IRB-approved protocol

Background and Significance

Body dysmorphic disorder (BDD) is a severe and relatively common disorder that consists of preoccupation with an imagined or slight defect in appearance that causes clinically significant distress or impairment in functioning. Individuals with BDD have markedly poor psychosocial functioning and high rates of morbidity, including psychiatric hospitalization and suicidality. The rate of completed suicide, while based on preliminary data, appears markedly high. Without effective psychiatric treatment, BDD appears to usually be chronic. Most individuals with BDD receive surgical, dermatologic, and other cosmetic treatments for their BDD symptoms, which are usually ineffective. Thus, there is a critical need for effective interventions for this severe illness.

Cognitive-behavioral therapy (CBT) is a time-limited treatment that includes cognitive restructuring, mindfulness/attention retraining, exposure, and response prevention, specifically tailored for BDD. CBT is the only fully developed psychosocial treatment for BDD. Preliminary data from case series and studies using waitlist controls suggest that CBT is very promising for BDD. However, no studies have more rigorously examined CBT's efficacy for BDD by comparing CBT to another treatment. The primary aim of this Collaborative R01 application is to examine the efficacy of a manualized CBT treatment in comparison to manualized enhanced supportive psychotherapy (SPT). SPT is the most widely received psychosocial treatment by persons with BDD. The CBT treatment we propose to test is a modular, manualized treatment developed in our recently completed R34 grant (R34MH70490). Data from the R34 study, which used a waitlist control group, suggest that our CBT treatment is acceptable to patients, feasible to implement, and appears promising for BDD, associated symptoms, and functional disability.

A recent Cochrane Collaboration review on the treatment of BDD, and a BDD treatment practice guideline from the United Kingdom's National Health Service, underscore the dearth of treatment research in BDD. They specifically call for more intervention research on this often-debilitating disorder. No prior studies have compared CBT for BDD to another treatment. The proposed study will fill a major gap in knowledge by testing the most promising psychosocial treatment (CBT) for this relatively common, severe, and understudied disorder.

Specific Aims

Primary Aim

1) To compare the efficacy of CBT to enhanced supportive psychotherapy (SPT) in reducing BDD symptom severity over a 24-week period.

   Hypothesis: After 24 weeks (22 sessions) of treatment, CBT will be more efficacious than SPT in reducing BDD symptom severity based on a clinician-rated measure.

Secondary Aims

2.1) To compare longer-term efficacy and durability of CBT versus SPT.

   Hypothesis: At follow-up (3 months and 6 months post-treatment), subjects in the CBT arm will have greater reduction in BDD symptom severity than those in the SPT arm, when examining changes from baseline (longer-term efficacy) and from post-treatment (durability).

2.2) To compare the efficacy of CBT to SPT with respect to secondary outcome measures.

   Hypothesis: At post-treatment, CBT will be more efficacious than SPT in improving depression, delusionality (insight) of BDD beliefs, psychosocial functioning, and quality of life.

2.3) To explore predictors of CBT-related improvement in BDD symptoms.

   Hypothesis: Within the CBT arm, subjects with less severe BDD, less delusional BDD beliefs, and/or less depression at baseline will have greater reduction in BDD symptom severity over time.

Exploratory Aim

3) To evaluate whether maladaptive beliefs, information processing and/or neuropsychological functioning partially mediate the efficacy of CBT compared to SPT in reducing BDD symptom severity.

   Hypothesis: The relative efficacy of CBT vs. SPT will be partially mediated by maladaptive beliefs (measured by the Appearance Schema Inventory-Revised), information processing (measured by the Emotion Recognition Task), and neuropsychological functioning (measured by the Rey-Osterrieth Complex Figure Test).

Research Design and Methods

Massachusetts General Hospital/Harvard Medical School and Rhode Island Hospital/Brown University will collaborate to recruit 120 adult participants to be randomly assigned to receive CBT or SPT. Approximately 150 participants will be enrolled in this study at Massachusetts General Hospital/Harvard Medical School in order to meet our target of 60 subjects who are eligible and able to complete study procedures.

Inclusion Criteria:

1) Outpatient men and women age 18 and older
2) DSM-IV BDD for at least 6 months (delusional patients will be included because delusional and nondelusional BDD appear to be the same disorder; including delusional patients will also broaden the generalizability of the results)
3) BDD is the most problematic psychiatric disorder (in the patient's and clinician's opinion) and the primary reason for seeking treatment
4) Minimum score of $\geq$24 on the BDD-YBOCS at both the screening visit (week -1) and baseline visit (week 0).

