

Recovery After an Initial Schizophrenia Episode (RAISE): A Research Project of the NIMH

RAISE

A Research Project of the NIMH
 Early Treatment Program

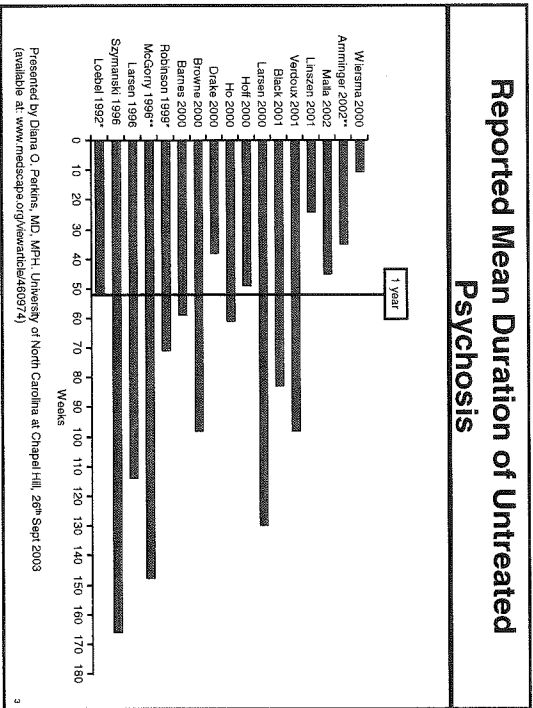
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 The Zucker Hillside Hospital/Hofstra University

John M. Kane Disclosures 2015

Dr. Kane has been a consultant for Alkermes, Eli Lilly, EnVivo Pharmaceuticals (Forum), Forest, Genentech, H. Lundbeck, Intracellular Therapeutics, Janssen Pharmaceutica, Johnson and Johnson, Otsuka, Reviva, Roche and Sunovion

Dr. Kane has received honoraria for lectures from Janssen, Genentech, Lundbeck and Otsuka

Dr. Kane is a Shareholder in MedAvante, Inc. and Vanguard Research Group



Implications of Delayed Treatment

- Greater decrease in functioning
- Loss of educational opportunities
- Impaired psychosocial and vocational development
- Personal suffering/family burdens
- Potential poorer response once treatment is provided
- Greater costs

A Systematic Review and Meta-analysis of Recovery in Schizophrenia

Elhan Jaskashvili^{1,2*}, Patricia Singh¹, Noreen Elthorpe³, John J. McGuffin⁴, Sushmita Saha¹, Shafiq Ishtiaque¹, Julia Vargish¹, and Ananda Mukhopadhyay^{5,6}

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Conclusions:

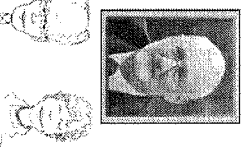
Based on the best available data, approximately 1 in 7 individuals with schizophrenia met our criteria for recovery. Despite major changes in treatment options in recent decades, the proportion of recovered cases has not increased

Jaskashvili et al. Schizophr Bull 2013;39(6):1296-1306

Timeline

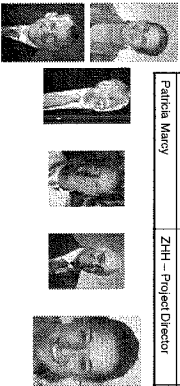
- NIMH Issues Request for Proposals June 2008
- Contract Awarded July 2009 (bolstered by funds from the American Recovery and Reinvestment Act of 2009)
- Enrollment Begins July 2010
- Enrollment Ends July 2012
- Last Patient In Reaches Two Years July 2014

RAISE-ETP: Executive Committee

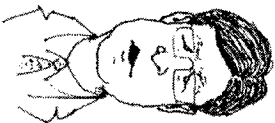


John Kane — Principle Investigator	The Zucker Hillside Hospital (ZHH)
Debra Robinson	ZHH
Nina Schindler	SUNY Downstate
Jean Adlington	University of Calgary
Sue Estroff	UNC
Christoph Correll	ZHH
Kim Mueser	Boston University
David Perrin	UNC
Robert Rosenheck	Yale University
Rachita Mory	ZHH — Project Director

