Research!America Alliance Discussion
Year 1 Update

November 16, 2023
About Bipolar Disorder

Types of Bipolar Disorder
There are two general categories of bipolar disorder: bipolar disorder type I and bipolar disorder type II.

Some individuals living with bipolar disorder experience a wide range of symptoms that may not align with those typically associated with bipolar I or bipolar II.

Bipolar I
Individuals with bipolar I have experienced at least one manic episode that impairs functioning lasting at least one week, and typically experience major depressive episodes lasting two weeks or longer.

Bipolar II
Individuals with bipolar II experience major depressive episodes and hypomania (a less intense manic episode), which does not impair functioning, that lasts four or more days.

Mania can cause people to experience euphoria. Symptoms also include irritability, racing thoughts, grandiosity, and increased energy with a decreased need for sleep. These symptoms may contribute to impulsive and uncharacteristic behaviors.

Depressive episodes may include sadness, hopelessness, insomnia, lethargy, indifference, fatigue, and thoughts of suicide.

Mixed states occur when symptoms of mania and depression occur at the same time.

The study of bipolar disorder has been complicated by the vast differences individuals living with the condition face. Bipolar disorder is now viewed as a collection of different conditions.
By the Numbers

Despite its prevalence in the population and costing an estimated $200 billion annually in health and economic burden in the US alone, bipolar disorder is often studied through the lens of other psychiatric conditions like schizophrenia, which receive far greater attention and funding.

**BD²: Breakthrough Discoveries for thriving with Bipolar Disorder** is the first organization focused on funding and advancing research and care for bipolar disorder on a global scale.

Bipolar disorder affects 40 million people worldwide

- 3% of adults experience bipolar disorder
- Fewer than 50% of individuals find effective treatments
- 7 year delay to correct diagnosis
- 10-20 years of lower life expectancy
People with bipolar disorder have 10 – 20 years lower life expectancy

No consensus upon standard of care

Estimated that only 50% of people with bipolar disorder can manage the disorder

Decentralized efforts chasing funding

No difference in life expectancy for people with or without bipolar disorder

Best in-class care regardless of location

All people with bipolar disorder not only manage the disorder but live thriving lives

Unified community driving improved outcomes for people with bipolar disorder
Over the past 10 years, due to a lack of focused funding, many researchers have moved away from bipolar disorder research. BD² was created to provide leadership and commitments that revitalize and expand the field, implement fundamental direction for research, and provide new hope to those with bipolar disorder and their loved ones.

BD²
Led by experts, informed by lived experience, committed to science and people above institution.

Convening Researchers, Care Providers, and Key Stakeholders

Advancing Clinical Outcomes

Deepening Understanding of Bipolar Disorder

Impact of Philanthropy
Our vision is that all people with bipolar disorder thrive.

Our mission is to accelerate scientific understanding of bipolar disorder and advance clinical care through cross-disciplinary collaboration, data sharing, and real-time learning.
The Growth of our Work in Bipolar Disorder

**Survey of Lived Experience**
A national survey that garnered 6,405 responses from people with depression and bipolar or providing care to someone with one of these conditions.

**Define Bipolar Disorder State of the Science**
Identified outstanding scientific questions, barriers to progress, and high-impact opportunity areas.

**Define Philanthropy’s Role in Advancing Care and Science**
Identified philanthropic opportunities to advance bipolar disorder research.

**Design Longitudinal Cohort Study**
Convened experts to develop a comprehensive prospective longitudinal cohort protocol for bipolar.

**Release Cycle 1 Funding**
BD² releases over $60 million of funding to bipolar research and clinical care.

**Develop Bipolar Research Roadmap**
Convened a Scientific Steering Committee and designed four integrated programs aiming to accelerate basic discovery and rapidly improve care for people with bipolar disorder.

**Launch BD²**
Three family philanthropies joined with the Milken Institute to launch BD²: Breakthrough Discoveries for thriving with Bipolar Disorder.
Our Theory of Change promises to break the mold in how the brightest scientific and clinical minds collaborate while continuing to engage people with bipolar disorder at every step.

This holistic approach features a continuous feedback loop across research programs, brain omics and genetics platforms, and clinical care.
Collaboration allows for rapid exchange of ideas, builds on relevant expertise, and can spark innovation. BD\textsuperscript{2} cultivates collaboration through multiple ways.

**Empowering Collaboration**

**The Hub**

The virtual community platform allows funded teams to connect with each other, share data and resources, and learn.

**Interest Groups** bring together teams across the network to share new data, and recent findings in relevant interest areas such as genetics and metabolism.

**Working Groups** bring teams together to solve a problem, align protocols, and standardize methods.

**Collaboration Grants**

New grants are available for funded investigators to form new, meaningful collaborations across the network.

