ORIGINAL RESEARCH

The RAISE Early Treatment Program for First-Episode Psychosis: Background, Rationale, and Study Design

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ABSTRACT

Objective: The premise of the National Institute of Mental Health Recovery After an Initial Schizophrenia Episode Early Treatment Program (RAISE-ETP) is to combine state-of-the-art pharmacologic and psychosocial treatments delivered by a well-trained, multidisciplinary team in order to significantly improve the functional outcome and quality of life for first-episode psychosis patients. The study is being conducted in non-academic (ie, real-world) treatment settings, using primarily extant reimbursement mechanisms.

Method: We developed a treatment model and training program based on extensive literature review and expert consultation. Our primary aim is to compare the experimental intervention to "usual care" on quality of life. Secondary aims include comparisons on remission, recovery, and cost-effectiveness. Patients 15-40 years old with a first episode of schizophrenia, schizoaffective disorder, schizophreniform disorder, psychotic disorder not otherwise specified, or brief psychotic disorder according to DSM-IV and no more than 6 months of treatment with antipsychotic medications were eligible. Patients are followed for a minimum of 2 years, with major assessments conducted by blinded, centralized raters using live, 2-way video. We selected 34 clinical sites in 21 states and utilized cluster randomization to assign 17 sites to the experimental treatment and 17 to usual care. Enrollment began in July 2010 and ended in July 2012 with 404 subjects. The results of the trial will be published separately. The goal of the article is to present both the overall development of the intervention and the design of the clinical trial to evaluate its effectiveness.

Conclusions: We believe that we have succeeded in both designing a multimodal treatment intervention that can be delivered in real-world clinical settings and implementing a controlled clinical trial that can provide the necessary outcome data to determine its impact on the trajectory of early phase schizophrenia.

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sychotic disorders such as schizophrenia are associated with enormous personal suffering, disability, family burden, and societal cost. The course is most often chronic, and recovery rates have been disappointingly low.^{1,2} Several single-element interventions (eg, pharmacotherapy,³ cognitive-behavioral therapy,⁴ family work,⁵ and supported employment⁶) have been shown to be effective at least over the short term. Although a number of innovative and integrated first-episode programs have been implemented,⁷⁻¹¹ there are remarkably few prospective, randomized controlled trials comparing a multimodal, multidisciplinary team approach to usual care.¹²⁻¹⁶ Such a study has never been conducted in the United States in real-world community clinics under extant reimbursement constraints. Even though academic centers play a key role in developing and testing new treatment strategies, unless such strategies can be implemented in typical, non-academic settings, it would be difficult to provide the necessary access and sustainability for the general population across the United States.

The National Institute of Mental Health (NIMH) issued a Request for Proposals entitled "Recovery After an Initial Schizophrenia Episode (RAISE)" in June 2008. The goal of the NIMH initiative is to change the trajectory and prognosis of first-episode psychosis (FEP). The premise is that by combining state-of-the-art pharmacologic and psychosocial treatments in a patient-centric fashion and having them delivered by a well-trained and coordinated, multidisciplinary team, the functional outcome and quality of life for first-episode patients treated in the community can be significantly improved.^{17,18} The specified aims of RAISE are, first, to develop a comprehensive and integrated intervention designed to promote symptomatic recovery, minimize disability, maximize social academic and vocational functioning, and be capable of being delivered in real-world settings utilizing current funding mechanisms and, second, to assess the overall clinical impact and cost-effectiveness of the intervention as compared to currently prevailing treatment approaches and to conduct the comparison in non-academic, real-world community treatment settings in the United States.

To respond to the NIMH requirements and achieve the desired goals, we assembled a leadership group representing expertise in early intervention and detection, psychosocial treatment, psychopharmacology, clinical trials, health economics, health policy, biostatistics, medical anthropology, and service system administration. In addition, we consulted with a range of experts including consumers, family members, advocacy groups, and state and federal governmental officials. The contract was awarded in July 2009, bolstered by funds from the American Recovery and Reinvestment Act of 2009.

In this report, we provide a description of the overall design of the research project, the RAISE Early Treatment Program (RAISE-ETP), and a discussion of the rationale for certain key decisions including

site selection, randomization strategy, and approach to assessment and analysis. The goal was to develop a treatment model and training program that would allow us to engage a broad range of clinics across the United States without prior experience or specialized programs for patients with FEP. We also sought a diverse group of sites from both a geographic and a demographic perspective so that the results would be as generalizable as possible. Ultimately, an important objective is to provide data-driven recommendations to the NIMH, health care policy makers, payers, and other stakeholders on how care for individuals experiencing a first episode should be delivered.

