

NAMI Responses to the House Energy & Commerce 21st Century Cures Proposal

On behalf of the National Alliance on Mental Illness (NAMI), I am pleased to offer our responses to the recent solicitation from the Energy & Commerce Committee on the bipartisan 21st Century Cures initiative.

NAMI is the nation's largest grassroots advocacy organization representing persons living with serious mental illnesses and their families. Through approximately 1,000 affiliates in all 50 states, we support education, outreach, advocacy and research on behalf of persons with serious mental illnesses such as schizophrenia, manic depressive illness, major depression, severe anxiety disorders and major mental illnesses affecting children.

An estimated 11.5 million American adults live with a mental illness that is often seriously disabling, such as schizophrenia, bipolar disorder, and major depression. Based on estimates for 2010, mental illnesses accounted for 21.3% of all years lived with disability in the United States. Among the top 20 causes of years lived with disability, five were mental illnesses: major depressive disorder (8.3% of the total), anxiety disorders (5.1%), schizophrenia (2.2%), bipolar disorder (1.6%) and dysthymia (1.5%). Suicide is the 10th leading cause of death in the US, accounting for the loss of more than 38,000 American lives each year, more than double the number of lives lost to homicide. The social and economic costs associated with these illnesses are tremendous. A cautious estimate places the direct and indirect financial costs associated with mental illness in the U.S. at well over \$300 billion annually, and it ranks as the third most costly medical condition in terms of overall health care expenditure, behind only heart conditions and traumatic injury.

Mental illness and substance abuse disorders account for more than 20 percent of overall national disability and mortality. However, our overall national investment in research on these disorders is lagging. The budget of National Institute of Mental Health (NIMH) is less than 5 percent of the NIH budget, the National Institute on Drug Abuse (NIDA) budget is less than 4 percent – less than half of what would be expected if NIH funding was allocated based on the consequences of the public health burden of specific illnesses.

Moreover, these costs are not only financial, but also human in terms of lost productivity, lives lost to suicide and broken families. Investment in mental illness research and services are – in NAMI's view – the highest priority for our nation, Congress and the Energy & Commerce Committee as you consider 21st century cures.

What is the state of discovery of cures and treatment for your disease? Are there cures and treatment on the horizon?

The reality is that the current treatments available for serious mental illnesses such as schizophrenia and bipolar disorder are palliative interventions, not curative. At their most optimal and effective use, they are able to improve functioning and allow some to experience

recovery and community integration. For major mental illnesses, we are still waiting for discreet novel interventions that can genuinely change the course of the illness and avoid lifelong disability and impairment. This includes development of a new third generation of antipsychotic medications to treat psychotic disorders.

In NAMI's view, it is critical for us to move beyond the current universe of palliative treatments for serious mental illness. The sad fact is that even with optimal care, some children and adults living with serious mental illness will not be able to achieve recovery (as defined as permanent remission). People living with serious mental illness and families desperately need rapid, effective treatments that target the core pathophysiology of serious mental illnesses and the tools for early detection. Mental illness research can develop new diagnostic markers and treatments, but this will require defining the pathophysiology of these illnesses.

NAMI also supports efforts at NIMH to translate basic research findings on brain function into more person-centered and multifaceted diagnoses and treatments for mental disorders. The Research Domain Criteria (RDoC) project is showing enormous promise toward efforts to build a classification system based more on underlying biological and basic behavioral mechanisms than on symptoms, RDoC should begin to give us the precision currently lacking with traditional diagnostic approaches to mental disorders.

What programs or policies have you utilized to support and foster research, such as patient registries, public private partnerships, and venture philanthropy?

NAMI is disappointed by the relative absence of innovative public-private partnerships and venture philanthropy focused on serious mental illness. While there is significant investment of private philanthropy on mental illness and suicide prevention research, these efforts tend to lack focus and coordination.

More importantly, NAMI has been frustrated by the lack of focus of burgeoning public-private partnerships on serious mental illness. NAMI was especially disappointed that the initial priorities undertaken by the Accelerating Medicines Partnership (AMP) between the NIH and the 10 largest pharmaceutical companies completely excluded serious mental illness, and that schizophrenia was actually dropped from a preliminary list of candidate disease states. AMP is a huge opportunity to develop and harness large scale collaborative efforts that can grapple with heterogeneous disease states and validate biomarkers in large patient populations. The removal of schizophrenia from the initial list of AMP priorities is a major disappointment. NIH and their industry partners must address this exclusion moving forward.

