

# care

COGNITIVE ASSESSMENT AND RISK EVALUATION

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Director and Principle Investigator

A Program for Adolescents  
and Young Adults



# CARE Program Overview

- Research: Established as a research, consultation and referral program in 1999 for young people in the early stages of psychosis.
- Treatment program, established in 2013, integrates clinical research and evidence based medicine in the treatment of early psychosis.
- Physical Location: The CARE Early Psychosis Treatment program is co-located with the research laboratory of Dr. Kristin Cadenhead on the 4<sup>th</sup> floor of the UCSD Outpatient Psychiatry facility in Hillcrest.

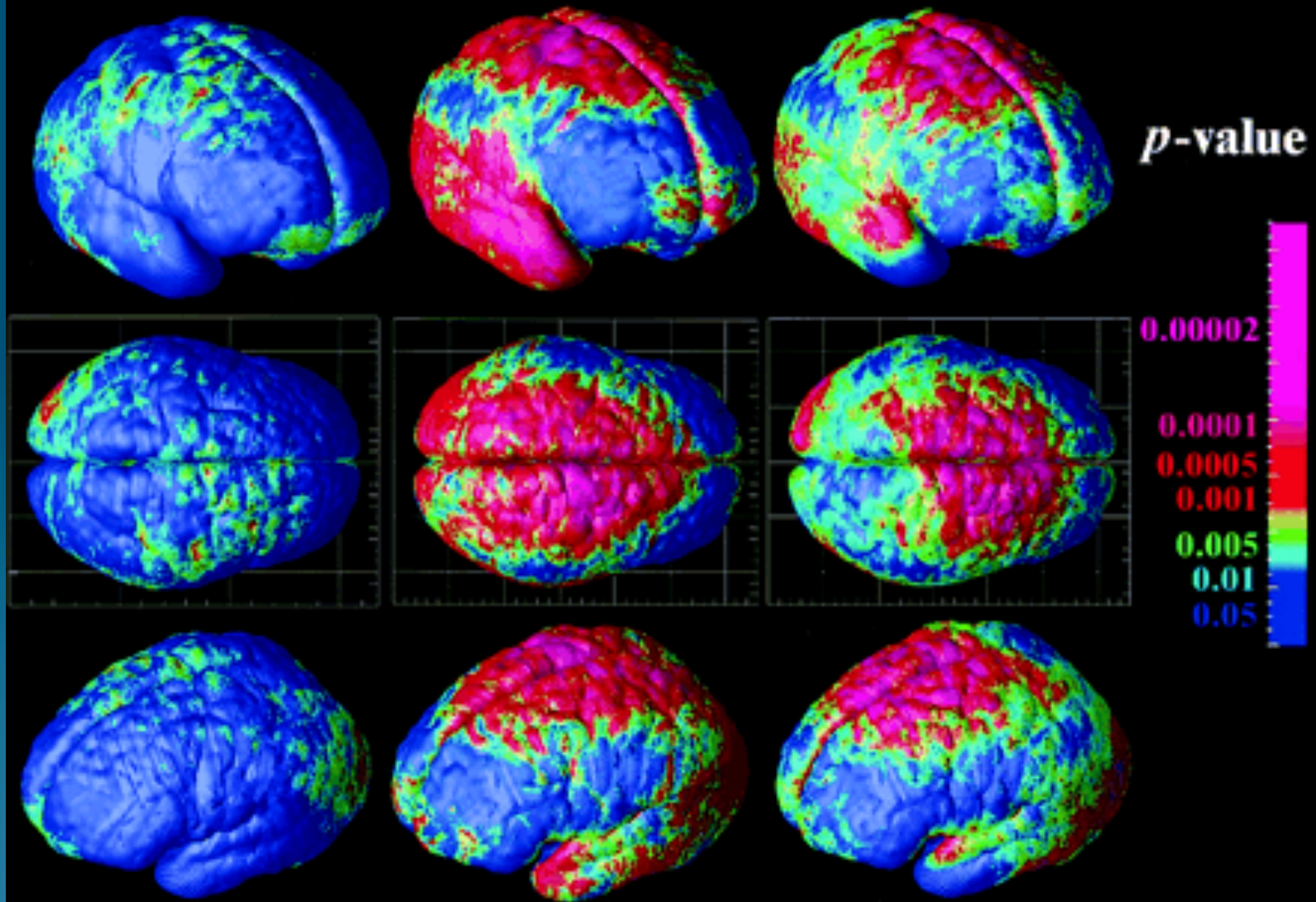
# Early Identification, Targeted Intervention and the Hope for Prevention in Early Psychosis

