


# A Precision Health Approach to Bipolar Disorder

Sarah H. Sperry, Ph.D.

September 12<sup>th</sup>, 2023



**Meet the  
Scientist**  
WEBINAR SERIES

I have no conflicts of interest



**Bipolar disorder** is one of the top 10 leading causes of disability worldwide.

# Mania

- Feeling elated, euphoric, or agitated
- Increased energy
- Reduced need for sleep
- Feeling invincible or superior
- Talking more and faster than normal
- Having racing thoughts
- Being hyper-focused on an activity
- Pacing or fidgeting
- Being impulsive or reckless
- Experiencing delusions or hallucinations

Must last at least one week or require hospitalization



# Hypomania

- Feeling elated, euphoric, or agitated
- Increased energy
- Reduced need for sleep
- Feeling invincible or superior
- Talking more and faster than normal
- Having racing thoughts
- Being hyper-focused on an activity
- Pacing or fidgeting
- Being impulsive or reckless

Must last at least 4 days and recognize unequivocal change





# Depression

- Prolonged low mood
- Loss of energy
- Loss of interest in pleasurable activities
- Feelings of worthlessness or guilt
- Withdrawal from social activities
- Appetite and weight changes
- Difficulty concentrating/making decisions
- Insomnia or hypersomnia
- Thoughts of death or suicide

Must last at least two weeks and cause impairment

A watercolor illustration of a human brain, split vertically. The left hemisphere is painted with cool colors: various shades of blue, teal, and green. The right hemisphere is painted with warm and vibrant colors: reds, pinks, purples, yellows, and oranges. A white outline defines the brain's shape. The text 'Mixed Symptoms' is centered in the white space between the two hemispheres.

# Mixed Symptoms



# Bipolar Spectrum

Bipolar I Disorder

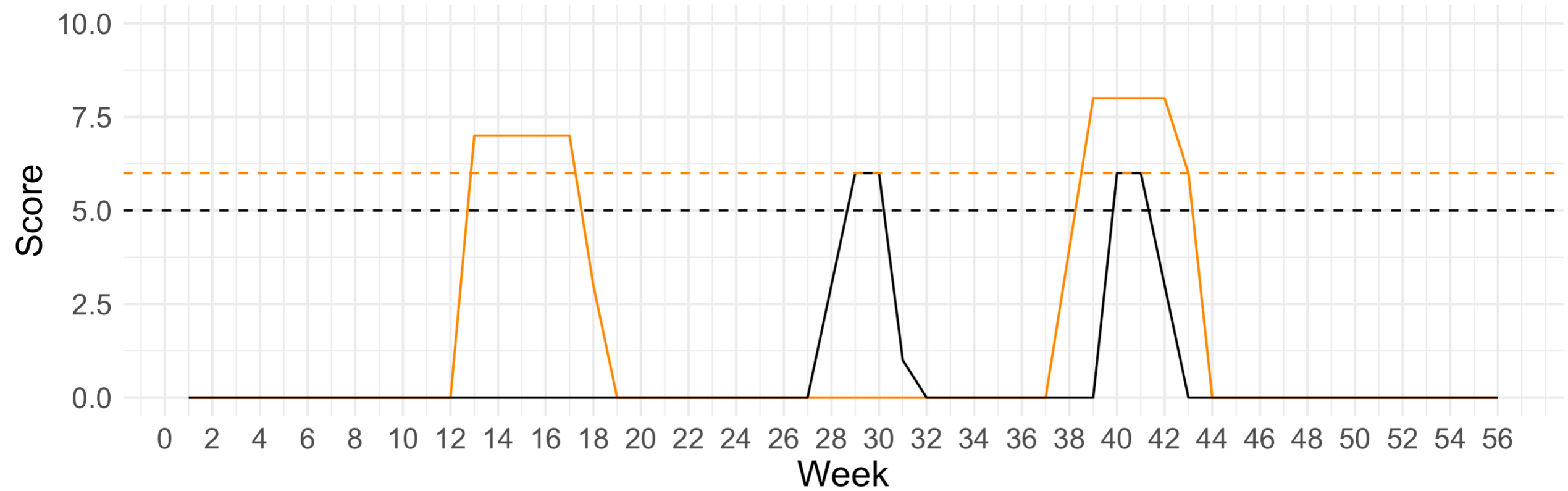
Bipolar II Disorder

Other Bipolar Disorder

Cyclothymic Disorder



# Bipolar I Disorder



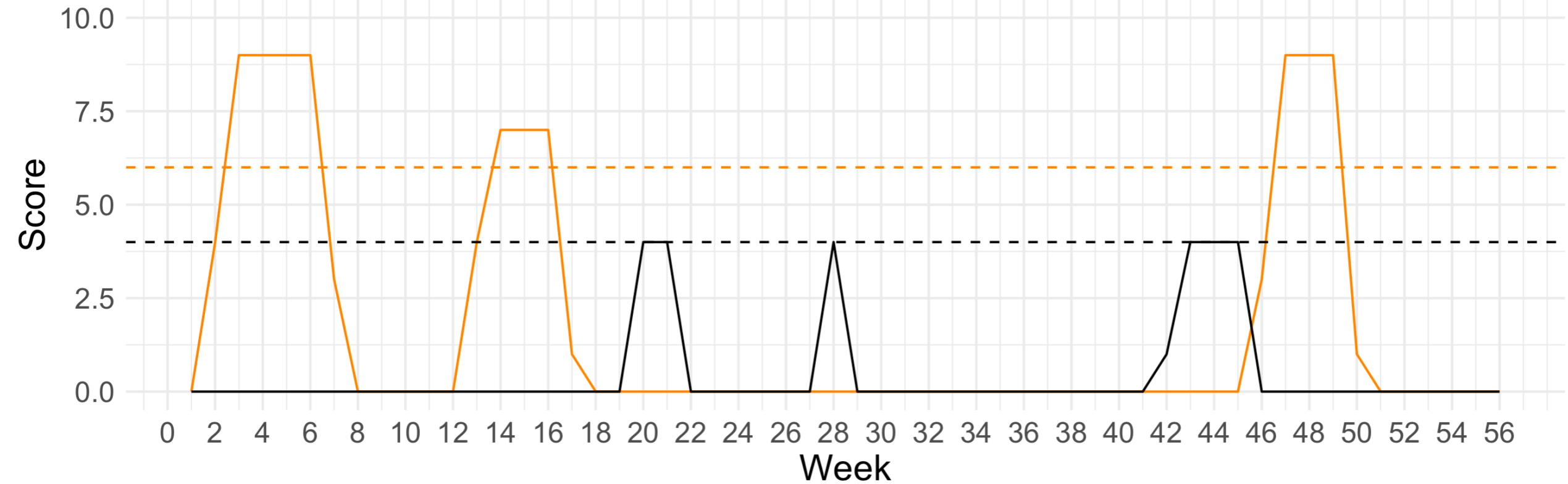
— Depression score

— Mania score

- - - Depression Clinical Severity

- - - Mania Clinical Severity

# Bipolar II Disorder



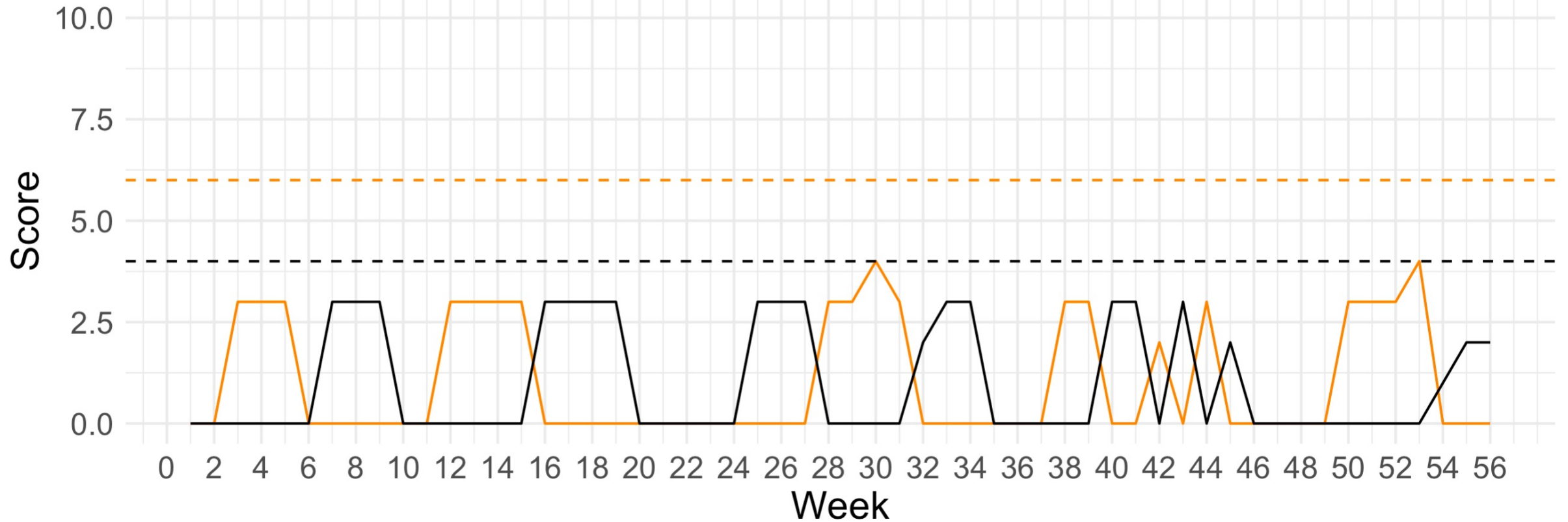
— Depression score

— Mania score

— Depression Clinical Severity

— Mania Clinical Severity

# Cyclothymia



— Depression score

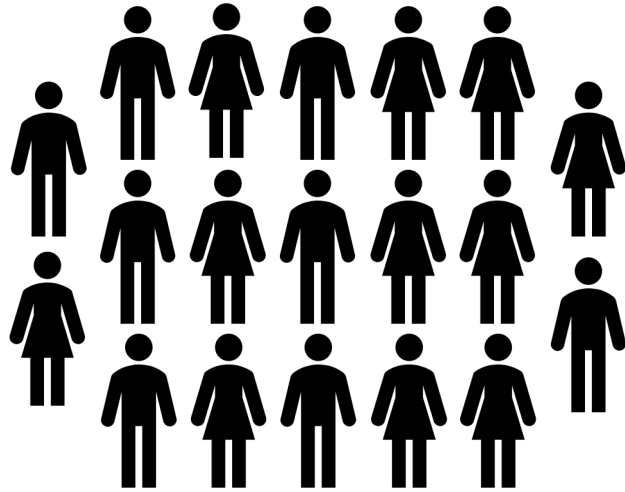
— Mania score

— Depression Clinical Severity

— Mania Clinical Severity

Things do not look this clean in **real-world data**

# PRIORI Ambient Study



6:22 4G LTE

Step 1 of 7 [Cancel](#)

## Mood Symptoms

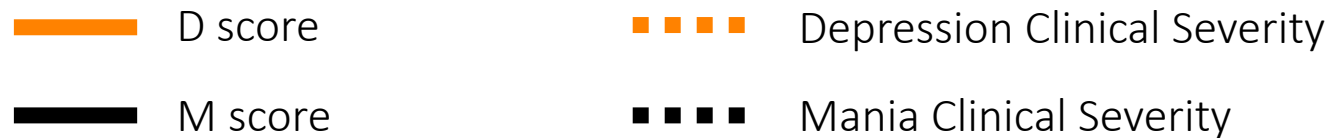
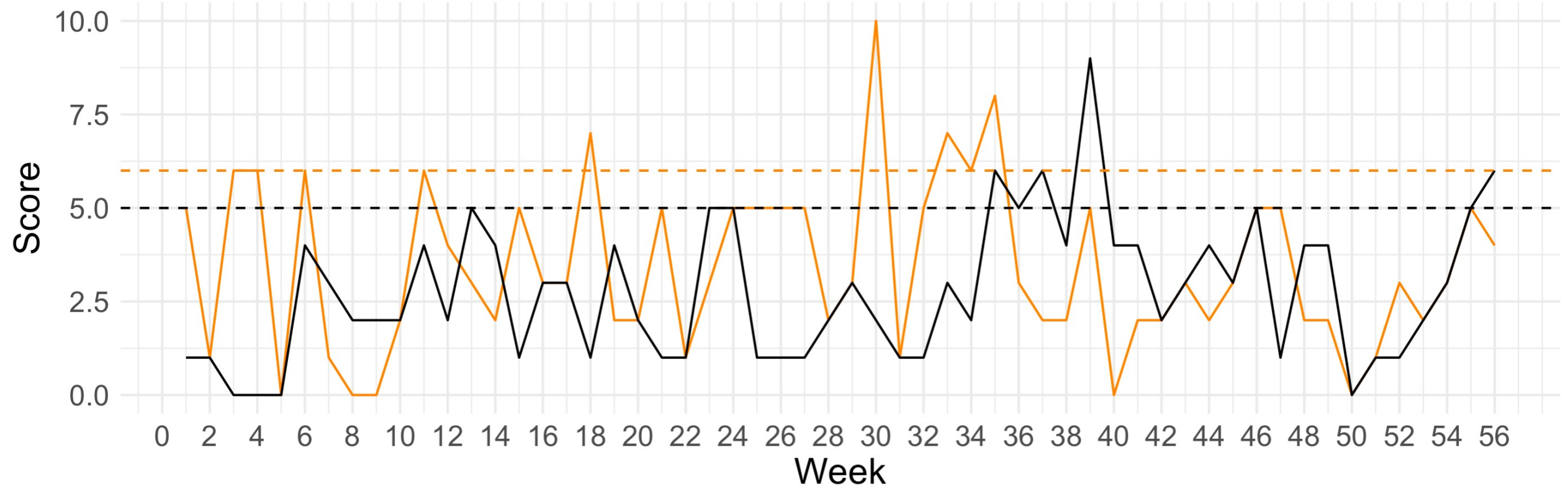
Please log your mood symptoms this evening using the following scale:

0 (absent or normal), 1 (mild), 2 (moderate), 3 (severe)