METHOD

Specific Aims

Our primary aim is to compare the impact of a multimodal, multidisciplinary team-based approach for FEP treatment to care usually delivered in community treatment settings ("usual care") on quality of life in a large, practical clinical trial. Secondary aims include comparisons with regard to remission, recovery, and cost-effectiveness.

Subjects

Inclusion criteria were (1) age of 15–40 years; (2) ability to participate in research assessments in English; (3) ability to provide fully informed consent (assent for those under 18); and (4) presence of definite psychotic symptoms and evidence that one of the following is included in the differential diagnosis: schizophrenia, schizoaffective disorder, schizophreniform disorder, psychotic disorder NOS, or brief psychotic disorder (according to DSM-IV).¹⁹ Exclusion criteria were kept to a minimum: patients were excluded who had clearly experienced more than 1 discrete psychotic episode; had a diagnosis of bipolar disorder, psychotic depression, substance-induced psychotic disorder, or current psychotic disorder due to a general medical condition; had neurologic disorders that would affect diagnosis or prognosis; or had clinically significant head trauma or other serious medical conditions that would significantly impair assessment, functioning, or treatment and thus make the patient unsuitable for the trial. To achieve a practical balance between proximity to first treatment with antipsychotic medication and feasibility to recruit an adequate sample with the budget available, we allowed patients with up to 6 months of cumulative exposure to antipsychotic medications to enter the trial. Subjects were recruited from inpatient and outpatient facilities.

All subjects aged 18 years or older were required to provide written informed consent for study participation. Subjects under 18 provided written assent and their parents/ guardians written consent. The study was conducted under the guidance of the Institutional Review Boards of the coordinating center and of the sites.

Site Selection

A critical early decision was whether to engage established community clinics and work with their existing personnel

- Functional recovery rates among patients with schizophrenia need to be improved substantially.
- A number of innovative and integrated first-episode programs have been implemented around the world.
- The premise of the RAISE ETP project is that by combining state-of-the-art pharmacologic and psychosocial treatments, delivered by a well-trained, coordinated multidisciplinary team, functional outcome and quality of life can be significantly improved.

or to establish a smaller number of new "specialty" FEP treatment centers designed specifically for this purpose and with personnel recruited especially for this project. We concluded that a program that could succeed across a range of diverse, existing community clinics and that included a broad representation of clinicians already working in such clinics who could be successfully trained by our team to deliver the enhanced intervention would provide generalizable information and be useful in establishing a national model that fits with the way health care is currently delivered and reimbursed in the United States. In some locales, specialized clinics might be an appropriate alternative based on geographic and population density opportunities; however, we believe that a major treatment need for FEP patients is to have appropriate care in readily accessible community clinics. The decision to conduct the project in community clinics had enormous implications for the development of our treatment and training model as well as for how the trial would be conducted.

We, therefore, sought a representative group of sites that (based on our evaluation) appeared capable of implementing the program and the study evaluation protocol while also recruiting the necessary number of FEP subjects. Sites with existing first-episode treatment programs were excluded. Via advertising, personal contacts, and outreach to The National Association of State Mental Health Program Directors, the NIMH Schizophrenia Trials Network, The National Council for Behavioral Health, and other organizations, we announced the opportunity for sites to participate in the project. Of the 79 potential sites that expressed interest in participation, 63 completed a detailed questionnaire about the populations that they served and their ability to provide study treatment (including all psychosocial treatments and recommended pharmacologic therapies) and support study assessments.

Questionnaire responses were reviewed by the study site selection committee; this review was followed by a telephone conference with the site. A site selection committee member visited all sites that remained potentials after the telephone conference and before final selection by the committee. Besides site capacity to perform the trial, geographic and demographic diversity was also considered in the selection process. Thirty-five sites were selected.