Exclusion Criteria:

1) Current clinically significant suicidality and/or score on the BDI-II suicide item (#9) >1
2) Any clinical features requiring a higher level of care
3) Mental retardation or borderline intellectual functioning (estimated IQ <80 on the Wechsler Abbreviated Scale of Intelligence) or dementia, brain damage, or other cognitive impairment that would interfere with ability to engage in CBT
4) DSM-IV substance use disorder in the past 3 months or use of an illicit drug that is not prescribed, as indicated by a urine drug screen and/or clinical inference
5) Current manic episode
6) Psychotic disorder (except for delusional BDD)
7) Borderline personality disorder
8) Body image concerns accounted for by an eating disorder
9) Previous treatment with $\geq$10 sessions of CBT similar to ours for BDD (we expect this to occur rarely)
10) Subjects cannot be receiving any other psychotherapy or begin such treatment during the study
11) Unstable dose of psychotropic medication for less than 2 months or discontinuation of psychotropic medication less than 2 months prior to study baseline; for benzodiazepine medication, discontinuation less than 2 weeks prior to study baseline. Patients can be receiving psychotropic medication if they have taken a stable dose for at least two months before the study baseline assessment and the dose remains stable during the study. We will include such patients because in our experience many patients interested in psychosocial treatment are taking psychotropic medication; including them will enhance recruitment and enable inclusion of a broader range of patients (e.g., those who are more severely ill), thus enhancing generalizability of the results. If a potential subject is taking psychotropic medication at the time of the phone evaluation or first in-person screening and wishes to discontinue it to enter the study, we will ask the patient to discuss with their prescribing physician whether medication discontinuation would be safe and in the patient's best interest. We will also obtain the patient's written consent to discuss this option with the treating clinician and will not influence the patient's decision. Subjects must agree not to begin psychotropic medication during the study. Subjects can be receiving non-invasive dermatologic agents (e.g., retin-A, oral or topical antibiotics, or Accutane). Due to the nature of the treatments and ethical considerations, subjects may discontinue use of these medications at any point during the study. Subjects must agree not to begin dermatologic medications during the study.
12) Presence of any behavior (e.g., violence) that would interfere with full cooperation with the protocol.
13) Medical illness or medical treatment that would likely interfere with participation.

Table 1: Assessment Measures by Study Visits: Most measures are administered at baseline, week 12, and post-treatment. Secondary outcome measures will be additionally administered at weeks 4 and 16 to increase the accuracy of analyses examining rates of change of these measures over time.

Form Type	Measure	Admin by	Wk	Wk 0 (Baseli	Wk	Wk	Wk	Wk	Wk	Wk 24 (Post-	Wk 37 (3 MO	Wk 50 (6 MO
Diagnosis & Screening	SCID-I/P	IE	x									
	SCID-II	IE	x									
	Physical Health Review:	-	-									
	Medical Systems (MSYS)	MD	x									
	Allergy (ALLG)	MD	x									
	Medications (MEDS)	MD	x									
	Surgical Procedures	MD	x									
	Urine Drug Screen (UDS)	MD	x									
	WASI	IE	x									
	WTAR	IE	x									
	History of Self-Harm	IE	x									
	Assessment of Risk (RISK)	IE	x									
	Demographics	Self	x									
BDD / Other Symptoms	BDD Data Form	IE	x									
	BDD-YBOCS	IE	x	x	x	x	x	x	x	x	x	x
	BDD-SS	Self		x	x	x	x	x	x			
	BABS	IE	x	x	x	x	x	x	x	x	x	x
	BDI-II	Self	x	x	*weekly at therapy*					x	x	x
	CGI-I: Clinician	IE			x	x	x	x	x	x	x	x
	CGI-I: Patient	Self			*weekly at therapy*					x	x	x
Safety	Concom. Meds/Ther	RA/Th			*weekly at therapy*					x	x	x
	Concom. Meds Log (CMED	RA/Th			*weekly at therapy*					x	x	x
	Concom. Therapies (CTHER	RA/Th			*weekly at therapy*					x	x	x
	Adverse Events (AES)	RA/Th			*every 4 wks at therapy*					x	x	x
	Adverse Events Log (AE Log)	RA/Th			*every 4 wks at therapy*					x	x	x
Functioning	Q-LES-Q	Self		x	x		x	x		x	x	x
	SDS	Self		x	x		x	x		x	x	x
Tx Details	Cred/Expectancy	Self		x	x							
	CSQ-8	Self					x			x		
	CBT Evaluation Form (CBT-	Self								x		
	SPT Evaluation Form (SPT-	Self								x		
Mediators	ASI-R	Self		x			x			x		
	ERT	Self		x			x			x		
	Rey (ROCF)	IE		x			x			x		
Other	Follow-Up (FUP)	IE									x	x
	Intent to Attend (ATTEND)	RA		Wk 0; weekly at therapy sessions; Wk 37								

Telephone Screening:

Our BDD programs have a telephone screening procedure that we will follow. The highly trained research assistant will ask screening questions to assess for BDD and determine whether study inclusion/exclusion criteria appear to be met. Callers will be given information about treatment options; those who appear to meet study inclusion/exclusion criteria and are interested in participating will be given information about the study. For potential subjects who are currently receiving psychotropic medication and wish to participate in our study (and we agree that this is a reasonable option), we will obtain their written consent to contact their treating clinician to determine the appropriateness of study participation. Callers who do not meet study entry criteria or do not wish to participate will be referred for treatment in our program or elsewhere. We will track the number of screens, number

of eligible subjects, and reasons for nonparticipation. Both programs have weekly meetings at which we discuss individuals who contact our program and their appropriate disposition. The PIs and their staff will also discuss recruitment issues on twice-monthly conference calls.

