiological human studies within the center and can thus readily inform the other projects. In Aim 1, we will investigate whether suicide-relevant phenotypes in mice induced with early life adversity are associated with indices of HPA dysregulation, neurobiological changes, and gene expression patterns in the brain. Heightened stress responsivity is risk factor for the emergence of psychopathology and this aim will establish the HPA function of maternally separated mice that exhibit risk phenotypes (anxiety-like, depressive-like, impulsivity/aggression). This aim will also determine the density of 5-HTT and 5-HT1AR binding in the brain as a function of maternal separation/risk phenotype and assess the expression of genes within serotonergic, HPA, and neurotrophic pathways, as these are biological phenotypes linked to suicide. In Aim 2, we will determine the role of epigenetic variation in the form of DNA methylation as a potential molecular pathway of maternal separation-induced effects. Aim 2 determines whether separation-induced epigenetic effects in the brain correspond to changes in blood and whether these peripheral epigenetic changes can be used to predict the later development of a suicide-relevant risk phenotype. In Aim 3 we will explore the reversibility of maternal-separation induced effects on suicide-relevant phenotypes using pharmacological targeting and environmental manipulations during the juvenile period.

NIH	2013	Neurotransmitter Imaging in Vivo in Mood Disorders and Suicidal Behavior	MANN, Joseph	Project 3 takes postmortem neurotransmitter findings in suicides with MDD and radioligand development of the last five years and brings them together in a fashion that is best done with in vivo positron emission tomography (PET). We and others find normalities of the serotonergic system, principally the serotonin IA receptor (5-HTIA) and serotonin transporter (5-HTT) postmortem in depressed suicides. We have pilot PET data indicating that low 5-HTT binding in the same brain regions as suicides in MDD suicide attempters compared with MDD nonattempters and healthy volunteers. This indicates a potential suicide-related biological endophenotype in suicides that may be detectable in MDD before the first suicide attempt. In this project we seek to determine whether this is an endophenotype that is present before the first suicide attempt or onset of MDD, and its relationship to childhood adversity. We have found that 5-HTT binding is lower in depressed patients with reported childhood adversity. Rodent studies indicate that early adversity alters 5-HTIA binding. Specifically, we hypothesize that [11C]DASB 5-HTT binding will be low in MDD attempters and childhood adversity will contribute to this effect. With our new agonist 5-HTIA radiotracer, [11C]CUMI-101, we predict higher 5-HTIA agonist binding in MDD attempters as seen in suicides. We hypothesize that the 5-HTIA and 5-HTT binding in MDD suicide attempters, compared with MDD nonattempters and controls, will parallel findings in suicides. Both PET tracers will be used in the same groups to determine which tracer is best to detect differences between the groups, and these data will be used by Dr. Ogden in P6. To determine if this is a potential endophenotype, we will scan a group of high-risk offspring of MDD attempters before their first suicide attempt or episode of MDD. In the last two years of the project we will study new neurotransmitter targets to expand our knowledge base about suicidal behavior. We will determine monoamine oxidase A (MAOA) levels in healthy volunteers and MDD suicide attempters. MAOA is upregulated in MDD and responsible for the degradation of synaptic serotonin, DA and NE. In the same patients/controls as for MAOA, we will evaluate the endogenous opioid neurotransmitter system, by quantifying the kappa opiod receptor. In collaboration with other Cores and Projects, we will examine the relationship between the binding measures, fMRI responses during appraisal, stress responses, aggressive traits and the effects of reported childhood adversity.
NIH	2013	Cognitive Phenotype Neural Circuitry in vivo in Mood Disorders and Suicidal Beha	OCHSNER, KEVIN	Over the past decade an important approach to describing and treating psychiatric disorders has been the application of cognitive neuroscience techniques to understanding the neural mechanisms underlying clinical dysfunction. For example, relative to healthy volunteers, individuals with major depressive disorder (MDD) may show hypoactivation of brain systems implicated in cognitive control (e.g. dorsal and ventrolateral prefrontal cortex, dlPFC and vlPFC) and hyperactivation of systems implicated in triggering emotional responses (e.g. the amygdala). Of particular interest is the extent to which such patterns may be related not just to MDD, but to suicide risk associated with depressive episodes. Although to date little functional imaging data have addressed this question, PET and postmortem work from Conte Center labs has shown that ventrolateral PFC and anterior cingulate hypofunction, as well as lower serotonin transporter binding in the amygdala and ventral/orbital PFC, may contribute to the risk of suicide or nonfatal suicide attempts. This proposal seeks to clarify these links, building on an emerging model of the cognitive control of emotion in healthy adults to examine the neural bases of a specific cognitive strategy for emotion regulation - known as reappraisal - in individuals with major depressive disorder who have attempted suicide (MDD-Atts), who have never attempted suicide (MDD-Non-Atts) and currently non-depressed adult offspring of MDD-Atts who may be at higher risk for suicide (HRs). In Aims 1-3, we will compare the neural correlates of reappraisal performance of MDD-Atts, MDD-NonAtts, and HVs to determine whether depressed individuals in general, and those who attempt suicide in particular (Aim 1) generate stronger negative emotions or have greater trouble down-regulating them, (Aim 2) generate weaker positive emotions or have greater trouble up-regulating them, or show patterns of regulation-related activity under Aims 1 and 2 that (Exploratory Aim 3) are related to abnormalities in 5-HT function (see P3), childhood adversity, stress responsiveness and/or aggression (see CEC). In Exploratory Aim 4 we ask whether HRs show response patterns under Aims 1-3 that resemble Atts, thereby suggesting a diathesis towards suicide.
NIH	2013	Suicidal Behavior: Aggression Subtypes, Childhood Adversity and Stress Response	STANLEY, BARBARA	Aggression, childhood adversity, and the response to stress are all critical factors contributing to risk for suicidal behavior. However, the relationships among these variables and their relative contribution to suicidal behavior are not well-understood, in part, due to limitations in measures. Conceptually, there may be multiple dimensions or subtypes of each that contribute to suicide risk in different ways The goal of this project is characterize the extent and nature of aggressive behavior exhibited by participants, relate it to detailed assessments of types of childhood adversity as well as to situational, psychobiological responses to stress, and ultimately relate all of these to suicidal behavior in suicide attempters and non-attempters with major depressive disorder, high-risk offspring of suicidal individuals, and healthy volunteers. Aggressiveness will be assessed via interview, self report and a behavioral measure (Point Subtraction Aggression Paradigm) to characterize the reactive vs. proactive nature of the behavior. While Reactive Aggression - characterized by acute responses to situational provocation and emotional volatility - is thought to underlie a substantial portion of suicidal behavior, Proactive Aggression - more deliberate behaviors with less overt emotional reactivity - has been less systematically studied, but has also been related to suicidal behavior Childhood adversity will be assessed via the Childhood Trauma Questionnaire, a measure that distinguishes among physical abuse, sexual abuse, and emotional abuse/neglect. Our preliminary data indicate that the effect of past abuse on suicidal behavior is mediated by aggression. Stress response will be assessed via behavioral and Cortisol responses to the Trier Social Stress Test. Our preliminary data indicate that heightened Cortisol response to this stressor is evident in those with high impulsive aggression, a group that does not encompass all suicide attempters. Thus, there is a subtype of attempter who appears more sensitive to these situational stressors, but another subtype - currently poorly characterized - that does not. Ultimately, this project will make a major contribution toward characterizing alternative pathways to suicidal behavior, with potentially different underlying neurobiological mechanisms. In conjunction with data from PET receptor studies of the serotonin transporter (Project 3) and functional magnetic resonance imaging studies of emotional regulation (Project 4), these studies will identify relationships among these biological and behavioral measures that can provide targets for intervention more closely tailored to individual needs.
NIH	2013	Statistical Models with High-Dimensional Predictors	OGDEN, TODD	Project 6 involves developing statistical methodology that will be applicable to many of the very high dimensional datasets that are being gathered as part of the Conte Center. In particular, we will focus on models with single outcome variables and very high-dimensional predictors, e.g., using gene expression data to discriminate between suicide attempters and depressed non attempters, or using brain imaging data to predict a patient's response to treatment for depression. This methodology will employ powerful newly developing statistical concepts and tools including functional data analytic methods, machine learning techniques, and prescreening algorithms. Emphasis will be on developing models that can both achieve accurate predictions and provide stable interpretable models, allowing for a deeper understanding of the biological basis of suicidal behavior and mental illness. The project involves development of appropriate methodology, application both to existing datasets and to those that will be gathered as part of the Conte Center, and comparison among the various modeling strategies using both simulation studies and real data validations.
NIH	2008	Alcohol and injury in adolescents, their families and their neighborhoods	BRANAS, CHARLES	DESCRIPTION (provided by applicant): In the US, injury is the leading cause of alcohol-related death and alcohol is the leading risk factor for injury. Injury is also the number one cause of death among adolescents in the United States. Across the nation, over 15,000 13-to-20 year olds die from injuries each year. Although adolescents are legally proscribed from consuming alcohol in the US, many still manage to do so and their consumption can be followed by an injury. This has led many policymakers to conclude that personal consumption is the primary mechanism by which alcohol enhances the risk of adolescent injury. However, we hypothesize that of potentially equal or greater influence on an adolescent's alcohol-related injury risk is their exposure to alcohol consumption by others around them. Many adolescents may risk injury simply by being in a family or a neighborhood environment where alcohol is present, regardless of their consumption -- being caught in the crossfire between intoxicated bar patrons, committing suicide in the absence of an alcoholic parent, or being hit by a drunk driver while walking to school. Using the entire City of Philadelphia as a research site, we intend to conduct a population-based case-control study to determine the risk of injury that exposure to alcohol creates for adolescents. As they occur, we will rapidly ascertain the injury times, locations, and alcohol exposure status for adolescent cases of homicide, suicide, and unintentional injury death between 13 and 20 years old. We will then use random-digit dialing and face-to-face interviews to survey adolescent controls from within Philadelphia as to their locations and alcohol exposures at the time of a matching case's injury. We will measure alcohol exposure in terms of individual, family, and neighborhood alcohol exposure. The proposed study will also uniquely make use of data from 17 local, state, and national sources as well as real-time surveys to identify cases of adolescent injury and measure personal, family, and neighborhood exposure to alcohol for both cases and their matched controls. In doing this, we specifically aim to answer the questions: (1) When considered separately, do baseline (crude) individual, family, or neighborhood exposures to alcohol increase the risk of fatal adolescent injury?; (2) When considered together, do individual, family, and neighborhood exposures to alcohol have a modifying (confounding) effect on each other's risks of fatal adolescent injury?; (3) When considered together, do individual, family, and neighborhood exposures to alcohol have a synergistic (interaction) effect on each other's risks of fatal adolescent injury?

NIH	2008	Alcohol, Suicide & HIV Prevention of Teens in Mental Health Treatment	ESPOSITO-SMYTHERS, CHRISTIANNE	DESCRIPTION (provided by applicant): This application was submitted in response to NIAAA PA-06-097 "Parenting Capacities and Health Outcomes in Youths and Adolescents". Alcohol and other drug (AOD) abuse/dependence, suicidal behavior, and HIV infection constitute three significant public health problems. Adolescents seeking treatment for mental health problems are at significantly greater risk for the development of AOD abuse/dependence, suicidal behavior, and risky sexual behavior compared to non-psychiatric adolescent samples. Prevention programs that target these three often inter-related self-destructive behaviors among youth seeking community mental health treatment have not been tested. The primary purpose of this proposal is to develop a family-based cognitive behavioral protocol designed to prevent AOD use disorder, suicidal behavior, and HIV risk behaviors among sexually active teens receiving community mental health services and then evaluate it in a randomized Stage I trial. This protocol will be developed by integrating key elements from two federally funded intervention protocols, Dr. Esposito-Smythers' (PI) cognitive behavioral individual and family based protocol for the treatment of adolescent alcohol abuse and suicidality and Dr. Brown's (PI) HIV prevention program for teens in mental health treatment. There are three primary aims in this project: 1) develop a manualized AOD, suicide, and HIV prevention protocol for adolescents receiving community mental health treatment; 2) pilot and refine the prevention protocol with 12 families; and 3) test this prevention protocol in a small randomized pilot trial. To accomplish these aims, a two step sequence of treatment development is proposed. Stage 1a activities include manual development, therapist training, and an open pilot trial. Stage 1b activities include a randomized pilot trial. One hundred twenty-five adolescents and their parents receiving community mental health treatment will be randomly assigned to the integrated prevention protocol or an assessment-only control condition as an adjunct to their outpatient mental health care. The prevention protocol will include attendance at two workshops and an individualized booster session. Outcome will be assessed at post-intervention, 6 month, and 12 month follow-ups. The long term objective of this research is to yield a comprehensive prevention program that can be used as an adjunct to mental health treatment in an effort to offset the developmental trajectory toward AOD abuse/dependence, suicidal behavior, and HIV risk behavior among youth with mental health problems. PUBLIC HEALTH RELEVANCE Adolescent alcohol and other drug (AOD) abuse/dependence, suicide, and HIV infection constitute three significant public health problems. Adolescents with mental health problems are at significantly greater risk for each of these self-destructive behaviors when compared to non-psychiatric adolescent samples. An integrated AOD, suicide, and HIV prevention program, delivered within community mental health centers, could offset the development of each of these outcomes among youth with mental health problems.
NIH	2011	Acute Alcohol Use and Suicide	KAPLAN, MARK	DESCRIPTION (provided by applicant): This proposal is a revision of R01 AA020063-01 that was reviewed in June 2010 by BGES. The revisions address methodological shortcomings. The project remains significant because suicide is a major national public health problem with about 30,000 deaths each year, representing the 11th leading overall cause of death and the 5th leading cause of years of potential life lost (YPLL) before age 65. Alcohol plays a key role in suicide and, indeed, according to the Centers for Disease Control and Prevention, 6,969 deaths and 235,865 YPLL resulted from alcohol-attributable suicides in 2001. Although alcohol use disorders and suicide have been intensively studied, there is comparatively little research on acute alcohol use and suicide (i.e., drinking prior to the event). Yet, data on acute alcohol use is essential for developing a comprehensive suicide prevention strategy. Research on toxicological characteristics of suicide decedents in the United States has been constrained by small samples and limited geographic coverage. This project will address these limitations using newly available data from the National Violent Death Reporting System (NVDRS), a large (47,398 suicide decedents in 2003-08) and demographically well-characterized database with toxicology information (blood alcohol concentration, BAC) as well as coroner and medical examiner reports pertaining to suicides. The project aims are as follows: (1) describe the epidemiology of blood-alcohol content among suicide decedents in the United States and among major subgroups defined by age, gender, and ethnicity; (2) compare BAC presence and levels at time of suicide to estimated BAC presence and levels in a matched general population control group; (3) examine blood-alcohol content presence and levels in relation to suicide involving different methods (e.g., firearm, hanging, or drug ingestion); and (4) test the effects of alcohol control policies on alcohol-related suicides compared to non-alcohol-related suicides. The project will also examine geographic and temporal variation among those who were and those who were not using alcohol at the time of suicide. The research is built on a multi-level framework in which counties are nested within states. Key environmental predictors will include data on population drinking patterns from the National Epidemiologic Survey on Alcohol and Related Conditions, alcohol availability indicators from the US Census Bureau Business and Industry Data, alcohol tax rates from the Tax Foundation, and firearm access indicators from the Behavioral Risk Factor Surveillance System. Documenting the alcohol-associated suicide mortality levels and trends over time, estimating the risk for the most commonly used method of suicide with alcohol involvement, and evaluating the effects of alcohol control policies on alcohol-positive suicides address fundamental gaps in the understanding of alcohol use in suicide with implications for the harmonization of alcohol policy and suicide prevention strategies. PUBLIC HEALTH RELEVANCE: The project is highly relevant to public health because some 30,000 Americans die by suicide annually with many of those deaths related to alcohol. Unfortunately, little is known about the role of acute alcohol use in suicide. This study will provide valuable information about suicide related to acute alcohol use. In turn, the data will inform development of prevention and treatment programs.
NIH	2012	Adolescents with Major Depression and AUD: Community-based Integrated Treatment	SPIRITO, ANTHONY	DESCRIPTION (provided by applicant): Studies have consistently shown an association between mental health disorders and alcohol use disorders (AUD) during adolescence. In particular, the comorbidity of AUD with Major Depressive Disorder (MDD) is well established and associated with a range of negative outcomes including longer and more severe episodes of illness and greater psychosocial impairment including behavior disturbance. This population may be even more challenging to treat than their adult counterparts because adolescents with MDD/AUD so often have other externalizing disorders besides AUD. Treatment research for this population is quite limited and Healthy People 2020 Objective MHMD HP 2020-14 directly addresses this area: "increase the proportion of persons with co-occurring substance abuse and mental disorders who receive treatment for both disorders". The purpose of this application is to conduct a randomized clinical trial comparing Cognitive Behavioral Therapy - Integrated (CBT- I) for adolescents with MDD and AUD to standard care (SC), i.e. an eclectic mix of therapy techniques. A two group randomized design will be used to test the primary hypothesis that the integrated CBT- I protocol designed to treat adolescents aged 12 to 18 years with AUD/ MDD will produce better treatment outcomes compared to standard care with respect to 1) heavy volume alcohol use/ alcohol problems which can contribute to both depression and externalizing behaviors, the most severe of which result in costly residential placements and arrests/incarceration; and 2) depression and suicidal events, the latter potentially requiring expensive Emergency Department visits and inpatient psychiatric hospitalizations. Both the integrated CBT-I and SC condition will be delivered by licensed mental health counselors at a community mental health clinic that uses an Intensive Outpatient Program model to treat adolescents with AUD and mental health disorders who have failed prior outpatient therapy and require more intensive services. Clinicians in the CBT-I condition will receive weekly supervision that focuses on use of the CBT-I protocol. Clinicians in SC will be provided standard clinic supervision that is more eclectic in nature, consistent with typical community care. Outcome data will be collected at one year post treatment. Successful completion of the project aims could change how services are delivered to this high risk group. Its clinical significance lies in ts addressing a critical barrier to the field: how to treat MDD/AUD adolescents. PUBLIC HEALTH RELEVANCE: Adolescents who have both alcohol use disorders and psychiatric disorders typically have major impairment that affects multiple aspects of their functioning. Improved methods for treating these individuals have the potential to decrease the morbidity associated with both conditions. The relevance of this problem is reflected in Healthy People 2020 Objective MHMD HP 2020-14 which reads: "increase the proportion of persons with co-occurring substance abuse and mental disorders who receive treatment for both disorders."

NIH	2013	Economic Contraction and Alcohol-Related Suicides: A Multilevel Analysis	KAPLAN, MARK	DESCRIPTION (provided by applicant): This proposal is a revision of R01 AA021791-01 that was reviewed in June 2010 by BGES. The revisions address methodological shortcomings. The United States economy contracted markedly starting December 2007. There is substantial evidence indicating the impact of contracting economies, particularly levels of unemployment, on suicide mortality risk. But less is known about the role alcohol misuse plays in the complex relationship between economic conditions and suicide. Preliminary data suggest that acute intoxication (blood alcohol concentration (BAC) e .08 g/dl) among male suicide decedents has increased at least 10% since the official start of the recession. Alcohol plays a key role in suicide and, indeed 7,235 deaths and 242,456 years of potential life lost resulted from alcohol-attributable suicides in 2001-09. This project will estimate the effect of the economic downturn on rates of suicide involving acute alcohol intoxication using newly available data from the National Violent Death Reporting System (NVDRS). The NVDRS is a large (57,813 suicide decedents in 2003-09) and demographically well-characterized database with toxicology information (i.e., BACs). The project aims are as follows: (1) describe suicides associated with acute alcohol ingestion by geographic region and by time from before (2003-07) to after the onset (2008-12) of the economic contraction; (2) examine the association between measures of economic distress and rates of alcohol-related suicide by geographic area and by time; (3) analyze the roles of alcohol consumption and alcohol availability in explaining connections (if any) between economic contraction and alcohol-related suicide; and (4) compare relationships among economic contraction, alcohol consumption, and alcohol-related suicide across age, gender, race/ethnicity, and socioeconomic sub-groups of the population. Several levels of data (state, substate, county, and individual) will be combined to capture the nested complexity between economic downturn and variation in alcohol-related suicides. The project will utilize multiple indicators of economic distress, including short- and long-term unemployment, median household income, poverty rates, home foreclosure rates, and median housing prices. Other key environmental indicators will include population drinking patterns, substance use, mental health status, and alcohol-control policies (i.e., alcohol taxes, density of alcohol outlets, and alcohol sales). These data will be obtained from the Bureau of Labor Statistics, Census Bureau, Realtytrac, Federal Housing Finance Agency, National Alcohol Beverage Control Association, Alcohol Policy Information System, state alcohol beverage control boards, Alcohol Epidemiological Data System, and the National Survey on Drug Use and Health. Documenting the effects of the economic contraction on alcohol- associated suicide mortality will be of considerable interest to state and federal decision-makers concerned about public health while dealing with budget deficits and a prolonged downturn.
NIH	2011	A Follow-up Study of Addictions and Co-Occurring Disorders in Older Adults	BLACK, DONALD	DESCRIPTION (provided by applicant): The goal of this application is to conduct a controlled, blind longitudinal follow-up (f/u) of older adults with pathological gambling (PG). This study will be the first of its type and set the standard. Pathological gambling is a formidable public health problem associated with other addictions, depression, domestic abuse, bankruptcy, and suicide. Pathological gambling has been ignored by researchers and is greatly understudied. It is particularly devastating to elders who form a vulnerable subset of persons at risk for PG. This project has important clinical implications because it will significantly advance understanding of PG course and outcome among the elderly, including its relationship with other addictions and co-occurring mental disorders, treatment utilization and response, suicidal behavior, and both risk and protective factors. Social networking, relationship loss, retirement, decision-making, and other issues pertinent to elders will be examined as potential modifiers of PG risk. This work will be accomplished through an intensive study of 75 older adults (e.g., >60 years of age) with lifetime PG and two comparison groups: 75 persons <40 years of age with lifetime PG and 75 elder controls (who gamble recreationally or not at all). Subjects with PG will meet DSM-IV criteria and have a South Oaks Gambling Screen (SOGS) score e 5. They will be recruited from 1) an ongoing family study or 2) from the community. Elder controls matched on important characteristics will have a SOGS score d 2. They will be recruited via random-digit dialing through a subcontract to the University of Northern Iowa to obtain an unbiased comparison group. Intake will occur in person and subjects will be re-interviewed by phone at six-month intervals through 48 months. The SCID, SIDP-IV, and other validated scales will be used to assess addictions and co-occurring mental disorders, gambling behavior, functional status, life events, personality, impulsivity, gambling-related cognitions, suicidality, social support, economic loss, and quality of life. Diagnostic reliability will be carefully monitored; new raters will be fully trained. Neurocognitive assessments will be administered at intake. The Longitudinal Interval Follow-up Evaluation (LIFE) will be used to track the trajectories of PG, other addictions and co- occurring disorders, suicidality, and functional status. The investigators will make every reasonable effort to maintain contact with subjects and document reasons for loss to f/u. Persons with PG who drop out will be replaced. The investigators hypothesize that elders with PG will have a higher level of gambling participation, greater percentage of time spent gambling, and fewer periods of abstinence than younger gamblers; that their gambling intensity/severity will vary in response to substance misuse and co-occurring disorders (e.g., major depression), life events (e.g., relationship loss, retirement), social support, proximity to casinos, and treatment; that those with the poorest outcome will have impulsive antisocial behavior, impaired decision making, and few protective factors. This work will push the field forward by leading to a better understanding of the course and trajectory of PG in elders and younger controls, and will inform the field regarding its proper classification and validity of subtyping schemes. This work will contribute to better and more targeted treatment/preventive strategies. PUBLIC HEALTH RELEVANCE: Pathological gambling (PG) is a significant and prevalent public health problem associated with other addictions, co-occurring mental health disorders, domestic abuse, bankruptcy, and suicide. This project will be the first detailed and controlled longitudinal follow-up of elders with PG; it is important because elders are uniquely vulnerable to develop problematic gambling behavior and to experience its devastating consequences. This work is essential to gain a better understanding of 1) the course and trajectory of PG in older adults and others, 2) its temporal relationship to other addictions and co-occurring disorders, 3) risk factors contributing to and protective factors mitigating against its development, and 4) its proper classification and validity of subtyping schemes. This work will ultimately contribute to better and more targeted treatment/preventive strategies.
NIH	2013	Adjustment Problems and Substance Use in 3 Generations	CAPALDI, DEBORAH	DESCRIPTION (provided by applicant): Three Generational Study We proposes to study intergenerational transmission of alcohol, tobacco, and other drug use (ATOD) across three generations (G1, G2, and G3). We will use children in the Three Generational Study (3GS), a community sample consisting of up to two of the biological children (G3) of at-risk early adult men (G2) in the Oregon Youth Study (OYS). Multiple indicators of ATOD in G3 will be assessed, including age of onset of use and growth in use over early to midadolescence. A dynamic developmental systems approach focusing on both general pathway psychopathology and outcome-specific risk factors will be used to examine the developmental pathways of precursors (e.g., ATOD awareness) and of the emergence of these behaviors from early childhood to adolescence. Hypotheses regarding cross-generational congruence in the onset and growth of ATOD also will be examined, as well as the transmission of contextual risk and problematic behaviors across three generations, and parenting behaviors and peer influences across two generations. Additionally, the role of ATOD in the etiology of three public health problems; namely health-risking sexual behavior, suicidal thoughts and behaviors, and dating violence will be tested. The OYS men show high levels of antisocial behavior (at age 25 years, 42% had two or more arrests) and substance use (estimated 50% lifetime diagnoses for alcohol dependence or abuse and 50% prevalence of marijuana use in the mid 20s). The men are currently ages 36-38 years and, with their parents (G1), have been involved in the OYS since the G2 men were ages 9-10 years. Specific Aims will be addressed through the collection and analysis of data that will expand the sample size for the early time points (ages 3 to 11 years) and extend the study to ages 19-20 years. Additionally, we will undertake secondary data analysis of the OYS, OYS-Couples Study, and 3GS extant data sets from the beginning of the proposed study period.

NIH	2012	Tracking Adolescents After Bariatric Surgery: Substance, HIV and Suicide Risks	ZELLER, MARGARET	DESCRIPTION (provided by applicant): Adolescence is a unique time in development-a period of rapid change in emotional, social and career/vocational domains. At the same time, rates of substance use (alcohol/tobacco/drug), risky sexual behavior, and suicidal behavior increase and peak in young adulthood, potentially compromising healthy psychosocial development. As bariatric surgery emerges as a viable treatment for adolescents with extreme obesity (BMI>40 kg/m2), it is critical to establish a comprehensive picture of the needs of these patients as they mature into young adulthood. Prior to surgery, adolescents with extreme obesity typically suffer from a range of weight-related medical and psychosocial comorbidities. Data from a nationally representative school-based sample indicated that adolescents with extreme obesity in engaged in many high-risk behaviors at comparable rates to healthy-weight peers, while also engaging in other behaviors in more dangerous ways (e.g., sexual activity in females while under the influence of alcohol/drugs, smoking in males before age 13). These risks, combined with the comorbidities associated with extreme obesity, illustrate the vulnerability of this subpopulation. The initial literature indicates that following bariatric surgry, adolescents experience improvements in physical and psychosocial health which have the potential to positively alter their life trajectory. However, some adolescents may encounter new or emerging risks, such as increases in substance use, risky sexual behavior (e.g., HIV-risk behaviors) and suicidal behavior that may threaten these improvements postoperatively. These are critical gaps in the literature currently being investigated by the PI and a multi- institutionl group of investigators through the Teen Longitudinal Assessment of Bariatric Surgery (Teen-LABS) consortium (U01 DK066568; PI: Inge), the PI's affiliated ancillary study TeenView (R01DK080020; PI: Zeller) and NIDA supplemental funds awarded to the consortium (TeenView2). Together, these landmark efforts represent the first prospective controlled observational studies to provide a foundation for the understanding of the impact of adolescent bariatric surgery on high-risk behaviors as well as the potential mediators/moderators of that pathway in the short term (1st two post-operative years). Our initial data suggest remarkably low rates of engagement in high-risk behaviors prior to surgery, with some high-risk behaviors appearing to increase to more "normative" levels at 24-months post-operatively. Of immediate importance, and the focus of the proposed study (TeenView3), is the longer-term (36, 48-month) observation of postoperative weight and psychosocial trajectories for adolescents during the transition to young adulthood, as well as a more comprehensive testing of relevant risk and protective factors affecting the pathway from bariatric surgery to engagement in high-risk behaviors. TeenView3 will provide critical information by identifying psychosocial risks and benefits which will define clinical decision-making and management for future adolescent patients. PUBLIC HEALTH RELEVANCE: Not only are adolescent high-risk behaviors (alcohol/tobacco/drug use, sexual behaviors, and suicidal behaviors) a public health focus, but the study of them in adolescents undergoing bariatric surgery is timely to determine the physical and mental health needs for the next generation of adolescent patients. Successful completion of the proposed study will provide evidence of the longer-term benefits of adolescent bariatric surgery and the unique or emerging risk factors associated with adolescent surgical weight loss that may impact health in the young adulthood. Hence, findings from the proposed study have the potential to markedly influence clinical practice, surgical candidacy and the development of post-operative care models for this specific age group.
NIH	2013	Culturally grounded early substance use prevention for American Indian families	WHITESELL, NANCY	DESCRIPTION (provided by applicant): Problematic substance use is widespread in many American Indian communities, and early adolescence is a critical period for the development of subsequent substance problems. Efforts to prevent early substance abuse are ongoing on many reservations but often are not informed by scientific evidence of effectiveness - largely because such evidence is sorely lacking. We propose to partner with a reservation community with high rates of substance problems to adapt, implement, and rigorously evaluate a program designed to prevent early initiation of substance use and the myriad of problems that accompany early use. The identification of early substance use as a target and the selection of the particular intervention approach we propose have directly resulted from a longstanding university-tribal community relationship and, in particular, from community input within the context of two recent projects funded by NIDA (RC4DA029974, Whitesell & Beals, PIs; and R01DA027665, Whitesell, PI). A clear message arising out of both projects has been the need to engage families and culture in the prevention of early onset substance use. In this project, we will continue this partnership to translate a rigorously evaluated evidence-based practice for use with tribal families, adapting and anchoring it within a cultural practice arising from within the community. We will draw on the strengths of both university and community partners, implementing innovative intervention development methods within a community collaborative research and evaluation context. We will address three specific aims: 1. Develop a culturally grounded, family-based early substance use prevention intervention tailored to a Northern Plains American Indian Reservation. "Use an evidence-based practice approach to implement a proven program (Iowa Strengthening Families Program/ISFP) within a new context, working with community partners to translate ISFP for the local context, including deep and meaningful adaptations in how the curricular content is delivered. "Use a practice-based evidence approach to integrate a cultural curriculum (Seven Directions/SD) developed within the community into the ISFP curriculum, drawing on local knowledge of effective practices to further ground substance use prevention efforts within the cultural context. 2. Pilot the adapted Seven Directions for Stronger Families (SDSF) program to determine feasibility, refine details, and maximize fit within the community. 3. Use the principles of the Multiphase Optimization Strategy (MOST) for intervention evaluation and development, to determine the relative effect size of different intervention components and inform a final SDSF program that balances effectiveness and efficiency. 4. Set the stage for broad implementation of SDSF by the tribal health administration and a randomized controlled trial of the full intervention.
NIH	2010	Quasi-experimental studies of early risk factors for severe psychopathology	D'Onofrio, Brian	DESCRIPTION (provided by applicant): Significance: Crime, substance use problems, suicide, and severe mental illness, such as schizophrenia and bipolar disorder, are associated with enormous personal distress and societal costs. Identifying the causes of these problems, especially very early in life, is a crucial research endeavor. Researchers have identified numerous putative environmental factors that are associated with increased risk for these severe problems, including maternal smoking during pregnancy, maternal stress during pregnancy, maternal age at childbearing, and advancing paternal age at childbearing. We do not know, however, whether these risk factors are casual risk factors for severe forms of psychopathology or are merely indices of family confounding. Our limited understanding of the underlying causal mechanisms is due, in part, to the fact that most existent studies of these risks have failed to use research designs that can test alternative hypotheses, especially the role of environmental and genetic selection factors. Innovation: We propose to utilize powerful quasi-experimental designs, natural experiments that can pull-apart co-occurring risk mechanisms and account for unmeasured genetic and environmental processes, to explore the effects of several putative early risk factors. In particular, we will compare differentially exposed full siblings, an approach that rules out all genetic factors that could account for the statistical association between early putative risks and later outcomes, as well as all environmental factors that siblings share. We will also compare differentially exposed half siblings, offspring of full siblings (full cousins), offspring of half siblings (half cousins), and offspring of twins. These additional comparisons will enable us to provide converging evidence for our findings and identify the source any familial selection factors (genetic and/or environmental). Detailed assessments of offspring, parental, and community- level risks will further enable us to identify the mechanisms through which early risk factors are associated with severe psychopathology. Approach: We propose to analyze a large dataset that includes information on every individual who was born or lived in Sweden from 1940-1995 (NH7,500,000), which includes measures of early environmental risks, correlated familial and community risks, and well-validated indices of severe criminal, substance use, suicide, and mental health problems from Swedish national registries. Because the dataset also includes information on the biological relatedness of each individual with all of their family members, we are able to conduct numerous quasi-experimental studies of the associations by comparing individuals who differ in both their environmental and genetic risk. Environment and Investigators: Our experienced team includes international experts in the risks associated with early prenatal and perinatal factors; the assessment and etiology of severe psychopathology; the use of large, national registries; and the use of quasi-experimental designs to study putative environmental factors. Indiana University and the Karolinska Institutet provide strong environments and relevant resources. PUBLIC HEALTH RELEVANCE: The staggering burden on individuals and society caused by violence, substance use problems, suicide, and severe mental illness has been well documented. Researchers have identified early risk factors that predict these major societal problems, but, it is still unclear whether putative early risks are truly causal or whether part-or most-of the associations with these risks are due to background familial factors. In order to improve prevention programs and our understanding of early risk factors, the current proposal seeks support to analyze a unique resource, a large dataset that includes every individual in Sweden for roughly five decades, relying on natural experiments to rigorously test causal hypotheses.

NIH	2010	Testing a Comorbid PTSD & Substance/Alcohol Use Intervention in Delinquent Girls	LANSING, AMY	DESCRIPTION (provided by applicant): Many youth with the most serious mental health problems resulting from violence exposure and maltreatment never receive mental health services [MHS].8,11 These youth are disproportionately found in juvenile delinquent populations where 67% - 75% have impairing psychiatric disorders, 20% have severe mental disorders and more than 1/3 need ongoing clinical MHS care- a figure twice the rate of the general adolescent population.7-10-12 Girls are the most vulnerable, understudied and underserved but fastest growing delinquent subgroup, with data strongly suggesting they have the most serious MHS needs: 75-95% have histories of child maltreatment, 95-100% have poly-trauma histories of violence exposure, sexual assault and child maltreatment, up to 50% have current Post Traumatic Stress Disorder [PTSD] and substance and alcohol use disorders [SAUD] and they have higher rates of PTSD and suicidality than delinquent boys.7,10,12,26-28 However there are few, if any, rigorously tested interventions available in the juvenile justice system [JJS] for youth with these comorbid problems. Our primary aim in this proposed study is to evaluate the efficacy of Seeking Safety [SS], an intervention for concurrently treating comorbid PTSD and SAUD that also addresses self harm and negative affect regulation, for female delinquents. This study lays the groundwork for developing a model for importing evidence based treatment [EBT] to high-risk youth who gain the attention of the JJS. We will recruit 250 female delinquents, 13 to 18 years old, with comorbid PTSD and SAUD through the San Diego Probation Department's Girls' Rehabilitation Facility. Our primary aims are to 1) use a randomized control trial design to determine the efficacy of an 8-week, 24 session manualized PTSD/SAUD intervention, 13 compared to the 'treatment as usual' [TAU] (8-week, 24 sessions) provided by the Probation Department for SAUD problems and 2) determine if cognitive factors (verbal skills, executive function) are related to treatment outcomes for SS and TAU. Our secondary aims are to 1) evaluate possible modifications to the SS treatment for improving services to the subject population and 2) use this study as a model for importing EBTs to other high-risk youth in Child Welfare and the JJS by partnering with (a) UC San Diego Comprehensive Research Center in Health Disparities to determine the best approach for fostering collaborative relationships within the alliance of San Diego's community clinics and identify funding streams to provide community-based services for a larger high- risk youth population and (b) Center for Criminality & Addiction Research, Training & Application to learn how to disseminate data about EBTs for youth in JJS across the nation and explore strategies to train correctional officers to work more effectively with traumatized and SAUD youth. With unprecedented support and access through the San Diego County Juvenile Court and Probation Department and a currently embedded multi- disciplinary, translational research program (spanning neurocognitive, psychiatric, imaging, genetics research), we are in a unique position to implement this proposed study that bears far reaching policy implications. PUBLIC HEALTH RELEVANCE: Youth who become involved with the Juvenile Court, either through the Child Welfare or Juvenile Justice system, demonstrate elevated rates of psychopathology and functional impairment, pose significant social and fiscal costs to society and often escape the attention of traditional mental health services. This research examines the efficacy of an evidence based intervention that simultaneously treats comorbid Post Traumatic Stress Disorder and Substance/Alcohol Use Disorders, the most prevalent comorbid pattern observed among high-risk and delinquent girls and a pattern that often results in future arrests (substance use, prostitution). This research will serve as a model for implementing and evaluating evidence based treatments with high-risk youth who gain the attention of the Juvenile Court but are traditionally underserved in the general community.
NIH	2013	Social Ecology and the Prevention of Suicide and Aggression in African American Y	ROBINSON, W	DESCRIPTION (provided by applicant): This indicated prevention intervention trial employs a randomized controlled design to examine the efficacy of a 15-session, culturally tailored, cognitive-behavioral group prevention intervention for urban, low income African American adolescents. The PI successfully adapted the Coping with Stress Course (Clarke et al., 1995) to be culturally sensitive and appropriate for use with urban, low-income African American adolescents. This culturally-adapted intervention (i.e., the Adapted-Coping with Stress Course [Robinson & Case, 2003]) will be significantly revised to enhance individual competencies believed to mitigate the risk for self-directed (i.e., suicidality) and inter-personal aggression. n addition, the proposed study aims to examine how neighborhood and family ecological characteristics moderate the effects of a culturally-adapted, cognitive-behavioral coping with stress prevention intervention on African American adolescents' self-directed (i.e., suicidality) and interpersonal aggression. This study is expected to have broad public health implications toward the reduction of African American youth health disparities and inform practice and policy on the development of effective violence prevention interventions for African American youth. It is expected that this study will inform a future large scale effectiveness study that will embed an evidence-based, culturally sensitive violence prevention intervention within a large urban school system.
NIH	2012	Epidemiology of Suicidal Behavior in Racially/Ethnically Diverse Older Americans	Byers, Amy	DESCRIPTION (provided by applicant): This application is in response to RFA-MD-12-001: NIMHD Health Disparities Research. One of the priority areas of this RFA is the study of health conditions associated with significant mortality that have been understudied in health disparity populations. In older Americans, suicide rates are 30% higher than in the general population, and five times higher in non-Hispanic white men age 85 years or older-as the nation continues to grow and racially/ethnically diversify with age so will the rates of suicide. Yet, little is knon about suicide-related behaviors (i.e., ideation, plans, and attempts) in older adults, which are strong risk factors for actual suicide and strong indicators of extreme emotional and mental distress. Even more so, differences in suicidal behavior by race/ethnicity have hardly been investigated at all, as most studies are from non-diverse clinic samples. Moreover, most of what we know about mental health services use related to suicide risk in older Americans comes from small non-diverse samples of suicide completers. However, understanding mental health services use and racial disparities in use is important, as all aging adults with emotional and mental distress related to suicidal thoughts and behaviors may benefit from service use and treatment. The proposed project will investigate the prevalence and predictors of suicidal ideation and related behaviors over the lifetime of older racially and ethnically diverse adults, that is, capturing transitions from ideation to plans and attempts and examining risk of late life and current suicidal behavior. It will also investigate mental health services use in those at increased risk of suicide. The aims will be addressed by studying three nationally representative aggregated data sets: 1) the National Co-morbidity Survey Replication (NCS-R), a probability sample of the general U.S.; 2) the National Survey of American Life (NSAL), a probability sample of African- American, Afro-Caribbean, and non-Hispanic White Americans; and 3) the National Latino and Asian American Study (NLAAS), a probability sample of Latinos and Asian Americans. The project proposes to make innovative use of the combined data and examine a large, nationally-based cohort of over 3,600 respondents aged 55 and older. In a very cost-efficient approach, this project will be the first comprehensive examination of the prevalence and predictors of suicide-related behaviors and mental health services use in older Americans. Key predictors, including sociodemographic variables, psychiatric disorders, and chronic medical conditions associated with suicidal behavior will be determined (Aims 1 and 2)-assessing differences of associations overall and by race/ethnicity, that is, in older non-Hispanic Whites, non-Hispanic Blacks, Hispanics, and Asians. In addition, racial disparities will be assessed separately for men and women (Aim 3), and key predictors of mental health services use will be examined overall and by race/ethnicity (Aim 4). Information stemming from this project will be important for identifying those older adults most at risk of suicide and with great need of care-helping to define national priorities for suicide prevention in late life for all Americans. PUBLIC HEALTH RELEVANCE: Suicidal risk profoundly impacts individuals, families, and society. Knowledge gained from this proposal will be both novel and critical for understanding the occurrence and predictors of suicide-related behaviors (i.e., ideation, planning, and attempts) in older Black, Hispanic, Asian, and White Americans, including use of mental health services in those at increased risk of suicide. Thus, this proposed project will have unique public health importance, because it will provide evidence for future psychiatric research and policy planning that will help to define national priorities for suicide prevention in late life for all Americans.

NIH	2008	Pediatric MDD: Sequential Treatment with Fluoxetine and Relapse Prevention CBT	EMSLIE, GRAHAM	DESCRIPTION (provided by applicant): This is a resubmission of a five-year competitive renewal of an ongoing programmatic research program of major depressive disorder (MDD) in children and adolescents (previously entitled "Childhood Depression: Remission and Relapse"). The first three studies were highly productive, demonstrating 1) continuity of the pathophysiology of depression in the pediatric age group, 2) efficacy of fluoxetine over placebo in pediatric depression, and most recently, 3) continued use of fluoxetine beyond acute treatment reduces relapse rates in this population. However, there continue to be major deficits in the research of pediatric depression treatment. Despite several positive RCTs in both psychotherapy and pharmacotherapy with relatively strong response rates (55-65%), remission rates (being "well") remain quite low (30-40%). Furthermore, early onset depression is often chronic, leading to high rates of relapse. In our recently completed continuation study, even with continued treatment of fluoxetine, 42% relapsed, with 22% experiencing a complete relapse of depression (CDRS-R =40 with 2 weeks of clinical deterioration). Residual symptoms were associated with higher relapse rates, especially in fluoxetine-treated patients. Although continued medication reduces relapse rates, other continuation phase treatments are needed, with particular emphasis on increasing remission and shortening the time to remission. Adult research suggests that adding cognitive behavioral therapy (CBT) following antidepressant treatment response reduces residual symptoms (which have been associated with lowering relapse rates) and reduces relapse rates. Utilizing the R34 mechanism, the investigators have developed a CBT treatment intervention, which focuses on improving residual symptoms and teaching wellness skills to youth who have responded to an antidepressant (R34 MH72737 "Continuation Phase CBT for Youth with MDD; PI: Kennard). We propose to determine if adding psychotherapy (CBT) following antidepressant response will improve remission rates and time to remission, as well as reduce relapse rates in children and adolescents compared to continued medication management. One hundred forty two youth (ages 7-18) with MDD who respond to 6 weeks of fluoxetine will be randomized to continued medication management alone (MM) or a sequential treatment strategy (STS) of medication management plus relapse prevention CBT (RP- CBT) for 6 months. Following randomization, all subjects will be evaluated every six weeks by an independent evaluator for the 6 month continuation phase. Remission is defined as CDRS-R total score =28. Relapse is defined as 1) CDRS-R score =40 with a history of 2 weeks of clinical deterioration or 2) CDRS-R<40, but with significant clinical deterioration. All subjects will be evaluated every 6 months for 1 year after completion of the continuation phase. Depression in youth is an underdiagnosed and undertreated illness, which can lead to long-term deficits in school, family, and overall functioning. Many pharmacological and psychotherapeutic interventions are available for this disorder; however, to date few treatments have been effective in treating youth to remission, or symptom free status, which is important as partial remission is related to relapse of depressive symptoms. The proposed project would test a treatment strategy combining medication treatment with fluoxetine and a new Relapse Prevention Cognitive Behavioral Therapy (RP-CBT) to maximize the benefits of both treatments to result in higher remission rates and reduced relapse rates.
NIH	2013	Adult Follow-up of Girls with ADHD: Predictors, Mediators, and Mechanisms	HINSHAW, STEPHEN	DESCRIPTION (provided by applicant): Attention-deficit/hyperactivity disorder (ADHD) is well known to be a highly impairing and strongly persistent condition in boys and men, but knowledge about its long-term consequences in girls and women is severely limited. The core objective is to redress the major dearth of longitudinal data on females with ADHD via a rigorous, prospective, 15-year follow-up investigation, into the age span of the mid-20s, of a well-characterized, ethnically- and socioeconomically-diverse sample of girls with carefully diagnosed ADHD (n = 140), plus an age- and ethnicity/race-matched sample of comparison girls (n = 88). To the investigator's knowledge, this sample comprises the largest in existence of girls with this disorder, ascertained prior to adolescence. During earlier iterations of the curren grant, participants were recruited and investigated between the ages of 6 and 12 years (Wave 1) and followed systematically in early to mid- adolescence (Wave 2, ages 11-18 years; 92% retention) and most recently in a 10-year follow-up in late adolescence/early adulthood (Wave 3, ages 17-24 years; 95% retention). Key aims for projected Wave 4 assessments, during the age span of 22-29 years, are to characterize outcomes of these women across multiple domains of functioning, including ADHD symptoms and subtypes, externalizing and internalizing behavior patterns (including antisocial behavior, mood disturbance, eating pathology, self-injurious and suicidal behavior), substance use/abuse, academic and vocational performance, neuropsychological skills, peer and family relations, health-related parameters, and service utilization. The overall goal is to understand trajectories of development, impairment, and (in some cases) positive adjustment, with the strongest focus on outcomes of major clinical and conceptual importance to female development: (a) educational attainment and employment status; (b) relationships/interpersonal functioning; (c) self-harm (i.e., suicidal behavior and sel-injury, which were present at strikingly high rates during the 10-year follow- up); (d) executive functioning; and (e) health-related behaviors. The project's established methods of ascertaining positive adjustment will be followed. A related aim is to characterize baseline predictors and moderators and adolescent mediators of adult functioning, via stringent and sophisticated statistical methods. The proposed Wave 4 assessments feature psychometrically rigorous, multi-method, and multi- informant measures, many of which are identical or parallel across all four waves, facilitating growth-curve and growth-mixture modeling. Because of (i) major gaps in knowledge surrounding adult adjustment of women with ADHD and (ii) the potential for unique findings to emerge during the age span of the mid-20s, examination of female developmental trajectories into adulthood is a key priority. Such aims will be met in this innovative and rigorou investigation, with the potential to enhance both basic and clinical science.
NIH	2012	Psychobiology of Suicidal Behavior in Borderline Personality Disorder	SOLOFF, PAUL	DESCRIPTION (provided by applicant): Psychobiology of Suicidal Behavior in Borderline Personality Disorder (BPD) is the first prospective study of clinical, psychosocial and biological risk factors for suicidal behavior in patients with BPD. The overarching goal of this work is to identify risk factors and clinical subtypes predictive of medically serious suicidal behavior. BPD is a highly prevalent psychiatric disorder, found in up to 2% of the population, and is the only psychiatric disorder defined, in part, by recurrent suicide attempts. With a suicide completion rate of 3%-10%, BPD is a clinically relevant model for the study of suicide. This study follows the stress-diathesis model of suicidal behavior, which predicts an increase in risk of suicide when acute stressors, such as interpersonal crises and depression, interact with personality traits such as impulsivity or affective instability. These personality traits are mediated by speciic brain networks and contribute a biologic diathesis to suicide under stress. At intake, subjects participate in a multidimensional assessment of risk factors associated with suicidal behavior. Systematic follow-ups are then conducted at 3 months, 6 months, and annually to define prospective predictors of suicidal behavior in short term (12 month), intermediate (2-4 years) and long term (6+-10 years) follow-up intervals. Currently, 245 BPD subjects are enrolled, with a 92% trace rate. By 2 year follow-up, 25% of subjects re-attempted suicide. Using trajectory analysis, a High Lethality BPD subtype has been defined by the increasing lethality of their recurrent suicide attempts. A recently completed 6 year follow-up analysis of 90 subjects identified poor psychosocial function as the most consistent predictor of suicidal behavior across all time intervals. This proposal will add 100 additional BPD subjects and 5 years of follow-up to increase statistical power of our analyses in all intervals, especially the long-term interval, whe many subjects will enter the age of highest risk for suicide. Additional assessments have been added for characterizing quality of life, stability of diagnosis and core dimensional traits, as these variables impact both psychosocial and suicidal outcomes. This study also investigates the neurobiologic diathesis to suicidal behavior using fMRI protocols, specifically targeting the neural basis of regulatory functions critical in responding to stress (e.g., response inhibition, conflict resolution, & autobiographic memory). A specific neural network is proposed as a mediator of suicidal behavior. fMRI protocols will test the functional connectivity of key structures in this neural network during negative affective stimulation. Preliminary studies indicate that negative affective stimulation produces interference with cognitive processing in these important regulatory functions. Affective interference increases the risk of suicidal behavior. The results of the longitudinal studies are immediately applicable to guide suicide risk assessment and treatment strategies; while the fMRI substudy may provide a biomarker identifying patients at highest risk for suicide, and a non-invasive method for following the progress of treatment. PUBLIC HEALTH RELEVANCE: This first longitudinal study of suicidal behavior in Borderline Personality Disorder identifies prospective predictors and high lethality BPD subtypes associated with suicidal behavior in short term (12 month), intermediate (2-4 year) and long term (6-10 years) follow-up. An fMRI substudy assesses the neurobiologic vulnerability to suicidal behavior through protocols measuring the effects of negative emotion on neural networks involved in responding to stress. The results of the longitudinal studies are immediately applicable to guide suicide risk assessment and treatment strategies; while the fMRI substudy may provide a biomarker identifying patients at highest risk for suicide, and a non-invasive method for following the progress of treatment.

