

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.



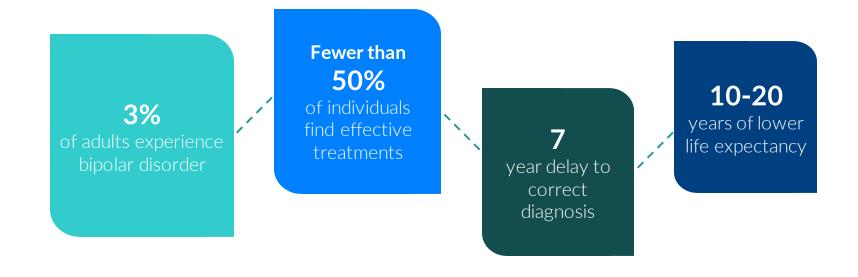
The study of bipolar disorder has been complicated by the vast differences individuals living with the condition face. Bipolar disorder is now viewed as a collection of different conditions.

By the Numbers

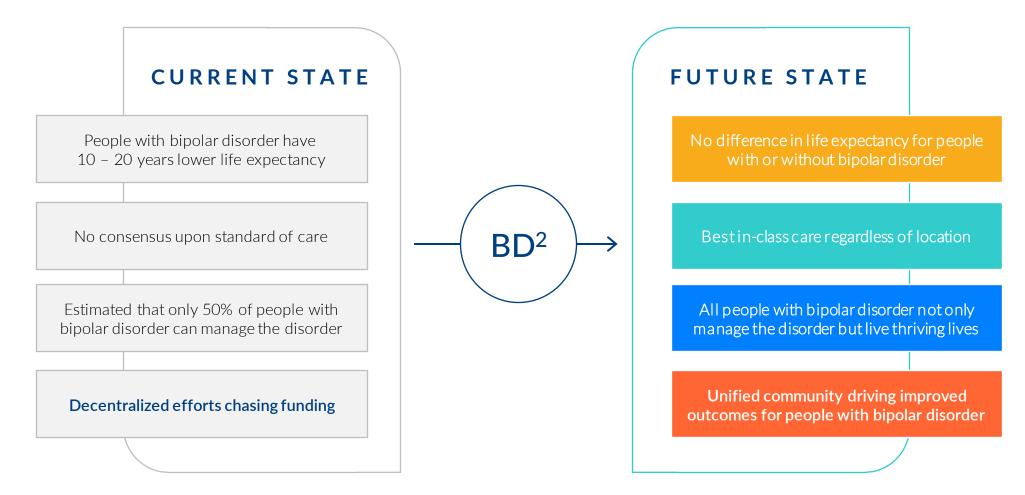
Despite its prevalence in the population and costing an est. \$200 billion annually in health and economic burden in the US alone, bipolar disorder is often studied through the lens of other psychiatric conditions like schizophrenia, which receive far greater attention and funding.

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



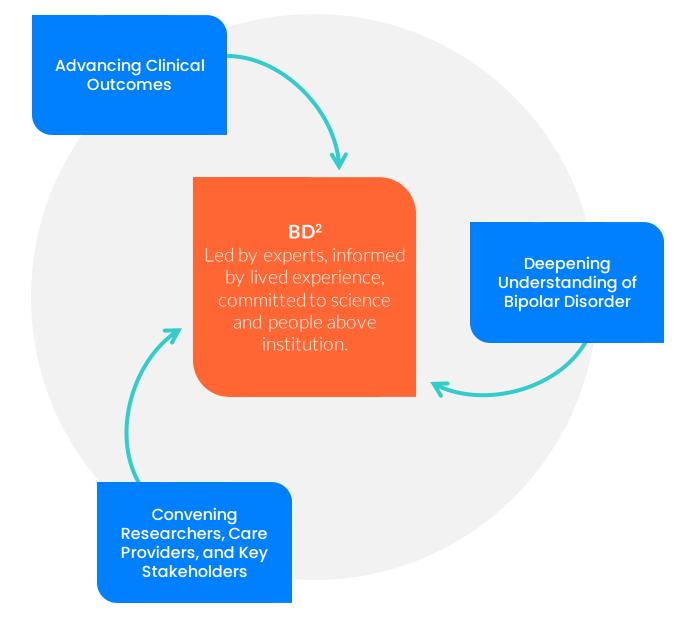
History of Bipolar Disorder Research and Care



Impact of Philanthropy

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.





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 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.



2018 2020

2021

2022

2023

Define Bipolar Disorder State of the Science

Identified outstanding scientific questions, barriers to progress, and high-impact opportunity areas.