Initial Evaluation Phase and Randomization:

Individuals who appear eligible for and interested in the study during the phone screen will then have an in-person screening assessment; the PIs or their doctoral level delegates will obtain informed consent. A highly trained IE (doctoral level clinician) will administer in-person assessments, and subjects will complete self-report questionnaires (see Table 2 below). Participants will complete a urine drug screen, physical health review, and will be screened for risk of violence by the IE. The IE will ask all participants about prior MGH research study participation. Eligibility for the study will be confirmed. When interviewed patients do not qualify for or choose not to participate in the study, reasons will be documented. The screening assessment will take an estimated 2.5 - 3 hours.

The IE will also conduct the baseline assessment. The baseline visit will require about 1.5 hours. At this visit, eligible subjects will be randomized in a one-to-one ratio to CBT or SPT. The MGH Biostatistics Center will randomize patients seen at both sites to ensure procedural consistency, and randomization will be stratified by site. Treatment assignment will be randomly generated using the randomization system (RS2) established by the MGH Biostatistics Center (and currently in use by large cooperative groups conducting multi-center clinical trials supported by NIH). The RS2 system allows for web-based randomization with stratification, using SSL to secure the transmission. The user authenticates to the system with a PIN and a password, and is then asked study-specific questions to determine the stratum to which the subject belongs. Once these questions have been answered, the system gives the user the subject's ID number and sends an email to confirm treatment assignment. The randomization system keeps detailed log files and maintains a list of randomized subjects, with the date and time of randomization and the treatment assigned. It also outputs summaries of enrollment, broken out by site and month or year.

Study Visits:

Both the SPT and CBT treatments will consist of 22 sessions over 24 weeks, followed by 3- and 6-month follow-up assessments. For both SPT and CBT, treatment sessions will last 60 minutes with additional time for assessments. The estimated time for assessments is: weekly, 10 minutes; monthly, 40-45 minutes; week 12, post-treatment, 3-month, and 6-month follow-up, 1.5-2.0 hours.

Alternative treatments include serotonin-reuptake inhibitors. However, SRIs have potential side effects, and relapse appears common upon SRI discontinuation. In addition, in our experience, some patients refuse pharmacotherapy. Our preliminary data show that CBT is a promising treatment whose efficacy has yet to be rigorously tested; the proposed study is a necessary step toward establishing the efficacy of CBT. Supportive psychotherapy is a non-medication treatment for BDD that is the most widely received psychosocial treatment by individuals with BDD in the community. The informed consent process will include a discussion of pharmacotherapy as an alternative to study participation.

Informed Consent: For participants who enter the study, written informed consent will be obtained using IRB-approved consent forms. The PIs or their doctoral level delegates will obtain informed consent from participants after a full explanation of the study and an opportunity for the participant to ask questions about the study. IRB-approved consent forms will be signed and dated by the participant and the PIs or their doctoral level delegates. Each participant will be given a copy of the signed and dated consent forms. The study and consent forms will be approved by each site's IRB.

The IRB-approved consent forms will inform the participant that all interviews and therapy sessions will be digitally recorded. The digital recordings will contain participant numbers but not names or other identifying information. Digital recordings will be rated and simultaneously entered in the REDCap data management system for analysis. The digital recordings will be kept by the research team in a password-protected file and destroyed after completion of the study.

***Protection Against Risks*:** The following procedures will be implemented to protect participants against risks. The information provided in this section pertains to both study sites.

