Supplementary Online Content

Ma J, Rosas LG, Lv N, et al. Effect of integrated behavioral weight loss treatment and problem solving therapy on body mass index and depressive symptoms among patients with obesity and depression: the RAINBOW randomized clinical trial. *JAMA*. doi:10.1001/jama.2019.0557

This supplementary material has been provided by the authors to give readers additional information about their work.

eAppendix 1. Reasons for Exclusions

	Frequency	Percent
Patient Health Questionnaire (PHQ) ineligible	3291	69.3
Move out of the area or transfer care outside of the health system during the study period	539	11.3
Other exclusions (age<18, low English proficiency, lack of Internet/email access, living in the same household with a person enrolled in or affiliated with this study, not interested, decline to answer an eligibility question)	262	5.5
CAGE Adapted to Include Drugs (CAGE-AID) Questionnaire score >= 2	165	3.5
Psychiatric care outside the health system	121	2.5
Exclusionary comorbidities (bipolar disorder, psychotic disorder, diabetes, active cancer, heart attack, stroke, congestive heart failure, or blood vessel surgery)	91	1.9
Pregnant, breast-feeding or planned pregnancy	89	1.9
Body mass index (BMI) ineligible	50	1.1
Active bulimia nervosa within the past three months	48	1.0
Suicide ideation	47	1.0
Haven't been a patient at the health system for at least 1 year	39	0.8
Recommended exclusion by study physician or coordinator due to health concern	7	0.1

eAppendix 2. I-CARE (Integrated CoAching foR bEtter mood and weight) Intervention Outline

Week	Visit	Time	Content
1	1	60 min	• Introduction to I-CARE Mood and I-CARE Lifestyle[1] sequenced integration (5 min) • Technology: Fitbit, MyFitnessPal - using, linking, friend requests to coach; My Health Online[2]. Encouragement to wear Fitbit and check uploads (10 min) • Physical activity safety guidelines handout (GLB Session 4, pages 3,4) • Evaluation of bathroom scale ownership • I-CARE Mood Session 1 (45 min)
2	2	60 min	• I-CARE Mood Session 2 (60 min) • Provision of bathroom scale to participants requiring one
3	3	60 min	• I-CARE Mood Session 3 (60 min)
4	4	60 min	• I-CARE Mood Session 4 (50 min) • Technology: MyFitnessPal - explanation of logging physical activity minutes and weight; introduction to logging diet; importance of self-monitoring (10 min)
6	5	60 min	• I-CARE Mood Session 5 (45 min) • I-CARE Lifestyle introduction and self-study guidelines (5 min) • Technology: MyFitnessPal - review of logging physical activity and weight; explanation of logging diet; importance of self-monitoring (10 min)
8[3]	6	60 min	• I-CARE Lifestyle Progress Check (5 min) • I-CARE Mood Session 6 (30 min) • Technology: MyFitnessPal , Fitbit, My Health Online check in (5 min) • Goals confirmation: weight, physical activity, steps (5 min) • Optional tools to reduce calorie intake: meal plans, packaged meals (5 min) • I-CARE Lifestyle Session (GLB Sessions #1,2) (10 min)
12	7	60 min	• I-CARE Lifestyle Progress Check (10 min) • I-CARE Mood Session 7 (35 min) • I-CARE Lifestyle Session (GLB Sessions #3,4,5,6) (15 min)
16	8	60 min	• I-CARE Lifestyle Progress Check (10 min) • I-CARE Mood Session 8 (35 min) • I-CARE Lifestyle Session (GLB Sessions #8,9,10)(15 min)
20	9	60 min	• I-CARE Lifestyle Progress Check (10 min) • I-CARE Mood Session 9 (35 min) • I-CARE Lifestyle Session (GLB Sessions #11,12)(10 min) • Overview of weeks 21-52 (5 min)
21-52	Phone	15-30 min	• I-CARE Lifestyle Progress Check (5-10 min) • I-CARE Mood Session(5-10 min) • I-CARE Lifestyle Session (5-10 min) • Discussion of maintenance plan when program goals met

[1] I-CARE Mood = PEARLS program
I-CARE Lifestyle = GLB program

[2] Participants receive Fitbit, MyFitnessPal, and My Health Online instructions via mail or e-mail prior to first session

[3] Expanded description of I-CARE Lifestyle content found on I-CARE Lifestyle Outline (next page)

