

Advancing Discovery Summit 2017 Summary Report

November 1, 2017

Summit Overview

On September 27, 2017, the Stanley Center for Psychiatric Research at the Broad Institute and National Alliance on Mental Illness (NAMI) hosted a half-day summit focused on exploring and discussing key issues relating to the advancement of neuroscience research that will lead to novel and effective treatments for people with mental illness. This invitation-only event was designed to build on the success of a similar gathering in the fall of 2016 and convened a diverse group of neuroscience thought leaders from academia and industry, leading advocates, and government and public policy experts. It also integrated the first-person and family experience of our current, imperfect treatment options. The discussion included overarching themes of developing more collaborative approaches, learning from our research setbacks, and seeking ways for greater innovation.

The primary objective of this summit was to strategize and develop an action plan for convening a larger group of key stakeholders in 2018 that will serve as a call to action for the research necessary to develop new and better treatments for schizophrenia and other serious mental illness.

The 2018 event is scheduled for March 22 and will also be held at the Broad Institute in Cambridge. Dr. Joshua Gordon, Director of the National Institute of Mental Health (NIMH), has agreed to participate. NIMH has a critical role in helping determine next steps in moving research forward. The Psychiatric Genetics Consortium (PGC) will also be participating as a convening partner along with NAMI and Broad.

Summit Hosts

NAMI is the nation's largest grassroots mental health organization. The organization brings the voice of the patient and their families to policymakers and researchers nationwide. NAMI has steadfastly supported resources for research; however, with the increasing recognition of the patient and family role in research, as well as changes in the rate of new treatments, NAMI is collaborating with the Broad Institute to convene leaders to promote acceleration of new discoveries and the sharing of information.

Broad Institute is the world's leading biomedical research institute dedicated to the bold mission of using the full power of genomics to transform the understanding and treatment of disease. The Stanley Center aims to exploit the most advanced technologies for human genetic analysis to study psychiatric disorders in order to understand disease mechanisms, identify potential biomarkers, and ignite needed progress in therapeutics.

Summit Format and Participants

Held at the Broad Institute in Cambridge, Massachusetts, the summit consisted of a four-hour working session.

Participants

- Anji Addington, Ph.D., Branch Chief of the Genomics Research Branch in the Division of Neuroscience and Basic Behavioral Science at NAMI
- Alexander Arguello, Ph.D., Acting Chief of the Functional Neurogenomics and Integrative Human Genomics Programs at NIMH
- Linda Brady, Ph.D., Director of the Division of Neuroscience and Basic Behavioral Science at NIMH
- Teri Brister, Ph.D., Director of Knowledge Integration at NAMI
- Tyler Brown, Ph.D., Program Manager at the Stanley Center for Psychiatric Research at the Broad Institute
- Sinéad Chapman, Associate Director, Genetic Project Management at the Stanley Center for Psychiatric Research at the Broad Institute
- Guang Chen, M.D., Ph.D., Scientific Director on Translational Research, Mood Disease Area Stronghold, Neuroscience Therapeutic Area at Janssen R & D, LLC, Janssen Pharmaceutical Companies of Johnson & Johnson
- Ken Duckworth, M.D., Medical Director at NAMI
- Mary Giliberti, J.D., Chief Executive Officer at NAMI
- Charles R. Harman, Chief Development Officer at NAMI
- Rosy Hosking, Ph.D., Manager of Scientific Operations and Programming at the Stanley Center for Psychiatric Research at the Broad Institute
- Steven E. Hyman, M.D., Harvard University Distinguished Service Professor of Stem Cell and Regenerative Biology and Director of the Stanley Center for Psychiatric Research at the Broad Institute
- Adrienne Kennedy, Executive Committee Secretary and Chair of Governance of the NAMI Board of Directors
- Kenneth Koblan, Ph.D., Head of Discovery and Global Translational Medicine and Early Development at Sunovion Pharmaceuticals Inc.
- Evan Macosko, M.D., Ph.D., Principal Investigator in the Stanley Center for Psychiatric Research at the Broad Institute and Assistant Professor of Psychiatry at Harvard Medical School
- Steven McCarroll, Ph.D., Dorothy and Milton Flier Associate Professor of Biomedical Sciences and Genetics at Harvard Medical School
- Mark Namchuk, Ph.D., SVP of Research, Non-Clinical and Pharmaceutical Development at Alkermes
- Benjamin Neale, Ph.D., Assistant Professor in the Analytic and Translational Genetics Unit at Massachusetts General Hospital, Assistant Professor in Medicine at Harvard Medical School, and Institute Member at the Broad Institute
- Ramiro (Raymond) Sanchez, Jr., M.D., Senior Vice President, Global Clinical Development at Otsuka Pharmaceutical Development and Commercialization