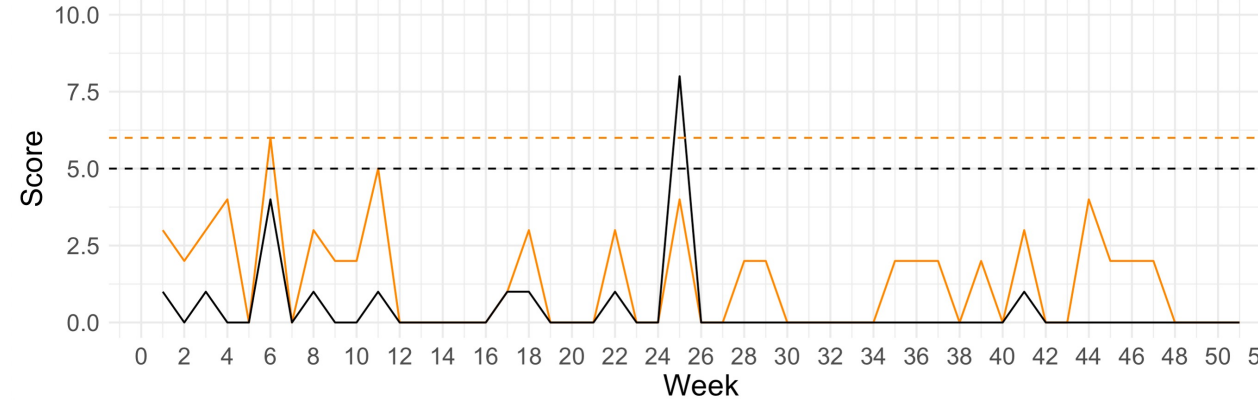
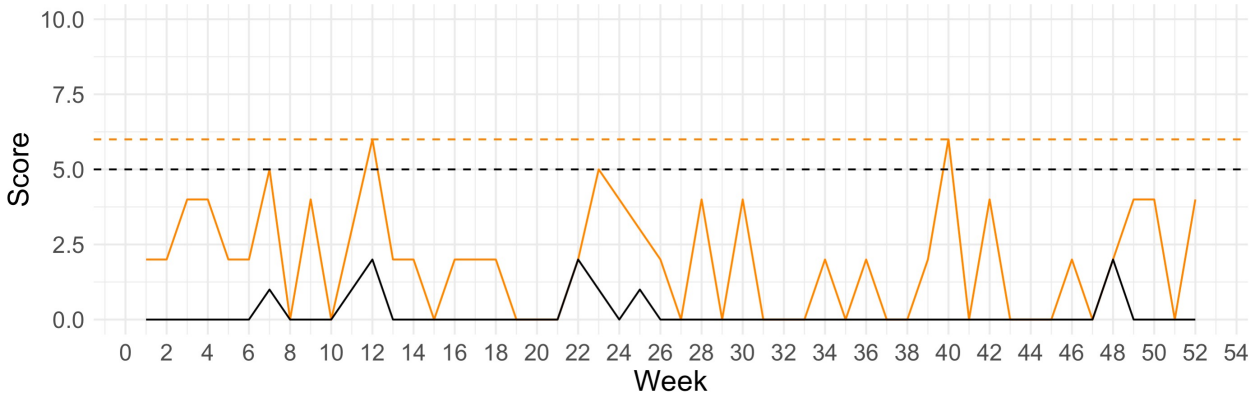
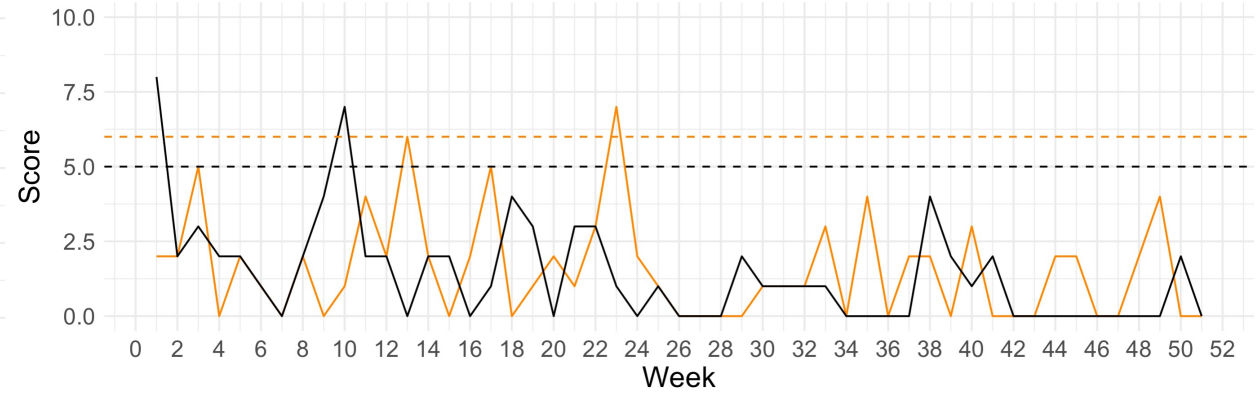
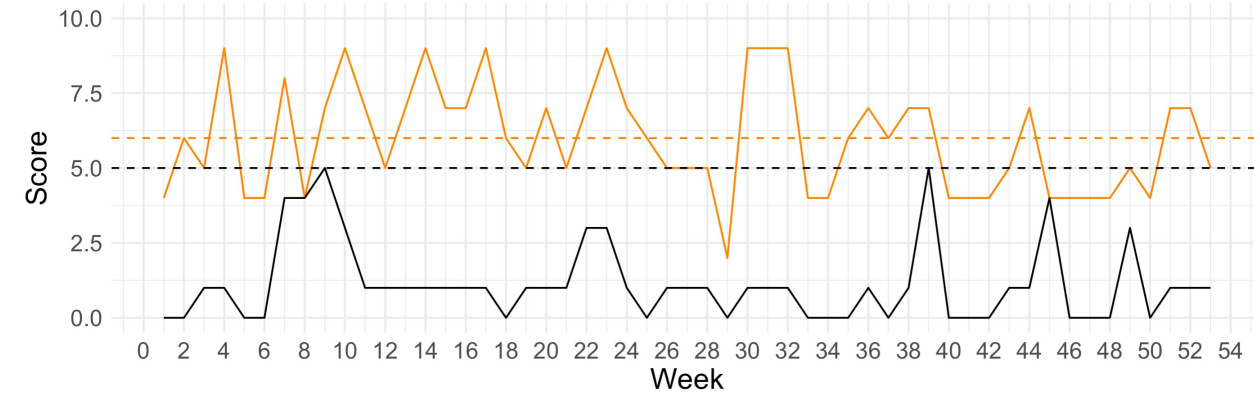
[Get Started](#)

- DigiBP (Gruichich et al., 2021)
- Once per week, 12 months
- D score = depressive symptoms
- M score = manic symptoms
- Clinical cutoffs determined from gold standard clinician measures

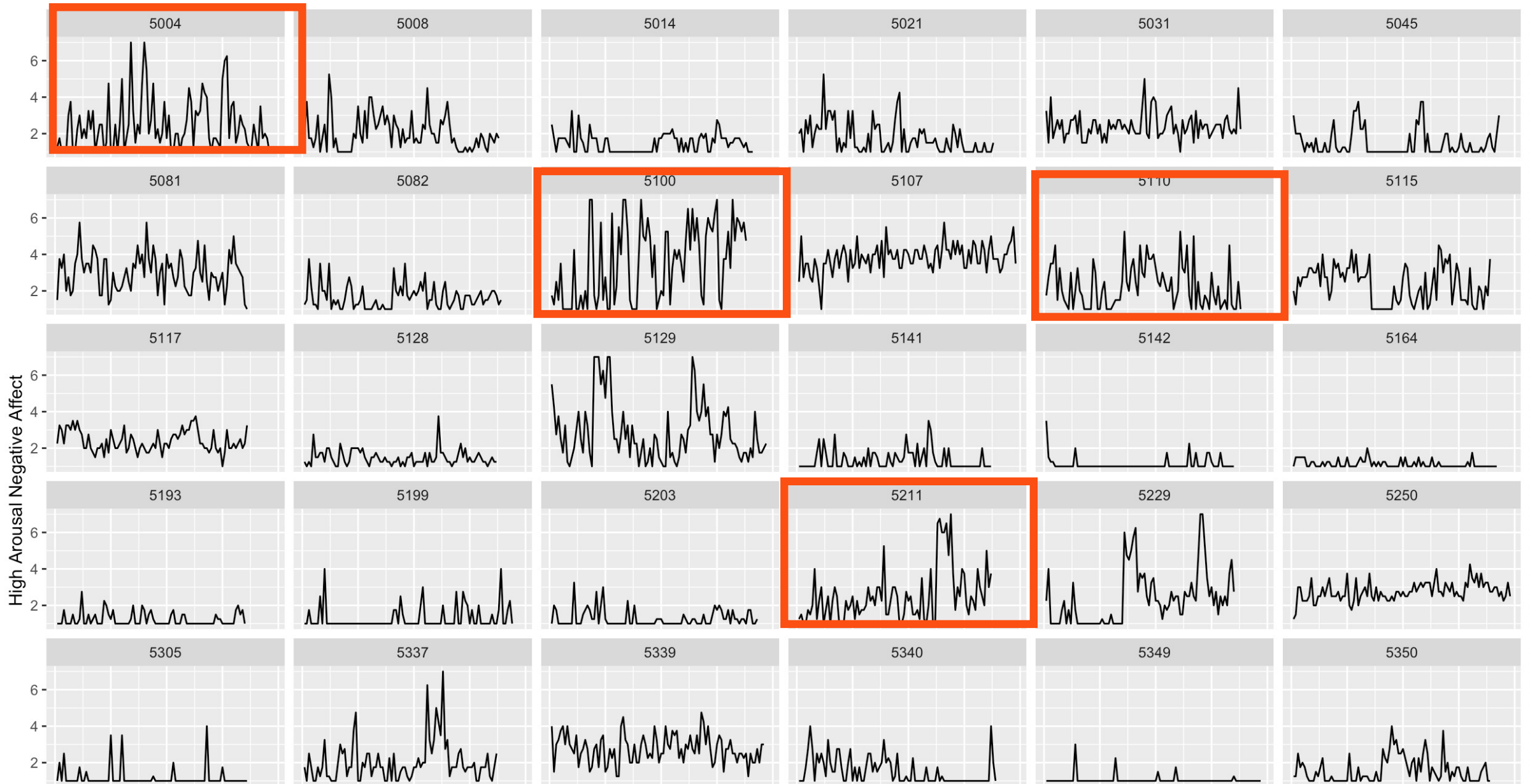
# Weekly mood for one participant over one year



# Four other participants



# APF Dissertation Award

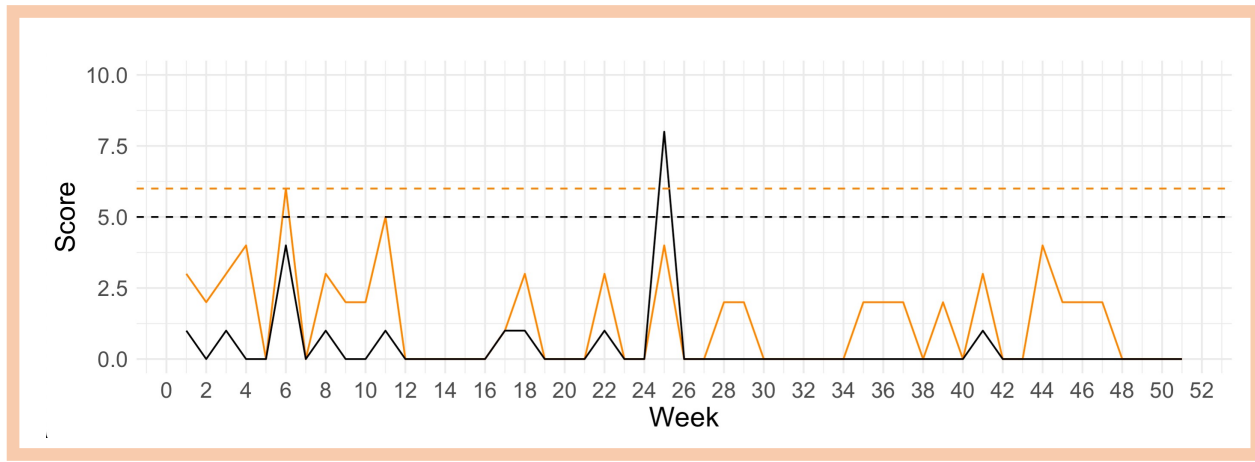
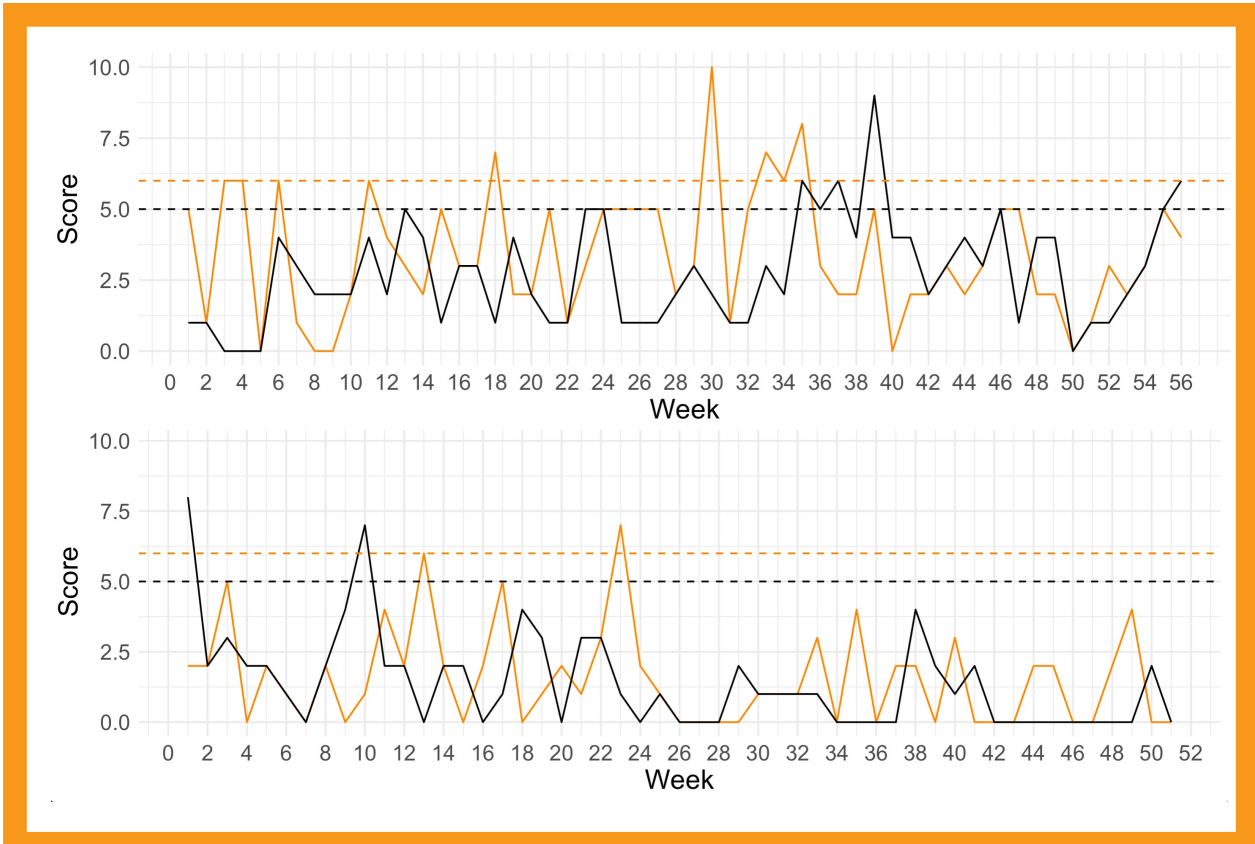
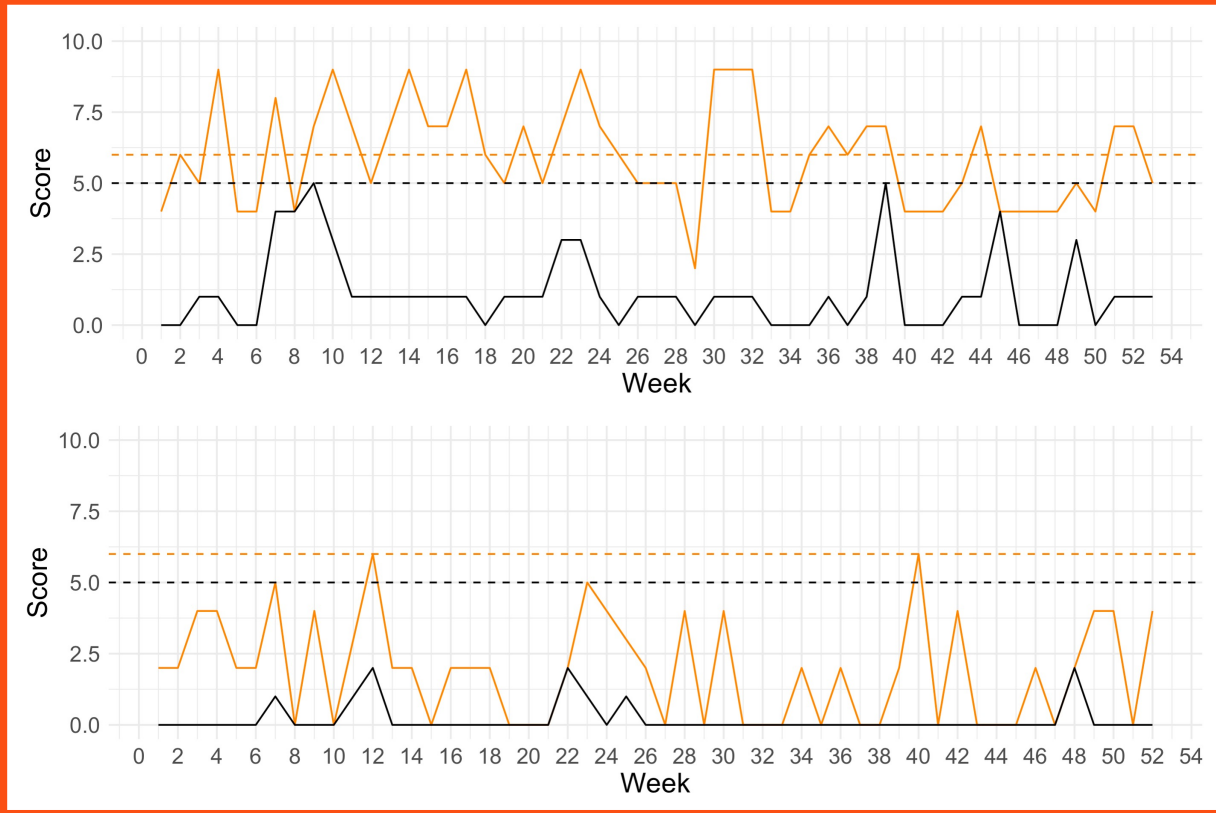




Individuals differ significantly in their presentation and course. This **heterogeneity** is complex and a challenge for research and treatment.