1) Screening procedures will exclude any potential subjects at potentially greater risk for psychiatric deterioration or an adverse outcome, or who are not clinically suitable for the study protocol.
2) All treatment will be provided by masters level or higher mental health professionals experienced in CBT or SPT and familiar with BDD.
3) All treatment sessions will be digitally recorded, allowing therapists to be closely supervised by Dr. Wilhelm and Dr. O'Keefe.
4) Independent evaluators will have a doctoral level degree in a mental health discipline and at least one year's experience in clinical assessment, and will receive formal training by Dr. Phillips in the protocol assessments. The IEs will be closely supervised, and these sessions will be digitally recorded for review by Dr. Phillips.
5) Therapists will be available to participants by phone, or in person if necessary, to discuss any concerns throughout the treatment period.
6) Drs. Wilhelm and Phillips will be available, if necessary, to discuss the study, alternative treatments, or any concerns about the study with participants if requested by the participant, therapist, or raters.
7) Drs. Wilhelm and Phillips (or covering clinician in their absence) will be available at all times to participants in the event of a clinical emergency; this will be clearly communicated orally and in writing to study participants. Participants will be given a letter from the investigators with information such as how to reach the investigators in an emergency. In addition, both sites have psychiatric emergency rooms that are available at all times to assist the investigators in the event of a clinical emergency. Subjects will be referred to a higher level of care (i.e., hospitalization) if needed.
8) Deterioration will be defined by a rating of 6 (much worse) or 7 (very much worse) on the global CGI during three consecutive, weekly assessments and clinician judgment that it would be in the best interest of the patient to be withdrawn. A patient may be withdrawn sooner than this, if in the judgment of the therapist and PIs, this is in the patient's best interest. As with all clinical intervention trials, participants in either condition could experience an increase in symptoms related to the natural waxing and waning of BDD symptoms. Participants may also experience a temporary increase in distress related to the treatment procedures, such as the behavioral experiments and exposure exercises, which may potentially provoke some anxiety. However, we will make all efforts to reduce such risk as described below (#12, #13). Participants in the CBT or SPT condition will be withdrawn from the study if their clinical condition deteriorates substantially. Participants may also be withdrawn if in the judgment of the PIs remaining in the study poses a substantial risk to the participant or a higher level of care is needed.
9) Ratings on the Beck Depression Inventory suicide item will be carefully monitored; any participant with a score >1 at any assessment will be immediately evaluated by the therapist and site PI and referred to a higher level of care if clinically indicated. If the assessment was conducted by a therapist, he/she will immediately contact the PI.
10) All participants who fail to respond to treatment or withdraw prematurely will be referred for alternative treatment. If withdrawal from the study is necessary, we will provide appropriate referrals for other treatment.
11) The study therapists and raters will make every attempt to help participants feel comfortable when discussing sensitive material.
12) If exposure exercises or behavioral experiments are too anxiety provoking, participants will be able to do alternative exercises that cause less anxiety.
13) The CBT treatment will initially emphasize cognitive restructuring, which we anticipate will be less anxiety provoking than exposure treatment alone and will make exposure more tolerable.
14) Many procedures will be used to protect the security of data obtained with REDCap, the platform for electronic data capture that will be used in this study. All users will have defined roles and privileges pre-determined by the system administrator. Thus, the PIs can set the level of access for each study staff such that only a limited number of people have access to sensitive study data. Data collected at both sites will be stored automatically and securely on an MS SQL Server, accessed over industry standard SSL-256 bit RSA encryption during data transfers. As part of the routine back up for all PHS systems, data are routinely backed up locally onto a redundancy server and stored in a separate database that is locked with 256 AES

encryption. Long-term storage on Partners servers occurs nightly and allows for incremental backup over multiple systems. Therefore, should one drive be physically damaged, there will be multiples within the chain to replace it. Both data servers are stored within the PHS IS corporate firewall, in a secure, key access facility with password protected computers. Only vetted PHS security officials will have access to physical machines storing study data. Since data are stored on a protected server, a compromise of any individual computer at a research facility will not lead to a breach of the secure database. Individual computers designated for data capture do not store participants' identifying information or study data.

Subjects may be withdrawn from the study for *any* of the following reasons:

1) A significantly deteriorating clinical course, such as emergence of active suicidal ideation or a need for hospitalization.
2) Score of >1 on the BDI-II suicide item (#9) and subsequent evaluation by the site PI indicating it would be unsafe for the patient to remain in the study.
3) Score of much or very much worse on the CGI for three consecutive weeks and therapist and PI judgment that remaining in the study is not in the subject's best interest; a patient may be withdrawn sooner than this, if in the judgment of the therapist and PI, this is in the patient's best interest.
4) PIs' decision that withdrawal from the study is in the subject's best interest.
5) Subject's decision to withdraw. In our experience with BDD treatment studies, patients rarely need to be withdrawn for the above reasons. Subjects who require medication changes or begin other types of therapy (e.g., family therapy) will be kept in the study even though such events violate study procedures. By comparing outcome data for compliant and non-compliant subjects, we will be able to assess any bias resulting from an intent-to-treat analysis. The data analysis section includes more detail on how data from subjects who are non-compliant will be analyzed, including sensitivity analyses to understand the impact of non-compliance on our findings.

The PIs will discuss and agree upon the withdrawal of any subject with each other, the therapist, and Dr. O'Keefe (for patients receiving SPT). If subjects are withdrawn from the study, an appropriate clinical referral will be made. The reason for withdrawal or dropout will be documented and the subject referred for appropriate treatment. Except for subjects who withdraw consent to participate, all who are withdrawn or drop out of the study will be asked to complete all remaining assessments (in-person or via phone). We will educate subjects about the importance of completing all scheduled assessments. As part of the informed consent process, we will ask subjects for contact information for four individuals (if possible) who could help us locate them if we lose contact with them. Based on our experience with our R34 study, we expect a high retention rate (about 80%).