Figure 1. Map of Sites



Interventions

The intervention was developed following an extensive literature review and consultation with appropriate experts in the United States and abroad. (A detailed description of the intervention is beyond the scope of this report and will be published separately.) Manuals designed for training in each component are now available online at www.raiseetp.org. We named our enhanced treatment program "NAVIGATE" in order to convey in an optimistic fashion its mission of helping individuals with a first episode of psychosis (and their families) in finding their way toward psychological and functional well-being and access to the services they need in the mental health system. The core interventions provided by the NAVIGATE clinical team include individualized medication management assisted by a computerized decision support system for the prescriber (the secure Web-based program named COMPASS was developed by us specifically for this project), family education, individual resiliency training, and supported education and employment. The coordinated implementation of the NAVIGATE program requires an approach to treatment that is shared by all team members. This approach includes shared decision-making, strengths and resiliency focus, recognition of the need for motivational enhancement, a psychoeducational approach, cognitive-behavioral therapy methods, and collaboration with natural supports. Regular team meetings are essential.

The control condition was designated "Community Care" and represented the routine treatment offered by that clinic for such patients with no additional training or supervision provided by the central team, except in relationship to retention in the research assessment and follow-up component.

Study Design and Implementation

Randomization. The study employed a cluster randomization design—that is, randomization by clinic/site rather than by individual patient. This decision was based on a number of critical factors. Patient randomization would have required each site to have a specialized, separate, systematically trained and supervised team to manage those patients randomized to the NAVIGATE intervention while maintaining a different group of clinicians to offer usual

Figure 2. Study Design



care to those randomized to the comparison condition. This would present challenges in terms of both establishing a viable NAVIGATE program with only half of the recruited patients being assigned to it and minimizing the risk of potential "spillover" or "contamination" effects when patients are assigned to two different "open" treatments within the same clinic. Further, community sites would rarely be able to staff separate study teams. An additional advantage of cluster randomization is that individuals do not have to agree to randomization, but only have to consent to participating in a study in which they will receive the treatment provided in their setting and to understand to which treatment condition the site has been randomized.

There are, however, risks associated with site randomization. One major risk is that cluster randomization will not be successful and that there will be systematic differences between the intervention and usual care sites and/or patients. However, with a sufficient number of sites, adjustments can be made in the statistical analysis for imbalances through measured covariates, allowing a valid comparison of the interventions. Given the practical advantages of site randomization, and the ability to make statistical adjustments if needed, we concluded that randomization at the level of site rather than patient was scientifically optimal. This was acceptable to sites, and none withdrew following randomization.

Thirty-five sites were randomized to either NAVIGATE or the Community Care condition. Following randomization and initial training, 2 of the sites were dropped from the trial before any subjects had been entered because they were unable to recruit. One site was subsequently added, resulting in 34 sites (17 in each treatment condition). Figure 1 shows site locations; the study included 21 of the 48 contiguous states. The study design of the RAISE-ETP Program is presented in Figure 2.

Research infrastructure. RAISE-ETP funded staffing for the research portion of the program at all sites: a part-time Study Director and Research Assistant to recruit, coordinate, and assess study subjects. All sites met together for an initial project meeting and orientation to overall study goals

| Y | Year 1 | | | | | | | | | | | | | | |
|--|--------|-------|-------|---|---|---|---|---|---|---|---|---|----|----|----|
| Month | Screen | BL1/0 | BL2/0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 |
| Procedure (P = phone interview, X = in-person assessment) | Ì | | | | | | | | | | | | | | |
| On-site assessments | | | | | | | | | | | | | | | |
| IRB-approved Informed Consent Form | Х | | | | | | | | | | | | | | |
| Screening form (inclusion/exclusion) | Х | | | | | | | | | | | | | | |
| Demographics and Psychiatric History Form | | | Х | | | | | | | | | | | | |
| Medical history and current medication | | | Х | | | | | | | | | | | | |
| SURF-Monthly ²⁴ | | | Х | Р | Р | Х | Р | Р | Х | Р | Р | Р | Р | Р | Х |
| SURF-Quarterly | | | Х | | | Х | | | Х | | | Р | | | Х |
| Antipsychotic Medication Adherence Assessment | | | Х | | | Х | | | Х | | | | | | Х |
| Prescription medication experience | | | Х | | | Χ | | | Х | | | | | | Х |
| Self-Report Assessment Form | | | Х | | | Χ | | | Х | | | | | | Х |
| Annual Demographic Update | | | | | | | | | | | | | | | Х |
| Intent to Attend Form ²⁵ | | | Х | | | Χ | | | Х | | | | | | Х |
| Family Assessment Scale | | | Х | | | | | | Х | | | | | | Х |
| Client Recovery Outcomes | | | Х | | | | | | Х | | | | | | Х |
| Physical assessment (sitting and standing blood pressure, sitting and | | | | | | | | | | | | | | | |
| standing pulse, weight, BMI, waist circumference, temperature, | | | Х | | | Χ | | | Χ | | | | | | Х |
| EPS, akathisia, and abnormal involuntary movements) | | | | | | | | | | | | | | | |
| Cognition (BACS) ²⁶ | | | Х | | | | | | | | | | | | Х |
| Laboratory tests—lipid panel, metabolic profile, HbA _{1c} and fasting | | | v | | | v | | | v | | | | | | v |
| insulin levels | | | Λ | | | Λ | | | Λ | | | | | | А |
| Urbanicity Questionnaire ²⁷ | | | Х | | | | | | | | | | | | |
| Remote telemedicine—MedAvante Assessments | | | | | | | | | | | | | | | |
| SCID—DSM-IV | | Х | | | | | | | | | | | | | Х |
| Psychopathology (PANSS/CGI/CDSS) | | Х | | | | | | | Χ | | | | | | Х |
| Functional outcome (QLS) | | Х | | | | | | | Х | | | | | | Х |

