The MoodNetwork: An Audacious Path to Better Treatments and Better Outcomes for Bipolar Disorder

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<table>
<thead>
<tr>
<th>Employee Of</th>
<th>Massachusetts General Hospital</th>
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<tbody>
<tr>
<td>Consultant For</td>
<td>Abbott Laboratories, Astra Zeneca, Basilea, BrainCells Inc., Bristol-Myers Squibb, Corcept, Eli Lilly &amp; Co., Epi-Q, Genaissance, Genetech, GlaxoSmithKline, Hoffman LaRoche, Innapharma, Janssen Pharmaceutica, Jazz Pharmaceuticals, Medavante, Merck, Methylation Sciences, Naurex, Novartis, PGx, Pfizer, Ridge Diagnostics, Sepracor, Schering-Plough, Shire, Somerset; Sunovion, Takeda/Lundbeck, Teva</td>
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<tr>
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# Disclosure Statement

## Andrew A. Nierenberg, MD

### Other Income
- MBL Publishing for past services as Editor-in-chief of CNS Spectrums; Slack Inc. for services as Associate Editor of Psychiatric Annals; Editorial Board, Mind Mood Memory, Belvoir Publications

### Patents and Copyrights
- Copyright joint ownership with MGH for Structured Clinical Interview for MADRS and Clinical Positive Affect Scale

### Additional Honoraria
- ADURS, ASCP, Brain and Behavior Foundation Colvin Prize, University of Pisa, University of Wisconsin at Madison, University Texas Southwest at Dallas, Health New England and Harold Grinspoon Charitable Foundation and Eli Lilly and AstraZeneca, American Society for Clinical Psychopharmacology and Zucker Hillside Hospital and Forest and Janssen, Brandeis University, International Society for Bipolar Disorder, NIMH
The Mood Patient Powered Research Network

www.moodnetwork.org

Or email

moodnetwork@partners.org
Improving lives and empowering people with mood disorders.
Decrease suffering.
Increase wellness.
Our clinical research system is not generating the evidence we need to support practice.

- Poor U.S. health status
- Most research fails to inform clinical care
- Progress slow
  - Randomized trials take 5 to 10 years to complete.
  - Only 14% of innovations enter the clinic.
  - Average of 17 years to implement innovation.
- Progress expensive
  - Lags behind technological advances

Riley et al. Clinical and Translational Medicine 2013, 2:10
Problem: Clinical care and research paradoxically not centered on patients.
Outcomes:
Disability
Premature Death
Psychiatric Disorders: Major Cause of Disability

Note: DALYs = disability-adjusted life years.
Premature Death; Schizophrenia or Bipolar Disorder

Solution:
Work together.
Collaborate

• People with lived experience
• Clinicians
• Researchers
• Funding agencies
• Healthcare systems
PCORnet: The National Patient-Centered Clinical Research Network

• Network of 29 networks
  – Clinical Data Research Networks (CDRNs)
    • 11 large conglomeration of health care systems
  – Patient Powered Research Networks (PPRNs)
    • 18 consortiums of people with related conditions
    • 9 rare disease networks, 9 common diseases

• Shared data models
  – Data stays behind firewalls at each network

• Minimum of 20 million people
PCORnet: The National Patient-Centered Clinical Research Network

Fleurence et al. JAMIA 21 (4); 2014: 578 – 582
The only psychiatric component of PCORnet.
Patient and Advocacy Group Partners

- Alies Muskin  ADAA
- Allen Doederlein  DBSA
- Ken Duckworth  NAMI
- Muffy Walker  IBPF
- Donna Barnes  NOCPAS
- Roberta Tovey  Director of Communications
- Dan Goodman
- Massoud Farahbakhsh
- Elizabeth Johnson
- Susan Edgman-Levitan
Patient/Stakeholder Partners in Governance

The MoodNetwork (Mood PPRN)

Data Safety Monitoring Board
Chair: TBD

Steering
Chair: Nierenberg

Executive
Co-Chairs: Nierenberg & Doederlein**

National Coordinating Center
Director: Nierenberg

Data Coordinating Center
Director: Schoenfeld

Contract/Budget
Chair: Hintlian

Quality Control
Chair: Schoenfeld

Clinical Events
Chair: Freeman**

CDRN Liaison
Chair: Nierenberg

Clinician
Chair: Alpert

Patient Centered Priorities
Chair: Deckersbach & Edgmen-Levitan**

Protocol
Chair: Nierenberg

Patient Stakeholder/Ombudsman
Co-Chairs: Sylvia & Walker**

Dissemination
Chair: Rubin**

** = Stakeholder Partners; * = Patient Partners
• **Transform** the lives of people with mood disorders

• **Conduct** prospective comparative effectiveness trials embedded within routine care

• **Collect** clinically useful data
  – patient reported outcomes
  – electronic medical records (EMR)
Who?

- People with depression or bipolar disorder
- Patient-partners/collaborators/citizen-scientists
- Advocacy Groups
  - DBSA
  - NAMI
  - International Bipolar Foundation
  - Anxiety Depression Association of America
  - National Association of Colored People Against Suicide
- Clinicians
- Researchers
Goal:

at least 50,000 patient-partners nationwide
Why should someone join the MoodNetwork?

• To improve their care
• To improve others’ care
• To use available treatments better
• To match people to the best treatment for them
• To find new treatments
• To advance research about causes
What will we invite people to do?

• Become a partner participant
• Sign informed consent
• Provide some basic data
• Report on how they are doing
• Determine research questions and priorities
• Consider participating in possible research studies on the MoodNetwork
What will people get out of the MoodNetwork?