*Affective instability* is present throughout much of the course, even outside of mood episodes.

Can we stratify individuals based on these  
patterns of affective instability rather than type of  
episode alone?



Sperry, McInnis, Mower Provost, unpublished data

# “Modeling and Predicting Mood Dynamics: A Precision Health Approach to Bipolar Disorder”



**FREDERICK & ALICE COLES AND  
THOMAS & NANCY COLES**

Frederick & Alice Coles and Thomas &  
Nancy Coles Investigators

**Sarah H. Sperry, Ph.D.**  
*University of Michigan*



# Prechter Longitudinal Study of Bipolar Disorder (PLS-BD)

Biological Samples  
Trauma history  
Personality  
Temperament  
Family history  
Cognitive functioning

Baseline

Repeated Assessments

Alcohol & Drugs  
Sleep Quality

Medical update  
Diagnostic update  
Treatment update  
Suicide update

2 months

6 months

1 year

2 year

5 year

Depression (PHQ9)  
Mania (ASRM)  
Anxiety (GAD7)  
Health functioning (SF12)  
Life functioning (LFQ)  
Life events (LEC)

Clinician rated mood  
(YMRS, HAMD)  
Family dynamics  
Chronotype  
Med update

Cognitive functioning  
Personality

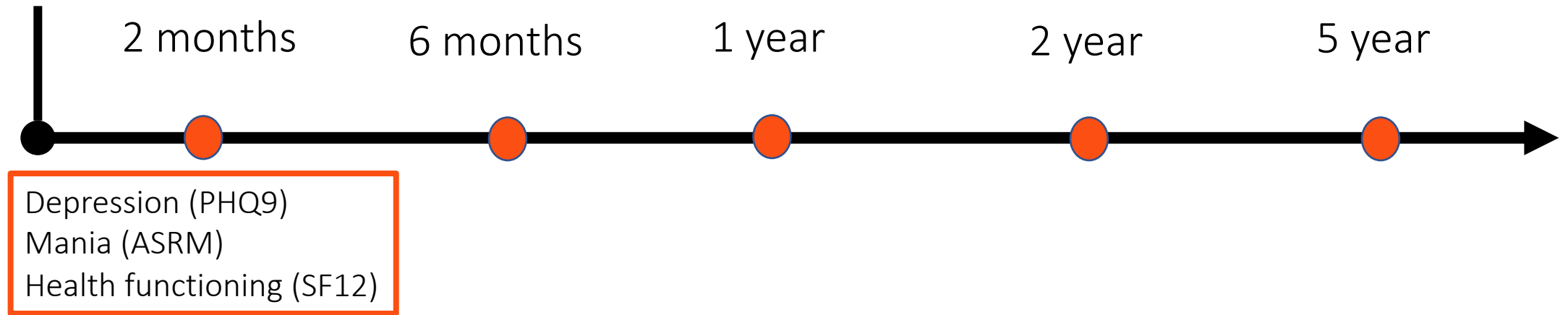
Electronic Health Record Data



# Prechter Longitudinal Study of Bipolar Disorder (PLS-BD)

Baseline

Repeated Assessments

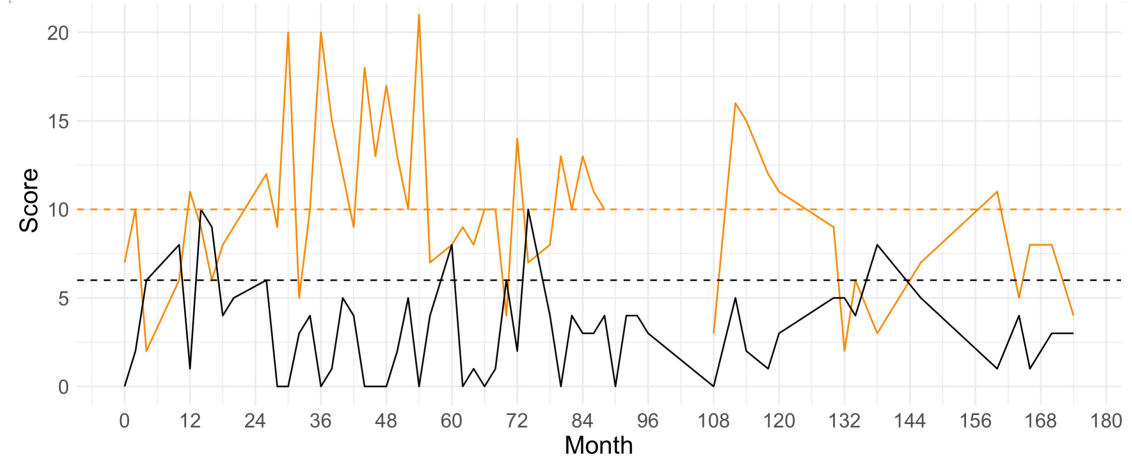
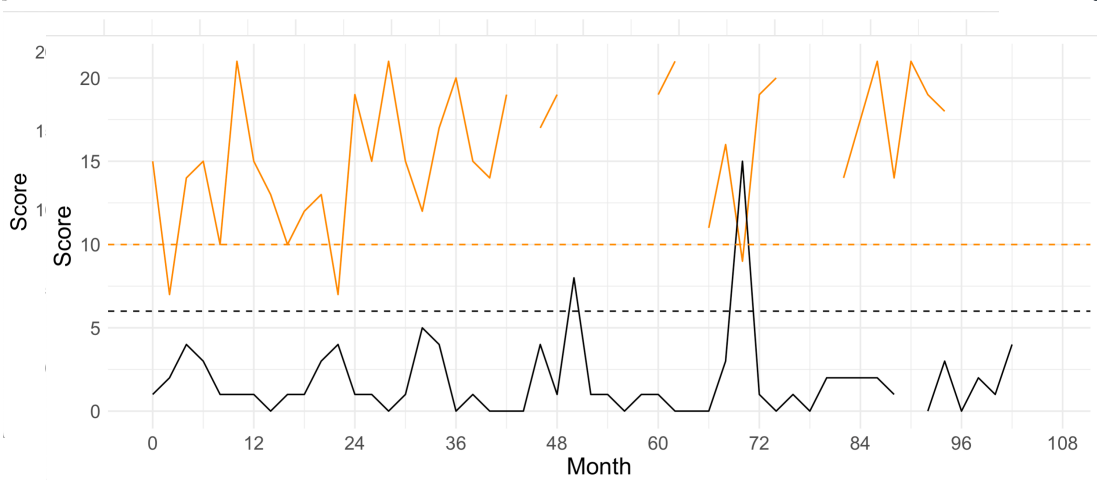
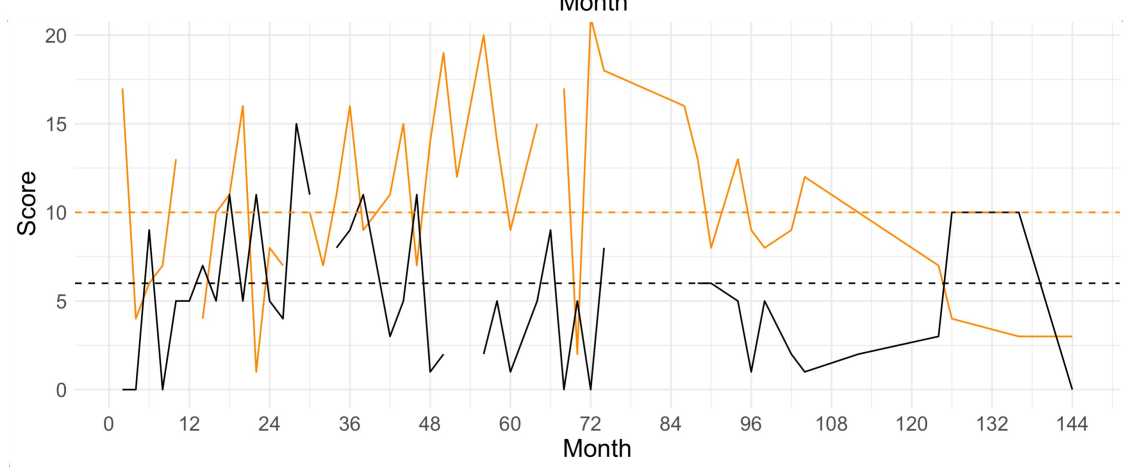
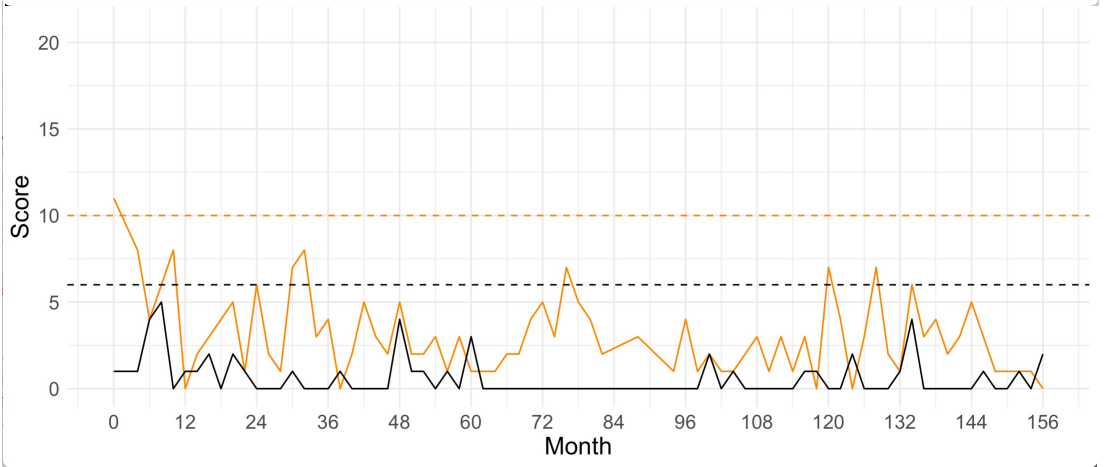
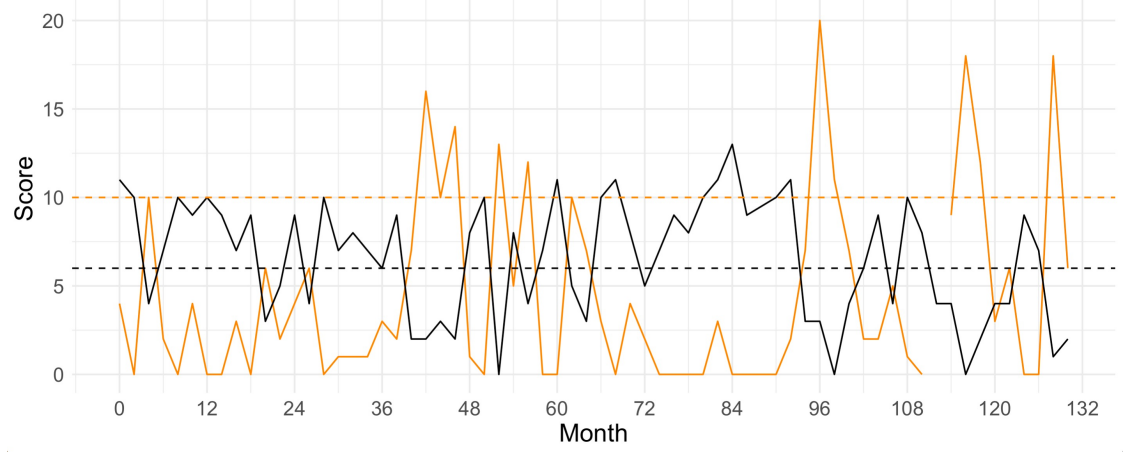
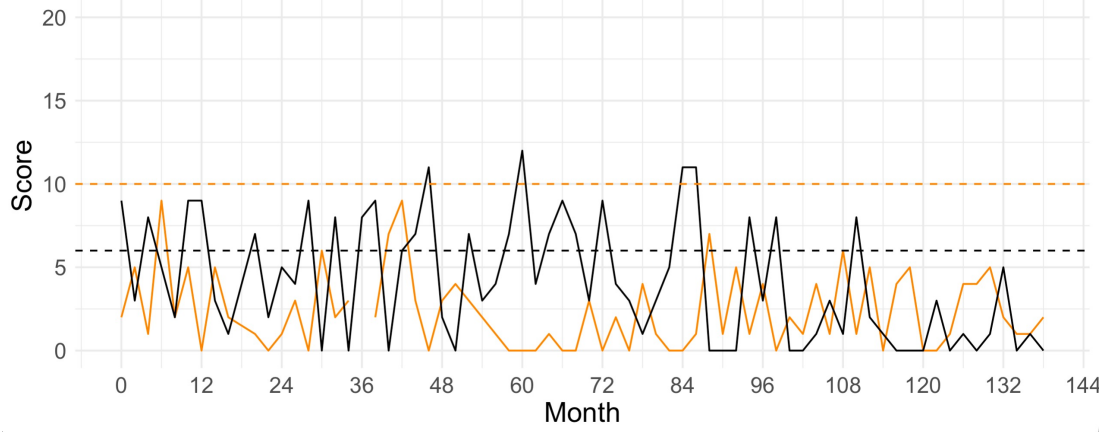


Depression (PHQ9)  
Mania (ASRM)  
Health functioning (SF12)

