Supplementary Online Content

Lam RW, Levitt AJ, Levitan RD, et al. Efficacy of bright light treatment, fluoxetine, and the combination in patients with nonseasonal major depressive disorder: a randomized clinical trial. *JAMA Psychiatry*. Published online November 18, 2015. doi:10.1001/jamapsychiatry.2015.2235.

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

eTable 1. Eligibility Criteria for Study

Inclusion criteria	1. Male and female outpatients aged 19-60 years. 2. Patients will meet DSM-IV-TR criteria for major depressive episodes as determined by a structured interview (Mini International Neuropsychiatric Interview, MINI). 3. A score of 20 or greater on the clinician-rated HAM-D, indicating at least moderately severe depression. 4. Competency to give informed consent.
Exclusion criteria	1. Pregnant women, lactating women and sexually active women of childbearing potential who are not using medically accepted means of contraception. 2. Serious suicidal risks as judged by the clinician. 3. The following DSM-IV diagnoses: • Major depressive disorder, recurrent, with a seasonal pattern • Organic mental disorders • Substance abuse/dependence, including alcohol, active within the last year • Schizophrenia, Paranoid or Delusional Disorders, or any other psychotic features • Obsessive-Compulsive Disorder, Post-Traumatic Stress Disorder • Panic disorder, Generalized Anxiety Disorder (if a primary diagnosis) • Bipolar Disorder 4. Serious illness including cardiac, hepatic, renal, respiratory, endocrinologic, neurologic and hematologic disease that is not stabilized, or a past history of convulsions. 5. Any retinal disease or systemic illness with active retinal involvement (e.g. diabetes) that precludes the use of bright light. 6. Patients who have a history of severe allergies and multiple drug adverse reactions. 7. Regular or current use of other psychotropic drugs including lithium, melatonin and tryptophan. 8. Patients treated with beta blocking drugs. 9. Hypertensive patients being treated with guanethidine, reserpine, clonidine or methyldopa (because of possible mood-altering effects of those drugs). 10. Use of monoamine oxidase inhibitors within 14 days of Visit 1 (to ensure no drug interactions between fluoxetine and MAOIs), or use of heterocyclic antidepressant within 7 days of screening Visit 1 (to ensure adequate washout period of two weeks between stopping previous drug and start of treatment at baseline Visit 2). 11. Previous use of fluoxetine or light therapy. 12. Treatment resistance in the current episode, as defined by failure (lack of clinically significant response) of two or more antidepressants given at therapeutic doses for at least 6 weeks. 13. Patients who started formal psychotherapy (e.g. cognitive-behavioural or interpersonal psychotherapy) within 3 months of Visit 1, or who plan to initiate such psychotherapy during the study. 14. Patients involved in any other form of treatment for depression.

eTable 2. Assessments Used in Study

Scale	Administration	Description
Hamilton Depression Rating Scale (HAM-D)[1]	Clinician-rated	The 17-item HAM-D is a widely used measure of outcome in depression studies. Higher scores indicate greater severity of depression.
Montgomery-Asberg Depression Rating scale (MADRS)[2]	Interviewer-rated	This 10-item scale is used widely for depression studies and is sensitive to change in clinical trials. Reliability is enhanced by using the Structured Interview Guide for the MADRS (SIGMA).[3] Higher scores indicate greater severity of depression.
Quick Inventory of Depressive Symptomatology, Self-Rated version (QIDS-SR)[4]	Patient-rated	This 16-item self-rated depression inventory rates the 9 DSM symptom criteria and is also widely used and validated in depression studies. Higher scores indicate greater severity of depression.
Clinical Global Impression scale, Severity (CGI)[5]	Clinician-rated	Used as a global measure of severity. Ratings range from 1=Normal, Not at all ill, 2=Borderline ill, 3=Mildly ill, 4=Moderately ill, 5=Markedly ill, 6=Severely ill, 7=Among the most severely ill patients. Higher scores indicate greater severity.
Clinical Global Impression scale, Improvement (CGI)[5]	Clinician-rated	Used as a global measure of improvement. Ratings range from 1=Very much improved, 2=Much improved, 3=Minimally improved, 4=No change, 5=Minimally worse, 6=Much worse, 7=Very much worse. Lower scores indicate greater improvement.
Expectation of Response Questionnaire (adapted from Borkovec and Nau)[6]	Patient-rated	This self-rated scale consists of 4 questions: Do you think you will benefit from this treatment? Do you think this treatment will make your symptoms worse? Do you think this is a logical treatment for depression? Would you feel confident in recommending this type of treatment for a friend? Responses are on a 5-point Likert scale ranging from “Not at all” to “Very Much.” Scoring is reversed for Question 2. Higher scores indicate greater expectation of response.
Adverse Events Scale[7]	Patient-rated	This self-rated scale assesses 41 adverse events and asks how troubling or disabling each one is (rated as Not at all, Slight, Moderate or Severe).

eTable 3. Results of Per Protocol Analysis for Completed Patients

	Conditions				
Measures	**Placebo (N=24)**	**Fluoxetine (N=27)**	**Light (N=28)**	**Combination (N=27)**	**Significant Comparisons**
Change in MADRS score, Baseline to endpoint, *mean (SD)*	7.9 (9.9)	9.3 (10.4)	13.6 (7.2)	16.5 (9.7)	L>P[1]; C>P[1] C>F[2]

[1] The ANOVA for change scores on the MADRS showed a significant overall effect (F=2.35, df=6,99, p=0.037) and a significant effect of condition (F=4.25, df=3,99, p=0.007). The preplanned simple contrasts found significant effects of light treatment versus placebo (p=0.04) and combination versus placebo (p=0.002), but not for fluoxetine versus placebo (p=0.63).

