

## A Randomized, Double-Blind, Placebo-Controlled Study of Light Therapy for Antepartum Depression

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**Objective:** Affective disorder during pregnancy is a common condition requiring careful judgment to treat the depression while minimizing risk to the fetus. Following up on promising pilot trials, we studied the efficacy of light therapy.

**Method:** Twenty-seven pregnant women with non-seasonal major depressive disorder according to *DSM-IV* (outpatients, university polyclinic) were randomly assigned to 7,000 lux fluorescent bright white or 70 lux dim red (placebo) light administered at home in the morning upon awakening for 1 h/d in a 5-week double-blind trial carried out between October 2004 and October 2008. Clinical state was monitored weekly with the 29-item Structured Interview Guide for the Hamilton Depression Rating Scale (HDRS) with Atypical Depression Supplement (SIGH-ADS). Changes of rating scale scores over time were analyzed with the general linear model. Differences from baseline of SIGH-ADS and 17-item HDRS scores at every time point were the dependent variables, time was the within-subjects factor, and treatment was the between-subjects factor. The model also included baseline score of depression and gestational age at intervention start.

**Results:** The superiority of bright light over dim light placebo was shown for both SIGH-ADS ( $R^2 = 0.251$ ;  $F_{3,23} = 3.91$ ;  $P < .05$ ) and HDRS ( $R^2 = 0.338$ ;  $F_{3,23} = 5.42$ ;  $P < .01$ ) when analyzing the week-by-week change from baseline, and HDRS scores showed a significant interaction of treatment with time ( $F_{4,92} = 2.91$ ;  $P < .05$ ). Categorical analysis revealed that the response rate (HDRS  $\geq 50\%$  improvement) at week 5 was significantly greater for bright light (81.3%,  $n = 16$ ) than for placebo light (45.5%,  $n = 11$ ) ( $P < .05$ ). Remission (final score  $\leq 8$ ) was attained by 68.6% versus 36.4%, respectively ( $P < .05$ ). Expectation ratings did not differ significantly between groups.

**Conclusions:** Bright white light treatment for 5 weeks improved depression during pregnancy significantly more than placebo dim red light. The study provides evidence that light therapy, a simple, cost-effective antidepressant modality with minimal side effects for the mother and no known risk for the unborn child, may be a useful non-pharmacologic approach in this difficult situation.

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Affective disorder during pregnancy is a common and severe condition. One in 10 pregnant women worldwide suffers from depression with severe risks.<sup>1,2</sup> Depression during pregnancy is the strongest predictor of postpartum depression.<sup>3</sup> Depression is associated with a higher risk for complications during pregnancy, requiring more frequent medical attention.<sup>4</sup> Many studies have reported that preterm delivery and low birth weight are associated with depression (overview in Bennett et al,<sup>1</sup> Douki et al<sup>2</sup>). Endocrine dysregulation due to maternal stress affects the fetus and birth outcome.<sup>5</sup> Depressed pregnant women are at risk for inadequate nutrition; poor weight gain; increased use of nicotine, drugs, and alcohol; failure to obtain adequate prenatal care; and poor mother-child attachment.<sup>6,7</sup> Furthermore, these women have a higher rate of surgical birth and vaginal operative delivery and their newborns have a higher rate of admission to neonatal intensive care.<sup>1,2</sup> Their infants have a higher risk for cognitive, emotional, and behavioral disturbance.<sup>6</sup>

Treatment of antepartum depression requires careful judgment to minimize risk to the fetus.<sup>8</sup> Pharmacologic treatment is an option, but all antidepressants cross the placenta, and both practitioners and patients are concerned about possible teratogenicity, prenatal and perinatal adverse effects for the infant, as well as negative effects on long-term development.<sup>2,8,9</sup>

Psychiatric medication use for depression in pregnancy may also pose a risk of fetal growth retardation and preterm delivery,<sup>10</sup> as well as withdrawal symptoms in the newborn, or pulmonary hypertension.<sup>2,8</sup> The safety of pharmacologic treatment of depression in the pregnant woman is still controversial,<sup>8,11,12</sup> with a lack of well-controlled studies. Many physicians and patients experience indecisiveness about the safety of antidepressant medication.<sup>13,14</sup>

Exploration of new approaches to treating the pregnant woman with major depression is therefore a priority. Interpersonal psychotherapy is a promising option (eg, Spinelli and Endicott<sup>15</sup>) but not readily available in practice settings and impractical for women limited in support resources such as transportation and childcare. Socioeconomically disadvantaged childbearing and childrearing women are difficult to engage and retain in adequate treatment, and many are left to suffer together with their newborns.