# *Significant* Progressive Gray Matter **Loss** in Schizophrenia

**NORMAL**

**SCHIZOPHRENIC**

**DIFFERENCE**



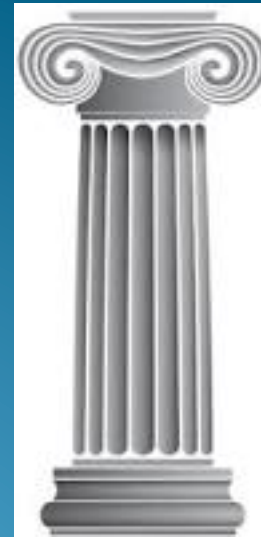
# Prevention



Prediction



Mechanisms of  
Onset

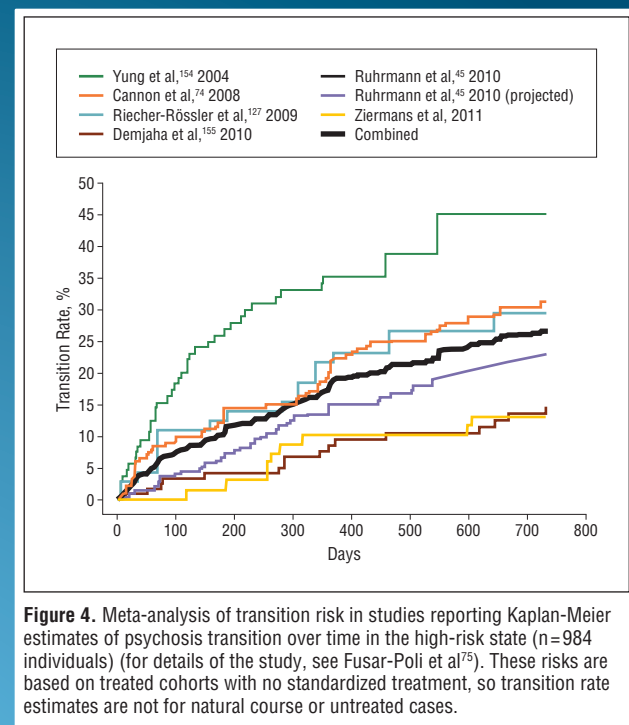
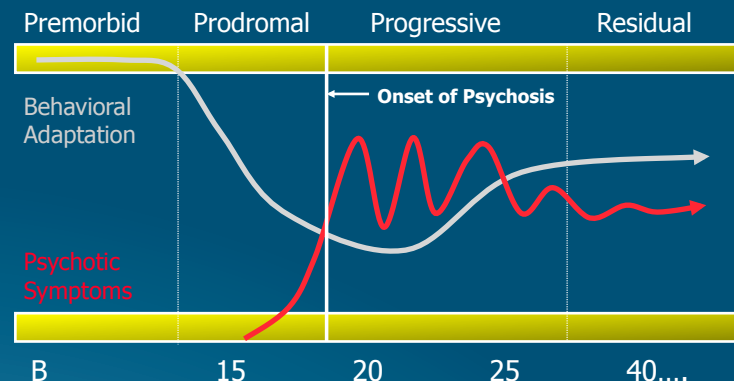


Intervention

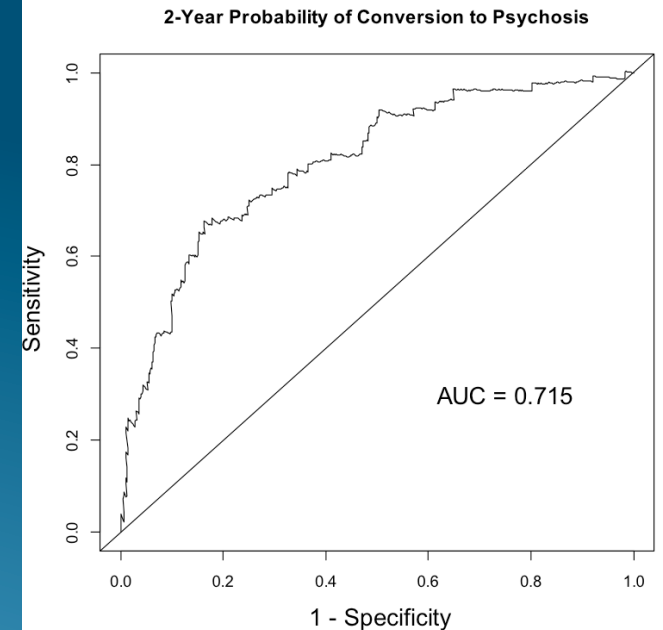
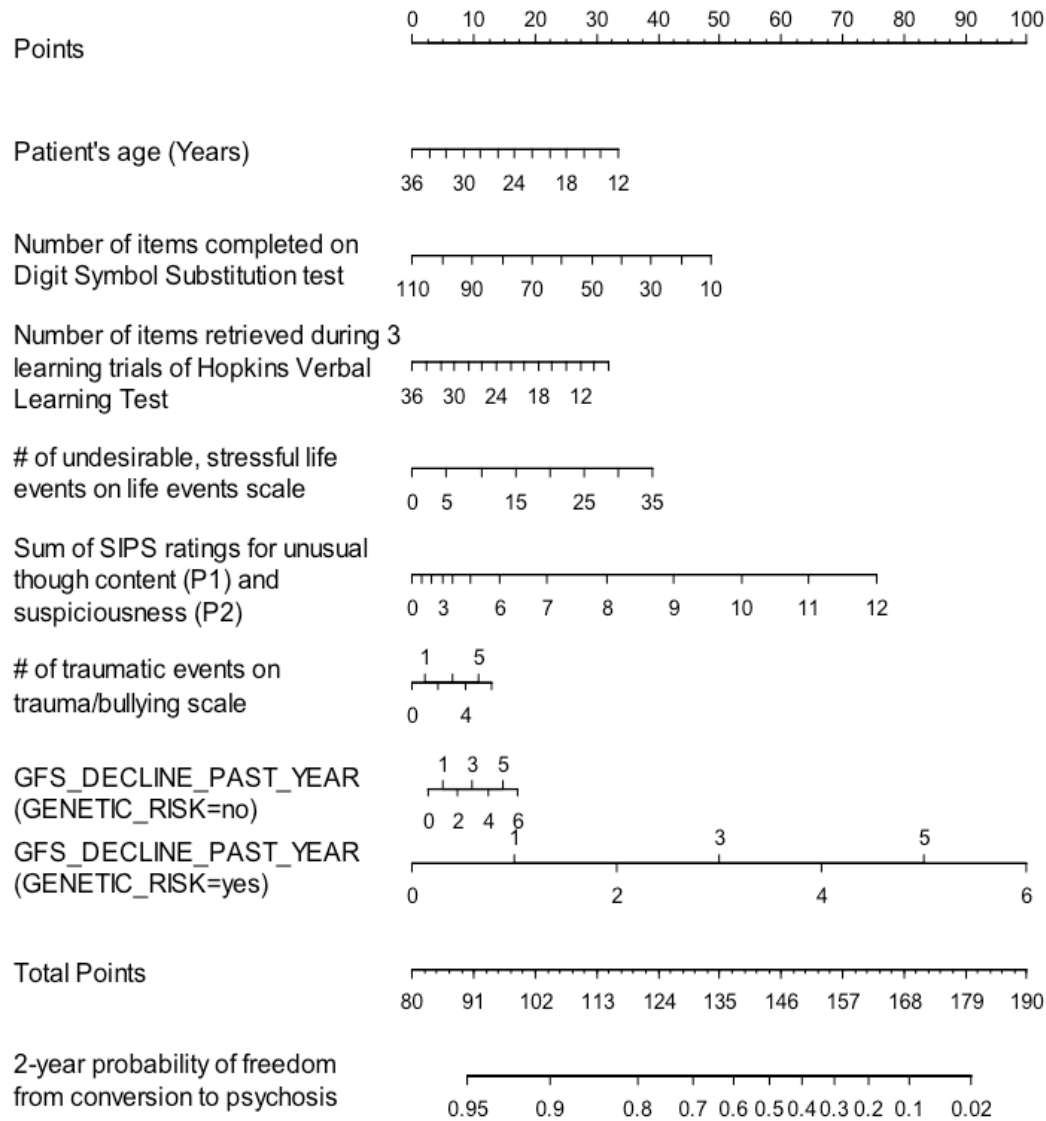