Table 1. Assessment Measures: Assessment Schedule A

and research procedures. Once the study teams returned home, they learned whether they had been randomized to NAVIGATE or Community Care. Those assigned to NAVIGATE next received initial training in the multimodal, team-based intervention and ongoing consultation and support. A procedure was in place to assess competence and monitor fidelity in the delivery of all components of the NAVIGATE intervention. A full description of these procedures is beyond the scope of this communication and is the focus of another report. Our clinical strategies for managing attrition at all sites include ongoing contact with sites to support their efforts to keep subjects in both treatment and assessment and a progressive subject reimbursement schedule that recognizes the importance of participation in assessments over time as allowed by the Institutional Review Boards.

Trial duration. The trial was designed to provide a minimum of 2 years of study treatment; subjects who entered early in the enrollment phase may have had treatment for up to 43 months. During this initial study treatment phase, patients could choose to continue to participate in research outcome assessments even if they were no longer receiving treatment in the NAVIGATE program or in Community Care. Treatment was allowed to be intermittent, if necessary, and patients were welcome to return to the treatment even after lengthy interruptions for whatever reason (eg, personal choice, incarceration). No threshold was in place for discontinuing patients from the trial. The study also includes a long-term follow-up phase: assessments continue for 5 years after subjects' study treatment began.

Assessment strategy and schedule. Because site-based personnel were not blind to treatment, the assessment

strategy combined site-based and centralized assessments. The site-based assessments were conducted by research assistants (RAs) who were trained to complete their assigned assessments, but were not required to have sufficient clinical background or the training necessary to administer research quality assessments. A major challenge in conducting, multisite studies at non-academic, community clinics is ensuring the availability of well-trained, calibrated interviewers/raters at each site. In addition, when a study involves different psychosocial treatment conditions, maintaining "blinded" assessment is very difficult. Therefore, remote, centralized personnel provided by MedAvante carried out diagnosis/assessment utilizing live, 2-way video. The centralized assessments were conducted by individuals with sufficient clinical experience and sufficient training to provide research quality diagnostic interviews and ongoing outcome assessments for psychopathology and quality of life-while remaining blind to treatment assignment and to the overall study design. Diagnosis (utilizing the Structured Clinical Interview for DSM-IV-SCID¹⁹) was done, duration of untreated psychosis was determined, and the Positive and Negative Syndrome Scale (PANSS),²⁰ Clinical Global Impressions scale (CGI),²¹ the Calgary Depression Scale for Schizophrenia (CDSS),²² and the Quality of Life Scale (QLS),²³ our primary functional outcome measure, were administered by the centralized raters. As shown in Table 1, the SCID¹⁹ was completed at baseline and at the 1-year assessment; other measures were completed every 6 months. Remote assessment utilizing 2-way video has been shown to be comparable to face-to-face assessments in patient acceptability and reliability.²⁸⁻³⁰ The remaining assessments were conducted by site-based personnel. Our primary tool