Treatment of depression during pregnancy that is efficacious, reliable, safe, and with minor side effects is an urgent unmet clinical need. Light therapy is well established

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as the treatment of choice for seasonal affective disorder. Some promising data are available for nonseasonal major depression,<sup>16</sup> suggesting that light therapy may provide a nonpharmaceutical alternative in this vulnerable patient group of nonseasonally depressed pregnant women. Because rapid improvement (within a week) had been shown in seasonal affective disorder, early studies of nonseasonal major depression were mostly short in duration. Given that pharmacologic trials of major depression are conventionally 5 weeks or more, light therapy has had little chance to reveal efficacy, although meta-analyses of light therapy trials for nonseasonal depression are positive.<sup>17-20</sup>

There have been 2 pilot studies of light therapy in antepartum depression. A single-blind, nonrandomized trial administered 3-5 weeks of light therapy (10,000 lux light treatment for 60 minutes daily, shortly after subjects awakened), and mean depression ratings improved by 50%.<sup>21</sup> A 5-week randomized controlled trial comparing 7,000 lux with 500 lux designated as placebo, for 60 minutes daily, found improvements of 60% and 41%, respectively,<sup>22</sup> which provided the rationale for the present study. Five weeks appeared sufficient to attain benefit without terminating treatment before the appearance of significant group differences.

We hypothesized that morning bright light therapy (7,000 lux white) is an effective treatment for major depression during pregnancy compared with low-intensity placebo light therapy (70 lux red) when administered 60 minutes daily for 5 weeks.

## METHOD

### Participants

Women were recruited through referrals from the University Psychiatric Outpatient Department and Department of Obstetrics/Gynecology, University Hospital Basel, from practitioners in the northwest Basel area of German-speaking Switzerland, and directly through the media.

Of 100 women screened (telephone interview and a score  $\geq 10$  on the Edinburgh Postnatal Depression Scale<sup>23</sup>), 70 met study entry criteria and came for assessment with the Structured Clinical Interview for *DSM-IV* Axis I Disorders<sup>24</sup> and a medical examination. The staff psychologist interviewed participants at the Psychiatric Outpatient Department, University Hospital Basel, or at home, if required.

**Inclusion criteria.** The inclusion criteria were women who were 18-45 years of age; German speaking; medically healthy, with normal ocular function; 4 through 32 weeks gestation based on first trimester ultrasound; *DSM-IV* diagnosis of major depressive disorder; Structured Interview Guide for the Hamilton Depression Rating Scale (HDRS)<sup>25</sup> with Atypical Depression Supplement (SIGH-ADS)<sup>26\*</sup> score

$\geq 20$ ; and ability to provide informed consent. Although the majority were untreated, we included 4 women who had taken an antidepressant for more than 3 months without any improvement and kept medication constant during the study (paroxetine 10 mg, paroxetine 20 mg, fluoxetine 20 mg, and citalopram 20 mg). Exclusion criteria were *DSM-IV* diagnoses of bipolar I or II disorder, seasonal affective disorder, any psychotic episode, substance abuse within the last 6 months, primary anxiety disorder, recent history of suicide attempt (6 months), delayed sleep phase disorder or hypersomnia with habitual sleep onset later than 1 AM or waking later than 9 AM, and obstetrical care or medications for medical disorders that might confound treatment results, fetal malformations, and intrauterine fetal death. After study completion, 6 patients reported that they had independently begun adjunct antidepressant medication during the trial and were excluded from the analyses.

### Study Design

The study was a randomized, double-blind, placebo-controlled clinical trial, with a parallel design and duration of 5 weeks, testing the hypothesis that 60 min/d of 7,000 lux white light is an effective antidepressant compared with 70 lux red (placebo) light. The primary endpoint compared reduction in depressive symptoms as documented by the SIGH-ADS 29-item version and the HDRS 17-item subscale. Further analyses compared percentage improvement and categorical response, as well as additional observer and self-report scales. The rationale for light treatment was explained to the patient, who also knew she had an equal chance of being assigned to different-colored light boxes. She was informed that standard psychiatric support, but not specific psychotherapy, also would be provided. The study design was approved by the Ethics Committee of the University of Basel, and patients signed informed consent. The study is registered at [clinicaltrials.gov](http://clinicaltrials.gov) (identifier: NCT01043289).