NIH	2009	Future Suicide Attempt: Psychobiological Features	Oquendo, Maria	DESCRIPTION (provided by applicant): Most studies evaluating risk for future suicide attempts in major depressive disorder (MDD) have methodologic limitations, e.g., no structured diagnostic interviews or restricted to one or other domain of potential predictors. However, determinants of suicidal behavior are derived from multiple domains including psychopathologic, neurobiological, neurocognitive, familial and psychosocial. As such, development of predictive or explanatory models of suicide attempt behavior requires assessment of potential risk factors from multiple domains in the same patient population in a prospective follow-up study. This prospective study of suicidal behavior in major depression utilizes a unique cohort of patients undergoing a baseline evaluation for MDD, comprising two comparable groups of past attempters and nonattempters. Patients receive extensive clinical and biological baseline assessments funded by the MH062185 Conte Center for the Neuroscience of Mental Disorders at NYSPI/Columbia University. This application provides funding to assess patients for clinical state, life events, treatment and suicidal behavior at 3, 12 and 24 months after discharge. The initial major emphasis had been to build a clinical predictive model and begin testing that model. In the current funding period, the utility of biological predictors was assessed. Promising results identify stress reactivity, neurocognitive indices, and PET quantification of the serotonin system as potential risk factors that principally target traits underlying the diathesis for suicidal behavior. The current application shifts the emphasis to an integration of these biological and neurocognitive predictors with previously identified clinical predictors into a explanatory AND predictive model of suicidal behavior. To that end, the application adds an evaluation of early childhood trauma, neurocognitive tests (decision-making and problem solving) and stress reactivity (Trier Social Stress Test) measures, to complement PET scans and clinical measures obtained in the Conte Center at baseline. Statistical model building methods and prediction strategies will construct optimal models with both heuristic and clinical value. PUBLIC HEALTH RELEVANCE: Most studies evaluating predictors of suicide attempts in major depressive disorder have methodologic limitations, e.g., no structured diagnostic interviews, restricted to one or other domain of potential predictor variables or chart reviews to quantify suicidal behavior. We have implemented the most comprehensive, neurobiological, neurocognitve and clinical prospective study of predictors of suicidal behavior in major depression. We will test behavioral predictors of suicide attempts from the following assessment in multiple domains: 1) stress responsiveness; 2) PET quantification of the serotonin transporter and 5-HT1A receptor; and 3) neurocognitive measures. This data will permit construction of predictive and explanatory models for suicidal behavior.
NIH	2009	2/2 - Familial Pathways to Early-Onset Suicide Attempts	MANN, JOSEPH	DESCRIPTION (provided by applicant): This 5-year, two-site A2 competitive renewal of "Familial Pathways to Early-Onset Suicide Attempts" seeks to identify familial and individual precursors of early-onset suicidal behavior and mechanisms by which suicidal risk is transmitted from parent to child. The cohort consists of 308 offspring of 135 probands with major depressive disorder (MDD) and a history of suicide attempt and a comparison group of 232 offspring of 120 non-attempters probands with MDD, all of whom have been followed for an average of 3.8 years. The aims of the study are to: (1) continue annual follow-up of offspring of attempters and non-attempters in order to document incident and recurrent suicide attempts; (2) characterize all subjects, probands and offspring, on four putative intermediate phenotypes (IP) (impulsive aggressive traits, early-onset depression, neuropsychological function, cortisol response to stress) as well as other risk (e.g., child abuse and neglect) and protective factors (e.g., family cohesion) for suicidal behavior; and (3) examine the role of IPs in mediating the familial transmission of suicidal behavior and predicting new-onset suicide attempts both alone and in interaction with early childhood abuse and neglect. In a projected 4,693 person years of follow-up, a total of 67 new-onset suicide attempts are expected, which will allow for adequate statistical power to test our hypotheses that IPs are familially transmitted, and mediate the familial transmission of suicidal behavior. The identification of IPs will facilitate future genetic studies of suicidal behavior. This study sample is unique because it permits identification of risk factors for familial transmission of suicidal behavior, and the identification of precursors of early-onset suicidal behavior. Because there are now no empirically validated interventions for suicidal youth, the findings from this unique cohort should help to frame treatment targets in high-risk families and individuals designed to alter prodromal at-risk behavior and psychopathology and prevent future suicidal behavior. This study is of public health importance because suicidal behavior is the single biggest risk factor for completed suicide, which is the third leading cause of death among adolescents and young adults in the United States. The aims of this study are consistent with several priorities of the NIMH and the Division of Pediatric Translational Research (DPTR): (1) reduction of the public health burden of suicide and suicidal behavior; (2) inclusion of family-genetic approaches to elucidate the interplay of biological and environmental factors to childhood psychopathology and to identify behavioral and biological markers of vulnerability and resilience; and (3) research that is likely to lead to novel psychosocial and pharmacological preventive and therapeutic interventions. This application is from the New York site (PI: J. John Mann, MH056390). PUBLIC HEALTH RELEVANCE: This study, "Familial Pathways to Early-Onset Suicidal Behavior," seeks to identify the familial and individual precursors of early-onset suicidal behavior and the mechanisms by which suicidal risk is transmitted from parent to child. We anticipate that certain traits, namely impulsive aggressive traits, early-onset depression, memory and decision making ability, and a greater physiological reaction to stress (measured by cortisol secretion) are familial and will: (1) explain how suicidal behavior runs in families; (2) predict suicidal behavior in the children of parents who have attempted suicide; and (3) yield intermediate phenotypes that can advance genetic studies of suicidal behavior. This study is important because suicide and suicidal behavior are leading causes of mortality and morbidity among adolescents, there are currently no empirically validated interventions to prevent or treat adolescent suicidal behavior, and the results of this study could frame targets for prevention and treatment.
NIH	2009	1/2-Familial Pathways to Early-Onset Suicide Attempt	BRENT, DAVID	DESCRIPTION (provided by applicant): This 5-year, two-site A2 competitive renewal of "Familial Pathways to Early-Onset Suicide Attempts" seeks to identify familial and individual precursors of early-onset suicidal behavior and mechanisms by which suicidal risk is transmitted from parent to child. The cohort consists of 308 offspring of 135 probands with major depressive disorder (MDD) and a history of suicide attempt and a comparison group of 232 offspring of 120 non-attempters probands with MDD, all of whom have been followed for an average of 3.8 years. The aims of the study are to: (1) continue annual follow-up of offspring of attempters and non-attempters in order to document incident and recurrent suicide attempts; (2) characterize all subjects, probands and offspring, on four putative intermediate phenotypes (IP) (impulsive aggressive traits, early-onset depression, neuropsychological function, cortisol response to stress) as well as other risk (e.g., child abuse and neglect) and protective factors (e.g., family cohesion) for suicidal behavior; and (3) examine the role of IPs in mediating the familial transmission of suicidal behavior and predicting new-onset suicide attempts both alone and in interaction with early childhood abuse and neglect. In a projected 4,693 person years of follow-up, a total of 67 new-onset suicide attempts are expected, which will allow for adequate statistical power to test our hypotheses that IPs are familially transmitted, and mediate the familial transmission of suicidal behavior. The identification of IPs will facilitate future genetic studies of suicidal behavior. This study sample is unique because it permits identification of risk factors for familial transmission of suicidal behavior, and the identification of precursors of early-onset suicidal behavior. Because there are now no empirically validated interventions for suicidal youth, the findings from this unique cohort should help to frame treatment targets in high-risk families and individuals designed to alter prodromal at-risk behavior and psychopathology and prevent future suicidal behavior. This study is of public health importance because suicidal behavior is the single biggest risk factor for completed suicide, which is the third leading cause of death among adolescents and young adults in the United States. The aims of this study are consistent with several priorities of the NIMH and the Division of Pediatric Translational Research (DPTR): (1) reduction of the public health burden of suicide and suicidal behavior; (2) inclusion of family-genetic approaches to elucidate the interplay of biological and environmental factors to childhood psychopathology and to identify behavioral and biological markers of vulnerability and resilience; and (3) research that is likely to lead to novel psychosocial and pharmacological preventive and therapeutic interventions. This application is from the Pittsburgh site (Principal Investigator: David Brent, MH56612). PUBLIC HEALTH RELEVANCE: This study, "Familial Pathways to Early-Onset Suicidal Behavior," seeks to identify the familial and individual precursors of early-onset suicidal behavior and the mechanisms by which suicidal risk is transmitted from parent to child. We anticipate that certain traits, namely impulsive aggressive traits, early-onset depression, memory and decision making ability, and a greater physiological reaction to stress (measured by cortisol secretion) are familial and will: (1) explain how suicidal behavior runs in families; (2) predict suicidal behavior in the children of parents who have attempted suicide; and (3) yield intermediate phenotypes that can advance genetic studies of suicidal behavior. This study is important because suicide and suicidal behavior are leading causes of mortality and morbidity among adolescents, there are currently no empirically validated interventions to prevent or treat adolescent suicidal behavior, and the results of this study could frame targets for prevention and treatment.

NIH	2011	Course and Outcome for Bipolar Disorder in Youth (COBY)	KELLER, MARTIN	DESCRIPTION (provided by applicant): This is a competitive renewal of "Course and Outcome of Bipolar Disorder in Youth (COBY)," a collaborative undertaking by University of Pittsburgh, Brown, and UCLA to collect long-term prospective data on children and adolescents with Bipolar-Spectrum Disorders (BP) across psychiatric (categorical and dimensional), familial, psychosocial, cognitive, and naturalistic treatment domains using state-of-the-art instruments. COBY successfully enrolled a total of 446 youth (197 children and 249 adolescents) with BP, the largest cohort of rigorously defined cases of early-onset BP described to date. Since 100% of subjects will be older than 18 years and 65% will exceed age 24 by the end the proposed extension, COBY now seeks 5 more years of follow-up in order to comprehensively describe, for the first time, the prospective course of pediatric BP into young adulthood. In accord with the current NIMH Strategic Plan, 5 more years of observation data across multiple disease-specific and functional domains will address fundamental gaps in our knowledge of this poorly understood childhood condition by: (a) identifying the differential long-term course trajectories extending from childhood/adolescence into young adulthood, and their predictors; (b) describing changes in clinical phenotypes that coincide with transitions across developmental periods; (c) determining the long-term developmental course of psychosocial functioning from intake into young adulthood; (d) documenting the prevalence and predictors of new psychiatric comorbidities shown to accentuate risk of treatment non- response in adult studies; (e) identifying risk and predictors of suicidality, smoking, and substance use disorder as subjects enter the peak risk period of young adulthood; (f) evaluating long-term bi-directional effects of BP and neurocognition from childhood into young adulthood; and (g) evaluating how naturalistic psychosocial and pharmacological treatments affect course and psychosocial outcomes, and determining how these effects change with age. In addition, two novel aims are proposed in this renewal. First, given overlap between BP and Borderline Personality Disorder and the risk of mistreatment that results from diagnostic error, COBY will prospectively evaluate the temporal relationship between these phenotypes. Second, reflecting mounting evidence linking BP to elevated risk of cardiovascular disease (CVD) and mortality, COBY will examine risk for CVD by prospectively assessing physical activity and diet, metabolic syndrome and its components (central obesity, hyperglycemia, hypertension, and dyslipidemia), and the presence of inflammatory markers associated with risk for CVD (interleukin-6, tumor necrosis factor-alpha and C-reactive protein). These data will be compared to a demographically matched sample of young adults reported in the Coronary Artery Risk Development in Young Adults (CARDIA) study. Findings from this effort will inform unanswered questions concerning long-term, cumulative, developmental effects of pediatric BP on adult psychiatric, functional, and health status, as well as the development of novel preventive strategies to enhance long-term management. PUBLIC HEALTH RELEVANCE: The Course and Outcome of Bipolar Disorder (BP) study has been interviewing children and adolescents with Bipolar Disorder (BP), every 6 months, for almost a decade, and COBY is proposing to continue the study for 5 more years to determine the impact of pediatric BP on adulthood. Since all of these youth will become young adults during the proposed project period, the results of this study will help us to better understand the clinical characteristics and the persistence of BP symptoms over time, the persistence or development of other psychiatric conditions (substance abuse, suicidal behaviors, personality problems), the risk for cardiovascular illnesses, and the social consequences of BP from childhood to adolescence and into young adulthood.
NIH	2011	Course and Outcome of Bipolar Disorder in Youth	BIRMAHER, BORIS	DESCRIPTION (provided by applicant): This is a competitive renewal of "Course and Outcome of Bipolar Disorder in Youth (COBY)," a collaborative undertaking by University of Pittsburgh, Brown, and UCLA to collect long-term prospective data on children and adolescents with Bipolar-Spectrum Disorders (BP) across psychiatric (categorical and dimensional), familial, psychosocial, cognitive, and naturalistic treatment domains using state-of-the-art instruments. COBY successfully enrolled a total of 446 youth (197 children and 249 adolescents) with BP, the largest cohort of rigorously defined cases of early-onset BP described to date. Since 100% of subjects will be older than 18 years and 65% will exceed age 24 by the end the proposed extension, COBY now seeks 5 more years of follow-up in order to comprehensively describe, for the first time, the prospective course of pediatric BP into young adulthood. In accord with the current NIMH Strategic Plan, 5 more years of observation data across multiple disease-specific and functional domains will address fundamental gaps in our knowledge of this poorly understood childhood condition by: (a) identifying the differential long-term course trajectories extending from childhood/adolescence into young adulthood, and their predictors; (b) describing changes in clinical phenotypes that coincide with transitions across developmental periods; (c) determining the long-term developmental course of psychosocial functioning from intake into young adulthood; (d) documenting the prevalence and predictors of new psychiatric comorbidities shown to accentuate risk of treatment non- response in adult studies; (e) identifying risk and predictors of suicidality, smoking, and substance use disorder as subjects enter the peak risk period of young adulthood; (f) evaluating long-term bi-directional effects of BP and neurocognition from childhood into young adulthood; and (g) evaluating how naturalistic psychosocial and pharmacological treatments affect course and psychosocial outcomes, and determining how these effects change with age. In addition, two novel aims are proposed in this renewal. First, given overlap between BP and Borderline Personality Disorder and the risk of mistreatment that results from diagnostic error, COBY will prospectively evaluate the temporal relationship between these phenotypes. Second, reflecting mounting evidence linking BP to elevated risk of cardiovascular disease (CVD) and mortality, COBY will examine risk for CVD by prospectively assessing physical activity and diet, metabolic syndrome and its components (central obesity, hyperglycemia, hypertension, and dyslipidemia), and the presence of inflammatory markers associated with risk for CVD (interleukin-6, tumor necrosis factor-alpha and C-reactive protein). These data will be compared to a demographically matched sample of young adults reported in the Coronary Artery Risk Development in Young Adults (CARDIA) study. Findings from this effort will inform unanswered questions concerning long-term, cumulative, developmental effects of pediatric BP on adult psychiatric, functional, and health status, as well as the development of novel preventive strategies to enhance long-term management. PUBLIC HEALTH RELEVANCE: The Course and Outcome of Bipolar Youth (COBY) study has been interviewing children and adolescents with Bipolar Disorder (BP), every 6 months, for almost a decade, and COBY is proposing to continue the study for 5 more years to determine the impact of pediatric BP on adulthood. Since all of these youth will become young adults during the proposed project period, the results of this study will help us to better understand the clinical characteristics and the persistence of BP symptoms over time, the persistence or development of other psychiatric conditions (substance abuse, suicidal behaviors, personality problems), the risk for cardiovascular illnesses, and the social consequences of BP from childhood to adolescence and into young adulthood.
NIH	2008	Treating Suicidal Behavior and Self-Mutilation in BPD	STANLEY, BARBARA	DESCRIPTION (provided by applicant): This application is in response to PA-07-079, "Research on the Reduction and Prevention of Suicidality" and is a competing continuation of R01MH 61017, "Treating Suicidal Behavior and Self-Mutilation in BPD." Suicidal behavior non-suicidal self-injurious behavior and depression are key problems in borderline personality disorder (BPD). Up to 10% of individuals affected with this disorder die by suicide, however, development of effective treatments for suicidal behavior and self-injury and understanding of mechanisms of action of treatment has received little attention. This project is a continuation of a randomized clinical trial of fluoxetine and Dialectical Behavior Therapy (DBT) for the treatment of suicidal behavior and non-suicidal self injury (NSSI). We achieved a nearly 80% reduction in suicide attempt rate comparing the treatment year to the year prior to study entry. DBT and fluoxetine have specific efficacy in achieving overall improvement at six months relative to supportive therapy and placebo. While at 12 months the differences in overall improvement are no longer present, the speed of response is important due to the seriousness of the problems being treated. Also, NSSI was significantly reduced in those with substance use disorders with DBT and fluoxetine. Furthermore, suicide attempts in the DBT condition were half the number of the supportive therapy condition. Fluoxetine at a high dose was associated with suicide attempts, thus, while helpful in overall improvement and NSSI, fluoxetine should be maintained at lower doses in order to avoid suicidal behavior. We now know, based on recent research from others in our group that almost complete serotonin receptor blockade is achieved at relatively low doses and, therefore, higher doses are likely to affect other systems and be responsible for side effects without additional therapeutic benefit. In our continuation, we plan to build on our current findings by comparing DBT to a strategy frequently used in clinical practice, clinical management with fluoxetine at lower dosage (no more than 40mg) with the option of switching to another SSRI. The project also uses translational neuroscience measures, neuropsychological testing, biobehavioral measures and fMRI at baseline and at the end of treatment, to evaluate emotion regulation and impulsivity, two key components of BPD, as moderators and predictors of treatment change. Furthermore, our preliminary data demonstrates that a 6-month treatment may be as effective in treating these behaviors and we plan to test this model. The findings of the proposed study will help to provide an accessible and rational treatment strategy for suicidal and self injuring individuals with BPD. This project is innovative in that: it is the first trial to compare DBT to a standard medication strategy; it uses a well-justified six month model instead of 12 months; it incorporates both biobehavioral and imaging measures at baseline and end of treatment to evaluate predictors and moderators of change; it addresses suicide-related outcomes and the risk of risk of antidepressant emergent suicidality. Suicide, suicide attempts and depression occur at a high rate in borderline personality disorder. The findings of the proposed study will help to provide an accessible and rational treatment strategy for suicidal and self injuring individuals and will also provide information on differential efficacy and mechanisms of action for these treatments.

NIH	2010	McLean Study of Adult Development	ZANARINI, MARY	DESCRIPTION (provided by applicant): We propose a 5-year (and final) renewal of the McLean Study of Adult Development (MSAD), the first large-scale, prospective study of the long-term course of borderline personality disorder (BPD). We will obtain a maximum of 20 years of follow-up data on 290 patients who met DIB-R and DSM-III-R criteria for BPD and 72 axis II comparison subjects who met DSM-III-R criteria for another personality disorder (and neither criteria set for BPD). After 14 years of follow-up, we are still following 88% of the surviving borderline patients (and 81% of the surviving axis II comparison subjects). During the years of follow-up, we have found that symptomatic remissions of BPD are far more common and stable than expected. We have also found that these remissions were driven more by the relatively rapid resolution of acute symptoms than the relatively slow resolution of temperamental symptoms. Taken together, these findings suggest that BPD has a better symptomatic prognosis than previously known. However, we have found more guarded and complex outcomes in other areas of investigation. More specifically, we found that recovery from BPD involving good social and vocational functioning as well as symptomatic remission from BPD was more difficult to achieve and maintain than symptomatic remission alone. In addition, we found that the physical health of many borderline patients has continued to decline, with obesity-related and smoking-related illnesses becoming more common over time, particularly among borderline patients who have not recovered from BPD (i.e., those with compromised psychosocial functioning). We believe that these findings warrant further investigation into the course of borderline psychopathology (particularly sustained remissions of BPD and its constituent symptoms), psychosocial functioning, recovery from BPD, co-occurring axis I and II disorders, psychiatric treatment, changes in temperament, and medical treatments (AIM 1: Description). We also believe that these findings warrant further investigation into the predictors of three main outcomes: recurrence of BPD, recovery from BPD, and completed suicide (AIM 2: Prediction). Subjects will be assessed at two-year intervals by raters who are blind to all previously collected information using semistructured interviews and self-report measures, including three new instruments assessing physical pain and sleep. This proposed continuation will result in crucial knowledge about the long-term course of BPD, with direct implications for patients, their families, and the clinicians treating them. PUBLIC HEALTH RELEVANCE: Borderline personality disorder (BPD) is a common and serious psychiatric disorder. The McLean Study of Adult Development (MSAD) is the first large-scale, prospective study of the long-term course and outcome of BPD. This study will provide patients, their families, and those treating them with crucial information they need to plan for the future.
NIH	2008	Impact of Sudden Parental Death on Children and Families	BRENT, DAVID	DESCRIPTION (provided by applicant): This is a 5-year A1 competitive renewal to study the impact of sudden parental death on children. During the initial project period, we recruited a cohort of 245 children who have lost a parent to suicide, accident, or sudden natural death, and a demographically similar, non-bereaved control group of 185 children and assessed them at 1 and 2 years after parental death. We find evidence of a persistent impact two years after the death: parental bereavement quadruples the risk for child depression, even adjusting for pre-death risk factors. We propose to reassess this cohort at 3 and 6 years after the parental death for a total of 4 follow-up assessment points in order to examine the relationship between parental loss and child outcomes in the domains of psychopathology (e.g., incident disorder, symptom trajectory), attainment of developmental competence (educational, vocational, relational), and health-related outcomes (e.g., BMI, impact on the hypothalamic pituitary adrenal [HPA] axis). We evaluate the construct and discriminant validity of complicated grief to determine if it has a stable factor structure and explains a unique proportion of the variance in outcome. We test an explanatory model by examining specific pathways that may mediate (e.g., child coping, family cohesion) or moderate (e.g., pre-death psychopathology, gender) the relationship between parental death and child mental health, developmental, and physical health outcomes. As an exploratory aim, we examine if polymorphisms in genes may moderate the relationship between parent death and cortisol response to a social stressor (e.g., glucocorticoid receptor) or depression (e.g., serotonin transporter promoter). This project will lead to new knowledge, because it: (1) is the only controlled, prospective study of parentally bereaved children with a follow-up period of longer than 2 years; (2) assesses outcomes complementary to psychiatric outcome, namely developmental competency, health, and the HPA axis; (3) tests models of mediation and moderation; (4) is large enough to assess if parental bereavement by suicide is uniquely deleterious; and (5) will address whether complicated grief in youth has construct and discriminant validity and has a direct impact on functional outcome. These results will help to identify bereaved youth and families at risk for sub-optimal mental and physical health and developmental outcomes, thus framing targets for future prevention and intervention studies.Project Narrative: The loss of a parent is widely recognized to be among the most stressful events that a child can experience, and numerous retrospective studies indicate that parent loss has serious and enduring mental health effects. However, there have been no long-term, controlled, prospective studies of the effects of parental bereavement on children.
NIH	2010	Long Term Effects of Depression Care on Services Use and Mortality in Late Life	Gallo, Joseph	DESCRIPTION (provided by applicant): The overarching goal of this amended proposal entitled "Long-term effects of depression care on services use and mortality in late life" is to assess the long-term effect on use of health care services and mortality of a primary care practice-based intervention for depression. Our work has shown that after 5 years of follow-up, older adults with major depression in practices randomized to the practice-based intervention condition were less likely to die over the follow-up interval. A goal of this competing renewal proposal to MH065539 is to extend our 5 year mortality follow-up to 8 years and to add claims data, supplementing available data on depression and depression interventions over 2 years with dates and causes of death from the National Center for Health Statistics (National Death Index Plus) and with health services claims data from the Center for Medicaid and Medicare Services. Specific aims of this study are: (1) to assess how the effectiveness of a practice-based intervention (intent-to-treat analysis) and increasing intensity of different types of depression treatment (as-treated analysis) in reducing all-cause mortality over the course of an 8-year follow-up interval differs between older adults with major depression, clinically significant minor depression, or suicidal ideation versus older adults without significant depression or suicidal ideation; and (2) to assess how the effectiveness of a practice-based intervention (intent-to-treat analysis) and increasing intensity of depression treatment (as- treated analysis) in reducing use of health care services over the course of an 8-year follow-up interval. To accomplish these aims, we will capitalize on screening, clinical assessment, treatment, and follow-up assessments of 1,226 persons which occurred for up to 2 years in PROSPECT, building on our work with 5- year mortality follow-up data. We propose to study the relationship of major depression, other depressive syndromes, and suicidal ideation with long-term outcomes (use of health services and mortality) in the context of an intervention directed at the practice level that increased individual-level exposure of older patients to antidepressant medication and psychotherapy. PUBLIC HEALTH RELEVANCE: Policy changes to improve reimbursement for collaborative care, to increase the use of care management, and to improve access to medications in primary care settings increase the urgency for information on the long- term individual and societal consequences of practice-based interventions. Our project is consistent with the NIMH Strategic Plan to reduce premature mortality among persons with mental illness.
NIH	2011	Culture, Risk Factors and Suicide Attempt in Rural China	ZHANG, JIE	DESCRIPTION (provided by applicant): Suicide by Chinese rural young women is an urgent focus in suicide research, because of the high suicide rates and the large population in China. Society and culture play an enormous role in dictating how people respond to and view mental health and suicide, and studies are needed to systematically examine the role of cultural factors (e.g. the value systems) in determining risk for suicide. Psychological autopsy (PA) studies with suicides are usually limited by their indirect evaluation and understanding of the suicides' neurocognitive functions, psychiatric disorders, suicidal intent, and conflicting social values, etc. However, studying serious suicide attempters can provide direct and comparatively more reliable information on why the victims are at high risk of suicide. This project is designed to study a cultural model of suicide using serious attempters in China. Confucian values, which are considered to be the cultural foundation in Asian societies including China, are supposed to explain the high suicide risks for young women and the comparatively low risks for young men. The deep-rooted Confucian sexism coupled with the communist egalitarianism advocated in China creates frustration or strain in the daily life of some rural young women. The strain resulting from the traditional reality and modern aspiration, interacting with other risk factors, is hypothesized to increase suicide risks for Chinese rural young women. In a case-control design, 800 serious suicide attempters (400 males and 400 females) and 800 community controls (400 males and 400 females) all aged 15-34 years will be randomly sampled from 16 rural counties selected in Liaoning, Hunan, and Shandong provinces of China. The study has the following four major aims: 1. To evaluate the direct effect of risk factors from four domains (personal factors, social structure, negative life events, and psychological/psychiatric factor) on young suicide attempters in rural China. 2. To test the Strain Theory of Suicide among suicide attempters (SAs) and community controls (CCs), by examining the impact of cultural factors related to Confucian values and communist ideology on attempted suicide in rural China and the role of gender in the relationship. 3. To test the moderating or intervening effects of the risk factors on the relationship between strain and attempted suicide in rural China. 4. To examine the relationship between strain and suicide intent among the suicide attempters Findings regarding the independent role of culturally defined beliefs and values in determining suicide risk will be generalizable to other Chinese and Asian populations in the United States and elsewhere in the world. PUBLIC HEALTH RELEVANCE: Suicide is a global public health problem and suicide by Chinese rural young women is an urgent focus of research. Complementary to the traditional approaches of suicide research and prevention, this study proposes and tests a cultural model in understanding and reducing suicide. Findings regarding the independent role of culturally defined beliefs and values in determining suicide risk will be generalizable to other Chinese and Asian populations in the United States and elsewhere in the world.

NIH	2012	Genetic Risk Factor For Suicidal Behavior	WILLOUR, VIRGINIA	DESCRIPTION (provided by applicant): This proposal aims to identify and characterize novel gene variants conferring susceptibility to suicidal behavior. We will do this both through intensive follow-up of a strongly implicated chromosomal region, and through performing the first ever exome-wide search for rare variants related to this phenotype. While suicidality is perhaps the most dreaded aspect of psychiatric disorders, relatively little research has been devoted to its biological basis. Yet family, twin, and adoption studies make clear that suicidal behavior has a substantial heritable component. While there is evidence that this heritability is accounted for in part by a liability to mood disorder, other evidence suggests an independent heritable facet that may cut across multiple psychiatric disorders. This independent feature has been hypothesized to be a liability to aggressiveness and impulsivity, the genetic study of which has focused on serotonergic genes. However, little systematic genetic investigation of the suicidality phenotype has been undertaken. In the first iteration of this grant, we conducted an attempted suicide genome-wide association study (GWAS), which generated an association signal on 2p25 at rs300774 (p=5.07 X 10-8), a finding that is on the threshold of genome-wide significance (p<5X10-8). The associated SNPs on 2p25 fall in a large linkage disequilibrium block that contains the ACP1 gene, whose expression is significantly elevated in bipolar disorder (BP) subjects who have completed suicide. Furthermore, the ACP1 protein is a tyrosine phosphatase that interacts with beta-catenin. The connection to beta-catenin, a key molecule in the Wnt signaling pathway, is noteworthy because the Wnt pathway is positively regulated by lithium, which has been shown to decrease suicidal behavior. The connection between suicidal behavior and beta-catenin was further supported by our gene set enrichment analysis of our attempted suicide GWAS dataset and by our initial whole-exome sequencing of 39 BP attempters and 60 BP non- attempters. We propose to follow up these findings by resequencing the 2p25 candidate region and by conducting a secondary analysis of whole-exome data from 800 attempters and 1,200 non-attempters, allowing us to search for functional variants influencing the risk for suicidal behavior on 2p25, in Wnt-related genes, and throughout the genome. To accomplish this, we will employ the diverse and complementary skill sets of an outstanding team of investigators including experts in molecular genetics, statistical genetics, bioinformatics, neurobiology, and psychopathology. The identification of candidate genes and functional variants associated with suicidal behavior would have a significant public health impact because it would provide new insights into the biological basis of suicidal behavior, provide new therapeutic targets, and provide the data needed to generate in vivo models in which to test therapeutic targets. PUBLIC HEALTH RELEVANCE: Suicidal behavior is perhaps the most dreaded aspect of psychiatric disorders and among the leading causes of death for young people. This proposal aims to identify genetic factors that increase the risk for suicidal behavior.
NIH	2008	5-HT1A receptor anti-apoptotic transduction pathways in suicide	ARANGO, VICTORIA	DESCRIPTION (provided by applicant): The 5-HT1A receptor is implicated in the pathology of anxiety, major depression and suicide. Studies with mutant mice indicate that the 5-HT1A receptor is necessary for the long-term viability of brain networks. Preliminary studies suggest that the activation of signaling molecules downstream of the 5-HT1A receptor is attenuated in the occipital cortex (OC) of suicides. We will determine whether this attenuation of signal transduction pathways is a characteristic of major depression or related to the diathesis for suicide by comparing suicides with major depression (MDD) to suicides with schizophrenia (SZ) and to nonpsychiatric, nonsuicide controls. We will evaluate four brain regions, one where we have found changes in both major depression and suicide (ventral prefrontal cortex, vPFC) and three regions where the findings seem more specifically linked to major depression (anterior cingulate cortex [ACC], dorsolateral PFC [BA9] and hippocampus). We predict signal transduction effects related to suicide will be present in both suicide groups and confined to the vPFC. We would predict the signal transduction changes related to MDD will be found in the MDD suicide group and not the other two groups and in the ACC and dorsal prefrontal cortex. We will test the hypothesis that 5-HT1A receptor-activated transduction pathways linked to cell survival are downregulated in specific brain regions relevant to major depression or for suicide. We will measure signaling proteins downstream of 5-HT1A receptors that are regulated via coupling to Gi/o and Gsubunits. One pathway involves the Gai-mediated inhibition of adenylyl cyclase (AC) and protein kinase A (PKA). The 5-HT-dependent inhibition of AC is normally counterbalanced by the concomitant activation of cell survival pathways. We propose that the reduced inhibition of AC in suicides represents a mechanism to counteract the reduction in the activity of the transduction pathways activated via the Gbg subunit. Investigating 5-HT1A receptor activation of NFkB, PI3-K/Akt and ERKs in suicide will advance our understanding of the role of 5-HT1A receptor signal pathways in depression and suicidal behavior. The cerebellar hemisphere will serve as a control region. We will also measure neuronal density, the levels of pro-apoptotic signaling molecules and death effectors. We hypothesize that the viability or functionality of brain cells that express 5-HT1A receptors is neuroendangered in major depression or suicide. Unraveling these events biochemically will yield crucial insights into the neurobiology of depression and suicide, major mental health problems in the US and the world. It may also identify novel drug targets for the treatment of depression and for the prevention of suicide. PUBLIC HEALTH RELEVANCE: Suicidal behavior is a major health problem in the United States and the world. With 30,000 deaths by suicide per year in the US, suicide is the 11th leading cause of death. We have data indicating that the neuroprotective cellular pathways associated with the serotonin 1A receptor are altered in suicide. We want to explore this further by studying these pathways in various brain regions of suicides (depressed and schizophrenic) and normal controls. We hope to gain insight into the neurobiology of suicide versus depression and identify novel drug targets for treatment of depression and prevention of suicide.
NIH	2008	Suicidality Associated with Antidepressants inTennCare Children and Adolescents	COOPER, WILLIAM	DESCRIPTION (provided by applicant): Depressive disorders account for substantial morbidity and mortality among children and adolescents and are most commonly treated with antidepressants. In recent years, increasing concerns have arisen that antidepressants in and of themselves might increase the risk of suicidality specifically among children and adolescents. However, the available evidence regarding suicidality and antidepressants in children is limited due to the small sample size of the clinical trials (even when combined in meta-analysis) resulting in insufficient power to assess the risk of suicide deaths and the risk of suicide-related behaviors for individual antidepressants. In addition, the short duration of clinical trials has precluded assessment of the risk of serious suicide attempts and suicidality over the course of treatment. Understanding the relationship between antidepressant treatment and injuries from suicidal behavior in children and adolescents is vital for clinical practice. The research described in this proposal will address three specific aims: 1) test the hypothesis that the risk of medically treated suicide attempts is lower for fluoxetine than for other antidepressants; 2) test the hypothesis that the risk of medically treated suicide attempts is increased in the time 4 and 12 weeks following initiation of antidepressant therapy; and, 3) test the hypothesis that periods on antidepressants represent greater risk for medically treated suicide attempts and suicide deaths than periods off antidepressants. To address these aims, a retrospective study cohort will be assembled from Tennessee Medicaid files and will include an estimated 85,000 6-18 year old children who are users of antidepressant medications with evidence suggesting treatment of major depression. Cohort follow up will be from 1995-2006 and will include an estimated 73,000 person-years of follow-up. Every person-day of follow-up will be classified by exposure to study medications and potential confounding factors. A case definition drawn from Medicaid claims, death certificates, and confirmed through medical record review will define medically treated suicide attempts and suicide deaths among children in the cohort. Poisson regression will be used to estimate the effects of the individual study drugs and the duration of study drug exposure on study endpoints. A case-crossover design will compare risk for periods on vs. off antidepressants. This research will address questions of enormous public health importance. Patients, families, and physicians urgently need to know whether or not individual drugs affect the risk of suicidality differently. Whether or not risk is increased early in the course of treatment will have implications for monitoring of children on these medications. Finally, understanding the risk of suicidality for periods off and on treatment will inform practitioners, patients, and families faced with treating an important condition.

NIH	2008	Reducing Disparities in Depression Care for Ethnically Diverse Older Men	HINTON, WALTER	DESCRIPTION (provided by applicant): The epidemic of suicide among older (i.e. age 60 and above) men in the US is a public health crisis. Older men have eight to ten-times higher rates of completed suicide than older women. Because depression is one of the strongest risk factors for suicide, improving care for depression in primary settings is a vital public health strategy to prevent suicide and other adverse outcomes of depression. Depression is more common in women than in men, but depressed older men and minorities are less likely to receive effective treatment. To address this knowledge gap and reduce disparities in older men and minorities, we propose a study that applies both qualitative and quantitative methods to better understand the perspectives, experiences, and preferences of care of ethnically diverse depressed older men and the primary care providers who treat them. Our focus gender-specific focus and attention to age-related factors will enable us to examine potentially important but under-studied variability among older men in how they experience and deal with their depression and will allow us to further develop our conceptual model and to develop strategies to engage more difficult to reach subgroups of diverse older men. Primary care is a logical site for this research because it is the setting where most depressed older men can potentially be recognized and treated. We will conduct systematic screening to identify a representative sample of 100 older men (50 Mexican-American and 50 white non- Hispanic) older men with treated and untreated clinical depression from primary care clinics in two cities and then conduct interviews with them and their primary care physicians (n = 48). This proposal's aims are 1) to examine how forms of masculinity and age-related changes and attitudes (i.e. health status, major role transitions, conceptions of normal aging) influence men's depression illness meanings, experience, and patterns of help-seeking, 2) to systematically examine older men's preferences for depression treatment, and 3) to identify factors that impede or facilitate depression care from the perspectives of primary care physicians. This proposal brings together an interdisciplinary group of investigators with extensive experience in working with older and minority populations and builds directly on published preliminary data (Hinton et al, 2006). It is the intention of this proposal to generate empirical data to help close the gender and ethnic gap in depression care, reduce associated health disparities, and mitigate high suicide rates in older men. Because depression is one of the strongest risk factors for suicide and because men who kill themselves frequently have had recent prior contact with their primary care physicians, improving care for depression in primary care settings is a vital public health strategy to prevent suicide and other adverse outcomes of depression. Depressed older men, however, are significantly less likely than women to receive effective depression treatment. Despite its public health importance, the barriers to depression care for older men are not well understood. Through a focused and in-depth examination of the perspectives and preferences of depressed older men and their primary care providers, this research will generate empirical data to reduce barriers to depression care for older men in primary care settings.
NIH	2008	Antidepressant Treatment and Suicidality: Biostatistical/Methodological Solutio	GIBBONS, ROBERT	DESCRIPTION (provided by applicant): ABSTRACT The purpose of this proposal is to develop, test, and apply new statistical methodologies that can be used to identify low base rate drug adverse event (AE) interactions. These new methods will then be applied to a wide range of existing non- experimental datasets to examine the relationship between antidepressants and suicide attempts and completion. We have designed this research project as an integral collaboration between biostatisticians, research psychiatrists and clinicians, economists, and pharmacoepidemiologists, working with large ecological and medical records/claims electronic patient databases covering years where antidepressant use is varying dramatically. Three major specific aims are proposed: (a) the development of new statistical surveillance methods for detecting drug-AE interactions, (b) the development and application of analytic methods for ecological and population data, and (c) the development of and application of statistical methods for analysis of person-level data from large scale medical records/claims databases both in the U.S. and in Europe. The datasets that we have been granted access to include the FDA spontaneous reporting system (SRS/AERS/MedWatch), electronic medical record/claims databases in the U.S. (VA, and PHARMetrics), and similar data from the Netherlands (PHARMO). The work in this proposal will be carried out by a research consortium that will study national and international drug safety issues. The multidisciplinary group includes the areas of statistics (Drs. Gibbons, (PI), Brown (co-PI), Bhaumik, Hur, Marcus, and Rosenbaum), psychiatry from adult (Mann), and child (Brent) perspectives, health economics/econometrics (Heckman), and pharmacoepidemiology (Valuck). Collaboration with members of the VA (Cunningham), and PHARMO (Erkens, Herings) is an integral part of the proposal. PUBLIC HEALTH RELEVANCE: The enormous human cost of suicide makes research and prevention a national priority. Traditional approaches to drug safety have proved inadequate to address current public health issues. Providing statistical and methodological advances for the active surveillance of Drug-AE interactions, such as antidepressants and suicide, is a necessary first step in the establishment of a science-based health policy system, and is the primary goal of this proposal.
NIH	2009	Impact of Adolescent Suicide Attempts on Parents	GOLDSTON, DAVID	DESCRIPTION (provided by applicant): The suicidal behavior of teenagers can be associated with considerable distress for parents, raising issues about the possibility of their unaddressed mental health needs. Parents' level of distress and their potentially higher risk for anxiety and depressive disorders may effect interactions with adolescents, parenting practices, and follow-through with treatment recommendations for youths or involvement with treatment. Nonetheless, little is known about which parents have the most difficulties following their teenager's suicidal behaviors, the nature of these difficulties, or how quickly these reactions resolve. This application is a proposal to address these issues, in response to the NIH Program Announcement 07-079, Research on the Reduction and Prevention of Suicidality. This program announcement invites applications that address the burden, and specifically, "the immediate and long-term mental health needs of family survivors who have experiences suicide attempts and/or deaths in the family." In this study, parents of 180 hospitalized teenagers who have made suicide attempts and 180 hospitalized teenagers who have not made attempts will be examined at 1,3, 6, and 12 months following a suicide attempt. The first specific aim of this project is to examine the distress and risk for anxiety and depressive disorders among mothers of suicidal teens relative to the mothers of other hospitalized youths, the diversity of these reactions, and the amount of time for resolution of these reactions. Using latent class trajectory methods, we will identify groups of parents with different patterns of symptoms over time following adolescents' hospitalization. The second Specific Aim of this proposal is examine child and maternal factors that are predictive of maternal emotional symptoms following adolescent suicidal behavior including high medical lethality of the attempt, number of prior attempts, family history of suicidal behavior, and past psychiatric treatment history. The third Specific Aim is to examine the association between material symptoms and anxiety/depressive disorders following adolescent suicidal behavior on parenting practices, mental health specialty service use, length of treatment and follow-through with the treatment recommendations. This project will help us to understand the mental health and treatment needs of mothers of adolescents who have attempted suicide. The results of this study will help shed light on the best strategies for meeting parental needs following adolescent suicide attempts, and involving parents in their son's and daughter's treatment.
NIH	2008	Suicidal Behavior in Mood Disorders:Genes and Intermediate Phenotypes	MANN, JOSEPH	DESCRIPTION (provided by applicant): This collaborative R01 involves three sites: New York State Psychiatric Institute/Research Foundation for Mental Hygiene, Inc., in New York City, USA (Mann), McGill University in Montreal, Canada (Turecki) and University of Munich, Germany (Rujescu) to examine the complex genetic basis of suicidal behavior. We have contributed to the original observations showing that suicide and nonfatal suicide attempts have biologic changes that are distinct from those of major psychiatric disorders that underlie suicide such as major depressive disorder or bipolar disorder. We have reported candidate gene associations that are independently associated with mood disorders or with suicide attempts. We believe the field is ready for a major effort to survey the genome to seek genes associated with suicidal behavior that are independent of the major psychiatric illnesses. We have developed and tested a potential predictive stress-diathesis model of suicidal behavior derived from a comprehensive assessment of risk factors. Depressed individuals with prominent (1) pessimism and (2) severity of life-time aggression/impulsivity are at greater risk for suicidal behavior and the effects are additive. These clinical phenotypic components can be measured in the field in patients and suicides. We now propose to use genome-wide screens to identify candidate genes and conserved haplotype blocks within those genes 4000 cases that span the higher severity range of suicidal behavior, namely completed suicide and attempted suicide compared to both psychiatrically matched controls and to healthy volunteers. We have data on Axis I and Axis II diagnoses and data on lifetime aggression scores and current severity of depression to permit assessment of these potential etiological factors and potential behavioral endophenotypes. We have data on childhood reported histories of physical or sexual abuse which will be a focus for an exploratory gene-early environment interaction analysis. Causal SNPs will be further identified by sequencing the most promising gene segments. PUBLIC HEALTH RELEVANCE: The predisposition to suicidal behavior is substantially determined by genetic factors independent of those associated with major psychiatric disorders. This study will screen the genome in the largest collection of samples ever assembled for such a study of suicidal behavior in order to identify the responsible genes.

