

#NAMIcon16

Bipolar Research Studies: Impact and Future State

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Heinz C. Prechter Bipolar Research Fund



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- Gloria Harrington – None
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Background



Heinz C. Prechter, 1942-2001



- Vision: To *personalize treatment* of bipolar disorder and *prevent recurrences* to enable those with bipolar to lead healthy and productive lives.



Bipolar Disorder

- Profound shifts in mood & energy
- Genes and environment interact
- Devastating effects on:
 - Social life
 - Vocation
 - Personal economics



Bipolar Disorder Facts

- 2 - 3% Prevalence (~6 million US adults)¹
- Average age of onset: 25
- At least 25 to 50% attempt suicide once¹
- Nearly 1 in 5 complete suicide²
- U.S. economic burden: \$45 billion annually³
- Personal economic burden: \$12,000 – \$650,000⁴

1. Jamison, K.R., (2000). Suicide and bipolar disorder. *J Clin Psychiatry*, 61(9), 47-51.

2. Goodwin , F.K., Jamison, K.R., (2007). Manic depressive illness: bipolar disorders and recurrent depression, vol. 1, Oxford University Press.

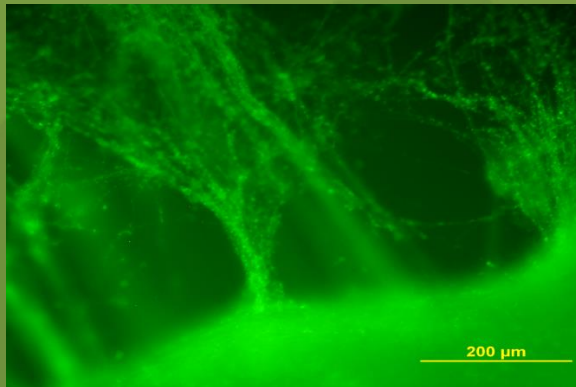
3. Williams, M. D., M.D., Shah, N. D., PhD., Wagie, A. E., B.S., Wood, D. L., M.D., & Frye, M. A., M.D. (2011). Direct costs of bipolar disorder versus other chronic conditions: An employer-based health plan analysis. *Psychiatric Services*, 62(9), 1073-8

4. Begley, C.E., et al., The lifetime cost of bipolar disorder in the US: an estimate for new cases in 1998. *Pharmacoeconomics*, 2001. 19(5 Pt 1): p. 483-95.



Emerging Bipolar Research Areas

- Induced Pluripotent Stem Cells – cell models
- Microbiome – to understand role of the gut flora
- Mobile Technology – to predict mood episodes



- Made possible through *longitudinal engagement*



Landmark Longitudinal Studies

- Cardiovascular

Framingham Study – cardiovascular disease

- Est. 1948; now in 3rd generation
- 1,200+ publications; prevention & risk identification
- Multiple cardiovascular longitudinal studies with thousands enrolled

- Mental Health

STEP-BD: Systematic Treatment Enhancement Program for Bipolar Disorder

- Est. 1998; follow-up every 3-6 months over 5 years
- 53+ publications; 4361 patients over 22 sites; primarily a treatment and treatment outcome study

Mental health longitudinal studies – in general have small sample sizes with limited number of follow-up years



Need for Longitudinal Studies

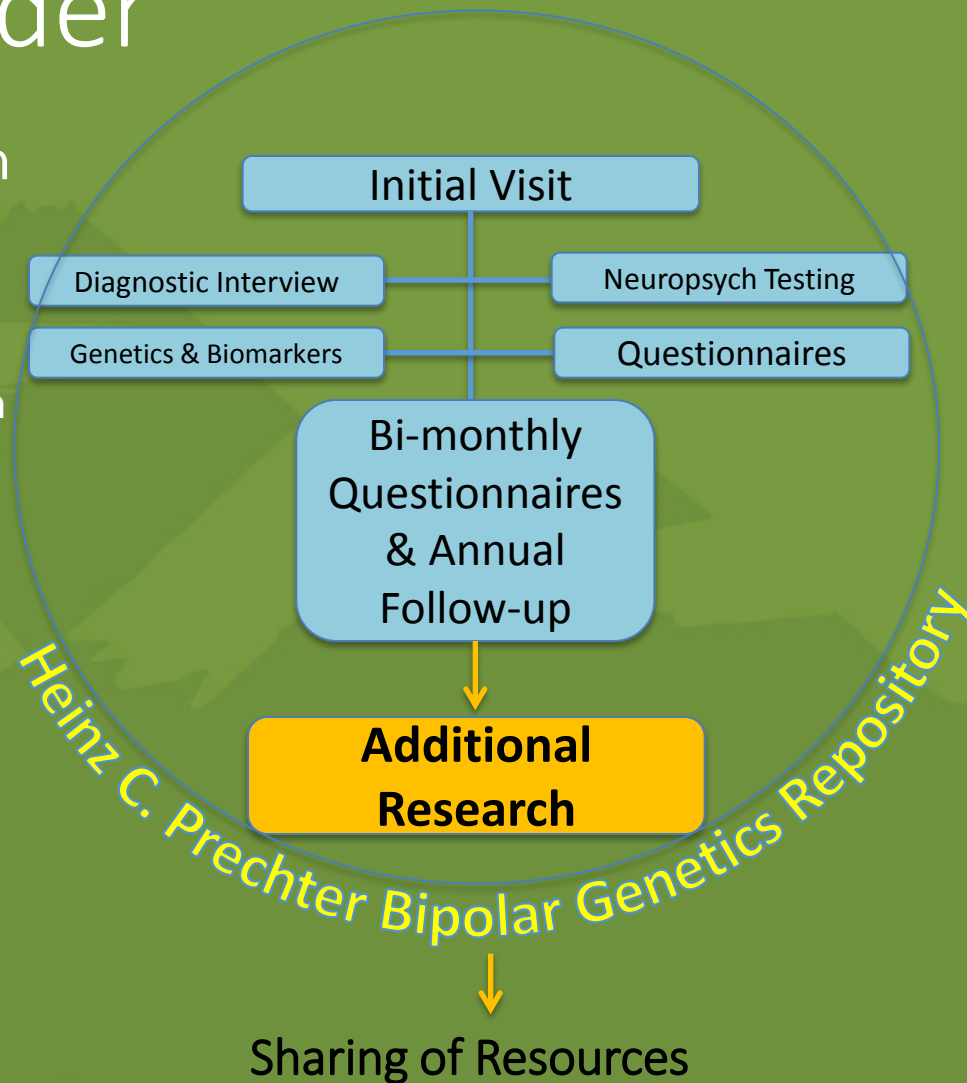
1. Applicable to study-defined populations
2. Provide estimates of distributions and prevalence rates
3. Used to assess risk factor trends over time
4. To observe relationships of various factors that impact outcomes¹