Because many patients with BDD are suicidal, and the suicide rate appears high, we will carefully implement safety precautions including:

1) exclusion of patients from the study who are actively suicidal
2) assessment and monitoring of suicidality with the BDI-II and clinician inquiry at each visit
3) withdrawal of any patient at higher risk as described above
4) availability of the PIs (or their covering clinician) and emergency services at all times. In addition, the PIs have extensive expertise in BDD.

During the study assessments, participants may experience some discomfort or anxiety from discussing personal material and completing self-report questionnaires. Likewise, some participants may feel uncomfortable about having assessment sessions or treatment sessions digitally recorded and reviewed by project staff (which is necessary for rater and therapist supervision as well as assessment of the reliability of ratings and treatment adherence and competence). The treatment procedures, particularly the behavioral experiments and exposure exercises, will potentially provoke some anxiety. To minimize these effects, our CBT treatment initially emphasizes cognitive restructuring, which we anticipate will be less anxiety provoking than exposure treatment alone and will make exposure more tolerable. Participants in the CBT or SPT condition could experience an increase in symptoms related to the natural waxing and waning of BDD symptoms; however, participants will be carefully monitored, and measures will be taken to minimize potential risks during this period (see Adequacy of Protection Against Risks section). Breach of confidentiality, which great care will be taken to prevent, represents a potential risk. As discussed below, we will take precautions to ensure that this potential risk is minimized. Participants will be

carefully monitored, and measures will be taken to minimize all potential risks during the project period (see Adequacy of Protection Against Risks below).

Participants may benefit from the comprehensive diagnostic assessment, potentially effective therapy, and careful clinical monitoring. This study has the potential benefit of improving the patients' BDD symptoms.

There will be no exclusion based upon gender or minority status. Based on the composition of the patient population at the OCD/BDD Clinic at MGH, we anticipate that at least 50% of the participants will be women. The percentage of minority participants is expected to be at least 10-12%. We will make vigorous attempts to increase this number by posting advertisement flyers in minority communities, community mental health centers, medical centers with a high percentage of minority patients, colleges, churches, and dermatology, dental, primary care, and cosmetic surgery settings.

Recruitment Procedures

Subjects will be recruited from BDD programs at MGH and RIH, which are nationally known for their BDD work and have excellent access to BDD patients. Recruiting patients from two sites will enable us to obtain the required number of subjects and potentially increase the sample's diversity and representativeness. At MGH, where Dr. Wilhelm directs the BDD Clinic and Research Unit and is Director of the OCD and Related Disorders Program, she reviews all new intakes and assigns new patients to clinicians. This will enable her to screen all new patients for BDD and invite patients who appear eligible to participate in the study. Dr. Phillips has a similar role in her BDD Program at RIH and will be able to similarly screen new patients for potential study participation. Per the timeline below, we will need to randomize subjects at a rate of 1.4-1.5 per month at each site. After reviewing enrollment rates at both sites for BDD intervention studies over the past several years and adjusting estimates for the proposed study's inclusion/exclusion criteria, we estimate that we will actually be able to randomize 1.8 subjects per month at each site. This estimated enrollment rate is slightly higher than what is needed for our target sample size of 120 subjects who are eligible in 42 months. In our R34 CBT treatment development study, we recruited 1.2 subjects per month per site with very limited advertising funds for the study. Thus, with advertising resources specifically allocated for this study, we expect to easily meet our recruitment targets.

We will use recruitment strategies that have been successful in our prior BDD treatment studies. We will advertise on our clinic websites. We will advertise on other websites, including BDD Central (which has about 20 million visitors a year), ADAA, NAMI, Craigslist, Facebook, and My Space, and will run sponsored ads on Google. We will advertise in newspapers, on radio stations, and in movie theaters, the Boston subway, and buses. We will send brochures to clinicians (mental health professionals, dermatologists, plastic surgeons, primary care physicians) and colleges describing our study. We will post flyers in the Boston and Providence areas and surrounding towns. We will also advertise on listservs for organizations such as the Massachusetts Psychiatric Society, the Rhode Island Psychiatric Society, the MGH and Partners employee broadcast, and the Brown University Department of Psychiatry. We will continue to do media interviews and local presentations on BDD, which enhances recruitment for our studies. Our books on BDD, written for both the public and professionals are expected to generate study referrals. Our recruitment strategies follow the guidelines on the NIH website to ensure racial/ethnic diversity, and many of our advertisement strategies (e.g., newspaper advertisements) specifically focus on minority groups.

Remuneration

We will reimburse subjects $25 for taking part in the week 12, post-treatment visit, the 3-month follow-up, and the 6-month follow-up, which should help minimize attrition. Participants will be given a voucher to cover the cost of parking should they drive to the clinic. All study evaluations and study visits will be provided at no cost.

