



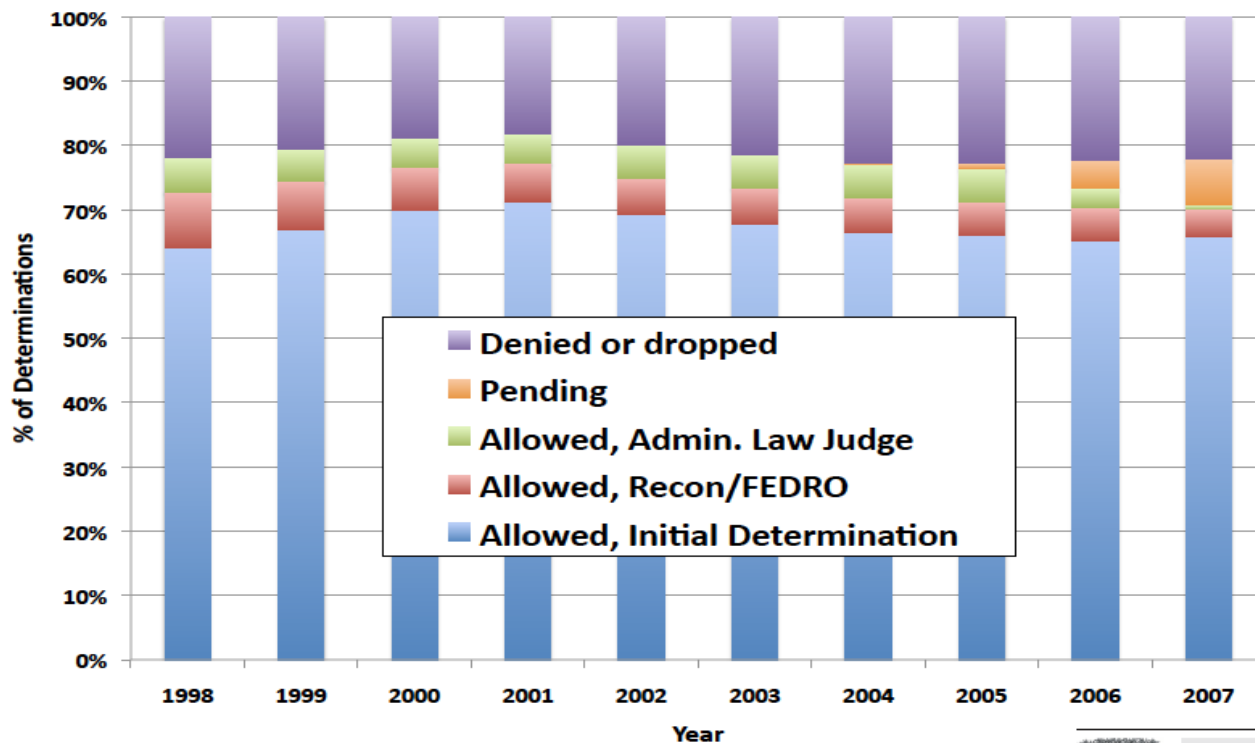
UNIVERSITY OF MIAMI  
MILLER SCHOOL  
of MEDICINE

# Biomarkers of Disability in Schizophrenia

Philip D. Harvey, PhD  
University of Miami Miller School of Medicine

# Rates of Disability Compensation in Schizophrenia

**Figure 2: Disposition of SSI/SSDI Applicants with Schizophrenia/  
Paranoid Functional Disorders (SSA Diagnosis Code 2950)**



Data provided by the SSA, 4/2010



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Schizophrenia Research

Journal homepage: [www.elsevier.com/locate/schres](http://www.elsevier.com/locate/schres)