These $150,000 annual grants must have at least two teams who are not yet collaborating.
Enabling Open Science

Open science produces more rigorous research, accelerates the pace of discovery, and better utilizes research dollars. BD² cultivates science through multiple ways.

Data from the Integrated Network are aggregated and standardized by the center to allow fast and accurate sharing across the network.

Data from participants include:
- Neuroimaging
- Clinical
- Psychometric
- Wellness metrics
- Sleep and actigraphy via mobile devices
- Whole genome sequencing
- Metabolic and immunological biomarkers

A written, detailed policy for open science is included in all Request for Applications and grant contracts to mandate true open science.

Research data, code, protocols, and publications must all be in open access, FAIR databases.
- Research data: Zeonodo
- Protocols: Protocols.io
- Code: Github
- Publications: Open access-enabled journals
After just one cycle of funding, BD² has connected 100+ scientists and clinicians in an initial network.

As BD² continues to build the community this map will grow and connections will strengthen, accelerating research progress to impact the care and outcomes for bipolar disorder.
The Integrated Network brings together researchers and clinicians from leading medical institutions to expand knowledge of bipolar disorder while accelerating the translation of that knowledge into clinical care. This unique and collaborative approach will advance clinical care and lead to better outcomes for those with bipolar disorder.

**FUNDING**

$2,300,000 over five years per site
The BD² Integrated Network will engage a multidisciplinary network of collaborating investigators and clinicians dedicated to improving care, interventions and outcomes for people living with bipolar disorder.
Longitudinal Cohort Study: Deep Phenotyping Protocol

**Screen Remote**
- Join study
- Receive onboarding materials
- Prescreen visit
  - Q&A with study representative
- Informed Consent
- Schedule first appointment

**Baseline Visit 1**
- Day 1. Check in
  - Fill out intake form
    - Demographics
    - Medical history
    - Family history
    - Comorbidities
  - Meet with Centralized Rater
    - Diagnosis: SCID
    - Mania: YMRS
    - Depression: MADRS
    - Psychosis: BPRS
    - Childhood experiences
- Day 2. Meet with study staff
  - Cognitive battery
  - Functioning: FAST
  - MRI/fMRI Imaging scan
  - Meet with Care Provider or study staff
    - Vitals and metabolic readouts
      - Weight, heart rate
      - BMI, waist-hip ratio, blood pressure
    - Blood draw
  - Prep for studies between clinical visits
    - Mobile apps
    - Participant dashboard

**Between Visits**
- Check into Participant Dashboard
- One-Time Surveys
  - Personality assessment
  - Resilience
  - Temperament
- Continuous Assessments
  - Mobile Apps
    - Sleep
    - Life stress
    - Wellness
    - PHQ, PMQ or digiBP

**Annual Follow-up In Person/Hybrid**
- Check in
- Fill out intake form
- MRI/fMRI Imaging scan
- Meet with Centralized Rater
  - SCID update
  - YMRS
  - MADRS
  - Psychosis
- Meet with study staff
  - Cognitive battery
  - FAST
- Meet with Care Provider or study staff
  - Vitals and Metabolic readouts
  - Blood draw
Principles of a Learning Health Network

Assemble patient data

Data are aggregated from various sources including EHRs, claims, wearables, patient & community input

Analyze patient data & interpret findings

Strive for data that are standardized, consistent & complete

Findings are aggregated from a “network of networks” are queried via a CDR

Identify key outcome measures

How do standardized outcome measures vary under different circumstances?

Determine variations in care associated with better outcomes

Scale change by clinic, institute, and beyond

Drive change in care to promote better outcomes

A sociotechnical system: Technical innovation informs change, interdisciplinary effort effects that change.
Integrated Network: Implementation Overview
The Discovery Research program is the cornerstone of BD²’s hypothesis-driven, cross-disciplinary approach. Each project will proactively share findings to facilitate progressive collaboration and the improvement of clinical care more quickly. Multidisciplinary research teams are examining the genetic, molecular, cellular, circuit, or behavioral mechanisms of bipolar disorder.

**FUNDING**

Awards of up to $4,500,000 support teams for three-year research projects.

Funded teams can also apply for $150,000 annual grants to form new collaborations across the BD² network.
The Brain Omics and Genetics Platforms aim to close fundamental gaps in scientific understanding of the biological and genetic foundations of bipolar disorder and generate data that can be used by all. The research and findings produced by the teams provide basic research for continued scientific exploration while also building the brain atlas and identifying the genetic architecture of bipolar disorder.

BD² funding also pioneers the sequencing of the largest (30,000) and most diverse set of samples from people with bipolar disorder from Africa, Central America, South America, and Asia.