Table 1. Assessment Measures: Assessment Schedule B

| Year 2 | | | | | | | | | | | | |
|---|----|----|----|----|----|----|----|----|----|----|----|----|
| Month | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | 21 | 22 | 23 | 24 |
| Procedure (P = phone interview, X = in-person assessment) | | | | | | | | | | | | |
| On-site assessments | | | | | | | | | | | | |
| SURF-Monthly | Р | Р | Р | Р | Р | Х | Р | Р | Р | Р | Р | Х |
| SURF-Quarterly | | | Р | | | Х | | | Р | | | Х |
| Antipsychotic Medication Adherence Assessment | | | | | | Х | | | | | | Х |
| Prescription Medication Experience | | | | | | Х | | | | | | Х |
| Self-Report Rating Form | | | | | | Х | | | | | | Х |
| Intent to Attend Form | | | | | | Х | | | | | | |
| Annual Demographic Update | | | | | | | | | | | | Х |
| Family Assessment Scale | | | | | | Х | | | | | | Х |
| Client Recovery Outcomes | | | | | | Х | | | | | | Х |
| Physical assessment (sitting and standing blood pressure, sitting and standing pulse, | | | | | | | | | | | | |
| weight, BMI, waist circumference, temperature, EPS, akathisia, and abnormal | | | | | | Х | | | | | | Х |
| involuntary movements) | | | | | | | | | | | | |
| Cognition (BACS) | | | | | | | | | | | | Х |
| Laboratory tests—lipid panel, metabolic profile, HbA _{1c} and fasting insulin levels | | | | | | Х | | | | | | Х |
| Remote telemedicine—MedAvante Assessments | | | | | | | | | | | | |
| Psychopathology (PANSS/CGI/CDSS) | | | | | | Х | | | | | | Х |
| Functional Outcome (QLS) | | | | | | Х | | | | | | Х |

Table 1. Assessment Measures: Assessment Schedule C

| Year 3 | | | | | | | | | | | | |
|---|----|----|----|----|----|----|----|----|----|----|----|----|
| Month | 25 | 26 | 27 | 28 | 29 | 30 | 31 | 32 | 33 | 34 | 35 | 36 |
| Procedure (P = phone interview, X = in-person assessment) | | | | | | | | | | | | |
| On-site assessments | | | | | | | | | | | | |
| SURF-Monthly | Р | Р | Р | Р | Р | Х | Р | Р | Р | Р | Р | Х |
| SURF-Quarterly | | | Р | | | Х | | | Р | | | Х |
| Antipsychotic Medication Adherence Assessment | | | | | | Х | | | | | | Х |
| Prescription Medication Experience | | | | | | Х | | | | | | Х |
| Self-Report Rating Form | | | | | | Х | | | | | | Х |
| Annual Demographic Update | | | | | | | | | | | | Х |
| Intent to Attend Form | | | | | | Х | | | | | | |
| Family Assessment Scale | | | | | | Х | | | | | | Х |
| Client Recovery Outcomes | | | | | | Х | | | | | | Х |
| Physical assessment (sitting and standing blood pressure, sitting and standing pulse, | | | | | | | | | | | | |
| weight, BMI, waist circumference, temperature, EPS, akathisia, and abnormal | | | | | | Х | | | | | | Х |
| involuntary movements) | | | | | | | | | | | | |
| Laboratory tests—lipid panel, metabolic profile, HbA _{1c} and fasting insulin levels | | | | | | Х | | | | | | Х |
| Remote telemedicine—MedAvante Assessments | | | | | | | | | | | | |
| Psychopathology (PANSS/CGI/CDSS) | | | | | | Х | | | | | | Х |
| Functional outcome (QLS) | | | | | | Х | | | | | | Х |