- Jordan W. Smoller, M.D., Sc.D., MGH Trustees Endowed Chair in Psychiatric Neuroscience, Professor of Psychiatry at Harvard Medical School, and Professor in the Department of Epidemiology at the Harvard School of Public Health
- Beth Stevens, Ph.D., Associate Professor at Harvard Medical School in the FM Kirby Neurobiology Center at Boston Children’s Hospital and Institute Member of the Broad Institute and Stanley Center for Neuropsychiatric Research
- Paul Surgenor, Ph.D., National Director of Information, Support and Education at NAMI
- Florence Wagner, Ph.D., Director of the Medicinal Chemistry Group in the Stanley Center for Psychiatric Research at Broad Institute

Facilitators

- Adam Kahane, Director, Reos Partners
- Elizabeth Pinnington, Ph.D., Principal, Reos Partners

Report Writer

- Janice Molloy, Principal, Espira Editorial

Convening Questions

The NAMI team posed three convening questions in advance of the session to help guide the group’s work together:

1. What is important to you (your organization) to help advance drug discovery for mental illness?
2. What outcome would you (your organization) like to see happen in the March summit to be able to move your vision forward?
3. What preliminary ideas do you have for communicating the outcomes of the March summit—white papers, consensus statement, call to action?

Summit Objective

To strategize and develop an action plan for convening a successful March 22, 2018 research event that will result in a call to action for the necessary research to develop new and better treatment for schizophrenia and other serious mental illness.

Pre-reading

Draft Conference Report, Psychiatric Genomics Consortium Meeting: Pathways to Drugs, London, March 2017

Background

Advancing Discovery Summit 2016

The Advancing Discovery Summit held on September 14, 2016, brought together leaders from industry, National Institute of Mental Health (NIMH), National Alliance on Mental Illness (NAMI), and the Broad Institute to evaluate what can be changed and improved to promote the ecosystem for new drug discovery for schizophrenia. The aim of this novel collaboration was to examine and change the variables that currently impede drug discovery—such as the paucity of biological markers—and to form new partnerships to address these challenges.

The public health need for better treatments for schizophrenia is compelling, and the market for these future compounds is substantial. This summit was part of an ongoing movement convened by NAMI and the Broad Institute to drive progress in this important area with industry and NIMH. Future meetings will include other partners, such as the FDA.

Takeaways from the meeting:

- The group agreed on the need to reassess the possibility of schizophrenia being reconsidered for the Accelerating Medicines Partnership (AMP). AMP is a creative public-private partnership to drive discovery in key illness areas. Unfortunately, schizophrenia did not make the list for this breakthrough model of discovery, but reportedly was close to being selected. Dr. Raymond Sanchez, Senior Vice President, Global Clinical Development at Otsuka Pharmaceutical, has volunteered to revisit the status of schizophrenia drug discovery with AMP and the Pharmaceutical Research and Manufacturers of America (PhRMA). NAMI will pursue this conversation with Dr. Josh Gordon, the Director of NIMH, at our next meeting. If this outcome could be achieved, it would be an elegant next step toward pulling together many public and private resources.
- Dr. Bob Heinssen, Director of the Division of Services and Intervention Research at NIMH, is committed to making the many new first episode of psychosis (FEP) programs friendly to research. These programs are sprouting up across the country as a result of the Substance Abuse and Mental Health Services Administration (SAMSHA) block grant program and will total approximately 150 in 2017. NAMI was a major force for advocacy for these programs. NAMI is also meeting with American Health Insurance Plans (AHIP) to promote alternative funding models to pay for these services.
- The Broad Institute is exploring ways to connect more closely with NAMI. The 2016 Advancing Discovery Summit was a strong beginning. Broad Institute leader Dr. Steve McCarroll also gave the research plenary lecture at the 2016 NAMI Convention in Denver and was one of the winners of the 2016 NAMI Inspiring

Hope Through Research award. Connecting NAMI to Broad’s genome-wide association studies is a future step under discussion.

Reconvening this group at the Broad Institute in Cambridge, MA, in September 2017 will provide an opportunity for this novel collection of leaders to assess scientific progress, changes in the regulatory culture after the election, and next steps to drive this needed change. NAMI and the Broad Institute will continue to convene this group and seek opportunities to advance this cause. NAMI would also like to give a special thanks to the industry partners that were part of the Advancing Discovery Steering Committee: Alkermes, Eli Lilly, Janssen, and Otsuka.

Process for the 2017 Summit

Steering Committee

The steering committee was composed of staff members from NAMI and Broad as well as representatives from industry sponsors. The committee met via teleconference twice monthly from June through the September meeting. The steering committee was responsible for compiling the invitation list as well as creating the agenda for the September summit.