I-CARE Lifestyle Outline

1. I-CARE Lifestyle Progress Check (5-10 min)
   - Evaluation of progress towards weight, physical activity, and step goals by review of self-monitored data
   - Strategies for improved monitoring, as needed
   - Identification of barriers and challenges to making progress towards goals, as needed
   - Problem solving around weight loss and physical activity challenges, as needed

2. I-CARE Lifestyle Session (10-15 min)

Week	Visit	Time	GLB Videos[1]	Content
8	6	10 min	1: Welcome to GLB Getting Started Losing Weight 2: Be a Fat and Calorie Detective	► Participant GLB DVD viewing progress and questions[2] ► Fat and calorie goals review/appropriateness (S2, P8)[3] • Identify 5 foods high in fat and/or calories and strategies to eat less fat or calories for each food (S2, P12,13)
12	7	15 min	3: Healthy Eating 4: Move Those Muscles 5: Tip the Calorie Balance 6: Take Charge of What's Around You	► Participant GLB DVD viewing progress and questions ► Progress review, structured meal plan and/or packaged meal use review (S5, P4,5) ► Physical activity plan (S6, P5) • Environmental cues activity (S6, P4) • My Plate as model for healthy meals experiences (S3,P12)
16	8	15 min	8: Four Keys to Healthy Eating Out 9: The Slippery Slope of Lifestyle Change 10: Jump Start Your Physical Activity Plan	► Participant GLB DVD viewing progress and questions ► Progress review (S9, P1) • Slips from healthy eating and being active (S9, P7,8) • Eating out problem (S8, P6)
20	9	10 min	11: Make Social Cues Work for You 12: Ways to Stay Motivated	► Participant GLB DVD viewing progress and questions ► Progress review (S12, P1) • Problem and positive social cues (S11, P6,7) • Personal lifestyle contract (S12, P11,12)
21-52	Phone	5-10 min	Supplements : 14: More Volume, Fewer Calories 15: Balance Your Thoughts for Long-Term Self-Management 16: Strengthen Your Exercise Program 19: Standing Up for Your Health 21: Stretching: The Truth About Flexibility 22: Looking Back and Looking Forward	► Participant questions ► Review of one session of supplementary material per call

[1] GLB main video 7 Problem Solving was intentionally excluded because of the Problem Solving Therapy component of the I-CARE intervention. Supplemental videos 13 Long-Term Self-Management, 17 Mindful Eating, and 18 Stress and Time Management were available for participant self-study.

[2] Participants receive EHR messages summarizing content of GLB DVD assigned sessions prior to visits 6, 7, 8, and 9

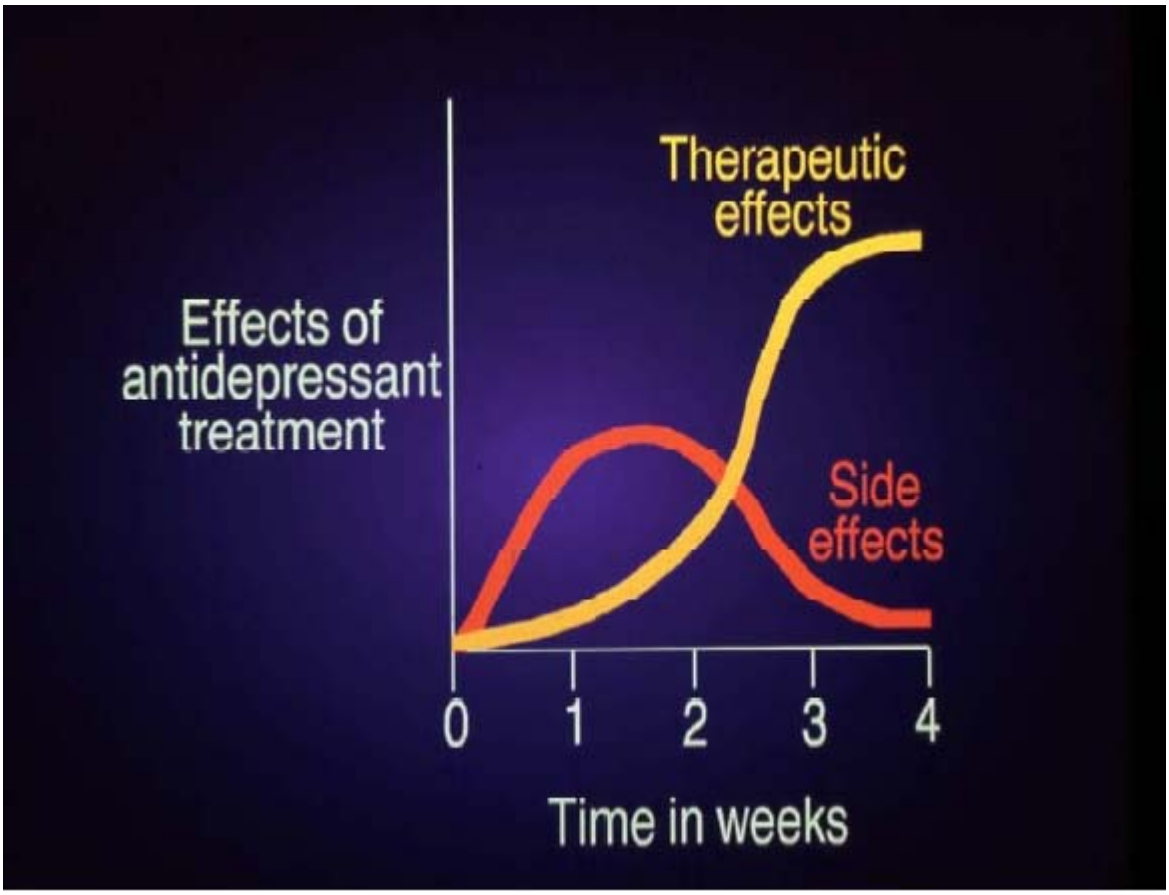
[3] S and P refer to session (S) and page number (P) in GLB session handouts