1. Szklo, M. (1998). Population-based cohort studies . Epidemiologic Review 20(1): 81-90.

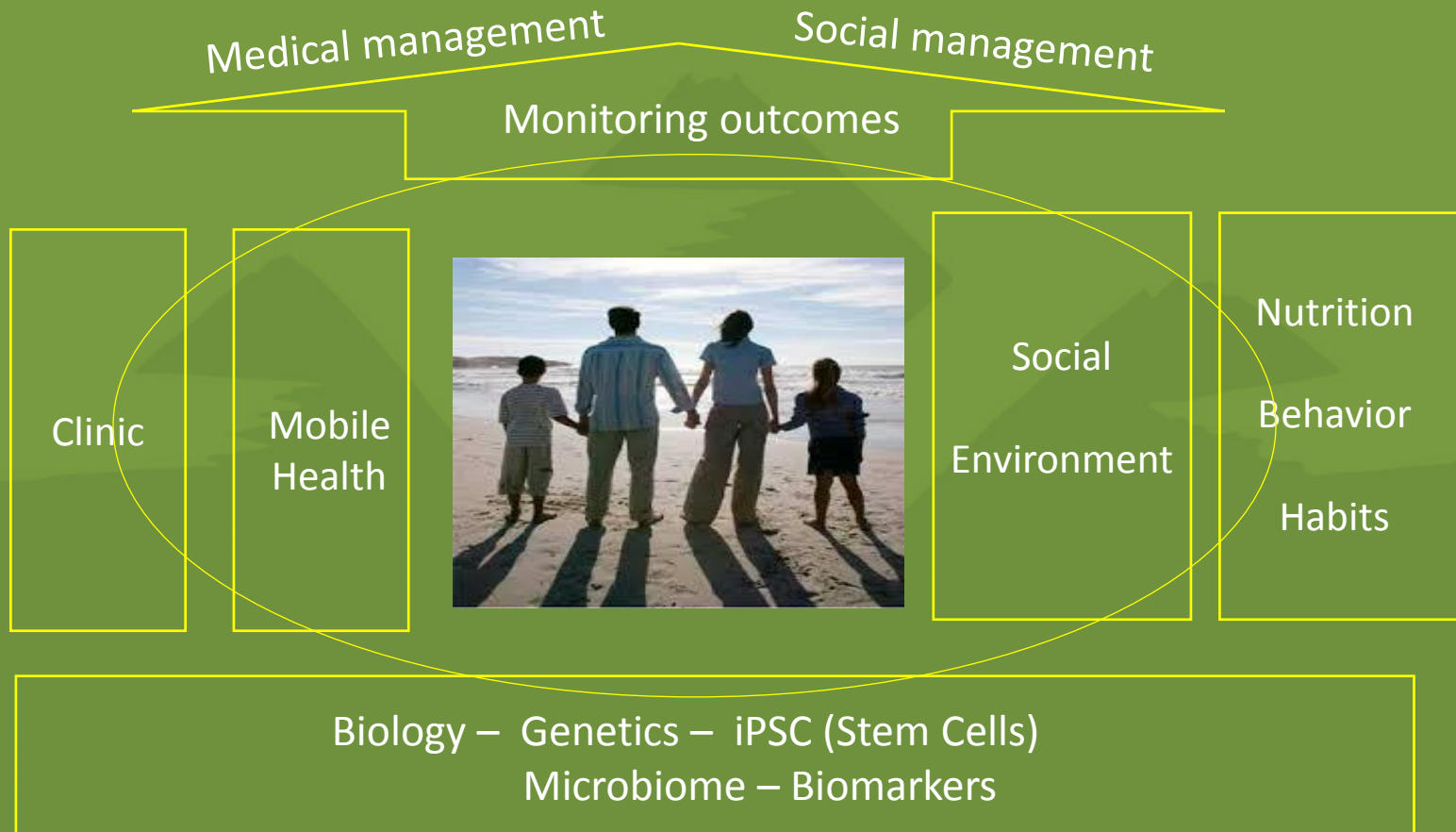


Prechter Longitudinal Study of Bipolar Disorder

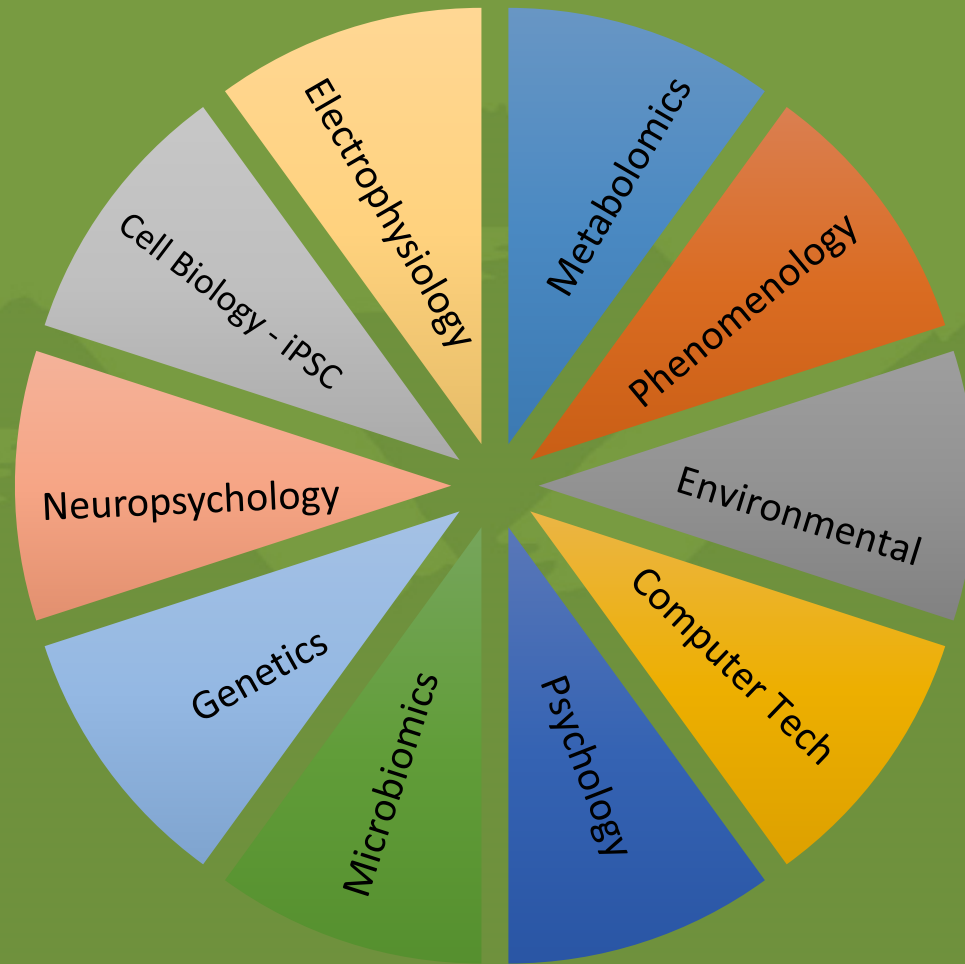
- Understand illness patterns in bipolar disorder:
 - through genetics
 - continued observation
 - additional research participation
- Over 1,200 enrolled
- 75% participants remain actively engaged
- Now in Year 10