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

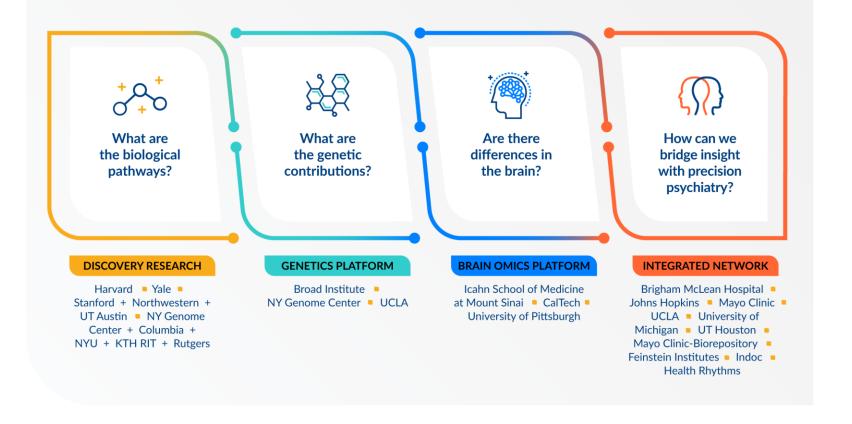
Three family philanthropies joined with the Milken Institute to launch BD²: Breakthrough Discoveries for thriving with Bipolar Disorder.



BD²'s Theory of Change

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.

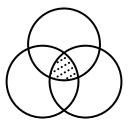
This holistic approach features a continuous feedback loop across research programs, brain omics and genetics platforms, and clinical care. Four foundational questions.
Four interconnected programs.
Zero silos. Closing the research and clinical gap.



Empowering Collaboration

Collaboration allows for rapid exchange of ideas, builds on relevant expertise, and can spark innovation.

BD² cultivates collaboration through multiple ways.

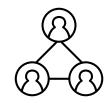


THE HUB

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

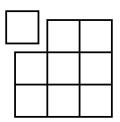
New grants are available for funded investigators to form new, meaningful collaborations across the network.

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 COORDINATING CENTER

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



OPEN SCIENCE POLICY

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.

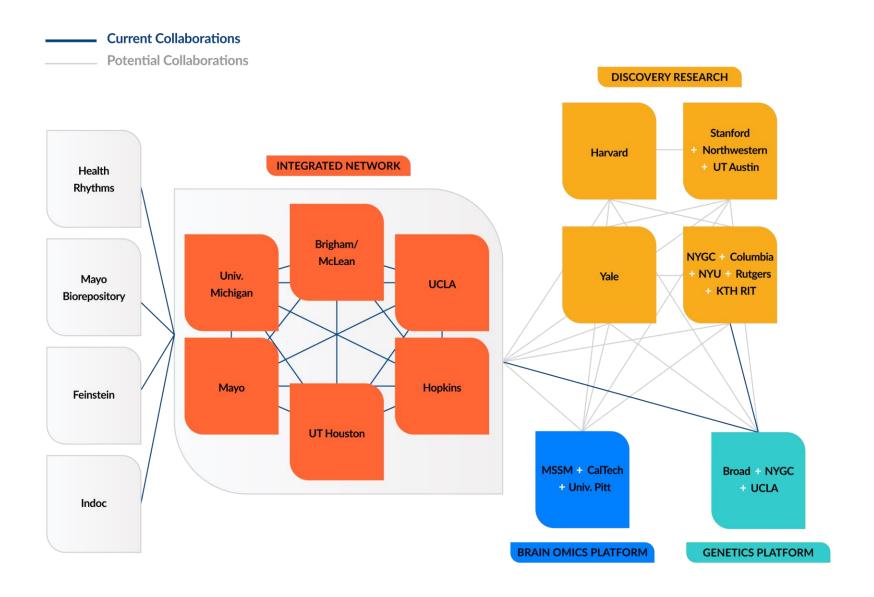
- Research data: Zeonodo
- Protocols: Protocols.io
- Code: Github
- Publications: Open access-enabled journals



Taking Science out of Silos

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.

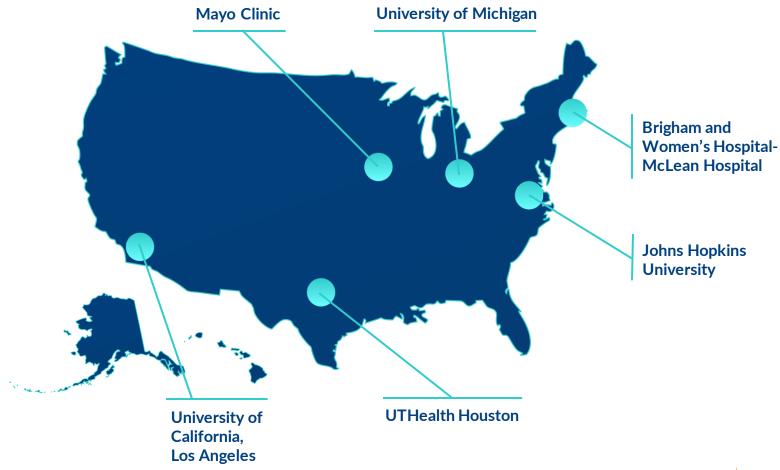


BD² Integrated Network

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



BD² Integrated Network

A novel design combining a longitudinal cohort and learning health network

Longitudinal Cohort Study

Collect in-depth clinical, cognitive, imaging and physiological markers from 4,000 participants over at least 5 years.

Learning Health Network

Engage a core team of clinicians and researchers supported by computational experts to provide on-the-ground, near-real-time data analytics on clinical carebased outcomes within the network that are re-invested back into practice.