► Priority discussion

• Optional discussion (time permitting)

eAppendix 3. I-CARE Medication Protocol

I-CARE Treatment of Depression with Medications
A. Initiating Antidepressants
When starting patients on antidepressants, they need to understand that side effects can occur before the medication's therapeutic effects help them to feel better. It is helpful to draw the figure below for patients, illustrating that side effects peak in the first 1-2 weeks and then subside, whereas therapeutic effects often peak at 3-4 weeks. This figure can prevent patients from getting discouraged prematurely and discontinuing medications.



These materials were adapted with permission from Dr. Wayne Katon, Principal Investigator for the TEAMcare trial (http://www.teamcarehealth.org).

B. Antidepressant Side Effects

Short-Term Side Effects:

These occur within the first several weeks and include jitteriness, insomnia, headache, and nausea, and other side effects that may be idiosyncratic to the individual patient. These symptoms are usually lessened by starting antidepressants at a low dose and increasing the dose weekly. Short-term side effects usually disappear within 2-3 weeks.

Long-Term Side Effects:

- *Diarrhea* is particularly common with sertraline (Zoloft), but can occur with other SSRIs or with bupropion (Wellbutrin). Changing to a low dosage of paroxetine (Paxil) at 5-10 mg and titrating upward by 5-10 mg every 7-10 days to a dosage of 20-50 mg may help because paroxetine (Paxil) has slight anticholinergic effects.

- *Sexual dysfunction* can occur in up to one third of patients receiving selective serotonin reuptake inhibitors (SSRIs), such as fluoxetine. It is important to ask about sexual function, since many patients with diabetes already have problematic sexual functioning. The most common sexual side effect is delayed orgasm or inability to experience orgasm. Patients can be switched or cross-tapered to bupropion SR if they experience this side effect on an SSRI. The addition of bupropion SR 100 mg twice a day or buspirone 15 mg twice a day to an SSRI regimen also often alleviates sexual dysfunction.