NIH	2008	Suicidal Behavior in Mood Disorders: Genes and Intermediate Phenotypes	Rujescu, Dan	DESCRIPTION (provided by applicant): This collaborative R01 involves three sites: New York State Psychiatric Institute/Research Foundation for Mental Hygiene, Inc., in New York City, USA (Mann), McGill University in Montreal, Canada (Turecki) and University of Munich, Germany (Rujescu) to examine the complex genetic basis of suicidal behavior. We have contributed to the original observations showing that suicide and nonfatal suicide attempts have biologic changes that are distinct from those of major psychiatric disorders that underlie suicide such as major depressive disorder or bipolar disorder. We have reported candidate gene associations that are independently associated with mood disorders or with suicide attempts. We believe the field is ready for a major effort to survey the genome to seek genes associated with suicidal behavior that are independent of the major psychiatric illnesses. We have developed and tested a potential predictive stress-diathesis model of suicidal behavior derived from a comprehensive assessment of risk factors. Depressed individuals with prominent (1) pessimism and (2) severity of life-time aggression/impulsivity are at greater risk for suicidal behavior and the effects are additive. These clinical phenotypic components can be measured in the field in patients and suicides. We now propose to use genome-wide screens to identify candidate genes and conserved haplotype blocks within those genes 4000 cases that span the higher severity range of suicidal behavior, namely completed suicide and attempted suicide compared to both psychiatrically matched controls and to healthy volunteers. We have data on Axis I and Axis II diagnoses and data on lifetime aggression scores and current severity of depression to permit assessment of these potential etiological factors and potential behavioral endophenotypes. We have data on childhood reported histories of physical or sexual abuse which will be a focus for an exploratory gene-early environment interaction analysis. Causal SNPs will be further identified by sequencing the most promising gene segments. PUBLIC HEALTH RELEVANCE: The predisposition to suicidal behavior is substantially determined by genetic factors independent of those associated with major psychiatric disorders. This study will screen the genome in the largest collection of samples ever assembled for such a study of suicidal behavior in order to identify the responsible genes.
NIH	2008	Suicidal Behavior in Mood Disorders: Genes and Intermediate Phenotypes	TURECKI, GUSTAVO	DESCRIPTION (provided by applicant): This collaborative R01 involves three sites: New York State Psychiatric Institute/Research Foundation for Mental Hygiene, Inc., in New York City, USA (Mann), McGill University in Montreal, Canada (Turecki) and University of Munich, Germany (Rujescu) to examine the complex genetic basis of suicidal behavior. We have contributed to the original observations showing that suicide and nonfatal suicide attempts have biologic changes that are distinct from those of major psychiatric disorders that underlie suicide such as major depressive disorder or bipolar disorder. We have reported candidate gene associations that are independently associated with mood disorders or with suicide attempts. We believe the field is ready for a major effort to survey the genome to seek genes associated with suicidal behavior that are independent of the major psychiatric illnesses. We have developed and tested a potential predictive stress-diathesis model of suicidal behavior derived from a comprehensive assessment of risk factors. Depressed individuals with prominent (1) pessimism and (2) severity of life-time aggression/impulsivity are at greater risk for suicidal behavior and the effects are additive. These clinical phenotypic components can be measured in the field in patients and suicides. We now propose to use genome-wide screens to identify candidate genes and conserved haplotype blocks within those genes 4000 cases that span the higher severity range of suicidal behavior, namely completed suicide and attempted suicide compared to both psychiatrically matched controls and to healthy volunteers. We have data on Axis I and Axis II diagnoses and data on lifetime aggression scores and current severity of depression to permit assessment of these potential etiological factors and potential behavioral endophenotypes. We have data on childhood reported histories of physical or sexual abuse which will be a focus for an exploratory gene-early environment interaction analysis. Causal SNPs will be further identified by sequencing the most promising gene segments. PUBLIC HEALTH RELEVANCE: The predisposition to suicidal behavior is substantially determined by genetic factors independent of those associated with major psychiatric disorders. This study will screen the genome in the largest collection of samples ever assembled for such a study of suicidal behavior in order to identify the responsible genes.
NIH	2009	Effectiveness of Suicide Hotline Training	GOULD, MADELYN	DESCRIPTION (provided by applicant): Crisis hotlines are one of the oldest suicide prevention resources in the United States, and are now ubiquitous sources of help worldwide. Yet, pervasive concerns exist about the clinical effectiveness of these services and the extent to which high-risk individuals are utilizing these resources. As such, we - from federal agencies to local communities - are relying on a relatively untested method of help for those individuals considered most at risk for suicide death. The current project is focusing on a situation of tremendous policy impact that has arisen: the National Suicide Prevention Lifeline's roll out (starting in winter of 2008) of a training program, using the LivingWorks' Applied Suicide Intervention Skills Training (ASIST), across its network of telephone crisis centers. A critical question to be answered by this resubmission is whether the training program is necessary, by virtue of its increasing the effectiveness of telephone crisis services. In recognition of the application 's policy import, due to the emergent use of hotlines and their expanded use by the Department of Veterans Affairs, as well as the innovativeness of the design, a one-year "NIH High Priority, Short-Term Project Award" (1R56MH082537-01) was granted to develop and implement the procedures that were planned for the first year of the study, including the commencement of data collection. The research protocol, timed to commence with NSPL's ASIST training, has randomized 18 centers to three training sessions (N= 6 centers per training) over a two year period, employing a dynamic wait-listed design for randomized trials (Brown et al., 2006). All 18 centers will receive the intervention, and the timing of the intervention is randomly assigned. Through the dynamic wait-listed design this will be the first controlled study of whether trained telephone crisis counselors adequately assess and refer callers. Assessments of each of the 18 centers commenced in June 2008 and will optimally conclude in December 2009. These assessments will include silent monitoring of calls linked to follow-up telephone interviews with callers (N = 1,920) to NSPL's 1-800 numbers. An assessment of the transfer/fidelity of the training will be incorporated into the design by the employment of "generation 1" trainer counselors' self-administered questionnaires, ratings of videotapes of the ASIST workshops they give to the "generation 2" counselors in their centers, and through the observation of calls via the silent monitoring. The dynamic wait-listed design will not be able to be completed without the funding of the current R01 application. The training of the 3rd cohort of 6 centers will not occur and data collection will have to end 9 months prematurely. This will clearly preclude our ability to address the aims of the study, needed to inform the future of the national network of telephone crisis services, which currently serves as the "safety net" for many national public health initiatives to prevent suicide and we will lose the rare opportunity for a research study to have such direct relevance to existing and future policy decisions. The roll out of the Applied Suicide Intervention Skills Training (ASIST) across the National Suicide Prevention Lifeline's network of telephone crisis centers and the expanded use of hotlines, particularly among the Department of Veterans Affairs and others, has prompted this application, which will answer whether the training program is necessary, by virtue of its increasing the effectiveness of telephone crisis services. This information is critically needed to inform decisions and plans regarding the optimization of a network of crisis services providing a "safety net" for imminently suicidal individuals. Few such opportunities arise for research studies to have such policy relevance, in other words, to have a direct impact on existing and future policy decisions.

NIH	2009	Course and risk factors for depression in late life	BOGNER, HILLARY	DESCRIPTION (provided by applicant): This application building on a randomized clinical trial carried out in primary care to study trajectories of depressive symptoms and medical comorbidity in relation to the outcomes of Major Depression and suicidal ideation at 2 years aligns with the NIMH Strategic Plan and is submitted in response to PA-07-082, "Risk factors for psychopathology using existing data sets," released 11 May 2007. Recent studies have demonstrated that a variety of primary care interventions can improve late life Major Depression outcomes. However, these interventions have not been found to be effective for minor depression. While some research has previously identified subtypes of depression, little work has focused on subtypes of late life depression, and that work has been conducted in cross-sectional data and not in the context of an intervention trial. The specific aims of this study are: (1) To identify subgroups of primary care elderly patients based on baseline characteristics and two different types of longitudinal profiles: 1) depressive symptoms and 2) overall medical comorbidity, and the association of subgroups with criterion-based Major Depression and/or suicidal ideation at 2 years; (2) To assess whether the different subgroups identified in Aim 1 on the basis of either depressive symptoms or overall medical comorbidity modify the effect of the collaborative care intervention on criterion- based Major Depression and/or suicidal ideation at 2 years, such that the intervention will show significant effects in certain subgroups; and (3) To assess how the effect modification of the intervention effect on criterion-based Major Depression or suicidal ideation at 2 years in Aim 1 is mediated by varying intensity of exposure to antidepressant medication or psychotherapy. To accomplish these aims, we will capitalize on screening, clinical assessment, treatment, and follow-up assessments which have occurred for up to 2 years in PROSPECT (the "Prevention of Suicide in Primary Care Elderly: Collaborative Trial"). In all, 1,226 patients, including all patients who screened positive for depression and a random sample of patients who screened negative, were enrolled in the 2-year longitudinal study. The primary care practices were randomized into: (1) treatment as usual by the primary care practice (n = 617 patients); and (2) a guideline management intervention consisting of antidepressant or psychotherapeutic treatment for depression following AHCPR guidelines, revised for the elderly, under the responsibility of the primary care physician who is assisted by a Masters-level specialist (the intervention condition; n = 609 patients). Among the sample of 1226 primary care elderly patients, we want to emphasize that our analysis will be based on course of depressive symptoms and not DSM-IV diagnoses. We propose to supplement PROSPECT data with medication records to classify and quantify medical comorbidity over the course of the 2-year follow-up interval. The foundation for the analysis to improve our understanding of the dynamic association of course of depressive symptoms and medical comorbidity will be the general growth curve mixture model (GGCMM). This project can have a significant public health impact because a further understanding of the association of the course of depressive symptoms and the onset and course of medical comorbidity among elderly primary care patients would be a key step in intervening to improve recognition and treatment of late life depression. PUBLIC HEALTH RELEVANCE: The overall goal of this application is to identify subgroups of primary care elderly patients, based on baseline characteristics and two different types of longitudinal profiles: 1) depressive symptoms and 2) overall medical comorbidity, for whom the collaborative care intervention reduces the persistence or onset of Major Depression and/or suicidal ideation. This project can have a significant public health impact because a further understanding of the association of the course of depressive symptoms and the onset and course of medical comorbidity among primary care elderly patients would be a key step in intervening to improve recognition and treatment of depression in late life.
NIH	2008	Religion and Suicidal Behavior Among Black Americans	JOE, SEAN	DESCRIPTION (provided by applicant): Remarkably little is known about protective factors that reduce Blacks' risk for suicide or attempted suicide. In particular, the link between religion and suicide risk reduction in blacks has never been demonstrated with a nationally representative sample, particularly one that also takes into account ethnic groups' differences. The death in suicide research among blacks is due primarily to not having data set with large enough numbers of black Americans from which to draw meaningful conclusions. The proposed research aims to provide a comprehensive examination of whether religious participation and spirituality are correlated with reductions in the risk for serious suicidal behavior (e.g., attempted suicide, suicide planning) in a nationally representative sample of 5,191 African Americans and Black Caribbeans. The public health significance lies in specifying religious factors related to lower suicide risk, which will inform subsequent suicide prevention interventions and strategies. The present study is designed to make four important contributions to the advancement of research on religion and spirituality's effects on suicidal behavior among African Americans, namely by: (1) capitalizing on the strengths of a large, nationally representative data set, the National Survey of American Life [NSAL]; (2) determining whether religiosity and spirituality are associated with reductions in the risk for suicide attempts and serious suicide planning by Blacks; and (3) investigating the relative effects of informal social support from both church members and family members on reductions in the risk for suicide attempts and serious suicide planning by Blacks. And whether and through what mechanisms informal social support (e.g., church and family social support) may moderate or mediate the pathways of religiosity to black suicidal behavior. The data analytic approaches to be used include regression, logistic regression, multi-nominal logistic regression, Cox proportional hazard model, and structural equation modeling. PUBLIC HEALTH RELEVANCE: The Institute of Medicine report (2002), "Reducing Suicide: A National Imperative," highlighted understanding the protective factors for suicidal behavior among Blacks, such as religion, as an emergent public health research priority.
NIH	2008	Prevention of Suicidality in College Students: A Common Core Process Approach	HAYES, STEVEN	DESCRIPTION (provided by applicant): Suicide and suicidality is a substantial public health problem among the 16 million college students in the United States: in a given year 9% seriously consider suicide and 1.3% reported having actually attempted suicide (American College Health Association, 2007). While treatment is helpful (Schwartz, 2006), 90% of those college students who commit suicide have never sought help within their institution (Gallagher, 2006). Prevention is a logical response, but few broad scale suicide prevention programs targeted specifically toward college students have been tested. Part of the problem is that suicidality is not just the end result of any one disorder it can be an aspect of a wide variety of problems including drug and alcohol abuse (Mean et al., 2005), affective disorders (Moscicki, 2001), anxiety disorders (Sareen, Houlahan, Cox, & Asmundson, 2005), thought disorders (Siris, 2001), problems in social relationships (Helliwell, 2007), and some physical health problems (e.g., Tang & Crane, 2006). There is substantial and growing evidence that experiential avoidance -- the tendency to avoid unwanted emotions and negative thoughts -- is a core common process that contributes to the diverse psychological and behavior problems that lead to suicidality and suicide (e.g., Hayes et al., 1996; Hayes, Strosahl, Wilson, Bissett, Pistorello et al., 2004). Acceptance and mindfulness-oriented interventions have been shown to reduce experiential avoidance and thereby reduce the common psychological problems that are predictive of suicidality (Hayes et al, 2006). This project proposes to evaluate an acceptance and mindfulness-based intervention Acceptance and Commitment Therapy (ACT; Hayes, Strosahl, & Wilson, 1999) -- in a randomized trial in which 720 18 to 20 year old college freshmen are assigned in three annual waves of 240 students each to receive either ACT or a didactic course on adjustment to the psychological challenges of college life. The impact of the intervention will be assessed on: (a) experiential avoidance, (b) a range of psychological, behavioral, health, and academic problems that are known to predict suicidality, and (c) the frequency or severity of suicidality, self-injury, suicide attempts, ER visits, and other risky behaviors. These processes and outcomes will be monitored for two to three years (depending on the wave of intervention). A preventive intervention for college students could be readily disseminated within the higher education structure, suggesting that a successful classroom-based preventative approach could have broad public health implications. PUBLIC HEALTH RELEVANCE: Suicide and suicidality among the nation's 16 million college students is a substantial public health problem (American College Health Association, 2007) that needs to be prevented. Because it is known that experiential avoidance -- the tendency to avoid unwanted emotions and negative thoughts -- is a core common process that contributes to the diverse psychological and behavior problems that lead to suicidality and suicide (Hayes et al., 1996; Hayes et al., 2004), the present project tests the impact of an acceptance and mindfulness-oriented intervention (Hayes et al., 1999) that has been shown to reduce experiential avoidance and thereby reduce the common psychological problems that are predictive of suicidality (Hayes et al 2006). If successful, a preventive intervention for college students could be readily disseminated within the higher education structure, giving such an approach broad public health implications.
NIH	2009	Citalopram in First Episode Schizophrenia	GOFF, DONALD	DESCRIPTION (provided by applicant): Depressive symptoms are common early in the course of schizophrenia and are associated with poor quality of life, relapse, and suicidality. As a result, selective serotonin reuptake inhibitors (SSRIs) are frequently prescribed, but their efficacy in first episode patients has not been studied. In a naturalistic study, prodromal patients treated with antidepressants were significantly less likely to progress to schizophrenia. SSRIs release brain derived neurotrophic factor (BDNF) which protects neurons from stress and stimulates neurogenesis. In schizophrenia, BDNF is dysregulated and BDNF genotype has been shown to predict cortical grey matter loss in first episode patients. These findings suggest that SSRI administration might protect against depression, relapse, and disease progression during the early course of the illness. Methods: We propose, in 100 first episode schizophrenia patients, a placebo-controlled, parallel-group, twelve month trial of citalopram added to risperidone treatment plus a psychoeducation protocol designed to enhance compliance and retention. Patients with significant depression or currently treated with an SSRI will be excluded from study and a CBT module targeting depression will be provided if depressive symptoms emerge during the trial. The primary outcome is depressive symptoms analyzed as the area under the curve per unit time. In addition, we will examine suicidality, negative symptoms, cognition, and relapse rates. Biomarkers will include BDNF Val66Met genotype, plasma BDNF concentrations, and gray matter volume to assess a possible relationship between SSRI treatment, enhanced BDNF activity, preservation of cortical gray matter, and improved clinical course. Significance: The evaluation of SSRI treatment for depressive symptoms, suicidal ideation and relapse in first episode patients is of considerable clinical importance. In addition, the potential role of SSRI-induced BDNF release in promoting neurogenesis and improving the course of the illness offers an exciting new direction for the pharmacology of schizophrenia.

NIH	2010	SSRIs and Self-harm in Borderline Personality Disorder	COCCARO, EMIL	DESCRIPTION: Suicide and lesser forms of intentional self-harm behaviors produce devastating medical, social and economic costs. Self-harm is integrally related to depressive disorders and Borderline Personality Disorder. Selective Serotonin Reuptake Inhibitors (SSRIs), like escitalopram, are front-line pharmacological treatments for these disorders, putatively regulating depressed mood and reducing suicidality. However, data from case studies and retrospective meta-analyses of depression clinical trials is mixed, with some (but not all) studies suggesting that during the first months of treatment, SSRIs may increase the risk of suicidal ideation in select individuals, particularly younger individuals. These post-hoc analyses, though informative, are based on studies that provide limited sampling of the self-harm domain. No study, to date, has implemented a direct prospective examination of the effects of early SSRI use on self-harm thoughts and behaviors using a multi-method measurement involving both the laboratory (standard self-aggression paradigm: SAP) and home environments (ecological momentary assessment: EMA). Also, no study has examined the influence of impaired 5-HT function and emotion dysregulation as moderators of outcome with escitalopram. The proposed randomized clinical trial will prospectively assess the impact of eight weeks exposure to SSRI treatment on self-harm ideation and behavior among a sample of 200 subjects with Borderline Personality Disorder and current major depression. After a one week single-blind placebo lead-in, participants will be randomly assigned double blind to either placebo or escitalopram for eight (8) weeks. The primary dependent variable will be EMA of self-harm ideation and behavior obtained several times each day. Self-harm will also be assessed using a laboratory analogue task (SAP) at baseline and again after the eight week trial. Age will be evaluated as a moderator of SSRI response. 5-HT dysfunction and emotion dysregulation will be evaluated as candidate moderators of SSRI response. 5-HT functioning will be assessed using psychophysiological (loudness dependence of the auditory evoked potential: LDAEP) and genetic (5-HT transporter promoter polymorphism: 5-HTTLPR) markers. Measures of emotion dysregulation will include trait aggression, impulsivity and socioemotional information processing. At the conclusion of the eight-week randomized trial, all participants will receive eight weeks of escitalopram administered single-blind, with continued EMA and other assessment. PUBLIC HEALTH RELEVANCE: The proposed randomized clinical trial will prospectively assess the impact of 8 weeks exposure to SSRI treatment on self-harm ideation and behavior among a sample of 200 subjects with Borderline Personality Disorder and current major depression. After a one week single-blind placebo lead-in, participants will be randomly assigned double blind to either placebo or escitalopram daily for eight (8) weeks. The primary dependent variable will be EMA of self-harm ideation and behavior obtained several times each day. Selfharm will also be assessed using a laboratory analogue task (SAP) at baseline and again after the eight week trial. Age, 5-HT dysfunction and emotion dysregulation will be evaluated as potential moderators of SSRI response.
NIH	2010	Suicide attempts and unintentional injury among older Americans on psychotropics	Miller, Matthew	DESCRIPTION (provided by applicant): The proposed cohort study will use a large health care utilization data set and novel pharmacoepidemiologic methods to determine whether the risk of injury from falls, motor vehicle crashes, and suicidal behavior applies equally to all antidepressant (and antipsychotic) classes -- or whether there are particular regimens of antidepressants (and antipsychotics) with safety advantages that should be prescribed preferentially. Analyses will examine how the risk of injury depends on socio-demographic factors, co-morbidity, co-medication, dose and duration of use. The proposed study addresses many of the limitations of prior observational work, including failure to account for dose-related effects, duration of use, confounding by indication, physician channeling bias, and distortions resulting from prevalent user designs. Data for the current application comprise information about prescription drug use and both medical and psychiatric conditions (including unintentional injuries and suicide attempts) for an annual population of over 15 million beneficiaries aged 50 years and older who received prescription drug benefits from managed care plans throughout the United States, 1997-2009. Descriptive analyses comparing the risk of unintentional injury among patients taking antidepressants or antipsychotics to those not (aim1) will place in context the two key aims of this application: to compare the risk of injury due to falls, motor vehicle crashes, and suicidal behavior (the leading causes of injury deaths in older Americans) among initiators of 1) SSRI vs. TCA vs. SNRI antidepressants (aim 2), and 2) conventional vs. atypical antipsychotics (aim 3). The proposed research responds to the NIMH's Strategic Objective 4: "Strengthen the Public Health Impact of NIMH-Supported Research". The proposed series of comparative studies on treatment emergent injury-related outcomes will advance understanding of the public health influence of the most common strategies used today to treat mental illness among older Americans. Because the therapeutic superiority of particular antidepressant (and antipsychotic) preparations have not been established for the conditions these agents are commonly prescribed to treat, 1-5 the potential clinical and possibly economic benefits of the proposed work could be large, since use of these agents is common and the consequences of injuries due to falls, motor vehicle crashes, and suicidal behavior are particularly untoward among older adults. PUBLIC HEALTH RELEVANCE: The current application will use novel pharmacologic methods and a large health care data set of Americans aged 50 and older to determine whether the risk of injury from a) falls, b) motor vehicle crashes, and c) suicidal behavior applies equally to all antidepressant (and antipsychotic) classes -- or whether there are particular regimens of antidepressants (or antipsychotics) with safety advantages that should be prescribed preferentially. Analyses will examine whether, and if so, how the risk of injury depends on socio-demographic factors, co-morbidity, co-medication, dose and time since starting an antidepressant or antipsychotic.
NIH	2009	Stress Responses as Prospective Predictors of Girls' Suicidality and Self-Injury	PRINSTEIN, MITCHELL	DESCRIPTION (provided by applicant): Especially among girls, the adolescent transition is associated with dramatic increases in the prevalence of suicidal ideation, and several forms of self-injury, including non-suicidal self-injury (NSSI; i.e., self-mutilation), suicidal gestures, threats, and attempts. This study proposes, and will test a theoretical model suggesting that biological and cognitive responses to social stressors explain the association between psychopathology (i.e., depression) and self-injury (i.e., mediation) and that specific interactions between stress responses (i.e., moderation) will help identify which girls with psychopathology are most likely to engage in self-injury longitudinally. Specific combinations of cognitive and biological stress responses are proposed to uniquely identify risks for different types of self-injury/suicidality (i.e., NSSI vs. suicidal ideation). Moreover, this study will examine trajectories of, and associations among self-injury constructs, addressing several limitations of past work. The aims of this research thus address several of the goals outlined in PA # 07-079, Research on the Reduction and Prevention of Suicidality as well as many of the goals articulated the NIMH Strategic Plan (NIMH, 2008) and the NAMHC Workgroup report on Transformative Neurodevelopmental Research (NAMHC, 2008). This study will use an innovative, lab-based methodological paradigm to examine cognitive (i.e., attributions, social problem solving) and biological (i.e., neuroendocrine, cardiovascular) responses to an in vivo social stressor. Participants will include 250 female adolescents from both outpatient and inpatient clinically-referred samples. Data will be collected from multiple informants (adolescents, parents) and multiple sources (observational methods, structured interviews, questionnaires, biological assays). It is expected that observed stress responses in the lab will interact with the experience of actual social stress measured during follow-up to predict self-injury trajectories over an 18 month interval. In other words, this study will address long-standing, but under-explored questions regarding why and how psychological symptoms, and/or the experience of stress, are associated with self-injurious behaviors. PUBLIC HEALTH RELEVANCE: Although much research has indicated that adolescents with a history of psychopathology are at increased risk for self-injury (e.g., self-mutilation; suicide attempts), little is known about why or how psychological symptoms lead to self-injury. Thus, there are few directions for evidence-based prevention/intervention. This research will examine specific psychological and biological responses to social stress that may increase the risk for girls' self- injury, and help to elucidate the development of self-injurious behaviors by exploring the course of these behaviors across a sensitive and critical developmental period.

NIH	2010	Identifying cognitive markers of late-life suicide	Szanto, Katalin	DESCRIPTION (provided by applicant): Although depression commonly precedes late-life suicidal behavior, clinicians still cannot confidently identify depressed elderly who are most likely to attempt or die by suicide. Thus, there is a great need for better predictive models regarding suicidal behavior in the elderly. This revised R01 (MH085651) application is to investigate specific cognitive vulnerabilities to late-life suicidal behavior. We focus on features that may cause accumulation of stressors, undermine deterrents, and facilitate the final decision to take one's life. Our preliminary data indicate that deficits in (1) specific aspects of cognitive control that involve reward/punishment processing, and in (2) social cognition distinguish depressed elderly suicide attempters from depressed non- suicidal elderly, while the two groups show similar global cognition, working memory, and forward planning. Building on this preliminary evidence, this new-investigator R01 will include key cognitive probes in a large- enough sample to test hypotheses that impairments in decision-making, affective processing, reversal learning, and social cognition are specifically associated with suicide attempts in depressed elders. We propose to assess 100 suicide attempters, 80 non-suicidal depressed individuals, and 60 non-psychiatric control subjects, aged 60 and older, using theory-driven computerized assessments as well as traditional tests of cognitive performance. Participants will undergo extensive clinical characterization of their suicidal behavior, psychopathology, psychosocial stressors, physical health, possible brain injury from suicide attempts, and medication exposure. The three groups will be similar in demographic characteristics and medical illness burden, and the two depressed groups will have similar severity of depression. To determine whether the identified impairments persist over time despite changes in mood state, we will repeat cognitive assessments four months after baseline (when substantial clinical improvement can reasonably be anticipated based on our pilot data). We will also prospectively explore the effect of cognitive status on suicide-related outcomes during this follow-up period. In collaboration with the biostatistical team of our late-life depression center and our external statistical consultant, we propose to use multivariate analyses of covariance to compare cognitive functions across groups, as well as discriminant function analysis to create a compact cognitive battery and to test its utility for correctly identifying suicide attempters beyond known risk factors. We will use mixed effects models to examine stability of cognitive impairments across mood states. Statistical analysis will account for factors that may affect cognition: severity of depression, medical illness burden, serum anticholinergicity, and other relevant factors identified by preliminary analyses. This project builds upon an ongoing K23, where the PI has shown the feasibility of recruiting, assessing, and longitudinally following suicidal elders with a high rate of suicidal behavior during follow-up. The research project will be conducted at the University of Pittsburgh, in collaboration with the Experimental Psychology Department, University of Cambridge. PUBLIC HEALTH RELEVANCE: Understanding cognitive deficits associated with late-life suicidal behavior and their relationship to other risk factors may help to advance translational neuroscience in geriatric mental health, identify elderly people at risk for suicide, and help to develop individualized treatment strategies in the service of preventing suicide in older people, who have the highest suicide rate in the US. The compact cognitive battery for assessing suicide risk derived from this research can be used in future prospective studies and in clinical settings.
NIH	2009	Understanding Social Contributions to Disparities in Depression Care: US and UK	Roter, Debra	DESCRIPTION (provided by applicant): Physicians' ability to communicate effectively with patients from ethnically and socially diverse backgrounds is essential to reducing health disparities. However, communication is not solely the task of medical professionals, patients also play a critical role in active participation in their care and in gaining the necessary confidence and competence to implement and continue treatment. The disparities that are evident within medical care reflect the interplay of social factors, including race, gender, age, literacy, and the cultural and normative expectations that guide the perspectives of both patients and physicians. The proposed investigation is designed to contribute to the disentangling of physician-derived and patient-derived contributions to social bias that may exacerbate health disparities associated with the provision and receipt of depression care and suicide risk assessment in the US and UK. In order to do so, we propose a novel approach in which videotape simulations are used to portray a depression -focused visit in primary care in which the ethnicity and gender of the participants have been experimentally manipulated. While sharing the context of a medical visit, the simulations differ in focus; one is designed to examine physicians' cognitive and clinical reasoning processes while the other explores patients' perceptions, responses and judgments related to the receipt of care. In the first study (for which data are already collected), visit simulations were shown to 128 US and UK physicians who were asked to take the role of the treating physician and provide a narrative account of their clinical reasoning. The second study shows simulated depression visits, in which patient and physician gender and ethnicity is experimentally manipulated, to 640 ethnically diverse male and female subjects in the US and UK. Subjects vicariously take the role of the depressed patient in the simulations to provide insights into their cognitive and affective reactions to care. In this way, we will be able to explore how subjects acting as analogue patients and physicians are influenced by gender and ethnicity in making medical care judgments in the context of the US and UK health care system and social structure. Study 3 will test the ecological validity of the analogue findings through the analysis of actual patient data in which physicians from different ethnic backgrounds have assessed patients' depression and suicide risk in an anonymised database. PUBLIC HEALTH RELEVANCE: ability to communicate effectively with patients from ethnically and socially diverse backgrounds is essential to reducing health disparities. However amelioration of disparities is not solely the task of medical professionals: patients also play a critical role in active participation in care and acquisition of the confidence and competence necessary to implement and continue treatment. The proposed investigation is designed to contribute to the disentangling of physician-derived and patient-derived contributions to social bias that may exacerbate health disparities associated with the provision and receipt of depression care and suicide risk in the US and UK so that more effective interventions may be designed and implemented.
NIH	2011	Cognitive Therapy for Suicidal Older Men	BROWN, GREGORY	DESCRIPTION (provided by applicant): There is a pressing need for clinical trials to test the efficacy of innovative treatments for persons at high risk for suicidal behavior. Men, 60 years of age and older, constitute one of the highest risk demographic groups for suicide in the United States. Yet, despite such statistics, there has been a very limited public health response that has specifically targeted this group for suicide prevention initiatives. One of the major roadblocks to addressing this profound public health problem involves the lack of evaluating innovative treatments that have been developed to reduce suicide risk specifically for this population. Therefore, the primary aim of the proposed study is to compare the efficacy of cognitive therapy (CT) with the efficacy of an enhanced usual care (EUC) intervention for reducing the rate of suicide ideation (SI) and the severity of depression and hopelessness among older men. Men who are 60 years or older and have reported an intent or desire to commit suicide in the month prior to screening will be recruited from the local health care systems. A total of 122 enrolled participants will be randomly assigned to receive either the CT or EUC condition. Patients in the CT condition will receive 12 to 16 weekly individual CT sessions plus 3 booster sessions. The CT intervention was developed to reduce SI as well as other psychosocial risk factors for suicide and focuses on an assessment of the participants' motivation for suicide, the development of an individualized safety plan to mitigate suicide risk, the development of a cognitive conceptualization of the presenting problems, improving patients' problem solving skills, facilitating treatment compliance, applying other cognitive and behavioral strategies to reduce suicidal crises, and increasing participants' reasons for living. Patients in the EUC condition will receive 12 to 16 weekly telephone calls, each approximately 15-30 minutes in duration, from the study therapists. The purpose of these calls will be to ensure patient safety and to provide some support. Patients in both study conditions will be allowed to receive usual medical care as practiced in the community and will receive assessment, referral, and crisis intervention services provided by the project staff. Study assessments of SI, depression, hopelessness, and other potentially relevant covariates or confounds will be conducted at baseline, and at 1, 3, 6, 9, and 12 months follow-up points. All study assessments will be administered by assessors who are blind to the assigned treatment condition. Participants in the CT condition are hypothesized to have lower rates of SI during the follow-up period than participants in the EUC control condition. In addition, participants in the CT condition are hypothesized to have lower levels of hopelessness and depression during the follow-up period than participants in the EUC control condition. Analyses will be conducted to test these hypotheses as well as to explore how post-baseline factors mediate or baseline factors moderate the effect of the CT treatment on outcomes. PUBLIC HEALTH RELEVANCE: Men, 60 years of age and older, constitute one of the highest risk demographic groups for suicide in the United States. Yet, despite such statistics, there has been a very limited public health response that has specifically targeted this group for suicide prevention initiatives. One of the major roadblocks to addressing this profound public health problem involves the lack of evaluating innovative treatments that have been developed to reduce suicide risk specifically for this population.

NIH	2010	2/2-Personalized Antidepressant Adherence Strategies for Depressed Elders	Kales, Helen	DESCRIPTION (provided by applicant): The goal of this proposed collaborative R01 randomized controlled trial is to test the effectiveness of a novel intervention, the Treatment Initiation and Participation (TIP) program, on depression treatment adherence and depression outcomes among geriatric primary care patients. TIP is a brief, psychosocial intervention aimed at reducing the multifaceted personal barriers to adhering to depression treatment. Adherence is a challenge across the lifespan, but among older adults with depression, this challenge is compounded by medical and psychiatric co-morbidity, medical regimen complexity, and skeptical attitudes towards mental illness and its care. For older adults, the effect of stigma on seeking care for mental health issues such as depression is particularly strong. The decision to begin treatment for depression entails both countering the ageist notion that depression is a normal outgrowth of aging and confronting the stigma of mental health treatment particularly prevalent in this cohort. The treatment gap created by non-adherence in later life is becoming an even more prominent issue as the nation's demographic profile shifts. The proposed RCT will be conducted with diverse community samples from two geographically complementary primary care centers (Ann Arbor, Michigan and New York City). The study will recruit 260 older adults who have been newly prescribed antidepressant medication by their primary care physician, and randomize participants to receive either the TIP intervention or usual care. To test the study hypotheses, research assessments will be conducted at study entry, and at 6, 12 and 24 weeks after enrollment. If the proposed intervention is useful in improving antidepressant adherence, it has the potential to decrease the deleterious effects of untreated depression in a growing number of older adults. As a brief manualized intervention, TIP-PC is designed to fit easily within primary care practices and to be delivered by non-MD staff. PUBLIC HEALTH RELEVANCE: Depression and its treatment in later-life presents many challenges for the growing number of older adults in our society; beyond personal suffering, untreated depression worsens the outcomes of many medical illnesses and increases the risk for falls, cognitive decline, and death. Older adults experience many barriers that interfere with their choice or ability to follow the treatment their doctor recommends. The purpose of this research is to test a personalized and flexible primary care-based program designed to help patients experience successful depression treatment.
NIH	2010	1/2-Personalized Antidepressant Adherence Strategies for Depressed Elders	SIREY, JO ANNE	DESCRIPTION (provided by applicant): The goal of this proposed collaborative R01 randomized controlled trial is to test the effectiveness of a novel intervention, the Treatment Initiation and Participation (TIP) program, on depression treatment adherence and depression outcomes among geriatric primary care patients. TIP is a brief, psychosocial intervention aimed at reducing the multifaceted personal barriers to adhering to depression treatment. Adherence is a challenge across the lifespan, but among older adults with depression, this challenge is compounded by medical and psychiatric co-morbidity, medical regimen complexity, and skeptical attitudes towards mental illness and its care. For older adults, the effect of stigma on seeking care for mental health issues such as depression is particularly strong. The decision to begin treatment for depression entails both countering the ageist notion that depression is a normal outgrowth of aging and confronting the stigma of mental health treatment particularly prevalent in this cohort. The treatment gap created by non-adherence in later life is becoming an even more prominent issue as the nation's demographic profile shifts. The proposed RCT will be conducted with diverse community samples from two geographically complementary primary care centers (Ann Arbor, Michigan and New York City). The study will recruit 260 older adults who have been newly prescribed antidepressant medication by their primary care physician, and randomize participants to receive either the TIP intervention or usual care. To test the study hypotheses, research assessments will be conducted at study entry, and at 6, 12 and 24 weeks after enrollment. If the proposed intervention is useful in improving antidepressant adherence, it has the potential to decrease the deleterious effects of untreated depression in a growing number of older adults. As a brief manualized intervention, TIP-PC is designed to fit easily within primary care practices and to be delivered by non-MD staff. PUBLIC HEALTH RELEVANCE: Depression and its treatment in later-life presents many challenges for the growing number of older adults in our society; beyond personal suffering, untreated depression worsens the outcomes of many medical illnesses and increases the risk for falls, cognitive decline, and death. Older adults experience many barriers that interfere with their choice or ability to follow the treatment their doctor recommends. The purpose of this research is to test a personalized and flexible primary care-based program designed to help patients experience successful depression treatment.
NIH	2011	1/2-Treatment of Suicidal and Self-Injurious Adolescents with Emotional Dysregula	LINEHAN, MARSHA	DESCRIPTION (provided by applicant): The long term aim of our research is to develop and evaluate effective treatments for adolescents at high risk for suicide that will reduce suicidal and self-injurious behaviors as well as improve functioning and the quality of life of teens and their families. The primary aim of the research proposed here is to evaluate the efficacy of dialectical behavior therapy (DBT) for adolescents by comparing it to a combined individual and group supportive therapy control condition (I/GST) chosen specifically to maximize internal validity. Subjects will be 170 teens 13-17 years old with borderline personality traits referred to treatment due to high risk for suicide. Outcome targets include reduced frequency and severity of suicidal behaviors, especially suicide attempts, inpatient or ER treatment for suicidality, increased maintenance in and compliance with treatment, and enhanced functioning across multiple domains. DBT has an empirical track record with adults of reducing the incidence, frequency and medical risk of suicide attempts and non-suicidal self-injuries among individuals meeting criteria for borderline personality disorder (BPD). However, although DBT is widely used with suicidal adolescents, particularly those with difficulties characteristic of BPD such as poor emotion regulation and impulse control, no randomized trial of DBT with adolescents has been conducted. Thus, although non- randomized trials suggest effectiveness, without a randomized trial we simply do not know whether DBT for adolescents is efficacious or not. Given the severity of the problem and the lack of alternative treatments for high risk adolescents, addressing this question is important. The second aim of this research is to analyze mediators of reduced suicidal and self-injurious behaviors in adolescents. DBT is based on a theoretical model that suicidal behavior is a combined outcome of high stressful events and emotion dysregulation together with inadequate behavioral skills for coping with negative emotions and life events. Risk factors for adolescent suicide and intentional self-injury include most importantly family conflict but also conflict with peers, teachers, losses, legal or disciplinary problems (stressful events) combined with high negative emotions and inadequate abilities in emotion regulation. We will analyze the potential mediating effects on suicidal behaviors of decreases in family conflict, increases in parent DBT behavioral skills, reductions in emotion dysregulation and increases in DBT behavioral skills. Preliminary data on cost-effectiveness will also be collected. PUBLIC HEALTH RELEVANCE: The primary aim of the research proposed here is to evaluate the efficacy of dialectical behavior therapy (DBT) for adolescents by comparing it to individual and group supportive therapy control condition (I/GST) chosen specifically to maximize internal validity. Subjects will be teens 13-17 years old referred to treatment due to high risk for suicide. Outcome targets include reduced frequency and severity of suicidal behaviors, increased maintenance in and compliance with treatment and enhanced functioning across multiple domains.
NIH	2011	Lithium's Molecular Mechanism of Action and the Pathology of Bipolar Disorders	Parsey, Ramin	DESCRIPTION (provided by applicant): Bipolar disorder (BPD) is a brain disorder characterized by recurrent manic and major depressive episodes with a one year prevalence rate between 1-2%.1 BPD ranked 20th in terms of causes of loss of disability- adjusted life-years in 19992 and is associated with a life time suicide risk of up to a 19%.3 The main burden of illness in BPD is in the depressive pole. A deficiency of serotonin (5-HT) function has been postulated to underlie depressive episodes yet few studies have examined indices of 5-HT neurotransmission in the brain in BPD. It is widely acknowledged that there are significant gaps in the current identification and treatment of bipolar depression.5-8 Better understanding of the neurotransmission deficits in BPD may aid diagnosis, identification of biomarkers and treatment targets to facilitate treatment development and ultimately to assist in treatment selection. Our preliminary data with [11C]DASB shows lower binding in BPD. We propose to determine the extent and nature of abnormalities in 5-HTT binding in vivo using positron emission tomography (PET) in medication-free bipolar I depression. We hypothesize that BPD has lower 5-HT binding compared to controls. We will also investigate the 5-HT effects of a common treatment for BPD, lithium. Discovered decades ago, lithium remains one of the few effective treatments in BPD, with evidence of mood stabilizing, antidepressant, antisuicidal, and even neuroprotective qualities and is considered to be first line treatment. The actions of lithium on 5-HT indices may be central to its antidepressive and antisuicidal properties. We hypothesize that lithium downregulates presynaptic 5-HT1A receptor binding, upregulates postsynaptic 5-HT1A binding, upregulates 5-HTT binding, and these molecular effects will be related to clinical improvement, both in depression and suicidality. 5-HT1A binding potential will be determined using [11C]WAY 100635. We propose to perform [11C]DASB and [11C]WAY 100635 scans in 38 medication free BPD I subjects during a major depressive episode and compare 5-HTT and 5-HT1A binding potential in 38 healthy volunteers. We will also examine the diagnostic specificity of lithium response by studying 10 unipolar depressed subjects in an identical manner. We will examine the pharmacological specificity of lithium by studying lamotrigine in BPD subjects. Finally, we will also assess the ability of baseline scanning to predict treatment response. All BPD subjects will be treated with lithium and have repeat scans with both radiotracers. Many with BPD do not tolerate lithium's side effect burden, and it has a narrow therapeutic window. In this grant period we will determine at which 5-HT protein(s) lithium exerts its antidepressant and antisuicidal properties. Ultimately this can lead to novel therapeutics that are better tolerated. We will independently advance our understanding of the molecular pathophysiology of BPD as well as characterize the mechanisms of action of lithium. PUBLIC HEALTH RELEVANCE: Bipolar disorder or manic depressive illness is a very common and devastating brain illness. Very little is known about the biological basis of this illness and less is known about the mechanism of action of our commonly prescribed medications. With this proposal we will significantly increase our understanding of both the illness and its treatment using state of the art brain imaging technologies.

NIH	2011	Attachment-Based Family Therapy for Suicidal Adolescents	DIAMOND, GUY	DESCRIPTION (provided by applicant): Suicide is the third leading cause of death for American adolescents. Nearly one million adolescents a year attempt suicide and about 500,000 adolescents a year are admitted to psychiatric hospitals for suicide attempts or serious suicidal ideation. This leads to high emotional costs for families and financial cost for the health system. Yet, no medication, and less than 10 psychotherapy studies have focused on suicidal youth and findings are mixed. Brent (2006) and Jensen's (2006) call for new and innovative approaches for depression treatment highlights the need for alternative interventions for suicidal youth as well. Attachment-Based Family Therapy (ABFT) offers a promising alternative to prior treatments. It is a manualized family therapy targeting processes associated with suicide and depression. ABFT seeks to improve the adolescent-caregiver relationship by increasing the family's capacity for discussing and negotiating affectively charged issues in the relationship. Improvements in the attachment relationship provide adolescents with improved capacity for affect regulation and the ability to use the caregiver as a source of protection and support. These strengths buffer adolescents against suicide and other risk behaviors. Four studies have demonstrated that ABFT can reduce suicidal ideation and depressive symptoms with an average effect size of .97. Unfortunately, interpretation of these studies is compromised by lack of a controlled comparison treatment. This study aims to test the efficacy of ABFT using a comparison group that controls for treatment dose, duration, therapist expertise, ecological factors, and family involvement. The study includes one year follow-up data, assessment staff blind to treatment condition and tests of the purported active ingredients of ABFT. Putative change processes will be tested including: a) adolescents' expectancies for parent availability, b) emotion regulation during parent-adolescent conflict discussions, and c) resolution of loss and abuse. To test this, Dr. Kobak, a leading adolescent attachment researcher, will use the Adult Attachment Interview and observational coding of the family interaction task to test these treatment mechanisms. If successful, the findings will provide evidence for both the efficacy and specificity of a family based treatment mechanism. We will recruit and randomize 130 adolescents to 16 weeks of ABFT or Family Enhanced-Non-directive Supportive Therapy (FE-NST). Assessments will be conducted at baseline, 8, 16, 32 and 52 weeks. The primary and secondary aims assess whether ABFT reduces suicidal ideation, depression, family conflict, and future suicide attempts more effectively than control. Exploratory aims test a) whether ABFT can improve parent-adolescent attachment, b) if attachment mediates outcome, and if a history of trauma, parental depression or family conflict moderate outcome. The study targets adolescents with severe and persistent suicidal ideation selected from inner city, minority youth. PUBLIC HEALTH RELEVANCE: Adolescent suicide is the third leading cause of death in adolescents and over one million adolescent a year attempt suicide, yet there are few effective treatments for preventing this serious public health problem. Building on very promising pilot data, this study will test the efficacy of Attachment Based Family Therapy for reducing the risk factors that are highly predictive of future suicide: suicide ideation, depression, and family conflict. The treatment model aims to achieve this goal by strengthening and or repairing the appropriate parent-adolescent attachment bond so that adolescents are more likely to turn to parents for support and protection the next time they feel suicidal.
NIH	2011	1/2-CBT Versus Supportive Psychotherapy for Body Dysmorphic Disorder	Wilhelm, Sabine	DESCRIPTION (provided by applicant): Body dysmorphic disorder (BDD) is a severe, often chronic, and common disorder consisting of distressing or impairing preoccupation with imagined or slight defects in appearance. Individuals with BDD have very poor functioning and high rates of hospitalization and suicidality. The rate of completed suicide, while preliminary, appears markedly high. A majority of patients receive surgical, dermatologic, or dental treatment for BDD, which is usually ineffective. Our prior work has shown that SRIs are often efficacious for BDD, but patients may not agree to try medication or may not benefit from it. Thus, there is a critical need for an efficacious psychosocial intervention for this severe disorder. Because BDD differs in important ways from other disorders, psychotherapies for other disorders are not adequate for BDD. There is no adequately tested psychosocial treatment of any type for BDD. An evidence-based treatment for this unique disorder is greatly needed. Cognitive-behavioral therapy (CBT) is the only psychosocial treatment for BDD that is fully developed and now ready for formal testing. Data from case series and studies using waitlist controls suggest that BDD- specific CBT is very promising for BDD. With an R34 grant, we developed a personalized, modular, manualized CBT treatment (CBT-BDD) that specifically targets BDD's unique and complex symptoms. The R34 study, which used a waitlist control group, suggests CBT-BDD is acceptable to patients, feasible to implement, and appears efficacious for BDD, associated symptoms, and functional disability. However, no study has adequately tested CBT's efficacy for BDD -- for example, by comparing it to another treatment that controls for therapist time, attention, and other non-specific treatment elements. Thus, there is a pressing clinical and public health need to test the most promising psychosocial treatment for BDD. This Collaborative R01 application's primary aim is to conduct the first study to adequately examine the efficacy of CBT for BDD. This study will compare our personalized and manualized CBT-BDD to manualized supportive psychotherapy (SPT). SPT appears to be the psychosocial treatment most often used for BDD, yet it appears to have a low response rate. Massachusetts General Hospital/Harvard Medical School and Rhode Island Hospital/Brown University will randomize 120 adults to CBT-BDD or SPT over 24 weeks followed by 3- and 6-month follow-up assessments. The primary outcome will be change in BDD severity assessed by a blinded Independent Evaluator. Secondary aims will examine change in depressive symptoms, delusionality of BDD beliefs, psychosocial functioning, and quality of life, as well as predictors of improvement in BDD. The United Kingdom's National Health Service treatment practice guideline on BDD and a Cochrane Collaboration review on BDD underscore the dearth of treatment research and call for more intervention research on BDD. The proposed study will fill a major gap in knowledge and patient care by conducting the first adequate test of any psychosocial treatment for a unique, disabling, common, and understudied disorder. PUBLIC HEALTH RELEVANCE: Body dysmorphic disorder (BDD) is a severe and common disorder characterized by high levels of functional impairment and markedly high rates of suicidality. The proposed study will be the first to adequately test the efficacy of the most promising psychosocial treatment for BDD -- cognitive behavioral therapy that specifically targets BDD's unique symptoms (CBT-BDD). Consistent with the NIMH strategic plan, we will test a new and personalized treatment for severely ill and suffering patients for whom no adequately tested psychosocial treatment of any type exists.
NIH	2011	Risk and Protective Factors for Suicide among Sexual Minority Youth	Grossman, Arnold	DESCRIPTION (provided by applicant): The risk for suicide is a major health concern for lesbian, gay, bisexual, and transgender (LGBT) youth. We propose a longitudinal study to recruit and follow a diverse sample of 1160 LGBT youth aged 15 to 21 youth from community-based organizations in three metropolitan areas across the United States. We will use snowball and respondent-driven sampling to increase the number and diversity of the participants. The youth will be assessed four times, post baseline, over a three-year period. These assessments will allow us to determine changes in constellations, magnitudes, and developmental sequences of risk and protective factors for suicidal behaviors with a particular emphasis on the major components of the interpersonal psychological theory of suicide: thwarted belongingness, perceived burdensomeness, and the capacity for self-lethal injury. We will simultaneously document whether or not risk and protective factors for suicide are uniquely related to LGBT youths' developmental milestones. Our emphasis will be comparing LGBT youth who do and do not experience any suicidal behaviors, i.e., ideation, threats, and serious attempts. Documenting the protective factors of the youth who emerge with positive psychological adjustment is crucial to the generation of knowledge of those youth whose adjustment is compromised by LGBT-related experiences emanating from society's negative view of youth who do not conform to sexual and gender role expectations. The knowledge we generate will allow us to more accurately assess LGBT youth at risk for suicidal behaviors, identify those risk factors that are malleable to change at various developmental milestones, and to create preventive messaging and intervention models that simultaneously increase protective factors and reduce risk factors. PUBLIC HEALTH RELEVANCE: Studies have repeatedly found higher rates of suicidal behaviors among lesbian, gay, bisexual, and transgender (LGBT) youth than their heterosexual peers. Recent studies have also found that compared to prior cohorts, contemporary LGBT youth are increasingly aware of, identifying and disclosing their sexual and gender identities earlier in their developmental trajectories; these factors have been related to suicidal risk factors such as bullying, harassment, marginalization, and victimization by family members and peers. As society has not been able to change the negative experiences that lead to suicidal behaviors among some LGBT youth, we need to provide public and mental health workers with evidenced-based research so that they can identify and enhance protective factors while simultaneously reducing malleable risk factors for suicidal behaviors when working with LGBT youth.