Sample size was determined by the cited pilot trials in which a reduction in SIGH-ADS scores of 8 points ( $SD = 9$ ),  $\alpha = .05$ , would achieve a power of 0.81 with 17 subjects in each group. To obtain 34 complete observations with an anticipated noncompletion rate of about 20%, we needed to enroll 42 women.

### Light Therapy

Patients were asked to maintain their habitual bedtime and wake-up time and not to change it for study entry. Light treatment was planned to commence within 10 minutes of habitual wake-up time. The light box (Healthlight, SphereOne Inc, Silver Plume, Colorado, <3 kg) could be conveniently transported and set up by pregnant women. During the 5-week treatment period in their homes, subjects sat in front of the light box daily for 60 minutes at a specified distance that provided an active dose of 7,000 lux white light ( $4.2 \times 10^5 \text{ lux} \cdot \text{min}$ ) or a placebo dose of 70 lux red light ( $3.0 \times 10^3 \text{ lux} \cdot \text{min}$ ). The active dose was found effective in the prior controlled treatment study.<sup>22</sup> The placebo

\*The SIGH-ADS, a rating scale for all subtypes of depression, contains the same items as used in the SIGH-SAD, originally developed for evaluating winter depression (seasonal affective disorder). The sleep items have been reformulated to require specific time-of-day estimates. The scoring structure remains the same.

70 lux red light box was chosen because the earlier study using 500 lux white light indicated some efficacy. Red is far from the proposed active wavelengths in the blue part of the spectrum,<sup>27</sup> and the intensity is below the threshold for phase-shifting circadian rhythms (< 100 lux).<sup>28</sup> Dim red light < 100 lux has been successfully used as placebo in several controlled light therapy trials.<sup>29-31</sup> Importantly, though, the patients perceived it as a credible light source according to their expectation ratings, and, therefore, it served as a plausible placebo.

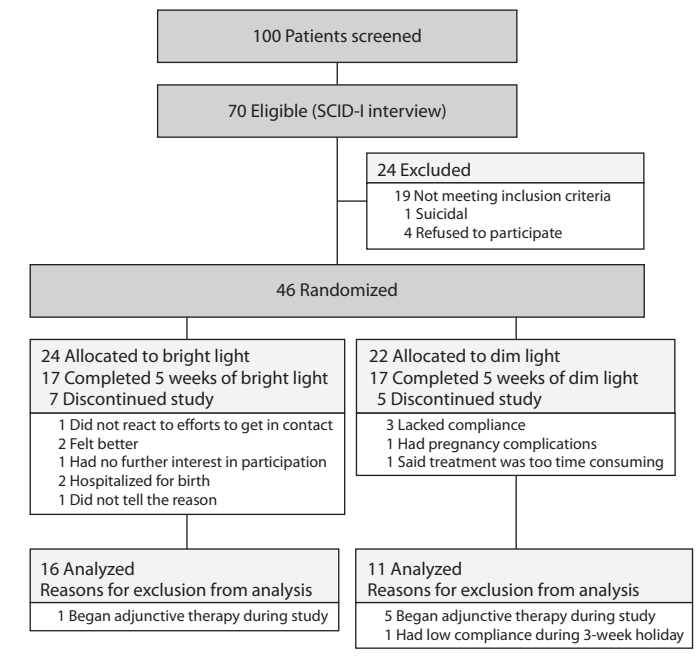
**Randomization: maintaining the blind.** An independent staff member provided the nonblind research nurse computer-generated random assignments in blocks of 6. The light boxes were in identical, coded cartons to preserve the blind and kept in a separate area of the hospital. The nurse allocated the lamps to the patients after they had entered the study and was the only staff member thus informed. Patients were instructed not to discuss the nature of their light box with the rating interviewer and told we were investigating different wavelengths to find the optimum color. After receiving the light box, each subject rated the degree to which she believed she would improve after 5 weeks of light therapy on a scale of 0 (ineffective) to 5 (complete improvement). Expectation ratings (mean ± SD) were similar and moderately positive for bright light (3.3 ± 1.1, n = 16) and placebo light (3.3 ± 0.9, n = 11). They were asked to rate their judgment of light therapy after completing 5 weeks of treatment as well, and, again, these ratings were similar and positive (for the bright-light group, 3.4 ± 1.1, and, for the placebo group, 3.0 ± 1.1 [ $t_{14} = 0.7, P = .49$ ]), which indicates that the blind had been maintained.