ETP—early treatment program



Principal NIMH Collaborators



- Robert Heinssen
- Susan Azrin
- Amy Goldstein



Specified Aims of RAISE

- Develop a comprehensive and integrated intervention to
 - Promote symptomatic recovery
 - Minimise disability
 - Maximise social, academic, and vocational functioning
- **Be capable of being delivered in real-world settings utilising current funding mechanisms**
- Assess the overall clinical impact and cost-effectiveness of the intervention as compared to currently prevailing treatment approaches
 - **Conduct the comparison in non-academic, real-world community treatment settings in the United States**

RAISE Trial Design: Subjects

- Sample size: 404
- Age 15-40
- The following diagnoses are included in the differential
 - schizophreniform disorder
 - schizophrenia
 - schizoaffective disorder
 - psychotic disorder NOS
 - brief psychotic disorder
- Less than six months of treatment with antipsychotic medications

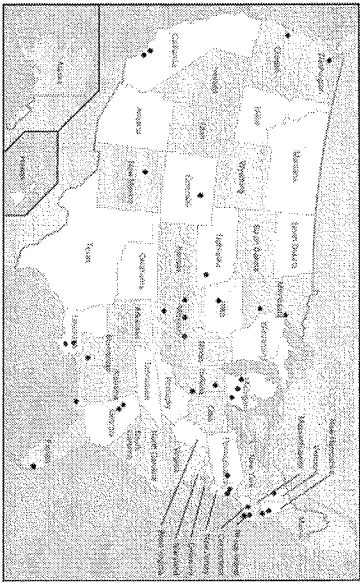
Tread softly because you tread on my dreams.

W.B. Yeats

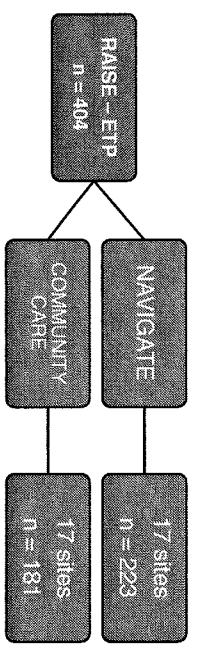
Randomized Controlled Trial (RCT)

- RCT to compare
 - NAVIGATE – experimental intervention
 - Community Care – treatment as offered in local clinics in the United States
- Cluster/site randomization of 34 sites in 21 states
- Two-year treatment period
- Assessment model includes
 - On-site recruitment, engagement and retention
 - Remote assessors of primary and secondary clinical outcome

**Conduct the Comparison in Non-academic, United States Community Treatment Settings
ETP Sites are in 21 US Contiguous States**



RAISE-ETP Study Design with Cluster/Site Randomization



Addressing the Problem of Masking Assessments

- Rigorous RCTs demand unbiased and therefore masked or blinded assessment
 - Masked Assessors at the site
 - Requires training of many assessors and insuring reliability over time
 - Needs oversight to insure masking is maintained
 - Masked, remote assessors
 - Clinical evaluators trained to determine diagnosis and evaluate symptoms and functional status
 - Insures that assessments are consistent across sites and treatment condition
 - Masked to which sites are in which treatment condition and what treatment participants are receiving
 - Participants are interviewed over live and secure two-way video connection

RAISE Trial: Outcomes

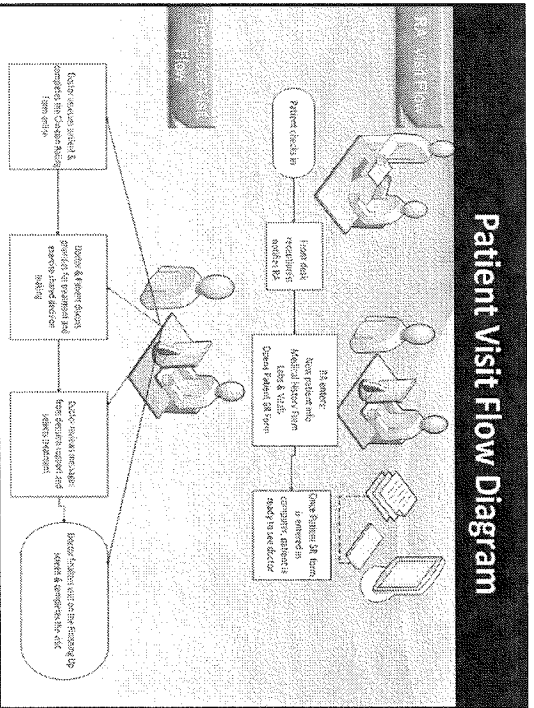
- Primary outcome measure: Quality of Life scale
 - Primary hypothesis
 - RAISE intervention compared to community care will improve Quality of Life
- Other measured outcomes
 - Service utilization
 - Cost
 - Consumer perception
 - Prevention of relapse
 - Enhanced recovery