NIH	2010	Effectiveness trial of youth suicide prevention delivered by teen peer leaders	WYMAN, PETER	DESCRIPTION (provided by applicant): This project responds to the need for (1) scientifically rigorous evaluations of interventions to prevent suicide in adolescents, and for (2) school-based suicide prevention programs that are suitable for rural and underserved communities where there is a scarcity of mental health services. Suicide accounts for more deaths among 10 - 24 year olds in the US than all natural causes combined; each year 5 - 9% of adolescents attempt suicide and 700,000 require medical attention. In most rural regions, adolescent suicide rates are 2 - 10 times above the US national average. This proposal seeks RO1 funding for a randomized controlled trial to evaluate the effectiveness of the Sources of Strength (SoS) intervention in reducing rates of attempted suicide among adolescents in rural communities. SoS builds social-ecological protective influences across a full population of high school students to reduce the likelihood that vulnerable youth will become suicidal and connects suicidal youth to capable adults at school and in the community. Trained 'peer opinion leaders' change the norms of students throughout their schools regarding the acceptability of suicide, help-seeking and youth-adult communication by conducting a set of well-defined messaging activities with ongoing adult mentoring. This approach draws on the major influence of adolescent peers that is powerful enough to affect drug use, sexual practices and other health behaviors. We have completed work to prepare SoS for a large scale trial, including conducting a preliminary study using a randomized design in 18 schools showing that the intervention modifies the norms of students school-wide about suicide and help seeking, with the largest changes occurring among suicidal youth. For the proposed 5-year study, 36 rural high schools in New York and North Dakota will be randomly assigned to immediate SoS or wait-list control conditions. We will survey students in the schools over 18 months to (1) compare intervention and control levels of self-reported suicide attempts, (2) determine differences in impact for low- and high-risk groups, (3) test multiple hypothesized mediators of SoS impact on reducing suicide attempts from our intervention causative model, (4) use social network methods in a subset of schools to identify network mediators of SoS impact, the extent of dissemination of peer-to-peer messages, and evaluate the efficiency of the current strategy for identifying student peer leaders. This project can have a positive public health impact through the potential to prepare a cost-effective intervention that can be implemented safely in diverse communities and is effective in reducing suicidal behaviors among adolescents. PUBLIC HEALTH RELEVANCE: This proposed 5-year project can have a positive public health impact by preparing Sources of Strength (SoS), a school-based suicide prevention intervention, for expansion as a cost-effective program that can be implemented safely in diverse communities and is effective in reducing suicidal behaviors among adolescents. The proposed study can also contribute to knowledge needed to strengthen social-ecological protective influences across a full population of high school students by peer opinion leaders to change the norms of students through their schools and reduce suicidal behaviors.
NIH	2010	Suicide Endophenotypes and Molecular Mechanisms of Lithium Action	Gould, Todd	DESCRIPTION (provided by applicant): Suicide has a devastating impact on victims, their extended families, and public health in the United States, as well as throughout the world. Few treatments have been shown to reduce risk. An exception, supported by extensive clinical evidence, is that lithium is effective in reducing the risk of both attempted and completed suicide. However, the mechanisms underlying lithium's antisuicidal actions are not yet known, limiting the development of improved prevention approaches. We intend to use the mouse as a model organism to elucidate molecular pathways by which lithium interacts with biological and behavioral factors associated with suicide in humans. However, rather than attempting the infeasible task of modeling suicide in mice, we will focus on approaches that assess mouse behavior in tests relevant to well validated endophenotypes (deconstructed components of complex behavioral phenotypes) associated with suicide including aggression and impulsivity. These endophenotypes will be used in combination with human genetic, biochemical, and pharmacological findings in suicide research to provide construct-valid animal models. Toward this end, clinical studies have implicated polymorphisms in a number of genes, including neuronal nitric oxide synthase (NOS1), with measures of impulsivity, aggression, and suicide. Similarly, the results of extensive research have implicated deficits in serotonin (5-HT) neurotransmission in the etiology of suicidal behavior as well as increased impulsivity and aggression. Data from preclinical and human genetic studies indicate that lithium may exert some of its mood stabilizing effects through inhibition of the enzyme glycogen synthase kinase-3! (GSK-3!). Intriguingly, emerging basic science evidence links NOS1 function, 5-HT neurotransmission, and GSK-3! activity suggesting that they may be causally linked in the pathophysiological processes relevant to the etiology and treatment of psychiatric diseases such as suicide, where impulsivity and aggression play a role. Thus, our Specific Aims are to: 1) Identify the effects of lithium on behavior in mice with genetically- and pharmacologically-induced decreases in 5-HT levels; 2) Identify the effects of lithium on behavior in mice with genetically- and pharmacologically-mediated deficiencies in nitric oxide synthase 1 (NOS1) activity; 3) Evaluate the role of glycogen synthase kinase-3!, a direct target of lithium, in modifying behaviors mediated by decreased 5-HT and NOS1 function. These studies will capitalize on current knowledge of lithium pharmacology and use mouse genetic knockouts and pharmacological approaches to dissect the molecular and neurobiological mechanisms whereby lithium may modify impulsive and aggressive behavior as well identify points of interaction between lithium and biological markers known to be associated with suicide. Public Health Relevance: The data derived rom these studies should promote the development of improved pharmacological interventions to modify aggressive and impulsive behaviors thereby decreasing the risk of suicide across all diagnostic categories. PUBLIC HEALTH RELEVANCE: A completed suicide has a devastating impact on families, society, and public health. Few treatments have been shown to result in reduced risk; however, lithium treatment is effective, for unknown reasons, in reducing the risk of both attempted and completed suicide. This application proposes experiments in the context of endophenotype strategies that will reveal molecular mechanisms whereby lithium acts to exert its therapeutics effects.
NIH	2011	Impulsive Aggression, Neurocognition, and Suicidal Behavior in Depressed Youth	BRIDGE, JEFFREY	DESCRIPTION (provided by applicant): Major Depressive Disorder (MDD) is the most potent psychiatric risk factor for suicidal behavior in adolescents, yet most depressed youth never attempt suicide, diminishing the positive predictive value of a diagnosis of MDD in gauging the risk of future suicidal acts. Efforts to prevent youth suicide would benefit greatly from a deeper understanding of precursors and pathways to suicidal behavior in depressed youth, particularly if such knowledge informs the development of effective risk evaluation and intervention strategies. Knowledge of measurable factors that increase the risk of future suicide attempts in depressed adolescents could prove critical to efforts to prevent youth suicide by virtue of: 1) aiding in the recognition of depressed youth at especially heightened risk for suicide, who at a minimum may require closer supervision and containment; 2) identifying targets for clinical intervention beyond the mood disorder per se; and, 3) contributing to the development of assessment tools and risk markers relevant to better gauging individual suicide risk and informing clinical intervention research with youth at risk for suicide. The proposed R01 application from an early stage investigator (ESI) will address critical gaps in knowledge by examining the role of impulsive aggression and neurocognitive functioning in the etiopathogenesis of suicidal behavior in adolescents with MDD. The central hypothesis is that impulsive aggression and deficits in executive function and decision making will contribute substantially to a model of future suicide attempts and add positive predictive value to traditional assessment approaches. Our hypothesis is informed by promising pilot work in which measures of impulsive aggression and decision making deficits sharply distinguished depressed adolescent suicide attempters from non-attempters. The design includes cross-sectional comparisons as well as a prospective longitudinal study of 300 depressed youth with and without a prior history of suicide attempt, followed from early to middle adolescence, the developmental period of highest risk for suicidal behavior. These results will contribute to the mission of the NIMH by improving our capacity to identify the temporal and likely causal sequence of antecedents to future suicidal acts in youth with MDD, thus framing targets for practical clinical risk assessment, intervention, and the prevention of suicidal behavior. PUBLIC HEALTH RELEVANCE: The severe consequences of adolescent suicidal behavior make the accurate identification of youth at high risk an important clinical, research, and public health objective. This is the first large-scale prospective study of the developmental antecedents of adolescent suicidal behavior to comprehensively address multiple risk and protective factors in depressed youth. With the use of a multi-method, state-of-the-art, and pilot tested approach for assessing impulsive aggression and an informative computerized battery of subtests of executive function and decision making, the proposed research may help to clarify the specific behavioral and neurocognitive pathways contributing to the etiopathogenesis of suicidal behavior. Thus, this work has the potential to inform the development of practical suicide risk evaluation tools, empirically-based treatments, and preventive interventions to reduce adolescent suicide.

NIH	2011	2/2-Treatment of Suicidal and Self-Injurious Adolescents with Emotional Dysregula	Berk, Michele	DESCRIPTION (provided by applicant): The long term aim of our research is to develop and evaluate effective treatments for adolescents at high risk for suicide that will reduce suicidal and self-injurious behaviors as well as improve functioning and the quality of life of teens and their families. The primary aim of the research proposed here is to evaluate the efficacy of dialectical behavior therapy (DBT) for adolescents by comparing it to a combined individual and group supportive therapy control condition (I/GST) chosen specifically to maximize internal validity. Subjects will be 170 teens 13-17 years old with borderline personality traits referred to treatment due to high risk for suicide. Outcome targets include reduced frequency and severity of suicidal behaviors, especially suicide attempts, inpatient or ER treatment for suicidality, increased maintenance in and compliance with treatment, and enhanced functioning across multiple domains. DBT has an empirical track record with adults of reducing the incidence, frequency and medical risk of suicide attempts and non-suicidal self-injuries among individuals meeting criteria for borderline personality disorder (BPD). However, although DBT is widely used with suicidal adolescents, particularly those with difficulties characteristic of BPD such as poor emotion regulation and impulse control, no randomized trial of DBT with adolescents has been conducted. Thus, although non- randomized trials suggest effectiveness, without a randomized trial we simply do not know whether DBT for adolescents is efficacious or not. Given the severity of the problem and the lack of alternative treatments for high risk adolescents, addressing this question is important. The second aim of this research is to analyze mediators of reduced suicidal and self-injurious behaviors in adolescents. DBT is based on a theoretical model that suicidal behavior is a combined outcome of high stressful events and emotion dysregulation together with inadequate behavioral skills for coping with negative emotions and life events. Risk factors for adolescent suicide and intentional self-injury include most importantly family conflict but also conflict with peers, teachers, losses, legal or disciplinary problems (stressful events) combined with high negative emotions and inadequate abilities in emotion regulation. We will analyze the potential mediating effects on suicidal behaviors of decreases in family conflict, increases in parent DBT behavioral skills, reductions in emotion dysregulation and increases in DBT behavioral skills. Preliminary data on cost-effectiveness will also be collected. PUBLIC HEALTH RELEVANCE: The primary aim of the research proposed here is to evaluate the efficacy of dialectical behavior therapy (DBT) for adolescents by comparing it to individual and group supportive therapy control condition (I/GST) chosen specifically to maximize internal validity. Subjects will be teens 13-17 years old referred to treatment due to high risk for suicide. Outcome targets include reduced frequency and severity of suicidal behaviors, increased maintenance in and compliance with treatment and enhanced functioning across multiple domains.
NIH	2011	Effectiveness of IPT for Men and Women Prisoners with Major Depression	JOHNSON, JENNIFER	DESCRIPTION (provided by applicant): At the end of 2008, state and federal prisons held more than 1.6 million prisoners. Major depressive disorder (MDD) is one of the most common disorders in prison settings, with 12 month prevalence rates that are 3 times those of individuals in the community (23.5%). The high rate of MDD among prisoners is of public health concern because prisoners are particularly vulnerable to the negative consequences of MDD, including suicide, dropout from correctional programming, rejection and victimization by other inmates, and difficulty addressing medical, family, and substance use problems. MDD also increases prison costs and risk of prison and substance use recidivism. Despite the prevalence and serious consequences of MDD among prisoners, the only randomized trial of treatments for MDD in prisons or jails larger than 10 people was conducted by the PI in pilot work for this proposal (see below). RFA- MH-11-061 calls for "studies that target disorders commonly encountered in justice settings for which there are existing mental health interventions with proven effectiveness in other settings... Of particular priority are studies addressing the delivery of mental health treatment during incarceration." This study will examine the effects of an evidence-based, first-line treatment for MDD, interpersonal psychotherapy (IPT), among prisoners, and will be the first fully-powered randomized trial of treatment for MDD in any incarcerated population. IPT's multicultural appeal and ability to be delivered by non-PhD or MSW level interventionists are assets in prisons, where many inmates come from minority groups and many front-line counselors have bachelor's degrees and little or no specialized mental health training. These features and IPT's effectiveness in a group format give it good potential for uptake within the prison system. Our prison pilot work (supported by an NIH K23 award to the PI) indicates that: (a) group IPT for MDD was feasible, acceptable, and effective among female prisoners; (b) prison stakeholders see MDD treatment as extremely important; and (c) non-specialty prison counselors can deliver IPT adherently and competently. This 3-year R01 will compare group IPT to treatment as usual (TAU) in a sample of 90 male and 90 female prisoners with MDD from 4 institutions during treatment and 3-month follow-up. Effectiveness outcomes include: 1. Depressive symptoms. 2. Suicidality. 3. In-prison functioning (i.e., enrollment and completion of correctional programs; disciplinary and incident reports; aggression/victimization; social support). Pilot implementation outcomes include: 4. Cost of group IPT and of TAU for MDD; 5. Feasibility and acceptability of IPT to all stakeholders; 6. Prison provider intervention fidelity; 7. Prison provider attitudes and competencies; 8. Stakeholder perspectives on barriers and facilitators to examine in a subsequent implementation study. We anticipate that this study will establish the effectiveness of IPT for MDD in prisons, will assess its cost, and will provide the foundation for research on implementation of evidence-based treatments for a severe and prevalent disorder among this vulnerable, understudied population. PUBLIC HEALTH RELEVANCE: Major depressive disorder (MDD) is a severe mental illness that is extremely common in prison settings. The high rate of MDD among prisoners is a concern because they are especially vulnerable to negative consequences of depression, including suicide, inability to protect oneself while incarcerated, dropout from correctional treatment and education programs, prison recidivism, relapse to addiction, and difficulty addressing a wide array of medical and psychosocial stressors such as HIV, trauma, poverty, and homelessness. This study will test an evidence-based treatment for MDD in men's and women's prisons, and will be the first large-scale randomized trial of treatments for MDD in any incarcerated population.
NIH	2012	1/3-Reducing Suicial Ideation Through Insomnia Treatment (REST-IT)	MCCALL, WILLIAM	DESCRIPTION (provided by applicant): Dozens of epidemiologic reports have linked insomnia to increased risk for suicidal ideation, suicidal behavior and suicide death in patients with major depression. The mechanism whereby insomnia increases the intensity of suicidal ideation may be mediated through dysfunctional beliefs and attitudes about sleep, somewhat similar to hopelessness. We have unpublished, preliminary data showing that the addition of the hypnotic eszopiclone to open-label fluoxetine in the treatment of depressed insomniacs is associated with a reduction in suicidal ideation, as compared with placebo added to fluoxetine. We now propose to confirm the premise that treatment of insomnia reduces suicidal ideation in a multi-site clinical trial. Wake Forest University (WFU) will be the coordinating site and a recruitment site, while Duke University (DU) and University of Wisconsin (UW) will also serve as recruiting sites. Outpatients (N=138) with major depression, insomnia, and mild- moderate suicidal ideation will be treated with open label fluoxetine for 8 weeks and will be further randomized to receive either eszopiclone or placebo at bedtime for the same period. Patients will have return office visits at 1, 2, 4, 6, and 8 weeks after treatment initiation. Assessments wll include measures of suicidal ideation intensity, overall depression severity, insomnia severity, dysfunctional cognitions about sleep, nightmare intensity, hopelessness, and actigraphy. All data will be entered in a WF-created web-based interface, and consistency of methodology across sites will be assured with regular teleconferences between sites. The sample size will be sufficient to allow 80% power to detect a 2.0 point difference in the Beck Scale for Suicide Ideation between treatment arms. Safety of participants will be assured by (1) exclusion of patients with more than severe suicidal ideation at baseline, (2) frequent follow up, (3) limited access to hypnotics, (4) access to university psychiatric inpatients units for psychiatric emergencies, (5) 24-hour per day emergency services available through the sites respective psychiatric residency programs, (6) involvement of families and loved ones, when available, in the consent process, (7) and the creation of a Data Safety Monitoring Committee that will include expertise in depression, insomnia, clinical trials, statistics, suicidology, biostatistics, ethics, and a patient advocate. The primary aim will be to assess the effect of treating insomnia with hypnotic medication on the intensity of suicidal ideation. The secondary aim will be to test whether reductions in suicidal ideation in depressed insomniacs is mediated through either reduced dysfunctional beliefs about sleep, reduced hopelessness, or through reduction in nightmares. The results of this study will inform the appropriate management of patients with mild-moderate suicidal ideation, insomnia and depression - representing an extremely common clinical scenario. PUBLIC HEALTH RELEVANCE: Insomnia is a common symptom of depression, and insomnia has been convincingly linked to suicidal ideation, suicidal behavior, and suicide death. This study will address whether cautious, judicious use of hypnotics will reduce suicidal ideation in depressed insomniacs who are already receiving antidepressant treatment.

NIH	2012	3/3-Reducing Suicidal Ideation Through Insomnia Treatment (REST-IT)	BENCA, RUTH	DESCRIPTION (provided by applicant): Dozens of epidemiologic reports have linked insomnia to increased risk for suicidal ideation, suicidal behavior and suicide death in patients with major depression. The mechanism whereby insomnia increases the intensity of suicidal ideation may be mediated through dysfunctional beliefs and attitudes about sleep, somewhat similar to hopelessness. We have unpublished, preliminary data showing that the addition of the hypnotic eszopiclone to open-label fluoxetine in the treatment of depressed insomniacs is associated with a reduction in suicidal ideation, as compared with placebo added to fluoxetine. We now propose to confirm the premise that treatment of insomnia reduces suicidal ideation in a multi-site clinical trial. Wake Forest University (WFU) will be the coordinating site and a recruitment site, while Duke University (DU) and University of Wisconsin (UW) will also serve as recruiting sites. Outpatients (N=138) with major depression, insomnia, and mild- moderate suicidal ideation will be treated with open label fluoxetine for 8 weeks and will be further randomized to receive either eszopiclone or placebo at bedtime for the same period. Patients will have return office visits at 1, 2, 4, 6, and 8 weeks after treatment initiation. Assessments wll include measures of suicidal ideation intensity, overall depression severity, insomnia severity, dysfunctional cognitions about sleep, nightmare intensity, hopelessness, and actigraphy. All data will be entered in a WF-created web-based interface, and consistency of methodology across sites will be assured with regular teleconferences between sites. The sample size will be sufficient to allow 80% power to detect a 2.0 point difference in the Beck Scale for Suicide Ideation between treatment arms. Safety of participants will be assured by (1) exclusion of patients with more than severe suicidal ideation at baseline, (2) frequent follow up, (3) limited access to hypnotics, (4) access to university psychiatric inpatients units for psychiatric emergencies, (5) 24-hour per day emergency services available through the sites respective psychiatric residency programs, (6) involvement of families and loved ones, when available, in the consent process, (7) and the creation of a Data Safety Monitoring Committee that will include expertise in depression, insomnia, clinical trials, statistics, suicidology, biostatistics, ethics, and a patient advocate. The primary aim will be to assess the effect of treating insomnia with hypnotic medication on the intensity of suicidal ideation. The secondary aim will be to test whether reductions in suicidal ideation in depressed insomniacs is mediated through either reduced dysfunctional beliefs about sleep, reduced hopelessness, or through reduction in nightmares. The results of this study will inform the appropriate management of patients with mild-moderate suicidal ideation, insomnia and depression - representing an extremely common clinical scenario. PUBLIC HEALTH RELEVANCE: Insomnia is a common symptom of depression, and insomnia has been convincingly linked to suicidal ideation, suicidal behavior, and suicide death. This study will address whether cautious, judicious use of hypnotics will reduce suicidal ideation in depressed insomniacs who are already receiving antidepressant treatment.
NIH	2012	2/3-Reducing Suicide Ideation Through Insomnia Treatment (REST-IT)	KRYSTAL, ANDREW	DESCRIPTION (provided by applicant): Dozens of epidemiologic reports have linked insomnia to increased risk for suicidal ideation, suicidal behavior and suicide death in patients with major depression. The mechanism whereby insomnia increases the intensity of suicidal ideation may be mediated through dysfunctional beliefs and attitudes about sleep, somewhat similar to hopelessness. We have unpublished, preliminary data showing that the addition of the hypnotic eszopiclone to open-label fluoxetine in the treatment of depressed insomniacs is associated with a reduction in suicidal ideation, as compared with placebo added to fluoxetine. We now propose to confirm the premise that treatment of insomnia reduces suicidal ideation in a multi-site clinical trial. Wake Forest University (WFU) will be the coordinating site and a recruitment site, while Duke University (DU) and University of Wisconsin (UW) will also serve as recruiting sites. Outpatients (N=138) with major depression, insomnia, and mild- moderate suicidal ideation will be treated with open label fluoxetine for 8 weeks and will be further randomized to receive either eszopiclone or placebo at bedtime for the same period. Patients will have return office visits at 1, 2, 4, 6, and 8 weeks after treatment initiation. Assessments wll include measures of suicidal ideation intensity, overall depression severity, insomnia severity, dysfunctional cognitions about sleep, nightmare intensity, hopelessness, and actigraphy. All data will be entered in a WF-created web-based interface, and consistency of methodology across sites will be assured with regular teleconferences between sites. The sample size will be sufficient to allow 80% power to detect a 2.0 point difference in the Beck Scale for Suicide Ideation between treatment arms. Safety of participants will be assured by (1) exclusion of patients with more than severe suicidal ideation at baseline, (2) frequent follow up, (3) limited access to hypnotics, (4) access to university psychiatric inpatients units for psychiatric emergencies, (5) 24-hour per day emergency services available through the sites respective psychiatric residency programs, (6) involvement of families and loved ones, when available, in the consent process, (7) and the creation of a Data Safety Monitoring Committee that will include expertise in depression, insomnia, clinical trials, statistics, suicidology, biostatistics, ethics, and a patient advocate. The primary aim will be to assess the effect of treating insomnia with hypnotic medication on the intensity of suicidal ideation. The secondary aim will be to test whether reductions in suicidal ideation in depressed insomniacs is mediated through either reduced dysfunctional beliefs about sleep, reduced hopelessness, or through reduction in nightmares. The results of this study will inform the appropriate management of patients with mild-moderate suicidal ideation, insomnia and depression - representing an extremely common clinical scenario. PUBLIC HEALTH RELEVANCE: Insomnia is a common symptom of depression, and insomnia has been convincingly linked to suicidal ideation, suicidal behavior, and suicide death. This study will address whether cautious, judicious use of hypnotics will reduce suicidal ideation in depressed insomniacs who are already receiving antidepressant treatment.
NIH	2012	Multi-Method Assessment of Emotion Reactivity: Translational Research in Suicide	Armey, Michael	DESCRIPTION (provided by applicant): Although advances have been made towards understanding and treating suicidal behavior, suicide rates in this country have not fallen appreciably over the last decade. One explanation for our limited ability to effectively treat suicidality may be our limited understanding of the phenomenology of suicidality as it occurs in the real world. The proposed study, US-TREAT (Understanding Suicide: Translational Research in Emotional Reactivity Assessment Technology), is the first to apply a combination of multimethod in-hospital assessments and ecological momentary assessment (EMA) procedures post-discharge from inpatient care to model a translational phenotype of emotional reactivity, a clinically- and theoretically-important influence on suicidality, and its prediction of future suicdal ideation and behavior. A sample of 300 individuals hospitalized for suicidal ideation and behavior and 50 non-suicidal psychiatric comparisons will participate in a laboratory paradigm to assess physiological response (i.e., heart rate variability, skin conductance, & startle) to standardized environmental stimuli, EMA of emotional reactivity (i.e., affect, affective valence, and rate of change in affect over time), and genetic biomarkers (e.g. serotonin system, neurotrophins). To better characterize and predict the phenomenology of suicidality, we will use analytical models of cyclical processes (i.e., dynamical systems) to permit non-linear modeling of discrete aspects of emotion (i.e., intensity, rate of affect change, cyclicality, and damping) a influenced by experienced (i.e. EMA assessed) life stressors. The US-TREAT approach will provide critical insight regarding the phenomenology of suicidality with clear treatment implications. PUBLIC HEALTH RELEVANCE: Suicidal ideation and behavior are a serious public health concern in the United States. Current treatments for suicidality show limited efficacy, possibly due to our limited understanding of the phenomenology of suicidality as it exists in the real world. The present study proposes a multimethod assessment of an emotion reactivity translational phenotype for suicide, using a combination of laboratory measures and ecological momentary assessment methods, to explore the relationship between biological, experiential, and dispositional risk factors and suicidal ideation and behavior.
NIH	2012	Ketamine vs Midazolam: Testing Rapid Relief of Suicide Risk in Depression	GRUNEBAUM, MICHAEL	DESCRIPTION (provided by applicant): Suicide and suicide attempts cost an estimated $33 billion annually in the U.S. and immeasurable pain and suffering. Most suicidal behavior is associated with a depressive disorder, yet medication guidelines for suicidal patients are virtually nonexistent. The evidence base is severely limited because suicidal patients are excluded from most antidepressant clinical trials. Several recent studies show rapid improvement in suicidal ideation, in as little as one hour, in depressed patients after intravenous infusion of sub-anesthetic ketamine, a glutamate antagonist and commonly used anesthetic. The improvement in suicidal ideation appears to last several days, however, depression and suicidality are usually chronic, recurring conditions. We propose a rigorous clinical trial in suicidal depressed patients to test random assignment to IV infusion of ketamine or midazolam control followed by open continuation treatment with antidepressant medication plus supportive case management. The primary goal is to test ketamine's potential anti-suicidal effects versus a similarly sedative control medication not known to reduce suicidal ideation. Exploratory aims include analysis of potential biological (salivary cortisol) and neuro-cognitive correlates as well as systematic assessment of suicidal ideation and behavior during continuation treatment. Establishing a strong anti-suicidal signal for ketamine in this high-risk population would support an innovative intervention that could change clinical care for a patient population of public healt importance. Exploratory assessment of suicidal ideation and behavior during continuation treatment could help target research on strategies to sustain the benefit of ketamine. PUBLIC HEALTH RELEVANCE: Suicide is the 10th leading cause of death in the U.S. resulting in more than 30,000 deaths annually, but there is a surprising lack of evidence-based treatment for suicidal depression. Studies suggest rapid improvement in suicidal ideation in depressed patients within hours after a single, low-dose intravenous infusion of ketamine. We propose a rigorous trial to test the efficacy of ketamine in improving suicidal ideation in depressed patients with clinically significant suicidal ideation, a key population for the public health goal of suicide prevention, but which is usually excluded from clinical trials.

NIH	2012	Metallothioneins and polyamines in major depression and suicide	Sequeira, Adolfo	DESCRIPTION (provided by applicant): Approximately 30,000 Americans die every year by suicide, more deaths than those caused by HIV and homicides combined. Major depressive disorder (MDD) patients have the highest rates of suicidal behaviors, however only a subset ever commit suicide, making the identification of a molecular signature for suicide a major clinical challenge in this high risk population group. We and others have observed specific gene expression alterations in two stress response molecular mechanisms, metallothioneins and polyamines, in brains of MDD suicide victims, with opposite effects however in MDD patients who died of other causes. These stress-related mechanisms have not been carefully studied at the genetic, epigenetic, RNA, and protein level in a sample of subjects allowing the comparison between suicide, non- suicide depressed cases, and normal controls in post-mortem brain tissue. The central hypothesis of this proposal is that metallothioneins, and polyamines, two key molecular stress-response mechanisms, are impaired in MDD subjects that commit suicide. This study proposes to investigate, at the molecular level, the role played by polyamines, and metallothioneins in suicide in MDD patients. (Aim 1) We hypothesize specific gene and protein expression alterations in suicide and non-suicide MDDs compared with control subjects. Twenty MDD suicides, 20 non-suicide MDDs and 20 controls matched in terms of age and gender will be analyzed for a total of 60 subjects. We will investigate six brain regions relevant to suicide, and mood disorders, including the anterior cingulate cortex (ACC), amygdala (AMY), dorsolateral prefrontal cortex (DLPFC), hippocampus (HIPP), nucleus accumbens (NAcc), and orbitofrontal cortex (OFC) which form circuits that regulate emotional stimuli processing and change in mood states. (Aim 2) We hypothesize that stable gene and protein expression differences in suicide will be associated with genetic and epigenetic variation for the genes selected from Aim 1 using the same cohort of subjects from Aim 1. (Aim 3.1) We hypothesize that relevant biomarkers will be found in subjects for which we have both blood and brain tissue. We will attempt to validate the identified molecular targets in a new cohort of subjects (20 MDD suicides, 20 MDD non-suicides, 20 controls) (Aim 3.2) We hypothesize that medications and cortisol will have differential effects on serious MDD suicide attempters compared to MDD non-attempters, and normal controls. We will determine the effects of cortisol and antidepressants on polyamine, and metallothionein gene and protein expression. These immortalized cell lines, derived from patients with severe suicide attempts, patients without suicide attempts or thoughts, and matched controls (25 cell lines per group, 75 in total). Taken together, this project involves a large number of high quality brain samples, blood samples and a mechanistic cellular confirmation component to identify potential biomarkers in molecular stress response systems. These biomarkers might play a significant role in the identification of MDD patients with high risk of committing suicide and might offer promising targets for pharmacological interventions. PUBLIC HEALTH RELEVANCE: Project Narrative 30,000 deaths each year in the US are due to suicide mainly among people suffering from psychiatric disorder and particularly from major depressive disorder. Current diagnostic algorithms are inadequate and the identification of individuals at high risk for suicide is frequently overlooked. The focus of this proposal is to stuy the role of three molecular response mechanisms to stress (polyamines and metallothioneins) in suicide predisposition for patients with major depressive disorder.
NIH	2012	Intensive Outpatient Protocol for High Risk Suicidal Teens	SPIRITO, ANTHONY	DESCRIPTION (provided by applicant): A significant subgroup of suicidal adolescents continues to demonstrate suicidal ideation and behavior after discharge from emergent psychiatric care. These adolescents are typically high utilizers of expensive follow-up psychiatric care after discharge from inpatient psychiatric settings. This group of adolescents is the focus of this application. We are aware of only 6 RCTs with suicidal adolescents, two using family therapy, two using group therapy, one using Multisystemic Therapy, and a study by our group using individual adolescent Cognitive Behavioral Therapy (Donaldson et al, 2005). Only one of these six studies reported a reduction in suicide attempts at follow-up. We recently completed a study (Esposito-Smythers et al, in press) using an integrated adolescent and parent CBT protocol for adolescents with depression, suicidality, and a substance use disorder. At follow-up, our protocol resulted in fewer suicide attempts, re-hospitalizations, ED (Emergency Department) evaluations, and residential placements relative to standard care. These data are remarkable for the cost savings in the experimental group if ED evaluations, repeat inpatient psychiatric hospitalizations and residential placements are considered. In addition, our 5% rate of repeat attempts in the experimental condition over 18 months is very low compared to naturalistic studies and other treatment studies. Our protocol required two therapists per family - one for the adolescent and one for the parent(s) due to the acuity and severity of these adolescents. Not all suicidal adolescents will need an intensive treatment protocol such as ours but many being discharged from inpatient psychiatric care will need such services. In this application, depressed, suicidal adolescents seeking emergency care in an ED or who are psychiatrically hospitalized are eligible for our study if they have at least one additional risk factor: a prior suicide attempt, nonsuicidal self-injury (NSSI), and/or a substance use disorder, because these factors are related to increased risk for continued suicidal behavior and expensive contacts with the health care system after discharge. These risk factors were also chosen for scientific reasons because they share common underlying mechanisms - affect regulation and impulse control - that can be addressed in an intensive treatment protocol. The purpose of this application is to conduct a two group randomized controlled trial to test the primary aim that an intensive protocol designed to treat depressed, suicidal adolescents with an additional complicating risk factor will produce better treatment outcomes compared to standard care at the end of the active treatment (6 months), end of maintenance treatment (12 months) and at the final follow-up point (18 months).. This application's clinical significance lies in its addresing a critical barrier to the field: how to best treat the most high risk, depressed and suicidal adolescents. PUBLIC HEALTH RELEVANCE: The purpose of this application is to conduct a two group randomized controlled trial to test the primary aim that an intensive outpatient protocol designed to treat depressed, suicidal adolescents with an additional complicating risk factor, substance use and/or nonsuicidal self-injury, will produce better treatment outcomes than standard care. This application's clinical significance lies in its addressing a critical barrier to the field: ho to best treat the most high-risk, depressed and suicidal adolescents. The public health relevance of this application is evident as it addresses Healthy People 2020 Objective MHMD HP 2020- 2: "Reduce suicide attempts by adolescents" as well as NIMH Strategic Objective 3.1 to develop interventions.
NIH	2013	Behavioral and Ecological Suicide Tracking: Attention, Interpretation, and Memory	Armey, Michael	DESCRIPTION (provided by applicant): Despite advances in understanding and treating suicidal behavior, suicide rates in this country have not fallen over the last decade. While previous research has identified several risk factors for suicidal behavior, the level of predictio afforded by these variables is inadequate. One major limitation of current risk factors is that the are almost exclusively based on patient report. Unfortunately, the utility of patient report may be compromised by factors such as patient resistance to reporting honestly regarding suicidal ideation and behavior or limited patient self- awareness related to cognitive and experiential risk factors associated with suicide. Recently, two areas of research have shown promise in identifying potent risk factors for suicidal behavior that may address these limitations. First, research in the area of implicit cognitive processes has shown that individuals at-risk for suicide and self-harm behavior have objectively detectable suicide-related associations of which they may not be aware or willing to disclose explicitly. Second, the application of ecological momentary assessment technology to self-harm behavior has produced encouraging results, with two studies indicating that shifts in affectivity, of which patients are largely unaware, are better predictors of future episodes of self-harm than dispositional measures alone. The BEST-AIM study proposes the first, fully powered, investigation of implicit and experiential measures of suicide risk in a high-risk sample of patients admitted to a psychiatric hospital due to significan suicide risk.

NIH	2012	Toll-like Receptors and Cytokines in Depression and Suicide Brain	PANDEY, GHANSHYAM	DESCRIPTION (provided by applicant): Suicide is a major public health concern. About 30,000 people die each year by suicide in the USA alone, and about one million people die from it worldwide. Depression is a major risk factor for suicide. Several studies indicate that suicide s also associated with abnormal neurobiology, such as altered serotonin function and signaling mechanisms. Some studies also suggest abnormality of the immune function in depression and suicide. This is based on the observation of increased levels of proinflammatory cytokines, which are major mediators of immune function, in the serum and CSF of depressed and suicidal patients and the observation that administration of cytokines, such as TNF-ï¿½, to cancer patients induces symptoms similar to those of depression. Some recent studies indicate abnormalities of proinflammatory cytokines in the brain of depressed and suicide subjects. Cytokines and chemokine are important biological mediators of immune function. However, it appears that Toll-like receptors (TLR), which may be the first line of defense against pathogens and tissue damage, are also major mediators of innate immunity. Upon activation by specific ligands, TLRs induce downstream signals that lead to cytokine and chemokine production, which can initiate a localized inflammatory response. In order to examine the role of cytokines and TLRs in depression and suicide, we are proposing a comprehensive study of TLRs, cytokines and chemokines in postmortem brain of depressed and suicide subjects. The proposed studies are also based on our preliminary findings from a gene profile study indicating alteration (up- or down-regulation) of 14 genes in depressed suicide victims. These altered genes include certain cytokines, chemokines and TLRs. The main objectives of our proposed studies are to examine in detail the specific TLR and cytokine genes that are altered in suicide and depressed brain, and if these altered genes are specific to suicide (independent of diagnosis) or these alterations are also shared by non-suicide depressed subjects. To achieve this objective we will conduct a gene profile study in the dorsolateral prefrontal cortex (DLPFC) and hippocampus of four groups of subjects which include: 1) normal controls, 2) depressed suicide, 3) non-depressed suicide, 4) non- suicide depressed subjects. We will then validate these findings by determining the mRNA and protein expression of altered genes, which we find to be about 14 in these subjects. These studies may be significant as they may result in identification of important bio- and vulnerability markers for depression and suicide and may provide useful targets, such as TLR-3, for developing newer therapeutic agents. This may be innovative as it may be the first comprehensive study of cytokines, chemokines and TLRs in depression and suicide and is significant for understanding the pathophysiology of depression and suicidal behavior and its treatment. PUBLIC HEALTH RELEVANCE: Suicide is a major public health problem and about 30,000 people die of suicide in the USA every year, and about one million people die from it worldwide. However, the neurobiology of suicide is unclear. Abnormalities of cytokines, which are considered hormones of the immune system, have been implicated in suicide. Besides cytokines, chemokines and Toll-like receptors (TLRs) are other mediators of immune functions. In order to examine if abnormalities of immune function are involved in the pathophysiology of suicide we are proposing a study of neuroimmune genes in the postmortem brain of normal controls, suicides victims and depressed subjects. These studies may identify vulnerability genes for suicide and newer targets for developing therapeutic agents for treatment of depression and prevention of suicidal behavior. These studies may also provide an understanding of the role of the immune function in depression and suicide.
NIH	2013	Genetic analysis of high-risk Utah suicide pedigrees	COON, HILARY	DESCRIPTION (provided by applicant): Suicide is a significant health concern. There are over 33,000 suicide deaths per year in the United States, accounting for 1.3% of all fatalities (WISQARS, 2005), and about 2% of deaths worldwide (World Health Organization, 2000). Aggregated data across multiple large studies has produced heritability estimates of completed suicide of 45%. The Rocky Mountain States have much higher age-adjusted suicide rates, and Utah is consistently in the top ten. In Utah, suicide is the leading cause of death for males between the ages of 15 and 54. Our project will use a large DNA resource already collected from decedents through a long-term collaboration with the centralized Utah State Office of the Medical Examiner (OME). Records of >2,000 decedents with DNA were linked to the Utah Population DataBase (UPDB), a computerized genealogy database that includes medical data, demographic information, and genealogical data for over 6.5 million individuals. Using the UPDB, we identified 27 high risk families containing ~150 suicide decedents with DNA. As a rare condition (1-2/10,000 per year), aggregation of suicide completion in high-risk pedigrees represents a unique resource to study risk factors. We will use the genealogical, demographic, and medical data in the UPDB to identify and focus on the most compelling of these high-risk suicide pedigrees; those that contain both a significant excess of suicide completion and that exhibit the most discriminating characteristics compared to non-familial suicide. By using these phenotypic comparisons to choose the most unique high-risk pedigrees, we will increase homogeneity and strengthen our ability to isolate genetic variants related to suicide risk. These discriminating phenotypes will also identify non-genetic factors associated with high familial risk that can foster other epidemiological studies, and can facilitate future gene x environment analyses. We currently have in hand a large resource of DNA and phenotype information from ~2500 additional Utah suicide decedents. This sample will grow to over 4000 DNAs by the end of the study, the largest population-based sample of DNA from suicide decedents ever collected. We propose to focus on unusual high-risk suicide pedigrees with increased likelihood for more penetrant rare genetic variation, followed by confirmation and follow-up analyses in large cohorts of Utah decedents and publicly-available psychiatric data sets. The detection of genetic variants associated with suicide could shed light on biological pathways leading to suicide risk in the population, or in association with specific disorders. We have chosen state-of-the-art analytical methods, and have assembled a team of experts (analytic, phenotypic, and molecular) to explore these unique data resources to identify genetic risk factors for suicide. The detection of rare variants associated with suicide could shed light on biological pathways leading to suicide risk in the population, or in association with specific disorders.
NIH	2013	Perturbed cell signaling network and suicide neurobiology	DWIVEDI, YOGESH	DESCRIPTION (provided by applicant): Suicide is a major public health concern. Suicidal behavior occurs in the context of a diathesis that is characterized by traits in multiple domains: behavioral, clinical, personality, and biologic. While the complexity of suicidal behavior requires a multi-faceted approach, the identification of neurobiological dysfunction is critical for the pharmacological interventions that may have protective effects against suicidal behavior. In this context, we have shown reduced BDNF gene expression and less activation of its cognate receptor TrkB in the brain of suicide subjects. In addition, we have found that p75NTR, a low affinity BDNF receptor is upregulated in the brain of these subjects. BDNF, which plays a critical role in neural plasticity and cell survival, essentially mediates its action via TrkB-mediated activation of extracellular signal-regulated kinase (ERK)1/2 and phosphoinositide 3 kinase (PI3K) signaling pathways. Abnormalities in these two signaling systems at the upstream levels were also found in the same brain areas of suicide subjects in which abnormalities were noted in BDNF/TRKB/p75NTR. These changes were present in all suicide subjects regardless of psychiatric diagnosis. To better understand the functional significance of altered BDNF signaling at molecular and cellular levels and their implications in the neurobiology of suicide, we propose to test the hypothesis that hypoactive BDNF/TrkB-mediated ERK1/2 and PI3K/Akt and overexpressed p75NTR will lead to modifications in the interaction and activation of downstream scaffolding/regulatory proteins, translational machinery, chromatin remodeling, and structural plasticity in the suicide brain. To test our hypothesis, in brain areas implicated in suicidal behavior, i.e., dlPFC and hippocampus (cerebellum as negative control brain region) from well-characterized and well-matched depressed suicide and non-suicide control subjects (n = 30 in each group), we aim to examine whether: 1) hypoactive ERK1/2 will lead to altered activation of substrates p90 ribosomal S6 kinase (RSK) and mitogen- and stress-activated kinase (MSK) and their mediated transactivation of transcription factors and chromatin remodeling; 2) hypoactive ERK1/2 and PI3K will lead to less active translational machinery, translation of postsynaptic genes, and altered dendritic morphology; and 3) altered PI3K/Akt and p75NTR will be associated with altered interactions of scaffolding proteins leading to c-Jun kinase (JNK) activation and altered expression and functional characteristics of downstream apoptotic regulatory proteins and neuronal apoptosis. To make sure that the effects are suicide specific, we will perform these studies in the same brain areas of an additional group of well-matched subjects who were depressed (no previous suicide attempt and no family history of suicide) and died by causes other than suicide (n = 30). Our proposed study will precisely and mechanistically assess the complexity of cellular signaling at the molecular, cellular, and functional levels in suicide brain and will have a significant impact in understanding not only the neurobiological basis of suicide but in designing more efficacious treatment strategies.
NIH	2011	Mood, Substance Use and Suicidality in Bipolar Adolescents: A Prospective Study	GOLDSTEIN, TINA	DESCRIPTION (provided by applicant): Youth suicide constitutes a major public health problem, ranking as the second leading cause of death for youth worldwide. Of all psychiatric disorders in youth, bipolar disorder imparts the greatest risk for suicide, followed by a substance use disorder. Mood disorder and substance use disorders commonly co-occur, and the combination increase the risk for completed suicide in adolescents exponentially over either disorder alone. Unfortunately, effective suicide prevention efforts, particularly for the ultra-high-risk population of youth with mood disorder and substance use, remain limited. This void in the treatment research may be understood by findings that a multitude of factors from a variety of domains contribute to suicidal risk; such factors remain too diffuse and multiply determined to be considered optimal targets for preventive interventions. Experts in the field have thus called for prospective, longitudinal studies in high-risk samples to systematically investigate specific mechanisms of suicide risk in adolescents. The American Association of Suicidology has specifically identified a need for research on proximal, dynamic and modifiable factors for suicidal risk in adolescents. PUBLIC HEALTH RELEVANCE: Youth suicide constitutes a major public health problem, ranking as the second leading cause of death for young people worldwide. Of all psychiatric disorders, bipolar disorder imparts the greatest risk for suicide, followed by a substance use disorder. Mood disorders and substance use disorders commonly co-occur, and the combination increases the risk for completed suicide in adolescents exponentially over either disorder alone. Improved understanding of the nature of these interrelated risk factors has the potential to inform targeted suicide prevention efforts for those at highest risk, thereby decreasing the morbidity, mortality and suffering associated with youth suicide.