Consent Procedures

Participants who appear eligible will attend an in-person screening assessment with the Independent Evaluator, who will do a standard clinical evaluation to confirm study eligibility and to discuss treatment options. The PI or a doctoral level delegate will obtain informed consent.

Data and Safety Monitoring

***Responsibility for Data and Safety Monitoring*:** The PIs will have overall responsibility for monitoring the integrity of study data and participant safety. In addition, Rebecca Betensky, Ph.D., Professor of Biostatistics, Harvard

School of Public Health; Stefan Hofmann, Ph.D., Professor of Clinical Psychology and Director of the Psychotherapy and Emotion Research Laboratory, Boston University; and Helen Blair Simpson, M.D., Ph.D., Associate Professor of Clinical Psychiatry, Columbia University and Director of the Anxiety Disorders Clinic, New York State Psychiatric Institute, will regularly review the progress of the trial as discussed below. These individuals have expertise in treatment research and are not otherwise involved in our study.

***Procedures for Monitoring Participant Safety*:** We will implement the following procedures to ensure data integrity and the safety of participants during the study:

1) A number of elements of the research plan are intended to minimize the risks of study participation (see above). For example, the study exclusion criteria exclude patients who are experiencing clinically significant suicidality or require a higher level of care than outpatient. We will also carefully monitor ratings on the Beck Depression Inventory suicide item (#9); any participant with a score >1 at any assessment will be immediately evaluated by the therapist and PI and referred to a higher level of care if clinically indicated. If the assessment was conducted by a therapist he/she will immediately contact the PI. The PIs, or a covering clinician in their absence, will be available at all times to discuss the status of the participant and treatment plan. Additional procedures for managing participant safety, including the response to clinical deterioration (as defined above) should it occur, are detailed above.

2) The investigators and study staff will discuss participant safety in person or via conference call at a minimum of every other week. They will also discuss and resolve any safety issues more frequently if necessary, as such issues arise -- e.g., the occurrence of adverse events (see below), possible participant withdrawal from the study, a score of >1 on the Beck Depression Inventory suicide item at any assessment, or deterioration as defined by a rating of 6 (much worse) or 7 (very much worse) on the global CGI during three consecutive assessments. The PIs will be responsible for preparing a summary of adverse events for distribution prior to these discussions and will also prepare a written report that summarizes these discussions and any decisions that are made pertaining to participant disposition.

3) We will review study risks and the status of participants' safety with our NIMH program officer per the required reporting process. These reports will include a discussion of adverse events that have occurred, a review and reassessment of possible risks to participants, and any ethical issues that may arise.

4) Rebecca Betensky, Ph.D., Professor of Biostatistics, Harvard School of Public Health; Stefan Hofmann, Ph.D., Professor of Clinical Psychology and Director of the Psychotherapy and Emotion Research Laboratory, Boston University; and Helen Blair Simpson, M.D., Ph.D., Associate Professor of Clinical Psychiatry, Columbia University, and Director of the Anxiety Disorders Clinic, New York State Psychiatric Institute, none of whom are otherwise involved in the study, will review the progress of the trial twice yearly, discuss any safety concerns that have arisen, and make recommendations to improve safety procedures if indicated. Dr. Betensky was chosen because she has provided statistical support for many therapy outcome studies, and has considerable experience with issues concerning human subjects research, including safety concerns related to treatment outcome research. In addition, she has served on the DSMB of another collaborative treatment study of the PIs and is therefore familiar with issues pertaining to BDD specifically. Dr. Hofmann was chosen because he has conducted several CBT studies on anxiety disorders and has conducted research with psychotic disorders. Dr. Hofmann served on the Charles River Campus IRB at Boston University, and is thus very familiar with safety and ethical concerns related to human subjects in clinical research. In addition, he is familiar with BDD and has served on the DSMB of another collaborative treatment study of the PIs and is therefore familiar with issues pertaining to BDD specifically. Dr. Simpson was chosen because she has been the PI on many NIMH-funded treatment outcome studies, including studies of CBT for OCD, a disorder that shares many clinical features with and commonly co-occurs with BDD.

5) Data integrity and confidentiality will be safeguarded as discussed above.

Reporting of Adverse Events

Reporting of adverse events will occur as follows:

1) Serious adverse events that are reportable according to the guidelines of the Office for Human Research Protections (OHRP) and FDA (e.g., death, suicide attempt, inpatient hospitalization) will be reported by telephone

within 24 hours to: 1) the IRBs of MGH and Rhode Island Hospital and 2) the NIMH program officer. A full written report of the event will be sent to the above entities within 1 week of the event's occurrence.

2) Any other unanticipated problems occurring at either study site will be reported to the IRB within 2 weeks, in accordance with guidelines of the Office for Human Research Protections (OHRP) and FDA.