Committee members included:

Broad:	Dr. Steven Hyman Dr. Rosy Hosking
NAMI:	Dr. Ken Duckworth Dr. Teri Brister Dr. Paul Surgenor
PGC:	Dr. Gerome Breen
Janssen:	Dr. Guang Chen
Lilly:	Dr. David Collier
Otsuka:	Dr. Raymond Sanchez

Facilitation Team

The Summit organizers sought a facilitation approach that would challenge participants to go beyond business-as-usual and stimulate out-of-the-box thinking. To achieve this goal, NAMI contracted Adam Kahane and Dr. Elizabeth Pinnington from Reos Partners to facilitate the meeting.

Reos Partners specializes in bringing people together from different parts of a system to make meaningful progress on complex, stuck challenges. They seek transformational rather than incremental change—something that NAMI and the steering committee

agree is a desired outcome for this project. Reos Partners facilitated the inaugural Advancing Discovery Summit in 2016 and will continue to work with steering committee to plan the March 2018 meeting.

Methodology

W. Edwards Deming said, “Every system is perfectly designed to get the results it gets.” If that is the case, then the way the current system around mental health is structured is at the root of the dangerously slow progress being made on prevention and treatment of serious mental illnesses.

Reos Partners’ approach for effecting systemic change begins with bringing together actors from different parts of the system to share their collective wisdom. The first step, which took place at this half-day meeting, is to map the structure—the relationships between the different parts that cause the current stuck behavior.

Based on this high-level map, participants consider questions, such as:

- Why are things stuck and how could they get unstuck?
- If there is a sense of frustration/blockage, what do we need to do to unblock it?
- Where is the leverage to change the structure so the pattern changes?
- What are the pinch points in the structure that, if unblocked, would result in new and better treatments?

Four Models

To provide a framework for the day’s work, Mr. Kahane and Dr. Pinnington introduced four models:

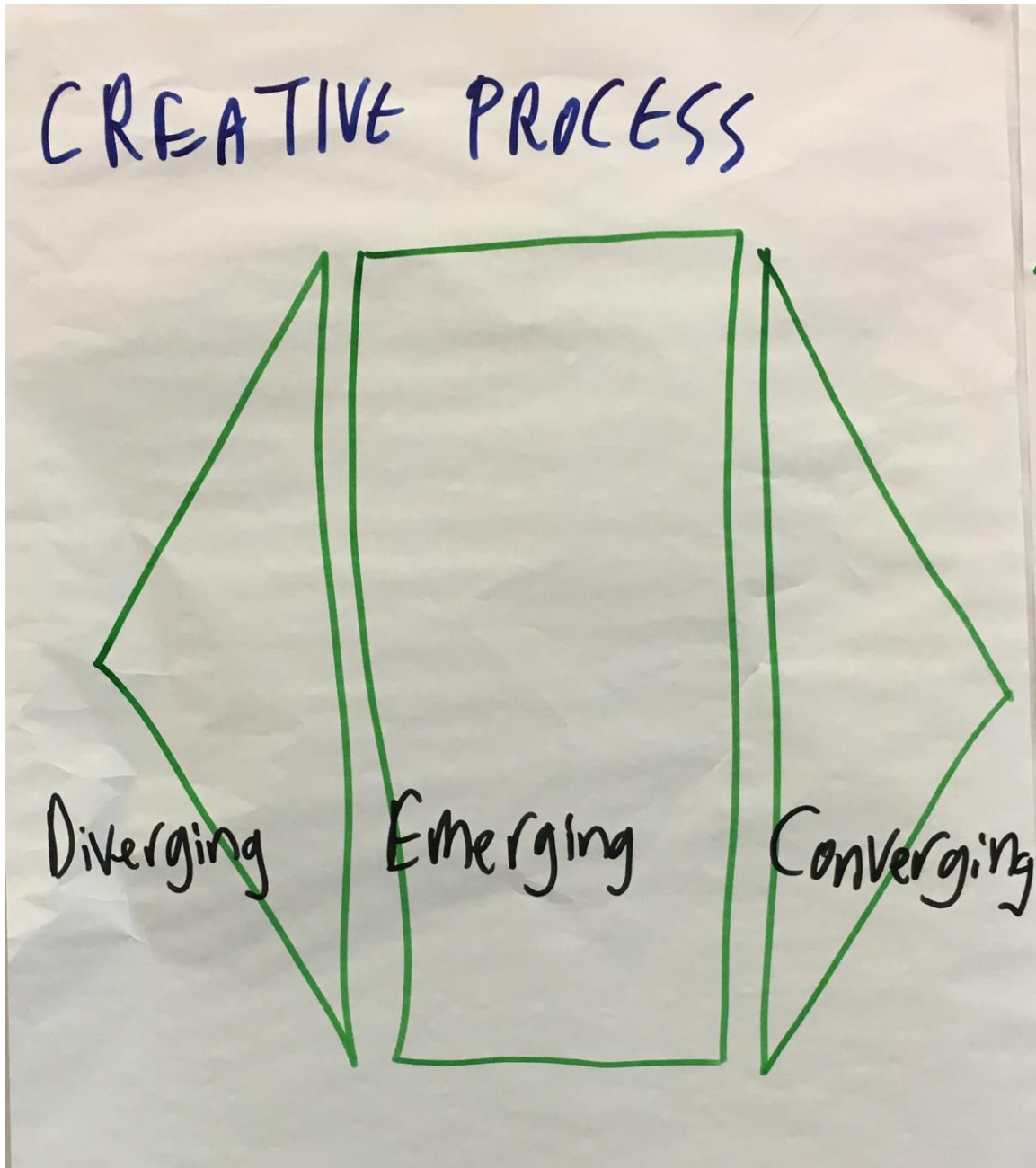
- Working with Complexity
- Creative Process
- Holonic Social Systems
- Systems Thinking Iceberg