Review

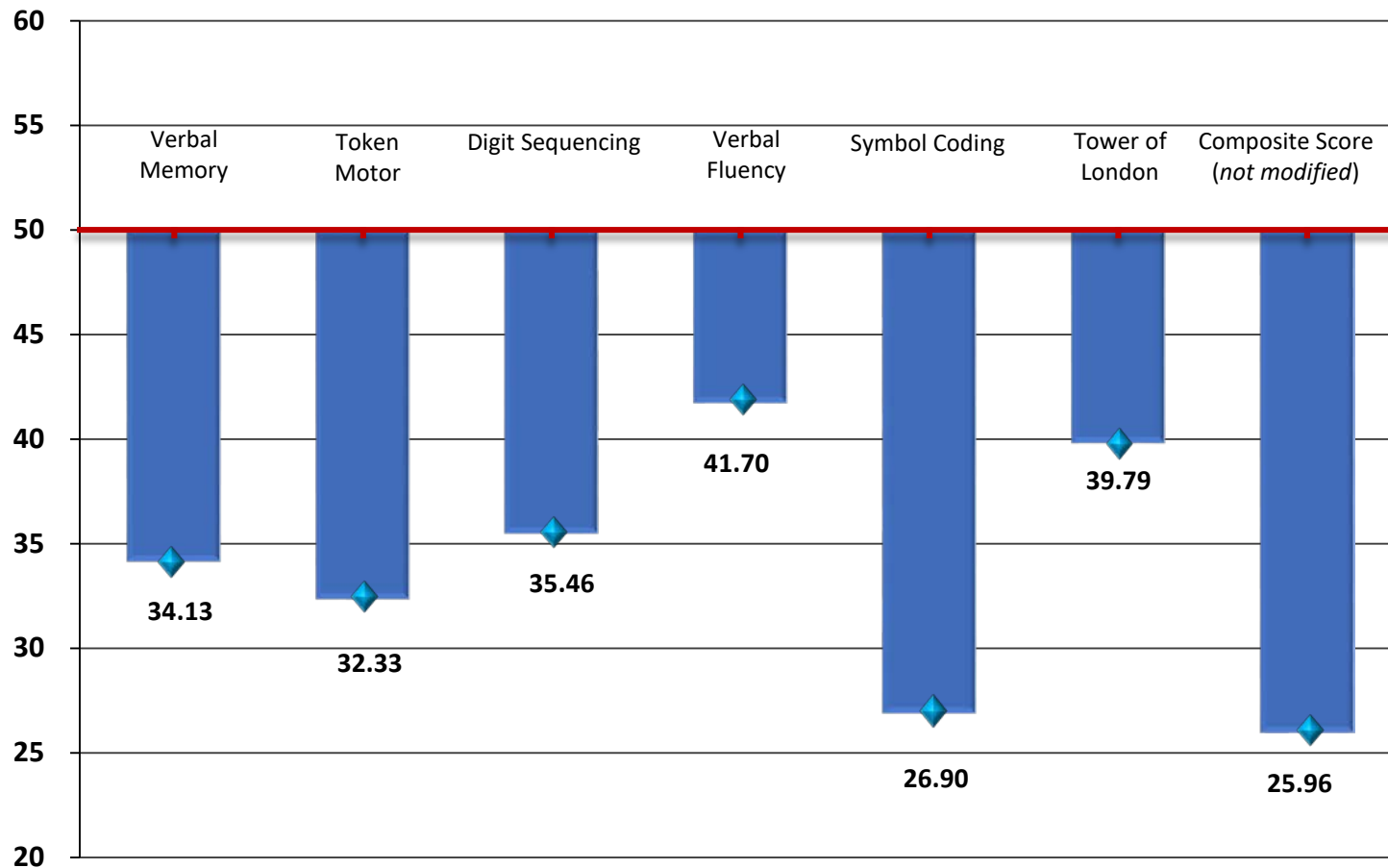
Functional impairment in people with schizophrenia: Focus on employability and eligibility for disability compensation

Philip D. Harvey <sup>a,\*</sup>, Robert K. Heaton <sup>b</sup>, William T. Carpenter Jr. <sup>c</sup>, Michael F. Green <sup>d</sup>, James M. Gold <sup>e</sup>, Michael Schoenbaum <sup>e</sup>