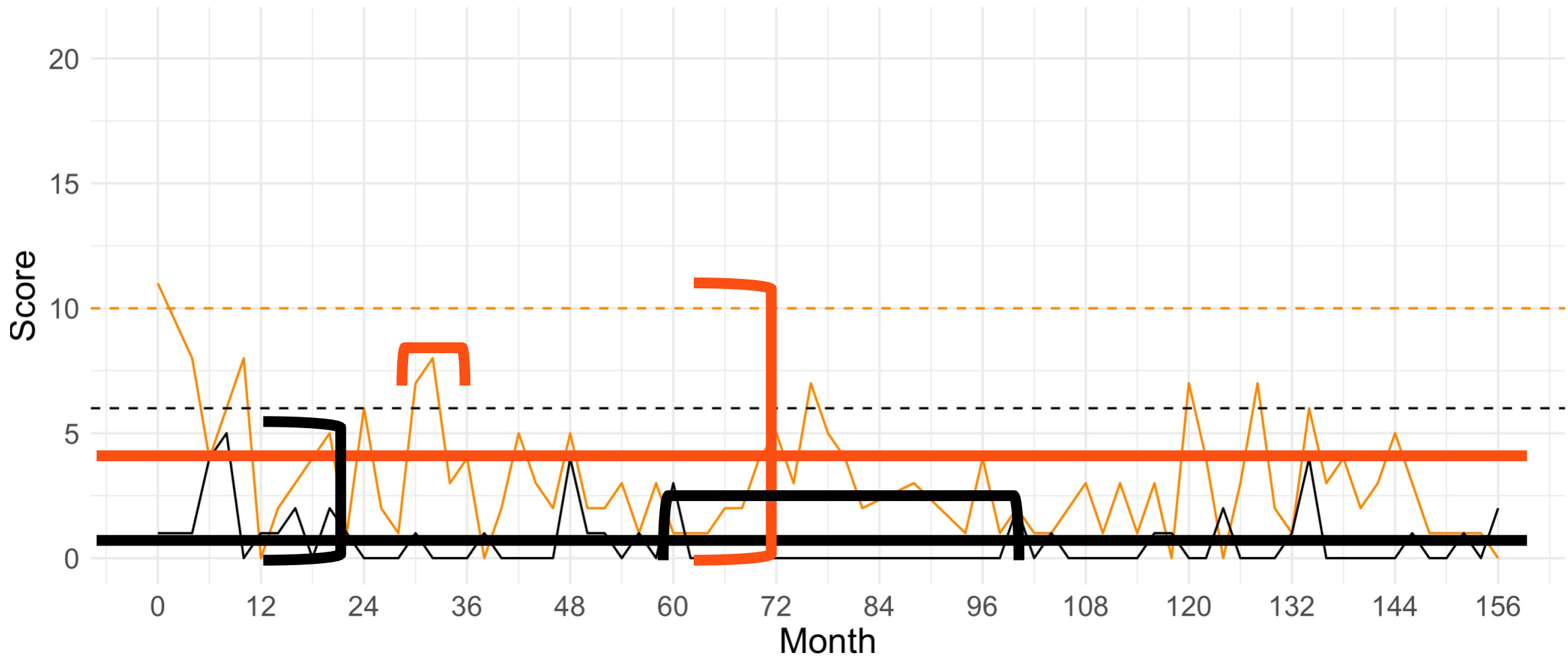
22,792 Depression Measures

23,106 Mania Measures





Sperry, Yocum, Tso, McInnis, unpublished data



Depression Mean

Depression Variability

Depression Autocorrelation

Mania Mean

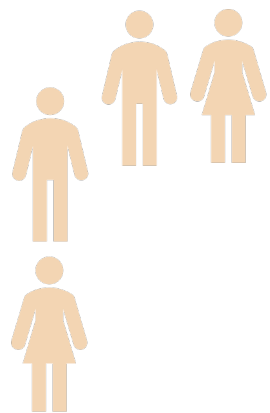
Mania Variability

Mania Autocorrelation

Sperry, Yocum, Tso, McInnis, unpublished data

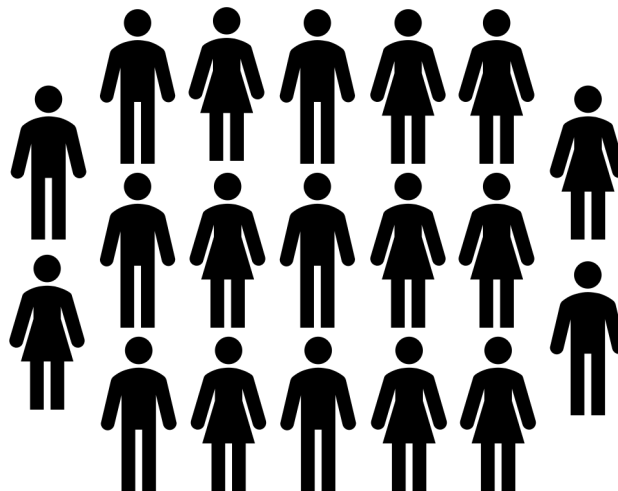
Depression Mean

Mania Mean



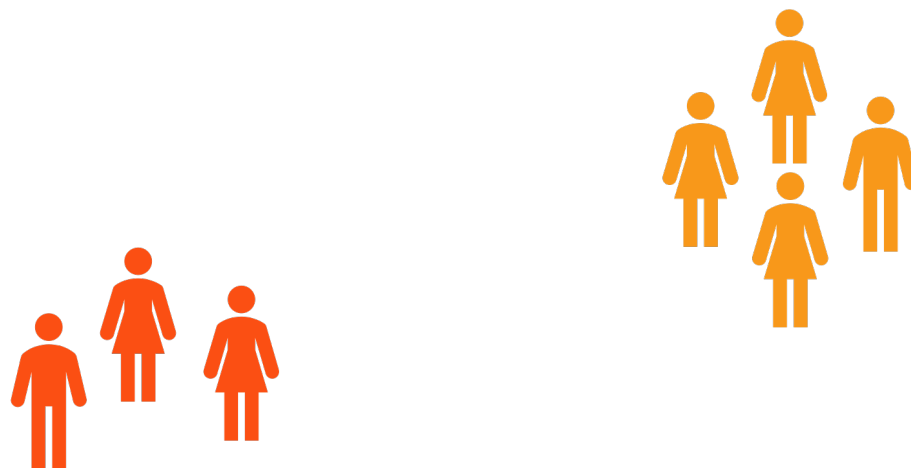
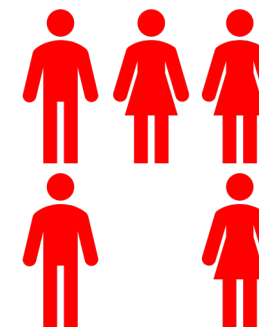
Depression Variability

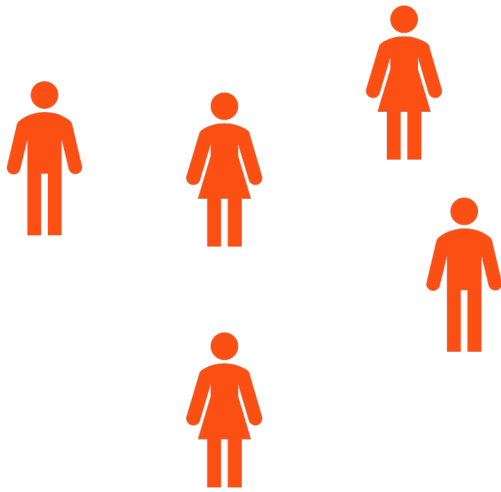
Mania Variability



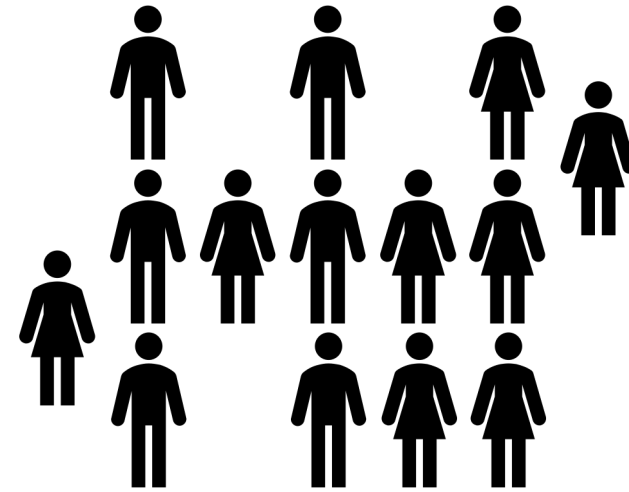
Depression Autocorrelation

Mania Autocorrelation



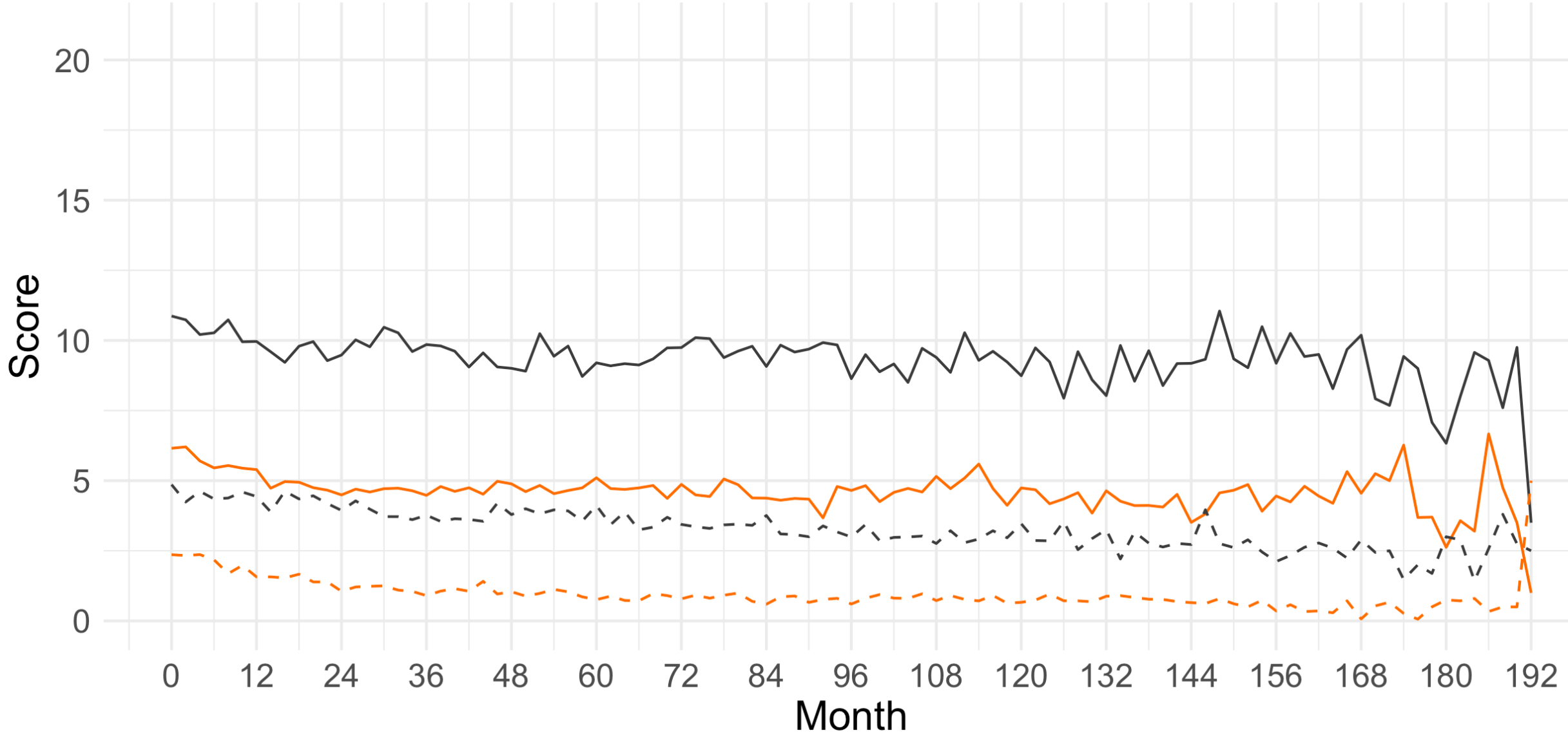


Group 1  
N = 253

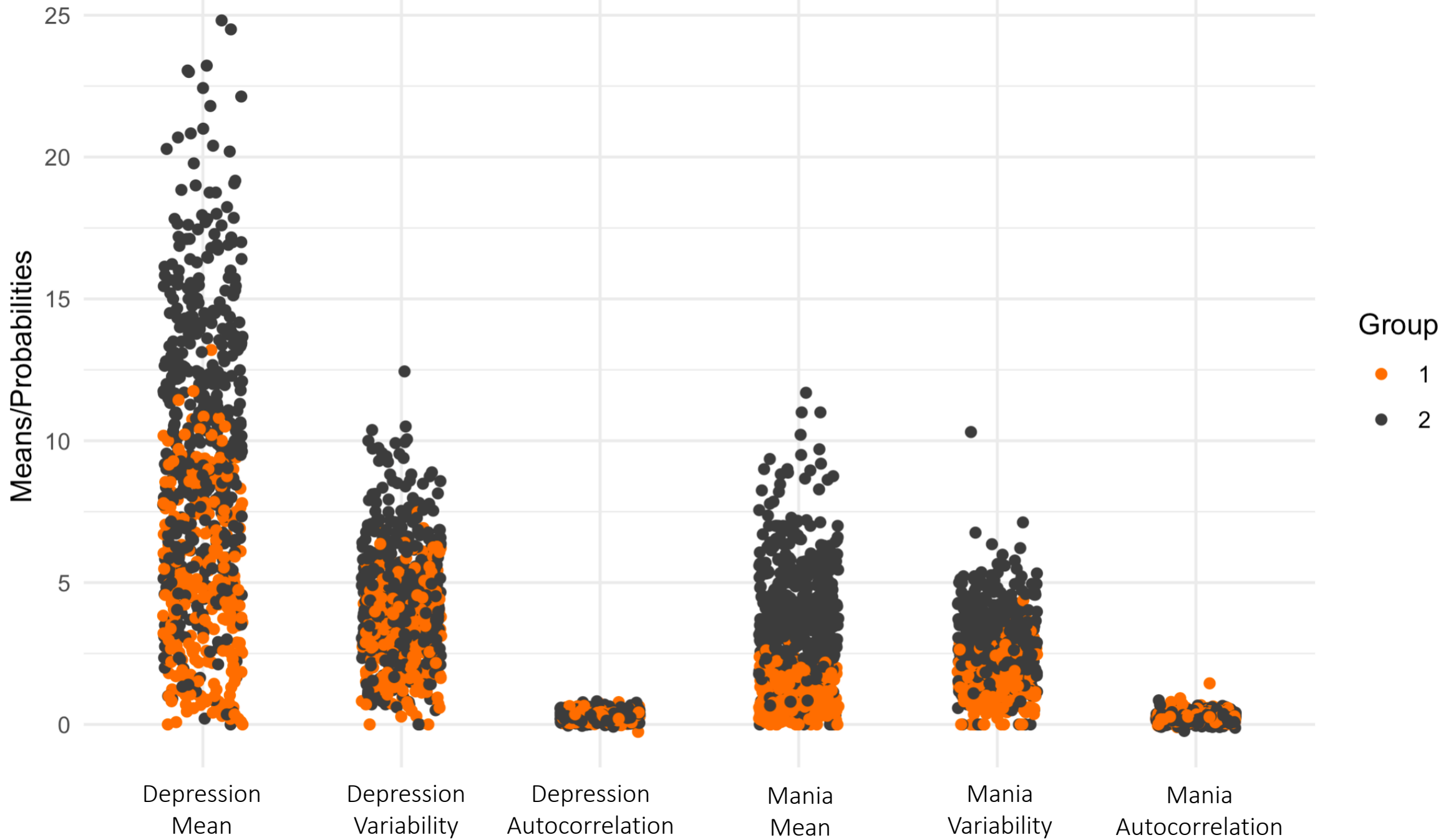


Group 2  
N = 478

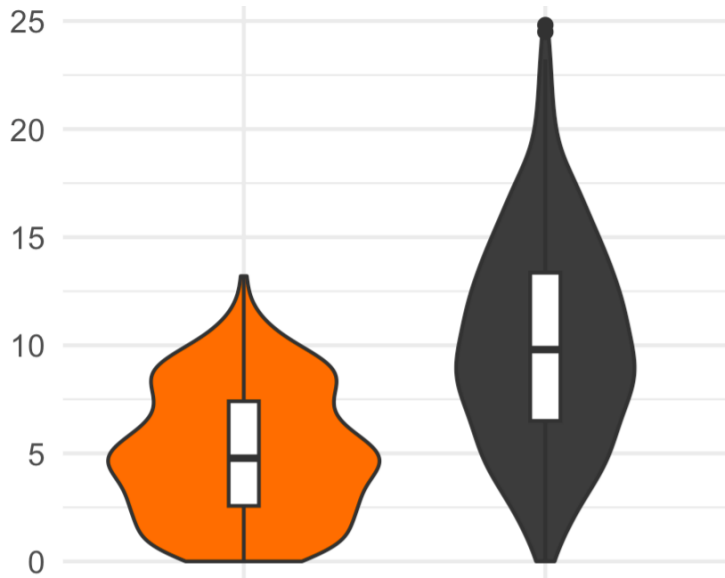
Class Probabilities		
	Group 1	Group 2
Group 1	.90	.10
Group 2	.03	.97