**Specific Instruments and Reliability Assessments**

The baseline interview collected information on ethnic group, age, marital status, education level, parity, as well as previous depressive episodes. Instruments written and tested in English were professionally translated with blinded back-translation.

The primary clinical outcome rating scale was the SIGH-ADS.<sup>26</sup> The 29-item scale incorporates the HDRS as well as assessment of atypical neurovegetative symptoms. This combined scale is the current benchmark for assessment of severity of depression in light therapy trials. Additional rating scales used to assess depth of depression were the Montgomery-Asberg Depression Rating Scale,<sup>32</sup> the Structured Interview Guide for the Hamilton Depression Rating Scale-Seasonal Affective Disorder Version-Self-Rating Version (SIGH-SAD-SR)<sup>33</sup> for self-ratings, and the Beck Depression Inventory (BDI).<sup>34</sup> Safety was monitored with the self-report version of the Systematic Assessment for Treatment Emergent Effects (SAFTEE), previously used to monitor side effects of light therapy.<sup>35</sup> Daily rating scales (mood and alertness ratings, sleep and light therapy logs) monitored compliance.

Figure 1. Patient Enrollment, Allocation, and Data Analysis



**Statistical Analyses**

The primary outcome measures were the SIGH-ADS and HDRS scores. Changes of rating scale scores over time (differences from baseline) were analyzed in the context of the general linear model. Differences from baseline of SIGH-ADS and HDRS scores at every time point were the dependent variables, time was the within-subjects factor, and treatment (bright light vs placebo) was the between-subjects factor. Baseline score of depression and gestational age at intervention start were included in the model. Post hoc power calculations were performed for the effect of the interaction between time and treatment on rating scale scores. We calculated the power of the within-between interaction for repeated measures using the O'Brien-Shieh algorithm, as implemented in G\*Power 3.0.<sup>36</sup> Finally, we analyzed categorical definitions of *response* (improvement ≥ 50%) and *remission* (improvement ≥ 50% to a final score ≤ 8) on both scales.

**RESULTS**

**Clinical Response**

Patient recruitment began in October 2004 and was completed in October 2008. Of 100 study applicants, 46 were enrolled and 34 completed the trial (12 dropouts). A further 6 were excluded from the analysis because of having begun adjunct therapy during the study and 1 because of poor compliance (Figure 1). Five of these 6 were in the placebo group. Thus, the analysis is based on 16 patients in the bright light group and 11 in the placebo group.

There were no significant differences between the bright- and dim-light groups in sociodemographic or clinical factors

**Table 1. Sociodemographic and Clinical Comparison of Bright- and Dim-Light Groups**

Variable	Bright Light (n = 16)		Dim Light (n = 11)		<i>P</i> <sup>a</sup>
	Mean	SD	Mean	SD	
Age, y	31.7	4.7	32.7	5.4	.621
Ethnicity, n					
Non-Swiss	5		3		
Eastern European	2		2		
Education (no. of school years)	12.4	4.4	10.8	2.7	.317
No. of previous depressive episodes	6.8 (0–85) <sup>b</sup>	20.9	1.1 (0–3) <sup>b</sup>	1.1	.382
Duration of present depressive episode at light start, wk	9.6	5.6	18.2	27.0	.227
Age at first onset of depression, y	23.5	9.1	28.0	6.6	.180
Gestational age at light therapy start, wk	18.9	6.3	22.5	6.1	.153
Gravidity	1.2	1.1	1.1	1.1	.799
Parity	0.87	0.74	0.66	0.67	.425

<sup>a</sup>2-Sided.<sup>b</sup>Mean (range).**Table 2. SIGH-ADS-29 and HDRS-17 Scores**

A. Over the 5 Weeks of Treatment (mean ± SD)						
Measure	Baseline	Week 1	Week 2	Week 3	Week 4	Week 5
SIGH-ADS-29						
Bright light (n = 16)	27.9 ± 6.3	23.2 ± 7.1	21.9 ± 7.8	17.6 ± 8.4	16.4 ± 9.0	12.3 ± 6.7
Dim light (n = 11)	27.5 ± 4.7	26.0 ± 5.6	18.1 ± 9.3	17.1 ± 8.0	16.6 ± 9.1	15.6 ± 7.7
HDRS-17						
Bright light (n = 16)	17.8 ± 5.1	14.4 ± 5.1	12.6 ± 5.0	10.4 ± 4.4	9.6 ± 5.8	6.6 ± 4.1
Dim light (n = 11)	17.7 ± 4.0	16.2 ± 5.1	12.2 ± 6.8	10.9 ± 6.0	10.4 ± 7.5	10.6 ± 6.0