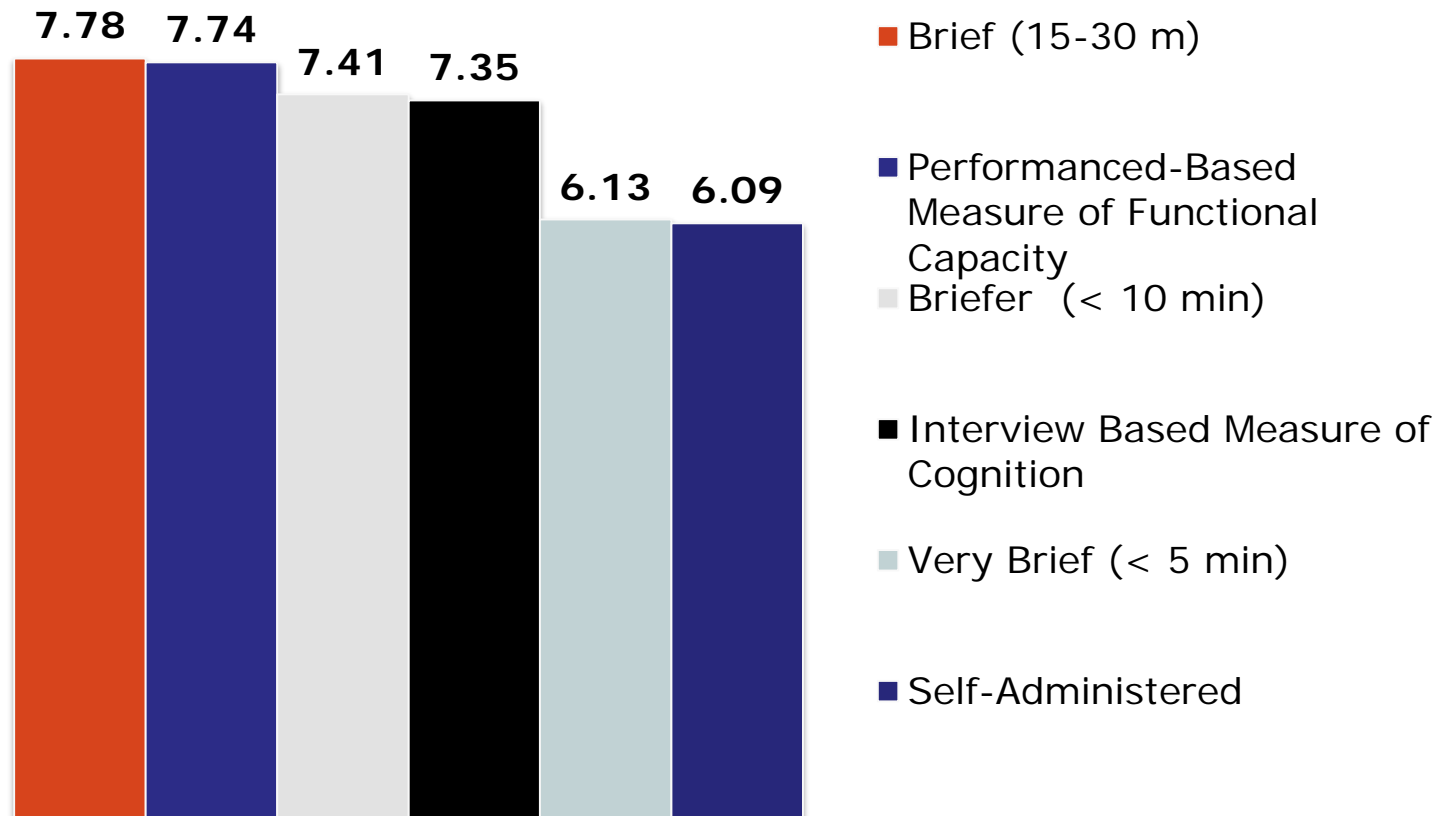
# What Predicts Everyday Disability in Schizophrenia?

