



December 17, 2019

NIMH Strategic Planning  
6001 Executive Boulevard, MSC 9663,  
Bethesda, MD 20892-9663

**Re: Request for Information (RFI) on the 2020 National Institute of Mental Health (NIMH) Strategic Plan for Research (NOT-MH-20-003)**

To whom it may concern:

The Treatment Advocacy Center appreciates the opportunity to provide comment on the National Institute of Mental Health (NIMH) draft 2020 Strategic Plan for Research.

The Treatment Advocacy Center is a national nonprofit dedicated exclusively to eliminating barriers to the timely and effective treatment of serious mental illnesses such as schizophrenia and bipolar disorder. Our organization promotes laws, policies, and practices for the delivery of psychiatric care and supports the development of treatments for and research into the causes of serious mental illnesses (SMI).

The National Institute of Mental Health (NIMH) is the main federal government agency for research into mental illness. The NIMH was authorized through the passage of the National Mental Health Act in 1946 to better help individuals with mental health disorders through better diagnosis and treatments. With a budget of almost \$2 billion in 2020, the NIMH conducts research and funds outside investigators to better understand mental illness and develop new treatments to reduce the burden these disorders have on individuals.

Despite the NIMH's vision that all mental illnesses should be prevented or cured, the NIMH has a history of ignoring those with the most severe mental illnesses, including markedly reducing treatment trials for medication treatments for schizophrenia in the last 15 years.

On December 2<sup>nd</sup>, the NIMH released a draft of its [five-year plan](#) for research and invited feedback from individuals and organizations. Again, it did not prioritize projects that will help those living with the most severe forms of mental illness, with little sense of urgency to improve the reality for those suffering right now and their families.

***Missing People who are Homeless or Incarcerated:*** The NIMH five-year plan lists suicide prevention and early intervention in psychosis under the section on 'Challenges and Opportunities,' which lays the groundwork for their plan. However, except for one passing

reference, the untreated individuals with serious mental illness who are homeless and incarcerated are entirely missing. At least one-third of the homeless, especially those who are chronically homeless and/or unsheltered, have serious mental illness. There are 10 times more individuals with serious mental illness in the nation's jails and prisons than there are in state psychiatric hospitals. Untreated individuals with serious mental illness are also overrunning the nation's emergency rooms and adversely impacting law enforcement in a variety of ways. The omission of this group under 'Challenges and Opportunities' suggests that NIMH does not regard them as a major problem to be considered for its research goals. The omission seems especially ironic given the fact that one week prior to the release of the NIMH draft research plan, the White House sent invitations for their upcoming White House Summit on Transforming Mental Health Treatment to Combat Homelessness, Violence and Substance Abuse.

***Out of Balance:*** The five-year plan is strongly weighted toward basic brain research to the exclusion of research that is of more immediate relevance for individuals who are currently affected. Basic brain research, such as biological or animal-based research into how the brain works, is of course part of the NIMH mission. Some of these brain research initiatives, such as the Human Connectome Project, may well lead to new treatments 20 or 30 years from now. But the authors of the report appear to believe that understanding the underlying biological mechanisms of how the brain works is the overriding goal of NIMH research.

The imbalance in NIMH research has been confirmed by an analysis of its research portfolio and was pointed out in 2016 in an editorial published in the *British Journal of Psychiatry*. Twenty current or former members of the NIMH National Advisory Mental Health Council noted that, in recent years, NIMH research has become increasingly centered on basic research, especially genetics and neural circuits, instead of research that might help people currently afflicted. In the editorial, they called for "an increase in public discussion of how to appropriate funding resources across mental health research domains." The current NIMH draft report appears to further increase the imbalance toward basic research.

***No New Treatments:*** According to the NIMH plan, no new treatments will be available until the distant future. The report assumes that the development of new treatments must await new research findings from basic brain studies. For example, Objective 3.1 states: "Develop new interventions based on discoveries in genomics, neuroscience, and behavioral science." There is a total disregard of current research findings which could lead to better treatments if they were pursued. In addition, NIMH has almost completely stopped doing any treatment trials for serious mental illness using currently available drugs. For example, in 2018, the most recent year for which complete data is available, NIMH supported just one treatment trial for schizophrenia among its 2,640 total grants.

The following are examples of research initiatives on serious mental illness that are currently being under-researched or not researched at all by NIMH. Each study has the potential to lead to better treatments and/or the prevention of these disorders.