**B. Score Changes Over the 5 Weeks of Treatment (difference from baseline, mean ± SEM)<sup>a</sup>**

Week of Treatment	Bright Light	Dim Light
SIGH-ADS-29		
1	-5.0 ± 1.3	-1.1 ± 1.6
2	-5.9 ± 1.7	-9.5 ± 2.0
3	-10.8 ± 1.8	-9.7 ± 2.2
4	-12.0 ± 2.0	-10.2 ± 2.5
5	-16.1 ± 1.6	-11.1 ± 2.0
HDRS-17		
1	-3.6 ± 1.0	-1.3 ± 1.3
2	-4.9 ± 1.3	-6.0 ± 1.6
3	-7.4 ± 1.3	-6.8 ± 1.6
4	-8.4 ± 1.6	-7.0 ± 1.9
5	-11.5 ± 1.2	-6.7 ± 1.4

<sup>a</sup>Adjusted for the covariates gestational age at baseline (20.37 weeks), SIGH-ADS score at baseline (27.70), and HDRS score at baseline (17.78).

Abbreviations: HDRS-17 = 17-item Hamilton Depression Rating Scale, SEM = standard error of the mean, SIGH-ADS-29 = 29-item Structured Interview Guide for the Hamilton Depression Rating Scale with Atypical Depression Supplement.

(Table 1). Light therapy logs (used to ascertain compliance) were similar in both groups.

Table 2 summarizes the means of the main outcome variables of clinical efficacy, the SIGH-ADS and HDRS, at weekly intervals throughout 5 weeks' treatment. The Levene statistic affirmed homogeneity of the variance for the SIGH-ADS and HDRS. At baseline, the ratings were similar ( $P > .05$ ). After 5 weeks, the SIGH-ADS score had dropped by 15.6 points in the bright-light group versus 11.9 points in the dim-light group; the HDRS score dropped by 11.2 points in bright light versus 7.4 points in dim light (Table 2A).

The superiority of light over placebo was shown on both SIGH-ADS and HDRS when analyzing the weekly change from baseline (Table 2B). A significant effect of the whole model on changes in severity of depression was found at

week 5 (SIGH-ADS,  $R^2 = 0.251$ ,  $F_{3,23} = 3.91$ ,  $P < .05$ ; HDRS,  $R^2 = 0.338$ ,  $F_{3,23} = 5.42$ ,  $P < .01$ ), which indicates that the included factors significantly influenced, as a whole, the observed improvement in depression.

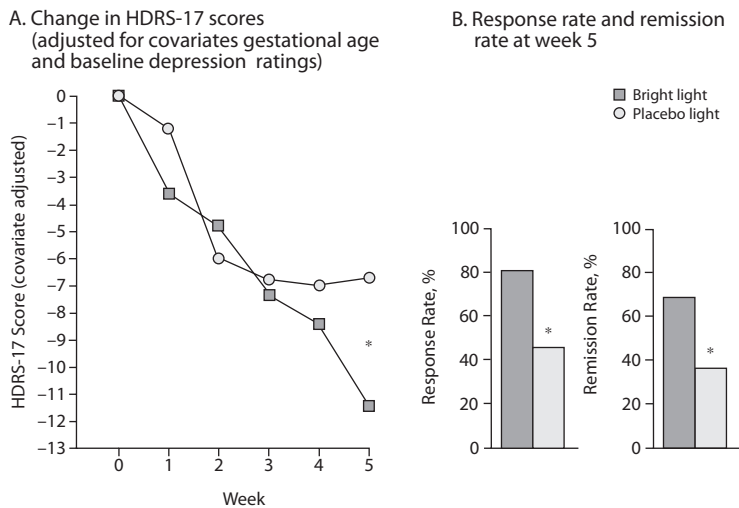
For the HDRS, there was a significant interaction of treatment with time ( $F_{4,92} = 2.91$ ;  $P < .05$ ), indicating that the decrease of depression severity did not follow parallel slopes of time course (Figure 2A). The contrasting curve shapes show a monotonic weekly improvement for bright light versus unchanged status after week 2 for dim light. The strongest effects were observed with bright-light treatment, with greater improvement than placebo at week 5 ( $\beta = 0.419$ ,  $t = 2.52$ ,  $P < .05$ ). Baseline depression severity was a significant main effect ( $F_{1,23} = 7.51$ ,  $P < .05$ ); higher severity led to better improvement ( $\beta = 0.498$ ,  $t = 3.12$ ,  $P < .01$ ) without a time interaction. Gestational age showed a significant interaction with time ( $F_{4,92} = 2.76$ ,  $P < .05$ ); the direction of effect suggests an inverse relationship with improvement, but univariate estimates were not significant at any time point.