Integrated Solutions for Bipolar Disorder



Key Multi-disciplinary Collaborations



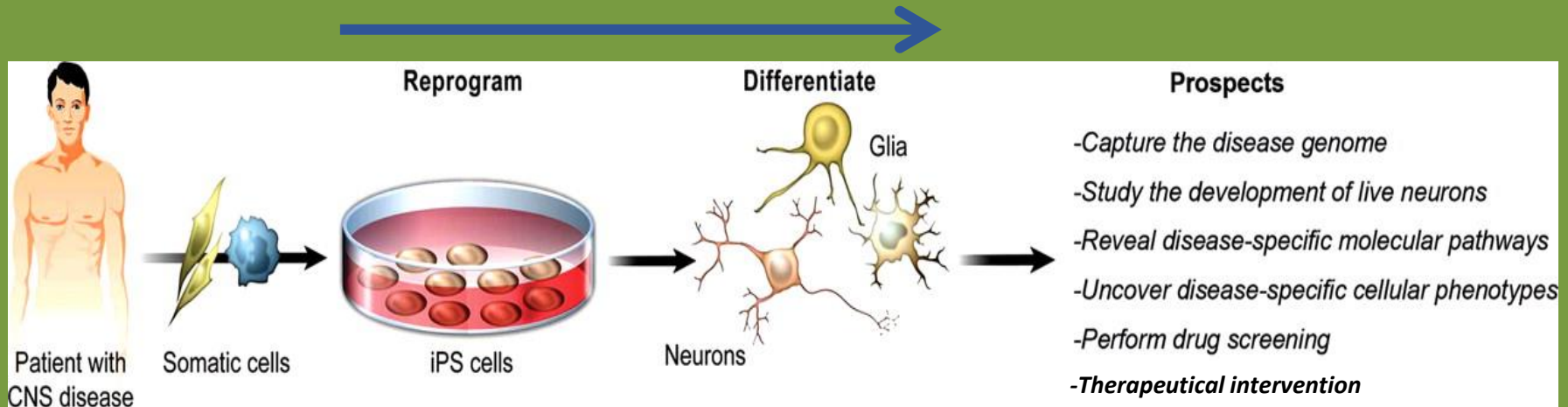
Induced Pluripotent Stem Cells

- Ideal method to study neurodevelopmental disorders
- Adult cells coaxed back to early stage of development (pluripotent) (not embryonic)
- Grown forward to cell type of interest (brain cells)
- Modeling of neural growth and development
- Evolution of pathophysiological development of disease states

(Melvin G. McInnis, MD)



iPSC Reprogramming Stages

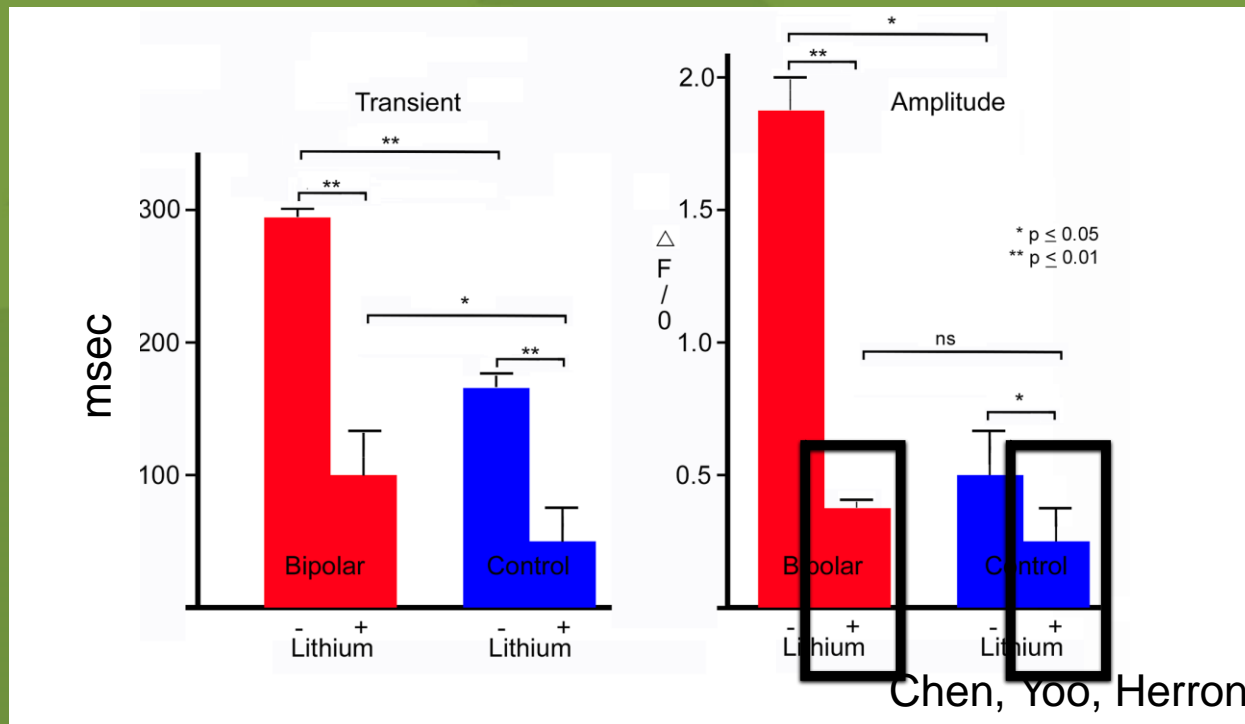


- Powerful model to study cell function
- Discovery of new molecules to help create and test new medications
- Leads to understanding of how individuals react to different treatments
 - **Personalized medicine**



What We've Learned from iPSCs

- Developmental Pattern Difference in Bipolar Cells
- Lithium pretreatment normalizes bipolar neuron calcium dynamics