3) All adverse events will be summarized in the NIMH and IRB annual progress reports.

4) We will inform the NIMH and the other site's IRB of actions, if any, taken by any of the sites' IRBs as a result of their continuing review.

Quality Assurance

Initial Therapist Training and Certification

In addition to the requirement for prior training in CBT or SPT, therapists will receive rigorous training before treating study patients. First, therapists will read the treatment manuals, related reading materials for the condition they will treat in (CBT or SPT), and readings on BDD. Therapists will then have to pass (i.e., 90% correct) a knowledge test about their reading material. Therapists for both conditions will attend a 2-day training. The first day (attended by all study staff [see below]) will be led by Drs. Wilhelm and Phillips and consist of an overview of the phenomenology and other important aspects of BDD, and implementation of the study protocol. On the second day, CBT and SPT therapists will meet with Dr. Wilhelm and Dr. O'Keefe, respectively, for a treatment-specific training on the manualized treatments, which will include slide presentations, role plays, and discussion. Dr. O'Keefe has expertise in SPT and teaches a course on supportive psychotherapy at MGH. In her role as Director of Internship and Psychology Training at MGH, she is highly experienced with therapist training and supervision. Drs. Wilhelm and O'Keefe will then hold a joint workshop for both groups of therapists highlighting the distinctiveness of the two treatments.

After this training, each therapist will be assigned a test case with BDD whom they will treat with the treatment they will deliver during the study (CBT or SPT). For certification, therapists' first six treatment sessions will be reviewed by Dr. Wilhelm (for CBT) or Dr. O'Keefe (for SPT), who will score the treatment fidelity measures developed with our R34. We have adapted these measures for SPT; similar SPT fidelity measures were used in our prior NIMH therapy studies. The treatment fidelity measures rate adherence to the treatment manual (on a scale from 1 to 7) and competent delivery of treatment procedures (on a scale from 1 to 5). Therapists with average scores of $\geq$ 6 (mostly or completely) on adherence and $\geq$ 4 (mostly or completely) on competence for each of these sessions will be certified to treat subjects. (Ongoing fidelity will be monitored as described below.) If these initial certification standards are not met, Drs. Wilhelm or O'Keefe will provide more training, and the next three consecutive sessions will be reviewed and must meet certification standards. In addition, the SPT therapist cannot provide any CBT strategies. Therapists who do not meet these initial certification standards will be replaced (although we do not expect this to occur, as we will use experienced therapists and provide rigorous training and ongoing supervision from CBT and SPT experts).

Ongoing Therapist Supervision

To ensure ongoing high-quality treatment, Dr. O'Keefe will provide weekly supervision in SPT, and Dr. Wilhelm will provide weekly supervision in CBT. Particular care will be taken in supervision to ensure that specific CBT techniques are not introduced into SPT. As discussed above, selection of CBT treatment modules will be discussed during supervision so modules can be consistently selected across patients and sites.

Ongoing Monitoring of Treatment Fidelity

All treatment sessions will be digitally audio recorded. Once therapists meet the initial certification standard, a doctoral level independent adherence rater will rate 15% of randomly selected sessions at regular intervals during the study using our adherence and competence measures. This will be done to ensure adherence to the treatment manuals, cross-site consistency of treatment delivery, and competent delivery of the treatments. The adherence rater will have experience with both CBT and SPT and will be further trained and supervised by Drs. Wilhelm and O'Keefe. He/she will attend the first day of the initial therapist training activities described above and will watch tapes of the CBT and SPT training that occur on the second day of training. Descriptive statistics on adherence and competence ratings will be obtained.

If minimum standards are not met (i.e., if two consecutive recorded sessions receive an adherence or competence rating below the above certification standard), the therapist will receive additional training from Drs.

Wilhelm or O'Keefe, and the next three consecutive sessions will be reviewed and must meet certification standards for continued treatment to occur. After the therapist is re-certified, the adherence rater will subsequently rate 15% of digitally recorded sessions (rather than consecutive recordings). Therapists who do not meet these standards will be replaced (although we do not expect this to occur, given that we will use experienced therapists and provide initial training and ongoing supervision from CBT and SPT experts).

Independent Evaluator (IE) Qualifications and Ensuring IE Blindness

A blinded evaluation of outcomes by an IE is essential to obtain unbiased information on treatment efficacy. IEs will have a doctoral degree in psychology or a related mental health field with at least a year of rating experience. We will take many steps to ensure that IEs remain blind to treatment condition throughout the study for all participants. IEs will not be told the treatment assignment for any participant. IEs will be trained to focus on outcome measurement only and to avoid any discussion of what treatment subjects are receiving. Moreover, patients will be reminded at each IE assessment not to discuss their treatment with the IE. Therapists and study staff will be regularly reminded of this as well. Supervisory discussions about treatment will occur in separate meetings attended only by therapists and supervising clinicians. In addition, the IE's office will be located in a separate area from therapists' offices so the blind will not be broken by the IE observing which clinician the patient is seeing. Treatment and assessment recordings will be kept in separate locations. Furthermore, the IE will be asked to guess the treatment condition of each participant after the completion of the follow-up assessments or, for dropouts, after the last treatment session.