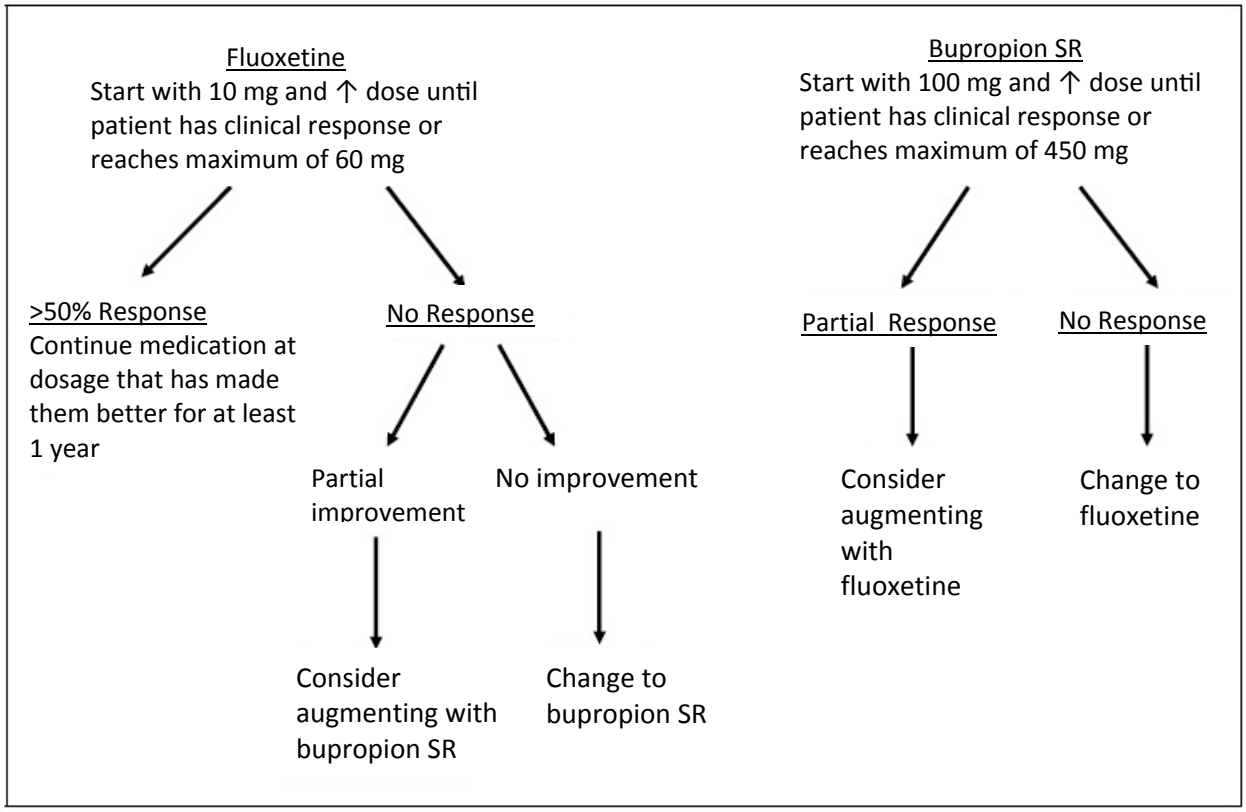
- *Sleep problems* continue to occur in approximately 25-33% of patients despite effective SSRI treatment. For people bothered by insomnia, trazodone could be prescribed, starting at 25 mg at bedtime and increasing the dose by 25 mg increments every 5 days until insomnia is successfully treated.

- *Weight gain*, a significant problem for many people with type 2 diabetes, is worsened for 5-10% of SSRI-treated patients. Paroxetine is the SSRI that has the most weight gain associated with it. Because bupropion and fluoxetine are not associated with weight gain, these antidepressants are good first choices for overweight people.

C. Choice of Antidepressant

For patients already taking an anti-depressant at a sub-therapeutic dose, the first treatment action step is to titrate up the antidepressant dosage. All titrations should be done slowly, on a weekly basis, until PHQ-9 score goals are achieved: either < 5 or a decrease of half the baseline total score.

For patients who have never taken antidepressants, fluoxetine or bupropion SR are good first-line antidepressant choices due to lack of weight gain with these medications. Initiation and titration are shown in the schematic below.



Patients who have tried one SSRI unsuccessfully in the past can be switched to either a second SSRI, bupropion SR, or venlafaxine XR.

Patients with coexisting anxiety can usually be effectively treated by starting on citalopram or sertraline.

Patients with moderate to severe neuropathy may be treated with either venlafaxine XR, duloxetine, or bupropion SR. These medications have been shown in randomized controlled trials in non-depressed individuals to reduce neuropathic pain.

Patients with pre-existing sexual dysfunction can usually be successfully treated with bupropion SR. While other antidepressants are likely to worsen problems with sexual response, initiating treatment with bupropion SR may improve function. Adding an antidepressant such as bupropion SR or an anti-anxiety agent such as buspirone to an SSRI can also help sexual function in patients with diabetes and may be viewed very positively. The TCM should work with the consulting psychiatrist when carrying out antidepressant augmentation strategies.