NIH	2008	The Functions of Adolescent Self-Injury: Measurement Structure and Clinical Imp	KLONSKY, E David	DESCRIPTION (provided by applicant): Non-suicidal self-injury (NSSI) refers to the intentional injuring of one's body tissue without suicidal intent and for purposes not socially sanctioned. Examples include skin-cutting, burning, and scratching. NSSI is a robust risk-factor for psychiatric disorders and suicide and has become a significant public health problem in adolescents. Recent research finds that approximately 8% of middle school students, 14-15% of high-school students, and 80% of adolescent inpatients have engaged in NSSI. Because most NSSI research has focused on prevalence and psychosocial correlates, little is known about the functions of NSSI in adolescents. Understanding the functions of NSSI would facilitate case conceptualization and treatment planning for patients who self-injure, and provide a meaningful context for research on the etiology, classification, prevention, and treatment of NSSI. The specific aims are to: 1) determine the suitability of a new, comprehensive measure of NSSI functions for adolescent populations, 2) establish the factor structure of NSSI functions in adolescents, and 3) examine the implications of different NSSI functions for diagnosis and treatment, including the identification of clinically distinct subgroups of self-injurers. Thus, the study will provide basic data on the covariation and clinical implications of NSSI functions, as well as produce the first comprehensive and valid measure of NSSI functions. PUBLIC HEALTH RELEVANCE: Non-suicidal self-injury (NSSI) is a robust risk-factor for psychiatric disorders and suicide and has become a significant public health problem in adolescents. Because most NSSI research has focused on prevalence and psychosocial correlates, the present project focuses on the functions of adolescent NSSI, including their measurement, structure, and clinical implications.
NIH	2008	Adverse Effects of Antidepressants in Pediatric Non-OCD Anxiety Disorders	BRIDGE, JEFFREY	DESCRIPTION (provided by applicant): The association between antidepressant treatment and suicidal thoughts and behavior in children and adolescents has been the topic of recent debate. Much of our knowledge about treatment emergent risks associated with antidepressant treatment in youth derive from short-term, randomized, controlled trials (RCTS). These trials are limited in detecting adverse effects of medications due to the relatively small number of participants required to test primary efficacy end points. The proposed R03 small grant project will address gaps in knowledge by determining the relative safety and tolerability of antidepressant medications in the acute treatment of childhood anxiety, based on a secondary analysis of individual patient-level data of all available randomized controlled trials (RCTs) comparing antidepressants and placebo for generalized anxiety disorder, separation anxiety disorder, and social phobia. Outcomes will include treatment emergent adverse events (TEAEs) and treatment-induced changes in vital signs, cardiovascular effects, height, weight, and clinical laboratory parameters. The study also aims to identify patient subgroups at highest risk of adverse outcomes during acute treatment. This work will build on the PI's existing databases of antidepressant RCTs for pediatric depression, OCD, and non-OCD anxiety disorders. Meta-analysis of individual patient data (MAP) has been proposed as the most rigorous empirical method available to determine the relative efficacy and safety of treatments. This study is novel in that MAP allows for statistically powerful time-to-event analysis, identification of subgroups of patients at differential risk of adverse outcomes, and adjustment for variables that may have confounded the original treatment comparisons. We will therefore be able to examine questions of safety and tolerability otherwise unanswerable by a single trial, a multi-center RCT, or a traditional study-level meta- analysis. The feasibility of this project is supported by existing commitments from PIs and industry sponsors to provide our team with the patient-level data necessary to accomplish the goals of this application. These findings will be of benefit to clinicians who manage and treat anxious youth with these medications. This preliminary research will also build the foundation for future work examining the treatment emergent risks and side effects burden of psychotropic medications in other psychiatric disorders, including MDD, OCD, and bipolar disorder.
NIH	2008	Social Inequalities in Outcomes for Treatment of Late-Life Depression	Cohen, Alexander	DESCRIPTION (provided by applicant): Late-life depression (LLD) is a major public health concern. It is associated with substantial impairment and disability in social and cognitive domains, increases risk for and exacerbates the severity of comorbid medical conditions [4-6], elevates risk for suicidality, and is a significant contributor to mortality. These associations and risks take on greater significance because LLD is commonly under-diagnosed and inadequately treated. Epidemiological research also suggests the presence of social inequalities in LLD. Socioeconomic status (SES), usually assessed by measures of education, income, wealth, occupation, and/or neighborhood characteristics, is associated with risk of depression in older adults (=60 years). Indeed, these risks appear to widen with age, with older adults of lower SES having markedly elevated risk for depression. Evidence is mixed about racial/ethnic inequalities. Whereas rates of LLD are higher among White males than among African-American and Hispanic males, older White males appear to have lower levels of depressive symptoms than older African American males. Furthermore, there is evidence that African Americans and Hispanics, in general, experience higher rates of chronic depression. The relationship between race/ethnicity and depression is itself, influenced by gender, income, and education. This application is for a small research grant (R03) to conduct secondary data analyses to investigate social and racial/ethnic inequalities in outcomes of antidepressant treatments in older adults. These analyses emerge from an initial study in which Cohen et al., (2006) reported SES (as measured by census tract median household income) was a significant moderator of antidepressant treatment in two clinical trials in which all subjects received high quality care. The proposed research will expand on this work by conducting an investigation of possible social inequalities in the effectiveness of PROSPECT (Prevention of Suicide in Primary Care Elderly: Collaborative Trial), a multi-site randomized clinical trial of an intervention (pharmacotherapy, interpersonal psychotherapy, and case management) for the treatment of LLD. We will also investigate whether the relative effectiveness of the intervention depended social inequalities in positive changes in social support during treatment and/or the extent to which patients took advantage of various components of the intervention. The proposed research will benefit from its use of data from a randomized clinical trial that was conducted in "real-world" primary care settings and included a heterogeneous sample of depressed older adults, as well as the availability of multiple measures SES and race/ethnicity at the level of individuals and the neighborhoods in which they lived. Results of this research may yield insights about: 1) the social factors that influence the effectiveness of treatments, even when controlling for access and the quality of treatment; 2) the clinical and public health needs of population subgroups; and, 3) the need for methodological changes in future clinical trials. More generally, we expect this research will make an important contribution to our understanding of health disparities. Late-life depression is a major public health concern in that it is associated with increased risk for functional disability, suicidality, and mortality. Expanding on preliminary research, which suggested social inequalities in the effectiveness of antidepressant treatments, the proposed research will investigate social inequalities (as measured by socioeconomic status and race/ethnicity) in the effectiveness of a primary care intervention for reducing depressive symptoms, hopelessness, and suicidality, and improving functional status in older adults. Results of this research may yield new insights about: 1) the social factors that influence the effectiveness of treatments, even when controlling for access and the quality of treatment; 2) the clinical and public health needs of population subgroups; and, 3) the need for methodological changes in future clinical trials.
NIH	2009	SUICIDAL BEHAVIORS AMONG DOMINICAN YOUTH	Pena, Juan	DESCRIPTION (provided by applicant): Since the inception of the Center for Disease Control and Prevention (CDC) surveillance system of U.S. high schools in 1991 called the Youth Risk Behavior Surveillance System (YRBSS), Hispanic youth have consistently reported among the highest rates of suicidal behavior of any major ethnic/racial groups including African Americans and Whites. Rates for suicide attempts are higher for U.S.-born Hispanic youth compared to their foreign-born counterparts suggesting that processes related to acculturation or immigration may be related to suicidal behaviors among Hispanics. However, the exact nature of these mechanisms remains to be understood in part because of lack of knowledge regarding suicide attempt rates, risk factors, and protective factors from Hispanic youth's countries of heritage. Our study will increase scientific knowledge of socio-cultural factors related to suicidal behaviors among D.R. youth and how they compare to their Dominican counterparts in NYC. We propose to survey a nationally representative sample of Dominican youth (N H 6,000) attending public secondary schools (grades 9 to 12) across the D.R. and estimate their rates of suicide attempts and ideation (Aim 1 of study). Pending availability of funds, the NYC Department of Health and Mental Hygiene has also agreed to collect data on ancestry on the 2009 NYC YRBSS which will allow us to identify a representative sample of Dominican youth attending NYC public high schools as a U.S. based comparison group (N H 1,229). Comparisons of suicide attempts, suicide ideation, and related risk behaviors will be made between D.R. youth and NYC Dominicans (Aim 3). Aim 2 of our study is to identify risk factors (e.g. family conflict, substance use, alcohol use, hopelessness, and violent related behaviors) and protective factors (e.g. family cohesion, familismo, and religiosity) for suicidal ideation and attempts among the youth of the D.R. As per PA-07-079, NIMH's PA-07-079, Research on the Reduction and Prevention of Suicidality, encourages research into "the role of cultural factors and acculturative processes that can modify risk and its perception as well as influencing protective factors." Our study will advance this research agenda. PUBLIC HEALTH RELEVANCE: Project Narrative Prevention of suicide attempts among adolescents has been identified as an urgent priority, and Hispanic youth have consistently reported among the highest rates of suicidal behavior of any major ethnic/racial groups including African Americans and Whites. Rates for suicide attempts are higher for U.S.-born Hispanic youth compared to their foreign-born counterparts suggesting that processes related to acculturation or immigration may be related to suicide risk among Hispanics. However, the exact nature of these mechanisms remains to be understood in part because of lack of knowledge regarding suicide attempt rates, risk factors, and protective factors from Hispanic youth's countries of heritage

NIH	2010	Longterm Treatment Effects on Juvenile Justice Girls' Depression and Suicide Risk	Kerr, David	DESCRIPTION (provided by applicant): The aims of the proposed project address gaps in the evidence base concerning interventions with girls in the juvenile justice system (JJS). All aims focus on the extent to which a delinquency-focused intervention disrupts depressive symptoms and suicide risk trajectories in young adulthood for these high-risk females. Participants are 164 women who were involved in the JJS as adolescents. The women initially participated at ages 13-17 in a randomized controlled trial to test the effectiveness of Multidimensional Treatment Foster Care (MTFC, Chamberlain, 2003) versus treatment as usual (TAU) at reducing delinquency and drug abuse. Delinquency, depressive symptoms, and suicidal thoughts were measured four times across the original 2-year follow-up period. A study is currently underway (R01 DA024672: February 2009-December 2012) in which in-person and telephone assessments of these women will be conducted across multiple 6-month intervals in young adulthood (18-28 years). The aims of this R01, however, do not address the course of depressive symptoms or suicide risk among these high-risk women. In the present application, we capitalize on rich existing longitudinal data and the active assessment phase in the R01 study to propose a new focus on the effects of MTFC on these problems. Specifically, we propose to 1) conduct a lifetime assessment of the number and timing of suicide attempts; and 2) augment R01 assessments planned at 6-month intervals to include self-reported suicidal thoughts and behaviors. Two of these assessments will occur prior to the proposed study, and will be supported with limited internal resources; we request funding for three additional measurement occasions (at 6-month intervals), for a total of five assessments in young adulthood. Using existing and proposed data collection, we will pursue three aims that estimate MTFC effects on depressive symptoms and suicide risk in young adulthood, and specify three key mechanisms of indirect effects. In Aim 1, we will use latent growth modeling to characterize the course of depressive symptoms across 9 time points in adolescence and young adulthood, and then to test intervention effects; girls randomly assigned to MTFC are expected to show decreases in depressive symptoms over time relative to girls assigned to TAU. Aim 2 tests whether changes in three domains already demonstrated to be impacted by MTFC (Chamberlain et al., 2007; Leve et al., 2007) mediate effects of the intervention on changes in depressive symptoms; specifically, MTFC is expected to reduce depressive symptoms through early adulthood via decreased delinquency and teenage pregnancy/child-bearing, and educational attainment. Aim 3 tests the effects of MTFC on suicide attempts and whether such effects are mediated by intervention-related reductions in delinquency and depressive symptoms. Findings will suggest directions for development and augmentation of interventions for JJS girls. Thus, the proposed study answers calls for innovative approaches to reaching high risk youth who do not benefit from existing depression prevention paradigms (Avenevoli et al., 2006). PUBLIC HEALTH RELEVANCE: Adolescent girls with serious conduct problems are at high risk for depression and suicide. Yet, effective treatments for these problems in this group are lacking. We examine whether a delinquency-focused intervention for girls in the juvenile justice system will reduce depressive symptoms and rates of suicide attempt into young adulthood via changes in delinquency, teen pregnancy rates, and educational attainment.
NIH	2010	Shared Task 2010 - Analysis of Suicide Notes for Subjective Information	Pestian, John	DESCRIPTION (provided by applicant): The objective of this virtual-conference is to conduct a shared task dedicated to developing and evaluating natural language processing methods that identify emotional language in suicide notes. Developing natural language processing methods that identify emotional language in suicide notes is an important responsibility. A responsibility that, as we will show, can immediately affect the care of suicidal patients. Additionally, these methods may be used by computers to understand other types of emotionally laden text. Shared tasks have a long history of contributing to the advancement of science. They are an efficient way of bringing together the efforts of large numbers of research groups to bear on important problems; they are, in fact, a virtual scientific conference. Our specific aims are 1) Select and develop methods for identifying emotional language in suicide notes; 2) Evaluate the accuracy of these methods; 3) Publish the results of the findings in an open-access journal.
NIH	2011	Suicidal Ideation and Alcohol Outcomes in Emerging Adult College Drinkers	Gonzalez, Vivian	DESCRIPTION (provided by applicant): This study is intended to advance our understanding of how suicidal ideation is functionally related to alcohol use and problems among emerging adult college students. Emerging adult college students have high rates of suicidal ideation and attempts and of alcohol use and problems. Among college students, individuals with suicidal ideation are more likely to binge drink and alcohol problems in this population are associated with increased rates of suicidal ideation and attempts. While the association between suicidality (ideation, attempts, and deaths) and alcohol is well documented in clinical and non-clinical populations, relatively few studies have applied relevant theory and research findings in both the areas of alcohol and suicidality to aid in the understanding of why they are linked. This study takes a conceptually driven and innovative approach to understanding the interplay of suicidal ideation and alcohol by developing and testing a model based on theory and research in the areas of both suicidality and negative affect related-alcohol outcomes. The primary aim of this study is to examine a conceptual model, using structural equation modeling, of the associations among depression, severity of suicidal ideation, problem solving skills, the use of avoidant coping, drinking to cope with negative affect, impulsivity in response to negative affect (i.e., negative urgency), and alcohol use and problems. Participants will be 400 college men and women between the ages of 18 and 25, who are current drinkers and who have experienced (at a minimum) passive suicidal ideation. Unlike typical alcohol research, which has relied on self-report measures of problem solving to explore models of alcohol use, this study will include the innovation of using a performance-based measure of participants' problem solving skills. This study also will use a more recent and refined measure of impulsivity in examining the relationships among suicidal ideation, impulsivity, and alcohol outcomes. Specifically, the role of negative urgency will be examined, as it is a facet of impulsivity found to be particularly associated with alcohol problems, it has been theorized to underlie the relationship between negative affect and alcohol problems, and our preliminary work suggests that it is particularly associated with suicidal ideation and alcohol problems among emerging adult college drinkers. This exploratory cross-sectional study will provide meaningful preliminarily data for longitudinal studies of the relationships among suicidality, coping skills, drinking to cope, negative urgency, and alcohol outcomes. The results of this study have the potential to contribute crucial knowledge by uncovering clinically malleable targets for secondary prevention and treatment efforts aimed at reducing suicidality and alcohol problems among emerging adults. PUBLIC HEALTH RELEVANCE: The results of this study have the potential to contribute knowledge crucial to the development of effective prevention and treatment efforts aimed at reducing suicidality (ideation, attempts, and deaths) and alcohol problems among emerging adult (18- to 25-year-old) college students, a population with high rates of both problems.
NIH	2012	The Acute Alcohol-Suicide Attempt Relation as a Function of Alcohol Use Disorders	BAGGE, COURTNEY	DESCRIPTION (provided by applicant): In the United States alone, more than 32,000 people commit suicide each year and it is estimated that for every death by suicide there are 8-25 nonfatal suicide attempts. Given the clinical and public health significance of suicide, there is considerable interest in identifying proximal factors that increase the risk for suicide attempts and that determine the timing of suicide attempts among individuals who often report persistent suicidal ideation. Despite consistent findings of an elevated prevalence of alcohol use surrounding suicide attempts, little is known about whether acute alcohol use serves as a trigger to suicide attempts, or whether the effect of acute alcohol use on suicide attempt differs as a function of chronic alcohol use. Disentangling the effects of acute alcohol use and risk of injury according to an individual's usual consumption pattern is a matter of great public health interest, and there are known differences in psychological characteristics (e.g., mood disorders, previous treatment history) between those who attempt suicide with and without alcohol use disorders (AUD), as well as between individuals who drink alcohol (A+) and who do not drink alcohol (A-) prior to their attempt. However, little is known about differences on such factors between suicide attempters with AUD+ (who do or do not use alcohol immediately prior to their attempt), AUD- individuals who use alcohol before their attempt, and AUD- individuals who do not consume alcohol prior to their attempt. In the proposed exploratory/ developmental study (R21), we will examine the unique triggering role of acute alcohol use on suicide attempts as a function of an individual's baseline AUD status, and will also examine distal psychological characteristics of distinct groups of attempters characterized by acute and chronic alcohol use. To this end, we will employ a case-crossover design with a between-subject comparison, recruiting 150 individuals presenting for medical evaluation after a suicide attempt. The one-session assessment will comprise a diagnostic measure of AUD, a battery of questionnaires assessing psychological characteristics, and a standard interview assessing substance use and other time-varying proximal risk factors during the six hours prior to the suicide attempt, as well as during two matched controls periods. This exploratory/developmental study will provide preliminary data on the magnitude of the unique within-subject relation between acute alcohol use and attempt among individuals with and without AUD, and will aid in identifying distinguishing characteristics of groups of attempters characterized by different patterns of acute and chronic alcohol use. These preliminary data and effect sizes will be used to inform the development of a larger study. Gaining a better understanding of the triggering effects of acute alcohol use on suicide attempts among those with and without AUD, and identifying psychological characteristics of individuals with different acute and chronic alcohol use patterns will facilitate future identification and treatment of alcohol-related suicide attempts. PUBLIC HEALTH RELEVANCE: Given the clinical and public health significance of suicide attempts and problematic alcohol use, there is considerable interest in their relation. Ultimately, identifying differences in the psychological characteristics of suicide attempters with different patterns of acute and chronic alcohol use, and gaining a better understanding of the triggering effects of acute alcohol use on suicide attempts among those with and without Alcohol Use Disorders (AUD), will facilitate future identification and treatment of alcohol-related suicide attempts. This is particularly important given that many who attempt suicide report persistent suicidal ideation, and thus the timing of these attempts is difficult to predict.

NIH	2009	Preventing Addiction Related Suicide	RIES, RICHARD	DESCRIPTION (provided by applicant): The key aims of this R21 exploratory research proposal are: 1) to develop the Preventing Addiction Related Suicide (PARS) module, a suicide risk reduction training and intervention program that can be incorporated into standard group-based, intensive outpatient program (IOP) addiction treatment; 2) to obtain pilot data on its acceptance and feasibility, as rated by IOP patients and counselors; and 3) to assess changes in knowledge, attitudes, and adaptive behaviors about suicide prevention following exposure to the PARS, as rated by addiction treatment participants and counselors at two NIDA CTN (Clinical Trials Network) addiction treatment agencies. PUBLIC HEALTH RELEVANCE: This proposal aims to improve drug and alcohol addiction treatment by developing and testing a behavioral suicide education and prevention module for integration into standard intensive outpatient addiction treatment. Addiction is a potent risk factor for suicide and suicidal behavior. Although studies show that suicide or suicide attempts are 10 to 50 times more frequent among people with addiction disorders-and even higher among people requiring addiction treatment-no suicide prevention efforts have been developed and tested specifically for addiction treatment settings.
NIH	2009	Developing an intervention to address suicide risk during substance use disorder	Ilgen, Mark	DESCRIPTION (provided by applicant): Suicide, with its related mortality and morbidity, represents a significant and preventable loss of human life. Existing research indicates that problematic alcohol and drug use are closely linked to both fatal and non-fatal suicide attempts. Given the strong association between substance use and suicide, an episode of substance use disorder (SUD) treatment provides a unique opportunity to decrease the likelihood of suicidal behaviors. However, there are no data on the effectiveness of specific interventions designed to decrease risk of suicidal thoughts and behaviors during an episode of SUD treatment in individuals at high risk for suicide. The proposed 2-year study will: (1) adapt and refine an existing cognitive-behavioral treatment (CBT) intervention designed to decrease suicidal thoughts and behaviors for use in SUD treatment settings; and (2) conduct a pilot randomized controlled trial with 50 patients in treatment for SUDs comparing the CBT intervention to usual care. This pilot randomized controlled trial will: (a) obtain information about the feasibility of these procedures in residential SUD treatment; (b) determine the distribution and variability of the primary (level of suicidal ideation) and secondary outcomes (suicide attempts, hopelessness, frequency of substance use) within intervention and control conditions. The strong existing data on the efficacy of the CBT intervention for use in other settings, combined with our prior knowledge of modifying interventions for individuals with SUDs, will allow us to progress quickly from the initial intervention modification process to conducting a pilot randomized controlled trial of this intervention. Patients will be screened at SUD treatment entry for a combination of a past suicide attempt and current suicidal ideation and will be randomized to CBT or control conditions. All participants in the pilot randomized controlled trial will be assessed at baseline, at the end of treatment, and at 3-month follow-up. From a public health perspective, SUD treatment programs contain large numbers of patients at high risk for future suicidal behaviors and therefore have the potential to play a central role in our nation's efforts to decrease suicide. The proposed project is the first step in our planned line of research intended to decrease the likelihood of suicidal thoughts and behaviors in individuals with SUDs and will provide all of the essential elements needed to design a large RCT in the future that is fully powered to test the impact of this intervention on post-treatment suicidal thoughts and behaviors in this high risk population. PUBLIC HEALTH RELEVANCE: The purpose of this project is to adapt an existing Cognitive-Behavioral Therapy (CBT) protocol to reduce suicidal thoughts and behaviors during an episode of substance use disorder treatment. The study will involve a pilot randomized controlled trial comparing this adapted CBT intervention to usual care in suicidal patients recruited from a residential substance use disorder treatment program in order to determine the distribution and variability of the primary and secondary outcomes within the intervention and control conditions.
NIH	2009	School -based Suicide Prevention: Building Skills, Resources and Capacity	WALSH, ELAINE	DESCRIPTION (provided by applicant): Despite prevention efforts, suicide remains a leading cause of death for adolescents. A key aspect of suicide prevention is identifying youth at risk, providing immediate support, and connecting them with appropriate re- sources. While schools are an ideal place for such prevention activities, for the most part prevention programs have not been translated adequately from the research to school setting. A critical prevention challenge is to create school capacity to implement and sustain efficacious suicide prevention programs. The goal of this developmental project is to implement a program that will increase the capacity of school districts to respond effectively to youth suicide risk behaviors, and to assess the feasibility of this capacity-building program. Capacity to respond will be increased by training school personnel to implement and sustain prevention interventions at three levels of expertise: awareness and case finding by all school staff members (Level I), intermediate assessment for all counselors (Level II), and advanced assessment/brief intervention for select counselors/mental health professionals (Level III). A secondary goal of this project is to develop and pilot a student surveillance model that assesses school climate. Study aims are to: (1) examine the feasibility of school-wide gatekeeper training (Level I) for increasing staff knowledge about warning signs for suicide risk and capacity to take action with students, (2) assess the feasibility of tiered assessment/brief intervention training (Levels II & III) by conducting in-depth assessments of trainees' opinions of and responses to training, (3) pilot a student surveillance model for assessing school climate characteristics, and (4) evaluate the feasibility of this focused capacity building approach from the perspective of school and district administrators. In Phase I of the study a combination of qualitative analyses and a limited, quasi-experimental pre-post test design are used. Focus groups will be conducted to assess Level II and Level III participants' perceptions about the training format, content, and utility. A within setting pre-post design and between setting post-test to pre-test with a selected comparison school district will be used to explore effects of training on Level I staff members' knowledge, skills, and willingness to intervene. In Phase II, we use a comparison school district to re-evaluate program changes made in the first implementation phase. We conclude by conducting interviews with school and district administrators to inquire about their perceptions of the overall feasibility of the project. This study responds to recommendations for systematic training in suicide prevention interventions through continuing education opportunities; addresses Healthy Youth 2010 objectives to reduce suicide rates and suicide attempts, and to increase the number of adolescents who receive treatment for mental health problems. It also responds to the Surgeon General's Call to Action recommendations to enhance community resources and train 'natural' gatekeepers. Findings will provide the foundation for an R01efficacy trial of the proposed capacity building model. PUBLIC HEALTH RELEVANCE: The purpose of this developmental grant application is to assess the feasibility of a program of suicide prevention activities designed to increase the capacity of high schools to respond effectively to youth suicide risk behaviors. In addition, we will pilot a student survey for assessing related school climate and organizational characteristics. All school staff members will be trained as gatekeepers who can identify and approach a distressed young person, provide support, and refer the young person to a school counselor for further evaluation. School counselors will be trained in suicide prevention assessment and intervention methods. Evaluation will include: changes in school personnel knowledge, willingness to take action and provision of help and support; trainee feedback on the format, content and utility of training; and successful administration of survey activities.

NIH	2010	Lumbee Rite of Passage: A Suicide Prevention Model for American Indian Youth	BELL, RONNY	DESCRIPTION (provided by applicant): Suicide is a threat to the health of all Americans, but some ethnic groups are more affected than others. Limited data indicate that American Indian (AI) youth experience high rates of suicide completions, suicide attempts, and suicidal ideation compared to their non-Latino white counterparts. Many factors contribute to suicidal ideation in AI youth, including depressive symptoms, low self-esteem, substance abuse, hopelessness, forced acculturation, and lack of social support. Cultural interventions (interventions that utilize cultural practices to intervene on health outcomes, as distinguished from interventions that are merely culturally appropriate) have recently been associated with positive health outcomes in AIs as well as other ethnic groups. Still, while it is highly recommended that interventions targeting mental illness in AI youth consider cultural constructs related to health, very few studies have used this approach to-date. North Carolina (NC) is home to the largest AI population east of the Mississippi River. The Lumbee Indian tribe, a non-reservation tribe with a population of about 50,000, is the largest tribe in the state and is largely concentrated in Robeson County. The overall goal of the proposed exploratory study, Lumbee Rite of Passage for Life, is to determine the impact of cultural programs, specifically a culture class conducted by the Lumbee tribe at three tribally owned Boys and Girls Clubs, on suicide ideation in American Indian adolescents between the ages of 12 and 17 years. The study will entail participation from the Lumbee community and will be conducted as a partnership between the Maya Angelou Center for Health Equity (MACHE) at Wake Forest University School of Medicine (WFUSM), the University of NC at Pembroke (UNCP), and the Lumbee Tribe of NC. This exploratory R21 will accomplish two specific aims: (1) to assess perceptions regarding suicidal behavior and risk factors for suicide and examine mental health needs among and services for Lumbee Indian youth (ages 12-17 years) in Robeson County, NC; and (2) to determine the impact of a tribally-run cultural program on suicidal ideation and its risk factors. A secondary aim to Specific Aim 2 is to examine the moderating effects of demographic variables (including gender), sexual orientation, and obesity on the relationship between participation in the culture classes and suicidal ideation. For Aim 1, we plan in-depth interviews with community gatekeepers regarding availability and quality of mental health resources and focus groups with Lumbee youth to identify impressions of mental health issues, particularly regarding suicide and its risk factors in their community. For Aim 2, investigators will conduct a feasibility study in conjunction with the Lumbee tribe to measure changes in suicidal ideation and its risk factors that occur as a result of participation in a cultural program that includes native dancing, pow-wow singing, NC Indian history, beading, and pottery. Participants will be randomized into intervention and delayed intervention (comparison) groups, and pre- and post-intervention measures of suicide ideation and factors associated with it will be collected via surveys. PUBLIC HEALTH RELEVANCE: Suicide and its risk factors remain a major public health concern in the United States, and American Indians bear an unequal burden of completed suicides, suicide attempts, and suicidal ideation compared to whites. The proposed exploratory study is a partnership with the Lumbee Indian tribe of North Carolina and will test the feasibility of using a tribally run culture class to promote positive mental health outcomes and reduce suicidal behaviors among Lumbee adolescents. While we acknowledge that culture may only be one of many things that promote good mental health among young people, innovative research such as this could lead to more comprehensive treatment and prevention interventions and therefore add to the body of public health knowledge.
NIH	2009	Varenicline Treatment for Smoking Cessation in Patients with Bipolar Disorder	CHENGAPPA, Kadiamada	DESCRIPTION (provided by applicant): As cigarette smoking decreases in the USA, it is startling to note that those with mental illnesses smoke nearly 45% of all cigarettes. Patients with Bipolar disorder are at least 3-4 times more likely to smoke as the general population, partly accounting for their much higher morbidity and mortality rates. Such patients are increasingly becoming the face of smoking and yet are typically excluded from clinical trials of cessation treatments. While systematic clinical trials for smoking cessation have been widely conducted in the general population and initiated for persons with schizophrenia, virtually none has been attempted for people with Bipolar disorder. The main objective of this study is to conduct a 3-month double-blind, placebo-controlled clinical trial of varenicline (the latest FDA approved agent for smoking cessation) combined with counseling in 80 smokers with bipolar disorder who are motivated to quit smoking, with follow up 3 months later to evaluate extended abstinence. By carefully screening and enrolling stable patients, the benefits and risks of varenicline in this population of smokers will be evaluated. To our knowledge, it will be the first controlled trial of medication for smoking cessation in patients with Bipolar disorder. Varenicline has been found to be the most effective cessation medication to date, providing a potentially robust treatment for smoking in this heavily dependent subpopulation that may be superior to the other approved medications of bupropion and nicotine replacement. Safety features have been built into the clinical trial to ensure safety of participants, especially monitoring for psychiatric symptom worsening, and to remove and stabilize participants if concerns arise. We will also assess craving, withdrawal, and smoking reward to gauge possible mechanisms of efficacy of varenicline versus placebo in this patient group. Results of this study will provide guidance on refining smoking cessation treatment in smokers with bipolar disorder and on designing clinical trials in other patient groups typically excluded from most clinical trials but in need of robust interventions for smoking cessation. Establishing effective cessation treatments for these smokers with disproportionate rates of morbidity and mortality could greatly reduce the public health toll of smoking. PUBLIC HEALTH RELEVANCE: This project aims to conduct the first formal placebo-controlled clinical trial of a smoking cessation medication in patients with Bipolar disorder. Patients will receive counseling plus medication or placebo for 3 months, with a 3-month follow-up to determine durability of treatment effects. Results will inform clinical care of smokers with Bipolar disorder, reducing their high risk of mortality, and help guide clinical trials in other patient groups currently overlooked in smoking cessation research.
NIH	2010	RNA editing in suicide, major depression and animal model of depression	DRACHEVA, STELLA	DESCRIPTION (provided by applicant): The estimated global burden of suicide is about one million deaths per year. Being one of the leading causes of death, suicide receives increasing attention worldwide, with many countries (including USA) developing national strategies for prevention. Up to 90% of adults who commit suicide have at least one psychiatric diagnosis (e.g., major depressive disorder (MDD), bipolar disorder (BPD), schizophrenia (SZ)). Whether the biological underpinnings of suicide are distinct from those of the comorbid psychiatric disorders is unclear. In our "initial study" we examined mRNA editing of 5-HT2CR in the prefrontal cortex (PFC) of persons who had suffered from BPD or SZ and died by suicide or other causes as well as in psychiatrically normal controls without suicides. We detected an increase in editing that was associated with suicide but not with the psychiatric diagnoses, demographic characteristics, psychoactive medications, alcohol or drug abuse. Based on these findings, we hypothesize that an alteration in the mRNA editing process may be one of the factors that predispose individuals toward suicidal behavior. The proposed application will investigate this phenomenon further to establish its specificity among different clinical populations and different brain regions as well as to elucidate molecular targets for future pharmacological interventions against suicidal behavior. Our initial study was focused on persons with BPD and SZ. However, given that the majority of suicides occur in persons with MDD, confidence in specificity of this phenomenon for suicidal behavior cannot be firmly established without studying 5-HT2CR editing in the context of MDD. In addition, our initial study was performed in the PFC that control decision-making and impulsivity. However, there is undoubtedly an affective component to suicide, which we will address in the proposed application by assessing editing in the amygdala and the anterior cingulate cortex. These two regions are the crucial elements of the corticolimbic circuitries that are involved in mood regulation and that are compromised in depression. In an attempt to tease out the anticipated 5-HT2CR editing changes in suicide from those that are induced by medications taken by the patients in the course of the disease, we will perform a parallel study using mice exposed to the unpredictable chronic mild stress (UCMS), which is an established model to study aspects of depression in animals. In particular, we will investigate editing alterations in UCMS-exposed mice with and without antidepressant treatment. The editing alterations (if observed) will be compared to those detected in humans with MDD and/or suicide. We will also take a first step toward elucidating the molecular mechanisms underlying the suicide-associated variations in editing. Although 5-HT2CR editing is influenced by many different factors, the most obvious explanation is an alteration in the activity of the editing enzymes (adenosine deaminases that act on RNA or ADARs). Thus, we will attempt to assess the activity of ADARs in suicide and/or MDD. PUBLIC HEALTH RELEVANCE: Despite dramatic improvements in the pharmacological treatment of psychiatric disorders associated with suicide, there has been relatively little change in suicide rates over the past 25 years. Effective pharmacological approaches toward suicidal behavior can be developed only if biological mechanisms specific for suicide are understood. According to our initial study, one of those suicide-specific mechanisms may initiate from an alteration in the mRNA editing process. The proposed application will investigate this phenomenon further, aiming to elucidate molecular targets for future pharmacological interventions against suicidal behavior.

NIH	2011	Developmental Pathways to Suicide Attempt	WILCOX, HOLLY	DESCRIPTION (provided by applicant): This exploratory study will examine if there are unique pathways to suicide attempt using 13 waves of prospective longitudinal data on two ongoing epidemiologically sampled cohorts of 2953 young adults (300 with a prior suicide attempt) originally recruited upon entry to first grade in 28 inner city Public Schools in Baltimore, Maryland. This project will assess the influence of individual psychiatric, familial (parenting, family history), environmental (exposure to violence, sexual/physical abuse), social, and high risk behaviors (sexual, drug use) during the course of development on distinct pathways to suicide attempt. Research has shown that it is very difficult to predict suicide deaths and suicide attempt, perhaps because there are multiple pathways or subtypes. The identification of subtypes is highly significant because appropriate intervention approaches for subtypes may differ. It is also possible that the SA subtypes could represent more homogeneous genetic groups yielding greater ability to detect genetic variation in vulnerability for SA. Studies have identified risk and protective factors but few have identified multiple factors prospectively through the course of development to identify processes or mechanisms. The majority of participants with SA in our community sample (~60%) have never met DSM-IV criteria for a major depressive episode. There is a growing literature on the importance of trait aggression/impulsivity as a strong indicator of suicide risk with a possible biological basis. It is unclear if there is a distinct subgroup defined by trait aggression with increased liability of SA. We will study multiple domains of childhood, adolescent and young adult experiences as reported by the participants, peers, parents, teachers, and public records (arrest records). The project will assess the effect of specific genetic markers of risk for suicide attempt (i.e., SLC6A4, TPH1, BDNF, FKBP5) overall and in subgroups, based upon the developmental pathways or trajectories identified. The results of this study will advance our current understanding of the processes and mechanisms associated with suicide attempts among ethnically diverse, urban community populations. PUBLIC HEALTH RELEVANCE: This R21 project entitled "Developmental Pathways to Suicide Attempt" aims to identify distinct pathways or trajectories to suicide attempt in 2953 young adults (300 suicide attempters) initially recruited upon entry to first grade in Baltimore City Public Schools. Improvement in the ability to predict suicide attempts through the identification of specific risk and protective factors experienced over the course of child and adolescent development is an important goal for the prevention of suicide.
NIH	2010	Epigenetic Studies in Suicide Brain	DWIVEDI, YOGESH	DESCRIPTION (provided by applicant): Suicide is a major public health concern. Although attempts have been made to investigate the neurobiology of suicide, the precise molecular mechanisms associated with this disorder are still unclear. It has been proposed that mood disorders/suicide result from an inability of the brain to make appropriate adaptive responses to environmental stimuli. Epigenomic processes are essential not only for normal cellular development and differentiation, but also critical for regulation of gene function through non-mutagenic mechanisms. DNA methylation is the major epigenetic approach for modulating the gene-environment interaction through alterations of promoter regulatory sequences and is associated with stable and adaptive changes in brain functions. In our previous studies, we have consistently shown that the expression of genes involved in neural and structural plasticity is significantly down-regulated in the postmortem brain of suicide subjects, suggesting that altered gene expression may be crucial in the etiology of suicide. Interestingly, a large number of genes exhibit an inverse correlation between the degree of methylation and the magnitude of gene expression. Therefore, the possibility that epigenetic modifications of DNA causing such alterations in the expression of certain genes in brain of suicide subjects, cannot be ruled out. In fact, research in the area of epigenomic regulation of gene expression has led to the hypothesis that the polygenic nature of complex psychiatric disorders might indicate that a common pathway is involved in the dysregulation of multiple genes through an epigenomic mechanism. Although still in infancy, recent evidence suggests that epigenetic factors may play a key role in the pathogenic mechanisms of psychiatric illnesses. To investigate whether epigenetic modifications of DNA play any role in suicidal behavior, we are proposing a pilot study to investigate large- scale epigenetic profiling in the prefrontal cortex of a cohort comprising depressed suicide, non-suicide depressed and well-matched non-psychiatric healthy normal comparison subjects. More specifically, we will examine the following: 1) DNA methylation pattern at the promoters of all known protein-coding genes; 2) confirm microarray results using sodium bisulfite modification-based mapping of metC/CAEC/T ratios in the CpG sites; 3) use a network-based approach to test the modularity of the epigenomic data; and 4) combined analysis of epigenomic profiles and global gene expression data. To further replicate the DNA methylation study, in another cohort of depressed suicide and healthy comparison subjects, we propose to follow-up 10 to 15 promoters of genes that exhibit the largest epigenomic differences between depressed suicide and normal control subjects. To our knowledge, the proposed research will be the first of its kind in suicide research, and will likely identify major epigenetic modifications in the suicide brain. The proposed studies will also pave the way for our future epigenetic studies and will be crucial for identifying the etiological and pathogenic mechanisms of suicide. PUBLIC HEALTH RELEVANCE: Our proposed study will yield important information on the neurobiology of suicide, which may eventually lead to better treatment and possibly prevention of suicide.
NIH	2011	Attempted Suicide Candidate Gene Resequencing	WILLOUR, VIRGINIA	DESCRIPTION (provided by applicant): This application aims to identify novel gene variants conferring susceptibility to suicidal behavior. While suicidality is perhaps the most dreaded aspect of psychiatric disorders, and among the leading causes of death among young people in the United States, relatively little research has been devoted to its biological basis. Yet family, twin, and adoption studies make clear that suicidal behavior has a substantial heritable component. While there is evidence that this heritability is accounted for in part by a liability to mood disorder, other evidence suggests an independent heritable facet that may cut across multiple psychiatric disorders. This independent feature has been hypothesized to be a liability to aggressiveness and impulsivity; the genetic study of this feature has focused on serotonergic genes because of neurobiological findings in suicidal subjects implicating this neurotransmitter. However, little systematic genetic investigation of the suicidality phenotype has been undertaken. Only in the last six years have the first attempts been made to examine the whole genome for linkage with this phenotype. The first two published studies of this kind, one using alcoholism pedigrees and the other using major depression pedigrees, both found evidence of linkage to the 2p11-12 region. Remarkably, when we examined the suicidal behavior phenotype in our bipolar disorder pedigree set, we found that the strongest evidence for linkage across the genome was in the same region, at the same markers implicated previously. This impressive confluence of findings across three genome-wide studies using differing sample types strongly suggests the presence of a gene predisposing to suicidal behavior in the 2p11- 12 region. We tested this hypothesis directly in a genome-wide association study by comparing genotypes from subjects with bipolar disorder and a history of attempted suicide (attempters) to those from subjects with bipolar disorder and no history of attempted suicide (non-attempters). This analysis identified the LRRTM4 gene, which encodes a nervous system transmembrane protein that triggers formation of excitatory synapses and localizes to 2p12. An independent case-control association study using the attempted suicide phenotype also identified the LRRTM4 gene. We propose to follow-up these results by conducting a large-scale resequencing effort designed to identify a catalog of risk alleles for LRRTM4, with the goal of identifying genetic variation that increases the risk of suicidal behavior, thereby providing unprecedented insight into the genetic basis of the phenotype. Our project will make use of the diverse and complementary skill sets of an outstanding team of investigators that includes experts in molecular genetics, statistical genetics, bioinformatics, and psychopathology. Finding genetic variants that influence suicidal behavior would allow for the identification of people with high-risk alleles and the identification of medications that influence suicidal behavior in individuals with these high-risk alleles. It would also provide new insights into the biological basis of suicidal behavior and provide new therapeutic targets. PUBLIC HEALTH RELEVANCE: Suicidal behavior is perhaps the most dreaded aspect of psychiatric disorders and among the leading causes of death for young people. This application aims to identify genetic factors that increase the risk for suicidal behavior.
NIH	2012	Constructing a Danish Reaction to Severe Stress Cohort	Gradus, Jaimie	DESCRIPTION (provided by applicant): The high prevalence of trauma in the US and around the world has made epidemiologic research on the sequelae of stressful and traumatic experiences of paramount importance. Unfortunately, large longitudinal cohorts of people who have experienced traumatic events, or received a psychiatric diagnosis as a result of these events, do not exist in the United States and cannot be easily constructed. General population cohorts that do exist are often limited in the amount of data that can be collected due to considerations about survey length, and are vulnerable to bias and loss to follow up. Denmark is the ideal location in which to study the longitudinal sequelae of disorders resulting from traumatic experiences, as national healthcare and social records have been catalogued for decades. The current application aims to create an ICD-10 reaction to severe stress (RSS) cohort in Denmark (including people with the diagnoses of acute stress reaction, posttraumatic stress disorder, adjustment disorder, and other reactions to severe stress), which can then be linked to other national Danish healthcare and social data to study various long term effects of these disorders. National Danish databases will also be used to collect data about traumatic events that have been experienced by all members of the cohort, where possible. Given that the current study proposes to use existing national healthcare data, the RSS cohort will ultimately provide an efficient resource to examine the short and long-term sequelae of RSS disorders, as well as modifiers of these associations. [Therefore, this project is well-suited to further the current NIMH strategic objective of "charting mental illness trajectories to determine when, where and how to intervene" (#2).] Further, the proposed open cohort will be an enduring resource, which can be continually updated to examine associations. Finally, because the cohort will contain prospectively collected data on all people who have ever received an ICD-10 RSS diagnosis in Denmark, the research produced from the proposed cohort will not be subject to the recall and selection bias issues common in studies that rely on retrospective reporting within subsets of populations. As an initial demonstration of the utility of the new cohort, we wil examine the associations between ICD-10 RSS disorders and all-cause mortality and mortality due to suicide. PUBLIC HEALTH RELEVANCE: The current project is of great public health relevance because it will establish a resource in which reaction to severe stress disorders can be examined at a national level. This includes examining the sequelae of reaction to severe stress disorders, modifiers of these associations, and identifying factors toward which public health intervention and prevention efforts can be aimed.