# Clinical High-Risk Paradigm

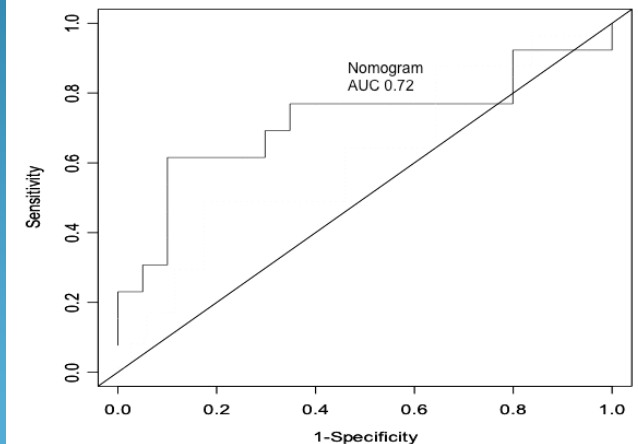
- Clinical high-risk criteria designed to capture population at risk of imminent onset
- Rates of conversion to full psychosis
  - 15% by 1 year
  - 30% by 2 years
- Diagnostic outcomes
  - ~80% schizophrenia spectrum
  - ~20% mood and atypical psychoses



# Nomogram for predicting 2-yr probability of freedom from conversion to psychosis



Breast Cancer Prediction: 17 Clinicians vs. Nomogram on 33 Patients



### Suspected Coronary Artery Disease

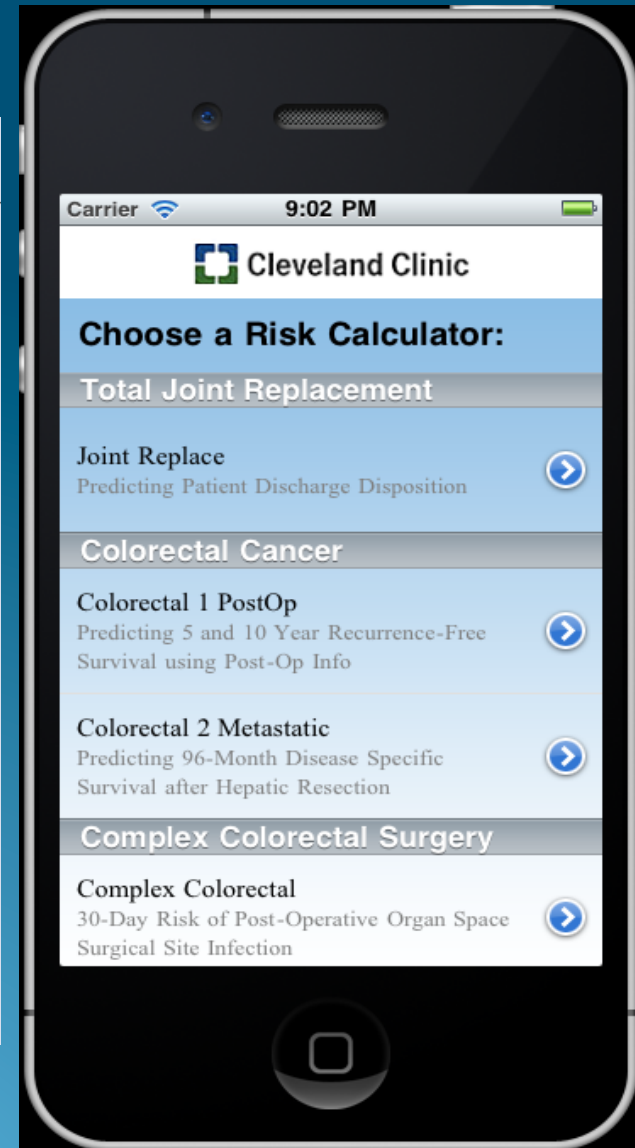
Predicting Long-Term Survival (for suspected patients with a normal electrocardiogram)

Age (years)	<input type="text" value="50"/>	<a href="#">?</a>
Male?	<input type="button" value="Yes"/>	<a href="#">?</a>
Typical Angina Pectoris?	<input type="button" value="Yes"/>	<a href="#">?</a>
Test-Induced Angina Pectoris?	<input type="button" value="No"/>	<a href="#">?</a>
Diabetic?	<input type="button" value="No"/>	<a href="#">?</a>
History of Smoking?	<input type="button" value="Yes"/>	<a href="#">?</a>
Hypertension?	<input type="button" value="No"/>	<a href="#">?</a>
Proportion of Predicted METs Achieved	<input type="text" value="2"/>	<a href="#">?</a>
ST-Segment Depression (mm)	<input type="text" value="1.5"/>	<a href="#">?</a>
Abnormal Heart Rate Recovery	<input type="button" value="Yes"/>	<a href="#">?</a>
Frequent Ventricular Ectopy during Recovery	<input type="button" value="No"/>	<a href="#">?</a>