D. Strategies for Overcoming Common Issues with Taking Antidepressants

A variety of strategies may help patients take antidepressants, including:

- Provide rationale for use.
- Pay vigorous attention to side-effects.
- Counter demoralization, fear of dependence, and loss of control.
- Enlist family/spousal support.
- Elicit resistance and relationship to prior experience with medication.
- Identify relevant illness aspects (phobic, paranoid).
- Increase contact with brief phone check-ins.
- Give specific instructions (take regardless of symptom change, don't stop on own).
- Use symptom scale PHQ-9 to chart progress.

Depression **Goal: PHQ-9 < 5 OR at least 50% decrease from baseline in PHQ-9**

- TCM to encourage patient to fill out PHQ-9 weekly until reaches a "steady state", then prn.
- TCM to discuss behavioral activation methods, medication adherence strategies, rationale for initial and long-term maintenance therapy with antidepressants (e.g., don't decrease dose or stop without checking with TCM or PCP; take regardless of symptoms), and side effects (most disappear at 2 weeks).
- TCM to contact PCP and team psychiatrist if patient has: acute suicidal symptoms, psychotic symptoms, manic symptoms, severe lack of appetite with insufficient oral intake or weight loss, suspected alcohol or drug misuse, or severe medication side effects.
- Create ***My Better Health Plan*** initially and update at each visit.

ANTIDEPRESSANT MEDICATION

_____ **Fluoxetine** 10 mg/day X 1 week; then 20mg/day X 1 week. If PHQ-9 hasn't decreased by 50% or more, increase to 30mg/day. At week 4, if PHQ-9 hasn't decreased by 50% or more, increase to 40mg/day. Can increase fluoxetine up to a maximum of 60 mg/day as needed/tolerated.

_____ **If two or more negative SSRI trials** or for those patients with preexisting diabetes-related sexual dysfunction, start Bupropion SR 100mg/day for 1 week; then 100mg 2X/day for a week; then 200mg in am & 100mg in pm. If PHQ-9 at 4 weeks isn't decreased by 50%, increase dose to 200mg BID.

_____ If patient doesn't fit above criteria, or has significant medical or psychiatric symptoms, antidepressant medications to be suggested by CAREteam consulting psychiatrist or PCP.

Antidepressant Medications				
Drug	**Starting dose**	**Usual Dose**	**Indications**	**Side Effects**
Starting antidepressants: improvement often seen in first two weeks. If not seen by 8 weeks, likely needs new agent or second agent. Check in at least weekly when starting antidepressants. 2/3 of people with depression will improve with antidepressants.				
Stopping antidepressants: Recurrence of depression is common. 64% of patients with depression had a recurrence 10 years after stopping their antidepressants. If patients do decide to stop their antidepressants, encourage them to talk with their PCP prior to stopping and help them understand that there are fewer problems when antidepressant dosages are tapered over a two week period.				
Selective serotonin reuptake inhibitors (SSRIs)				
Citalopram (Celexa)	10	20-40	Max FDA daily recommended dose for patients >60 yrs old is 20 mg	Jitteriness, restlessness, agitation, headache, GI distress, nausea, diarrhea, insomnia usually improve in 2 weeks. Weight gain for some patients.
Fluoxetine (Prozac)	10	20-60	-First line (weight gain less likely) -Also used to treat binge eating disorder (BED) and post traumatic stress disorder (PTSD)	
Fluvoxamine (Luvox)	50	50-300		
Paroxetine (Paxil)	20	20-60	Worst for sexual dysfunction, weight gain, sedation; mild anticholinergic effects (helps diarrhea)	Same as above.
Paroxetine CR (Paxil CR)	25	25-75		Same as above.
Sertraline (Zoloft)	50	50-200		Same as above.
Escitalopram (Lexapro)	10	10-20	Also used to treat BED	Same as above.
Dopamine-norepinephrine reuptake inhibitors				
Bupropion SR (Wellbutrin SR) ***When dose > 100 mg give bid.*	100	300-400	Weight gain rare. May improve sexual functioning. Useful for lethargic patients.	***Contraindicated in patients with seizure history or eating disorders.***
Serotonin-norepinephrine reuptake inhibitors (SNRIs)				
Venlafaxine XR (Effexor XR)— *****When dose > 75 mg, give bid.***	37.5, 75 & 100	75-300		Effective for diabetic neuropathy, fibromyalgia, chronic pain.
Duloxetine (Cymbalta)—	30	60-120		Effective for diabetic neuropathy, fibromyalgia, chronic pain.
Serotonin modulators				
Trazodone (Desyrel)	*25-50*	50-300	Useful for insomnia associated with depression/anxiety.	Doses > 50 mg can cause orthostatic hypotension or (rarely) priapism.
Tricyclics and tetracyclics				
Amitriptyline (Elavil)	25-50	100-300		Anticholinergic side effects and weight gain. Elders particularly susceptible to memory change, confusion, hallucinations, sedation and orthostatic hypotension.
Amoxapine (Asendin)	50	100-400		
Clomipramine (Anafranil)	25	100-250		
Maprotiline (Ludiomil)	50	100-225		
Doxepin (Adapin, Sinequan)	25-50	100-300		
Imipramine (Tofranil)	25-50	100-300		
Desipramine (Norpramin)	50	100-300		
Nortriptyline (Pamelor)	25	50-200		