Table 1. Assessment Measures: Assessment Schedule D

| Year 4 | | | | | | | | | | | | |
|---|----------------|----------------|----------------|----------------|----------------|----|----------------|----------------|----------------|----------------|----------------|----|
| Month | 37 | 38 | 39 | 40 | 41 | 42 | 43 | 44 | 45 | 46 | 47 | 48 |
| Procedure (P = phone interview, X = in-person assessment) | | | | | | | | | | | | |
| On-site assessments | | | | | | | | | | | | |
| SURF-Monthly | P ^a | Х | P ^a | Х |
| SURF-Quarterly | | | Pa | | | Х | | | Pa | | | Х |
| Antipsychotic Medication Adherence Assessment | | | | | | Х | | | | | | Х |
| Prescription Medication Experience | | | | | | Х | | | | | | Х |
| Self-Report Rating Form | | | | | | Х | | | | | | Х |
| Annual Demographic Update | | | | | | | | | | | | Х |
| Intent to Attend Form | | | | | | Х | | | | | | |
| Family Assessment Scale | | | | | | Х | | | | | | Х |
| Client Recovery Outcomes | | | | | | Х | | | | | | Х |
| Physical assessment (sitting and standing blood pressure, sitting and standing pulse, | | | | | | | | | | | | |
| weight, BMI, waist circumference, temperature, EPS, akathisia, and abnormal involuntary movements) ^a | | | | | | Х | | | | | | Х |
| Laboratory tests—lipid panel, metabolic profile, HbA _{1c} and fasting insulin levels ^a | | | | | | Х | | | | | | Х |
| Remote telemedicine—MedAvante Assessments | | | | | | | | | | | | |
| Psychopathology (PANSS/CGI/CDSS) | | | | | | Х | | | | | | Xb |
| Functional outcome (QLS) | | | | | | Х | | | | | | Х |

| Table 1. Assessment Measures: | Assessment Schedule E |
|-------------------------------|-----------------------|
|-------------------------------|-----------------------|

| Month | 54 | 60 |
|---|----|----|
| Procedure (P = phone interview, X = in-person assessment) | | |
| On-site assessments | | |
| SURF-Monthly | Х | Х |
| SURF-Quarterly | Х | Х |
| Client status update | Х | Х |
| Physical assessment (sitting and standing blood pressure, sitting and standing pulse, weight, BMI, waist circumference, temperature, EPS, akathisia, and abnormal involuntary movements) ^a | Х | X |
| Laboratory tests—lipid panel, metabolic profile, HbA1c and fasting insulin levels ^a | Х | Х |
| Remote telemedicine—MedAvante Assessments | | |
| Psychopathology (PANSS) | Х | Х |
| Functional Outcome (QLS) | Х | Х |

^aData collected for only a subset of participants.

^bPANSS only.

Abbreviations: AIM = Abnormal Involuntary Movements, BACS = Brief Assessment of Cognition in Schizophrenia, BARS = Brief Adherence Rating Scale, BL = baseline, BMI = body mass index, CDSS = Calgary Depression Scale for Schizophrenia, CGI = Clinical Global Impressions scale, EPS = extrapyramidal symptoms, IRB = Institutional Review Board, PANSS = Positive and Negative Syndrome Scale, QLS = Quality of Life Scale, SCID = Structured Clinical Interview for *DSM-IV* Axis I Disorders, SURF = Service Utilization and Resources Form for Schizophrenia.

for assessing cost of services is the Service Use and Resource Form (SURF),²⁴ completed monthly, that documents all inpatient, residential, emergency department, and outpatient mental health and medical services used in the past month. At less frequent intervals, insurance coverage information is collected as well. The SURF has been used in several previous multisite clinical trials of both pharmaceutical and psychosocial interventions³¹ and is not influenced by the mix of payers. Subject reimbursement was provided for each assessment. Subjects are also assessed for the presence of 21 antipsychotic side effects (side effects were chosen for assessment based on a review of the frequency of occurrence reported in first episode medication trials—see Table 1).

Data management and statistical analysis. Data management is conducted by Innovative Clinical Research Solutions at The Nathan Kline Institute. The analysis of the primary outcome will compare the treatment differences in the overall quality of life (total QLS score) and over time during the first 2 years (baseline and 6, 12, 18, and 24 months). A 3-level nested mixed-effects linear model^{32,33} will include a fixed effect for the treatment indicator, terms of time, and their interactions; a random intercept at the patient-level; and a random intercept at the site level. The terms of time are coded as different levels of the categorical time. The effect of the interactions between the treatment and the terms of time will be tested for the treatment difference in overall functional outcome. Treatment difference will be declared if the interaction terms are statistically significant with 4 degrees of freedom at 2-tailed α -level of 0.05. To test the rate of improvement in QLS score between the 2 intervention groups over the course of the treatment (difference in slope), time will be used as a numerical variable and the interaction term with 1 degree of freedom will be tested. In addition, the model fit with a first-order autoregressive (AR1) covariance structure will be tested against the independent structure.³⁴ Likelihood ratio tests will be used in all tests. Sample size requirements for mixed-effects linear regression analyses were based on RMASS.³⁴ We assumed that the intraclass

correlation (ICC) within subjects will range from 0.30 to 0.60 and the ICC within site is 0.10. We have at least N = 145 per group, even after accounting for 20% attrition, and the proposed design will provide power in excess of 0.90 to detect an overall group difference and the difference in rate of change over time for a standardized effect size at the 24-month visit as small as 0.40 SD units. We consider a difference of this magnitude, which represents 9 points of the QLS, clinically meaningful. Thus, given the assumptions, the sample size should provide sufficient power to test our primary hypothesis regarding quality of life.