[?](#)

10-Year Survival Percentage

**97%**





# Biomarkers –Prediction, Mechanism, Personalization

- Neuroimaging (Structural, Functional, DTI, MRS)
- Electrophysiology (MMN, P300, Startle, LTP)
- Neuroendocrine (Cortisol)
- Inflammation/Oxidative Stress
- Neurocognition
- Genetic (DNA, Gene Expression)

# New Studies

- **“NAPLS3”** - Predictors and Mechanisms of Conversion to Psychosis. MH081944-06 (R01) (**Cadenhead, PI**) 10/1/14-9/30/19.
- **“ReGroup”** - Cognitive Behavioral Social Skills Training for Youth at Risk of Psychosis. MH105243-01(R01) (**Cadenhead, PI**)10/1/14-9/30/19
- **“Progresa”** Compensatory Cognitive Training in Clinical High Risk Latino Youth. MH105247-01 (R34) (**Cadenhead, PI**) 10/1/14-9/30/17
- **Inflammatory Biomarkers in First Episode Psychosis: A Mexico/US Collaboration.** MH102374-01(R21) (**Cadenhead, PI**) 5/1/14-4/30/16

# Pilot Studies

- Mindfulness based therapy in early psychosis
- Mu Suppression and Mirror Neuron Circuitry in Early Psychosis
- Neurofeedback in Early Psychosis
- Metabolic measures as predictors of early psychosis
- Visual Contrast Sensitivity in the Prodrome and First Episode of Psychosis
- Duration of Untreated Psychosis
- Co-morbidity of OCD with Prodromal Symptoms
- Cortical Thickness and Neurotoxicity in First Episode

# care

Cognitive Assessment and  
Recovery Enhancement Early  
Psychosis Treatment Program

# Problem

- Incidence of Psychotic Disorders
  - 50/100,000 new cases of psychosis in the US
  - 15/100,000 new cases of schizophrenia per year in the US
  - **1500 new psychosis cases/yr in San Diego County**
- Prevalence of Psychotic Disorders
  - 30/1000 diagnosed with a psychotic disorder in the US
  - 7.2/1000 diagnosed with schizophrenia in the US
  - **San Diego County: 21K schizophrenia, 90K psychosis**
- Concerns:
  - Duration of Untreated Psychosis is 1-2 years in most studies
  - Significant cause of lifetime disability in young adult population
  - Early intervention can improve prognosis, reduce costs
  - **Effective Psychosocial/Pharmacologic Treatment models are not readily available for all patients in Southern California**

# Solution

- UCSD CARE program
  - Comprehensive Assessments and Consultation, Psychosocial Treatments, Pharmacologic Management
- IOP located in shared research space 140 Arbor
  - Prevent hospitalization or as a step down from inpatient
- Staff: Expertise in Psychotic disorders, Psychologists, Psychiatrists, Social Workers, Psychometrists
- Coordination with Inpatient at UCSD and Children's
  - Family intervention and psychoeducation can bridge inpatient and outpatient services
- Coordination of care with clinicians in the community who already refer patients for evaluation, research and consultation.



# International Integrated Programs for Psychosis

- EPPIC (Australia)
  - Emphasis on early detection, low-dose antipsychotic medications, a less restrictive environment, and psychological intervention
  - Symptomatic Remission observed in 37%-59% of the cohort.
- OPUS (Denmark)
  - Integrated treatment with 2 years of specialized, enhanced service
  - Patients in integrated treatment had 3X as many contacts than those in standard care, perceived reduction in family burden and reported less substance use than those in standard care.
- LEO(London)
  - Community outreach with psychosocial interventions
  - Compared to standard care there were fewer hospital re-admissions, relapses and treatment drop-outs

# First Episode Programs in the US/Canada

- **EDAPT (Early Diagnosis and Preventive Treatment)** Sacramento
- **OASIS** – UNC Chapel Hill
- **First Episode and Early Psychosis Program (FEPP)** and **Prevention and Recovery in Early Psychosis (PREP)** at Massachusetts General Hospital.
- **First Episode Clinic - Maryland Psychiatric Research Center** at University of Maryland School of Medicine.
- **First Episode Psychosis Program** at the University of Illinois Medical Center at Chicago
- **Specialized Treatment Early in Psychosis (STEP)** Yale University
- **First Episode Psychosis Program** University of Minnesota
- **The Toronto First Episode Psychosis Program**
- **Early Psychosis Intervention Program** British Columbia
- **RAISE (Recovery After an Initial *Schizophrenia* Episode)** – Multisite NIMH funded community clinics