[2] *Post hoc* Tukey's Highly Significant Difference tests showed a significant effect of combination versus fluoxetine (p=0.03).

MADRS, Montgomery-Åsberg Depression Rating Scale; SD, standard deviation; P, Placebo; F, Fluoxetine; L, Light; C, Combination; >, superior to.

eTable 4. Results of Season of Treatment Analysis

	Season of Treatment[1]				
Measures	**Winter**	**Spring**	**Summer**	**Autumn**	**Significant Comparisons**
All conditions: Change in MADRS score, Baseline to endpoint, *mean (SD)*	9.9 (10.4) N=34	15.2 (9.3) N=27	10.9 (9.7) N=29	10.1 (9.3) N=32	No significant differences[2]
Light conditions only: Change in MADRS score, Baseline to endpoint, *mean (SD)*	14.0 (8.6) N=15	19.0 (9.0) N=13	13.1 (8.4) N=18	15.1 (7.7) N=15	No significant differences[3]

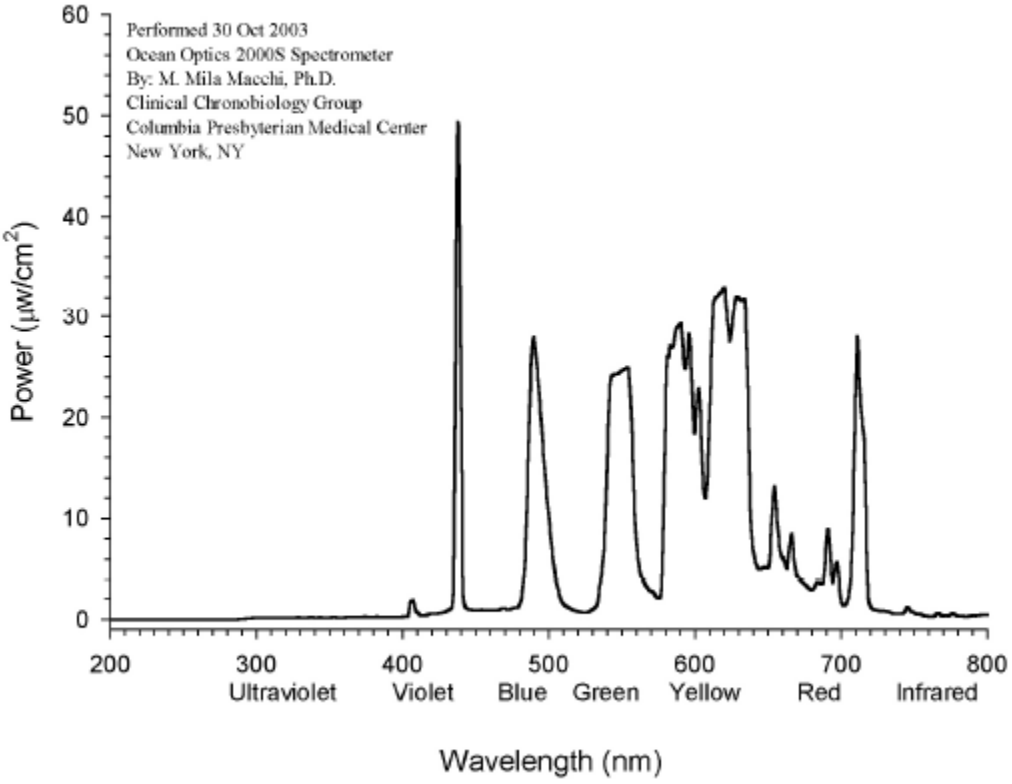
[1] Season of treatment was determined by the month of randomization and defined as winter (December, January, or February), spring (March, April, May), summer (June, July, August) and autumn (September, October, November). Results are shown in eTable 4. An ANOVA was conducted with MADRS change as the dependent variable and season of treatment as the fixed variable.

[2] For all conditions, the ANOVA for change scores on the MADRS showed no significant overall effects (F=1.66, df=6,115, p=0.168) and no significant effect of season (F=2.21, df=3,115, p=0.090).

[3] For the light conditions only, the ANOVA for change scores on the MADRS showed no significant overall effects (F=1.41, df=6,54, p=0.227) and no significant effect of season (F=1.43, df=3,54, p=0.245).

MADRS, Montgomery-Åsberg Depression Rating Scale; SD, standard deviation.

eFigure. Spectral Emission at 10,000 lux for Carex Day-Light Classic Model



Performed 30-Oct-2003, Ocean Optics 2000S spectrometer, by: M. Mila Macchi, PhD, Clinical Chronobiology Group, Columbia Presbyterian Medical Center, New York, NY.

eReferences

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