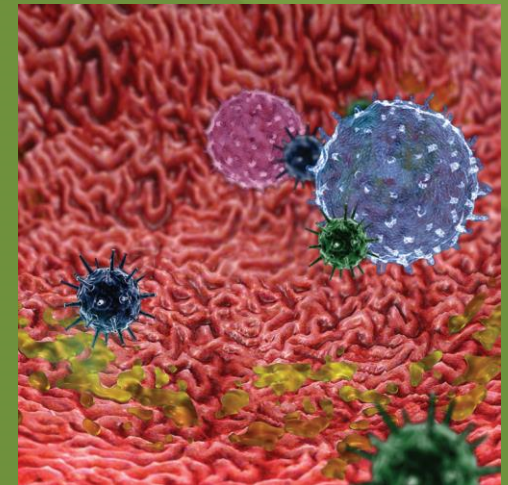
Next Steps for iPSC Research

- Lithium mechanisms – can novel interventions be developed?
- Mechanisms of other bipolar medications will be studied to advance research in therapeutics
- Developmental patterning research involves the study of the developing brain that is at risk for bipolar disorder



Microbiome: Gut-Brain Interaction

- Gut microbiome: influence on brain development, function, and behavior
- The microbiome responds to stress, diet, and medications
 - impact sleep, anxiety, mania, and depression
- Longitudinal study:
 - Leverage historical data to inform microbiome analysis



What We've Learned from the Microbiome

- The bacterial gut community is different in individuals with bipolar disorder.
- Specific gut bacteria associate with sleep quality, anxiety, and depression in bipolar disorder.
- Specific gut bacteria associate with intake of specific dietary nutrients.

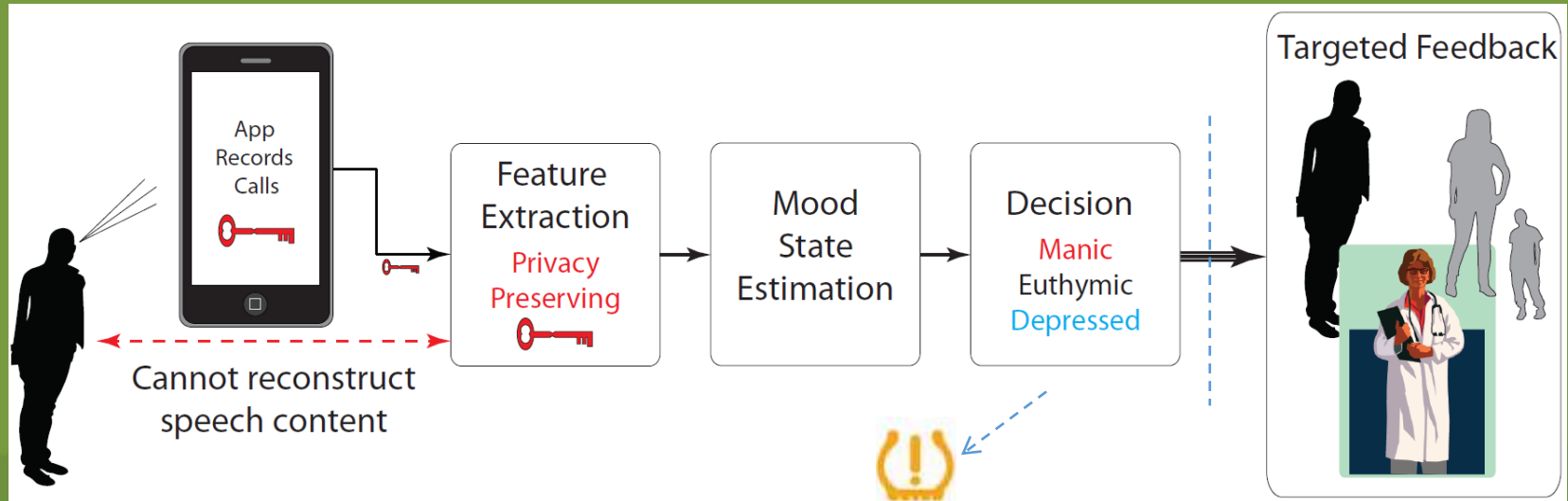


Next Steps for the Microbiome Studies

- Can specific diets improve the bacterial complement of the gut microbiome?
- Do dietary-induced changes in the microbiome extend to improved clinical outcomes over time?
 - Better sleep
 - Lower anxiety
 - Reduced depression and mania