# OASIS (UNC Chapel Hill)

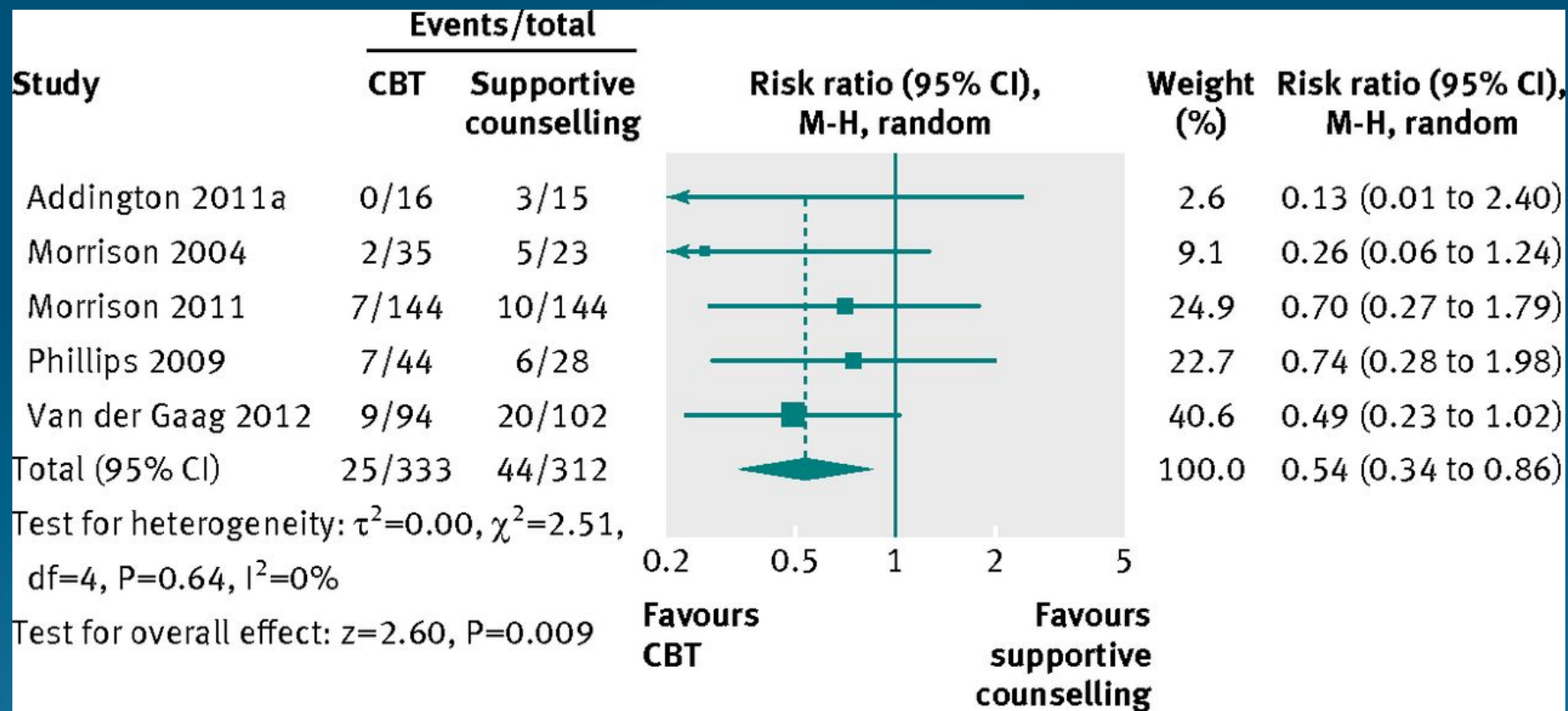
- Clinic Configuration: 70% insured, 20% indigent, 10% self pay
- Budget: 500K - Revenue: 350K plus 200K through state funds
  - 0.4 Administrator
  - 0.6 FTE Family therapist
  - 2 FTE Therapists
  - 1.8 FTE Psychiatrists
  - 0.5 FTE Administrative Assistant
  - 0.25 FTE Nursing Assistant
  - 0.25 Computer support
  - rent, utilities, copier costs, etc
- Clinicians average 25 billable hours/week
- Psychotherapy (CBTSST, stress reactivity, mindfulness, Functional Support, Supported employment/education)
- Psychoeducation
- Family therapy and multifamily groups
- Medication management
- Contracted case management
- Faculty provide services for individual payment

# PREP Clinic (Harvard)

- Clinic Configuration: ~50 young adults (age 16-30)
- Budget: 560K (supported by Department of Mental Health)
  - 0.5 Administrator
  - 2.0 FTE Therapists
  - 0.5 FTE Psychiatrist/Medical director adult and adolescent
  - 1.8 FTE clinical social worker
  - 1.0 FTE Psychologist
  - 0.75 FTE Advanced practice psychiatric nurse
  - 1.0 FTE milieu workers
  - 0.5 FTE Peer receptionist
  - Residents, psychology trainees social work intern
- Twice weekly group therapy
- Family education, treatment and support
- Preventive physical health and self-care
- Cognitive remediation and enhancement of social cognition
- Promotion of medication adherence, early initiation of decanoate, early consideration of clozapine
- Empirically supported psychotherapy
- Substance misuse treatment