A handwritten table on a piece of paper titled "WORKING WITH COMPLEXITY". The table is organized into three columns and three rows. The first column is labeled "Dimension". The second column is labeled "Approach for Simple systems". The third column is labeled "Approach for complex systems". The rows are labeled "Dynamic", "Generative", and "Social". The corresponding approaches are "Piece by piece", "Systemic", "Best practice", "Experimental", "Experts & authorities", and "Collaborative".

Dimension	Approach for Simple systems	Approach for complex systems
Dynamic	Piece by piece	Systemic
Generative	Best practice	Experimental
Social	Experts & authorities	Collaborative

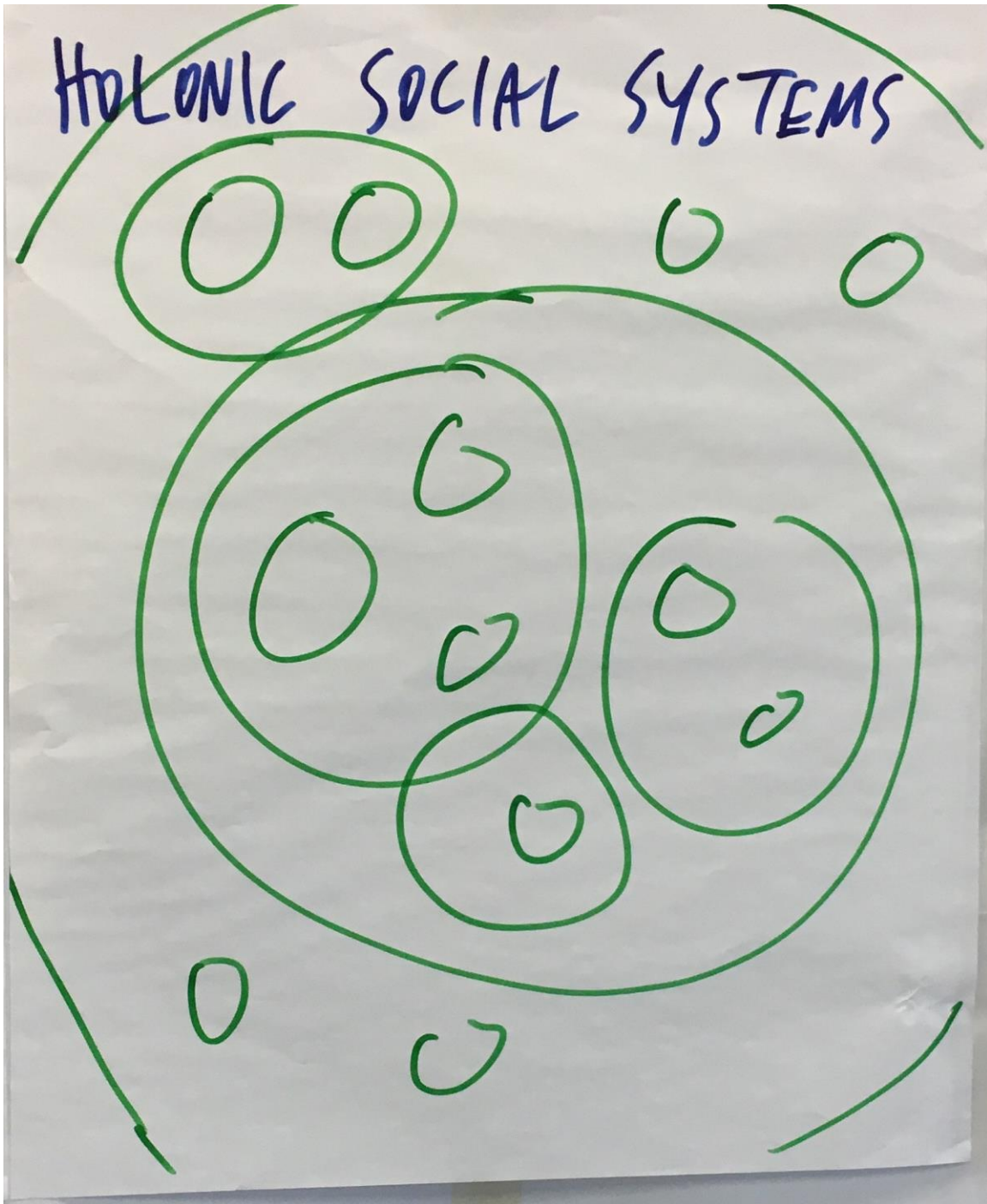
Reos Partners believes that, when dealing with complex challenges, we need to use approaches that are *systemic*, *experimental*, and *collaborative*.