At the same time, NAMI does support President Obama's BRAIN Initiative (Brain Research through Advancing Innovative Neurotechnologies) and the request for a \$40 million increase for FY 2015, up to \$100 million. The BRAIN Initiative shows promise for a multi-agency collaboration with a number of foundations designed to unleash new technologies and undertake basic mapping of circuits and neurons in the most complex organ in the human body. NAMI is hopeful that it will yield tremendous advances in understanding the foundations and future of neurosciences. The BRAIN Initiative's three federal funding agencies, NIH, National Science Foundation (NSF) and Defense Advanced Research Projects Agency (DARPA), are already

collaborating with private organizations to leverage advances in nanoscience, imaging, engineering and informatics. The coordination of scientific advances to a common purpose – improving neurological research tools -- will accelerate the development of better diagnostics and treatments for brain ailments. NAMI urges the Committee to support this vital research program.

How can Congress incentivize, coordinate and accelerate basic research for diseases we know relatively little about?

In NAMI's view, there is an urgent need for new medications to treat serious mental illness. Existing medications can be helpful, but they often have significant limitations; in some cases requiring weeks to take effect; failing to relieve symptoms in a significant proportion of patients; or, resulting in debilitating side effects. However, developing new medications is a lengthy and expensive process. Many promising compounds fail to prove effective in clinical testing after years of preliminary research. To address this urgent issue, NAMI is encouraging NIMH in working to accelerate the pace of drug discovery through an 'experimental medicine' approach to evaluate novel interventions for mental illnesses. This "fast-fail" strategy is designed not only to identify quickly candidates that merit more extensive testing, but also to identify targets in the brain for the development of additional candidate compounds. Through small trials focused on proof-of-concept experimental medicine paradigms, we can make progress to demonstrate target engagement, safety, and early signs of efficacy.

How can we work together to better translate advances in science into safe and effective new therapies for patients?

Over the years, NAMI has worked hard to develop strong alliances with major research institutions across the nation and the world --- in government, academia, private industry and philanthropy. These collaborations are now beginning to deliver promising results in for newer and more effective interventions, particularly with respect to early intervention in psychotic disorders. As many as 100,000 young Americans experience a first episode of psychosis (FEP) each year. The early phase of psychotic illness is a critical opportunity to alter the downward trajectory and social, academic, and vocational challenges associated with serious mental illnesses such as schizophrenia. The timing of treatment is critical; short- and long-term outcomes are better when individuals begin treatment close to the onset of psychosis. Unfortunately, the majority of people with mental illness experience significant delays to seeking care—up to two years in some cases. Such delays result in periods of increased risk for violence, especially suicide.

NIMH-funded research has focused on the prodrome, the high-risk period preceding the onset of the first psychotic episode of schizophrenia. Through North American Prodrome Longitudinal Study (NAPLS) and other studies focused on early prediction and prevention of psychosis, NIMH has launched Early Psychosis Prediction and Prevention (EP3) initiative. EP3 is showing promise in detecting risk states for first episode psychosis.

NAMI also supports efforts on the part of the federal government to advance "translational" research. The National Center for Advancing Translational Sciences (NCATS) is the newest of

27 Institutes and Centers (ICs) at the National Institutes of Health (NIH). This Center was established in December 2011 to catalyze innovative methods and technologies to enhance the development, testing, and implementation of diagnostics and therapeutics across a wide range of human illnesses. Among NCATS' important initiatives is the "Discovering New Therapeutic Uses for Existing Molecules" program. NCATS collaborated with four private pharmaceutical companies to make 26 therapeutic agents available to researchers to crowdsource ideas for new uses. NIH, working together with industry partners, can improve therapeutic development process and speed treatments to patients in need.

Both the BRAIN Initiative and NCATS are supported with from existing appropriations; not additional funding support. As important as the BRAIN Initiative and NCATS are to overcoming regulatory barriers; neither is a substitute for sustained, robust funding of biomedical research. NAMI urges the Committee's support to encourage Congressional appropriators to restore NIH's eroded purchasing power.

How do you coordinate research and outreach with other patients?

NAMI is proud of its longstanding collaboration with the NIMH. Our most recent collaboration with NIMH involved services intervention research. The NIMH Recovery After an Initial Schizophrenia Episode (RAISE) Project is aimed at preventing the long-term disability associated with schizophrenia by intervening at the earliest stages of illness. The RAISE Early Treatment Program (RAISE ETP) will conclude in 2014. The RAISE Connection Program has successfully integrated a comprehensive early intervention program for schizophrenia and related disorders into an existing medical care system. This implementation study is now evaluating strategies for reducing duration of untreated psychosis among persons with early-stage psychotic illness.

NAMI is also coordinating with NIMH on a research agenda to address early mortality in serious mental illness. When individuals with schizophrenia and bipolar disorder progress to later stages of their illness, they become more likely to develop—and die prematurely—from medical problems such as heart disease, diabetes, cancer, stroke, and pulmonary disease than members of the general population. NIMH funded research is demonstrating progress advancing the health of people with serious mental illness. NAMI supports efforts at NIMH to advance this research to large-scale clinical trials aimed at reducing premature mortality with people living with serious mental illness.

