Working Together to Advance Discovery and Reignite Hope:

Advocacy, Academia, Industry and Government Push for New Mental Health Treatment Options

Ken Duckworth M.D., NAMI
Rosy Hosking Ph.D., Stanley Center for Psychiatric Research at Broad Institute
Teri Brister Ph.D. LPC, NAMI
Elizabeth Stafford MPH, NAMI

NAMI
National Alliance on Mental Illness

STANLEY CENTER
FOR PSYCHIATRIC RESEARCH
AT BROAD INSTITUTE

Introduction

Advances in science and technology have improved the health of billions of people. From the early discoveries of pasteurization and penicillin to modern methods of minimally-invasive surgery, we have made longer and better lives possible. We have made measurable progress against some of the most significant threats to health, improving quality of life for people with HIV and increasing rates of survivorship for many types of cancer. Progress is not evenly-distributed, however. There are still many conditions that do not receive the attention and investment required for meaningful advancement. This disparity is particularly noticeable, and concerning, in the context of serious mental illness.

In 2014 the National Institute of Health (NIH) and U.S. Food and Drug Administration (FDA), along with twelve biopharmaceutical and life science companies and thirteen nonprofit organizations, launched the Accelerating Medicines Partnership (AMP). The public-private partnership was created with the ambitious goal of eliminating barriers to the research and development of new diagnostic and therapeutic options for highly complex conditions. The first four conditions of focus were Alzheimer's disease, type 2 diabetes, rheumatoid arthritis and lupus; a new project on Parkinson's disease was launched in 2018.

The AMP represents exactly the type of transparent, cooperative, guided effort that is needed to develop more effective treatment options for serious mental illness. As the largest grassroots advocacy organization representing individuals and families affected by mental illness, The National Alliance on Mental Illness (NAMI) was strongly in favor of including schizophrenia as a condition of focus for AMP. Ultimately, however, schizophrenia was not included on the final list of conditions. In response to that decision Dr. Steven E. Hyman, Director of the Stanley Center for Psychiatric Research at the Broad Institute, wrote a compelling editorial in *Science* calling for "the scientific community, including industry, academia, patient groups, and government" to develop a well-governed partnership to share financial risk and translate basic scientific research into meaningful new treatments for schizophrenia.[1]

Upon reading that editorial NAMI's medical director Dr. Ken Duckworth and CEO Mary Giliberti recognized a common interest and unique opportunity for collaboration. Although schizophrenia's missed opportunity in the AMP was disappointing, it inspired a different partnership, with new opportunities – the Advancing Discovery Summit series.

Background

In the 1950s, the dawn of psychopharmacology generated immense excitement and, for the first time, hope for individuals with mental illness and their families. With the introduction of new medications like lithium and chlorpromazine, clinicians could treat the manic and psychotic symptoms of various conditions on an outpatient basis. It began to feel possible to imagine a world without the need for mental institutions or straightjackets, where treatment and recovery could be facilitated in a community and family setting – thanks to the remarkable dedication of researchers pressing forward to advance discovery.

Of course, no single therapeutic tool is perfect, and science does not progress in a straight and predictable line. Seventy years later, much of that excitement and hope remains unfulfilled. Lithium, shown to be effective in 1949, is still the first-line treatment for symptoms of mania in bipolar disorder.[2] It remains one of the most effective treatments, so this persistence might be acceptable if there were few side effects – but many

people treated with lithium experience weight gain and tremor and have heightened risk of renal and thyroid disorders.[3] Chlorpromazine, the first antipsychotic, inspired the development of several other medications now referred to as "typical" or "first generation" antipsychotics. These medications are effective in treating hallucinations and delusions but do little to improve the difficulties with focus and emotion that commonly occur in schizophrenia.[4] Over time, it has become clear that these medications frequently lead to the development of disorders such as tardive dyskinesia, which can cause involuntary movements of the face and body.

The early 1990s saw a flurry of innovation in the "atypical" or "second generation" antipsychotics (SGAs), but those also fail to deliver on the promise of highly effective treatments with low risk of side effects. The SGAs are associated with lower risk of movement disorders, but unacceptably high risk of metabolic disorders, such as diabetes and weight gain, as a consequence of treatment.[5] For many people with mental health conditions and those who care about them, the current reality of treatment simply doesn't live up to the excitement and hope of the 1950s.

The lack of observable, satisfying progress in psychopharmacology is not due to lack of dedication from researchers, or lack of passion from advocates, or callousness from pharmaceutical companies. It is not due to any one simple factor, because nothing in the field of psychiatric drug development is simple. Every step of the process, from identifying which chemical compound has which effect on which neuronal pathway to communicating vital safety and compliance information to research volunteers, requires multiple stakeholders to commit their energy and resources to a common goal of scientific and therapeutic progress. When funding is limited, and success is not guaranteed, a unified call to action is critically important.

We have witnessed this type of call in other areas of scientific and medical research. The field of cancer research in particular has been radically transformed in a relatively short time. Many of us remember a time when a cancer diagnosis was something to be discussed behind the closed doors of a doctor's office, if at all. Clinicians might even refuse to use the word "cancer" with their patients. But with the advent of new therapies, increasing survival rates, and a casting off of stigma and fear, advocates brought cancer out into the open. Now, patients and advocates, researchers and clinicians, pharmaceutical companies and celebrities proudly proclaim their support and engagement with the continuing effort to bring better treatments and hope to people affected by cancer. Witnessing this type of cooperation is inspiring. And, as many in the mental health community anticipate, replicable.