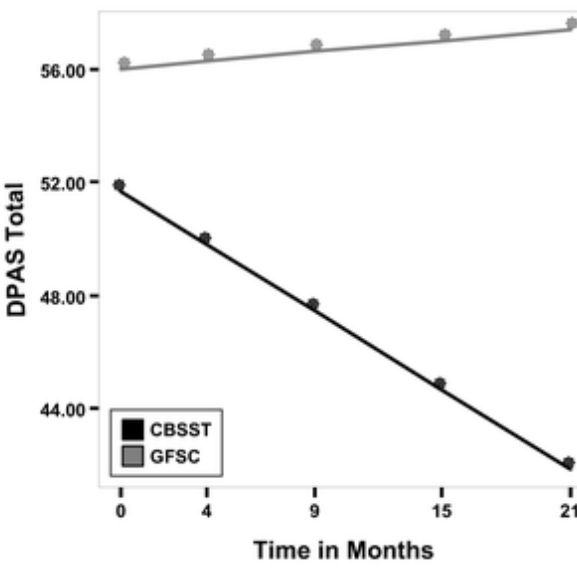
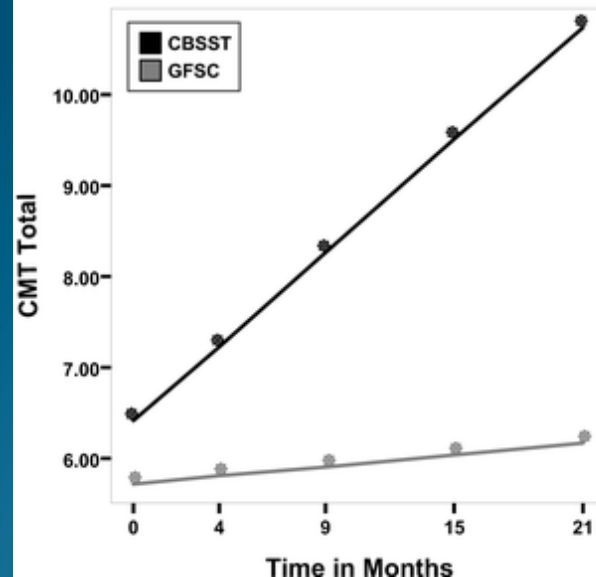
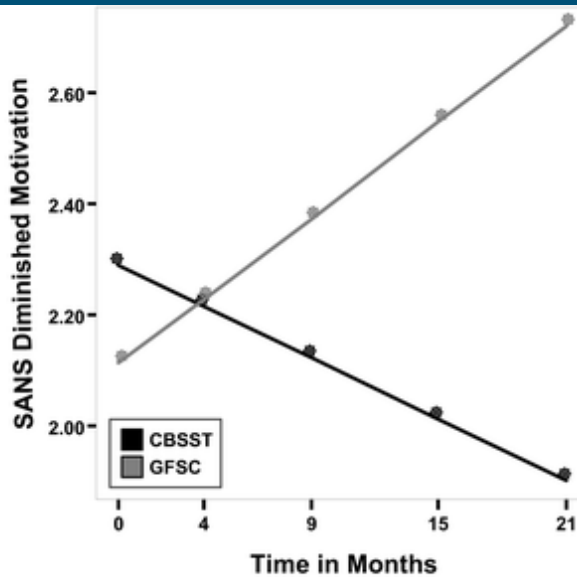
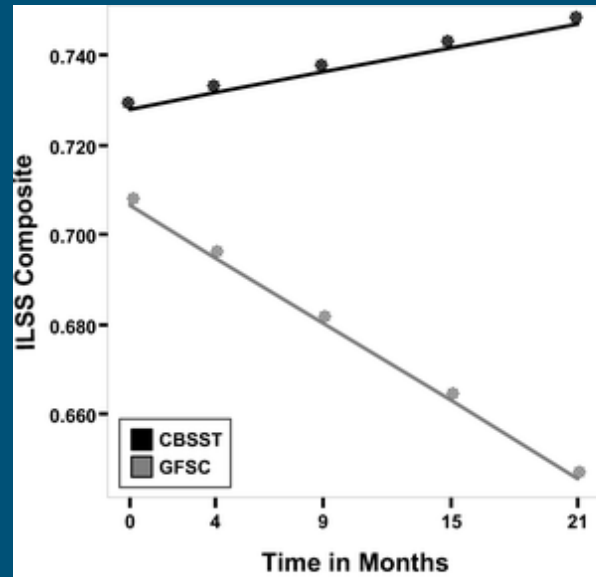
# Evidence Based Treatment for Early Psychosis

# Cognitive Behavioral Therapy versus Supportive Therapy and Prevention of Psychosis



*Early interventions to prevent psychosis: systematic review and meta-analysis*  
 Stafford MR et al BMJ 2013; 346





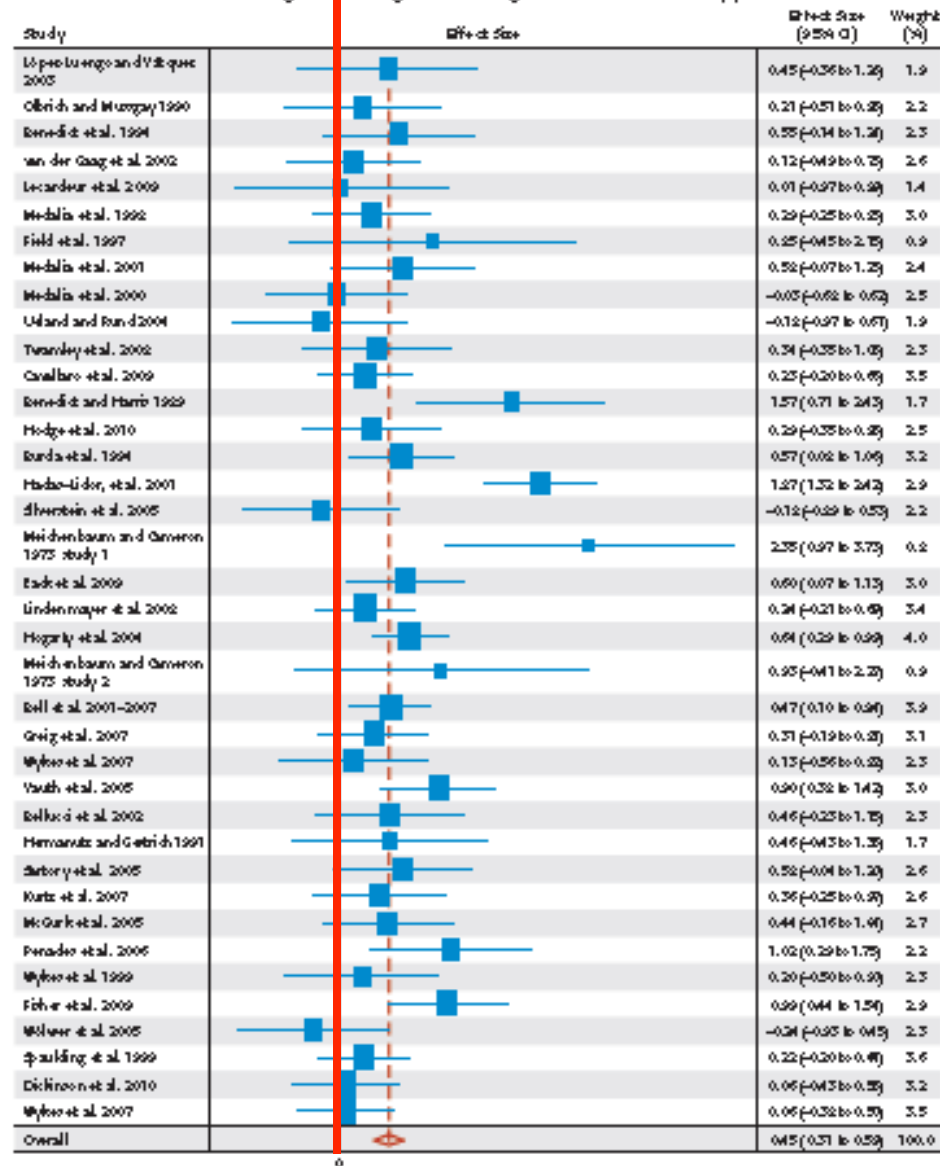
Randomized clinical trial of cognitive behavioral social skills training for schizophrenia: Improvement in functioning and experiential negative symptoms.