- The usual suspects include:
  - Cognition
  - Negative Symptoms
- New evidence is emerging on physical functioning and physical fitness as well

# Cognitive Impairments in Schizophrenia

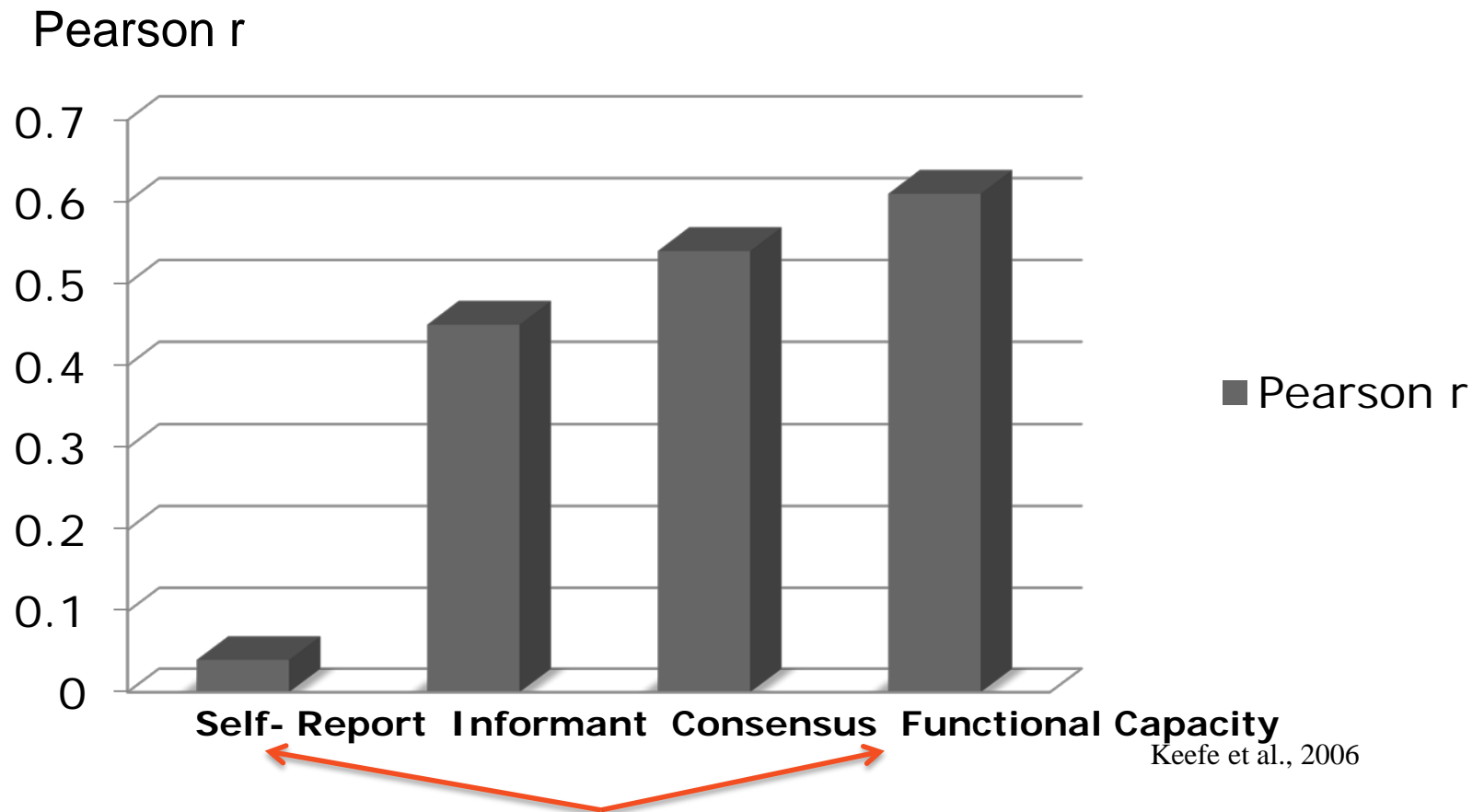


# No Consensus on Assessment for Measuring Cognition Among Psychiatric Clinicians



Keefe et al, Report on ISCTM Consensus Meeting on Clinical Assessment of Response to Treatment of Cognitive Impairment in Schizophrenia. Schizophr Bulletin, 2015