Integrated Network

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

Annual Follow-up
In Person/Hybrid

Check into Participant Dashboard

One-Time Surveys

- Personality assessment
- Resilience
- Temperament

Continuous Assessments

- Mobile Apps
 - Sleep
 - Life stress
 - Wellness
 - PHQ, PMQ or digiBP

Check in

Fill out intake form

MRI/fMRI Imaging scan

Meet with Centralized Rater

- SCID update
- YMRS
- MADRS
- Psychosis

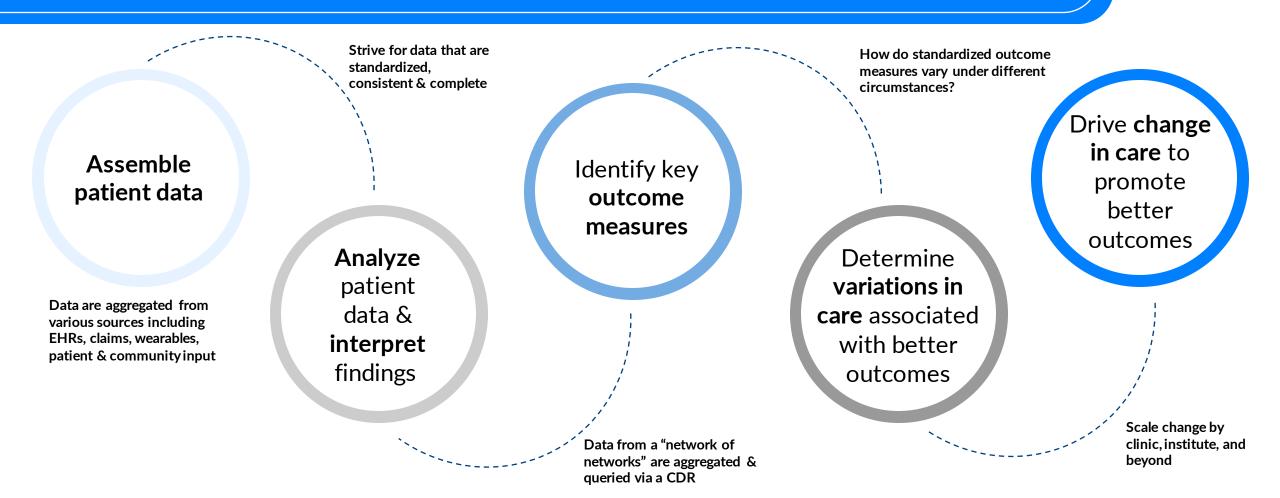
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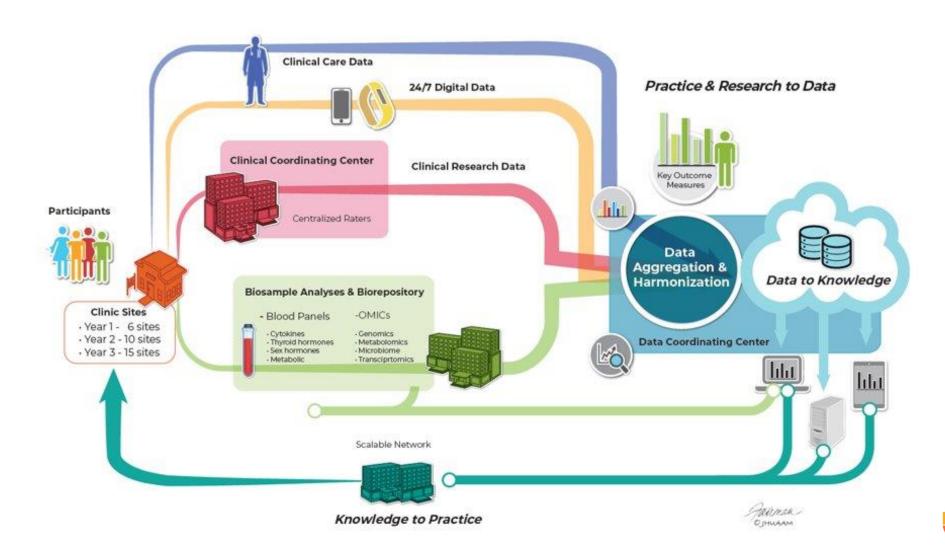
Principles of a Learning Health Network



A sociotechnical system: Technical innovation informs change, interdisciplinary effort effects that change.



Integrated Network: Implementation Overview



Discovery Research

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.

YALE UNIVERSITY

Mechanisms of Mitochondrial Dysfunction

STANFORD UNIVERSITY

Mechanisms of Sleep and Circadian Rhythms

NEW YORK GENOME CENTER

Genetics of Bipolar Using Stem Cells

HARVARD UNIVERSITY

Mechanisms of Current Treatments



Brain Omics and Genetics Platforms

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.

BRAIN OMICS PLATFORM

Icahn School of Medicine at Mount Sinai

FUNDING

\$5,000,000 over three years

GENETICS PLATFORM

Broad Institute

FUNDING

\$10,000,000 over two years