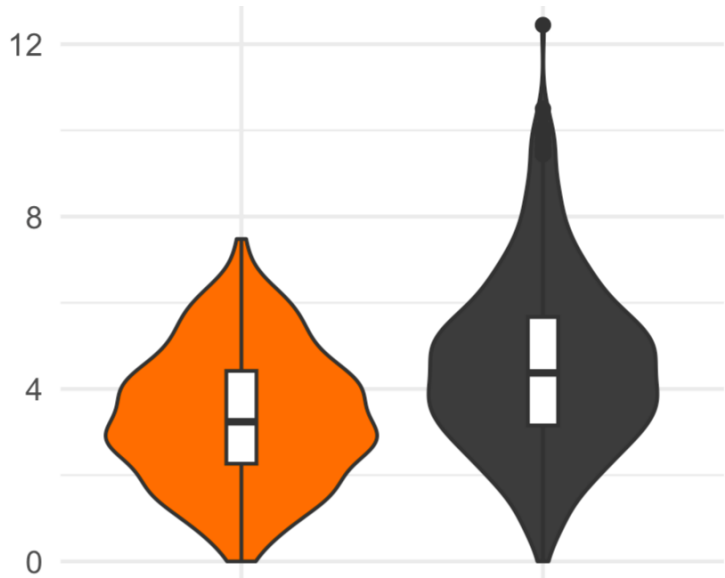
Group 1 depression      Group 2 depression  
Group 1 mania      Group 2 mania



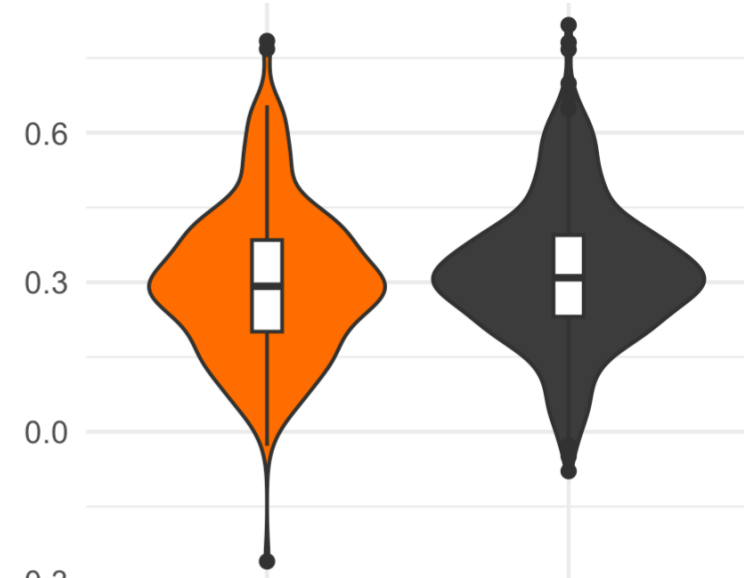
Depression Mean



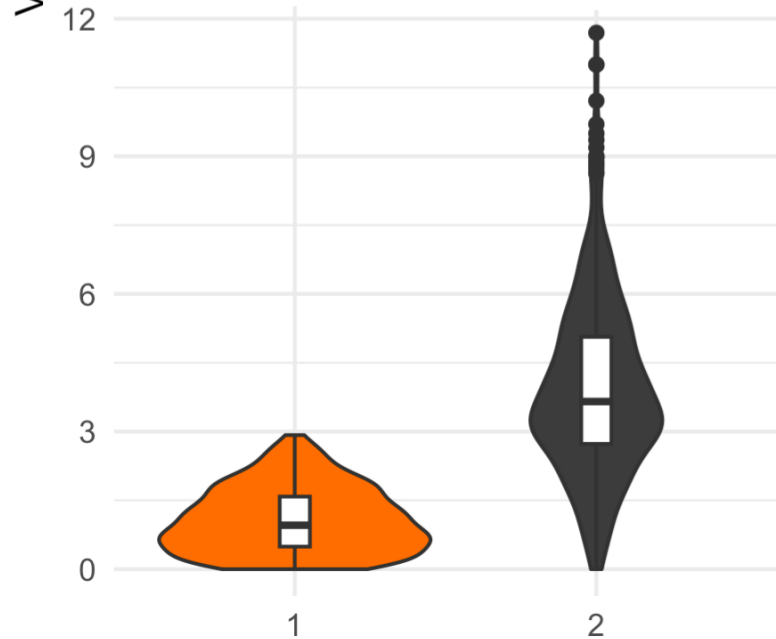
Depression Variability



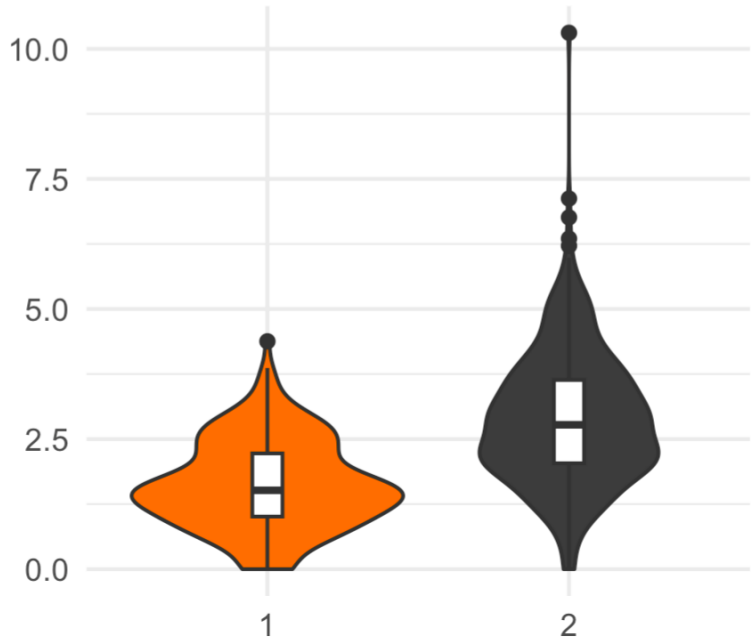
Depression Autocorrelation



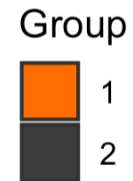
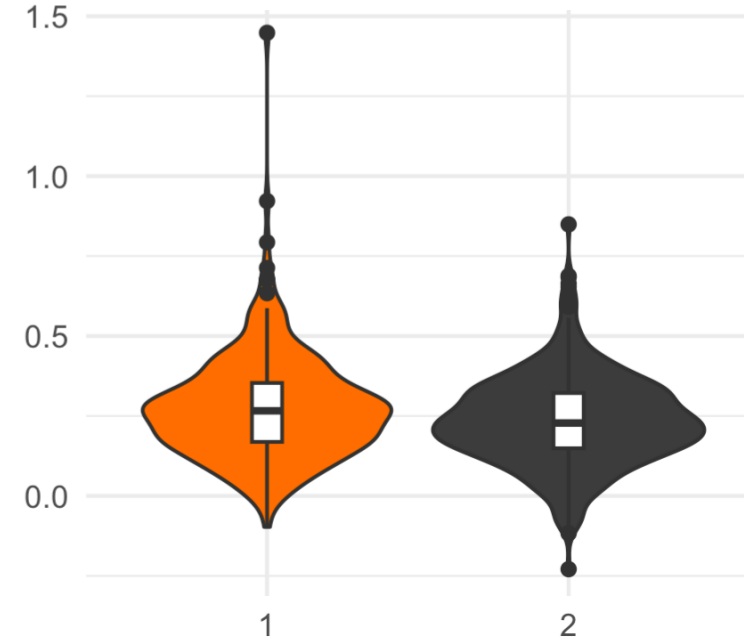
Mania Mean



Mania Variability



Mania Autocorrelation

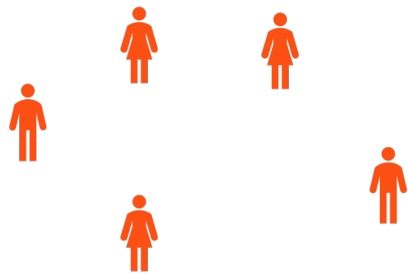


Group

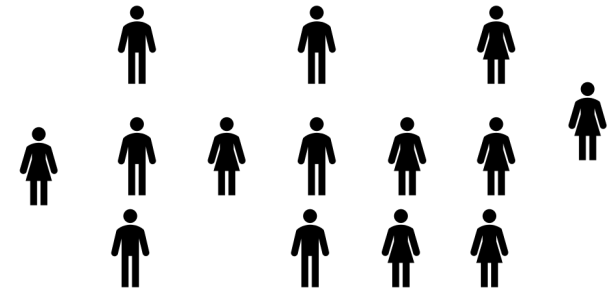
Sperry, Yocum, Tso, McClinnis, unpublished data

Are their **predictors** that help us know who likely gets classified in group 1 vs. 2?





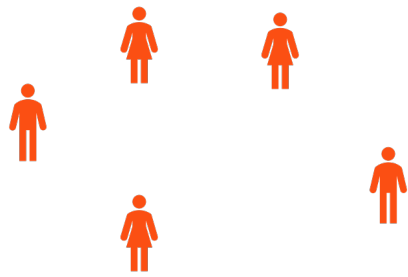
Group 1 (n = 253)



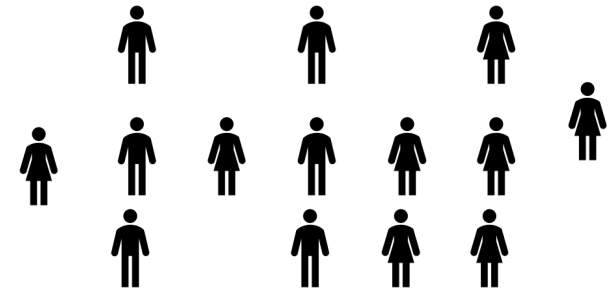
Group 2 (n = 478)



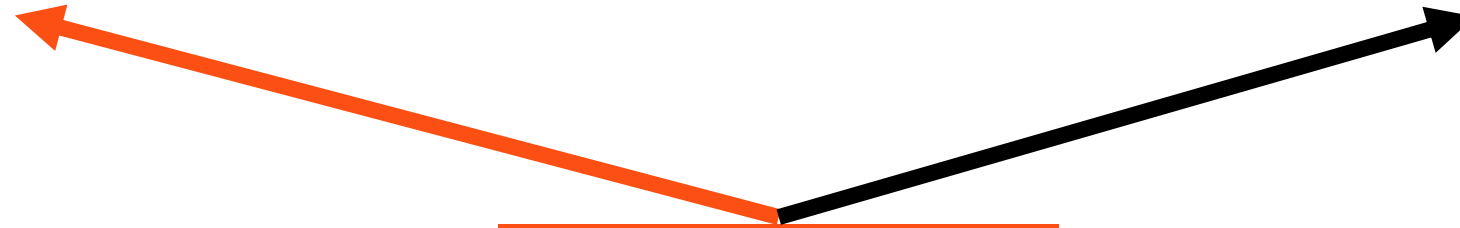
- Age of onset of mania
- Age of onset of hypomania
- Age of onset of depression
- Number of episodes of mania
- Number of episodes of hypomania
- Number of episodes of depression
- Sex (male, female, other)
- Race (White, BIPOC)
- Diagnosis (BD1, BD2, BDNOS)



Group 1 (n = 253)



Group 2 (n = 478)



Age of onset of mania

Age of onset of hypomania

Age of onset of depression

Number of episodes of mania

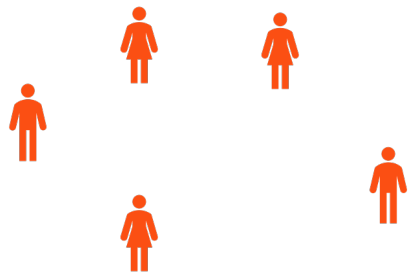
Number of episodes of hypomania

Number of episodes of depression

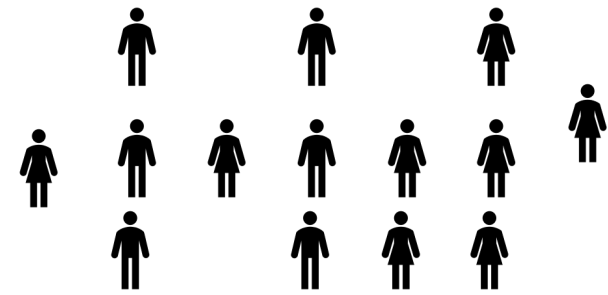
Sex (male, female, other)

Race (White, POC)

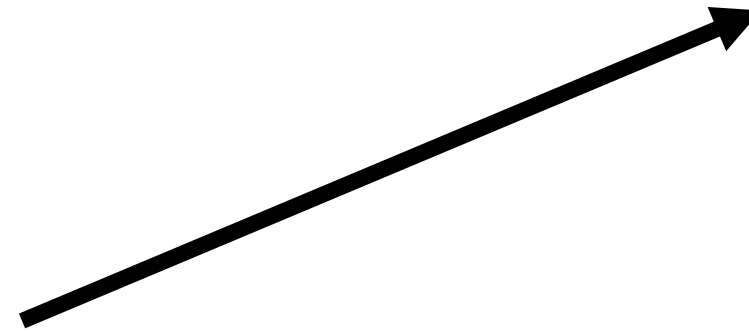
Diagnosis (BD1, BD2, BDNOS)



Group 1 (n = 253)



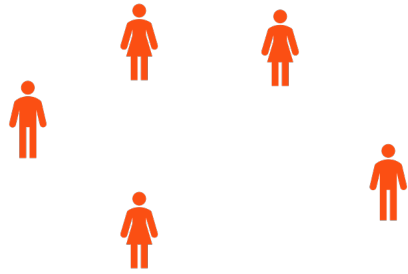
Group 2 (n = 478)



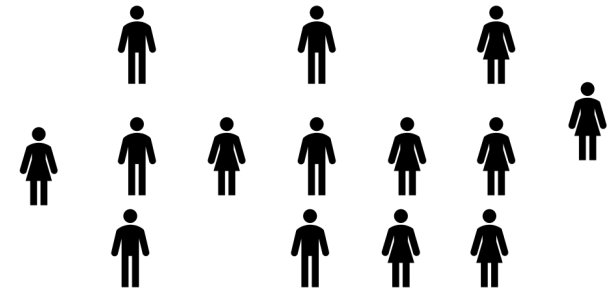
Younger age of onset of mania  
Older age of onset of depression  
Greater number of episodes of mania  
POC

Diagnostic status did not predict group membership – diagnosis does not differentiate patterns of affective instability over time!