Navigate

- Team based
- Shared decision-making
- Strength & resiliency focus
- Psychoeducational teaching skills
- Motivational enhancement teaching skills
- Collaboration with natural supports
- Four components
 - Psychopharmacology – COMPASS
 - Individual Resiliency Training (IRT)
 - Family psychoeducation
 - Supported employment/education

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Patient Visit Flow Diagram



COMPASS

A computer decision support system to facilitate patient provider communication and medication choice within a **shared decision making** framework.

A Web-Based application available on Desktops, Laptops or iPad

Patient Self Report Form

RAISE	Self Report Questions
<p>1. How often do you experience the following symptoms? 1 = Never, 2 = Rarely, 3 = Sometimes, 4 = Often, 5 = Always</p>	<p>1. I feel that my medication is helping me feel better. <input type="checkbox"/> Yes, about every day <input type="checkbox"/> No, I haven't had any problems</p>
<p>2. How often do you experience the following symptoms? 1 = Never, 2 = Rarely, 3 = Sometimes, 4 = Often, 5 = Always</p>	<p>2. I feel that my medication is making me feel worse. <input type="checkbox"/> Yes, I have had problems <input type="checkbox"/> No, I have not had any problems</p>
<p>3. How often do you experience the following symptoms? 1 = Never, 2 = Rarely, 3 = Sometimes, 4 = Often, 5 = Always</p>	<p>3. I feel that my medication is making me feel worse. <input type="checkbox"/> Yes, I have had problems <input type="checkbox"/> No, I have not had any problems</p>
<p>4. How often do you experience the following symptoms? 1 = Never, 2 = Rarely, 3 = Sometimes, 4 = Often, 5 = Always</p>	<p>4. I feel that my medication is making me feel worse. <input type="checkbox"/> Yes, I have had problems <input type="checkbox"/> No, I have not had any problems</p>
<p>5. How often do you experience the following symptoms? 1 = Never, 2 = Rarely, 3 = Sometimes, 4 = Often, 5 = Always</p>	<p>5. I feel that my medication is making me feel worse. <input type="checkbox"/> Yes, I have had problems <input type="checkbox"/> No, I have not had any problems</p>

Little red boxes indicate items not yet addressed

Clinician Rated Form Includes Information From Patient Self-Rated Form On Corresponding Items And Adjusts The Prompt Questions Accordingly

1 Depressed Mood
 I've been depressed in the past 6 months (60) (not rate symptoms influence or severity noted here - only mood likely to associated with a certain emotional feeling)

Patient did not endorse 'depressed' mood on self-report
 You start on the questionnaire that you care and all your questions about being depressed, sad, or down. Any questions not being answered (filling) for likely 60% of 45% grade for the presence of depressed mood.

Not reported

- Very Mild: occasionally feels sad or down - at questionnaire cannot interpret
- Mild: occasionally feels moderately depressed or often feels sad or down
- Moderate: occasionally feels very depressed or often feels moderately depressed
- Moderately Severe: often feels very depressed
- Severe: feels very depressed most of the time
- Very Severe: constant and/or nearly constant feelings of depression

Unable to assess if a subject endorsement is in the

2 Anxiety / Worried
 Subjective experience of worry, apprehension, concern, or concern for the future (60) (not rate symptoms influence or severity noted here - only mood likely to associated with a certain emotional feeling)

Patient endorsed anxious mood on self-report
 You start on the questionnaire that you care and all your questions about being depressed, sad, or down. Any questions not being answered (filling) for likely 60% of 45% grade for the presence of depressed mood.