# Correlation Between Performance-based Cognition Scores, Functional Capacity, and Ratings of Impaired Cognition in Schizophrenia



# Cognition: Biomarker Status

- Little question that cognition is related to brain function, even with contributions of physical functioning
- Also, impairment is fully developed by the time of first identification of psychotic symptoms
- So, useful as an early predictive indicator of risk for disability compensation
- Seems like there are multiple feasible assessment strategies that could even be conducted remotely, such as remote cognitive assessments or informant interviews

# Negative Symptoms

- Reduced emotional experience
  - Avolition-Anhedonia; Amotivation
    - Highly related to reduced social drive and functioning
- Reduced emotional expression
  - Blunted affect, reduced volume of speech, reduced intonation
    - Highly visible to observers
- These are real symptoms and not produced by other features of the illness
- Multiple studies have suggested the importance of negative symptoms and avolition-anhedonia in particular
- Reduced expression does not predict disability as well as Avolition-Anhedonia



# Negative Symptoms are an early Marker of Risk

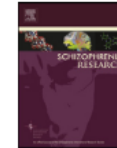
Schizophrenia Research 161 (2015) 407–413



Contents lists available at ScienceDirect

Schizophrenia Research

journal homepage: [www.elsevier.com/locate/schres](http://www.elsevier.com/locate/schres)



Negative symptoms and functioning during the first year after a recent onset of schizophrenia and 8 years later



Joseph Ventura<sup>a,\*</sup>, Kenneth L. Subotnik<sup>a</sup>, Michael J. Gitlin<sup>a</sup>, Denise Gretchen-Doorly<sup>a</sup>, Arielle Ered<sup>a</sup>, Kathleen F. Villa<sup>c</sup>, Gerhard S. Helleman<sup>a</sup>, Keith H. Nuechterlein<sup>a,b</sup>

Schizophrenia Research 203 (2019) 24–31



Contents lists available at ScienceDirect

Schizophrenia Research

journal homepage: [www.elsevier.com/locate/schres](http://www.elsevier.com/locate/schres)



Cognitive remediation can improve negative symptoms and social functioning in first-episode schizophrenia: A randomized controlled trial



Joseph Ventura<sup>a,\*</sup>, Kenneth L. Subotnik<sup>a</sup>, Denise Gretchen-Doorly<sup>a</sup>, Laurie Casaus<sup>a</sup>, Michael Boucher<sup>a</sup>, Alice Medalia<sup>c</sup>, Morris D. Bell<sup>d</sup>, Gerhard S. Helleman<sup>a</sup>, Keith H. Nuechterlein<sup>a,b</sup>

# Assessment of Negative Symptoms

- It is clear that assessment of negative symptoms can be challenging and requires clinical experience
- Its not productive to just ask a family member
- Newly developed strategies have focused on “digital biomarkers”
  - Active and Passive Assessment Strategies
  - Facial and vocal Emotional Expression
  - Actigraphy