Creative Process

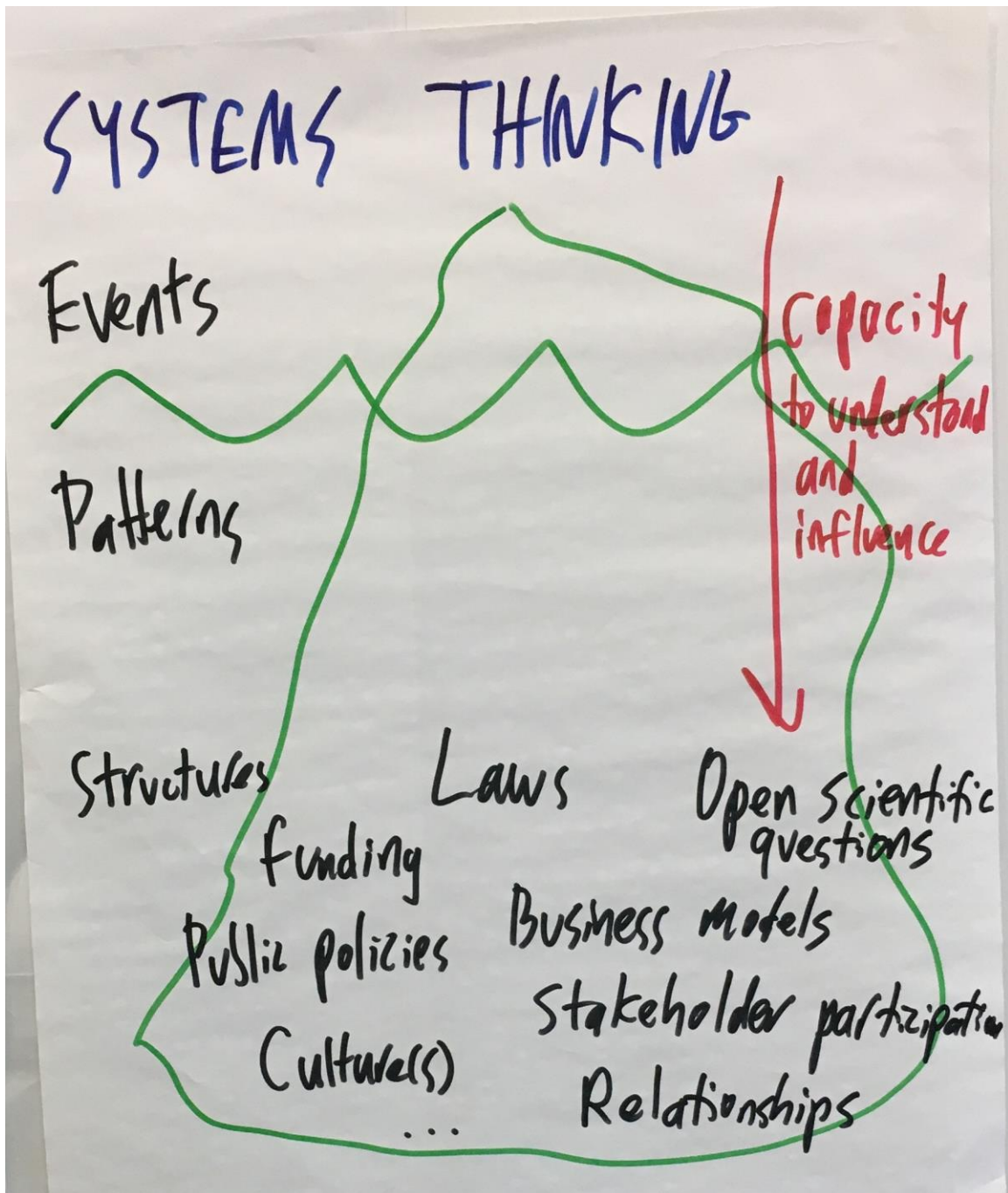


Because the challenges we're struggling with are complex, we're lost and trying to find our way forward. For that reason, we're going to spend most of our time in today's session—and perhaps in the months to come—in an *emergent* space.