- *Update of CATIE study:* The Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study, funded by NIMH, compared more recently introduced antipsychotics with the older antipsychotics. The results, published in 2005, were extremely helpful in guiding the treatment of schizophrenia. Since that time, five new antipsychotics have been introduced. Doing a CATIE-type trial comparing the effectiveness of these medications would be very useful in guiding treatments.
- *Efficacy of generic drugs:* Psychiatric patients being switched from brand-name to generic psychiatric medications frequently complain about loss of efficacy. NIMH should support studies of generic drug efficacy for psychiatric illnesses.
- *Long-term injectable antipsychotics:* In recent years, several new long-term injectable antipsychotics have been introduced. Although each was approved by the FDA for being better than a placebo, almost nothing is known about their comparative efficacy against each other. NIMH funded trials on these medications would help physicians make more informed decisions on medications for their patients.
- *Long term effects:* Many of the psychotropic drugs commonly administered to millions of patients in the United States were only studied for their acute effects. Very little is known about the long-term effects of treatment with these medications regarding side effects, maintenance dose, and use of blood levels. These should be systematically studied. The results of such studies might enable treatment using doses which are lower than those currently used, reducing side effects and improving medication compliance.
- *Duration of treatment:* Current guidelines are not clear regarding how long patients should be treated after a first episode of psychosis. In practice, many clinicians recommend stopping after one year, often increasing risk of relapse. RCTs should be done randomizing patients to continuation of low dose antipsychotic treatment 1, 2 and three years after their first psychotic episode, to see if continued treatment reduces risk of relapse, while monitoring side effects.
- *ECT:* Electroconvulsive therapy (ECT) is underused in the United States compared to other developed nations. Randomized, sham-controlled studies using modern research designs should be conducted in the United States testing the efficacy and safety of ECT. This might encourage the use of this unpopular, but safe and efficacious evidence-based treatment.
- *Medication compliance:* Patients often do not come in to the clinic to receive long-acting injections. While in some cases this is due to active refusal of treatment, in many cases this is due to negative symptoms, disorganization and poor insight. Randomized studies showing that nurses who travel to patients' homes and administer long acting injections once a month are predicted to show lower rates of treatment discontinuation and decrease in hospitalization.
- *Disease markers:* Clinicians are badly in need of accessible biological markers for the diagnosis and monitoring of treatment for psychiatric patients. NIMH should be collecting blood, saliva, and other accessible specimens from large groups of patients for population-based analytics.
- *Infections in childhood:* Several European studies have reported that infections in childhood are risk factors for the later development of serious mental illnesses. The studies need to be replicated in the United States with its more diverse population.

- *Anti-inflammatory medications:* Multiple studies have reported that serious mental illnesses have an inflammatory component. Sixteen different anti-inflammatory agents, some with promising results, have been tried for schizophrenia and/or bipolar disorder. NIMH is not currently supporting treatment trials for any of them but should be doing so.
- *Probiotic treatment trials:* Studies of the gut-brain axis and associated microbiome hold great promise for the development of new psychiatric medications. NIMH should be supporting treatment trials of probiotics and prebiotics for people with serious mental illness.
- *Estrogen:* Estrogen has been shown to be relevant to schizophrenia. There are well-replicated sex differences in the age of onset and disease course of schizophrenia that indicates that hormone differences between sexes might have an influence. Several randomized controlled trials administering estradiol patches to female patients with schizophrenia reported a beneficial effect. Further RCTs should be done, taking into account the risk for cancer, and the brain mechanism by which estrogen improves symptoms should be explored.
- *Herpes viruses:* Several studies have reported increased antibodies to various herpes viruses in individuals with schizophrenia and bipolar disorder. The viruses include cytomegalovirus, herpes simplex virus, Epstein-Barr virus, and others. Most recently, for example, aberrant immune responses to the Epstein-Barr virus were found in many individuals with schizophrenia and major depressive disorder. Studies of these viruses and the use of anti-viral medications could be very beneficial to those suffering from serious mental illness.
- *Toxoplasmosis:* Four studies have reported that cat ownership in childhood is a significant risk factor for later developing schizophrenia. *Toxoplasma gondii* is a parasite carried by cats and increased antibodies to this parasite have been reported in multiple studies of individuals with schizophrenia. Research on the role of this parasite and the development of drugs against it could lead to improved treatments.
- *Urban risk:* Multiple studies have shown that being born in, or raised in, an urban area doubles the risk of later developing a serious mental illness. Understanding the cause of this could lead to better treatments or even prevention of these diseases.
- *Migrant risk factor:* Multiple European studies have shown a dramatic increase in serious mental illness in individuals who migrate from one specific country to another, for example Jamaica to England or Morocco to the Netherlands. This is not true of all migrants but only specific groups. The increase in incidence of serious mental illness is as much as six-fold. Doing studies of these migrants could lead to understanding the cause and better treatments for these illnesses.

In summary, the draft plan for NIMH research goals for 2020-2025 further exacerbates the existing imbalance in NIMH research. It offers little hope for new or better treatments for individuals who are currently afflicted with a mental illness during their lifetime, especially a serious mental illness. Like NIMH's present research portfolio that includes only one treatment trial for schizophrenia

among its 2,640 grants, the proposed 5-year research plan is completely unacceptable to individuals with severe mental illness and their families. It is also inexcusable given the large increase in research funding given to NIMH by Congress in recent years. Such funding should have been, and should be, used to correct the existing imbalance, not to further exacerbate it. Those with the most severe forms of mental illness deserve to be prioritized.

Sincerely,

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