[Granholm, et al. Journal of Consulting and Clinical Psychology 82.6 \(Dec 2014\): 1173-1185.](#)

Worse

Better

FIGURE 1. Forest Plot of Global Cognition Among Studies in Cognitive Remediation Therapy\*



\* studies are listed by their clinical trial assessment measure scores (Table 1) in ascending order.

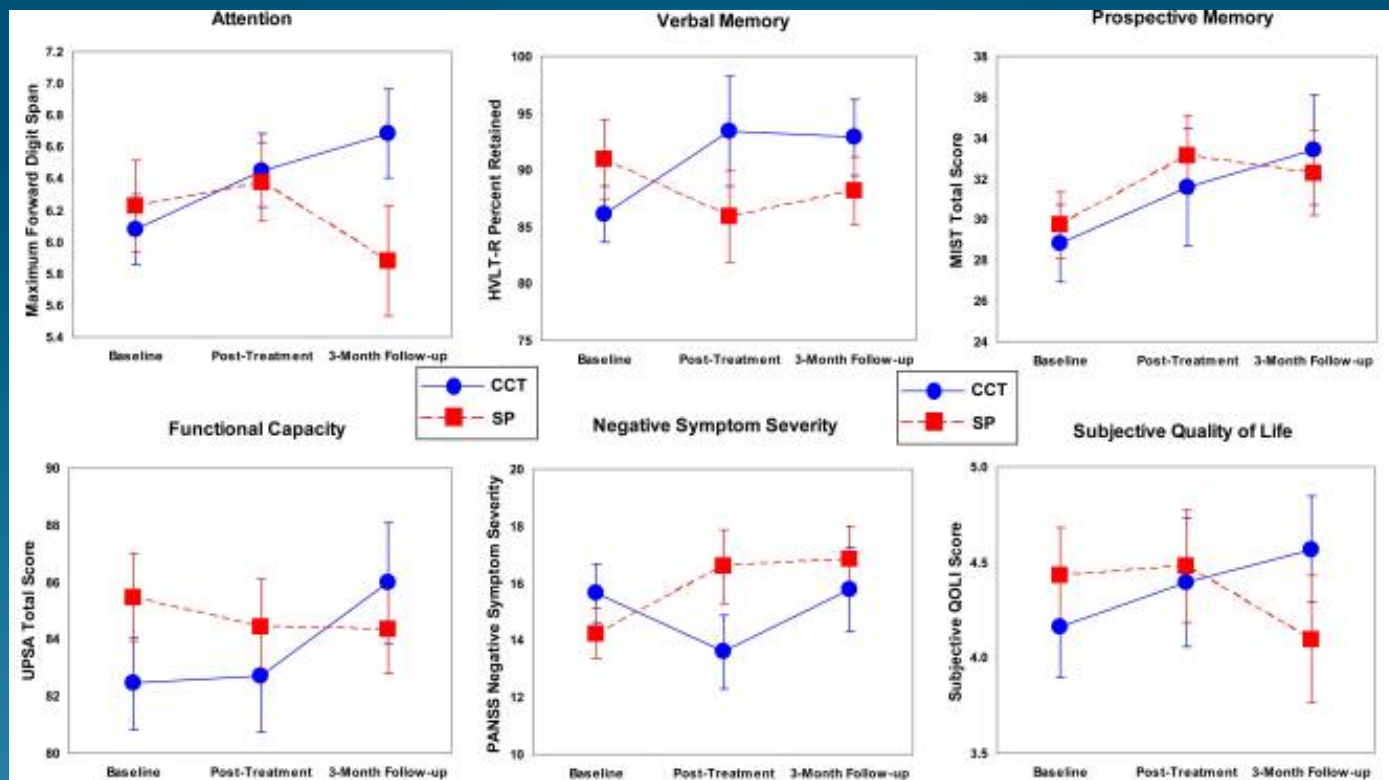
Efficacy of Cognitive remediation in schizophrenia

Til Wykes et al Am J psychiatry 2011

The meta-analysis (2,104 participants) yielded durable effects on global cognition and functioning.