NIH	2012	NA	Tseng, George	DESCRIPTION (provided by applicant): Major depressive disorder (MDD) is a heterogeneous illness with many clinical variables - such as sex, age, alcohol, antidepressant drug, recurrence or death by suicide -- as potential factors characterizing subtypes of MDD, making it difficult to fully understand its underlying mechanisms and heterogeneous genetic underpinnings. Many transcriptomic studies have been generated in the literature, including those from Dr. Sibille, the co-PI on this proposal. We propose to apply state-of-the-art statistical integrative analyses tailored to combine multiple MDD transcriptomic studies that will address the specific issues of case-control pairing design, confounding clinical variables and small sample size. Our study will detect novel MDD associated biomarkers, pathways and co-expression modules, and elucidate the magnitudes of transcriptomic changes attributable to substance abuse, recurrence, disease severity, age and sex. The results will enhance our understanding to MDD genetic mechanisms and lead to better and individualized therapeutic solutions. PUBLIC HEALTH RELEVANCE: Our proposed research is to develop and apply modern genomic meta-analysis methods to combine multiple major depressive disorder (MDD) transcriptomic studies that will adequately model the specific data structure of case-control pairing design, confounding clinical variables and small sample size. The goal is to detect novel MDD associated biomarkers, pathways and co-expression modules, and elucidate the magnitudes of transcriptomic changes attributable to substance abuse, recurrence, disease severity, age and sex. The results will enhance our understanding of MDD genetic mechanisms and lead to better and individualized therapeutic solutions.
NIH	2012	Suicide Epigenetics	WILLOUR, VIRGINIA	DESCRIPTION (provided by applicant): Suicidal behavior is a complex phenotype that includes both attempted and completed suicide. Family, twin, and adoption studies provide strong evidence for a heritable component to suicidal behavior. This heritability appears to be partly dependent on the presence of psychiatric disorders such as bipolar disorder, depression, and alcoholism. Importantly, the heritability also appears to be partly independent of them. Our ongoing studies on the genetics of suicidal behavior have identified linkage regions on 2p11-12 and 6q25-26 and one genome-wide association signal on 2p25 (p=5.07 X 10-8), findings that may lead to important advances in understanding the biological basis underlying suicidal behavior. However, a fuller picture will only emerge as the interaction of genetic susceptibility variants with other factors, such as personality traits and environmental risk factors, are established. Environmental stressors, such as child abuse and early parental loss, are known to play important roles in triggering suicidal behavior, likely through interaction with genetic vulnerability factors. Recent work showing stress-mediated epigenetic control of BDNF, a gene implicated in suicidal behavior, provides molecular evidence that epigenetic mechanisms can mediate this interaction (Tsankova et al., 2006). These results suggest the possibility that new insights into the etiology and pathophysiology of suicidal behavior can be gleaned from further study of epigenetic modifications in post-mortem brains of suicide completers. The tools to perform large-scale epigenetic studies have only just become available, and our Epigenetics Center at Johns Hopkins has been a leader in the development of such tools, having created the Comprehensive High-throughput Arrays for Relative Methylation (CHARM) method for genome-wide DNA methylation (DNAm) studies (Irizarry et al., 2008). We are now proposing to conduct a genome-wide assessment of DNAm using CHARM and samples from the frontal cortex (BA10) of post-mortem brains taken from mood disorder suicide completers and controls. Promising DNAm regions will then be validated using bisulfite pyrosequencing, and validated candidate genes will be screened for differential expression in suicide completers. To accomplish this, we have assembled an outstanding team of investigators with expertise in epigenetics, genetics, biostatistics, and psychopathology. The identification and characterization of differentially methylated genes and genomic regions in suicidal behavior would a) provide new insights into the biological basis of suicidal behavior; b) provide new therapeutic targets; and c) provide the data needed to generate in vivo models in which to test therapeutic targets. These new insights into suicide pathogenesis might allow for dramatic advances in our ability to reduce the global burden of this devastating phenotype. PUBLIC HEALTH RELEVANCE: Suicidal behavior is perhaps the most dreaded aspect of psychiatric disorders and among the leading causes of death for young people. This application aims to identify epigenetic modifications that increase the risk for suicidal behavior.
NIH	2013	Biomarkers in HPA axis and inflammatory pathways for suicidal behavior in youth	Melhem, Nadine	DESCRIPTION (provided by applicant): There is a pressing need to detect biological signatures, or biomarkers, for psychiatric diseases that will improve our understanding of their architecture of risk and methods of diagnosis and treatment, as their public health burden continues to grow alarmingly. This is especially true for suicide and suicidal behavior, the most serious sequelae of psychiatric diseases and the 3rd leading cause of death among adolescents and young adults. While suicidal behavior occurs in the context of psychiatric disorders, relatively few subjects with psychiatric disorders attempt suicide. Hypothalamic-pituitary-adrenal (HPA) axis dysregulation is postulated as one of the pathways between stress, psychiatric diseases, and suicidal behavior. In this R21 pilot study, we propose to examine hair cortisol concentrations (HCC) in psychiatric inpatients, 13-25 years of age, admitted for suicide attempt (n=35) and compare them to psychiatric inpatients with suicidal ideation but no previous history of attempts (n=35) and healthy controls (n=35). HCC is a marker of chronic activation of the HPA axis as it provides a retrospective assessment of cortisol levels over the past few months and thus will provide an assessment of cortisol levels prior to suicide attempt. This temporal assessment is not possible using standard methods of HPA axis measurement. This R21 study is the first to use this innovative method in the context of suicidal behavior. HPA axis dysregulation also affects the inflammatory response. We propose a model for the biological pathways to suicidal behavior where we will examine the pathways from gene expression in the HPA axis and inflammatory pathways in peripheral blood to HCC, glucocorticoid receptor (GR) sensitivity, systemic levels of inflammation (Interleukin-6, C-reactive protein), clinical correlates of suicidal behavior, and suicidal behavior. This study is also the first to examine peripheral gene expression and the relationship between the HPA axis and inflammatory pathways in relation to suicidal behavior. We hypothesize that suicide attempters will have decreased GR expression, increased HCC, decreased GR sensitivity, increased expression of inflammatory genes, and increased inflammation as compared to the other two groups. These biological measures will be associated with increased sleep disturbances, impulsive aggression, emotion dysregulation, and reduced distress tolerance. Biological and clinical measures will together predict suicidal behavior. This study is in line with NIMH's Research Domain Criteria (RDoC) where we are measuring the sustained threat construct of the negative valence systems in subjects who are on the spectrum of suicidal behavior from normal to ideation and attempt. This R21 study is the first exploratory stage of a future project that will examine the clinical efficac of HCC and test our proposed model for the biological pathways of suicidal behavior in larger samples. Achieving these goals will bring innovative methods to clinical practice to detect individuals at high risk and will result in the development of new treatment approaches, which will both lead to a significant reduction in psychiatric morbidity and mortality resulting from suicidal behavior in youth.
NIH	2008	Elluam Tungiinun - Toward Wellness	ALLEN, JAMES	DESCRIPTION (provided by applicant): Alaska Natives face significant health disparities associated with alcohol use disorders and suicide. Elluam Tungiinun is a Yup'ik Eskimo term translatable as "towards wellness." Elluam Tungiinun (ET) is a culturally-based preventative intervention to reduce suicide risk and co-morbid underage drinking among Alaska Native Yup'ik Eskimo youth. The ET process approach contextualizes its intervention program to the local needs and culture of each rural Alaska community it serves through a set of intensive community co-researcher adaptation process procedures. This proposal seeks funding for a five-year CBPR prevention trial of the ET intervention with 239 youth, ages 12 through 18, in five rural, remote Yup'ik communities. A sample of 159.in three communities will test effectiveness two years post intervention using a randomized dynamic wait list control design, along with the fidelity of the ET contextualizing process approach to the intervention model. A sample of 80 will test durability and sustainability of impact over five years in two additional communities with whom we have worked in the past three years developing and piloting the ET intervention. This proposal represents the next stage in a 15-year CPBR process with Alaska Natives. Elluam Tungiinun has three specific aims: Specific Aim 1: Test the effectiveness of the ET intervention through contrasts of impact on outcome measures using a randomly assigned, staggered baseline, dynamic wait list control design with three remote, rural AN villages at completion of the intervention. Specific Aim 2: Test the fidelity of implementation of the ET toolbox local contextualization approach to the ET intervention model in three communities, and impact of fidelity on outcomes. Specific Aim 3: Monitor the sustainability and durability of intervention impact on outcome measures in randomly assigned communities 1- 3 at year 1 and 2 post intervention, and in communities 4- 5, where the intervention was developed and piloted, at year 1-5 post intervention. The ultimate goal of this project is to create evidence-based prevention practices for Alaska Natives. The project has three direct contributions to public health relevance. It seeks to (1) reduce the most significant source of health disparity of public health importance disproportionately affecting Alaska Natives and American Indians, (2) advance CBPR methods in health related research with tribal communities and other ethnic minority, low socioeconomic status, medically underserved, and rural populations, and (3) enhance understanding of factors predictive of health among indigenous and other ethnic minority groups.

NIH	2009	DBT for Self-Harm: A Clinical/Research Training for Psychiatry Residents	Brodsky, Beth	DESCRIPTION (provided by applicant): Over the past decade, much effort has been directed toward the development and empirical testing of comprehensive psychotherapy interventions designed to target suicidal and non-suicidal self-injurious behaviors. Less effort has been devoted to incorporating these treatments into clinical training programs, or to training clinicians to conduct psychotherapy research. Dialectical Behavior Therapy (DBT) was identified in the RFA as a "scientifically validated behavioral treatment" for self-harm behaviors. The treatment is primarily taught in doctoral programs that train clinical psychologists. Yet, psychiatrists are often on the front lines of treating suicidal patients. We propose to develop, implement, evaluate and disseminate a comprehensive psychotherapy and research training curriculum for psychiatry residents using Dialectical Behavior Therapy for self- harm behaviors. We propose a 12-month DBT clinical/research training for psychiatry residents at Columbia University that combines didactic seminars, videotape rating and training, and case supervision. The curriculum has two integrated components. One is a comprehensive clinical training program for residents to learn the principles, concepts and interventions of conducting DBT for self-harm behaviors. A concurrent research curriculum will teach basic principles of conducting psychotherapy research, specifically to conduct research testing the efficacy of DBT in the reduction of self-harm behaviors. The faculty will consist of senior DBT trainers and researchers. The clinical component will include a 5 -day clinical DBT intensive along with weekly group consultation team supervision sessions and 15 hours of clinical training through peer videotape coding and rating. The research component will consist of 25 one- hour didactic sessions related to the conduct of psychotherapy efficacy trials and suicide intervention research on topics of study design, procedures for psychotherapy trials, the role of the psychiatrist in psychotherapy research, data analysis, manualization and adherence. The specific aims of this application are to: 1) develop a core curriculum for training psychiatry residents in DBT clinical interventions and research methods with suicidal and self-harming clinical populations; 2) develop a criterion-based evaluation of basic skill in DBT; 3) disseminate this training and the evaluation to other psychiatry residency training programs in the country. The proposed evaluation component includes the development and validity testing of a new measure designed to assess the achievement of clinical skill in DBT. This measure will be compared with reliable DBT adherence ratings. Basic knowledge of DBT principles, interventions and research methodology will be assessed by a final examination. The dissemination of this curriculum and evaluation plan will take place through workshops at residency training administrative conferences, publications, website postings, and consultation to residency training programs throughout the country. PUBLIC HEALTH RELEVANCE: Suicide and self-harm behaviors have been identified by the Surgeon General to be high priority public health concerns. The proposed research plan is to teach psychiatry residents to conduct Dialectical Behavior Therapy (a psychotherapy empirically shown to reduce self-harm behaviors), and to conduct psychotherapy research to further test the efficacy of DBT in reducing self-harm behaviors. The proposed curriculum will serve as a model to incorporate such trainings into residency programs throughout the country to effectively reduce and prevent suicide and self-harm behaviors.
NIH	2008	Adapting Exercise Treatment for Depression to Adolescents: A Pilot Study	DUNN, ANDREA	DESCRIPTION (provided by applicant): Adolescent depression is a major public health problem in the United States and throughout the world. Major depressive disorder (MDD) in adolescence is common with point prevalence rates of 3% to 9%. In the U.S., it is estimated that by the time adolescents reach the age of 17, 14% will have experienced at least one episode of major depressive disorder. Effective treatments of adolescent depression are clearly needed despite the fact that in the past 10-15 years, there has been a dramatic increase in studies of the efficacy of medications, primarily the selective serotonin reuptake inhibitors (SSRIs) and of cognitive behavioral therapy (CBT). Medications and CBT rarely result in complete and lasting remission of symptoms, and residual symptoms are associated with a high rate of relapse. In most studies, a positive response is defined as a 30-50% improvement in symptoms and/or a global rating that the subject is much or very much improved. In adults, exercise has been used as a mono-therapy and as an augmentation therapy with antidepressant medication. Our recently completed randomized trial of exercise treatment in adults found response and remission rates of 46% and 42%, in those randomized to a public health dose of exercise. In adolescents, data on the use of exercise to treat MDD is relatively sparse. A 2006 Cochrane review of exercise to prevent and treat depression in adolescents found a small effect size in support of exercise, but the conclusion is based on evidence from a small number of randomized clinical trials of low methodological quality. In this exploratory R34, the specific aims of this application are to: 1) Develop a detailed Manual of Procedures (MOP) to conduct an acute-phase randomized trial of exercise to treat adolescent depression; 2) Develop estimates of recruitment yield from tests of various recruitment strategies; and, 3) Pilot test trial methodologies in (n=40) adolescents diagnosed with depression to ascertain estimates of treatment effect sizes, adherence and drop-out rates. To achieve these aims, the project is organized into 3 phases. Phase I will be the development of the first draft MOP that will adapt procedures developed from a previous trial examining two doses of exercise in treatment of adult MDD. Phase II will test specific recruitment methodologies to determine recruitment yields for each strategy and will pilot test screening procedures developed in Phase I. Phase III will be a pilot test of the intervention and will include development of baseline and outcome measures of exercise and depression; development and implementation of the experimental exercise treatment; and determination of the effects of exercise on depressive symptoms. Following the pilot study, we will finalize all procedures for the MOP and obtain estimates of effect sizes, adherence and drop out rates. These data will allow us to specify all study procedures necessary to meet standards of high methodological quality for a future, larger-scale, controlled study of exercise in depressed youth and will provide us with needed experience. Additionally, the results of the pilot study will enable us to more precisely quantify sample sizes for a future R01 application. This pilot study may yield important research findings on how to adapt exercise treatment for depression among adolescents. Potential public health benefits from this study include a reduction of adolescent depression and problems associated with untreated depression in young adults including suicide, substance abuse, cigarette smoking, teen pregnancy, impaired psychosocial functioning and school failure. In addition, because this study prescribes physical activity as a treatment for depression, additional public health benefits may include a reduction in chronic diseases such as obesity, diabetes and heart disease, all of which are associated with sedentary behavior.
NIH	2009	Concurrent Treatment for Parents and Adolescents Who Attempt Suicide	SPIRITO, ANTHONY	DESCRIPTION (provided by applicant): Approximately 2 million adolescents attempt suicide each year and 700,000 receive emergency medical treatment each year (Shaffer & Pfeffer, 2001). Treatment of adolescent suicide attempters is complicated by parental psychopathology, which has been found to be significantly elevated in this group compared to normal controls. There are several pathways by which all parents' psychopathology may be related to their adolescent's suicidality. First, genetic transmission of either suicidal behavior and/or more general psychopathology, such as an affective disorder, may be the mechanism by which parent functioning affects adolescent suicidal behavior. Indeed, a number of studies have found high rates of parental suicidal behavior among adolescents who attempt suicide. Second, parents with a history of past or current suicidality may model suicidal behavior for their adolescent. Third, family processes in these families may be especially sensitive to suicidality. For example, these families may inadvertently reinforce suicidal behavior via attention, or adolescents may use suicidal behavior to terminate aversive family relationship patterns. Fourth, parental psychiatric disorders may lead to aversive parenting in such a way that it may lead to an adolescent's suicidal thinking or behavior (Downey & Coyne, 1990). Finally, parental functioning may affect a parent's ability to follow through with their adolescent's treatment attendance, which in turn can affect progress made in therapy. The purpose of this application is to develop a treatment protocol that simultaneously treats the adolescent who attempts suicide and his/her parent, most typically a mother, if the parent is diagnosed with major depressive disorder. A two-step sequence of treatment development is proposed. Phase I includes therapist training, pilot testing, and protocol revisions as well as a small open trial. The concurrent treatment protocol will include both individual sessions for adolescents and parents but also parenting and family sessions. In Phase II we will conduct a small randomized trial and compare the experimental concurrent treatment protocol to treatment of the adolescent alone. Adolescents hospitalized on a psychiatric inpatient unit or treated in the Emergency Department following a suicide attempt will be recruited to participate in the study. Outcome will be assessed at the end of treatment and 6 months post-treatment. By integrating the treatment of these adolescents with that of their parents and using the same treatment principles for both, we hypothesize that the experimental protocol will lead to greater improvements in suicidal ideation and treatment success (i.e., no repeat suicide attempts, no repeat hospitalizations) than that typically found when an adolescent is treated individually. Adolescent suicide is the third leading cause of death during adolescence. This application tests an integrated protocol for suicidal adolescents and a depressed parent. Reducing the incidence of injurious suicide attempts among adolescents 14 to 17 years old and completed suicide among youth 15 to 19 years old are Year 2010 objectives addressed in this application.

NIH	2009	College Students with Elevated Suicide Risk: Enhancing Treatment Linkage	KING, CHERYL	DESCRIPTION (provided by applicant): Suicidal behavior is a significant concern on college campuses and suicide is the third leading cause of death in the U.S. college-aged population. Consistent with recommendations in the National Strategy for Suicide Prevention (2001) and spearheaded by organizations such as the American Foundation for Suicide Prevention, several universities have initiated voluntary web-based screening to identify students at elevated risk for suicide and in need of mental health services. This is a promising direction; however, research is needed to determine how to most effectively link students with positive screens to professional services. We propose to develop and pilot test a theoretically-driven intervention, Students' e-Bridge to Treatment (e-Bridge), which aims to identify students with elevated levels of known suicide risk factors and facilitate these students' linkage to mental health services. e-Bridge will incorporate motivational interviewing principles and draw from health behavior promotion models. Our initial aim is (1) to develop the e-Bridge intervention for students at risk for suicidal behavior due to depression and alcohol/substance misuse, or suicidal thoughts or behavior. e-Bridge will include (a) a web-based screen using standardized instruments to identify students at elevated suicide risk; (b) personalized feedback; and (c) the opportunity to correspond online with a professional who has been trained in motivational interviewing and is knowledgeable about local resources. This is consistent with a model emphasizing autonomy and self-determination. Additional aims are (2) to conduct a pilot feasibility study with a small number of college students at elevated risk, and (3) to conduct a pilot randomized controlled trial comparing e-Bridge to a control condition (personalized feedback and list of mental health resources). The primary quantitative outcome, assessed two months after screening, will be linkage to mental health services. Qualitative data will be collected about what students found to be most and least helpful about each intervention component. Secondary outcomes will include: a) suicidal thoughts and behavior; b) depression severity and alcohol/substance misuse; and c) the costs of the intervention. If the intervention is shown to be promising and then demonstrated to be effective in larger studies, it could prevent suicides and other adverse consequences among college adults nationwide. Suicide is a leading cause of death among young adults. Moreover, recent national surveys indicate that 10% of college students have seriously considered attempting suicide within the past year. In keeping with recommendations in the National Strategy for Suicide Prevention (2001), this project will develop and pilot test Students' e-Bridge to Treatment. This intervention will identify students at elevated risk for suicidal behavior and facilitate their linkage to appropriate treatments.
NIH	2010	Group IPT For Major Depression Following Perinatal Loss	JOHNSON, JENNIFER	DESCRIPTION (provided by applicant): Perinatal loss includes early (before 20 weeks; miscarriage) and late fetal death (after 20 weeks; stillbirth) and the death of a liveborn neonate in the first 28 days after birth (neonatal death. Despite medical advances, spontaneous miscarriages occur in 10-15% of recognized pregnancies, with stillbirth occurring in 1 in 160 live births and neonatal death occurring in an additional 1 in 145 live births. Overall, about 650,000 women in the United States experience perinatal loss each year; of these, 11-13% (71,500 - 84,500) will experience a related major depressive episode. The rates of major depressive disorder (MDD) among women who have recently experienced perinatal loss are 3 times the rates of MDD among matched samples of community women. An elevated prevalence of MDD relative to other women of childbearing age is notable given that MDD already is twice as common in women as men, with peak onset during the childbearing years. Women who meet criteria for MDD following perinatal loss are at risk for severe and enduring morbidity and impairment, which can persist up to 30 months after the loss. Moreover, they have increased rates of both completed suicides and hospitalization for suicide attempts. In addition, regardless of the circumstances surrounding its onset, MDD is the leading cause of lost years of healthy life among women worldwide and the leading cause of non-obstetric hospitalization in young women in the United States. Despite recognition that MDD following perinatal loss is an important public health concern, that it causes significant impairment, and that treatment as usual has been inadequate, virtually no treatments have been developed for or tested in this population. Group Interpersonal Psychotherapy (IPT-G) has been shown to be efficacious in treating MDD in other populations and may be especially pertinent to the treatment needs of women experiencing MDD following perinatal loss because many of these needs are social and interpersonal in nature. The purposes of this application are to (a) adapt group interpersonal psychotherapy (IPT-G) to address the unique needs of women with MDD that occurs following perinatal loss, and (b) to collect preliminary data on its feasibility, acceptability, and initial efficacy relative to a dose-matched standard depression treatment (the Coping with Depression course) in a sample of 60 women to lay the groundwork for a larger clinical trial. Primary outcomes are treatment acceptability, time to remission from MDD, and reduced depressive symptoms. Secondary outcomes are social support and social functioning, couple distress, and grief. From a longer term perspective, this program of research will result in the adaptation of a specialized, efficacious treatment for a vulnerable and understudied population whose distress has historically been minimized. PUBLIC HEALTH RELEVANCE: Overall, about 650,000 women in the United States experience perinatal loss (including miscarriage, stillbirth, and early neonatal death) each year; of these, 11-13% (71,500 - 84,500) will experience a related major depressive episode. Women who meet criteria for major depressive disorder following perinatal loss are at risk for severe and enduring morbidity and impairment, which can persist up to 30 months after the loss, yet virtually no treatments have been developed or tested for this population. This project will adapt and test an interpersonally-based treatment to address the specific needs of this vulnerable and understudied population.
NIH	2011	Coping Long-Term with Attempted Suicide Program - Adolescents	YEN, SHIRLEY	DESCRIPTION (provided by applicant): Suicide is the third leading cause of death in the 15-24 age group and accounts for more deaths than all natural causes combined. In 2007, 14.5% of U.S. high school students seriously considered suicide, 6.9% reported making at least one suicide attempt in the previous twelve months, and 2% of students reported making at least one suicide attempt in the previous twelve months that required medical attention. Despite the high public health significance of suicide and suicide attempts, there has been relatively little research devoted to developing or testing interventions that directly target suicidal behavior. There is no gold standard treatment for adolescent suicidality; reviews of published randomized controlled trials for adolescent suicidality conclude that treatments to date have been minimally efficacious. Thus, the consideration of new multi-modal interventions that can be applied to suicidal adolescents during the high risk transition period from inpatient to outpatient care, irrespective of diagnosis, is clearly warranted. The purpose of this R34 treatment development grant is to develop the "Coping Long-term with Attempted Suicide Program - Adolescents (CLASP-A)," an integrated, adjunctive intervention program for adolescents who have made a previous suicide attempt. The goals of CLASP-A are to reduce continued suicidal behavior and ideation, reduce risk behaviors for suicide, and improve adherence to psychosocial and psychopharmacologic treatments. It is comprised of three major components: a) three individual meetings while the patient is in the hospital, b) one in-person meeting with the patient and his/her parent/guardian in the hospital and c) a series of scheduled telephone contacts with the patient and parent/guardian for six months following discharge from the hospital. CLASP-A is based on a risk reduction model, and specifically targets four generic and potentially modifiable risk factors: hopelessness, impaired family support, problem solving deficits, and treatment non-adherence. The overall aim of this proposal is to further develop the CLASP-A intervention to address the needs of adolescents and to examine the feasibility and acceptability of this intervention program in adolescents. We propose a development phase which includes an open trial and iterative revisions to the treatment manual, a pilot study phase which includes a randomized trial (n=50), and a revision phase. Based on our findings, we will revise CLASP-A, with the objective of creating a flexible protocol in which emphasis can be shifted based on the presenting problems of the patient/family, and strategies can be selected to accommodate the developmental stage of the patient. The results from this pilot study will lay the groundwork for a larger clinical trial evaluating this new adjunctive intervention for suicidality for this high risk group of patients during the high risk period of transition from inpatient to outpatient care. PUBLIC HEALTH RELEVANCE: Adolescent suicidality is a growing public health concern. However, relatively little research has been devoted to developing or testing interventions that directly target suicidal behavior. The goal of this treatment development grant is to develop an adjunctive intervention for adolescents who have made a suicide attempt.

NIH	2012	Outcomes in Callers to the VA's 24/7 Veterans Crisis Line	KNOX, KERRY	DESCRIPTION (provided by applicant): If we are ever to know with any certainty that crisis lines are effective in reducing deaths from suicide, or in managing distress levels in individuals before they are suicidal, three essential questions must be addressed: 1. Of the entire population of potential callers to a crisis line, what are the characteristics of individuals who cll a crisis line? 2. What are the key behavioral characteristics of responders that moderate individual characteristics of callers, resulting in acceptance of a referral given from a responder to the caller? 3. Is there an impact on important outcomes: death from suicide, suicide attempts and reattempts, hospitalization for suicidal behaviors, engagement in an ongoing safety planning process, and overall reductions in psycho-social distress? PUBLIC HEALTH RELEVANCE: We view a study of the Department of Veterans Affairs' (VA's) 24/7 Crisis Line (formerly called the VA Suicide Hotline) as significant since suicide prevention crisis lines continue to be an intervention of great interest, while still defying reaching a high standard of proven effectiveness. Due to the very nature of community crisis lines, by virtue of their anonymity, it is difficult to answer three questions that must be addressed if we are ever to know with any certainty that crisis lines are effective in reducing deaths from suicide, or in managing distress levels in individuals before they are suicidal. These questions underscore the significance of this application because of our distinct ability to address issues that cannot be done in any other crisis line setting: 1. Of the entire population of potential callers to a crisisline, what are the characteristics of individuals who call a crisis line? 2. What are the key behavioral characteristics of responders that moderate individual characteristics of callers, resulting in acceptance of a referral given from a responder to the caller? 3. Is there an impact on important outcomes: death from suicide, suicide attempts and reattempts, hospitalization for suicidal behaviors, engagement in an ongoing safety planning process, and overall reductions in psycho-social distress? We recognize that considerable advances have been made in addressing Questions 1 and 2; indeed, Dr. Madelyn Gould who is a Co-Investigator on this study has been a leader, with others, in the field of examining the utility of suicide crisis lines But a critical difference between the national network of suicide crisis lines across the United States (National Suicide Prevention Lifeline, or NSPL) and VA's Crisis Line is that the VA's Crisis Line has the enhanced ability to study characteristics of callers and responders, the capacity to provide nation-wide services through immediate referral and follow-up care, and the critical capacity to identify outcomes in callers to the Crisis Line. Through the use of some new, innovative methods, including causal modeling, we have developed a study that we strongly believe has the potential to have a high impact on delivery of care through suicide crisis lines. I summary: This may not be the perfect study of the effectiveness of a suicide crisis line, but it overcomes many of the limitations inherent to studies of community crisis lines.
NIH	2012	Pilot Study of Online Interventions for Population-Based Suicide Prevention	WHITESIDE, URSULA	DESCRIPTION (provided by applicant): Reducing the risk of suicide attempt and suicide is a public health priority. In the United States, 36,000 people die annually from suicide and it is our nation's 10th leading cause of death. There has been no substantial decrease in suicide for the past two decades. Prevention efforts to date have focused on primary (e.g. public service announcements) and tertiary (e.g. interventions following suicide attempt) methods. Secondary or indicated prevention has been relatively unexplored. Secondary prevention requires both accurate screening methods and effective interventions. These essential elements are now available. Our recent research demonstrates that responses to the suicidal ideation item of the PHQ depression scale are a powerful predictor of subsequent suicide attempt and death. Availability of the PHQ in electronic medical records creates an opportunity for accurate population-level screening. Dialectical behavior therapy (DBT) has strong evidence of tertiary efficacy for preventing suicide attempts in clinical populations. Brief outreach tertiary interventions such as caring messages have some evidence for preventing suicide attempts. These clinical or tertiary prevention interventions provide the best available evidence for use in building secondary prevention programs. Resulting programs could then be linked to population-level screening data in electronic medical records. The first goal of the research plan is to adapt DBT and caring messages to fit delivery models suitable for the large numbers of at-risk patients identifiable in healthcare settings. The second goal is to evaluate the feasibility, acceptability, and safety of these alternative online suicide and self-injury secondary prevention programs. Online delivery models are suitable because they are scalable and can be provided securely, cheaply, and utilizing existing systems in healthcare. Three brief online interventions will be evaluated: caring email (CE); CE + DBT online program; and CE + DBT online program + coach. Each intervention will supplement usual care among high- risk patients identified via PHQ depression scales collected at outpatient primary care and mental health visits. Intervention content will be drawn from the principles of DBT and caring messages. The study design will be additive in order to examine alternative intervention models that vary widely in resources required for large- scale delivery. However, these interventions will require vastly fewer resources than in-person or telephone interventions. The project will involve intervention feasibility (pretesting, N=60) and acceptability and safety testing (pilot, N=400). Acceptability wll be assessed by patient intervention engagement levels (requiring the large pilot sample) and qualitative/formative intervention feedback from patients. Safety will be assessed via rates of psychiatric hospitalizations and self-injury diagnoses in the medical record in the intervention conditions compared to those receiving just continued usual care. Results of the pilot study will inform the design of a full-scale effectiveness trial examining the impact of one or more of these interventions on risk of suicide attempt and/or suicide death. PUBLIC HEALTH RELEVANCE: Pilot study of Online Interventions for Population-Based Suicide Prevention PROJECT NARRATIVE th In the United States, 36,000 people die annually from suicide and it is our nation's 10 leading cause of death. Suicide prevention is a national priority and yet secondary prevention programs targeting those most at risk are lacking. The purpose of the current research is to develop and pilot test three promising suicide prevention programs that, if found acceptable to high-risk individuals, could be further evaluated and eventually offered broadly and affordably to the public.
NIH	2013	Developing an intervention to promote API women's sexual and mental health	Hahm, Hyeouk	DESCRIPTION (provided by applicant): Our objective for this R34 is to systematically modify the existing evidence-based intervention, "Seeking Safety" (SS), by integrating a gender-specific HIV intervention (Project FIO) and critical cultural components for Asian-Pacific Islander (API) women who report a history of violent traumatic experience or a diagnosis of Post-Traumatic Stress Disorder (PTSD). This proposal is significant because it aims to reduce two public health problems among API women: 1) the rapidly rising incidence of HIV/STIs, and 2) the highest rates of completed suicide between the ages 15 to 24 among all racial groups of women. A preliminary study based on a K01 identified a strong association between lifetime sexual and physical trauma and health risk behaviors in API women. Specifically, those who experienced trauma had elevated risks of suicidality, substance use, and HIV risk behaviors. To date, no specific intervention that integrates sexual and mental health promotion has been tested for the APIs population, despite it is the fastest growing in the US. The most commonly applied, empirically-supported intervention for women who have experienced trauma is SS.1 However, the intervention should be culturally appropriate and grounded in "the real world" of API women affected by trauma. Thus, we will develop new protocols, which incorporate SS, Project FIO (Future is Ours), API women's unique experiences and voices, and feedback from intervention experts and an API Community Advisory Board (CAB) (Aim 1). We propose to test the feasibility and safety of a pilot randomized clinical trial (RCT) using a two- armed design (with an intervention group of 36, and a wait-list control group of 36) (Aim 2). We will launch AWARE (Asian Women's Action for Resilience and Empowerment) to screen at least 400 women in the greater Boston area and recruit a total of 72 women who meet the criteria for PTSD and traumatic history. The 10-week intervention will be given group psychotherapy along with secure daily mobile text messages ("AWARE Stories"). Adherence to group psychotherapy, utilization/satisfaction of secure mobile messages, and safety (suicidality and intimate partner violence) will be tested as feasibility outcomes. We also aim to test the efficacy of AWARE (Aim 3). We will measure HIV-related outcomes (primary outcomes) and psychiatric symptoms and substance use (secondary outcomes) at baseline, week 10, and 3 months to determine effect sizes for outcomes of the adapted intervention. This integrative, holistic approach is innovative in multiple ways: (1) the study will be the first pilot RCT study to target traumatized API women, (2) it incorporates a culturally appropriate intervention to be widely available, acceptable, and feasible, (3) it is designed to reduce HIV risk behavior, and (4) it tests the feasibility of a moble technology. The proposed research project responds to multiple priorities of NIH, NIMH, and Healthy People 2010. In the future, the findings can be translated into a larger RCT. It is our aim that these efforts will ultimately lead to the reduction of HIV transmission, suicidality, and psychiatric symptoms among API women.

NIH	2013	Skills to Enhance Positivity in Suicidal Adolescents	YEN, SHIRLEY	DESCRIPTION (provided by applicant): The prevalence of suicidal behaviors in adolescents remains unacceptably high. Reviews of published randomized controlled trials (RCTs) for adolescent suicidality conclude that treatments to date have been minimally efficacious. The preponderance of interventions focus on crisis intervention, underlying psychiatric disorders, regulating negative affect and reducing cognitive distortions. However, our pilot work and other recent data suggest the importance of considering how low positive affectivity contributes to suicide risk independent of other risk factors and may be another mechanism that leads to suicidal behaviors. Our model is based on Fredrickson's empirically-supported Broaden and Build model which asserts that the function of positive affect (PA) includes helping individuals thrive by improving social supports, problem-solving, and personal resilience. Each of these areas is instrumental in decreasing suicidal behavior. We propose that PA increases survival directly by decreasing suicidal ideation and indirectly by increasing social support and problem-solving. In this R34 treatment development grant we seek to develop a novel, individual skills-based, PA intervention, delivered adjunctively to treatment as usual (TAU), targeting the highest risk adolescents - those hospitalized due to suicide risk. We focus on three strategies that have been demonstrated to increase sustainable (vs. transient) PA in community and depressed adults: meditation, gratitude, and savoring. There are several ways to practice each strategy; we take into account patient preferences in a personalized approach in which patients select the practice(s) that fits best with their needs and circumstances. We propose using multiple means of intervention delivery that includes a new technology medium of their choosing, to reinforce in-vivo practice. Our intervention, Skills To Enhance Positivity Program (STEPP) includes two phases: a) in-person phase consisting of 3 individual in-person sessions and 1 joint parent session during the inpatient hospital stay to teach PA skills and develop a personalized intervention; b) remote delivery phase which consists of weekly telephone booster calls and daily text or email messages over 4 weeks post-discharge. The phone calls will be used to review or adjust personalized intervention components and reinforce use of skills. The text/email messages will include self-scripted reminders to practice skills and links to online resources. Text vs. email delivery will be based on accessibility and preference. STEPP will be tested in an open trial with 20 participants, and after further revision, in a pilot RCT, compared to TAU in a sample of 50 adolescents. The primary goal of this intervention is for patients to increase positive affect by incorporating skills and practices into their normal home-based routines, which we believe will lead to increases in problem-solving and social support and decreases in suicidal ideation. Our proposal meets NIMH Strategic Objective #3. This is a novel intervention for a high-risk acute population via a different mechanism (i.e. PA), and conceptually distinct from other empirically examined theoretical approaches.
NIH	2009	Enhancing Clergy Suicide Prevention and Referral	Goldsworthy, Richard	DESCRIPTION (provided by applicant): Suicide is the 2nd leading cause of death in persons aged 25-34, the 3rd leading cause of death among people in the age groups 10-14 and 15-24, and the 8th leading cause of male deaths. Faith leaders and clergy have been identified in national strategic public health documents as important front-line gatekeepers for suicide prevention. Preliminary research by the Indiana Partnership to Prevent Violent Injury and Death (IPPVID) has identified strong interest among clergy in training materials regarding suicide prevention. However, to date, no evidence-based training materials are available to facilitate adoption of suicide-related risk reduction and mitigation behaviors among faith leaders. The goal of this project is to fill this need by developing and validating evidence-based and theory-driven training materials to increase suicide awareness and suicide prevention skills among faith leaders. Across both phases, a multipronged approach will be used to generate the content of the faith leaders' suicide prevention curriculum: the effort will (1) capitalize on a pilot curriculum developed by our research partner (IPPVID), (2) draw upon emerging suicide prevention training programs for mental health professionals and general audiences that can be tailored to the specific practical and sociocultural needs of faith leaders, and (3) involve stakeholders and subject-matter experts in the articulation and validation of the curriculum outlines, lessons, and learning activities. Design and development of educational lessons and activities will be guided by a constructivist pedagogical theory, an integrated performance support model, and a well- established instructional design process. Phase I will deliver an overall curriculum design document by conducting structured audience analysis regarding faith leaders' needs, barriers, and common situations as well as content analysis of existing suicide training curricula. Interviews (n=20) with clergy will elicit factors affecting engagement in the target behaviors and will gather reactions to existing curricula; a survey (n=200) of identified beliefs will be conducted, and the results of the survey will drive motivational and other elements of the media. Content from IPPVID pilot trials will be further refined through the multipronged approach described above. Phase I will then develop prototype web-based interactive lessons and activities focusing primarily on awareness and risk identification. The resulting lessons and activities will be evaluated in a small scale RCT (n=60). PUBLIC HEALTH RELEVANCE: Suicide prevention is a vital public health concern. A large number of individuals use religious leaders as their first and often primary source of mental health support. Faith leaders have been identified as important points of leverage for addressing suicide through their ability to directly and immediately engage in identification, brief diffusion, and referral of individuals at risk. Yet faith leaders are often not adequately prepared for this role. There currently exist no evidence-based suicide prevention educational programs tailored for faith leaders' particular practical, organizational, and cultural workplace needs. This project will develop a suicide prevention professional development curriculum customized to the unique needs of faith leaders. The curriculum will draw upon existing evidence-based suicide training efforts and state-of-the-art pedagogical theory and technology. It will be deliverable as individualized instruction over the web as well as through facilitator led training. The proposed effort meets an important, recognized, need with an innovative, easily dessiminable, and customizable educational solution. As such, the resulting products should be well-received by faith leaders and their organizations as well as institutions which provide pre-professional and continuing education to them.
NIH	2010	Automated Interactive Text Messaging to Assess Adolescent Depression	MUNDT, JAMES	DESCRIPTION (provided by applicant): New interactive communication technologies continue to expand in modern society. Children and adolescents are frequently among the earliest adopters of new technologies. Communication via Short Message Service (SMS) "text messaging" is one example. This application proposes to develop computer-automated methods for interactively assessing clinical states in children and adolescents using dynamically branching SMS "text" messaging. Assessment of depression will be used as a template for the proposed research. Study aims are to (1) evaluate the technical feasibility of a computer-automated interactive SMS messaging system, (2) assess acceptance of the technology among depressed children and adolescents, and (3) collect reliability and validity data on a version of the Quick Inventory of Depressive Symptomatology specifically designed for use by adolescents and delivered by SMS (QIDS-A-SMS). Long-term objectives for the development of an interactive SMS technology are to provide clinically valid, widely available, internationally accessible, easily used, and user- acceptable tools for obtaining patient reported outcomes across a wide range of conditions in pediatric patient populations. If successful, the research proposed by this application will support use of the QIDS-A-SMS as a valid treatment outcome measure in pediatric antidepressant clinical trials. Twenty-five outpatients, 8-17 years old, diagnosed with major depression will be recruited from the NIH-sponsored "Pediatric MDD: Sequential Treatment with Fluoxetine and Relapse Prevention CBT" (MH039188; Dr. Graham Emslie, PI). During office visits at baseline and at the end of 6 weeks of treatment with fluoxetine, study participants will use cell phones to complete interactive QIDS-A-SMS assessments via "text replies" to a series of dynamically branching, computer-automated SMS messages. User feedback regarding the assessment experience will be collected. Independent evaluators at the University of Texas - Southwestern Medical School will also assess depression severity using the Child Depression Rating Scale-Revised (CDRS-R) for comparison with the QIDS-A-SMS data. Technical measures of system performance such at time to complete the assessments and error frequencies, user acceptance feedback, and psychometric reliability and validity of the QIDS-A-SMS will be analyzed. PUBLIC HEALTH RELEVANCE: Modern technologies, such as "text messaging" via cellular telephone, are attractive to adolescents and may provide new opportunities to provide behavioral and mental health interventions. The technology may also be helpful for assessing the impact of such interventions in pediatric populations. Major depression is a disabling condition that often begins between the ages of 15-19 years, disrupting development, impairing functioning, and increasing risk for substance abuse, suicide, and adulthood depression. Recent concerns about an increased risk of suicide in adolescents being treated with antidepressants have focused public attention on the need for closer monitoring of adolescent signs and symptoms of depression.

NIH	2010	Chromatin Immunoprecipitation (ChIP) Assay Development for FFPE human brain secti	Jelinek, Mary	DESCRIPTION (provided by applicant): Depression is the leading cause of disability among individuals between the ages of 15-44, affecting approximately 21 million Americans and is the leading cause of suicide. Current diagnostic tools available for medical professionals are limited to questionnaires and other inherently subjective approaches. Improving accuracy of diagnosis has been cited as a pressing need in the field. Recent advances have shed light on the genetic basis for psychopathological conditions, which not only includes changes in gene expression, but also epigenomic changes as well. Epigenomic mechanisms, which regulate gene activity without altering the DNA code, consist fundamentally of DNA methylation of CpG-dinucleotides, which occurs at the fifth position of the cytosine pyrimidine ring, and regulation of chromatin structure through post-translational modification of histones. In this Phase I proposal , we intend to develop a Clinical Chromatin ImmunoPrecipitation assay (C- ChIP), for use with formaldehyde-fixed paraffin embedded (FFPE) human brain specimens, which will enable analysis of changes in histone post-translational modifications in normal and suicide brains samples. Chromatin immunoprecipitation is a powerful technique that captures DNA bound proteins, and enables quantification of the specific immunoprecipitated DNA sequences relative to input. Development of the C- ChIP assay will be achieved by first establishing a rat tissue model system, and in conjunction with the isolation of a panel of highly characterized and specific monoclonal antibodies to histone modifications associated with either transcriptionally active or repressed loci, will be used to systematically adapt existing ChIP protocols developed for in vitro cultured cells, into a highly sensitive assay compatible for use with FFPE sections. Assay validation with clinical samples will be performed collaboratively on a rat maternal care model and subsequently on FFPE control and suicide brain samples. The successful development of the C-ChIP assay will have two effects. First, would be the commercialization of the C-ChIP assay for the broad research market, providing for the first time, an assay which enables the functional genomic analysis of archived clinical samples. The second outcome of this Phase I application will enable subsequent Phase II studies in which genomic-wide survey of a large cohort of suicide brains specimens will be examined for epigenetic alternations which could possibly serve as biomarkers for depression. With this information, it may be possible to subsequently identify peripheral markers that correlate with the brain markers, leading to the development of a diagnostic assay for assessing depression and suicide risk. PUBLIC HEALTH RELEVANCE: 1-3 Suicide and depression are major public health concerns . Recent studies have identified some of the molecular mechanisms involved in suicide and depression and these 7-15 mechanisms include changes in the regulation of gene expression in the brain . This Phase 1 application describes the development of an assay that will enable identification of gene expression changes through the whole genome, which could subsequently lead to the development of a much needed diagnostic for depression and suicide risk.
NIH	2013	American Indian Suicide Prevention Interactive Resources	RAGHUPATHY, SHOBANA	DESCRIPTION (provided by applicant): Suicide is the second leading cause of death for Native youth ages 15-24 residing in IHS service areas and is the third leading cause of death of children aged 10-14 years. Exacerbated by factors such as extreme poverty, substance abuse and inadequate mental health service, suicidal deaths among American Indian/Alaska Native (AI/AN) teens has reached the level of a crisis. In addition, many troubled Native adolescents choose to forego seeking help during times of distress due to privacy concerns, a sense of isolation, hopelessness and stigma. The present proposal will use emerging trends in interactive technology and Web 2.0 tools to develop ASPIRE (American Indian Suicide Prevention Interactive Resources) for Native youth in high schools. ASPIRE will offer schools and youth serving organizations, three distinct-yet complementary-resources: (a) an online modular, suicide prevention curriculum with multimedia activities that is customizable to the practitioner's needs and logistical constraints; (b) online training for teachers and practitioners to implement suicide prevention programming; (c) an online resource for Native teens that will promote knowledge, resilience, and help-seeking behavior among AI/AN teens and young adults. The goal of the ASPIRE project is to create a curriculum that is dynamic and engaging; is culturally-relevant to Native youth; is cost-effective, and most importantly, incorporates youth content and helps peer-to-peer connections within a safe, discreet and monitored community. ASPIRE will be based on the American Indian Life Skills (AILS) Development program, an evidenced-based intervention developed by Prof. Teresa LaFromboise that has been successfully replicated in multiple Native communities.
NIH	2012	Suicide Safety Net: Multimedia Tools for Reliable Risk Management Documentation	DIMEFF, LINDA	DESCRIPTION (provided by applicant): Suicide is the 11th leading cause of death in the United States, accounting for approximately 34,000 deaths per year [1]. Despite the prevalence, many clinical research trials routinely exclude suicidal individuals due to the lack of appropriate tools and protocols to adequately manage suicide risk. Similarly, clinicians are hesitant to treat suicidal patients, fearing the possibility of legal action by bereft family members should their loved one kill him/herself. The overarching goal of this project is to improve the availability and quality of mental health care for suicidal individuals by: 1) increasing the ability of clinicians'to implement best practice techniques for suicide risk assessment and management, and 2) reducing clinicians' fear of litigation following a suicide by reducing the actual risk of litigatin. This will be accomplished by designing and developing an innovative, web- based tool that guides clinicians through an empirically-derived suicide risk assessment and management protocol, while also providing thorough documentation that suicide risk was managed according to state-of-the- art procedures. Suicide Safety Net: Multimedia Tools for Reliable Risk Management Documentation (SSN) is based on the University of Washington Risk Assessment and Management Protocol (UWRAMP), a tool developed and used extensively by Linehan and colleagues at the UW, and by other treatment outcome researchers working with highly suicidal patients. All content will be thoroughly reviewed and critiqued by a consortium of suicide and forensic experts for accuracy of content. Specific aims for the present Phase I application are as follows. Aim 1: Iteratively develop content and implementation guidelines for a Suicide Safety Net (SSN) prototype utilizing a consortium of forensic suicide experts. Aim 2: Conduct a formative evaluation of the SSN prototype to determine usability, acceptability and perceived barriers to use among target end-users (i.e., clinicians and researchers). Aim 3: Conduct an open feasibility trial with practicing clinicians (N=30) who treat suicidal patients from eight diverse settings to evaluate the SSN prototype and identify additional barriers to use. Pending positive Phase I outcomes, we will: 1) complete development of the full SSN system, 2) produce an e-Learning curricula providing instruction in how to use the SSN in routine clinical practice and within clinical research trials, and 3) conduct a pilot feasibility trial with clinicians in mutiple mental health settings using the full SSN system with suicidal adult clients.

NIH	2009	Biomarkers of Suicide Risk in Adolescents and Young Adults: Factors that Co	BLUMBERG, HILARY	This application addresses the broad Challenge Area (03) Biomarker Discovery and Validation and specific Challenge topic, 03-MH-101: Biomarkers in Mental Disorders and is entitled: Biomarkers of Suicide Risk in Adolescents and Young Adults: Factors that Contribute to High Risk in Bipolar Disorder. The proposed study addresses a critical gap in knowledge that could have a major impact on progress in suicide prevention: identification of neural circuitry biomarkers of adolescent and young adult suicidality and the biological and environmental factors that contribute to their development. Each year, over one million individuals lose their lives to suicide worldwide, including more than 32,000 Americans. For adolescents and young adults, suicide is the 3rd leading cause of mortality. Suicide is preventable. The critical issues in its prevention are its early identification and addressing its risk factors; however, biomarkers for adolescent and young adult suicidality have not been identified. The development of biomarkers of suicide in adolescents and young adults is especially critical, as it could contribute not only to prevention of suicide in this age group, but evidence suggests that antecedents to suicide through adulthood are present in childhood and adolescence during which biological and environmental factors alter the development of neural circuitry leading to lifelong increases in suicide vulnerability. The proposed study brings together a new multidisciplinary team of investigators to focus on the identification of neural circuitry biomarkers of adolescent and young adult suicidality. This includes investigators with expertise that spans basic molecular neuroscience, genetic, development, child and adult psychiatry, neuropsychology and neuroimaging study. Adolescents and young adults with bipolar disorder (BD) with a history of suicide attempts will be compared to adolescents and young adults with BD without a history of suicide attempts, as well as adolescents and young adults who do not have a psychiatric disorder. Suicidality in BD will be the focus of this project, initiating this new program of research in adolescent/young adult suicide, as BD is associated with one of the highest rates of suicide from amongst psychiatric disorders and is associated with a high rate of suicide in adolescents and young adults. Thus, study of development of suicide in BD could lead to the development of biomarkers associated with high risk for suicide and aid the development of prevention strategies that could be targeted to this high-risk group. The adolescents and young adults participating in this study will complete comprehensive assessments of psychiatric diagnosis, illness course features and symptoms, cognitive testing, and multi-modality magnetic resonance imaging brain scanning including functional magnetic resonance imaging (fMRI) and diffusion tensor imaging (DTI). Preliminary findings of the research team implicate the brain circuitry of emotion and impulse regulation. This brain circuitry will be investigated intensively using state-of-the-art brain scanning image analysis methods. Study of specific genetic variations will be performed and comprehensive information regarding psychosocial and environmental factors, including history of early stress and substance abuse, will be collected in order to study genetic and environmental factors that might influence risk for suicide. This project will initiate this program of research focused on identifying the causes and biomarkers for adolescent and young adult suicide. Long-term goals for this program include the development of new methods for early detection of risk for suicide and effective prevention methods. Relevance: Each year, over one million individuals lose their lives to suicide worldwide, including more than 32,000 Americans, and suicide is the 3rd leading cause of death in adolescents and young adults. It is preventable; however, in order to detect who is at risk and to develop effective prevention methods, identification of the brain circuitry biomarkers of suicidality in youth and the factors that contribute to the development of this circuitry are needed. This study would be one of the first investigations to utilize a comprehensive and intensive approach to elucidate brain circuitry biomarkers for suicide among adolescents and young adults and to study their genetic and environmental causes in a disorder associated with one of the highest risks for suicide among youths, bipolar disorder. PUBLIC HEALTH RELEVANCE: Each year, over one million individuals lose their lives to suicide worldwide, including more than 32,000 Americans, and suicide is the 3rd leading cause of death in adolescents and young adults. It is preventable; however, in order to detect who is at risk and to develop effective prevention methods, identification of the brain circuitry biomarkers of suicidality in youth and the factors that contribute to the development of this circuitry are needed. This study would be one of the first investigations to utilize a comprehensive and intensive approach to elucidate brain circuitry biomarkers for suicide among adolescents and young adults and to study their genetic and environmental causes in a disorder associated with one of the highest risks for suicide among youths, bipolar disorder.
NIH	2010	Measurement of Social-Cognitive Risk Factors for Suicidal Ideation and Behavior	Miranda, Regina	DESCRIPTION (provided by applicant): As one of the top three leading causes of death among teenagers and young adults, suicide has become an issue of increasing public health concern. Hopelessness has been identified as a cognitive risk factor for suicidal thinking and behavior, but the precise ways of thinking through which hopelessness arises and through which it leads to suicidal thoughts and behaviors is not well understood. This proposal for a SCORE Research Advancement Award seeks to fill this gap in the literature by 1) identifying differences in how two different subtypes of rumination prospectively predict suicidal ideation among previous suicide attempters and non- attempters, 2) examining rumination about the future as another type of process through which individuals develop hopelessness, along with modeling a procedure through which these thoughts might be changed; and 3) examining the specific cognitive content characteristic of hopeless that predicts risk for future suicidal thoughts and behavior. These aims will be addressed via a longitudinal study of a sample of young adults - screened for a history of suicidal ideation and attempts - who complete a battery of cognitive measures over 6, 12, and 18 months. Data will be analyzed via mixed model regression to examine the pathways through which two verbal-linguistic forms of rumination lead to suicidal ideation and behavior. These data will also be analyzed via multi-level modeling to examine whether rumination about the future - assessed with a newly- developed measure - is a procedure through which depressive predictive certainty and hopelessness develop. To examine the third aim, this study will utilize a cognitive fluency paradigm to test the hypothesis that young adults with reduced cognitive fluency in expecting positive future outcomes, along with certainty about an absence of positive outcomes -- are at increased risk of future suicidal ideation and attempts. Finally, individuals with and without a history of suicidal ideation or attempts will be trained to mentally rehearse making optimistic future-event predictions, to determine whether inducing optimistic future expectations leads to reduced depressive predictive certainty and hopelessness among individuals with a history of suicidality. PUBLIC HEALTH RELEVANCE: This research will contribute to the understanding of thinking processes that result in suicidal behavior. In addition, it has implications for the assessment and treatment of suicidality.
NIH	2010	Research Training for Prevention of Suicide and Pyschosis: A Public Health Model	BECK, AARON	DESCRIPTION (provided by applicant): The primary aim of this training program is to promote academic research careers for postdoctoral trainees in researching the treatment and prevention of suicide, depression, and schizophrenia. In response to a pressing need for clinical researchers to translate relevant clinical findings Into community mental health services, this program will provide the next generation of researchers with an understanding of the complexities involved in clinical intervention research and the strategies to translate and disseminate such findings into public health settings. Within this context, the program includes a focus on evidence-based interventions for mental disorders and suicide including cognitive, behavioral, dynamic, family, and pharmacological treatments. This application requests support for a two-year Postdoctoral Training Program (3 trainees in Year 1, 5 trainees in Years 2-5). This program will provide trainees with knowledge and experience in the proper conduct of clinical intervention research, ethics, human subjects issues, consent procedures, clinical measurement of symptoms, as well as in research design, statistical analytic approaches, and preparation of peer-reviewed articles and research grant applications. The training will be delivered through three major components: (1) a core curriculum of didactic presentations and workshops on a variety of topics related to clinical intervention research, (2) a year-long mentored clinical research experience with a core faculty member's research group and an optional secondary research experience with another faculty member, and (3) a mentored independent clinical research project that will lead to an application for independent research funding by the conclusion of this training program (e.g., NIH K-Award, foundation grant). In addition, in order to prepare for an academic research career, trainees will have access to a broad array of research and professional development resources, including research meetings, statistical courses, career development mentoring and case consultations. The internationally recognized faculty has many years of experience collaborating with one another and training research fellows. PUBLIC HEALTH RELEVANCE: Suicide is a leading cause of death. Depression and schizophrenia are two of the ten leading mental disorders that generate disability, and are significant risk factors for suicide. Evaluating, refining and disseminating programs for the treatment and prevention of suicide, depression and schizophrenia are crucial for reducing the global burden of disease associated with these conditions.