PRIORI: Predicting Individual Outcomes for Rapid Intervention



AUC 0.70 – 0.81

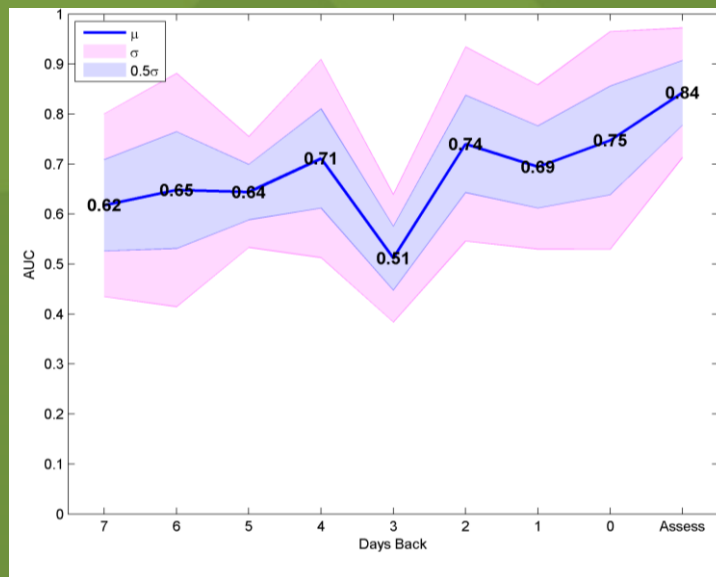
- n = 50
- 6 – 12 months
- 45,000 calls

(Emily Provost, PhD)
Computer Science & Engineering

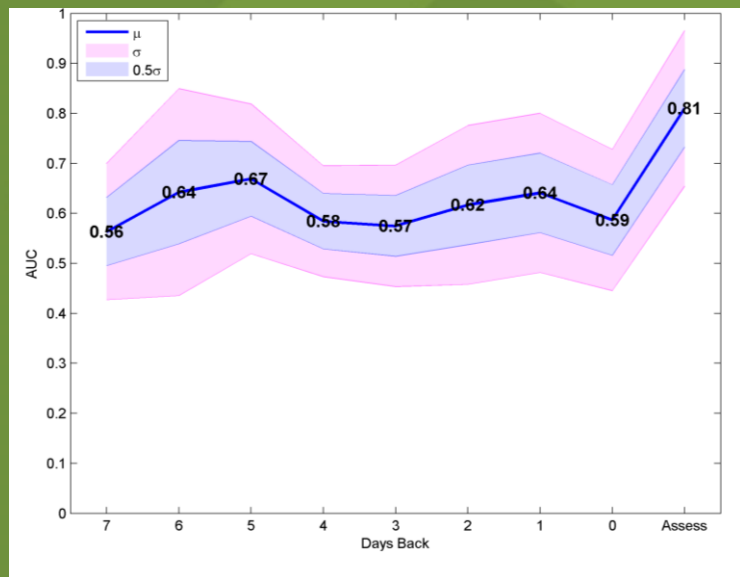


What We've Learned from PRIORI

- Mood can be detected using speech characteristics