The Advancing Discovery Summit Series

In September 2016, representatives from the Broad Institute and NAMI convened a meeting with National Institute of Mental Health (NIMH) and industry leaders to evaluate the "ecosystem" of new drug discovery for schizophrenia, identifying the most glaring challenges that must be addressed to kickstart and sustain progress. A primary outcome of this first Summit was the recognition that although schizophrenia must remain a key condition of focus, many mental health conditions will benefit from shared research and advocacy efforts. By broadening the working group's mission and bringing in more diverse stakeholders, the initial Summit organizers created new flexibility and

opportunities for collaboration. A steering committee comprised of NAMI, Broad Institute, Psychiatric Genomics Consortium (PGC), and industry representatives formed to help shape the Summit's newly diversified strategic goals. Over the next 18 months the steering committee conducted a series of in-depth dialogue interviews with leading researchers, advocates, and policymakers. A working session in 2017 further refined and solidified this progress. The culmination of this work was the 2018 Advancing Discovery Summit held in Cambridge, Massachusetts.

The 2018 Advancing Discovery Summit, co-hosted by NAMI and the Broad Institute, convened over thirty thought leaders from academia, industry, government and private research institutions across the country. A professional facilitator guided the Summit participants through structured discussions, kinetic activities, and a free-form "marketplace of ideas" – practices designed to encourage creative thinking on the major challenges and opportunities identified during the steering committee's dialogue interviews and the 2017 working session. Participants tackled diverse topics including "keeping the vein open" during the multi-year period from initial scientific breakthrough to new drug approval, combatting stigma to engender broad public support, and structuring data-sharing agreements for cross-company and trans-national consortium studies.

On the second day of the 2018 Summit NIMH Director Dr. Joshua A. Gordon presented on the institute's current priorities. As a significant source of support for many researchers, NIMH programs are critical to both foundational research and therapeutics development. One such program, *All of Us*, will collect medical and behavioral information and biological samples from at least one million volunteers. Having access to this data, particularly the data from historically underrepresented populations, is incredibly valuable to researchers who may otherwise be limited to their own institution's siloed datasets. To reduce barriers in the drug development pipeline, NIMH regularly provides grants to investigators in the first stages of testing potential therapeutic compounds. From protein assays to toxicology evaluations, NIMH performs processes that many investigators would struggle to complete without an industry sponsor. Critically, NIMH is engaged in the Accelerating Medicines Partnership program – and has begun a proposal for the inclusion of schizophrenia as a condition of focus in 2019.

As a significant source of support for many researchers, NIMH programs are critical to both foundational research and therapeutics development.

Conclusions and Recommendations

The goals of the 2018 Summit were not only to facilitate conversation and generate inspiration among a diverse stakeholder group, but to establish concrete plans of action. At the close of the Summit, participants established six key outcomes-based initiatives and drafted strategic plans with measurable benchmarks.

Advancing Discovery Summit Key Initiatives:

- Identify biomarkers, genes linked for schizophrenia
- Create mechanisms for improved data sharing
- Establish a public-private partnership venture
- Embrace the role of advocacy organizations
- Develop a strategic communications plan
- Educate the public and recruit to patient registries

The Summit's initiatives are unique in that they were established by stakeholders from many different fields, with diverse areas of expertise, who may never have found themselves on a shared project if they had not been brought together by the Advancing Discovery Summit Series. The common thread that ties them all together is the understanding that in order to improve the lives of people impacted by mental health conditions, we must be bold enough to create and communicate a real vision for the future – dialogue between stakeholders is essential.

Two initiatives have celebrated significant progress in the time since the 2018 Summit, and now have formal working groups to advance their goals. In November 2018, representatives from the Broad Institute hosted a meeting to assess interest in forming a consortium focused on cerebrospinal fluid-based schizophrenia biomarkers. The meeting brought together representatives from NIMH, Yale, Harvard, and Mount Sinai Medical Center, as well as a representative from the Michael J. Fox Foundation to share expertise from the field of Parkinson's disease biomarker discovery. The consortium on biomarkers will launch in 2019, initially with academic leadership; the eventual aim will

be to partner with industry collaborators as well. A similar round-table discussion tackling the feasibility of efficiently sharing genomic and imaging data, hosted by the Data Sharing working group, is planned for early 2019.

All of the Summit's work is based on the principal that people must not be asked to choose between managing the symptoms of their mental health condition and maintaining their physical health and wellness. As scientists, advocates, friends and family, we must continue to strive for new and better treatment options. This will be a complex and long-term effort, as the challenges are diverse and significant. Genetics and brain science are immensely difficult even with the most cutting-edge technologies, funding for research with no guaranteed return on investment is rare, and stigma against mental health conditions isolates potential allies. The Advancing Discovery Summit Series is a powerful first step to bring together representatives from academia, government, industry, and advocacy – breaking down barriers, sharing resources, and strategizing for our common progress. As more partners join the effort, we will grow even stronger – and continue to gain hope.

The Advancing Discovery Summit will reconvene in April 2019 in Rockville, MD, hosted by the Broad Institute and NAMI. Please contact Elizabeth Stafford at research@nami.org with any questions.

[1] Hyman S, "Time for new schizophrenia Rx," *Science*, 2014 March;343(6176):1177.
[2] Shorter E, "The history of lithium therapy," *Bipolar Disorders*, 2009 June;11(s2):2-9.
[3] Gitlin M, "Lithium side effects and toxicity: prevalence and management strategies," *International Journal of Bipolar Disorders*, 2016;4:27.
[4] Hyman S, "Time for new schizophrenia Rx," *Science*, 2014 March;343(6176):1177.
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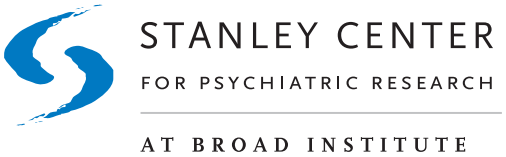
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