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Demographics Adjusted for Cluster Design

	NAVIGATE	Community Care	p-value
Age and Gender			
Age (mean)	23.5	23.2	
Males (%)	77.6	66.2	.05
Race			
White (%)	65.9	49.9	
African American (%)	25.4	44.1	
Other (%)	8.7	6.0	
Role Functioning			
In school (%)	14.9	25.5	.03
Working (%)	12.6	16.6	
Prior Hospitalization (%)	76.2	81.6	.05

Clients' Baseline Characteristics

Figure 1: Clients' Baseline Characteristics

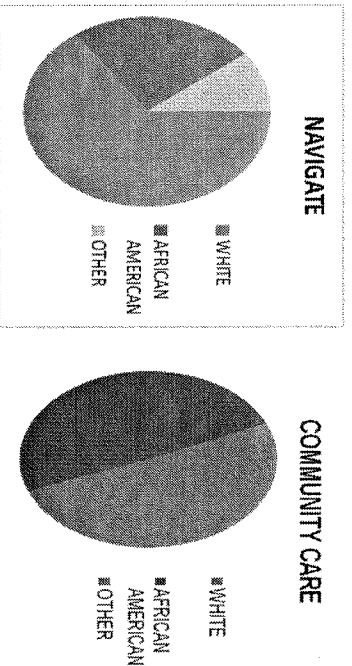
Figure 2: Clients' Baseline Characteristics

Figure 3: Clients' Baseline Characteristics

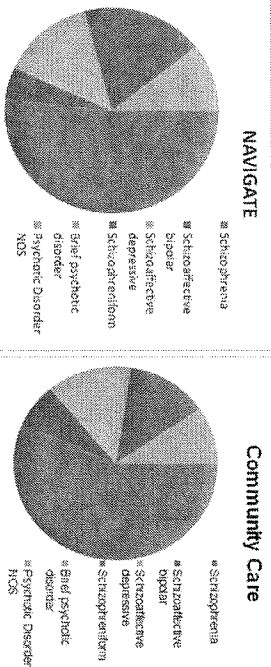
Figure 4: Clients' Baseline Characteristics

Figure 5: Clients' Baseline Characteristics

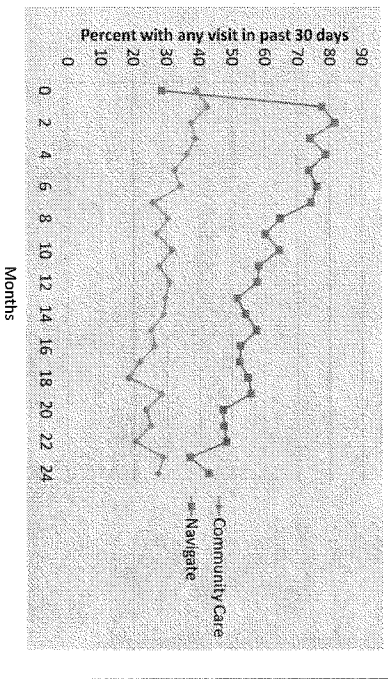
RAISE ETP Demographics – RACE (p<0.0001)



Baseline Diagnoses Adjusted for Cluster Design

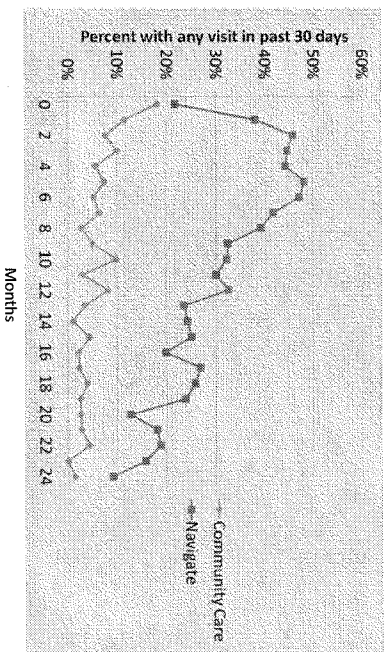


Have You Had Individual Sessions with a Mental Health Provider Who Helps You Work on Your Goals and Look Positively Towards the Future? (%)