NIH	2009	4/8-Prolonging Remission in Depressed Elderly (PRIDE)	PETRIDES, GEORGIOS	DESCRIPTION (provided by applicant): While advances have been made in the acute treatment of geriatric depression, failure to maintain remission following successful treatment remains a major public health problem. In particular, loss of antidepressant response can result in ongoing functional impairment and increased risk of suicide. This is especially salient for severe and/or treatment resistant illness, even after successful ECT. This competing continuation application builds upon our prior work demonstrating that continuation pharmacotherapy and continuation ECT were equally but only modestly effective over 6 months. These results highlight the need to develop improved strategies to maintain remission and optimize functional outcomes. The current application tests a novel strategy that utilizes pharmacotherapy-enhanced ECT in the acute phase. It then combines the 2 continuation modalities [pharmacotherapy and continuation ECT], and introduces a novel patient-focused individualization of the ECT schedule (Symptom-Titrated, Algorithm-Based Longitudinal ECT (STABLE)) to enhance long-term outcomes in late-life depression. In STABLE, the ECT schedule is clinically driven to prevent over-treatment of those who do not need it, and to permit re-capturing clinical response for those patients who might have otherwise relapsed with a rigid dosing schedule. STABLE combines a fixed ECT taper followed by an individualized, flexible ECT schedule responsive to symptom re-emergence. This approach provides the first operationalized guidance to the field regarding how to conduct continuation ECT. The primary aim of the Prolonging Remission In Depressed Elderly (PRIDE) trial is to compare, in a randomized clinical trial of patients with late-life depression, the relative efficacy, functional outcomes, and tolerability of two strategies to sustain antidepressant effect after successful acute treatment: 1) combination pharmacotherapy with venlafaxine and lithium (PHARM) and 2) the same combination of pharmacotherapy plus symptom-titrated ECT (STABLE). At 7 sites, 322 patients receive an acute course of ECT augmented by standardized medication (Phase 1); 188 remitters are randomly assigned to one of the 2 groups and followed for 6 months (Phase 2). The primary outcome measure is the longitudinal continuous Hamilton Rating Scale for Depression (HRSD-24). Secondary outcomes are measures of function and tolerability validated in the geriatric sample. By 2020, depression is predicted to become the 2nd leading cause of disease burden worldwide and a major cause of suicide. Late-life depression is particularly important given the rapid growth of the geriatric segment of the population. Patient-focused approaches will guide the development of targeted strategies to reduce disease burden and to enhance quality of life for older patients with severe mood disorders who are at significant risk for suicide.
NIH	2009	Emergency Department Safety Assessment and Follow-Up Evaluation (EDSAFE) Trial	BOUDREAUX, EDWIN	DESCRIPTION (provided by applicant): The NIMH?s RFA-Suicide Prevention in Emergency Medicine Departments recognizes the emergency department (ED) as an important setting to increase suicide detection and prevention efforts but observes that evidence-based practice guidelines do not exist. In response, we have designed the ED Safety Assessment and Follow-up Evaluation (EDSAFE) trial. Two inter-related studies will be conducted using a quasi-experimental design appropriate for studying systems-based change. The studies will share three phases of data collection: Treatment as Usual, Screening Alone, and Intervention. During each phase, 472 suicidal patients (1,416 total) will be enrolled and followed using multiple methods for 12 months. The first study, the Screening Outcome Study, will use data collected during the first two phases (Treatment as Usual and Screening Alone). Primarily, it will focus on testing a practical approach to screen ED patients for suicidal ideation and behavior and will assess its impact on suicide detection, process outcomes, and suicide behaviors. The second study, the Care-chain Evaluation Study, will use data collected during the last two phases (Screening Alone and Intervention). Primarily, it will evaluate the impact of a multi-component intervention on suicide outcomes. The intervention blends conceptual underpinnings from screening, brief intervention, and referral to treatment (SBIRT) models for health behaviors with empirically grounded strategies for suicide prevention. It will involve (1) Question, Refer, Persuade counseling provided by the treating nurse, (2) incorporation of a Comprehensive Suicide Management Protocol into clinical practice, and (3) post-discharge telephone counseling. Our overarching hypotheses will be tested using a combination of both studies. We predict that screening will improve detection of suicidal ideation, and the intervention will enhance the quality of care and reduce suicide outcomes. Our studies offer the following innovations and strengths: (1) inclusion of eight general medical EDs representative of broad geographic regions, patient demographics, and catchment areas (i.e., urban, suburban, rural); (2) use of the EMNet, which was awarded a best practice designation by the NIH-funded Inventory and Evaluation of Clinical Research Networks (IECRN); (3) a structured intervention that is empirically based, practical, and flexible enough to accommodate a full spectrum of suicidal ideation and behavior; (4) stratification of the sample and planned analyses to examine whether the intervention?s effectiveness differs based upon baseline suicide risk; (5) a multi-method outcome attainment strategy; and, (6) a multi-component evaluation that will help determine effectiveness, feasibility, and sustainability. Public Health Relevance: The lack of implementation of screening and brief interventions for suicidal ideation in the ED setting is a significant problem with far-reaching consequences, including excess morbidity and premature mortality. Our study focuses on examining the effectiveness, feasibility, and sustainability of a multi-component screening and intervention for suicide within general ED settings. Our study should hold important implications for a variety of stakeholders, including patients, family members, healthcare providers, financial managers, health insurers, administrators, and policy makers.
NIH	2010	SSRI's and Suicidality	SIMON, GREGORY	Introduction and Overview: Our objective in this study is to evaluate the possible unintended consequences ofthe FDA decision to issue a warning regarding the prescribing of SSRIs to children and adolescents and require a BBW on antidepressant labels. Depression is prevalent among youth in the US and is a risk factor for suicide.(21) Thus, it is of critical importance that the public health implications of possible decreases in antidepressant treatment rates be fully understood. While much research has been conducted in this area, suboptimal study design, absence of long-term trend data, and/or lack of statistical power have left important questions about the effects ofthe warnings on suicidality unanswered. Below we review the important studies to date and highlight how our proposed research will fill gaps in our understanding ofthe relationships among FDA warnings (and associated media reports), antidepressant treatment in youth, and risk of suicidal behavior.
NIH	2012	Pragmatic trial of population-based programs to prevent suicide attempt	SIMON, GREGORY	DESCRIPTION (provided by applicant): Suicide ranks tenth among all causes of mortality in the US, accounting for over 38,000 deaths in 2010. Suicide attempts result in 600,000 emergency room visits and nearly 200,000 hospitalizations each year. Reducing this potentially preventable morbidity and mortality is a public health priority. Recent developments create an opportunity to evaluate population-based selective prevention programs for suicidal behavior. First, increasing use of standard depression severity measures will allow timely and efficient identification of people at risk for suicidal behavior. Second, efficient and scalable intervention (both structure risk assessment / care management programs and low-intensity emotion regulation skills training) have shown promise for reducing risk of suicide attempt in at-risk populations. Third, the NIMH-funded Mental Health Research Network has established a nationwide infrastructure large enough to test prevention programs. We propose a large, pragmatic trial to examine two specific selective prevention programs. The trial would be conducted in three or more large, integrated health care systems, enrolling approximately 16,000 adults for whom responses to item nine of the PHQ depression scale indicate elevated risk. Participants will be randomly assigned to usual care or one of the two prevention programs: a systematic outreach and care management program including structured assessment linked to specific care pathways. This would be based on a model successfully implemented at Henry Ford Health System. The assessment component would be informed by the recently developed Columbia Suicide Severity Rating Scale. Care pathways would include specific guidance regarding type and timing of recommended service. Electronic medical records will be used to support and monitor intervention quality. Outreach and assessment will continue through the one-year intervention period, with frequency depending on risk level; an online psychoeducational program focused on development of emotion regulation skills and prevention of suicidal behaviors, supported by coaching to promote engagement and adherence. The online program will incorporate components of Dialectical Behavior Therapy shown to mediate treatment effects on suicidal behaviors. Based on previous research with online interventions, we anticipate that coaching support will be necessary to promote initial engagement and continued participation. This coaching will be delivered by telephone and/or secure online messaging following a specific motivational enhancement protocol. Both programs would be intended as supplements to usual care, in addition to any risk assessment or treatment provided by primary care or mental health providers. The primary outcome will be documented suicide attempt during the following year - ascertained automatically using computerized records. A pragmatic trial of selective prevention of suicide attempts would fill a major gap in current suicide prevention efforts. Methods developed through such a trial could dramatically accelerate suicide prevention research. PUBLIC HEALTH RELEVANCE: A large pragmatic trial in three or more large health systems will evaluate the effectiveness of two programs to prevent suicide attempts among patients who report suicidal ideation on routine depression questionnaires. One program includes an online program to develop emotion regulation skills, supported by outreach and coaching. The other program includes systematic outreach to assess risk and encourage follow-up care.

NIH	2009	Modifiable Risk and Protective Factors for Suicidal Behaviors in the US Army	URSANO, ROBERT J.	DESCRIPTION (provided by applicant): This application is submitted in response to RFA-MH-09-140 by an interdisciplinary team from four institutions: the Uniformed Services University of the Health Sciences (USUHS), Harvard Medical School (HMS), the University of Michigan (UM), and Columbia University (CU), The team has unparalleled expertise in research on military mental health (USUHS), general population psychiatric epidemiology (HMS), large-scale epidemiological data collection (UM), and neurobiological-clinical research on suicidal behaviors (CU). We propose a multi-phase epidemiological study that considers diverse psychosocial and neurobiological risk and protective factors for suicidal behaviors and secondary outcomes in order to make evidence-based recommendations for implementation of Army suicide prevention interventions. An enriched version of the Army Suicide Event Report (ASER) system will be developed to define the primary outcomes incorporating information from the DoD Medical Mortality Registry (MMR) and Total Army Injury and Health Outcomes Database (TAIHOD). Our study design will include both a retrospective case-control component for quick efficient hypothesis testing and a prospective survey component to predict subsequent suicidal behaviors and secondary outcomes (onset, persistence, worsening of DSM-IV disorders, suicide ideation, suicide plans). We will also use data from the ongoing Pre- and Post-Deployment Health Reassessment Program (PDHRP) surveys as secondary outcomes. The case-control survey will study soldiers who made nonfatal attempts and relatives of soldiers who committed suicide in a psychological autopsy framework. Parallel data will be collected from carefully matched controls. Blood samples and, in the case of nonfatal attempters and their controls, saliva samples will be collected to allow neurobiological risk and protective factors to be studied. The survey component will include active duty personnel across all phases of Army service. Survey reports will be link to subsequent ASER records and PDHRP reports to study prospective associations of predictors with suicidal behaviors and secondary outcomes. A number of innovative measurement, design and analysis features will be used to increase chances of discovering effective intervention possibilities. RELEVANCE: The problem of Army suicide is one of great importance because an effective military force requires its members to be not only physically healthy but also mentally healthy. The relevance of a current study of Army suicide is heightened by the alarming rise in the suicide rate of US Army personnel over the past five years. The research proposed here has the potential to be of great value in helping the Army select optimally effective interventions to address this problem.
NIJ	2011	Unobtrusive Suicide Warning System	Jeffrey Ashe	Despite many improvements, inmate suicide remains a longstanding problem for correctional institutions. In addition to the fundamental tragedy of loss of life, suicide incidents place huge burdens on the institution that contributes to the tarnishing of the reputation of law enforcement, increasing the costs of litigation, and driving new needs to continuously monitor inmates. In completing Phase I and Phase II of this multi-phase program, GE has developed a prototype demonstration system that can measure an inmate?s heart rate, breathing and general body motions without being attached to the inmate. The system is based upon measuring a ballistogram using a modified version of a commercialized Range Controlled Radar (RCR) that was originally designed as a motion detector for home security systems. The detection of the ballistogram (subtle motions on the surface of the body due to the motion of internal components such as the heart and lungs) required modifications to the RCR hardware for increased physiological sensitivity and the development of new signal processing algorithms to detect and classify features.
NIJ	2013	Reducing Youth Access to Firearms through the Health Care Setting	Eric Sigel	The purpose of this project is to examine the implementation and effectiveness of an intervention, delivered in a health care setting, to decrease home firearm access by youth. A total of 800 youth, age 12-17, attending a large urban outpatient adolescent health clinic and their parents will be enrolled in the study. Youth coming to the clinic for routine physicals will be screened for risk and clinicians trained in using a tested means restriction education protocol will deliver means restriction counseling randomly to half of all families reporting guns in the home. Self-reported parental behaviors to follow firearm means restriction recommendations will be compared on the basis of responsiveness and between families in which the adolescent test as high risk for violence or depression to those testing at low risk. The implementation process will also be assessed to guide future dissemination.
NSF	2011	THE LIVED HISTORIES OF VULNERABLE PEOPLES: UNDERSTANDING DIFFERENTIAL SOCIAL HEALTH IN MARGINAL POPULATIONS	Gerald Sider	One significant social problem in many countries is the very poor social health in indigenous communities. While every native community has a substantial proportion of people who are healthy and well, there are also often a proportion of the population suffering from substance abuse, including especially from alcohol and gasoline sniffing; from suicide and domestic violence. The rates of these indicators of poor social health can be much higher in native communities than in either the general population or among ethnic minorities in the general population. This comparative research project will work with four native populations: two small groups in North and South Carolina, which although historically stressed by poverty and prejudice have very good social health, and two northern (sub-arctic) populations (both Inuit and Indian/Innu) where the social health is less good. This research project will focus on developing and refining the concept of lived history: the various ways native people see and live the connections between a not-quite-past and their sense of an impending future. This sense of a continuing history that people live, in their everyday lives, will be examined to see what role it plays in the production and maintenance of social health in native communities.
NSF	2008	SGER: Coming Home: Exploratory Research on the Reintegration of National Guard Troops to Rural Native Alaskan Communities	Linda Green	This Small Grant for Exploratory Research, Linda Green, proposes to do exploratory investigation of the social and cultural reintegration of Alaska Native troops, serving in Iraq and Afghanistan, into their communities in southwestern Alaska. Green notes that of the approximately 2000 Alaska Army National Guard troops serving outside of the United States, most of them are from rural communities, 10% of whom are serving on the Kuwait-Iraq border and are from 25 Yup'ik villages located in the Yukon-Kuskokwim Delta region of Alaska. Green points out that there is a growing body of research that shows an "alarming rise in mental and behavioral health issues affecting active duty soldiers, reservists, National Guard troops, and veterans returning from the Middle East war theater." Examining the statistics, it is possible to predict that rural Alaska Native communities will be disproportionately affected by the anticipated increases in suicide, depression, alcohol and drug abuse, and an increase in domestic violence that has been reported for returning veterans. In small rural villages, where populations frequently number under 100 occupants, the affect of one individual's experience is dramatically magnified. Green proposes this SGER as an exploratory project to build a community collaborative project for research on how communities are affected by the reintegration of returning veterans; how the veterans' experiences affect their own social and cultural integration; and how to explore these issues in the historic framework of experiences previous veterans. The PI correctly states that a subject of such political and ethical considerations could only occur by building strong community and individual collaborations that include active participation, input, exchange and cooperation between the people of the region and the researcher.
NSF	2009	Coming Home: The Reintegration of Native Yup'ik Soldiers/Veterans into their rural communities	Linda Green	This award is funded under the American Recovery and Reinvestment Act of 2009 (Public Law 111-5). This research explores the potential and multiple risks of suicide for Native (Yup'ik) Alaskan soldiers and veterans returning from the Middle East war theatre as they reintegrate into their rural isolated communities located in the Yukon - Kuskokwim Delta of southwest Alaska. Native Alaskan communities in general - and Yup'ik communities in particular - have some of the highest suicide rates of anywhere in the United States and young Native men are at the greatest risk (Perkins 2006). Insofar as veterans from the Middle East war theatre are committing suicide at an alarming rate these Native soldiers/ veterans are returning to a doubly charged social and emotional landscape (Tanielian, 2008). Moreover, two of the primary factors that can inhibit soldiers and veterans from obtaining the needed behavioral and mental health services are access to care and willingness to seek care. The exploratory study has three key objectives; first, to investigate the multiple strategies utilized by Native soldiers and veterans to negotiate this dual risk environment. Secondly, to examine the particular ways in which the struggles that some of these young Native men face affect their everyday lived experience, that is social relations with their families, their peers and their community. Lastly, to explore under what circumstances these young Native adults may or may not choose to seek help for what has been characterized as the "invisible wounds of war" (Tanielian, 2008). The researcher's hypothesis is that without a culturally - sensitive, community - based modality of care - a middle ground - that can serve as a bridge between not seeking any care at all, ie., "going it alone" and actively engaging with evidenced based medical care for suicide ideation and associated problems of depression, PTSD, substance abuse, these Native soldiers/veterans in rural communities are doubly at risk for suicide as they are isolated - not only from their military peers (Messinger 2008) - but also from their families and their community (Lifton, 1973; Appendix C). This study seeks to understand what the parameters of that middle ground might look like that is at once socially, culturally and historically contextualized. This phase of the research contributes to our understanding of the complexity of the social and emotional problems faced by these young Native Alaska soldier/veterans in new ways that allows for more in depth insights usually missed by more prosaic community research methods. Although many community studies have now incorporated an ethnographic component into their research design, it is usually delimited by rapid response techniques, which usually involved a stay in village a week or so, thus mitigating an understanding of a locally lived social lives embedded within local history. This study not only explores the lived experiences of individuals at risk for suicide, but places them within the context of their families, their history, their community and their culture. In doing so both the strengths as well as the vulnerabilities of such emerge that may map new ways to reach and reach out to people in such circumstances.

NSF	2008	Collaborative Research: IPY: Negotiating Pathways to Adulthood: Social Change and Indigenous Culture in Four Circumpolar Communities	Stacy Rasmus	Contemporary dynamics of rapid social change have dramatically affected the political, cultural, and economic systems of circumpolar Indigenous people. In line with three of the International Polar Year (IPY) priority areas, this project intends to (1) increase international collaboration between circumpolar institutions, (2) leave a legacy of infrastructure and data, and (3) increase Indigenous capacity for research and action. The Pathways study is a comparative, collaborative, and participatory circumpolar research project. Its aims are to explore responses to rapid social transition through the life experiences of circumpolar youth. The proposed study will examine 80 youth life history narratives. These narratives will come from an Alaska Inupiat, Alaska Yupik, Canadian Inuit, and Siberian Eveny community. In addition, the research team is developing collaborations using additional funding sources to examine the narratives of an additional 40 youth from a Norwegian Sam?and Greenlandic community. In this study, the team intends to identify shared and divergent stressors and patterns of resilience in the transition to adulthood across these different circumpolar settings. Youth resilience is defined as the ability to overcome acute and on-going difficulties in the pathway to adulthood. The investigators seek to identify cultural strategies and resources that characterize resiliency across two age groups, ages 11-14 and 15-18, and across gender. The impact of a shared colonial history and contemporary social suffering among indigenous communities in the Arctic has been extensively documented through decades of Arctic social science research. The issue of healthy adaptation and resilience among Indigenous youth has not been adequately considered, leaving developmental trajectories of healthy adaptation and resilience relatively unexplored. This research aims to build on Indigenous categories to describe the social experiences and resources shaping culturally patterned resilience strategies of young people responding to challenges distinct from those of their parents and grandparents. This will provide insights into the family, community, and cultural contexts that support healthy youth development, and identify key ingredients to successful prevention and intervention health strategies for Indigenous young people. Study across six circumpolar communities will also provide unprecedented insights into the effect of diverse social, political, cultural, and economic systems on youth development, and inform effective social policy for circumpolar youth. This project builds on and sustains long-term participatory research relationships between local community institutions, community co-researchers, and a multidisciplinary team of international university researchers. Indigenous community co-researcher involvement and direction is emphasized throughout all phases of this project, whose aims respond to strong local interest in youth resilience and wellbeing. Development of interview schedules, data collection procedures, and the analysis will be in col+X367laboration with Local Steering Committees (LSC) to ensure their cultural grounding. A representative from each LSC will be actively involved in the cross-site work through membership in an international Circumpolar Steering Committee. Dissemination with communities and regional Indigenous organizations will contribute to a developing network of circumpolar communities engaged in suicide prevention, promotion of collective wellbeing, and development of a circumpolar Indigenous identity. The study will also establish tracking procedures, participatory research infrastructure, and international circumpolar collaboration for future longitudinal, prospective study of safe passage into adulthood.
NSF	2008	Collaborative Research: IPY: Negotiating Pathways to Adulthood: Social Change and Indigenous Culture in Four Circumpolar Communities	Michael Kral	Contemporary dynamics of rapid social change have dramatically affected the political, cultural, and economic systems of circumpolar Indigenous people. In line with three of the International Polar Year (IPY) priority areas, this project intends to (1) increase international collaboration between circumpolar institutions, (2) leave a legacy of infrastructure and data, and (3) increase Indigenous capacity for research and action. The Pathways study is a comparative, collaborative, and participatory circumpolar research project. Its aims are to explore responses to rapid social transition through the life experiences of circumpolar youth. The proposed study will examine 80 youth life history narratives. These narratives will come from an Alaska Inupiat, Alaska Yup?ik, Canadian Inuit, and Siberian Eveny community. In addition, the research team is developing collaborations using additional funding sources to examine the narratives of an additional 40 youth from a Norwegian Sam?and Greenlandic community. In this study, the team intends to identify shared and divergent stressors and patterns of resilience in the transition to adulthood across these different circumpolar settings. Youth resilience is defined as the ability to overcome acute and on-going difficulties in the pathway to adulthood. The investigators seek to identify cultural strategies and resources that characterize resiliency across two age groups, ages 11-14 and 15-18, and across gender. The impact of a shared colonial history and contemporary social suffering among indigenous communities in the Arctic has been extensively documented through decades of Arctic social science research. The issue of healthy adaptation and resilience among Indigenous youth has not been adequately considered, leaving developmental trajectories of healthy adaptation and resilience relatively unexplored. This research aims to build on Indigenous categories to describe the social experiences and resources shaping culturally patterned resilience strategies of young people responding to challenges distinct from those of their parents and grandparents. This will provide insights into the family, community, and cultural contexts that support healthy youth development, and identify key ingredients to successful prevention and intervention health strategies for Indigenous young people. Study across six circumpolar communities will also provide unprecedented insights into the effect of diverse social, political, cultural, and economic systems on youth development, and inform effective social policy for circumpolar youth. This project builds on and sustains long-term participatory research relationships between local community institutions, community co-researchers, and a multidisciplinary team of international university researchers. Indigenous community co-researcher involvement and direction is emphasized throughout all phases of this project, whose aims respond to strong local interest in youth resilience and wellbeing. Development of interview schedules, data collection procedures, and the analysis will be in collaboration with Local Steering Committees (LSC) to ensure their cultural grounding. A representative from each LSC will be actively involved in the cross-site work through membership in an international Circumpolar Steering Committee. Dissemination with communities and regional Indigenous organizations will contribute to a developing network of circumpolar communities engaged in suicide prevention, promotion of collective wellbeing, and development of a circumpolar Indigenous identity. The study will also establish tracking procedures, participatory research infrastructure, and international circumpolar collaboration for future longitudinal, prospective study of safe passage into adulthood.
NSF	2008	Collaborative Research: IPY: Negotiating Pathways to Adulthood: Social Change and Indigenous Culture in Four Circumpolar Communities	Lisa Wexler	Contemporary dynamics of rapid social change have dramatically affected the political, cultural, and economic systems of circumpolar Indigenous people. In line with three of the International Polar Year (IPY) priority areas, this project intends to (1) increase international collaboration between circumpolar institutions, (2) leave a legacy of infrastructure and data, and (3) increase Indigenous capacity for research and action. The Pathways study is a comparative, collaborative, and participatory circumpolar research project. Its aims are to explore responses to rapid social transition through the life experiences of circumpolar youth. The proposed study will examine 80 youth life history narratives. These narratives will come from an Alaska Inupiat, Alaska Yup?ik, Canadian Inuit, and Siberian Eveny community. In addition, the research team is developing collaborations using additional funding sources to examine the narratives of an additional 40 youth from a Norwegian Sam?and Greenlandic community. In this study, the team intends to identify shared and divergent stressors and patterns of resilience in the transition to adulthood across these different circumpolar settings. Youth resilience is defined as the ability to overcome acute and on-going difficulties in the pathway to adulthood. The investigators seek to identify cultural strategies and resources that characterize resiliency across two age groups, ages 11-14 and 15-18, and across gender. The impact of a shared colonial history and contemporary social suffering among indigenous communities in the Arctic has been extensively documented through decades of Arctic social science research. The issue of healthy adaptation and resilience among Indigenous youth has not been adequately considered, leaving developmental trajectories of healthy adaptation and resilience relatively unexplored. This research aims to build on Indigenous categories to describe the social experiences and resources shaping culturally patterned resilience strategies of young people responding to challenges distinct from those of their parents and grandparents. This will provide insights into the family, community, and cultural contexts that support healthy youth development, and identify key ingredients to successful prevention and intervention health strategies for Indigenous young people. Study across six circumpolar communities will also provide unprecedented insights into the effect of diverse social, political, cultural, and economic systems on youth development, and inform effective social policy for circumpolar youth. This project builds on and sustains long-term participatory research relationships between local community institutions, community co-researchers, and a multidisciplinary team of international university researchers. Indigenous community co-researcher involvement and direction is emphasized throughout all phases of this project, whose aims respond to strong local interest in youth resilience and wellbeing. Development of interview schedules, data collection procedures, and the analysis will be in collaboration with Local Steering Committees (LSC) to ensure their cultural grounding. A representative from each LSC will be actively involved in the cross-site work through membership in an international Circumpolar Steering Committee. Dissemination with communities and regional Indigenous organizations will contribute to a developing network of circumpolar communities engaged in suicide prevention, promotion of collective wellbeing, and development of a circumpolar Indigenous identity. The study will also establish tracking procedures, participatory research infrastructure, and international circumpolar collaboration for future longitudinal, prospective study of safe passage into adulthood.

NSF	2010	The Invisible Wounds of War: An Ethnographic Investigation of Yup'ik combat veterans' problematic reintegrations into communities in southwestern Alaska	Linda Green	This research study is to understand how Yup'ik veterans from villages in the Yukon-Kuskokwim Delta of southwestern Alaska who face significant problems of access to services reintegrate into communities with the accompanying stresses of combat, that are only partially visible. This project is an ethnographic investigation with three key objectives: First, to grasp the human and social consequences of war on the lives of those Yup'ik community members who have served in combat in the US military. The study examines the multidimensional aspects of reintegration of Yup'ik solders into their communities from three eras; the Vietnam War, the First Gulf War, and the ongoing conflicts in Iraq and Afghanistan. Secondly, the study explores how individual soldiers as well as their families make sense of, give meaning to, and cope with the partially visible wounds of war in their daily lives in the aftermath of combat. As such the investigator will explore the impact, both positively and negatively, of external forces and internal disruptive pressures on people's everyday lives and livelihoods and how these processes are understood. Thirdly, to gain an understanding under what circumstances Native veterans may or may not choose to seek help for their battle trauma; when and why do they choose to "go it alone" or to actively participate in medical care. In the context of this planned ethnographic research the investigator will explore to what extent and under what conditions kinship, community, and culture can be helpful in healing and contributing to successful reentry as these outcomes are reported by veterans, their families and their community. The central concern of this proposed research is to gain a long-term historical perspective on how people manage psychological and social trauma. As such this study focuses on how soldiers cope with coming home from combat -- from Vietnam to the present -- and places their experiences within a social milieu, one, like many aboriginal communities from Australia to the Circumpolar North struggle with devastating rates of suicide, interpersonal violence and substance abuse. The need for this research is pronounced. In the absence of substantial VA interventions in the researcher's perspective what is crucial is to investigate the kinds of issues families and communities face as they try to help in the reintegration process of veterans. Importantly, this study will contribute to an understanding of the kinds of problems Native veterans are facing, the effects on kin and families and the panoply of coping strategies that are utilized by communities. The data produced by this project will help community residents and leaders, as well as social service organizations responsible for assisting them to better understand the social needs that are crucial in helping veterans, kin and communities cope with this added layer of social stress, loss and trauma. Moreover this study by design includes Alaska Native residents/under-represented groups in the research planning and data collection process - including the innovative community-based Elders Advisory Councils. While the research will produce academic articles and a monograph, the findings will also be presented at scientific meetings and conferences. The summaries of the research will also be presented to local indigenous associations in Alaska, particularly in the Yukon-Kuskokwim Delta, village tribal councils, the Yukon-Kuskokwim Health Corporation, the Veterans Administration in Bethel and Anchorage, The Alaskan Tribal Health Consortium. And in keeping with the Principles for the Conduct of Research in the Arctic the Principle Investigator will return to each village for public presentations of the research findings.
SAMHSA	2012	Native Aspirations Evaluation	Christine Walrath	The Native Aspirations Evaluation aims to produce findings and tools that can be used for programs targeting suicide prevention in specific American Indian/Alaska Native (AI/AN) sub-populations. The evaluation will produce three reports: (1) Suicide Prevention in Alaska; (2) Preventing and Responding to Suicide Clusters in AI/AN Communities; and (3) Sustaining Successful Suicide Prevention Activities in AI/AN Communities. Suicide Prevention in Alaska: This report will synthesize findings from multiple data sources for Alaska communities involved in Native Aspirations as well as communities impacted through Garrett Lee Smith Youth Suicide Prevention and Early Intervention Program resources. It will describe the communities? awareness, knowledge and behaviors related to bullying, suicide, violence and other risk and protective factors; prevention models used in these communities; service and infrastructure related to health; the relative impact of prevention resources on attempts and referrals; and the sustainability of programs. The report will also describe the implementation of Native Aspirations projects and community successes and challenges related to implementation, as well as recommendations for additional support and service, particularly to address gaps in service availability. Preventing and Responding to Suicide Clusters in AI/AN Communities: This report will describe American Indian/Alaska Native (AI/AN) community efforts to respond to and prevent suicide clusters. It will include descriptions of the impact of GLS-/Native Aspirations-funded suicide prevention activities in tribal communities that had experienced clusters, and discusses the conditions under which cluster prevention has been most effective. The analysis will contain an inventory of the tools developed, and describe how and when these tools were used to contain/prevent a cluster. It will also discuss the role of surveillance of youth suicidal behavior and proactive follow up of at-risk youth within communities that previously experienced a cluster. Finally, the report will describe the factors to which these communities attribute their ability to recover, improve, and strengthen their mental health support systems. Sustaining Successful Suicide Prevention Activities in American Indian/Alaska Native Communities: This report will review the suicide prevention strategies that were most effectively implemented, as well as strategies that were sustained after the project ended, with a focus on community outcomes. The report will compare communities that received only a Native Aspirations grant with communities that received, at a later date, a grant through the Garrett Lee Smith Youth Suicide Prevention and Early Intervention Program. The report will be informed by a wide variety of data sources, including a comprehensive analysis and summary of findings from the Native Aspirations Community Knowledge and Behaviors Survey (CKABS). It will also include recommendations for additional supports and services, particularly to address gaps in service availability.
SAMHSA	2009	Garrett Lee Smith Youth Suicide Prevention and Early Intervention Cross-site Evaluation	Christine Walrath	As mandated by the Garrett Lee Smith Memorial Act (GLSMA), SAMHSA must report on a cross-site evaluation for both the State/Tribal Youth Suicide Prevention and Early Intervention Grant Program as well as for the Campus Suicide Prevention Program. The Garrett Lee Smith Youth Suicide Prevention and Early Intervention Cross-site Evaluation is an integral part of the GLSMA and is the most comprehensive data collection effort dedicated to youth suicide prevention ever undertaken. The cross site evaluation's design, support infrastructure, and technical assistance approach were designed to generate information corresponding to GLSMA requirements, fulfill program performance monitoring requirements, and contribute substantially to the field of suicide prevention. The cross-site evaluation provides continuous documentation of the context in which the funded suicide prevention activities are being implemented; the utilization of products and services being generated and supported through grant funding; the impact of training activities being supported through grant funding; the impact of training activities being supported through the grant program, and the impact of grant funding on identification, referral, and follow up activities. Collectively, this information will help guide the field of suicide prevention across the Nation's communities.
SAMHSA	2009	National Suicide Prevention Lifeline Evaluation	Christine Walrath	The National Suicide Prevention Lifeline (NSPL) Evaluation builds upon previous NSPL evaluation projects funded by SAMHSA (see Suicide and Life Threatening Behavior, June 2007) to continue to help inform and shape SAMHSA's NSPL. The NSPL evaluation assesses the Lifeline?s objectives of offering effective quality services, access to care, and continuity of care through three primary components: (1) NSPL Follow-up Evaluation; (2) NSPL Imminent Risk Evaluation; (3) Emergency Department Discharge Pilot Evaluation. Using data from the Follow-up Evaluation, callers? perceptions of care are examined as one indicator of the quality of follow-up services offered by Lifeline crisis centers. Demographic and clinical factors impacting callers? perceptions of care are also explored to provide preliminary impressions regarding which callers may experience the most benefit from follow-up, and what follow-up procedures are most appreciated by them. Data from the Imminent Risk Evaluation describe how Lifeline counselors define imminent risk and the interventions they use to mitigate it, and also provides the basis for understanding the extent to which counselors are applying the Lifeline?s guidelines. The Emergency Department Discharge Pilot Evaluation seeks to address another important measure of the effectiveness of crisis centers? follow-up services: their impact on emergency department readmissions for suicidal behavior. Findings from these ongoing evaluations will be used to inform the future directions of the NSPL.

VA	2009	Telehealth Care Management and Tobacco Cessation for Veterans with PTSD	Catherine Battaglia	Veterans smoke at a higher rate (30%) than the U.S. adult population (21%), and veterans with PTSD have even higher rates of smoking (53-66%). Evidence has shown that any tobacco dependence treatment strategy must be integrated in the health care system because consistent and effective delivery of tobacco cessation requires coordinated interventions. Persistent tobacco users typically cycle through multiple periods of relapse and remission. Veterans with PTSD (279,256 in 2005) who are treated for smoking cessation may need more comprehensive aid to be successful. Failure to appreciate the chronic nature of tobacco dependence may impede comprehensive and consistent treatment. Care management using telehealth has been shown to improve access to care while reducing costs for veterans with chronic diseases and has the potential to coordinate smoking cessation with care for other chronic diseases. Nurses have successfully managed chronic diseases using telehealth by focusing on increasing self-management, positive behaviors and knowledge. Nurses are vital to increasing the level of support in the community through education and motivation and by responding to medical events in order to improve veterans' health. Objectives: The study is designed to determine if adding motivational counseling and care management using the PTSD Health Buddy to usual care improves smoking quit rates of veterans with PTSD. Specific Aims are to compare: 1) self-reported quit attempts, progression through the stages of change, and quit rates, 2) patient perception of care coordination, and 3) changes in PTSD symptoms in veteran smokers with PTSD who receive a nurse-driven telephonic motivational counseling intervention triggered by responses to stage-based smoking cessation questions in addition to usual care to those who receive usual care only. Methods: This randomized controlled trial will assess the effectiveness of tobacco cessation treatment for veterans with PTSD. We will recruit 120 veterans who smoke and who are using or are eligible to use the PTSD Health Buddy program from the Eastern Colorado Health Care System in order to detect a 24 percent increase in quit attempts. Subjects will be randomized to usual tobacco cessation care (control) and care management using telehealth and stage-based motivational counseling in addition to usual care (experimental). The PTSD Health Buddy has an already-developed smoking cessation module which will be the telehealth system used in this trial. Standardized instruments will be used to assess stage of change, care coordination, and PTSD symptoms in all subjects. Demographics, clinical characteristics and outcome measurements will be compared between groups. Outcome measurements will occur at the end of the three- month intervention, and at six-month post-study follow-up. Chi-square tests for quit rate and other categorical variables and t-tests for continuous variables will be used. PUBLIC HEALTH RELEVANCE: : Anticipated Impacts on Veteran's Healthcare: Our study provides a nurse-driven integrated care management model of care using telehealth and stage-based motivational counseling to help veterans with PTSD quit smoking. This is important because veterans with PTSD have higher rates of smoking and are less likely to successfully quit than other veterans. Given the high rates of PTSD in veterans and the lifetime ill effects of tobacco abuse, this is a particularly timely and critical endeavor.
VA	2011	Pain and Suicidal Behaviors Among Veterans in Care in the VA	Joseph Goulet	Suicide rates in the VA healthcare system are higher than in the general population, and they are increasing. VA patients may be at increased risk as a result of the high prevalence of many well known risk factors. Chronic pain is an additional risk factor for suicide, but research on this association among Veterans is lacking. This pilot project will inform the development of a Merit Review application to perform an in-depth patient level study of potentially modifiable risk and protective factors for suicide and suicide attempts highly prevalent among Veterans, in particular, chronic pain. However, before that can be undertaken, pilot work must define and validate information that can be gathered from VA data which may be used to constitute the sample of Veterans at risk for suicide or suicide attempts. The aims of this pilot project are to: 1. Abstract data from electronic medical records to ascertain the completeness and determination of the provider's evaluation of suicide risk in a sample of Veterans who screen positive for depression during a VA primary care visit 2. Determine the agreement between the providers evaluation of suicide risk and the suicide risk assessment from the data entered into the Health Factors file 3. Examine the correlates of discrepant findings of suicide risk, including patient demographics and pain assessment as well as severity of pain Design This study will develop and conduct a structured retrospective chart review to determine the provider's evaluation of suicide risk among Veterans who screen positive for depression. We will select and review the charts of 300 Veterans who screen positive for depression on at least one primary care visit at the VACHS West Haven campus during the period 1 October 2008 until 31 September 2009. We will then compare results from the provider's evaluation of suicide risk to Health Factors based assessment results. We will then examine correlates of discrepant findings (e.g. assessment is positive for risk but clinician evaluates the patient as negative), including patient demographics and pain scores. Integration of Pilot Study with Larger Study Because "suicide prevention programs depend on the accuracy with which assessments of suicidality are conducted", a review of the completeness and discrepancies in the suicide risk screening is crucial. Given that the VA uses a "single, integrated electronic medical record (EMR) system for all of its clinical activities", this can be assessed. The preliminary work of this pilot project will be the basis of a Merit Review application to be conducted in collaboration with members of the Canandaigua VA Medical Center Mental Health Center of Excellence which focuses on suicide prevention. We plan to constitute a multi-site cohort study of Veterans with suicide risk in order to examine the longitudinal course of pain and its likely substantial effect on suicidal risk and attempts. Ultimately, we will determine whether high prevalence conditions among Veterans in care, such as chronic pain and pain conditions, can be used to more effectively target suicide and suicide attempts prevention and intervention efforts. PUBLIC HEALTH RELEVANCE: Significance: Inaccurate suicide risk screening may result in many 'false positives', leading to an overestimation of the risk among Veterans in care, or more catastrophically, to 'false negatives', wherein a Veteran at risk is not detected or treated. This project and the studies to result from our findings represent a unique opportunity to examine the accuracy and completeness of the results of our suicide risk screening, and to compare those results to an in-depth examination of the Veterans EMR data to more clearly elucidate which Veterans are at risk, and to determine whether conditions that are peculiar to Veterans in care, such as the high prevalence of chronic pain and pain conditions, can be used to more effectively target suicide and suicide attempts prevention and intervention efforts.
VA	2011	Brain pH and Acid Sensing in Depression-Related Behavior	John A. Wemmie	Depression is consistently one of the top causes of morbidity and mortality, and veterans are afflicted more commonly than non-veterans. In addition, veterans are more than twice likely to die from depression-related suicide than the general population. Despite current antidepressant medications, a disappointingly large number of patients are refractory to current treatments, all of which target similar mechanisms. Thus, new medications with novel mechanisms of action are urgently needed. Using animal models that can predict antidepressant and anti-anxiety effects in humans, we identified a novel molecule in depression and anxiety-related behaviors, the acid-sensing ion channel 1a (ASIC1a). Pharmacologically inhibiting and genetically disrupting ASIC1a in mice produced antidepressant-like effects in the forced swim test, tail suspension test, and following chronic unpredictable stress. Moreover, the effects were independent of and additive to several currently used antidepressant medications. Disrupting ASIC1a also reduced conditioned and unconditioned fear behaviors, which model post-traumatic stress disorder (PTSD) and other anxiety disorders. Together these findings suggest the exciting possibility that targeting ASIC1a will relieve depression and anxiety through a novel mechanism of action. To take full advantage of this possibility we need to know more about how ASIC1a is activated in the brain. The exquisite sensitivity of ASIC1a to low extracellular pH suggests that acidic pH might play an important signaling role. We hypothesize that emotionally distressing stimuli lower pH in the amygdala, which in turn activates ASIC1a to promote stress responses including depression and anxiety-related behaviors. To test this hypothesis we propose to answer the following questions: 1) Does manipulating ASIC1a pH sensitivity alter its effects on depression-related behavior? 2) Does altering the expression of ASIC1a and other ASIC subunits influence depression-related behavior? And, 3) can pH be therapeutically targeted to reduce depression? Our planned experiments take advantage of several recent advances including: our ability to measure brain pH in behaving mice with a fiber optic pH sensor, and our ability to alter the pH sensitivity of ASIC1a channels and assess the behavioral consequences. If pH dependent signaling contributes to depression and anxiety, then manipulating pH or ASICs could provide novel therapeutic opportunities that may be rapidly translated to human research and treatment. For example, a number of techniques can be used to safely alter human brain pH, and might be used to intervene in depression and in other psychiatric consequences of severe emotional stress. PUBLIC HEALTH RELEVANCE: Depression is a leading cause of disability and mortality that affects veterans even more frequently than non-veterans. Moreover, veterans are more than twice as likely to die from depression-related suicide. Unfortunately, a large number of veterans do not respond to current medications. Thus, new treatments with novel mechanisms of action are desperately needed. Using animal models that can predict antidepressant efficacy in humans, we found a novel ion channel that when disrupted or inhibited produces antidepressant and anti-anxiety-like effects in mice. This channel, called acid-sensing ion channel-1a (ASIC1a), is activated by acidic pH. The pH sensitivity of these channels, coupled with evidence that pH fluctuations occur in the brain with neural activity, suggests that pH might play an important signaling role in the brain to promote depression and anxiety. In this proposal, we will determine the contribution of brain pH to ASIC1a channel activity, and test whether ASIC1a and brain pH might be targeted to reduce depression.