Does group membership predict **outcomes**?



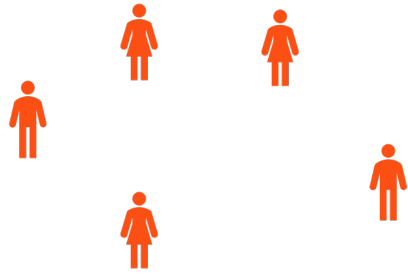
Group 1 (n = 253)



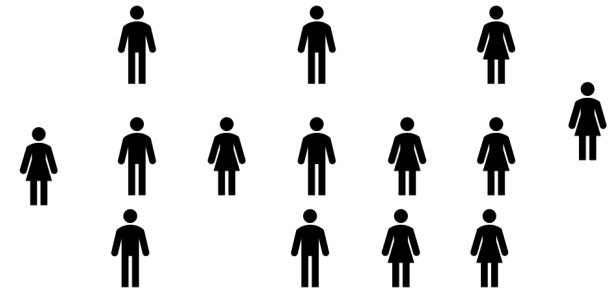
Group 2 (n = 478)



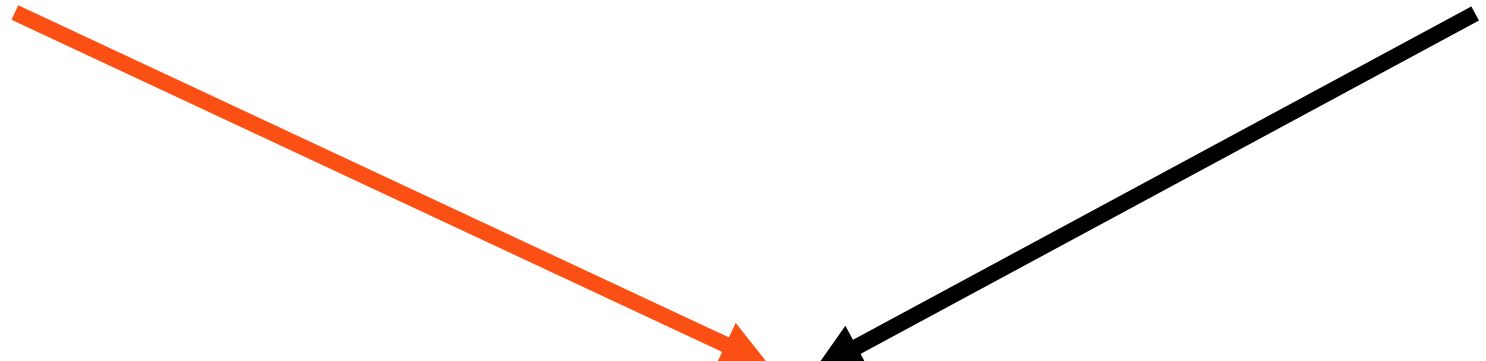
Longitudinal mental health functioning  
Longitudinal physical health functioning



Group 1 (n = 253)



Group 2 (n = 478)



Individuals in Group 2 have lower mental and physical health functioning over the course of their illness by an average of .5 standard deviations

1. Individuals with bipolar disorder experience **inter-episodic affective instability**
2. They **can be stratified** into a group with higher instability and lower instability
3. **Demographics and age of onset** predict group membership
4. Group membership **predicts functioning**

What about all those other measures you get in the longitudinal cohort? Thanks for asking! Here are **next steps...**



# Prechter Longitudinal Study of Bipolar Disorder (PLS-BD)

Biological Samples  
Trauma history  
Personality  
Temperament  
Family history  
Cognitive functioning

Baseline

Repeated Assessments

Alcohol & Drugs  
Sleep Quality

Medical update  
Diagnostic update  
Treatment update  
Suicide update

2 months

6 months

1 year

2 year

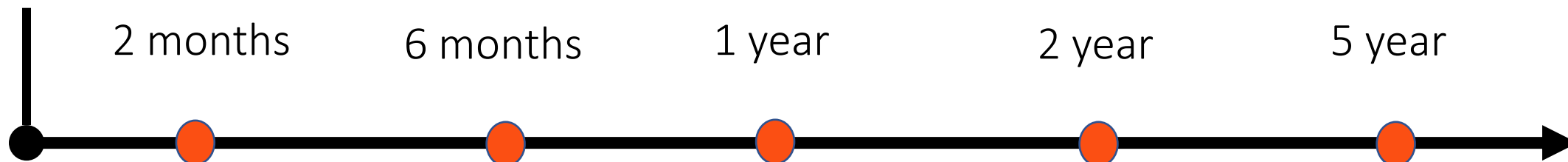
5 year

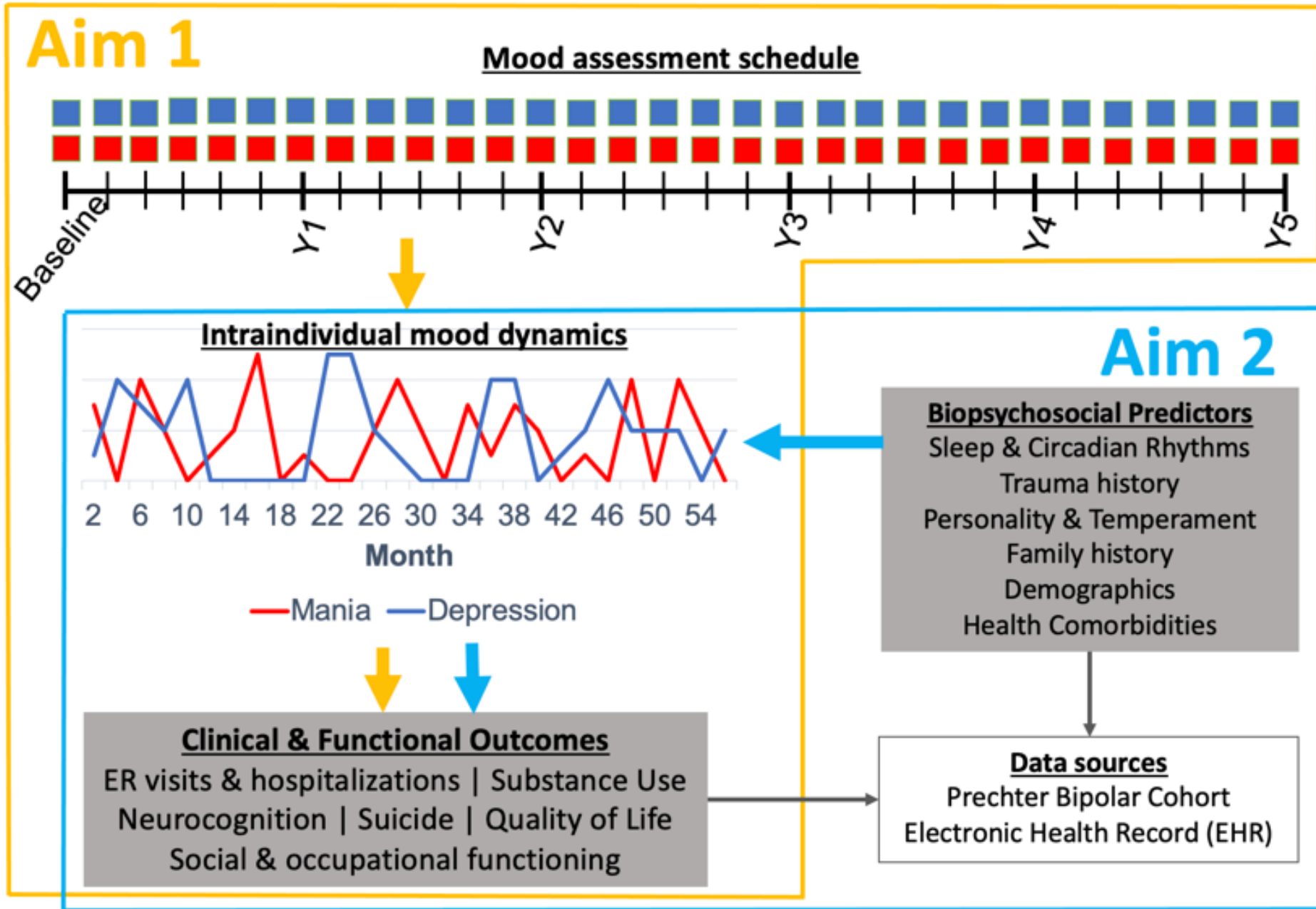
Depression (PHQ9)  
Mania (ASRM)  
Anxiety (GAD7)  
Health functioning (SF12)  
Life functioning (LFQ)  
Life events (LEC)

Clinician rated mood  
(YMRS, HAMD)  
Family dynamics  
Chronotype  
Med update

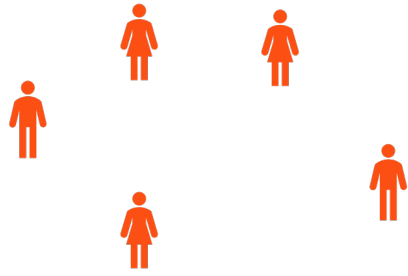
Cognitive functioning  
Personality

Electronic Health Record Data

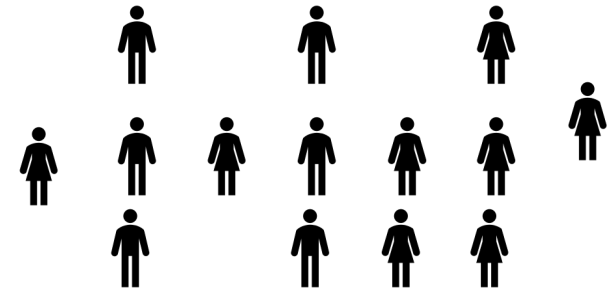




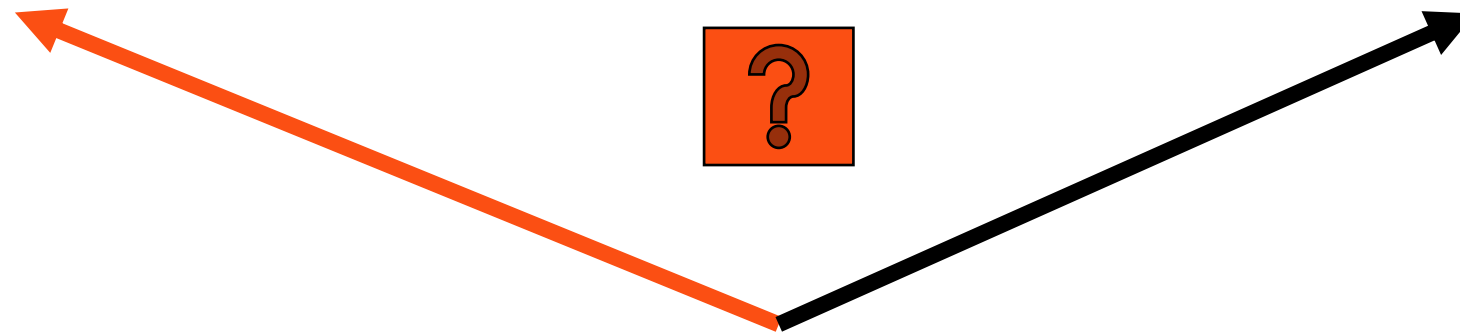
**Figure 1.** Overview of specific aims of this project.



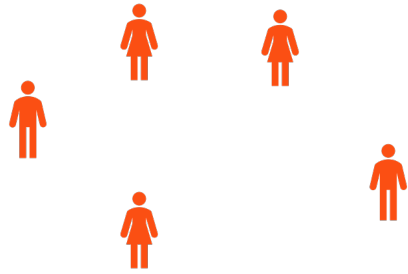
Group 1 (n = 253)



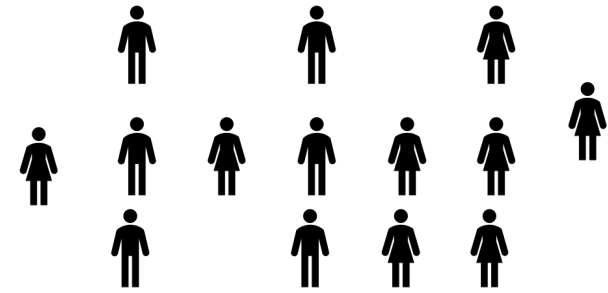
Group 2 (n = 478)



Sleep & Circadian Rhythms  
Trauma history  
Personality and temperament  
Family history  
Health comorbidities



Group 1 (n = 253)

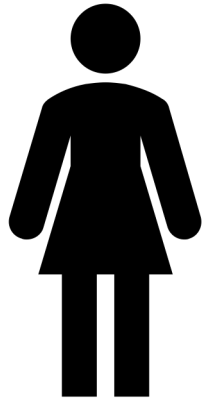


Group 2 (n = 478)



- ER visits & hospitalizations
- Substance Use
- Cognitive functioning
- Suicide risk
- Quality of life
- Medication & therapy response

How can this impact **who gets what treatment?**



Traditional  
diagnostic  
interview

Bipolar I

Bipolar II

Bipolar NOS

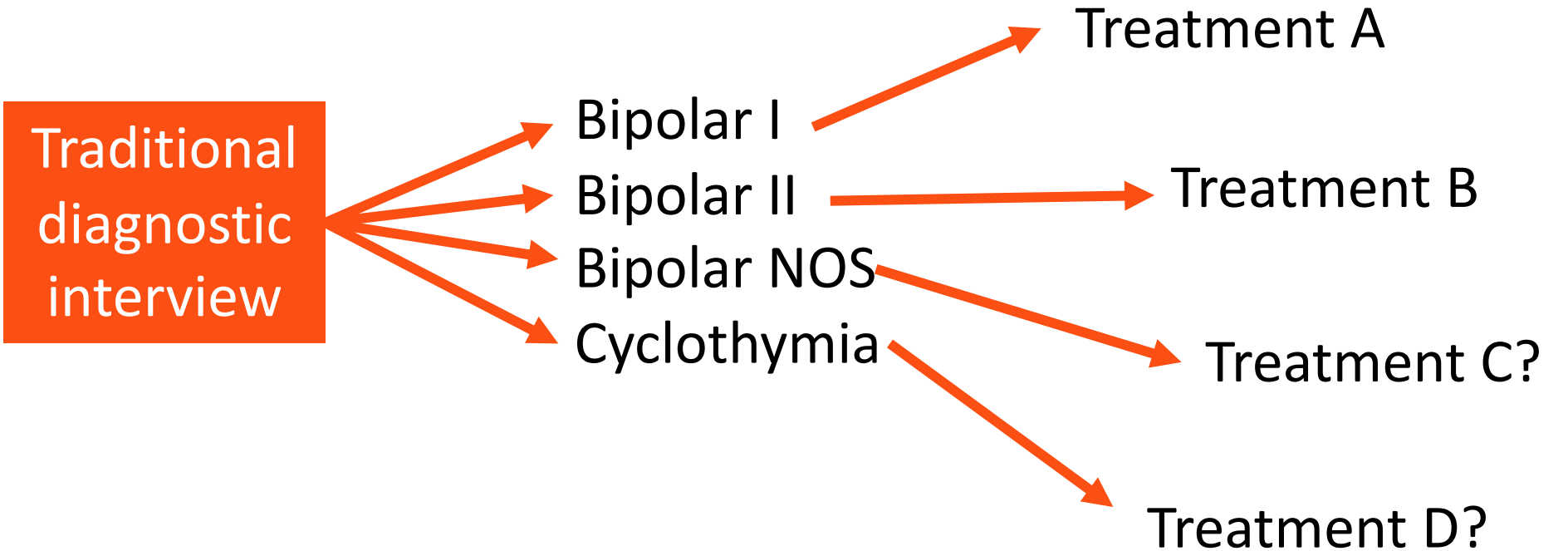
Cyclothymia

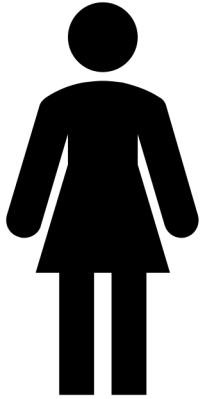
Treatment A

Treatment B

Treatment C?