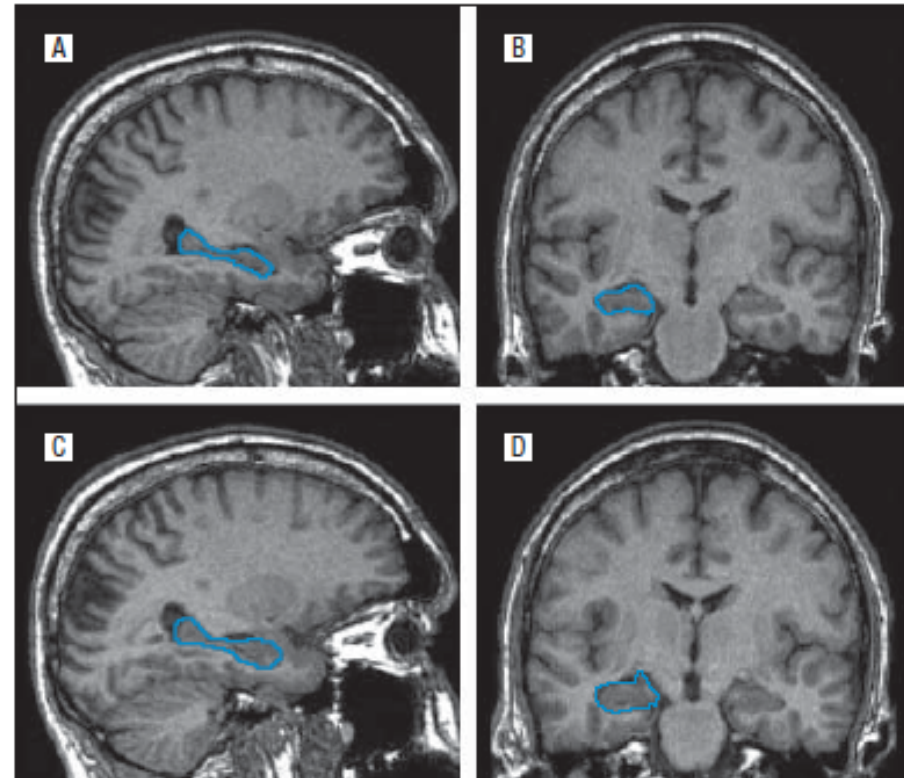
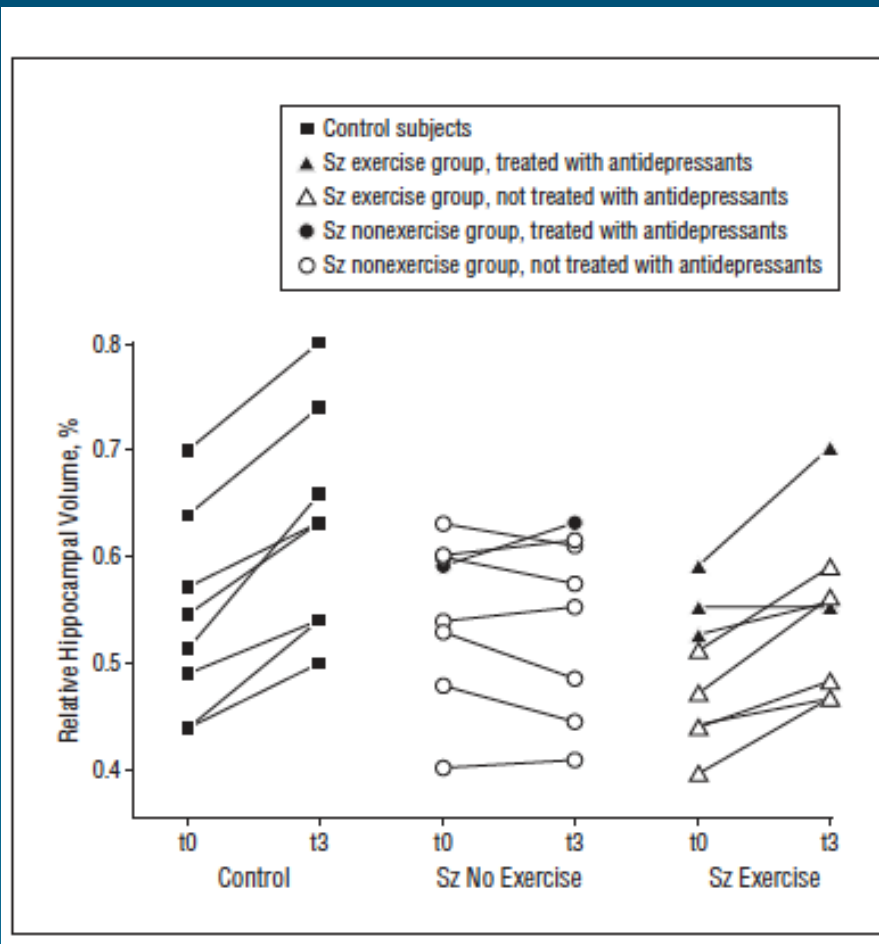
# Compensatory Cognitive Training for Psychosis: Effects in a Randomized Controlled Trial

Elizabeth W. Twamley et al, J Clin Psychiatry. 2012 Sep; 73(9): 1212–1219.



Note. CCT = Compensatory Cognitive Training; HVL-T-R = Hopkins Verbal Learning Test-Revised; MIST = Memory for Intentions Screening Test; PANSS = Positive and Negative Syndrome Scale; QOLI = Quality of Life Interview; SP = Standard Pharmacotherapy; UPSA = UCSD Performance-based Skills Assessment

# Exercise increases hippocampal volume and improves verbal learning in patients with schizophrenia



# CARE Early Psychosis Treatment Program

- Clinical consultation
- Diagnostic assessment
- Neuropsychological assessment and evaluation
- Pharmacologic management including complimentary medicine
- Intensive Outpatient Treatment (M,W,F 9:00-3:00)
- Individual and group psychotherapy (cognitive behavioral, social skills)
- family therapy
- psychoeducation
- lifestyle counseling
- mindfulness
- cognitive remediation
- case management
- supported employment/education
- research opportunities



# CARE Program



Isabel Domingues, MD  
Psychiatry Resident



Kristin Cadenhead, MD



Heline Mirzakhanian, PhD



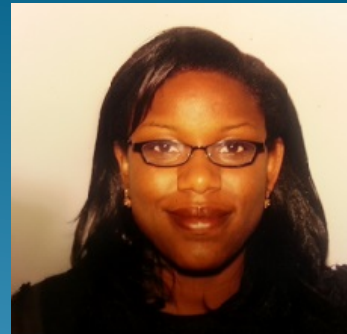
Kathleen Shafer



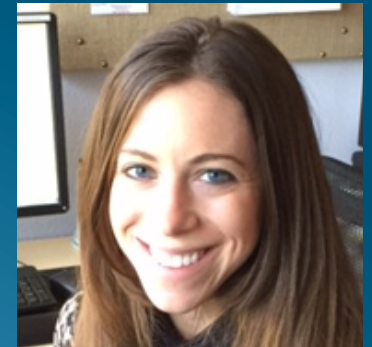
Sara Hansen, MD  
Psychiatry Resident



Clara Robles, MFT



Teela Davis, MSW



Lauren Stern, MSW



Manju Ilipakurti, MD  
Psychiatry Resident



Amedeo Minichino, MD  
Visiting Scholar



Marta Francesconi  
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COGNITIVE ASSESSMENT AND RISK EVALUATION

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