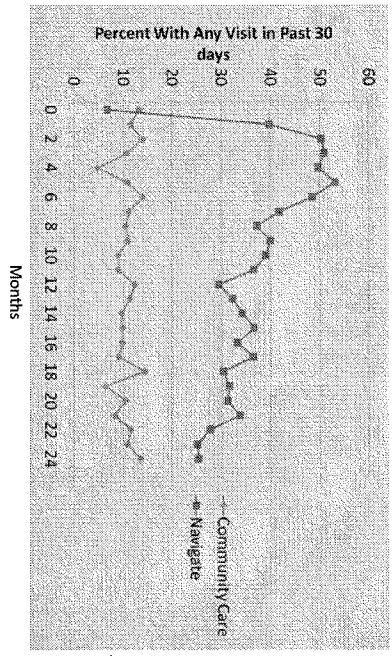


Clients' Perceptions of Treatment

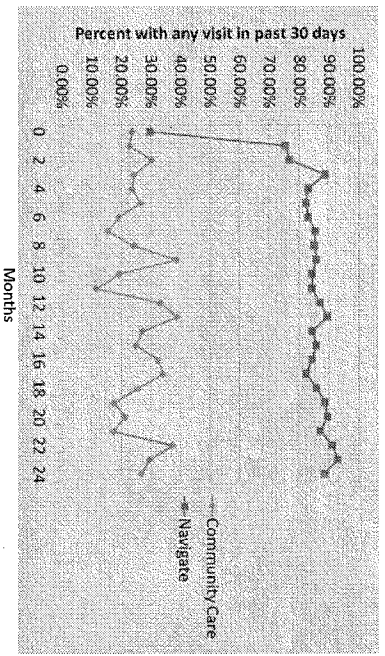
Has Your Family Met With a Mental Health Provider to Help Them Understand and Address Your Situation? (%)



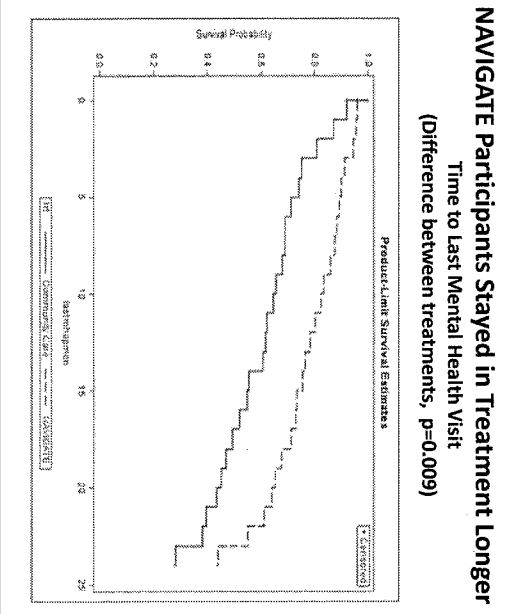
Have You Met With a Person Who is Helping You Get a Job in the Community or Furthering Your Education? (%)