• Change the research agenda for mood disorders
• Confirm diagnoses
• Track symptoms and functioning
• Communicate
  – others with lived experience
  – experts
• Learn new research findings
Participate in studies.
NIMH Cogito Study

• **Challenge**
  – Detect mood episodes before they begin

• **Study**
  – Use an app to securely track
    • Movement
    • Location
    • Phone use
    • Voice patterns
    • Audio diary
PCORI Proposed Comparative Effectiveness Trial

Should young people with bipolar disorder be treated with a second generation antipsychotic (SGA) alone or with a combination of a SGA and a mood stabilizer?
PCORI Proposed Comparative Effectiveness Trial

- Examine benefits and harms
- Examine how long people stay with the randomized treatment
  - All cause discontinuation
- Examine what other treatments are needed
- Match people with treatments
Process

• Prioritized questions with stakeholders
• Reviewed competing designs with stakeholders
• Proposed vetted design for a letter of intent to PCORI
### Table. Study Designs Suggested for Top-Tier Future Research Needs for Management Strategies for Bipolar Disorder

<table>
<thead>
<tr>
<th>Rank</th>
<th>Prioritized Future Research Need</th>
<th>Recommended Study Design</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>What are the comparative safety and effectiveness of antipsychotic monotherapy compared with combination therapy with medications from the “mood-stabilizing” class in adolescents/young adults with bipolar disorder?</td>
<td>RCT or observational study using existing data</td>
</tr>
<tr>
<td>2</td>
<td>What are the comparative effects of antipsychotics on social, academic, and occupational functioning in adolescents/young adults with bipolar disorder?</td>
<td>RCT or observational study involving new data collection</td>
</tr>
<tr>
<td>3</td>
<td>What are the key patient- and family-centered outcomes for adolescents/young adults with bipolar disorder and their families, and how are these outcomes affected by different antipsychotic classes/agents?</td>
<td>Observational study involving new data collection</td>
</tr>
<tr>
<td>4</td>
<td>What are the comparative safety and effectiveness of concurrent psychiatric medications not belonging to the “mood-stabilizing” class given as adjuncts to antipsychotics in adolescents/young adults with bipolar disorder?</td>
<td>RCT or observational study using existing data</td>
</tr>
<tr>
<td>5</td>
<td>What are the comparative safety and effectiveness of “mood-stabilizing” medication classes compared with antipsychotic drugs in adolescents/young adults with bipolar disorder?</td>
<td>RCT or observational study using existing data</td>
</tr>
<tr>
<td>6</td>
<td>What are the comparative safety and effectiveness of antipsychotic drugs alone compared with the combination of antipsychotic drugs plus other nonpharmacologic interventions in adolescents/young adults with bipolar disorder?</td>
<td>RCT or observational study involving existing or new data collection</td>
</tr>
<tr>
<td>7</td>
<td>What are the adverse effects of short- and long-term medication exposure between and within antipsychotic classes for adolescents/young adults with bipolar disorder, and how do these adverse effects vary on the basis of patient characteristics?</td>
<td>RCT or observational study involving existing or new data collection</td>
</tr>
<tr>
<td>8</td>
<td>How do the comparative safety and effectiveness of antipsychotic treatment in adolescents/young adults with bipolar disorder differ depending on demographic differences?</td>
<td>Meta-analysis of observational studies or observational study involving existing or new data collection</td>
</tr>
<tr>
<td>9</td>
<td>How do the comparative safety and effectiveness of antipsychotic treatment in adolescents/young adults with bipolar disorder differ depending on socioeconomic factors?</td>
<td>Meta-analysis of observational studies or observational study involving existing or new data collection</td>
</tr>
<tr>
<td>10</td>
<td>What are the comparative effects of antipsychotics on core disease features in adolescents/young adults with bipolar disorder, both immediately and in the long term?</td>
<td>RCT, meta-analysis, or individual-patient data analysis of existing RCTs, or observational study using existing data</td>
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**RCT** = randomized controlled trial.
Design

• 5000 bipolar youth
• Ages 10 to 24
• Randomize to SGA alone vs SGA plus MS
• Treat for 2 years
• Recruit 500 interested clinicians
  – MGH Psychiatry Academy (>40,000)
  – PCORnet sites
• Collaborate with advocacy groups
• Link interested parents and patients to interested clinicians
Patient Centered Outcomes from Stakeholder Partners

- Irritability
- Fatigue
- Social functioning with friends and
- Activities
- Functioning at school and at home.
How will we get this done?

- Cluster randomize clinicians
  - Each agree to treat at least 10 patients
  - Each agree to provide the cluster randomized treatment for those 10 patients
  - For example, Dr. X gets randomized to treat her patients with SGA alone
  - She then invites her patients to partner with her
  - Patient partners join the MoodNetwork
  - Dr. X starts her patients on the SGA alone
What does Dr. X get by participating?

• Expert systematic diagnosis
• Progress report about patient progress
• Exclusive community of clinicians
  – Start Patients-like-Mine
• Private grand rounds
• Private journal club
• Exclusive on-line access to experts
• Free CME and Maintenance of Certification
What does the parent or patient get by participating?

• Free expert diagnosis by Vidyo
• Ongoing feedback about their progress
• Provide essential feedback about their lived experience
  – Observations about side effects
  – Perspective of benefits and risks
  – Assessment of things that matter to them
• Join a community to share experiences
Aspirations

- Patients-like-me type of functionality
- Options for real-time monitoring
  - Cogito
  - Ginger-io
- Provide data to clinicians
  - “Patients-like-mine” type of functionality
- Option to “TestMyBrain”
- Funding for biomarkers