Similarly, the SIGH-ADS showed an interaction of treatment with time ( $F_{4,92} = 2.87$ ;  $P < .05$ ), with greater effect under bright light. Baseline severity of depression and gestational age both showed trends toward a main effect at week 5 in a similar direction as found for HDRS (SIGH-ADS at baseline:  $F_{1,23} = 4.04$ ,  $P = .056$ ; gestational age:  $F_{1,23} = 3.60$ ,  $P = .070$ ).

The general linear model repeated-measures analysis of variance was also performed, including as factors clinical variables that might affect the pattern of change of depressive ratings: age at onset of illness, number of previous depressive episodes, and duration of current depressive episode. Among these, only the number of previous recurrences showed a significant interaction with time (HDRS:  $F_{4,72} = 2.88$ ,  $P = .029$ ; SIGH-ADS:  $F_{4,72} = 3.82$ ,  $P = .007$ ). The direction of the effect supports the hypothesis of better effects in more severe patients: the more previous depressive episodes, the better the improvement. Adding this factor to treatment, baseline severity of depression, and pregnancy week did not significantly change the overall goodness-of-fit of the model and confirmed the significant time × treatment interaction (HDRS:  $F_{4,88} = 3.00$ ,  $P = .023$ ; SIGH-ADS:  $F_{4,88} = 3.02$ ,  $P = .022$ ).

Post hoc power analyses of the multivariate time × treatment interactions showed large effect sizes (SIGH-ADS, Pillai  $V = 0.403$ ; O'Brien-Shieh algorithm,  $f[V] = 0.822$ ; HDRS,

Figure 2. Depression Score Change and Response and Remission Rates



\**P* < .05.

Table 3. Categorical Response and Remission Rate

Measure, n (%)	Response		<i>P</i> <sup>a</sup>	Remission		<i>P</i> <sup>a</sup>
	Bright Light (n = 16)	Dim Light (n = 11)		Bright Light (n = 16)	Dim Light (n = 11)	
SIGH-ADS-29	12 (75.0)	4 (36.4)	.023	5 (31.3)	2 (18.2)	.223
HDRS-17	13 (81.3)	5 (45.5)	.027	11 (68.8)	4 (36.4)	.048

<sup>a</sup> $\chi^2$  (1-sided).

Abbreviations: HDRS-17 = 17-item Hamilton Depression Rating Scale, SIGH-ADS-29 = 29-item Structured Interview Guide for the Hamilton Depression Rating Scale with Atypical Depression Supplement.

Pillai *V* = 0.378; O'Brien-Shieh algorithm, *f*[*V*] = 0.780), thus achieving sufficient power (0.88 and 0.84, respectively) to detect the observed differences.

Percentage improvement showed the significant advantage of bright light across time on the SIGH-ADS ( $F_{4,100} = 17.88, P < .001$ ), with a significant interaction ( $F_{4,100} = 2.72, P < .05$ ). The HDRS also showed improvement over time ( $F_{4,100} = 12.06, P < .001$ ) but only a trend for interaction ( $F_{4,100} = 1.89, P = .118$ ).

A paired *t* test comparison of baseline week 0 with week 5 yielded significance for bright white light over placebo for HDRS values ( $t_{25} = 1.97, P_{1-sided} < .05$ ) but not for the SIGH-ADS. The percentage improvement at week 5 was significant for both SIGH-ADS ( $57.5\% \pm 4.6\%$  vs  $41.2\% \pm 8.8\%$ ;  $t_{25} = 1.78, P_{1-sided} < .05$ ) and HDRS ( $63.9\% \pm 5.1\%$  vs  $37.5\% \pm 10.7\%$ ;  $t_{25} = 2.45, P_{1-sided} < .05$ ). Categorical analyses (Figure 2B, Table 3) also showed the superiority of bright light, with higher response rate on both scales and higher remission rate on the HDRS.