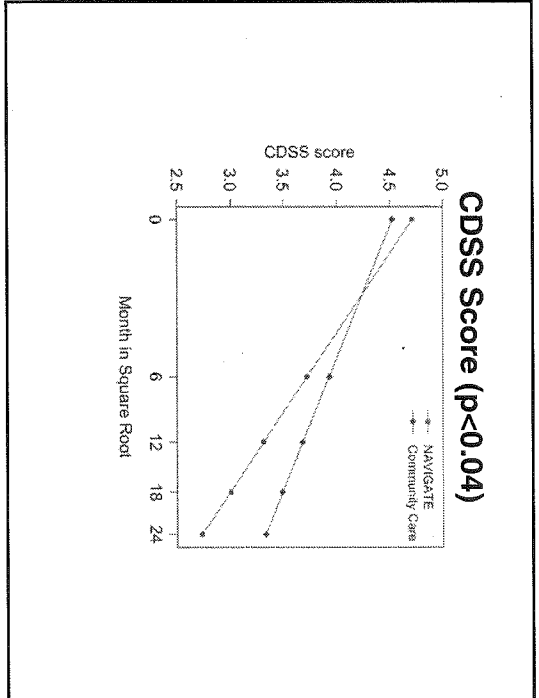
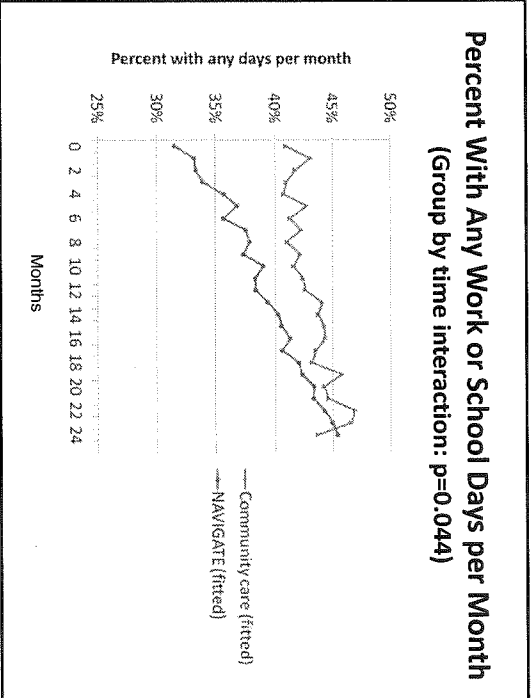
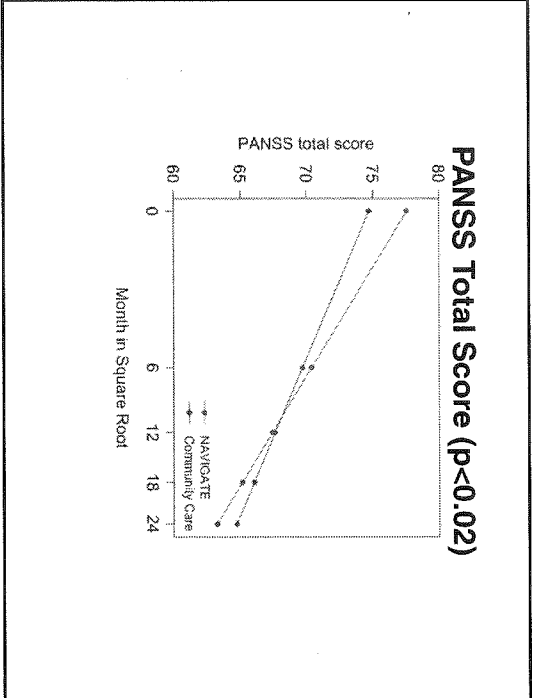
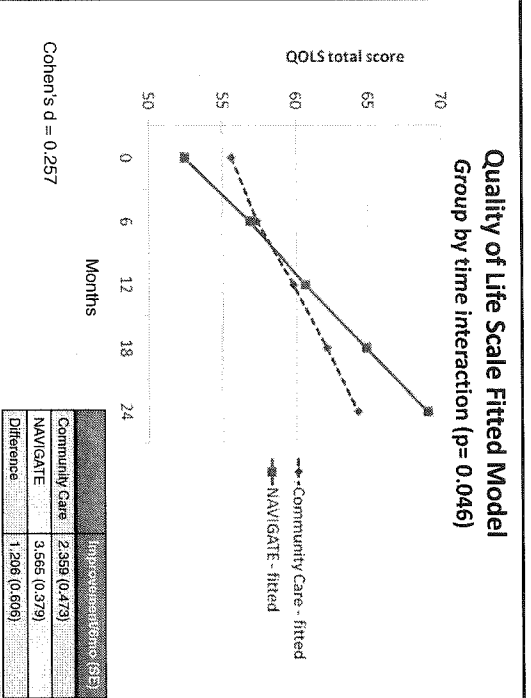
Were You Asked to Record Your Symptoms and Side Effects Before You Met With Your Psychiatrist or Nurse Practitioner? (% among responders: 44% in CC, 65% in N)



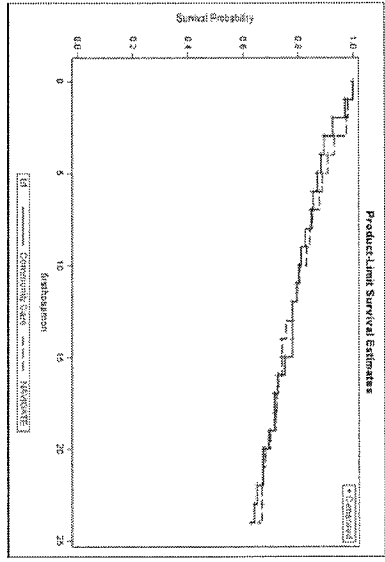
Major Study Outcomes



NAVIGATE Participants Stayed in Treatment Longer Time to Last Mental Health Visit (Difference between treatments, p=0.009)