VA	2009	Neurobiology of Suicide Risk in Traumatic Brain Injury and Substance Abuse	Deborah Yurgelun-Todd	Efforts at understanding the neurobiological correlates of traumatic brain injury (TBI), prefrontal function and suicidal ideation have thus far provided inconclusive results. Primary blast-related TBI is common in returning veterans and appears to produce neurophysiological changes that resemble diffuse axonal injury (DAI). Disruptions in brain neural circuits that support cognitive processing in individuals with TBI may result in deficits in executive function including reduced problem solving and decision-making capacity. Moreover, veterans with TBI are often co-morbid for substance abuse and it has been shown that use of alcohol and illicit drugs can further compromise executive mediated functions known to depend on the frontal cortex. It has been proposed that these functional deficits may lead to cognitive rigidity and psychological distress and thus may serve as markers for suicidal risk. The proposed research builds on existing neurobiologic models of frontal function and will extend our understanding of TBI related brain changes by applying functional magnetic resonance imaging (fMRI) and diffusion tensor imaging (DTI) techniques. Accordingly, we will examine blood oxygen level dependent (BOLD) signal changes within the cingulate and dorsolateral prefrontal cortices as well as the amygdala in TBI subjects, with and without a history of substance abuse, to characterize the nature of these patterns of signal change (higher/lower) in relation to healthy control subjects. We will determine whether measures of white matter microstructure, as measured by DTI methods, are abnormal in TBI subjects, with and without a history of substance abuse compared with healthy control subjects. We will also examine the relationship between BOLD signal changes and reduced FA values and suicidal ideation. Lastly, we will test the hypothesis that reduced FA and reduced activation in frontal regions in both substance abusing and non-substance abusing TBI veteran groups is significantly correlated with suicidal ideation, and that the correlation will be stronger for the TBI plus substance abuse cohort. We believe the proposed studies will impact veteran's health by providing important insights into the neurobiological correlates of suicide and TBI that may lead to new approaches for identification and treatment of behavioral consequences of TBI. PUBLIC HEALTH RELEVANCE: Traumatic brain injury (TBI) is an important medical problem for active combat veterans. The return of veterans from Operation Enduring Freedom/Operation Iraqi Freedom (OEF/OIF), many of whom have suffered mild TBI, has emphasized the crucial importance of understanding the neurobiologic and neuropsychological consequences of this type of brain injury. Furthermore, several studies point to the urgent need to define the neurobiological and cognitive underpinnings of suicidal ideation and behavior in veterans with TBI with and without comorbid substance abuse/dependence disorders. The evaluation of the neurophysiologic and cognitive predictors of suicide risk and recovery are needed to improve treatments. We believe the proposed studies will impact veteran's health by providing important insights into the neurobiological correlates of suicide that may lead to new approaches for identification and treatment of behavioral consequences of TBI.
VA	2013	Brain Chemistry and Altitude in Bipolar Disorder	Perry Renshaw	Bipolar disorder is a prevalent and severe psychiatric disorder marked by alternating episodes of depression and mania. In the Department of Veterans Affairs (VA), nearly 80,000 Veterans received care for bipolar disorder in 2004, a 40% increase from 1999. Bipolar disorder imposes a substantial medical burden on Veterans, and is associated with the highest health care costs of any psychiatric disorder in the VA system. Moreover, in male Veterans bipolar disorder is a significant risk factor for suicide. The World Health Organization ranks bipolar disorder as the sixth leading cause of global medical disability. Despite decades of research, the illness remains poorly understood, and no new treatment has surpassed lithium's effectiveness for the majority of patients. There is a critical need for research studies aimed at understanding the neurobiology of bipolar disorder, to improve our diagnostic and treatment strategies. Brain pH is closely linked to affective functioning, and is influenced by a range of internal and external factors. One such environmental factor may be altitude. Extreme altitudes are associated with a decreased partial pressure of inspired oxygen, and this hypobaric hypoxia results in significant cognitive impairment. However, the effect of moderate changes in altitude on brain chemistry is not well understood. Recent publications show that within the U.S., altitude is associated with an increased rate of suicide that begins at the modest altitude of ~2,000 feet, an effect that may be strongest in bipolar disorder. In terms of endogenous factors, it is hypothesized that decreased brain pH in bipolar disorder may represent a biologic trait of the illness. Decreased brain pH has been linked to altered brain lactate and glutamate levels in bipolar disorder. Research is needed to clarify the relationship between mood, brain chemistry and altitude in bipolar disorder. To address this need, we propose to use magnetic resonance spectroscopy (MRS) neuroimaging together with clinical assessments, to study the relationship between brain pH, glutamate, lactate and altitude in Veterans with bipolar disorder. The proposal features a novel cross-sectional study design, in which brain scans will be performed on subjects with bipolar disorder at two altitudes: Salt Lake City, UT (4,700 feet) and Belmont, MA (44 feet). A total of 120 subjects will be enrolled, including 40 depressed bipolar subjects (20 per site), 40 euthymic bipolar subjects (20 per site), and 40 healthy controls (20 per site). All subjects will undergo MRS brain scans to measure their brain pH, glutamate and lactate levels. The proposed study will provide insight into the interrelationship of brain chemistry, mood state and altitude in bipoar disorder. The results of the study may help scientists develop new diagnostic methods, or new treatment approaches for Veterans with bipolar disorder.
VA	2013	Risk of death among veterans with depression	Kara Zivin	The Global Burden of Disease study projected that depression will be the second leading cause of disability worldwide by 2020, and there is substantial (but not unequivocal) data from community studies indicating that it is a key risk factor for mortality. Both older veterans and newly returning veterans have high mental health service needs, and VA patients are particularly vulnerable, with higher rates of depression (~12% prevalence), poverty, comorbid medical illness, and disability than the general US population. The proposed study builds on our existing research on the impact of depression on Veteran suicide (IIR 04-211) and cost-effectiveness of VA depression treatment (CD2 07-206) to examine all causes of death associated with depression among VA service users. Our research team is uniquely qualified and has the necessary data resources and expertise to examine overall death rates as well as deaths from specific causes while accounting for baseline and time-varying risk factors and other potentially influential sociodemographic and clinical characteristics through its extensive administrative, survey, and cause of death data sources. Objectives: The objectives of this study are: 1) to examine the potential risks of all-cause and cause-specific mortality associated with depression among VA patients, 2) to characterize the impact of modifiable health behaviors on the relationships between depression and all-cause mortality, and mortality due to cardiovascular disease and cancer, and 3) to examine the associations between receipt of depression treatment and mortality. Methods: To achieve these objectives, we will create a new panel dataset with health and sociodemographic information on all VA service users nationwide (N~4,700,000) from FY03 followed for up to five years. We will conduct analyses with merged secondary data from existing data sources. The VA's National Patient Care Database (NPCD) will provide detailed inpatient and outpatient clinical data identifying depression and other disease diagnoses as well as health care utilization including prescription medications. Medicare utilization data will be linked for eligible patients. The National Death Index (NDI) will provide mortality data, including cause and date of death. The 2003 Survey of Healthcare Experiences of Patients (SHEP) will provide sociodemographic and health behavior information not available from administrative resources. We will use survival analysis techniques, specifically Cox regression models, as well as logistic regression analysis to examine the impact of depression on timing and causes of death in our VA patient cohort. We will examine the independent association of depression with death, as well as the impact of potential confounding factors, including medical and psychiatric comorbidity, health behaviors, and sociodemographic characteristics. In analyses using statistical methods to control for possible treatment selection biases, we will examine the impact of depression treatment on mortality. In sensitivity analyses, we will examine regional variation in the relationship between depression and timing, causes, and correlates of death. Through this work, we will not only be able to provide detailed information from the largest health-system- wide cohort ever studied on how depression is associated with mortality, but we will also be creating a unique data resource that can potentially be made available for other VA researchers and policy makers to identify causes of death in the VA patient population. PUBLIC HEALTH RELEVANCE: The proposed study will provide the first large scale assessment of depression-related mortality among patients treated in a large healthcare system. By examining the risk of death among depressed VA patients, the VA may be better able to understand the long term health and social consequences of this highly prevalent and disabling disorder. This research will contribute toward identifying ways to reduce identified mortality risks associated with depression and potential health care system gaps, as well as identifying opportunities for enhancing the VA's ability to meet the needs of the large group of veterans with depression.

VA	2013	Improving Outcomes in Suicidal Veterans with Schizophrenia	John Kasckow	Suicide is a serious public health problem among Veterans with schizophrenia. Risk for suicidal behavior is elevated among this group of Veterans when they are discharged from the hospital following an admission for suicidal behavior. Many Veterans with schizophrenia have difficulty monitoring their symptoms and adhering to outpatient treatment. Cognitive deficits associated with the illness likely play a role, and individuals who are isolated with limited social support are particularly vulnerable. This inability to self-monitor can lead to escalating symptoms and the potential tragic outcome of suicidal behavior and even possibly premature death. To address this problem, we have designed and piloted a home-based telehealth system using the Health Buddy(R) monitoring device for Veterans with schizophrenia who have been recently hospitalized for suicidality. Our intervention is targeted for the critical transition from inpatient to outpatient care. In pilot work, our research team has been able to help patients better monitor their symptoms and improve outcomes. In comparison to a control group, our group with the telehealth monitoring has experienced a more rapid improvement in suicidal and depressive symptoms. However, we have noted some problems which need to be addressed before initiating a randomized controlled trial: (1) Some Veterans have not been able to set up the system; and (2) some Veterans who have been able to start using the system have not done so in a consistent and sustained manner. This Health Services Research and Development Pilot proposal brings together a team with expertise in key content and methodological areas (e.g., schizophrenia, telehealth interventions, health services implementation research) to identify barriers to optimize the intervention for broader implementation and testing. We plan to enhance the system for ease of Veteran use with the help of an expert panel of academic and consumer leaders. Our panel members have expertise in suicidology, recovery, substance use disorders and early warning signs of relapse, as well as in telehealth, and health services. We will then field test the enhanced telehealth system at the VA Pittsburgh Healthcare System (VAPHS) where rates of suicide are high in this Veteran population. Our overarching aim is to enhance, implement, and test the Health Buddy(R) telehealth system in order to improve the outcomes of Veterans with schizophrenia and suicidality. The specific aims for this pilot project are to: (1) evaluate and refine the telehealth system with the help of a panel of experts to optimize the utility of the intervention; and (2) field test the refined system in a group of eligible Veterans at risk for suicide. With our field test, we will administer the intervention for a 3 month period to 15 Veterans recently discharged after admission for escalating suicidal behavior. With this pilot project, we will establish project feasibility, test and refine study procedures, and obtain preliminary data for effect size and power calculations for the full scale randomized clinical trial to follow. PUBLIC HEALTH RELEVANCE: Veterans who have schizophrenia and suicidal behaviors comprise a population of patients who represent a serious public health concern. Treating and preventing suicide is an important treatment goal in this population. This project proposes to improve upon a telehealth system using the Health Buddy(R) to monitor, treat, and prevent suicidal behavior in these Veterans. The proposed project will refine this system with the help of a panel of academic and consumer experts in the fields of suicidology, recovery, substance use disorders, early warning signs of relapse, telehealth, and implementation research. We will then implement a field test of the improved telehealth system in suicidal Veterans with schizophrenia. With this pilot project, we will establish project feasibility, test and refine study procedures, and obtain preliminary data for effect size and power calculations for the full scale randomized controlled trial to follow.
VA	2012	Veteran Interactions with VA Primary Care Prior to Suicide	Steven Dobscha	Study results have the potential to 1) identify gaps and barriers within the primary care setting in the identification and treatment of veterans at high risk for suicide completion, 2) identify specific characteristics of patients seen in VA primary care that are associated with high risk of suicide completion, 3) identify patient, provider and system characteristics that are associated with receipt of care related to suicide prevention, and 4) shape healthcare and suicide prevention efforts to the unique needs of Operation Enduring Freedom/Operation Iraqi Freedom (OEF/OIF) veterans. Project Background: Prior research suggests that veterans are twice as likely to die by suicide compared to non-veteran civilians, and each year, as many as 6,500 veterans take their own lives. Many patients visit healthcare clinicians prior to suicide. Primary care clinicians may be in a unique position to intervene with these patients. Unfortunately, little is known about the characteristics of patients who make contact with primary care clinicians prior to suicide, as well as the content of these patient-clinician interactions. It is thus unclear what opportunities may exist within primary care for intervening with individuals at highest risk for suicide. Project Objectives: The goal of this project is to inform VA suicide prevention strategies by describing and evaluating the VA primary care received by veteran suicide decedents in the year prior to death. Specifically, we will 1) describe characteristics of, and healthcare received by suicide decedents in VA primary care settings in the year prior to death, and compare this healthcare to healthcare received by a matched sample of veterans who did not complete suicide; 2) evaluate content of last interactions of veteran suicide decedents with VA primary care teams; and 3) describe characteristics of, and VA primary care received by OEF/OIF veteran suicide decedents and compare these characteristics and care to those of other veteran patient groups. Project Methods: This is a retrospective descriptive and case-control study. We will link National Violent Death Reporting System Data (NVDRS) from 10 States with the VA Decision Support System (DSS) to identify veterans who completed suicide from 2005 to 2009 and who received VA healthcare in the 12 months prior to death. NVDRS data include demographic information (including patient identifiers), means of death, and other variables. DSS will provide additional demographic, clinical (general medical and psychiatric diagnoses), and healthcare utilization (types and numbers of visits, medications) data. The OEF/OIF Roster will be used to identify OEF/OIF status and will provide military history information for the subgroup of OEF/OIF veterans. We will conduct medical record review using VA VistAWeb to access individual medical records (including progress notes) from all VA sites within participating states, and gather information on the content of healthcare visits. Medical record review variables include whether clinicians screened or assessed for depression, substance use disorder, post-traumatic stress disorder, suicidal ideation, predisposing and protective factors for suicide, reasons for last contacts, and presence of emotional distress at last contacts. Analyses will be stratified by sex. We will summarize demographic and clinical characteristics, variables describing primary care team assessments, and clinical actions taken for veterans who completed suicide. We will compare characteristics of, and healthcare received by, suicide decedents to those of a 1:1 control sample of age, sex, and primary care provider-matched veterans who did not complete suicide. Robust estimates of the standard errors will be used to adjust for clustering within states. Regression models will be adjusted for covariates identified in preliminary analyses. We will also compare characteristics of and healthcare received by OEF/OIF veterans to 1:2 matched control samples of 1) other veterans who completed suicide, and 2) OEF/OIF veterans who did not complete suicide. PUBLIC HEALTH RELEVANCE: Suicide rates are higher among veterans compared to the general population, and veterans have high rates of risk factors for suicide. The proposed study directly responds to the HSR&D mental health priority to improve identification and treatment of suicidality by aiming to identify what opportunities may exist in VA primary care settings to intervene with veterans at high risk for suicide. This retrospective descriptive and case-control study will link National Violent Death Reporting System Data (NVDRS) from 10 states with VA administrative data to identify veterans who completed suicide from 2005 to 2009 who received VA primary care in the year prior to death. We will review medical records, describe the primary care received by veteran suicide decedents, and identify potential gaps in identifying and addressing suicide risk. The information collected in this study can be used by the VA and by individual states to further suicide prevention efforts.
VA	2013	Increasing Treatment Seeking Among Suicidal Veterans Calling the Crisis Line	Tracy Stecker	Building on theory and previous empirical findings, we propose a randomized controlled trial to test the effectiveness of a brief, individualized cognitive-behavioral (CB) intervention to promote entry into behavioral health treatments for at-risk Veterans who call the VA's National Crisis Line and are resistant to initiating behavioral health treatment. The goal of this research is to evaluate the effectiveness of the intervention for increasing engagement to behavioral health treatment services. Specific aims are to test the effectiveness of the intervention on (1) attitude toward behavioral health treatment, and (2) the initiation of and adherence to behavioral health treatment. The effectiveness of the brief, individualized cognitive-behavioral (CB) intervention will be tested on 275 Veterans who call the Crisis Line but are resistant to mental health services to determine whether the intervention modified beliefs about treatment including the intention to initiate behavioral health treatment services. We will also test to determine whether the intervention impacted the decision to engage in behavioral health treatment and the number of sessions attended. Logistic and mixed effects models will be used to determine whether the intervention increased the initiation of and number of sessions attended. A secondary objective of this aim will be to test the effectiveness of the intervention on mental health outcomes. Treatment initiation rates among at-risk Veterans are alarmingly low, and research is urgently needed to develop and test interventions to improve treatment initiation. We anticipate that if the intervention is found to be effective that it will be implemented by the VA's National Crisis Line and/or the DoD as a part of their outreach efforts. PUBLIC HEALTH RELEVANCE: The goal of the proposed research is to test the effectiveness of an intervention, which promotes the initiation of mental health and/or substance use treatment among at-risk Veterans who call the VA's National Crisis Line and are resistant to treatment services. The findings help at-risk Veterans initiate treatment for mental health or substance-related problems in order to reduce the risk of suicide, as well as to improve mental health outcomes and quality of life.

VA	2013	Mindfulness-Based Cognitive Therapy for Preventing Suicide in Military Veterans	Anna Kline	Mindfulness-Based Cognitive Therapy for Preventing Suicide in Military Veterans Investigator: Anna Kline, Ph.D. Objectives: The aim of this proposal is to implement and evaluate a mindfulness-based group intervention for patients on the VA high risk for suicide list based on the Mindfulness Based Cognitive Therapy (MBCT) program for depression, modified to address the special needs of suicidal veterans (MBCT-S). MBCT has shown positive outcomes with depressed patients, while the mindfulness approach has demonstrated effectiveness in managing the emotional dysregulation and impulsivity that frequently accompany suicidal behavior. The primary aim of this proposal is to conduct a randomized controlled trial comparing MBCT-S to treatment as usual (TAU) to obtain data on key treatment outcomes. Primary outcomes of interest include suicide events (defined broadly to include a range of suicide-related thoughts and behaviors) and suicide attempts. Both outcomes will be operationalized using items from the Columbia Suicide Severity Rating Scale. Additionally, we will explore the effects of the intervention on suicide ideation, depression and hopelessness measured by the Beck Scale for Suicide Ideation, the Beck Depression Inventory and the Beck Hopelessness Scale. Methods: The study will involve a randomized-controlled trial, in which 164 veterans assigned to the high-risk for suicide list at the VA New Jersey Health Care System (VANJ) will be randomly assigned to MBCT-S plus treatment-as-usual (TAU) or TAU only. The two groups will be compared at baseline and at 4, 8, 24 and 52 weeks post-baseline on standardized measures of suicidal ideation, attempts and other outcomes of interest. Our large, two-campus facility, which sees 12,000 unique mental health patients per year, adds approximately 15 new patients to the high risk list per month, insuring an ample population for study enrollment at this single site. Outcomes: This study has the potential to increase the range of cost effective treatment alternatives for the sizeable number of suicidal veterans for whom evidence-based psychotherapies are severely limited. It may also initiate a new line of research addressing a key gap in interventions for suicide. If effective, the therapy will enhance the VA's existing suicide prevention efforts and reduce the number of veterans who attempt or complete suicide. PUBLIC HEALTH RELEVANCE: : Every month the VA becomes aware of approximately 1,100 veterans in VA care who attempt suicide. While the VA has implemented a comprehensive, multifaceted suicide prevention approach, it has yet to implement nationally any evidence-based psychotherapies targeting suicide, a gap due largely to the dearth of evidence- based therapies for suicide. Primary aims of this proposal are to conduct a randomized controlled trial testing an adaptation of a cognitive-behavioral intervention, Mindfulness-Based Cognitive Therapy (MBCT), for veterans on the VA's High Risk for Suicide List. Our adapted version of MBCT for suicide (MBCT-S) integrates mindfulness meditation techniques with standard cognitive therapy into a low-intensity group therapy format and builds on the VA Safety Plan to enhance patients' awareness of suicide triggers and appropriate coping strategies. This study has the potential to increase the range of cost effective treatment alternatives for the large number of suicidal veterans for whom evidence-based therapies are severely limited.
VA	2012	Executive Dysfunction and Suicide in Psychiatric Outpatients and Inpatients	Lisa Brenner	Individuals with a history of Traumatic Brain Injury (TBI) are at increased risk for suicidal behavior. Researchers have also found suicidal behavior to be associated with executive dysfunction as measured by indices of poor decision making, laboratory-measured impulsivity, and aggression; however, such studies were not focused on individuals with histories of moderate to severe neurologic disease or damage. To date, a clearly defined study has not been conducted to explore the relationship between executive dysfunction, as a multidimensional construct and suicidal behavior in the vulnerable population of those with a history of moderate to severe TBI. The purpose of this study is to explore a potential risk factor that could impact assessment and intervention practices for those with moderate to severe TBI. Specifically, this study will examine whether the effect of suicidality on different dimensions of executive functioning is different for those with a history of moderate to severe TBI compared to those without a history of TBI.
VA	2013	Variation in Implementation of the Partners in Care (PIC) Program	Angie Waliski	Gatekeeper training for suicide prevention is an evidence based intervention that has been used extensively by VA, primarily through the Office of Mental Health Services (OMHS)-sponsored Operation SAVE program. To date, research has shown that gatekeeper training for suicide prevention increases knowledge of suicidal warning signs and referral for veterans exhibiting warning signs among samples of VA clinical and non-clinical staff. The objective of this study is to evaluate the implementation of Partners in Care (PIC), which includes training in Operation SAVE and works with National Guard State/Joint Forces Chaplains to provide training to the state wide faith based community on how congregations/clergy can provide supportive services and resources for Veterans, military service members, and their families. Our objectives include 1) document PIC implementation and the use of Operation SAVE skills and to identify sources of variability in implementation within different states and sites, and 2) identify and characterize features of highly effective PIC program implementation. Research Plan: The present study will use mixed quantitative and qualitative methods to characterize multiple stakeholders' perspectives of the evidence, context, and facilitation needs related to PIC program implementation. There are two sources of study data. The first is data collected as part of standard program evaluation practices. This includes (1) Pre-Post training evaluations conducted on-site the day of the PIC Summit and (2) Summit Planning Interviews with NG Chaplains which will document the training team development, recruitment strategies, topics included in the trainings and opinions of the support provided by project partners. The second data sources will be jointly collected by the VISN 2 Center of Excellence, Epidemiology Core, Call Center staff and by the research team outlined in the project management plan. This data consists of semi-structured surveys of training attendees and key informant interviews of NG Chaplains and a subset of attendees. Clinical Relevance: Clergy are being utilized to encourage military service members and Veterans to seek help for suicide ideations. PIC incorporates Operation SAVE with a multi- layered approach that utilizes community stakeholders to provide support services for Veterans and their families. Results collected from this study will inform the National dissemination of PIC. Relevance to QUERI: MH QUERI's Strategic Plan identifies suicide prevention as a priority focus area for implementation research. Further, supporting adoption and implementation of the VA Enhanced Care Package for Suicide Prevention is one of two areas of emphasis identified by MH QUERI's Suicide Prevention Coalition. Gatekeeper training and Operation SAVE are components of this Package. Therefore, this study is directly responsive to priorities of OMHS and those specified within the MH QUERI Strategic Plan. PUBLIC HEALTH RELEVANCE: Partners in Care (PIC) is a program conducted by State NG State/Joint Forces Chaplains that coordinates support for National Guard (NG) members and their families by building partnerships with local faith based communities. PIC uses a gatekeeper model to inform faith based community leaders about military life, deployment, and warning signs of suicide. By expanding the faith-based resources, NG Chaplains are able to refer NG members and their families to local faith communities for diverse kinds of support, without implied endorsement of a particular religion. Faith based organizations are not limited in applying these skills to NG members but rather can conduct outreach to all military personnel, Veterans and their families. The proposed project is seeking funding to evaluate the implementation of the PIC pilot program.
VA	2012	Motivational Interviewing to Prevent Suicide in High Risk Veterans	Peter Britton	The purpose of this project is to conduct a randomized controlled trial (RCT) with psychiatrically hospitalized Veterans who are at high-risk for suicide. Participants will be recruited from the Acute Psychiatric Inpatient Unit at the Syracuse VAMC. To meet high-risk criteria, Veterans must score over two on the Beck Scale for Suicidal Ideation (SSI), which is prospectively predictive of death by suicide. After providing informed consent, participants will complete a screening assessment to confirm eligibility and a baseline assessment of risk- factors for suicide. Participants will then be randomized to receive Motivational Interviewing to Address Suicidal Ideation (MI-SI) plus treatment as usual (TAU), or TAU alone. The MI-SI group will receive two sessions of MI- SI during hospitalization and one MI-SI telephone booster sessions after discharge. Participants in both conditions will be asked to complete telephone follow-up interviews at one, three, and six months after discharge. The primary outcome will be change in the severity of suicidal ideation as measured by the SSI. Exploratory analyses will examine the impact of MI-SI on treatment engagement, and treatment engagement as a partial mediator of the impact of MI-SI on the severity of suicidal ideation. PUBLIC HEALTH RELEVANCE: Veterans who receive health care from the VA are at elevated risk for suicide, and the number of Veterans at high risk may be growing. Although the months following discharge from psychiatric hospitalization are a period of acute risk for Veterans, there is a dearth of empirically supported treatments tailored to psychiatric inpatients and no studies examining treatments for psychiatrically hospitalized Veterans. The purpose of this RCT is to test the efficacy of an adaptation of Motivational Interviewing to Address Suicidal Ideation (MI-SI) on the severity of suicidal ideation in psychiatrically hospitalized Veterans at high risk for suicide. Findings will set the stage for an RCT examining the efficacy of MI-SI on risk for suicidal behavior in Veterans, research examining mechanisms by which MI-SI may work, and ultimately contribute to the implementation of effective preventive interventions for high-risk Veterans across VA.
VA	2010	Assessing Medications as Interventions to Prevent Suicide in the VHA	Eric G. Smith	Background: Suicide prevention is a major clinical and programmatic focus of the VHA. For patients with mood disorders, stronger evidence exists for lithium as a suicide preventative than any other medication. However, the evidence base is still thin, with little randomized evidence and with observational evidence that frequently is confounded and/or lacks active controls. Most recently, a small randomized trial comparing lithium and divalproex for preventing suicide attempts failed to find a significant difference between the medications, so the potential of lithium as a suicide preventative within or outside the VHA is still unresolved. OBJECTIVE(S): Objectives: The primary objective of this study is to assess, using modern comparative effectiveness methods such as high-dimensional propensity scores, whether use of lithium is associated with reduced risks of suicide for VHA patients compared with anticonvulsant mood stabilizers (with initial focus on valproate, the most popular anticonvulsant mood stabilizer). Secondary objectives include assessing and accounting for "healthy adherer" effects, risks associated with discontinuation/nonadherence that might limit usefulness in a real-world setting, and addressing potential unmeasured confounding in administrative data through chart review.

VA	2009	Outcomes and Correlates of Suicidal Ideation In OEF/OIF Veterans	Steven Dobscha	In 2007, the Department of Veterans Affairs (VA) introduced a national performance measure requiring suicidal ideation (SI) assessment for all Veterans with positive depression screens. To date, there is little empirical evidence supporting the use of population-based SI assessment for improving outcomes. Operation Enduring Freedom (OEF) and Operation Iraqi Freedom (OIF) Veterans frequently have risk factors for suicide. It is important to know if the VA's structured SI assessment process facilitates delivery of timely and appropriate mental health care. OBJECTIVE(S): The main objective of this study was to identify process outcomes among OEF/OIF Veterans with depression who received brief structured assessments for SI in VA facilities. Specifically, our goals were to 1) Identify process outcomes following positive SI assessments, comparing post-assessment care of Veterans with positive assessments to Veterans with negative assessments, 2) Identify key correlates of positive SI assessments, and 3) Evaluate clinician adherence to recommendations for suicide risk assessment following positive SI assessments, 4) Explore Veterans' experiences of SI assessments and their perceptions of clinicians' responses to assessment results. Additional aims included identifying the prevalence of positive assessments among OEF/OIF Veterans who screen positive for depression; comparing accuracy of depression, SI, PTSD, alcohol, and pain screening data in local and regional VA databases; and describing rates and correlates of SI assessments within one day of positive depression screens.
VA	2009	Patient and Provider Outcomes of E-Learning Training in CAMS	Kathryn M. Magruder	Multiple policy reports have underscored the elevated risk of suicide in veterans, increased rates of suicide morbidity and mortality, and the need for veteran-specific interventions. The Collaborative Assessment and Management of Suicidality (CAMS) is a proven approach that is suitable for VHA settings and is now encouraged in VISN7 for all mental health providers; however, it is only available as an in-person training experience and there is only one trainer. Given the increasing numbers of providers being hired and the limited numbers of learners that can be accommodated for in-person training sessions, it is clear that there will be difficulties in accomplishing this training mission in an acceptable time frame. In addition to these inefficiencies, there is the expense of providing in-person training (and "make-up" training sessions). An efficient and effective alternative is needed. There is evidence that e-Learning has similar impacts on provider knowledge as In-person learning. OBJECTIVE(S): The overall objective of this proposal is to develop and test the effectiveness of an electronic learning alternative to the CAMS in-person approach. There are four specific aims: 1) Refine a CAMS e-learning course that covers the same material and meets the same learning objectives of CAMS in-person training; 2) Test the effectiveness of the CAMS e-Learning modality compared to the CAMS In-person modality and a no-CAMS condition in terms of provider evaluation and behavior; 3) Test the effectiveness of the CAMS e-Learning delivery compared to the CAMS In-person delivery and a no-CAMS condition in terms of patient outcomes; and 4) Assess factors that facilitate or inhibit adoption of CAMS through e-Learning or In-person.
VA	2009	Management of Suicidal Veterans during Substance Abuse Disorder	Mark Ilgen	Many veterans receiving treatment in the VHA have risk factors that have been associated with suicide deaths and accidental overdose, including substance use disorders (SUDs). SUDs are highly predictive of both suicide and accidental overdose and VHA SUD treatment programs have the potential to have a major impact in preventing suicide and accidental overdose. Several practice guidelines outline strategies for reducing and managing suicidal risk; however, the degree of adoption of these practices in VHA SUD programs is unknown. Additionally, a greater understanding of current practices for patients at known risk for accidental overdose, such as those receiving SUD treatment, is needed. Developing a measure of utilization of suicide and overdose risk reduction strategies in VHA SUD programs is a first step to understanding potential gaps in the current treatment system. OBJECTIVE(S): The objective of this study was to develop a data collection instrument that would allow us to gather information on suicide risk management practices in VA SUD treatment programs. The survey was designed to measure three guideline-concordant, suicide-related practices that include the need to: (a) assess for suicidal behavior risk, (b) integrate information about suicide risk into treatment plans, and (c) monitor at-risk patients for their suicide risk during the course of treatment. We also added an objective to help us assess clinician practices in VA SUD treatment programs that addressed accidental overdose risk.
VA	2008	Serotonin 2C Receptor mRNA Editing in Suicide	Stella Plevan (Dracheva)	Suicide is the eleventh leading cause of death in the U.S., accounting for 32,439 deaths in 2004. Up to 90% of adults who commit suicide have at least one DSM-IV psychiatric diagnosis. A question that has remained unanswered is whether the molecular factors predisposing to suicide are distinct from those of the psychiatric disorders in which it occurs. Our study during the current funding period (01/05 - 12/07) provides evidence that they are. In this initial suicide study we examined the mRNA variants of one of the serotonin receptors --2C (5-HT2CR)--previously implicated in depression and suicide. We compared postmortem specimens from the prefrontal cortex (PFC) of patients who had suffered from one of two psychiatric conditions (Bipolar Disorder (BPD) or Schizophrenia (SZ)) prior to death and subsequently committed suicide, to those subjects who died of other causes (this second group included psychiatric patients (BPD or SZ) and normal controls). We detected variations in the mRNA editing of the 5-HT2CR that were associated with suicide but not with the comorbid psychiatric illnesses, demographic characteristics, alcohol or drug abuse. These variations predict a significant increase in the VSV isoform of the receptor that has decreased activity and potency compared to the non-edited receptor. Over-representation of the VSV isoform in the PFC may, therefore, represent a vulnerability factor that predisposes some individuals to suicidal behavior irrespective of BPD or SZ. We now propose several lines of investigation that will broaden our understanding of these initial findings. Our first aim is to elucidate the molecular mechanisms underlying the increased 5-HT2CR editing in suicide. We will accomplish this by examining a number of candidate targets that are involved in the process of editing in order to determine whether their function is altered in the PFC of suicide victims. These studies aim to identify some of the factors responsible for the observed differences in 5-HT2CR editing and will allow us to determine whether suicide-associated changes are restricted to the 5-HT2CR or are present in other editing targets. In our initial study we found that 5-HT2CR editing varied with history of suicide rather than with SZ or BPD; however, tissue specimens from suicides with MDD were not available for us to study. Because, more than 30% of all suicides occur in MDD patients, it is crucial to examine 5-HT2CR editing in this population. Our second aim is to investigate whether suicide in the context of MDD is associated with variations in editing similar to those that we have detected in SZ and BPD suicide victims. If so, the evidence will be strengthened that increased 5-HT2CR editing constitutes a true and specific suicide-associated factor.
VA	2009	Implementation and Refinement of the Suicide Classification System	Lisa Brenner	Suicide is the number one sentinel event reported to the Joint Commission on Accredited Health Organizations. In recent years, suicide prevention has received increased focus within the VA. This is in part, related to concerns regarding the mental health and associated suicide risk of OEF/OIF military personnel, and a recent study highlighting the increased risk of death by suicide for members of the Veteran population. A number of initiatives have been mandated and implemented by the VA with the goal of averting Veteran suicides. Ultimately, all of these efforts could be enhanced if a clinically feasible uniform language regarding self-directed violence (SDV) was readily available and adopted throughout the VA system. The VISN 19 MIRECC staff joined efforts with the Centers for Disease Control and Prevention (CDC) to finalize the Self-Directed Violence Classification System (SDVCS). The SDVCS is a taxonomy of terms and corresponding definitions for thoughts and behaviors related to suicidal and non-suicidal SDV. Data regarding implementation (feasibility and acceptability) of the SDVCS and Clinical Tool (CT) were collected as part of this VISN 19 MIRECC Rapid Response Project. OBJECTIVE(S): The aims of this investigation were as follows: (1) to implement the VISN 19 MIRECC training program for the SDVCS and CT in two clinical settings; (2) to evaluate organizational- and provider-level factors associated with implementation, including barriers and facilitators to change, and the feasibility of a QUERI Service Directed Project (SDP); and (3) to analyze the programmatic impact on health care system processes in the areas of suicide risk assessment and clinical decision making.
VA	2012	Stakeholder Perspectives on Improving Access to VHA's Suicide Prevention Services	Monica M. Matthieu	In the United States and in the Department of Veterans Affairs (VA), suicide prevention has been declared a national priority. The current national statistics indicate a suicide rate of 11.5 per 100,000 with 34,598 Americans dying by suicide in 2007. In a study of VA healthcare seeking Veterans as compared to the general population, the suicide rate among Veterans was 43.13 and 10.41 per 100,000 person-years for men and women, respectively. Although this study is limited to Veterans seeking VA health care in 2001 prior to Operation Enduring Freedom/Operation Iraqi Freedom (OEF/OIF) and prior to suicide prevention initiatives in the Veterans Health Administration (VHA) facilities, this data confirms that both older and younger Veterans using VA health care services are at heightened risk for death by suicide. Among those Veterans who die each year by suicide, it is still unknown how many of these deaths are among community-dwelling Veterans who do NOT go to VHA for care. Epidemiological data on previous combat Veteran cohorts and data on underutilization of VHA services among OEF/OIF Veterans suggest that suicide risk among our newest cohort of Veterans as well as other Veterans not enrolled in VHA care, is of great concern. OBJECTIVE(S): The overall objective of the study is to examine the need for suicide prevention services in the local communities where Veterans live from the perspective of a diverse group of VHA and community providers. The study will identify provider and organizational barriers to care with a focus on those unique to OIF/OEF Veterans living in rural areas that are at risk for suicide.

VA	2012	Documenting Variability in Suicide Event Reporting	Robert Bossarte	Processes and standards for reporting of known suicide events were implemented in all VHA facilities in 2008. However, there is evidence of variability in reporting across VISNs. Results from an internal comparison of 2009 reported versus estimated (expected) deaths from suicide suggest that the SPAN database contains approximately 40% of all expected suicide deaths among Veterans receiving VHA services; with substantial variability across administrative units (range: 17-66%). There are two possible hypotheses that could explain the observed variability in suicide case ascertainment: H1: Population-level variability in patient characteristics and service utilization is associated with differences in the number of observed vs. expected suicide events within each VISN, H2: VISN- level variability in suicide event reporting is a function of differences in the processes associated with implementation of suicide event reporting. OBJECTIVE(S): Despite evidence of increased risk for suicide among Veterans and variability in suicide event reporting across VHA facilities, the degree of underreporting and most effective strategies for enhancing the quality of case reports have not been determined. The primary objectives of the proposed project are to identify sources of variability in suicide event reporting and to develop recommendations for enhancing current reporting practices to improve case ascertainment.
VA	2013	Using Photo-Elicitation to Explore Suicide Risk and Protective Factors among High-Risk Homeless and Marginally Housed Veterans	Samantha Farro	The purpose of this exploratory research project is to understand the lived experiences of homeless Veterans as related to suicide risk and protection. It utilizes a novel strategy that prioritizes the participant voice and elicits real-time information in a non-intrusive, non-burdensome manner (Frith & Harcourt, 2007). This project aligns with the VISN 19-MIRECC because homelessness is a known suicide risk factor including among Veterans (Bickley et al., 2006; Dasai, et al., 2003; Hwang et al., 2009; Prigerson et al., 2003; Schinka, et al., 2012). Additionally, Veterans are overrepresented among the homeless population (Fargo et al., 2011; Gamache, Rosenheck, & Tessler, 2001; VA National Center on Homelessness among Veterans, 2011). The primary aim of this project is to explore, identify, and understand homeless Veterans? suicide risk and protective factors. The small body of research on homelessness and suicide that exists is based primarily on epidemiological studies that identify population-level trends and risk factors. However, individual-level research exploring homeless and marginally housed Veterans' every day, lived experience related to suicide is needed, as it may meaningfully inform suicide treatment and prevention. The current pilot project proposes to address this gap by conducting an individual-level research project on suicide among homeless Veterans.
VA	2010	Housing instability and mental distress among Veterans	Robert Bossarte	Collaboration with the Center for Homeless Among Veterans using BRFSS data from Nebraska to examine how housing instability (i.e., stress paying rent/mortgage) may be associated with suicidal ideation among Veterans. Results showed a significant independent association between housing instability and suicidal ideation, even after controlling for psychiatric diagnosis. This manuscript is accepted for publication. Results suggest that housing instability may be an independent risk factor for suicidal thoughts, and that interventions to promote stable housing should be considered in developing interventions for at-risk Veterans.
VA	2012	The Influence of PTSD on Perceptions of Injury	Nazanin Bahraini	Given high rates of mTBI and PTSD co-morbidity in Operation Enduring Freedom/Operation Iraqi Freedom (OEF/OIF) Veterans, it is important to understand how PTSD interacts with cognitive processes (e.g., beliefs, perceptions) that have been shown to impact recovery and functioning following mTBI. The purpose of this pilot study is to examine the effect of PTSD on perceptions and beliefs about physical injury in Veterans with a history of combat mTBI or non-TBI injury. This research may provide a greater understanding of how co-occurring affective responses to trauma can impact the way individuals perceive and respond to different bodily injuries.
VA	2009	Service Utilization and Suicide in Veterans Treated for Alcohol Use Disorders	Kenneth Conner	There are 4 aims to this study: 1) to document the prevalence of suicide in Veterans with an AUD, 2) identify aspects of recent treatment utilization as predictors of suicide in Veterans with AUD's, 3) identify whether the overall pattern of treatment utilization changes prior to suicide, 4) gather greater qualitative information about the care received prior to suicide. We will examine the demographic and diagnostic indicators of risk of suicide in Veterans with AUD's.
VA	2011	Brief CBT for Insomnia in VA Primary Care Patients with Depression & Insomnia to Reduce Suicide Risk	Wilfred Pigeon	Treating depression in primary care is one of a very limited number of evidence based practices for suicide prevention. Perceived stigma and resistance to treatment are major barriers to treating depression in primary care, particularly among men. In contrast, insomnia, which frequently co-occurs with depression, blunts treatment response to depression therapies, and contributes to the recurrence of depression, carries less stigma than depression and is a comparatively non-threatening topic. Moreover, treatments for insomnia can be highly efficacious in treating not only insomnia, but comorbid conditions. Research is needed to see if these findings extend to Veterans in primary care settings. Interventions that can be delivered briefly and adapted to primary care settings are needed for a variety of conditions served by VA behavioral health and mental health providers (including for insomnia), although there is a paucity of data to inform practice. The VA is an optimal environment in which to further this line of inquiry given the presence of integrated behavioral health providers within each primary care clinic. Overall, insomnia provides an evidence-based intervention target for depression that is generally non-threatening; the intervention has the potential to reach a broad group of depressed primary care patients and has potential implications for primary care based suicide prevention. Cognitive Behavioral Therapy for Insomnia (CBT-I) is a multi-component intervention that includes the application of several evidence-based, behavioral and cognitive techniques to address insomnia, including stimulus control, sleep restriction, sleep hygiene, cognitive therapy and relaxation training. Accordingly, the purpose of the proposed intervention study is to deliver and test a brief version of CBT-I that would be more in keeping with an integrated healthcare approach and has the potential to reach a greater number of Veterans. As proposed the study will be a randomized controlled trial of CBT-I versus a control condition of Sleep Hygiene (a common control condition in insomnia trials).
VA	2008	CBT for Insomnia and Nightmares in Veterans with Combat Exposure	Kerry Knox	This was the CoE?s s first pilot treatment trial, an uncontrolled test of a behavioral intervention for insomnia and nightmares. Results showed large changes in participants? sleep outcomes, moderate changes in PTSD and depression severity, and a cessation in suicidal ideation in Veterans reporting such ideation at baseline. The manuscript is under review. Although limited by the uncontrolled design and the small sample size, the study was an important learning experience for the center in conducting intervention research in local VA clinics and has set the stage for additional sleep intervention studies with Veterans.
VA	2013	Examining Variability in Risk Assessment for Suicidal Veterans	James Pease	This study seeks to learn more about the risk assessment practices of providers throughout VA facilities nationwide. The purpose of the proposed study is threefold: (1) to capture how clinicians assess for risk of suicide; (2) to measure the variability between clinicians in categorizing risk (e.g., high, medium, low); and (3)to measure the consistency with which an individual clinician makes risk assessments between cases. This projects meets the VISN 19 MIRECC mission by providing important data on the suicide risk assessment practices of VA providers. More information is needed about these risk assessment practices of providers in order to provide a foundation for future studies that inform risk assessment practice and competency. Background: Suicide is a formidable problem, ranking as the 11th leading cause of death in the United States. Veterans are at particular risk for suicide. While there is no nationwide system for tracking the suicide rate among U.S. Veterans, the National Violent Death Reporting System (NVDRS) estimates that approximately 6,500 Veterans or those who have served die by suicide each year, accounting for approximately 20% of the annual suicides nationwide (CDC, 2006). Although much has been written about risk factors for suicide (e.g., Beck, Steer, Kovacs, & Garrison, 1985; Jobes & Mann, 1999), this knowledge does not always translate into accurate risk assessments. In fact, not only are risk assessments often incorrect, studies have shown that there is great variability in how clinicians assess risk (Cahill & Rakow, 2011). In addition, suicide measures have been shown to be poor predictors of suicidal ideation and behavior(Brown, 1999). Judgment is the primary factor that determines how a clinician determines risk (Dawes, Faust & Meehl, 1989; Doyle & Dolan, 2002). This judgment, acquired through professional training and experience in the field, varies due to differences in opinion about what constitutes risk factors, the theoretical orientation of the clinica1 field, psychiatry,psychology, nursing, social work, and differing risk assessment protocols in clinics and hospitals.
VA	2013	VA Augmentation and Switching Treatments for Improving Depression Outcomes (VAST-D)	Sidney Zisook	The overall purpose is to determine research based 'next-steps' for outpatients with major depressive disorder who have not had satisfactory outcomes to standard 'first-step' treatments. The primary objective is to compare the acute (up to 12 weeks) treatment effectiveness of augmenting an antidepressant with aripiprazole or with bupropion-SR vs. switching treatment to bupropion-SR monotherapy on symptom remission in Veterans with Major Depressive Disorder (MDD) who have not achieved optimal response after an adequate trial on antidepressant (SSRI or SNRI) monotherapy. The secondary objectives are to compare the acute (up to 12 weeks) and long term (up to 36 weeks) efficacy, safety, effects on functioning, suicidality, quality of life, anxiety and other associated symptoms, costs and cost-effectiveness of each of the three treatments.

VA	2009	Improving Depression Management Through Peer Support	Marcia Valenstein	Although effective treatments are available for depression, remission is often incomplete and relapse is common. Thus, many patients must cope with longer term depressive symptoms that decrease their quality of life and compromise functioning. As with other chronic conditions, frequent, proactive, and supportive contacts may assist depressed patients in maintaining the motivation and self-management skills needed to reach valued life goals despite continuing symptoms. Peer-support interventions that supplement usual mental health care, allow for frequent contacts, build on key elements of chronic illness care, mutual self-help, and recovery may be beneficial for patients dealing with depressive symptoms over the longer term. OBJECTIVE(S): We will conduct a randomized controlled trial (RCT) that compares the effectiveness of a telephone delivered, recovery focused, peer-support intervention to enhanced usual care for VA patients with depression. Our primary aims are to evaluate the effects of the peer-support intervention on: a) functional status, b) quality of life, c) depressive symptoms, and d) suicidality. We will also evaluate intervention effects on recovery orientation (self-efficacy for depression management, empowerment, and hope). Our secondary aims are to assess potential mediators of changes in functional status and quality of life, and our exploratory aims are to evaluate the relative effectiveness of the intervention among identifiable subgroups of depressed patients. METHODS: In this study, each participant was matched with another participating veteran and the pairs randomized to enhanced usual care or to the telephone based peer-support intervention (DIAL-UP). All study participants will receive usual care plus in-person training and written materials outlining depression self-management strategies, behavioral activation, and recovery. DIAL-UP participants will also receive: a) a peer-support manual that outlines these principles and provides peer discussion topics and b) access to a specialized telephone platform that permits free calls to their partners, ready access to mental health staff for back-up and advice, and recorded tips on depression management. Patients will be encouraged to call their partners at least once per week during the 6-month intervention period. Patient outcomes will be assessed at 3, 6, and 12 months following enrollment.
VA	2013	A Randomized Double-Blind Placebo-Controlled Trial of Lithium Augmentation and Enhanced Suicide Prevention Management in Preventing Suicide Re-Attempts in Individuals with Depression and Bipolar Disorder	Ira Katz	The study is a double blind, placebo controlled, randomized clinical trial testing the effectiveness of lithium augmentation of enhanced usual care for prevention of repeat episodes of suicidal self-directed violence including suicide attempts, interrupted attempts, hospitalizations for the prevention of suicides, and deaths from suicide, as determined by the Outcomes Adjudication Committee, over a one year period. The study sample will include patients with depression or bipolar disorder, with or without non-psychotic comorbid conditions, who have survived a suicide attempt, experienced an interrupted attempt, or were hospitalized to prevent suicide within three months prior to enrollment. The primary hypothesis is that lithium is superior to placebo for the prevention of episodes of suicidal self-directed violence over time. The primary outcome measure is time from randomization for treatment allocation to the first episode, either a suicide attempt, an interrupted attempt, a hospitalization specifically to prevent suicide, or death from suicide. As secondary objectives of the study, the efficacy of lithium will be evaluated for the prevention of subtypes of suicidal self-directed violence, for all suicidal self-directed violence events (even after the first recurrence), for the prevention of repeated events in subgroups as well as the entire sample, and to identify potential mediators. The tertiary objective of the study is to extend the follow up period using electronically available data to describe patterns of lithium use following active participation in the study participants, as well as to evaluate rates and determinants of suicide reattempts and all cause mortality over a longer follow up period. The study will enroll and randomize 1,862 patients to receive either lithium or placebo with enhanced usual care. The study is projected to run a total of 4.5 years with 3 years of recruitment, 1 year of follow-up on lithium or placebo, and time for start-up and closeout as indicated in the study budget. We expect to enroll, on average, 65 patients per site at 29 VA medical centers.