SUMMARY AND CONCLUSIONS

The project was initiated on July 13, 2009, and completed enrollment of the 404 subjects in July 2012. We believe that we have succeeded in both designing a multimodal treatment intervention that can be delivered in real-world clinical settings under extant reimbursement constraints and implementing a randomized, controlled clinical trial that can provide the necessary outcome data to determine its impact on the trajectory of early phase schizophrenia. We are very grateful for the help of numerous consultants and advisors, the outstanding participation of our core collaborators, and the terrific efforts of all of the treatment teams at the 34 participating sites. We also extend our thanks to all of the patients and families who have agreed to work with us in this effort.

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See supplementary material for this article at PSYCHIATRIST.COM.



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Supplementary Material

- Article Title: The RAISE Early Treatment Program for First-Episode Psychosis: Background, Rationale, and Study Design
- Author(s): John M. Kane, MD; Nina R. Schooler, PhD; Patricia Marcy, BSN; Christoph U. Correll, MD; Mary F. Brunette, MD; Kim T. Mueser, PhD; Robert A. Rosenheck, MD; Jean Addington, PhD; Sue E. Estroff, PhD; James Robinson, MEd; David L. Penn, PhD; and Delbert G. Robinson, MD
- **DOI Number:** 10.4088/JCP.04m09289

List of Supplementary Material for the article

1. <u>eAppendix</u> RAISE-ETP Sites

Disclaimer

This Supplementary Material has been provided by the author(s) as an enhancement to the published article. It has been approved by peer review; however, it has undergone neither editing nor formatting by in-house editorial staff. The material is presented in the manner supplied by the author.

Appendix A: RAISE-ETP Sites

| | Site Name | Address |
|----|--|--|
| 1. | Burrell Behavioral Health (Columbia) | 601 Business Loop 70 West, Suite 215, |
| | Key Personnel: Gary Stoner, Pam Williams | Columbia, MO 65203 |
| 2. | Burrell Behavioral Health (Springfield) | 1423 N. Jefferson, Ste D-200, Springfield, MO |
| | Key Personnel: Paul Thomlinson, Melissa | 65802 |
| | Daugherty | |
| 3. | Catholic Social Services of Washtenaw County | 4925 Packard, Ann Arbor, MI 48108-1521 |
| | Key Personnel: David Garvin, Lorin Burgess | |
| 4. | Center for Rural and Community Behavior | MSC09 5030, 1 UNM, Albuquerque, NM 87131- |
| | Health New Mexico | 0001 |
| | Key Personnel: Stephen Lewis, Tammy Seaman | |
| 5. | Cherry Street Health Services | 100 Cherry Street SE, Grand Rapids, MI 49503 |
| | Key Personnel: Eric Achtyes, Heather Mayle | |
| 6. | Clinton-Eaton-Ingham Community Mental Health | 812 E. Jolly Road Ste. G-12, Lansing, MI 48910 |
| | Authority | |
| | Key Personnel: Angela Pinheiro, Catherine | |
| | Adams | |
| 7. | Cobb County Community Services Board | 6133 Love Street, Austell, GA 30168 |
| | Key Personnel: Asha Pandya, Bryan Stephens | |
| 8. | Community Alternatives | 3738 Chouteau Ave., Ste. 200 St. Louis, MO |
| | Key Personnel: Tony Hilkin, Ana Savu | 63110 |
| 9. | Community Mental Health Center of Lancaster | 2201 South 17th Street, Lincoln, NE 68502 |
| | County | |