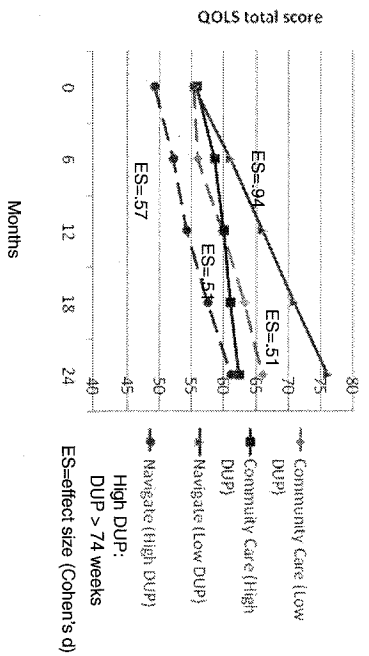


Time to First Psychiatric Hospitalization
 (Difference between treatments, p=0.75)

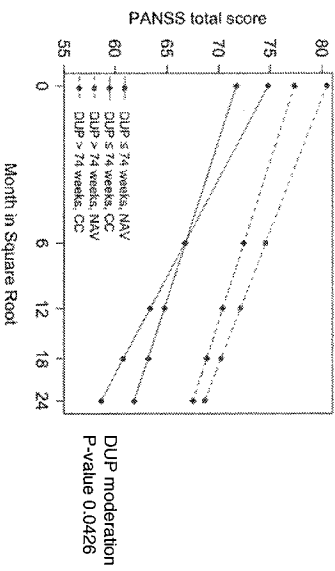


Predictors of Outcome

Quality of Life Scale: Effects of Shorter vs Longer Duration of Untreated Psychosis (DUP; p<0.03)



Moderation of PANSS Total Score by DUP



Acknowledgements

We are grateful to all of our core collaborators and consultants.

We thank and acknowledge the terrific work of many clinicians, research assistants and administrators at the participating sites.

We are very grateful for the participation of the hundreds of patients and families who made the study possible with their time, trust and commitment.

Community Mental Health Center of Lancaster County
Clinton-Eaton-Ingham Community Mental Health Authority
North Point Health and Wellness Park Center
PeaceHealth Oregon
Pine Bluff Mental Health Center
The Providence Center
River Parish Mental Health Center
St. Clare's Hospital
South Shore Mental Health Center
Terradome Mental Health Center
Cherry Street Health Services
UMKC School of Pharmacy
Starr Clinia Mental Health Center
San Fernando Mental Health Center
United Services
Center for Rural and Community Behavior Health New Mexico
Staten Island University Hospital

With Thanks to Our 34 Sites: Clinicians and Participants

Burrell Behavioral Health- Springfield
Burrell Behavioral Health- Columbia
Catholic Social Services of Washitawak County (CSSW)
Cobb County
Places for People
Community Mental Health Center, Inc. Evely Ball
Grady Health System
Greater Nashua Mental Health Center @ Community Council
Henderson Behavioral Health
Howard Center
Human Development Center
Lehigh Valley Hospital
Life Management Center of Northwest Florida
Mental Health Center of Denver
The Mental Health Center of Greater Manchester

Conclusions

- Recipients of NAVIGATE were significantly more likely to remain in treatment and experienced significantly greater improvement in the primary outcome measure (i.e., quality of life).
- They were more likely to be working or going to school.
- NAVIGATE participants showed a significantly greater degree of symptom improvement on PANSS and CDSS.
- DUP appears to be an important moderator of NAVIGATE effectiveness.
- These results show that a coordinated specialty care model can be implemented in a diverse range of community clinics and that the quality of life of first episode patients can be improved.

Hospitalization Rates in Controlled Trials of Comprehensive Care in FE Individuals

Study	Length of Trx	Hospitalization Rates During Follow-Up Interval	
		Experimental Intervention	TAU
RAISE-ETP (1)	24 months	34%	37%
STEP (2)	12 months	23%	44%
LEO (3)	15 months	33%	51%
OPUS (year 1) (4)	1-12 months	59%	71%
OPUS (year 2) (5)	13-24 months	26%	39%