- Quality of data varies by phone models
- Area under curve (AUC) for participants from assessment to 7 days prior:



Hypomanic vs. Euthymic



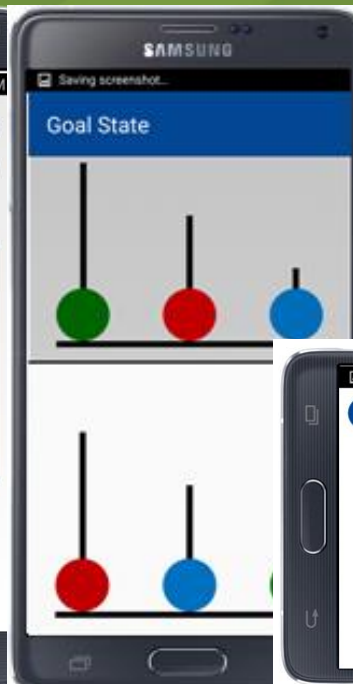
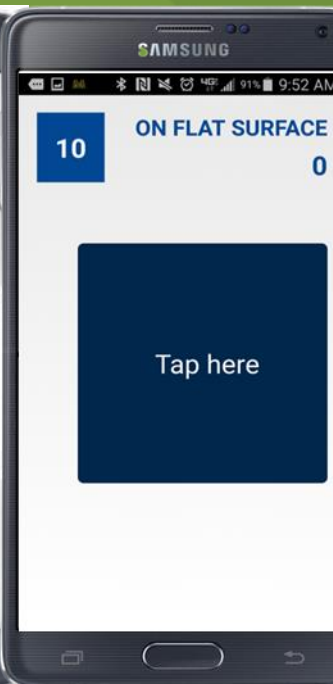
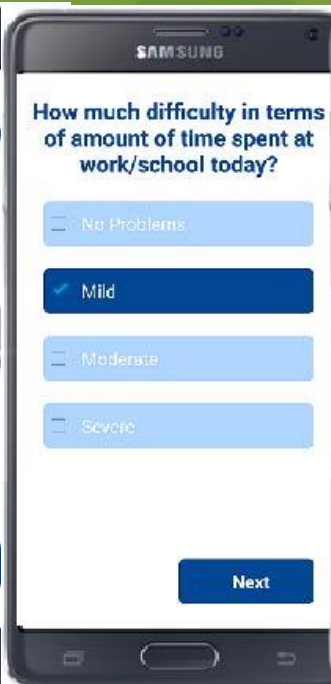
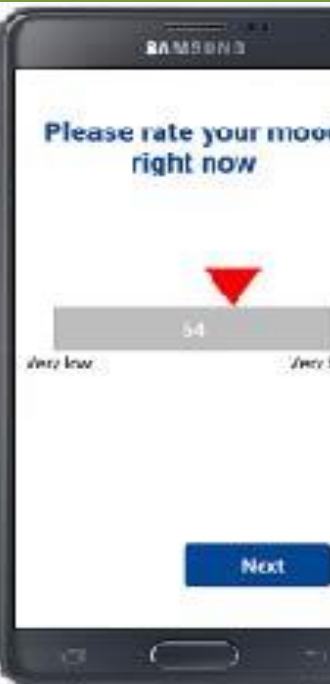
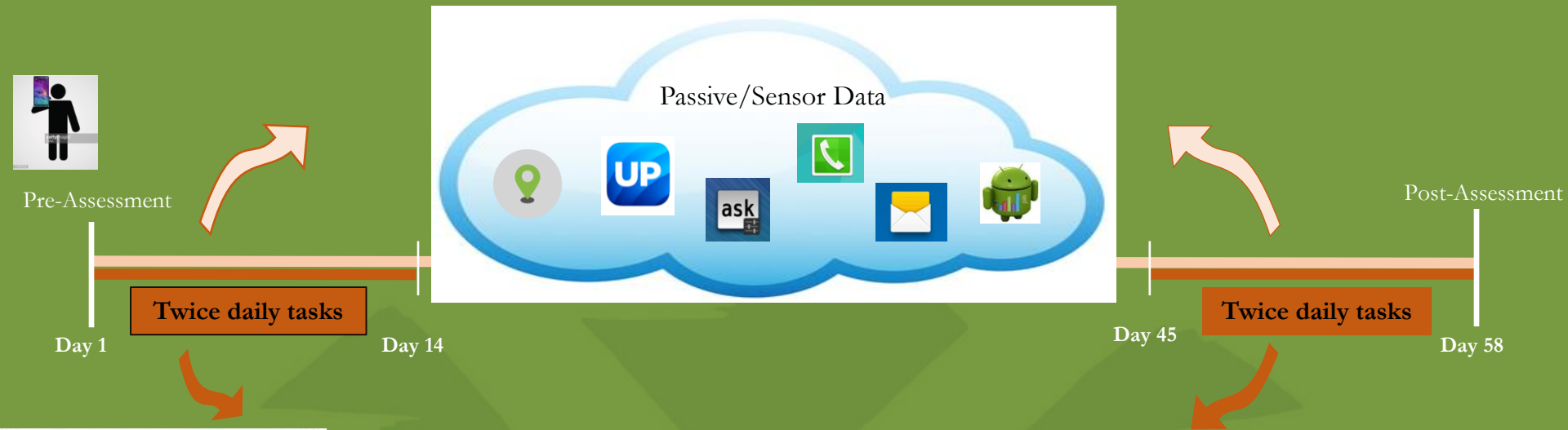
Depressed vs. Euthymic