Treatment D?





Traditional  
diagnostic  
interview

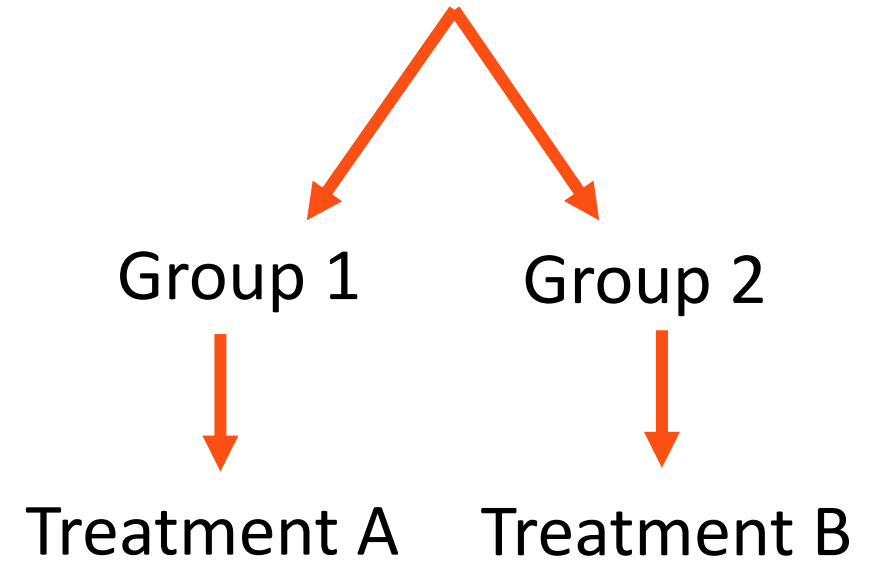
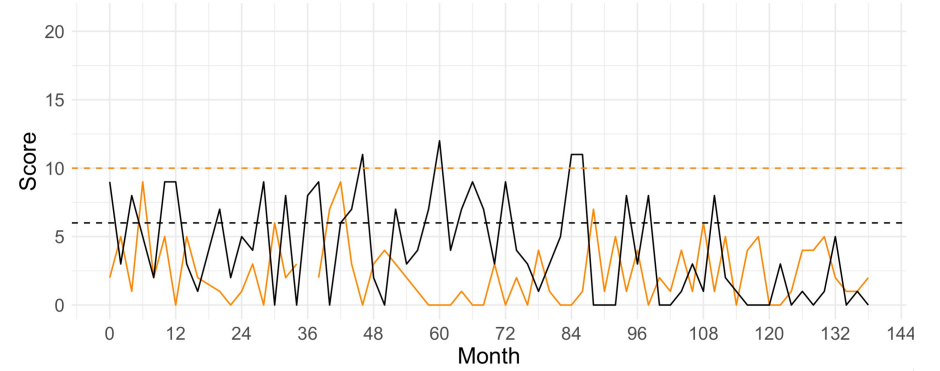
6:22 4G

Step 1 of 7 Cancel

Mood Symptoms

Please log your mood symptoms this evening using the following scale:  
0 (absent or normal), 1 (mild), 2 (moderate), 3 (severe)

Get Started



...but not everyone is in a longitudinal research cohort. How can we measure and classify people in **real-world clinical settings**?



6:46 PM Mon Sep 11

65%

MyUofMHealth - Login P: X +

myuofmhealth.org



Ver en Español

MyUofMHealth Username

Password

Sign in

Forgot username?

Forgot password?

New User?

New User Sign Up

Frequently Asked Questions

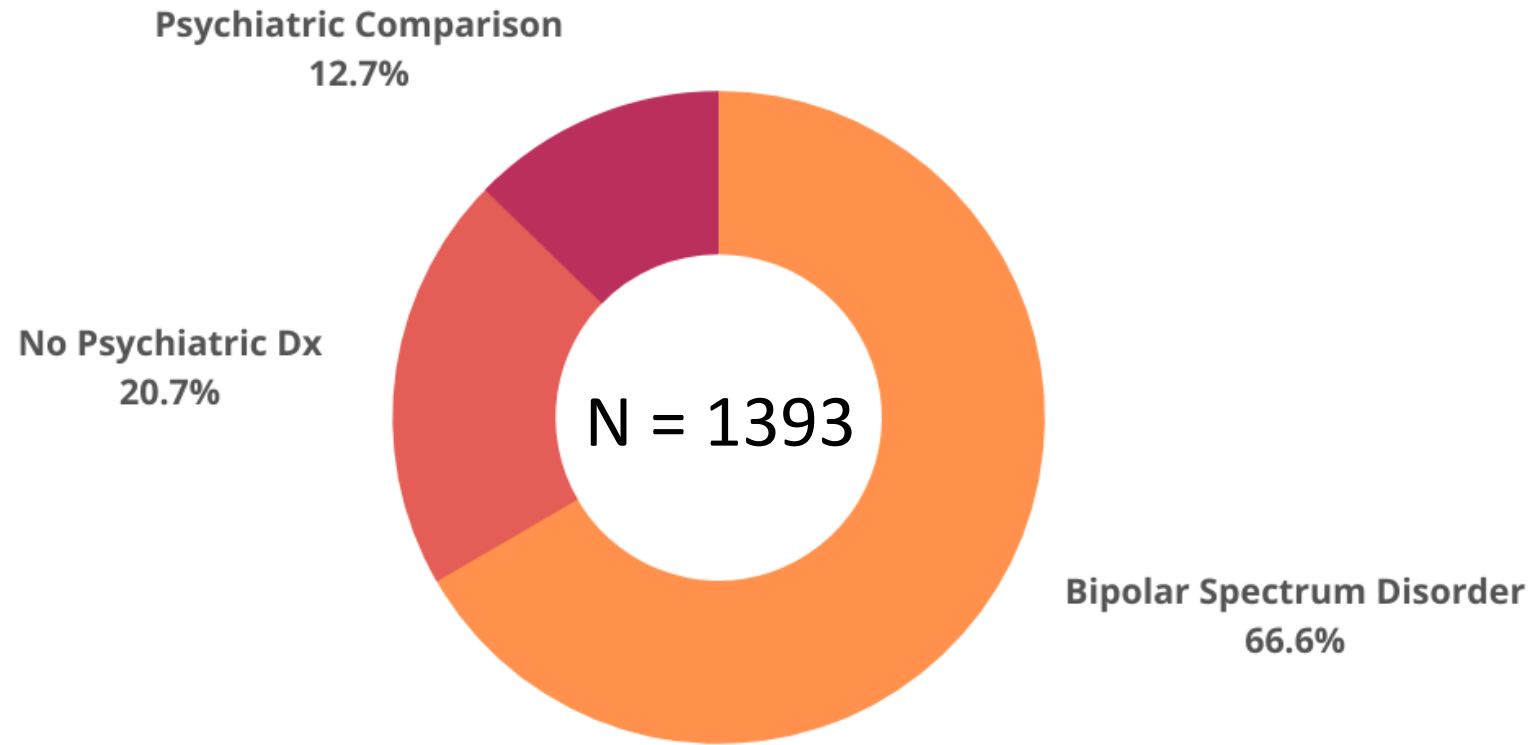
Parents / Caregivers

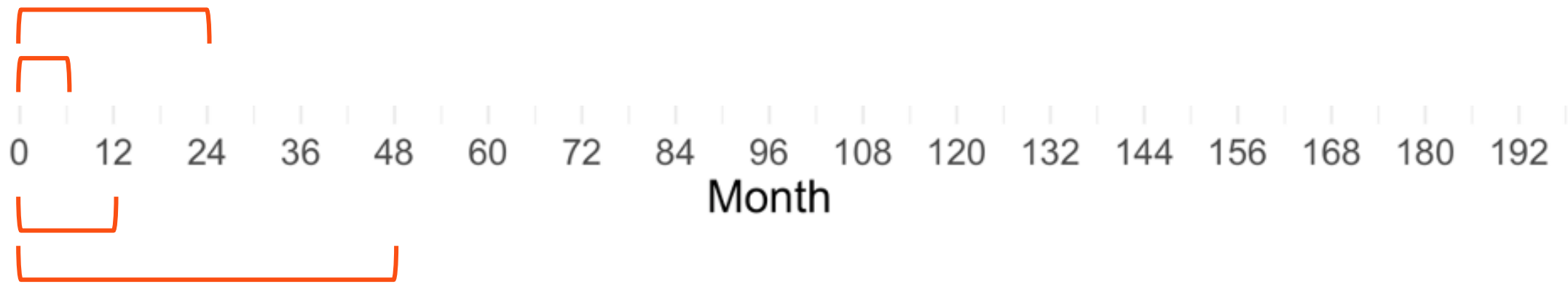
Request Proxy Access

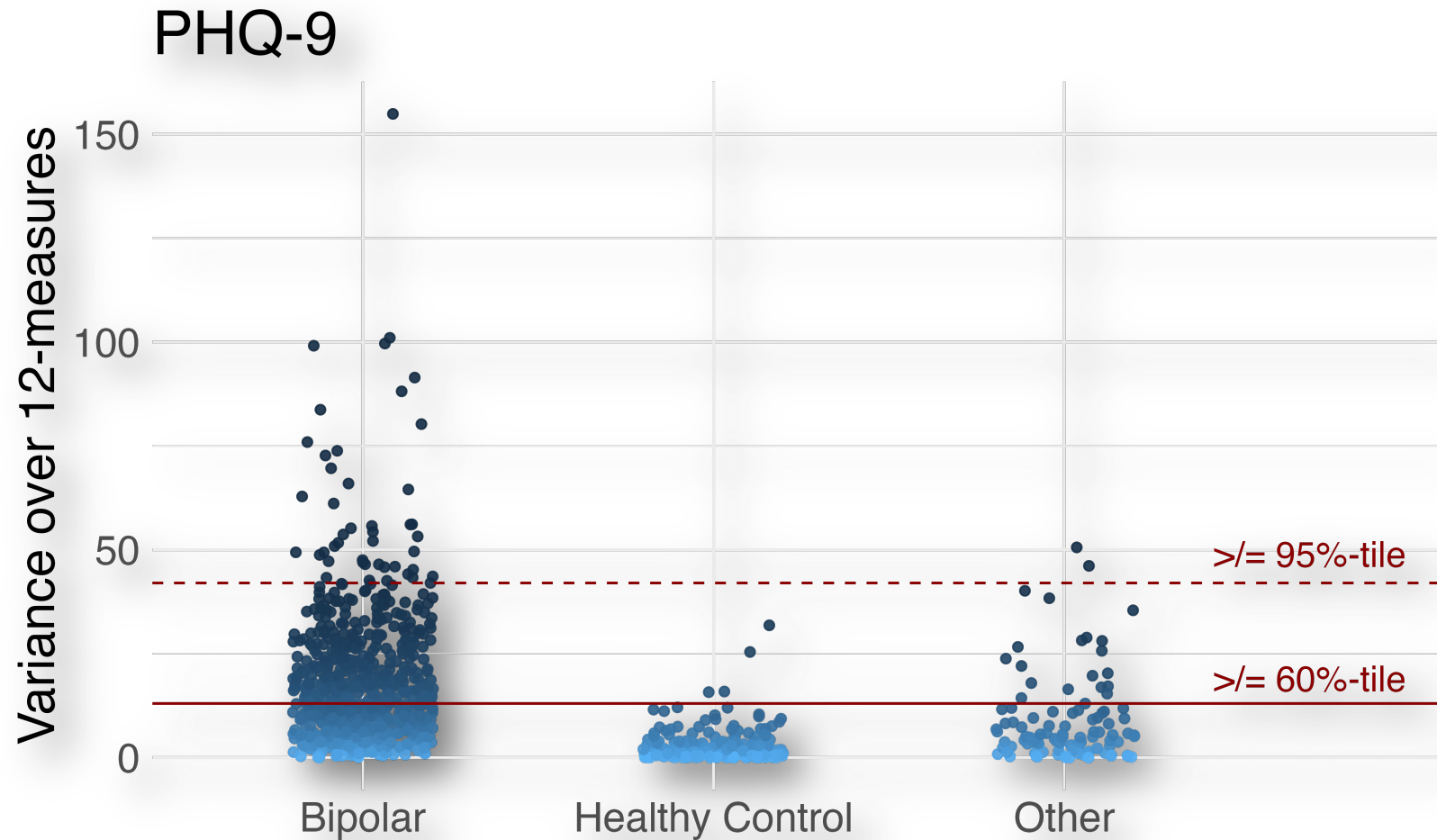
Online Bill Payment

Pay as a Guest

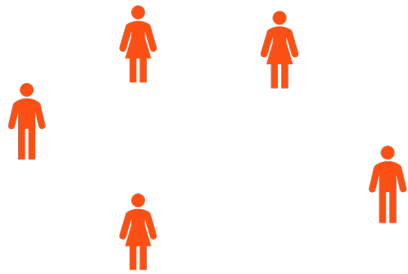
# Prechter Longitudinal Study of Bipolar Disorder (PLS-BD)



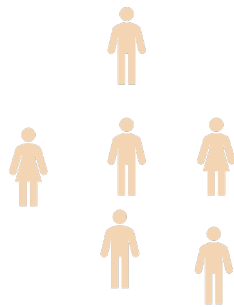




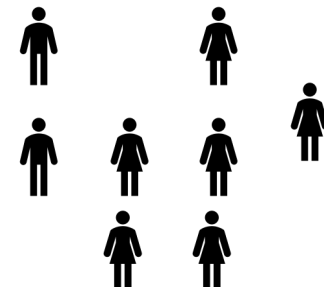
You can stratify people based on variability with measures taken over **just 12 months**



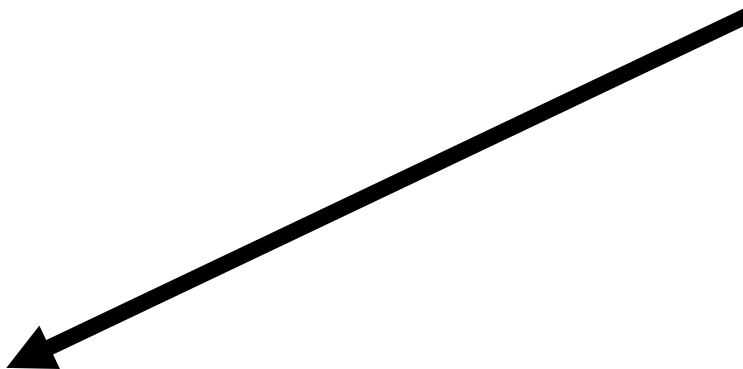
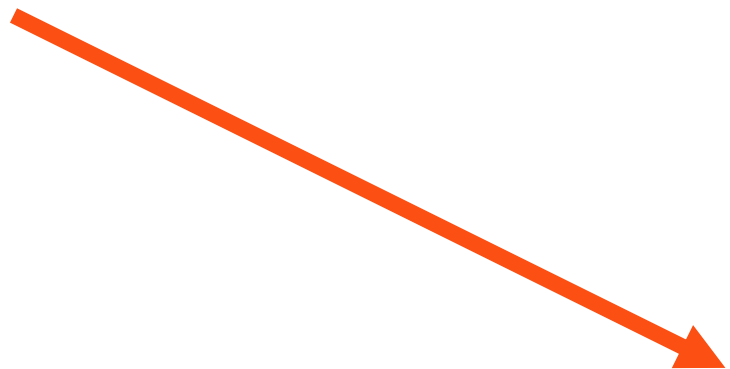
Average instability