# Paging Strategies

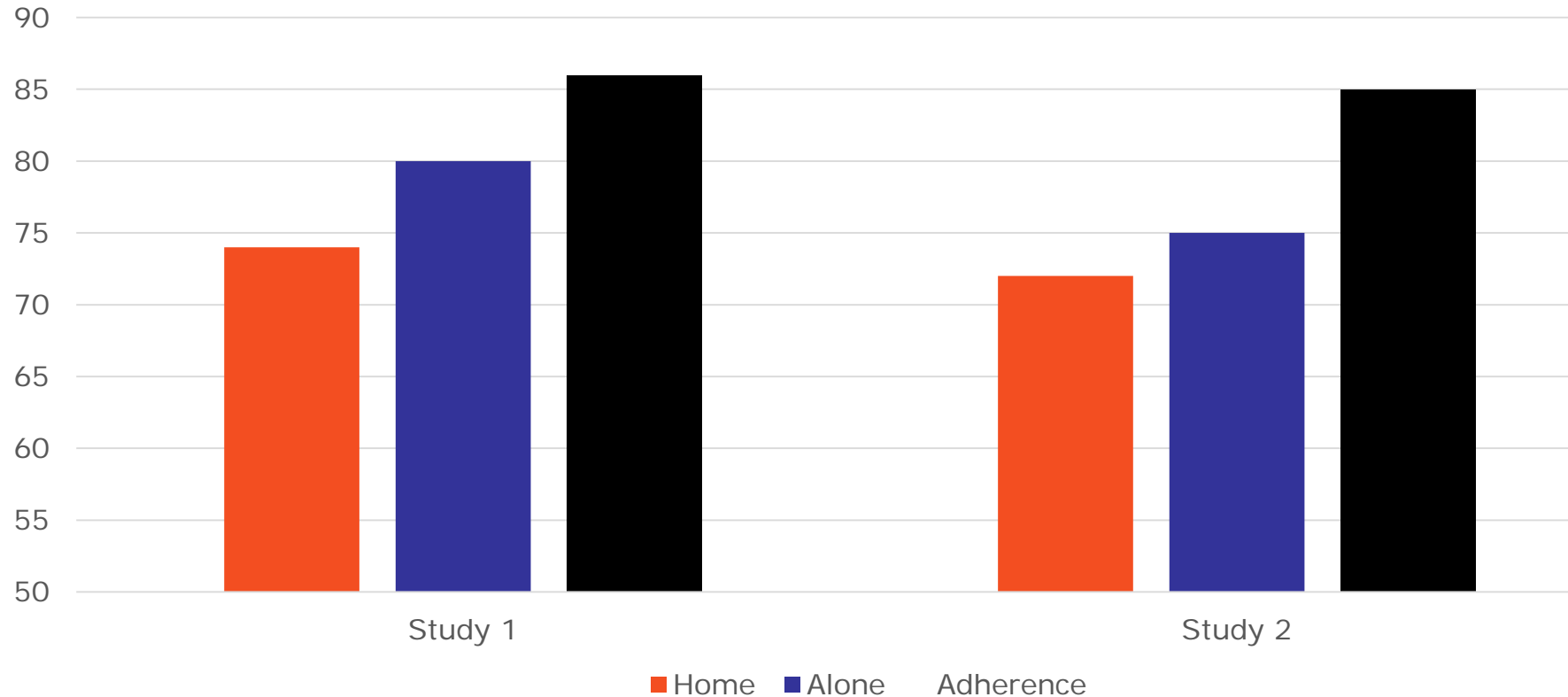
- **Where** are you?
  - Home vs Away
- **Who** are you with?
  - Alone or with someone
- **What** are doing?
  - Activity survey
- **How** are you feeling?
  - Mood and psychosis

# Two Psychosis Studies

- Study 1: 100 outpatients with SCZ
  - 4200 total surveys
- Study 2: In process, 104 outpatients with SCZ, 71 with BPI
  - 12,540 surveys to date