Holonic Social Systems



Arthur Koestler introduced the term “holon” in his 1967 book *The Ghost in the Machine*. The word refers to something that is simultaneously a whole and a part. The different stakeholders confronting the complexity of mental health issues—academia, government, industry, advocacy groups—are both systems and parts of a larger system.



The iceberg is a key metaphor used for dealing with complex systems. The *events* we see are at the surface level. If we delve slightly below the surface, we may be able to see individual events as part of an ongoing *pattern*. Patterns of events, in turn, are created by underlying structures—policies, laws, beliefs, and so on—that drive behavior. As we go down the iceberg and design interventions at the structural level, our ability to effect lasting change increases.

Example:

- **Event:** A pharmaceutical company withdraws from the mental health market.
- **Pattern:** Multiple pharmaceutical companies withdraw. Progress of treatments for mental health issues remains slow.
- **Structure:** Laws, funding streams, etc.

Ground Rules for the Summit

The facilitators introduced simple ground rules for participants' conduct during and after the session. These expectations encouraged attendees to participate in the discussion openly and fully:

- **Be present.**
- **Keep confidences.** You can say who was here, you can say what was said, but you can't say who said what (without permission).
- **Practice democracy of time.** The summit isn't based on an expert model. The more we can hear each other's ideas, the better we can think together. Move from trying to convince everyone else that things will get better if they apply your idea to hearing others' ideas. Pay attention to how much you are talking versus how much you are listening. Avoid jumping to action; instead, slow down to notice what is emerging.

Working Session

Introductions

Mary Gilberti, CEO of NAMI

Mary began the session with a story about receiving a call from someone whose son is in prison. The call from this parent reminded Mary about the need for early intervention in mental health crises—a lesson we can take from Alzheimer's research. She expressed her excitement about building on the work started at last year's summit.

Until recently, advocates' voices weren't heard. Mary feels the inclusion of this constituency is an important step. She posed the question, "When industry, academia, advocacy groups, and government form partnerships, what could we do together?"

The March meeting provides both challenges and opportunities. What can we do to make that an impactful conversation? One message from the March 2016 summit was that this is a time to be bold.

Steve Hyman, Director of the Stanley Center for Psychiatric Research at the Broad Institute

Steve reflected on the Stanley Center Symposium, held on the two days prior to this summit, in which participants "completed two days of cherry picking the best science related to schizophrenia, bipolar disorder, and some autism."

He mentioned the following takeaways:

- Our science is really hard. Cancer is “an easy hard problem.” We know how to work on those things and are gaining real traction.
- Genetics is opening new opportunities.
- It’s difficult to get academics to embrace the complexity nature has given us rather than running from it. But they have to embrace it for industry partners to invest.
- Government and academia have to provide a platform or it’s hard for industry to get involved. Fortunately, NIMH is aligned with this position.
- Biomarkers have forever changed Alzheimer’s research and treatment. We need to find biomarkers for mental health issues, and for that to happen, we need the participation of families in the cohort.
- There’s a role for everyone to play.

Ken Duckworth, Medical Director at NAMI

As a follow-up to last year’s summit, this is the second step in a long journey. The Alzheimer’s breakthroughs began with a small meeting 20 years ago. In the mental health arena, we need new partners, such as the Psychometric Genetics Consortium, industry, and advocates.

Josh Gordon from NIMH will participate in the March meeting. NAMI members have been excited to participate in the National Institute of Health’s All of Us Research Project—it makes them feel engaged and part of something bigger.

Opening Activities

Front-to-Front/Back-to-Back

Knowing that the diverse group of participants from different disciplines needed to accomplish considerable work in a short amount of time, Mr. Kahane and Dr. Pinnington introduced the “Front-to-Front/Back-to-Back Activity” as a way to quickly build social capital and a level of trust within the team. Their objective was for participants to form relationships across specialties and be comfortable in sharing their knowledge and contributing openly to the conversation.