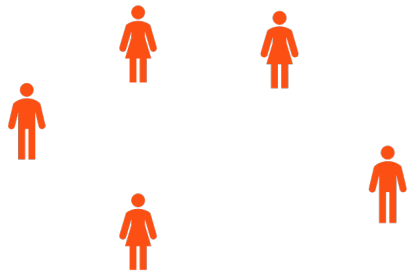
Moderate instability



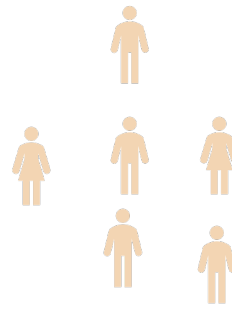
High instability



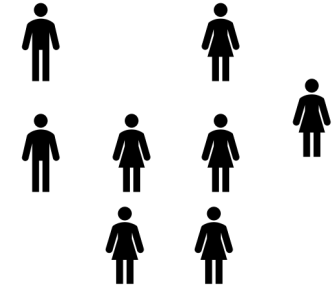
Longitudinal mental health functioning  
Longitudinal physical health functioning



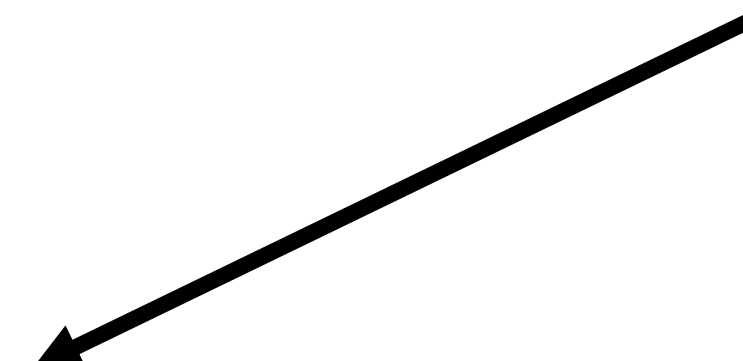
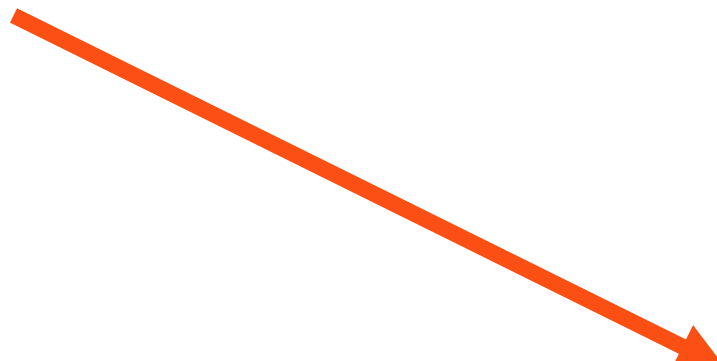
Average instability



Moderate instability



High instability



If you are in the moderate variability or high variability your functioning level is between .25 and .5 standard deviations below those in average variability

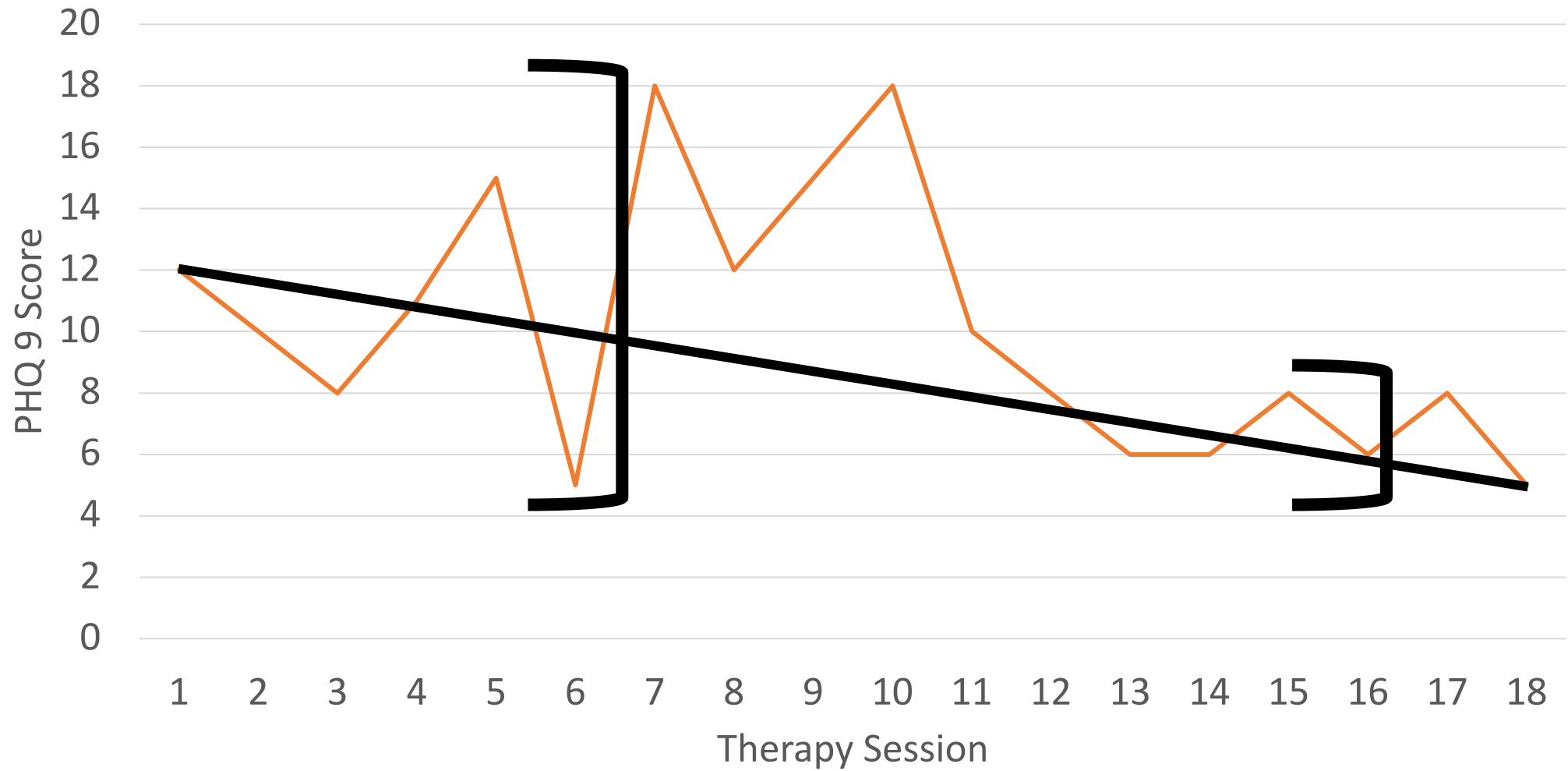
1. Individuals **can be stratified** into groups based on affective instability even with just a few measures collected over 12 months.

2. This can be done with traditional patient reported outcomes measures (PROMs) like the **PHQ9** that are often delivered now in the context of **routine** physical and mental health care.

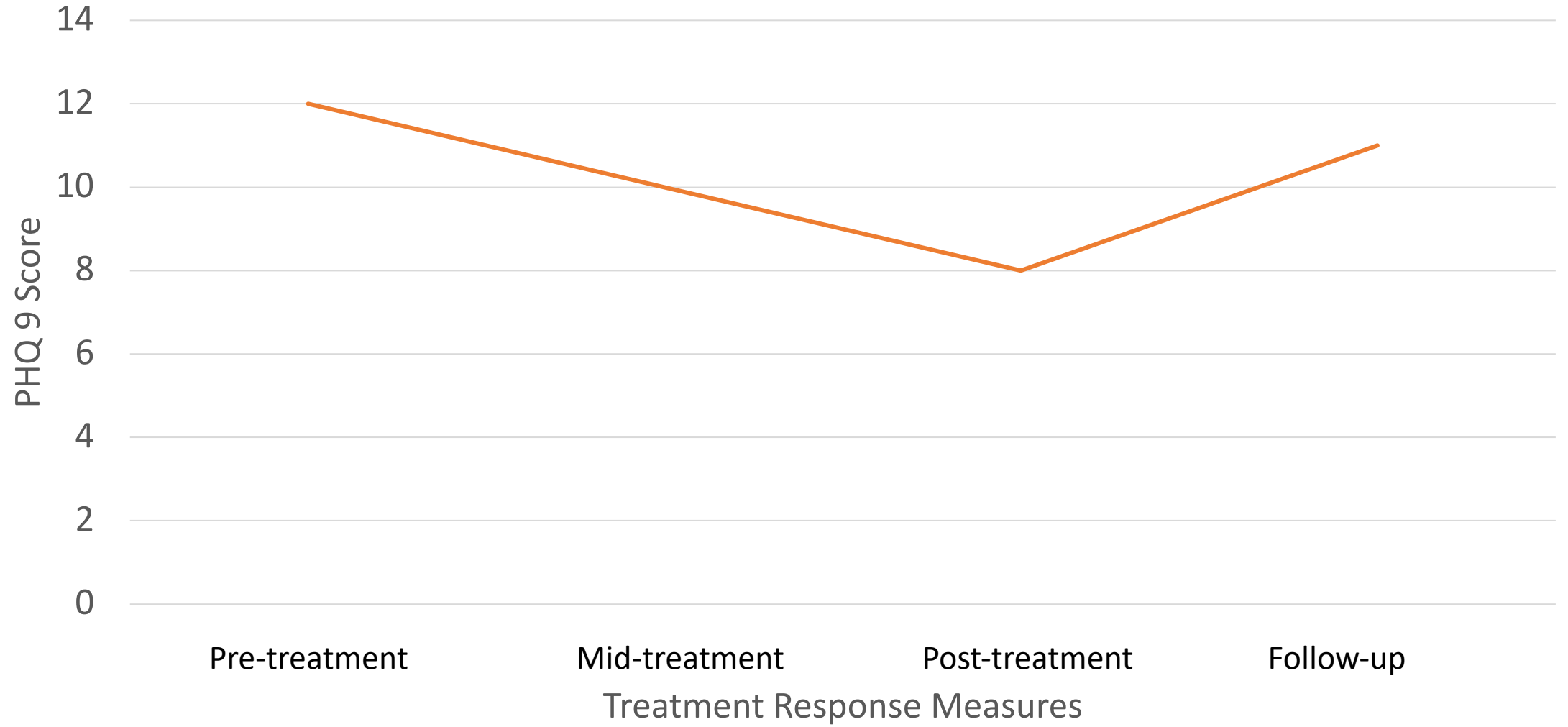
Affective instability is something we must to pay more attention to!

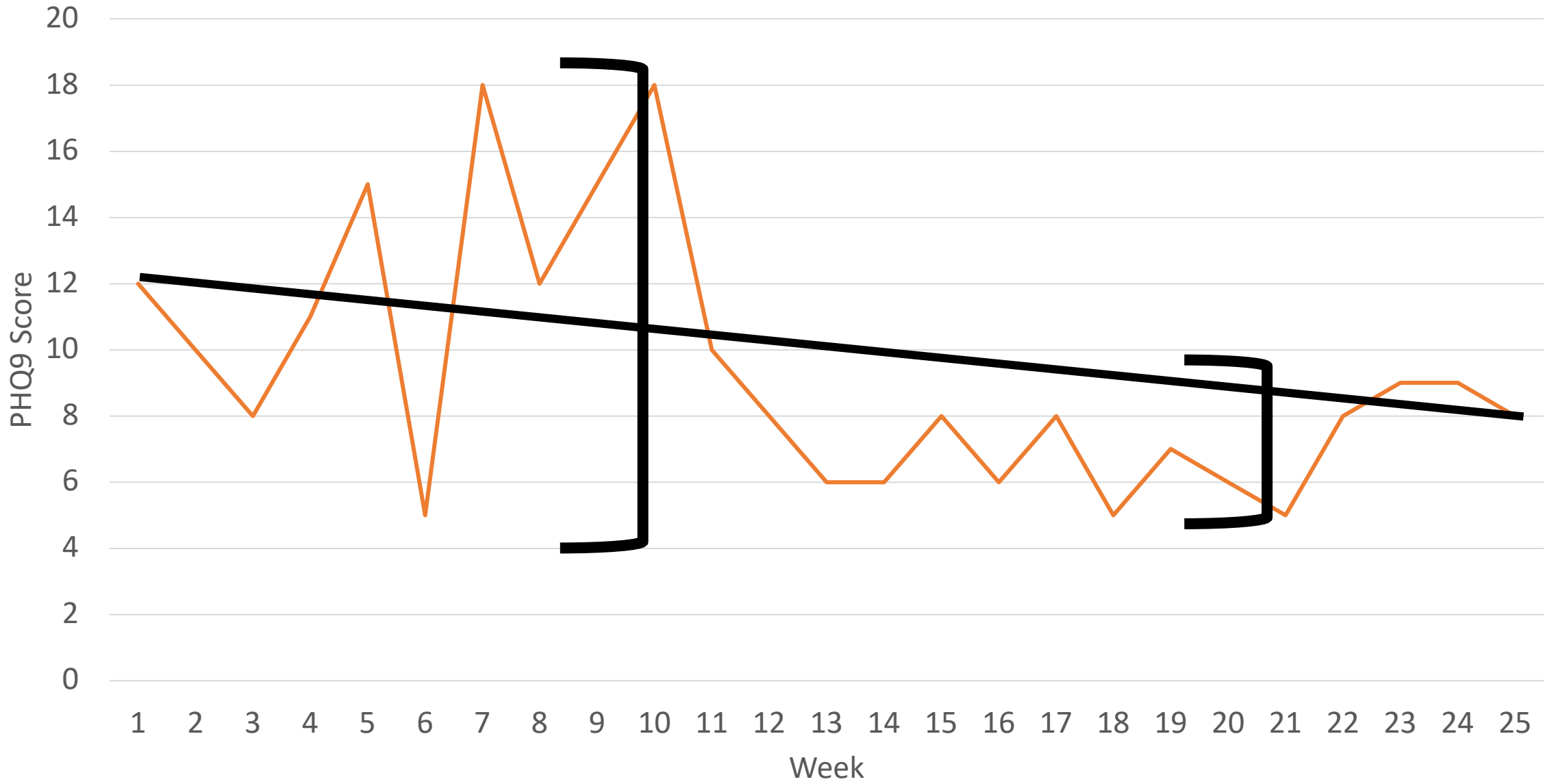


# Therapy measurement-based care



# Clinical trials





You can measure and use **ffective instability** as a treatment outcome measure!



**M** HEINZ C. PRECHTER BIPOLAR RESEARCH PROGRAM  
MICHIGAN MEDICINE

I'd like to thank all the participants of the PLS-BD for whom this research would not be possible. I'd also like to thank the Prechter family and Dr. Melvin McInnis— without your support and vision the PLS-BD would not exist.



BBRF Mentor:  
Ivy Tso, Ph.D.

# Questions?



<https://sperry.lab.medicine.umich.edu/>



<https://medicine.umich.edu/dept/prechter-program>