Key Personnel: Lisa Young, Mary Sullivan

| 10. Community Mental Health Center, Inc. | 427 W. Eads Parkway Lawrenceburg, IN 47025 |
|---|--|
| Key Personnel: Nancy Janszen, Michelle Menke | |
| 11. Eyerly Ball Iowa | 1301 Center Street, Des Moines, IA 50309 |
| Key Personnel: Zach Pacha, Anthony Zamudio | |
| 12. Grady Health Systems | 49 Jesse Hill Jr. Drive, SE, Atlanta, GA 30303 |
| Key Personnel: Patrick Amir, Stephanie | |
| Johnson | |
| 13. Henderson Mental Health Center | 4720 North State Road 7, Ft. Lauderdale, FL. |
| Key Personnel: Elise Ward, Steve Ronik | 33319 |
| 14. Howard Center | 300 Flynn Avenue, Burlington, VT 05401 |
| Key Personnel: Sandy Steingard, Lisa Martiny | |
| 15. Human Development Center | 1401 E 1st St Duluth, MN 55805 |
| Key Personnel: Saprina Matheny, Christine | |
| Hakala | |
| 16. Lehigh Valley Hospital | 17th & Chew Sts. 3rd FL, Allentown, PA 18104 |
| Key Personnel: Ralph Erickson, Heather | |
| LaBarre | |
| 17. Life Management Center of Northwest Florida | 525 E. 15th St., Panama City, FL 32405 |
| Key Personnel: Bernard Bergman, Cheryl Fields | |
| 18. Mental Health Center of Denver | 4353 E. Colfax Ave., Denver, CO 80220 |
| Key Personnel: Cheryl Clark, Stephen Fisher | |
| 19. Greater Nashua Mental Health | 7 Prospect Street, Nashua, NH 03060 |
| Key Personnel: Nancy Gilbert, Sandy Palladino | |
| 20. North Point Health and Wellness | 1313 Penn Ave N, Minneapolis, MN 55411 |

| | Key Personnel: Rabindra Tambyraja, Thomas | |
|-----|--|---|
| | Recht | |
| 21. | Park Center | 909 East State Blvd., Fort Wayne, IN 46805 |
| | Key Personnel: Jason Cook, Rochelle | |
| | Bloomfield | |
| 22. | Peace Health Oregon/Lane County Behavioral | 2411 MLK Blvd, Eugene, OR 97401 |
| | Health Services | |
| | Key Personnel: Tom Akins, Carla Gerber | |
| 23. | Pine Belt Mental HC | 103 S. 19th Ave.Hattiesburg, MS 39403 |
| | Key Personnel: Rita Porter, Ragan Downey | |
| 24. | River Parish Mental Health Center | 1809 W. Airline Hwy LaPlace, LA 70068 |
| | Key Personnel: Danny Sansovich, Theresa | |
| | Honey | |
| 25. | San Fernando Mental Health Center | 10605 Balboa Blvd., Granada Hills, CA 91344 |
| | Key Personnel: Konstantinos Tripodis, Roberto | |
| | Zarate | |
| 26. | Santa Clarita Mental Health Center | 23501 Cinema Drive, Valencia, CA 91355 |
| | Key Personnel: Alex Kopelowicz, Richard | |
| | Franco | |
| 27. | South Shore Mental Health Center | 4705A Old Post Rd Charlestown, RI 02813 |
| | Key Personnel: Claire Perretta, Megan McDavitt | |
| 28. | St. Clare's Hospital | 50 Morris Ave., Denville, NJ 07834 |
| | Key Personnel: David Ruiz, Warren Ververs | |
| 29. | Staten Island University Hospital | 475 Seaview Ave Staten Island, NY 10305 |
| | Key Personnel: Timothy Sullivan, Stacy Bruno | |

| 30 | Terrebonne Mental Health Center | 5599 Hwy. 311, Houma, LA 70360 |
|-----|--|--|
| | Key Personnel: Melanie Vega, Stephany | |
| | Hillman | |
| 31. | . The Mental Health Center of Greater | 1555 Elm St., Manchester, NH 03101 |
| | Manchester | |
| | Key Personnel: Harry Cunningham, Jason | |
| | Welsh | |
| 32 | . The Providence Center | 530 North Main Street, Providence, RI 02904 |
| | Key Personnel: Kazi Salahuddin, Anthony | |
| | Parente | |
| 33. | . United Services | 132 Mansfield Ave, Willimantic, CT 06226 |
| | Key Personnel: Jay Patel, Sandra Long | |
| 34 | University of Missouri-Kansas City School of | 2464 Charlotte Street, Kansas City, MO 64108 |
| | Pharmacy | |
| | Key Personnel: Stephen Jarvis, Leigh Anne | |
| | Nelson | |