Establishing and Monitoring Interrater Reliability

We have extensive experience with the measures we propose to use in this study. Training and reliability checks will be done to ensure that IEs at each site conduct ratings in a uniform way. Raters will first receive instruction in the SCID-I/P, SCID-II, BDD-YBOCS, BABS, BDD Data Form, and CGI from Dr. Phillips, who developed the BDD measures, at the two-day start-up meeting. The Clinical Assessment and Training Unit in the Department of Psychiatry and Human Behavior at the Alpert Medical School of Brown University will provide both sites with SCID-I/P training via DVDs, which cover an introduction to the SCID-I/P and detailed instructions on administering each module. Dr. Phillips, who has clinical and research experience in personality disorders, will provide training on the SCID-II. In addition, IE's will observe their site's PI administering these measures to four patients; both PIs have extensive experience administering these measures. Subsequently, IEs will additionally rate BDD-YBOCS, BABS, and SCID-II training tapes of interviews conducted by Dr. Phillips, and rate interviews on the SCID-I/P training DVDs. The raters will discuss their ratings of these tapes and DVDs with Dr. Phillips. They will then begin to administer and record interviews for review by Dr. Phillips. IEs will be certified when they reaches reliability criteria with Dr. Phillips for the BDD-YBOCS, BABS, SCID-I/P, and SCID-II on four consecutive tapes. Reliability criteria will consist of ICC=.8 or higher for the BDD-YBOCS and BABS total score, kappas of .8 or higher on the SCID-I/P and SCID-II, and 100% agreement on BDD diagnosis on the SCID-I/P. Ratings will be submitted via REDCap to MGH statisticians for statistical analysis.

To maintain inter-rater reliability during the study and reduce rater drift, all assessments will be audio recorded digitally. Dr. Phillips will review and rate 15% of randomly selected digitally recorded interviews at regular intervals during the study. If reliability with Dr. Phillips falls below the above criteria we will institute retraining procedures. Dr. Phillips will also conduct weekly phone supervision meetings with IEs during which diagnostic and assessment interviews from the past week will be discussed. Any problems in interview content and diagnostic disagreements will be addressed during supervision. Reliability statistics for diagnoses (kappa) and continuous ratings (intraclass correlations) will be included in our publications.

For training on our neurocognitive measures, our consultants Drs. Buhlmann and Savage will attend the second day of the start-up meeting to train the IEs to administer and score the neurocognitive measures. Dr. Savage will also train the IEs in administering the WASI. In addition, Drs. Buhlmann and Savage will participate in our cross-site conference calls every other month to discuss any rating issues. Dr. Savage will score 15% of tests, and reliability on the ROCF will be established, as described in Deckersbach and colleagues.

Research Team Meetings and Conference Calls

All study personnel will attend a two-day meeting before subject enrollment to discuss the protocol, study procedures, rating scales, recruitment, and other issues; therapists and IEs will receive additional training specific to their roles in the study. All MGH and RIH study personnel will also attend one in-person meetings a year to discuss issues such as the study's progress, recruitment, treatment fidelity, and interrater reliability. The two PIs, study

coordinators, and research assistants will also have twice monthly 90-minute conference calls to discuss the study, including recruitment, new subjects to ensure inclusion/exclusion criteria are met, withdrawal of any subject, any safety issues, and other topics. Our consultants Drs. Buhlmann and Savage will participate in these calls as described above. In addition, the PIs will discuss the study on their regular monthly 60-minute conference calls, and each site will discuss the study at their site-specific weekly research meetings. Dr. Steketee will consult on treatment procedures on an as-needed basis. Dr. Wilhelm will meet weekly with Ms. Keshaviah and monthly with Dr. Schoenfeld from the MGH Biostatistics Center. Drs. Wilhelm and Phillips will have a twice yearly conference call with the Data and Safety Monitoring Board.

Privacy and Confidentiality

The following methods will be used to protect the confidentiality of information provided by study participants:

a) Data will be encoded using patient IDs but not names. IDs will be assigned sequentially, in a manner unrelated to name, social security number, or other easily identified information.

b) Names will not be included on digital recordings, in computerized data files, or in any published reports.

c) Digital recordings for interrater reliability, treatment adherence, or competence will be returned to the data management site at MGH and stored securely in the BDD Clinic.

d) Study data will be reviewed only by study personnel or, if necessary, by institutional, state, or federal regulatory personnel.

e) All personnel will be trained in research confidentiality procedures and will be educated about the importance of strictly protecting participants' rights to confidentiality.