An item-by-item validation of the German SIGH-ADS was carried out.<sup>37</sup> Many somatic symptoms of depression in pregnant women improved with light therapy (none related to sleep and appetite). We therefore extracted a short, 7-item scale for future clinical use that could differentiate

between responders and nonresponders (items: depression, work and activities, feelings of guilt, psychic anxiety, somatic anxiety, social withdrawal, and fatigability/lack of energy).<sup>37</sup>

Examination of daily logs showed that sleep was not disrupted by light treatment, although there was individual variability in wakeup time and/or interval between wakeup and light therapy. No patient showed a sudden switch out of depression, as might be found with sleep deprivation<sup>16</sup>—rather, improvement was gradual over the 5 weeks' treatment.

The ancillary rating scales all revealed score reductions from baseline to week 5. Fewer patients completed these ratings, which lessens the likelihood of finding significant differences. After 5 weeks of bright-light treatment, patients in the bright-light group tended to have lower Montgomery-Asberg Depression Rating Scale scores than patients in the placebo group ( $t_{20} = -1.55, P = .068$ ) (Table 4). Self-ratings also

improved with time, but neither BDI nor SIGH-SAD-SR differed significantly between groups after 5 weeks of treatment (Table 4).

Only 4 patients were taking antidepressants (and had not responded to them). They were in the bright-light group, and all improved.

Among study completers, 6 patients decided to start a drug treatment, and 5 of them were receiving placebo light. The decision to combine antidepressant drugs was then marginally higher in the placebo group ( $\chi^2_1 = 3.57, P = .059$ ).

Although no patients fulfilled criteria for seasonal affective disorder, the screening questionnaire for seasonality<sup>38</sup> yielded 8 patients with seasonal affective disorder-equivalent symptoms (2 in the bright-light group) and 1 with subsyndromal seasonal affective disorder. However, there was no correlation between clinical improvement and degree of seasonality. There were also no differences in the final scores of the depression scales between the seasonal and nonseasonal subjects. In addition, we checked the season in which patients were treated with light (slightly more in the winter months). Again, there was no correlation between season of treatment and response.

Using the SAFTEE questionnaire weekly, we found no clinically meaningful side effects at any time point. All women gave birth without perinatal complication.

## DISCUSSION

Although both groups showed similar baseline severity, bright-light therapy showed greater reduction in depression ratings than placebo dim light after 5 weeks of treatment. A difference of 4 points in the HDRS at week 5 is impressive for an antidepressant trial—the majority of placebo-controlled drug studies show a difference of about 2 points with far larger sample size.<sup>39</sup> A similar effect was seen for the expanded

**Table 4. Supplementary Observer-Based and Self-Report Scales<sup>a</sup>**

Measure	n	Baseline		Posttreatment	
		Mean	SD	Mean	SD
<b>Observer rating scale</b>					
<b>MADRS</b>					
Bright light	13	20.5	6.0	7.5	7.0
Dim light	8	21.1	6.1	12.4	8.4
<b>Self-report scales</b>					
<b>BDI</b>					
Bright light	13	24.9	12.0	12.2	9.6
Dim light	10	21.8	7.8	12.0	9.0
<b>SIGH-SAD-SR<sup>b</sup></b>					
Bright light	12	28.6	7.4	15.3	4.7
Dim light	9	31.7	9.3	18.1	13.6

<sup>a</sup>All group comparisons were nonsignificant (*t* test).

<sup>b</sup>The SIGH-SAD-SR, a rating scale for all subtypes of depression, contains the same items as used in the SIGH-SAD, originally developed for evaluating winter depression (seasonal affective disorder) and the renamed observer rating SIGH-ADS. The sleep items have been reformulated to require specific time-of-day estimates. The scoring structure remains the same.

Abbreviations: BDI = Beck Depression Inventory, MADRS = Montgomery-Asberg Depression Rating Scale, SIGH-SAD-SR = Structured Interview Guide for the Hamilton Depression Rating Scale-Seasonal Affective Disorder Version-Self-Rating Version.