# Who and where

EMA Activity-based Sampling two Studies



# GPS Validation of Survey Results

ARTICLE

OPEN

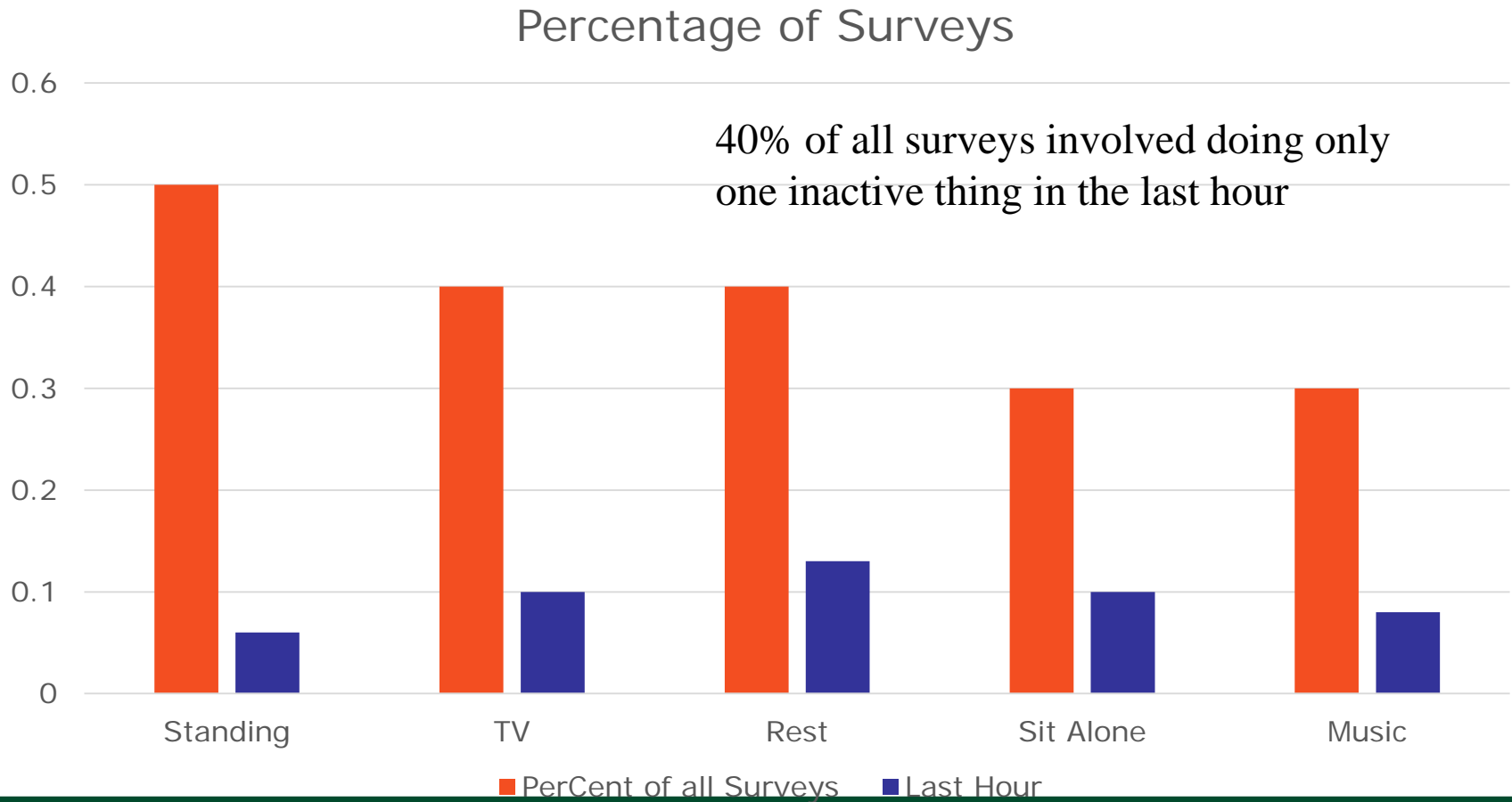
## GPS mobility as a digital biomarker of negative symptoms in schizophrenia: a case control study

Colin A. Depp<sup>1,2\*</sup>, Jesse Bashem<sup>2</sup>, Raeanne C. Moore<sup>1,2</sup>, Jason L. Holden<sup>1</sup>, Tanya Mikhael<sup>3</sup>, Joel Swendsen<sup>4</sup>, Phillip D. Harvey<sup>5</sup> and Eric L. Granholm<sup>1,2</sup>