(Emily Provost, PhD)

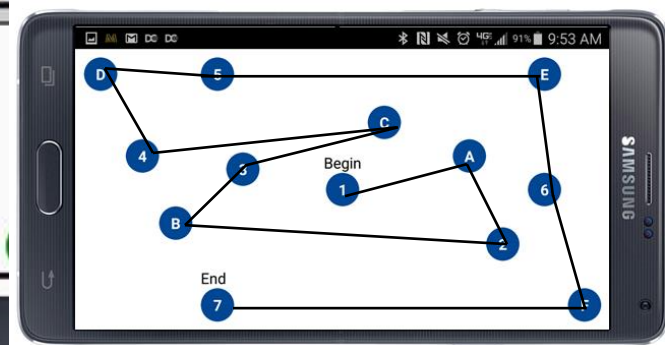
Computer Science & Engineering



Other Mobile Technology Apps



(Kelly Ryan, PhD)
Department of Psychiatry



Next Steps for Mobile Technology Studies

- Need larger sample sizes
- Need for clinical trial
 - Can we measure or redefine core features, such as psychomotor activity, using technology?
 - Can we predict changes and alter the course of bipolar disorder using PRIORI and other mobile applications?

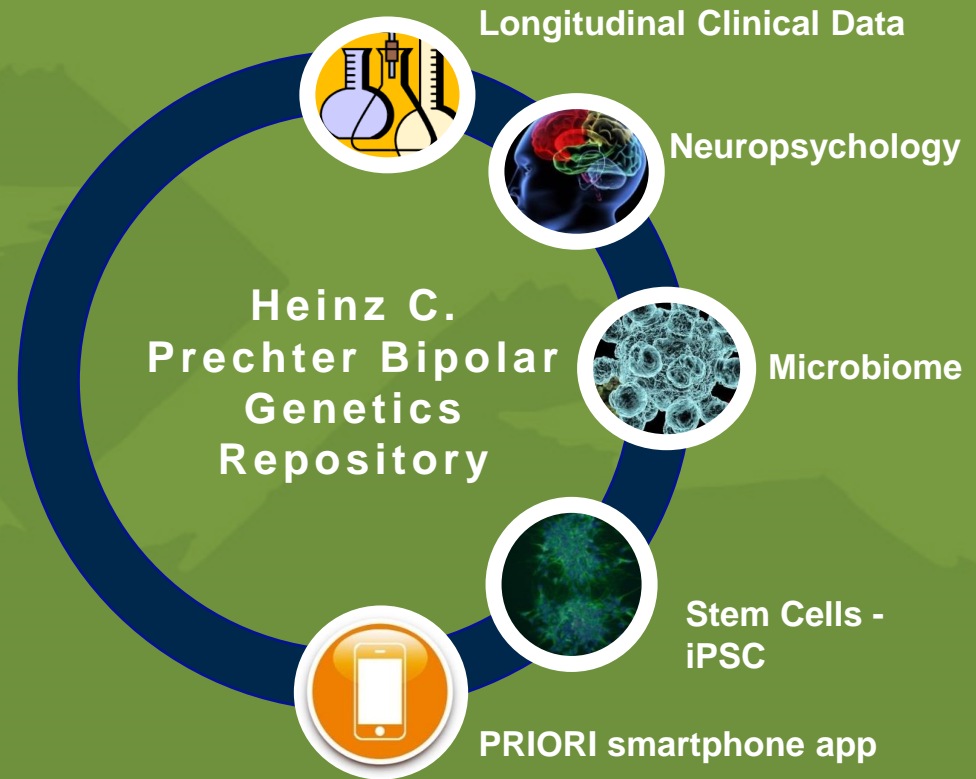


Heinz C. Prechter Bipolar Genetics Repository

- **Clinical data and biological samples**

- Bipolar disorder
- Healthy controls

- **Integrated solutions**



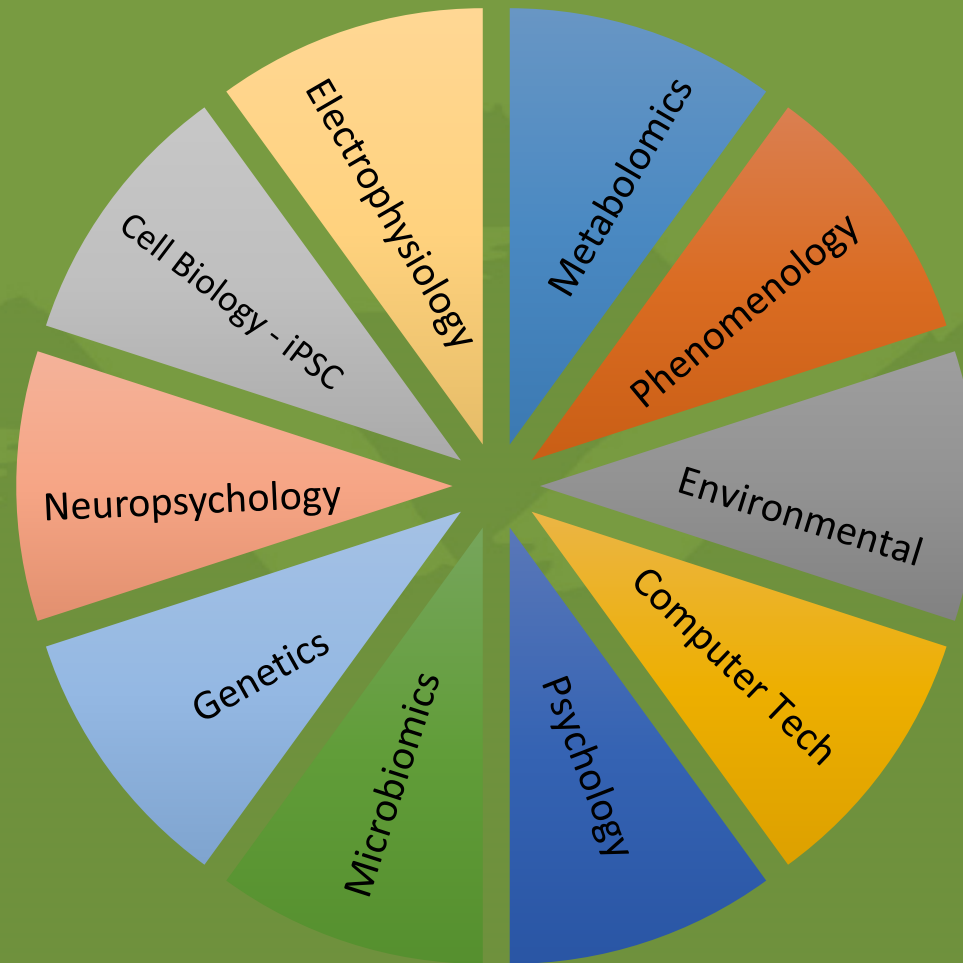
Longitudinal Studies: Engagement

1. Maintain good relationships with longitudinal members
2. Securing health-care provider support for cohort with key health issues¹
3. Creating an Executive Committee (community) to assist with¹:
 - Program planning
 - Translate study findings to community
 - Active participation in organizational aspects of the study
4. Overall, our participants report doing better by being involved in research
 - Clinicians do check-ins when there are safety concerns
 - Depression and mania scores are showing improvement over time

1. Szklo, M. (1998). Population-based cohort studies . Epidemiologic Review 20(1): 81-90.



Key Multi-disciplinary Collaborations



Conclusion

- Living a healthy life with bipolar disorder is possible.

Strategies to consider:



- **Work-life balance**
 - **Regular exercise**
 - **Get enough sleep**
 - **Eat a healthy diet**
 - **Collaborate with your care providers (& your research team!)**
 - **Engage support of friends and family**
- For more information, visit us at **Booth #219**
 - www.prechterfund.org



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