How do you learn about new treatments and cures? How do you communicate with other patients regarding treatment and cures?

NAMI collaborates closely with senior staff at NIMH and in academia to access and disseminate the latest scientific findings. This includes regular meetings with the leadership at NIMH and participation in the semi-annual NIMH Alliance for Research Progress meetings. In addition, NIMH Director Tom Insel regularly presents at our annual convention. Finally, we also use broad range of publications and on-line tools to share research results with our membership of people living with mental illness and their families.

How should regulators evaluate benefit risk? How do you work with regulators regarding benefit-risk? Can this process be improved?

NAMI is supportive of the risk-benefit framework that was included in the FDA Safety and Innovation Act of 2012 (FDASIA, P.L. 112-144). These changes were an important step forward in bringing greater transparency to the benefit-risk assessments at the FDA. Prior to FDASIA, the interests of patients and their families were not taken into account makes that too many of us has often been opaque and difficult to understand, especially when decisions have been made across multiple divisions and offices. The improvements in this Agreement should bring more transparency to this process. Increasing the public's understanding of this process should also help improve public confidence in the agency's decisions.

NAMI is pleased that FDASIA and the PDUFA V Agreement are already bringing greater transparency to the benefit-risk assessments FDA makes that too many of us has often been opaque and difficult to understand, especially when decisions have been made across multiple divisions and offices. The improvements in this Agreement should bring more transparency to this process. Increasing the public's understanding of this process should also help improve public confidence in the agency's decisions.

What is the role of public and private funding in the research and development of cures and treatments?

Both public and private investments in scientific research aimed at developing newer and more effective treatments are critical. Each has unique and complimentary roles – the NIH in basic scientific, translational and services research and private industry in developing and bringing to market both breakthrough therapies and incremental improvements that can improve adherence and respond the complex needs of individual patients. The new challenge new is that the severe constraints placed on federal discretionary spending in recent years – changes likely to stay in place over the coming decade – are likely to keep funding at the NIH flat or below the cost of research inflation.

On the private industry side we have seen more and more companies pull back from investments in neuroscience research in recent years. This is occurring as a result of the high failure rate that too often occurs in clinical trials involving not only serious mental illness, but across all of neuroscience. We know that the brain is the most complex human organ. Molecular targets are elusive and there are few animal models to assist in development of biomarkers.

At the same time, there are promising developments on the horizon. New genomic technologies, combined with global collaborations are showing promise in identifying and growing number alleles associated with schizophrenia and bipolar disorder. Molecular pathways involved in neuronal function are emerging and beginning to suggest valid drug targets. Animal and in vitro models in which to investigate hundreds of gene variants of small effect are still elusive. However, promising tools are emerging here as well. When combined with new genome engineering tools, these approaches permit the study of individual risk alleles, multiple alleles in molecular pathways, and the correction risk alleles in neurons derived from patient samples.

NAMI is hopeful that the early stages of the successful Alzheimers Disease Neuroimaging Initiative can serve as a model to identify new biomarkers in schizophrenia.

It is critical for NIH and industry to use AMP as a tool to foster greater collaboration to jumpstart these opportunities for development of new treatments.

How can Congress help?

NAMI urges Congress to move forward on legislation to better align incentives for drug discovery and promote development of new therapies and diagnostics. In particular, NAMI urges Congress to pass the MODDERN Cures Act (HR 3116), sponsored by Representative Leonard Lance of New Jersey. HR 3116 would update the current drug evaluation process to encourage the discovery and development of new treatments for chronic and rare diseases. It would also provide a pathway to bring promising new compounds to market and establish a predictable timeline for the introduction of generic equivalents. In addition, it advances creative solutions for developing companion diagnostic tests and create a system that rewards efficiency and effectiveness to the benefit of people living with serious and disabling illnesses, including serious mental illnesses such as schizophrenia and bipolar disorder.

NAMI also supports the Youth Mental Health Research Act (HR 4170), authored by Representative Chaka Fattah of Pennsylvania. By authorizing a Youth Mental Health Research Network at the NIH, HR 4170 would advance mental illness research and ensure better focus on early detection, greater coordination of multisite clinical trials of available early intervention therapies and more rapid dissemination of scientific findings resulting from such trials. This will promote greater replication and adherence to the guidelines, protocols, and practices developed and validated in important studies on early intervention in psychosis such as the North American Prodrome Longitudinal Study (NAPLS) and the Recovery After an Initial Schizophrenia Episode (RAISE) study. NAMI urges the Committee to support HR 4170.

Respectfully Submitted,

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National Alliance on Mental Illness

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