**Table 2.** Spearman correlations between GPS metrics and EMA metrics in total sample ( $n = 142$ )

	GPS median daily distance traveled (miles)	GPS median daily distance traveled from home (miles)	GPS median percent of samples at home
<i>Total sample</i>			
EMA time spent at home in past hour	−0.575 ( $p < 0.001$ )	−0.623 ( $p < 0.001$ )	0.684 ( $p < 0.001$ )
EMA percent of samples at home	−0.551 ( $p < 0.001$ )	−0.582 ( $p < 0.001$ )	0.658 ( $p < 0.001$ )
<i>Healthy comparators</i>			
EMA time spent at home in past hour	−0.375 ( $p = 0.004$ )	−0.422 ( $p = 0.001$ )	0.546 ( $p < 0.001$ )
EMA percent of samples at home	−0.366 ( $p = 0.006$ )	−0.406 ( $p = 0.002$ )	0.539 ( $p < 0.001$ )
<i>Schizophrenia</i>			
EMA time spent at home in past hour	−0.569 ( $p < 0.001$ )	−0.601 ( $p < 0.001$ )	0.681 ( $p < 0.001$ )
EMA percent of samples at home	−0.550 ( $p < 0.001$ )	−0.560 ( $p < 0.001$ )	0.640 ( $p < 0.001$ )
Spearman Rho value ( $p$ value); EMA ecological momentary assessment			

# Most Common Activities: All Surveys vs One Activity in the Last Hour

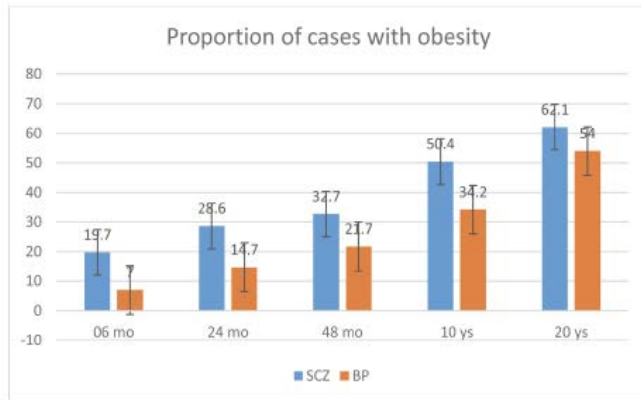


# Activity Levels, Disability, and Schizophrenia

- Co-morbid conditions in schizophrenia lead to employment challenges as well
- These include metabolic syndrome and related conditions
- These problems start early
- Our patients are doing lots of seated single and multi-tasking
- This activity information may provide a link between negative symptoms, sedentary behavior, and physical limitations interfering with employment



# Rates and Importance of Obesity for Employment



“In the model for *labor force participation*, chair stands entered the equation first, and accounted for 9% of the incremental variance ( $p < 0.001$ ). SANS total scores were entered next and accounted for another 5% of the variance ( $p < 0.005$ ). Thus, impairments in mobility and negative symptoms predicted 14% of the variance in the final model for labor force participation; the other variables were nonsignificant.”

.... “BMI at illness onset predicted employment significantly at 20-year follow-up ( $b = -0.05$ ,  $p = 0.03$ ). This finding indicated that the higher the individual's BMI at illness onset, the less likely that individual was to be employed at 20-year follow-up.”

## BIPOLAR DISORDERS

AN INTERNATIONAL JOURNAL OF PSYCHIATRY AND NEUROSCIENCES

ORIGINAL ARTICLE

**Twenty-year progression of body mass index in a county-wide cohort of people with schizophrenia and bipolar disorder identified at their first episode of psychosis**

Martin Strassnig<sup>a,\*</sup>, Roman Kotov<sup>a</sup>, Danielle Cornaccio<sup>a</sup>, Laura Fochtman<sup>a</sup>, Philip D Harvey<sup>a</sup>, Evelyn J Bromet<sup>a</sup>



Journal of Psychiatric Research 94 (2017) 180–185

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Journal of Psychiatric Research

journal homepage: [www.elsevier.com/locate/psychires](http://www.elsevier.com/locate/psychires)

**Health status and mobility limitations are associated with residential and employment status in schizophrenia and bipolar disorder**

M. Strassnig<sup>a,\*</sup>, D. Cornaccio<sup>b</sup>, P.D. Harvey<sup>c</sup>, R. Kotov<sup>d</sup>, L. Fochtman<sup>d</sup>, E.J. Bromet<sup>d</sup>

# Conclusions

- Cognition, activity, and weight are all biological factors that predict unemployment
- All are present early in the illness; all can be measured with existing tools
- All are directly relevant to work outcomes