- They instructed participants to find a partner and stand front-to-front with that person, that is, facing them.
- When given the instruction, they were to turn and stand back-to-back with that partner.
- When given the instruction, they were to switch partners while keeping the same back-to-back orientation.
- When given the instruction, they were to stand front-to-front with the new partner.
- While standing face-to-face with the partner, when given the instruction, they were to take turns answering a question.

Questions included:

- What is your favorite home-cooked meal?
- What is your favorite vacation destination?
- What is one lifelong dream you have yet to realize?

Check-In

To begin the session, Mr. Kahane and Dr. Pinnington asked participants to introduce themselves and briefly share the frustration that underlies their commitment to the work they do.

Here are some of the themes that emerged from the check-in:



Map the Current Structure

After introducing Reos Partners' approach and the session objectives, Dr. Kahane and Dr. Pinnington assigned participants to groups to start to map the current structure: "Why are things the way they are?"

Participants were randomly assigned to tables, which were furnished with blank cards and markers. They were then instructed to:

- **Do silent brainstorming.** Some people can think out loud while others need to think then talk. The silent brainstorming gives the latter group a chance to gather their ideas before sharing their thoughts with others. Participants were asked to record three ideas on three cards.
- **Share ideas with the group.** Participants took turns sharing their ideas.
- **Use the cards to make a map.** Participants were asked to stand up around the table and physically move their cards to group like ideas. They used the markers

to draw arrows to show the connections between different parts of the existing structure.

- **Record the most significant blockages.** Group members then recorded the three most significant blockages they had identified on three hexagonally shaped sticky notes (“hexagons”).

Key Structural Blockages

Participants then moved to sitting in chairs arranged in a semicircle that faced the front of the room. Each group chose someone to read their three hexagons and post them on the chart in the front of the room. The different groups posted the following hexagons:

Group 1:

- Lack of collaboration
- Lack of data sharing
- Lack of proof-of-concept biomarkers

Group 2:

- Lack of incentives for scientists to embrace new tools and get outside their comfort zones—companies and academics value certainty, which squelches innovation
- Lack of “open science” infrastructure—sharable at publication and pre-publication levels
- Social stigma—patients, providers, researchers, politicians

Group 3:

- Lack of collaboration and openness and associated reward structures
- Stigma
- Reinforcing loop with a lack of scientific progress leading to lack of patient involvement and vice versa

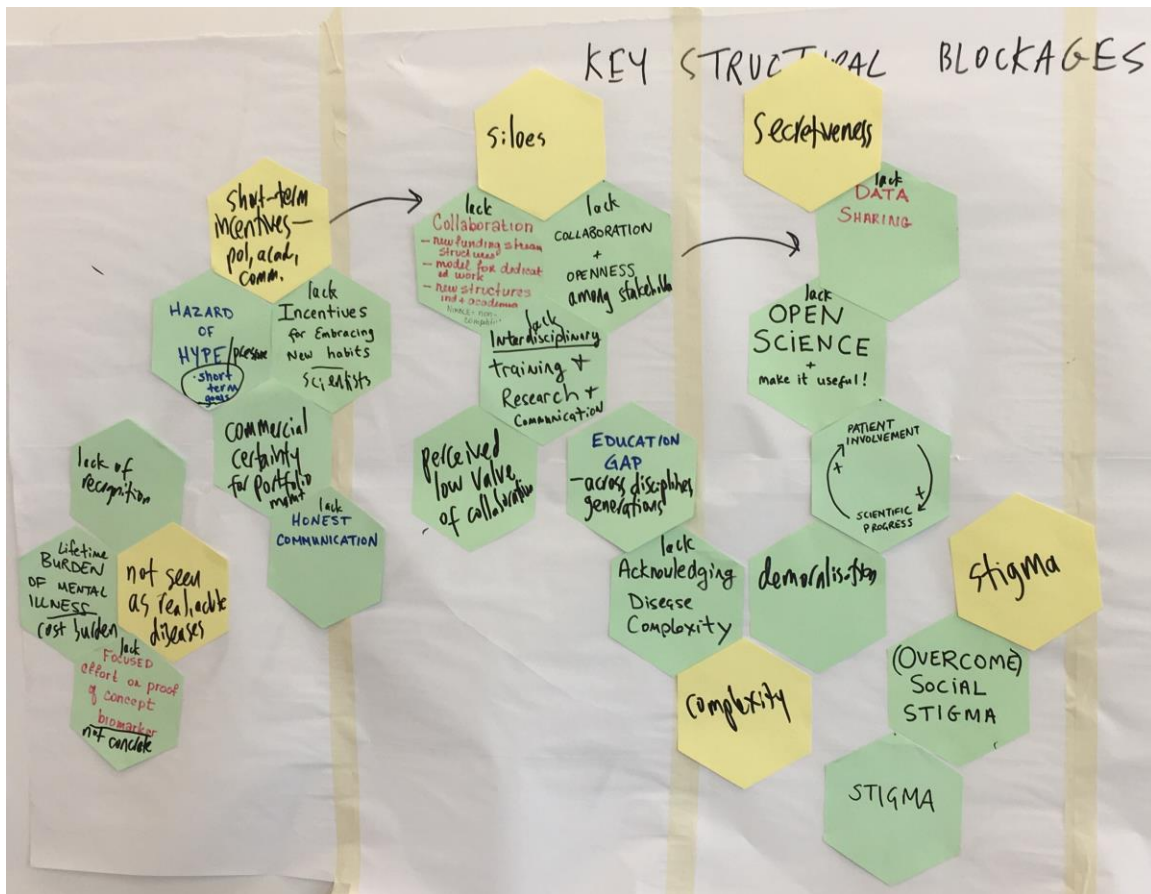
Group 4:

- “Hazard of hype” around short-term gains
- Education gap—lack of information shared between sectors/stakeholders, between generations of researchers
- Lack of honest communication—it’s difficult to communicate across areas that require deep expertise

Group 5:

- Lack of interdisciplinary training, research, communication
- Lack of acknowledgement of disease complexity
- Lifetime burden of mental illness

Mr. Kahane then helped to group the hexagons around key themes:



The clusters the group identified were:

- Short-term incentives
- Siloes
- Secretiveness
- Not seen as real illness
- Complexity
- Stigma

Mr. Kahane pointed out that, through these clusters, the underlying structure is becoming a bit clearer. The group had started to tease out some of the elements causing lack of traction and a pattern of frustration.

Feelings About the Map

The question, "What do you feel when you look at this map?" elicited the following responses: daunting, "Sisyphus must win," determination, challenge, frustration, humbled, motivated.

Implications

What does this map imply for the effort in March? It suggests that:

- The March meeting isn't primarily on scientific questions but on policy/commercial incentives.
- Meaningful improvement on one element could lead to improvement on others. What aspect offers the highest leverage? What are the possible areas that could shift the system?
- We must learn from the success of Alzheimer's research and also that there's not just one biomarker.
- It's important to be able to stay in the emerging stage—the not knowing or what poet John Keats called “negative capability”—for a long time.
- We can't fix human nature in one meeting.

Proposed Process

A small group met over lunch and came up with a proposal regarding a possible process for starting to shift the system:

Gather an international group of key stakeholders to:

- Define a roadmap with short- and long-term goals to expand R&D in mental illness.
- Identify a uniform message.
- Identify collaborative next steps (together and in parallel).

The group as a whole raised the following points during the conversation:

- Create a long-term collaborative network and focused leadership structure.
- Figure out how to take collaboration to the next level.
- Decide on a structure and goals that allow you to get these things done.
- Recognize that early success will help galvanize people.
- Frame the project so that, if you are serious about solving mental illness, you need to be part of this group—“the cool kids.”
- Determine where the most leverage exists—the first domino to knock over within the roadmap that will start a chain reaction.
- Identify a rallying cry—message or vision for people to rally around (perhaps a logo)—before the March meeting.

Process Fork in the Road

To start to put these ideas into action:

- A) Hold conference calls and small-group meetings leading up to the March meeting to get us as far as we can.
OR
- B) Set up a small-group meeting right before the March meeting to design more time for thinking together at the summit.

Guidance to the Steering Committee

- List of blockages
- Potential guidance from lunch group
- Two possible paths/processes for action
- Candidates for parallel sessions to be held at the March meeting (for example, biomarkers as a game changer, forces that would promote more data sharing, public-private partnership models, etc.)

Request from Steering Committee

- Submit names of potential steering committee members.
- Walk away with something actionable in March.

Check-Out

What is one thing that is becoming clearer to you?

- Alignment
- Increasing focus and clarity
- Need for something actionable in the near term
- Need for a communication strategy
- Need to decrease the education gap between siloes
- Themes that cut across siloes
- Cohesive
- Convergence of diverse perspectives
- Organizing and aligning messages
- Specificity and inclusiveness
- Broad spectrum of commitment
- Not one solution
- Cognizant of long term
- Creativity needed to change human nature
- Not simpler than the scientific problem
- Alignment in the room—need a communication structure to move forward
- Need to start somewhere
- Common goals
- Big thinkers needed for big public health problem
- Highest leverage—build momentum for people to stay engaged
- Sense of urgency

Next Steps

- Convene steering committee.
 - Invite new members to include volunteers from the summit.
 - Debrief the summit.
 - Make decisions about format of 2018 event – one day or two days.
- Share notes with all participants.