Supplementary Table 2: Considerations for Relative Contraindications to Fluvoxamine

Patient Factors	Reasoning (if not obvious)
Allergy to fluvoxamine	
Moderate to severe depression within 6 weeks of enrollment	If the patient would need to be switched to fluvoxamine from another agent due to drug-interactions, this would ideally be done with explicit supervision
Previous or current diagnosis of manic depression / bipolar disorder	If the patient would need to be switched to fluvoxamine from another agent or if there would be concern that adding fluvoxamine might trigger a manic episode
Hepatic impairment defined as known Cirrhosis of any severity	Fluvoxamine metabolism is altered in patients with cirrhosis
Hospitalization for gastrointestinal or other non-traumatic bleeding within the last year	Fluvoxamine can impact platelet aggregation and these patients were excluded from the trial. This decision could be individualized.
Concurrent Medications	
Caffeine	Fluvoxamine leads to substantial increases in caffeine levels. In the trial, we encouraged no caffeine for participants. At the very least they were told avoid more than 1 small cup of coffee's worth of caffeine (and to stop caffeine if they felt it was "too energizing").
Patients taking warfarin	Increased bleeding risk due to increased AUC of warfarin
Patients taking clopidogrel	Increased risk of ischemic event due to metabolism
Patients taking 2 or more of the following: aspirin, NSAIDS, ticlopidine, prasugrel, ticagrelor, direct oral anticoagulants	Assuming NSAIDs cannot be held. Fluvoxamine can impact platelet aggregation and these patients were excluded from the trial. This decision could be individualized.
Donepezil	This is a Sigma-1-receptor (S1R) agonist and we excluded patients from the trial given that fluvoxamine was being used for its S1R activity
Other antidepressant medications	For any patient already on a tricyclic antidepressant, SSRI, or SNRI, we evaluated whether it could be held or reduced under medical supervision during the time they were prescribed fluvoxamine. If the patient was taking a low dose of another medication (e.g., citalopram 10mg) and there was low risk of serotonin syndrome, concurrent use was allowed.
Use within 14 days of an MAO inhibitor [e.g., Isocarboxazid (Marplan), Phenelzine (Nardil), Selegiline (Emsam), Tranylcypromine (Parnate)]	Important drug interactions risking serotonin syndrome

Patients taking astemizole, cisapride, mesoridazine, ramelteon, or terfenadine	Contraindicated due to hepatic CYP3A4 interaction
Patients taking phenytoin or valproic acid	Potential interaction leading to seizure
Patients who are taking mirtazapine, melatonin, tramadol, or triptan medications	If these drugs could not be held, there was a risk of drug interaction increasing levels of these medicines
Participants taking alosetron, clozapine, flutamide, mexiletine, olanzapine, rasagiline, ropinirole, tacrine, theophylline, tizanidine, triamterene	Drugs are primarily metabolized by CYP1A2, which is inhibited by fluvoxamine.
Diazepam or alprazolam users	Due to interactions, we recommend reducing the dose by 25% unless the patient has a known seizure disorder (in which case they were excluded).