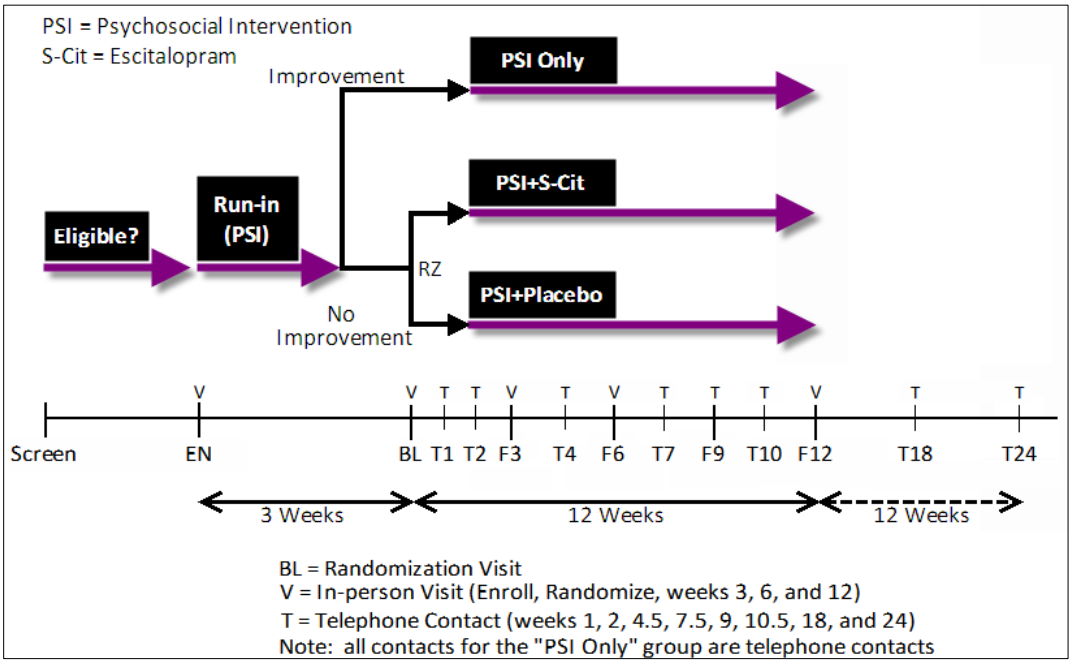
SCOPE OF WORK AND PAYMENT FOR AFFILIATED CLINICAL CENTERS

The S-CitAD Chairman's Office (CO) will establish a sub-contract with each affiliated clinical center selected to participate in the study. Clinical centers will be responsible for conducting the trials according to ICH Good Clinical Practice Guidelines (*Federal Register, 9 May 1997, 62 FR 25692*), which include the following: obtaining appropriate Institutional Review Board approval (S-CitAD will offer services from an optional Single IRB); following the procedures described in the study protocol for evaluation, enrollment, and follow-up of study patients; expedited reporting of urgent safety matters following procedures distributed by the Coordinating Center (CC); ensuring that subjects' Protected Health Information remains confidential; and adhering to study policies and procedures to ensure that study data are accurate, complete, and submitted in a timely manner to the CC.

Clinic personnel are expected to work with the CO and CC to develop recruitment plans with an emphasis on underrepresented minority recruitment; to obtain site certification in a timely manner once certification activities begin; to attend the annual investigators meetings, including the initial training meeting; and to participate in regular conference calls for S-CitAD clinical sites as scheduled by the study leadership. Study protocols will also require clinic personnel to screen for eligible participants; obtain participant consent; administer study treatments, including a structured psychosocial intervention (PSI) as specified; collect data on participants' medical history and demographic characteristics; conduct clinical examination procedures including collecting blood specimens and performing electrocardiography; and other research activities as will be specified in the study protocol and Manual of Procedures. Sites will collect data according to procedures disseminated by the CC and will transmit these data to the CC using the S-CitAD data system. It is critical that data entry occur quickly following collection, and that responses to queries about entered data be investigated and resolved quickly. The timeliness of these activities will be a key performance metric tracked by S-CitAD with the expectation that data entry and query responses will occur within a week. A schematic of the study design is shown below.

S-CitAD Study Design Schematic



Affiliated clinical centers will receive quarterly capitation payments from the CO for screening and randomization activities as follows:

• $1,500 on completion of a patient screening and enrollment into the 3-week PSI run-in
• $7,000 for successful completion of an RZ visit and entry of a study participant into the 24- week follow-up period (12 weeks with in-person visits and 12 weeks of extended follow-up with telephone contacts. Payments will include F&A (overhead) of 25%.

See below for more detailed information regarding the definitions of “screening” and “entry”. Screening and entry activities will be tabulated based upon the completion and entry of study data into the S-CitAD data system.

For purposes of the capitation payments, we will use the following definitions:

Screening ($1500): the screening capitation payment will issued upon the completion of a successful screening visit (including administration of the PSI) that enrolls an eligible participant into the 3-week PSI run-in. A screened participant is an individual who signs informed consent, meets entry criteria, and initiates the three-week PSI.

RZ Visit ($7000): the RZ capitation payment will be issued upon the completion of a successful randomization visit and entry of an eligible patient into the follow-up period, regardless of whether the patient shows no improvement to the run-in PSI and is randomized to masked treatment or instead does show improvement to the run-in PSI and is entered into the “PSI Only” long-term follow-up arm. An enrolled participant is one who continues past the three-week period either through randomizing (into masked study treatment, escitalopram or placebo) because of non-improvement, or continues in the study without randomization and without masked study treatment because of improvement during the run-in period.

In order to manage the overall study budget, we will monitor the number of patients that complete screening but do not complete the RZ visit and may need to cap the number of screening payments relative to the number of RZ payments (i.e., no more than four screening payments for every three RZ payments).

Once the study is initiated, accepted sites will be prepaid $2500 of their capitated payments to help with startup costs. However, we remind sites that we will provide the services of a Single IRB at no cost to participating sites and we encourage sites to use our Single IRB. Once a site is certified and "released" to begin recruiting, it will be eligible to invoice on a quarterly basis for *per subject* payments as described above. We emphasize that payment for participants screened or enrolled will occur once data are entered for the initial screening or enrollment visits. We will not pay on the basis of completed follow-up visits; full payment for each enrolled participant will be made upon randomization. However, we will track the completion and entry of all follow-up visits and sites that show high rates of missed visits or loss to followup may be restricted from further randomization until a plan of corrective action can be developed and implemented.

The CC will provide funds for travel to the Research Group and Training meetings for affiliated sites. The Research Group meetings (1/year) will last 1 day, and the Training meeting will last 2 days (a single meeting expected in late summer of 2017). Travel funds will be provided for 1 PI (or designee), and 1 study coordinator, from each site. All meetings will be held in the Baltimore, Maryland area.

S-CitAD will not limit the number of patients a particular site may enroll, but instead will use the traditional “competitive enrollment” model. This will support flexible recruitment and encourage sites that are able to recruit faster. Recruitment is expected to last up to 3 years. As a hypothetical, if a clinic completes 6 screening visits and 4 RZ visits annually the award amount would be about $37,000, plus F&A (overhead) at 25%, totaling $46,250 per year.