Antidepressant Medications				
Drug	**Starting dose**	**Usual Dose**	**Indications**	**Side Effects**
Protriptyline (Vivactil)	10	15-60		**Contraindicated in patients with recent MI, cardiac conduction problems**
Noradrenergic and specific serotonergic antidepressant				
Mirtazapine (Remeron)	15	15-45		Causes weight gain in 50% of patients. Helpful for anxious patients with insomnia and no appetite.

eAppendix 4. Study Measured Weight Loss Outcome

	Unadjusted Estimates		Treatment Difference	
	Intervention	Usual Care	Adjusted difference in means	*P* Value
	n=169	n=169	(95% CI)*	
BMI, mean (SD)				
6 months	36.0 (7.2)	36.4 (5.8)	-0.9 (-1.2, -0.5)	<0.001
12 months	36.0 (7.3)	36.4 (6.1)	-0.7 (-1.3, -0.2)	0.01

Abbreviations: BMI, body mass index; CI, confidence interval; SD, standard deviation.
*Adjusted analysis for intervention vs usual care: adjusted difference in means for BMI and 95% CI. Linear mixed-effects model accounting for the random effects of repeated measures and primary care providers was adjusted for baseline value of the outcome of interest, clinic, age, sex, race/ethnicity, education, any antidepressant medications (if taken at the time of enrollment), and number of hospitalizations during 12 months before randomization.

eAppendix 5. Participants Who Were Prescribed Antidepressant Medications during 12 Months Pre and Post Randomization, No. (%)

	Pre randomization		Post randomization	
	Intervention	Usual care	Intervention	Usual care
	n=204	n=205	n=204	n=205
No antidepressant medication	105 (51.5)	108 (52.7)	76 (37.2)	119 (58.0)
Bupropion	27 (13.2)	21 (10.2)	32 (15.7)	23 (11.2)
Sertraline	25 (12.3)	18 (8.8)	27 (13.2)	13 (6.3)
Citalopram	16 (7.8)	18 (8.8)	12 (5.9)	18 (8.8)
Escitalopram	13 (6.4)	10 (4.9)	18 (8.8)	9 (4.4)
Fluoxetine	9 (4.4)	14 (6.8)	18 (8.8)	11 (5.4)
Trazodone	13 (6.4)	13 (6.3)	16 (7.8)	9 (4.4)
Venlafaxine	8 (3.9)	9 (4.4)	12 (5.9)	8 (3.9)
Amitriptyline	4 (2.0)	8 (3.9)	5 (2.5)	4 (2.0)
Duloxetine	9 (4.4)	7 (3.4)	16 (7.8)	9 (4.4)
Nortriptyline	3 (1.5)	4 (2.0)	2 (1.0)	3 (1.5)
Paroxetine	4 (2.0)	3 (1.5)	5 (2.5)	2 (1.0)
Desvenlafaxine	1 (0.5)	1 (0.5)	0 (0.0)	0 (0.0)
Mirtazapine	1 (0.5)	1 (0.5)	3 (1.5)	2 (1.0)
Naltrexone-Bupropion	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.5)
Vilazodone	1 (0.5)	0 (0.0)	1 (0.5)	0 (0.0)
Desipramine	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)
Doxepin	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)