SIGH-ADS scale, which includes 8 atypical neurovegetative items, and the 4 last items on the 21-item HDRS. Even though the SIGH-ADS is weighted toward somatic factors prevalent in pregnancy independent of depressive symptoms, it provided results similar to the HDRS.<sup>37</sup> The effect sizes of 0.78 for the HDRS and 0.82 for the SIGH-ADS are large,<sup>40</sup> yet they may indeed be conservative: 5 of the 6 patients who began antidepressant drug treatment during the trial were in the placebo group, which suggests that placebo produced less benefit than bright light, leading subjects to seek additional treatment off protocol.

The decrease of depression severity did not follow parallel slopes of time course for bright light and placebo. This pattern of treatment-emergent medication-placebo difference is closely similar to that observed with antidepressant drugs. Clinical trials that explore the hypothesized superiority of antidepressant drugs over placebo have consistently affirmed that no difference can be expected between the treatments during the first 2 weeks, as conclusively confirmed by meta-analysis,<sup>41</sup> and, recently, that placebo-controlled antidepressant clinical trials do not yield significant differences at less than 4 weeks' duration.<sup>42</sup> The similarities between the time course of the effects of light therapy and of pharmacologic antidepressant treatments, as reported in independent studies, increase the confidence in our results, which merit replication in an independent, larger sample, as well as consideration of optimum light intensity and duration of treatment.

Given the limited treatment options for pregnant women with depression, the potential benefit of light therapy is promising. The side effect profile of light therapy is attractive. Although as yet there are no data to verify that light therapy incurs minimal risk to the fetus, a simple analogy can be made. One hour of light therapy provides light exposure

similar to 1 hour of outdoor light. Indeed, in patients with winter depression, a regular 1-hour morning walk outdoors provides therapeutic effect similar to a light box.<sup>43</sup> At typical daily exposures, natural light is safe for the eyes. Obstacles to prescribing outdoor treatment, of course, include variable weather conditions and seasonal light availability.

In terms of ophthalmologic safety, patients with retinal or other eye disorders should consult an ophthalmologist before using light therapy and periodically thereafter. Long-term studies in seasonal affective disorder patients have not found any clinically significant emergence or exacerbation of ocular symptoms.<sup>44</sup> Lithium reduces light sensitivity, which may require longer exposure duration for clinical response, but its effect on retinal sensitivity is reversible.<sup>45</sup> There are no ophthalmologic studies investigating interaction with antidepressant drugs. Clinical trials of light plus medication suggest a potentiation of the therapeutic effect.<sup>31,46</sup> None of our patients used photosensitizing psychotropics.

There were no switches into hypomania in our study. There is a potential for light to induce a switch in patients with bipolar disorder, but it is low if the patients are on prophylactic treatment.<sup>47</sup> Moreover, when deciding to choose early morning light therapy versus antidepressant drug treatment in patients with a personal or family history of bipolar illness, it should be noted that the most powerful chronotherapeutic interventions have been associated with a risk of manic switches not exceeding 10% versus a risk of development of treatment-emergent mania in roughly one-quarter of bipolar patients administered antidepressant drugs.<sup>47,48</sup>

The light box used in this study has been tested in a several clinical trials and conforms to stringent standards, such as adequate size for illuminating a broad visual field, lighting from above to avoid glare, and ultraviolet screening. Many light therapy devices on the market have not undergone any clinical trials, so generalizations cannot be made, except in the case of similar designs (but not for pocket lighting devices nor for blue-enhanced ones).

The strengths of this study were the stringent entry and response criteria and the placebo-controlled protocol; a limitation was the number of patients. In order to optimize effects, treatment duration may need to be longer than the 5 weeks studied here. The earlier placebo-controlled pilot study found only a trend toward better improvement with bright light at week 5, which became significant after 10 weeks.<sup>22</sup> Women beyond the 36th week of gestation may thus not derive immediate benefit during pregnancy. However, continued treatment postpartum has promise, given that antepartum depression predicts postpartum depression.<sup>3</sup> Several patients have elected this option following completion of the protocol, with success.

Although there are many studies of light therapy for non-seasonal depression, none have been without antidepressant drug treatment, and too many protocol differences exist to make a confident comparison.

In summary, light therapy is perceived as "natural" and therefore appeals to pregnant women, since most of them

wish to avoid medication. Light therapy may prove more practical in community mental health and nonpsychiatric medical settings than specialized types of psychotherapy for the disorder and may also be combined with psychotherapy. It could provide a long-sought therapeutic modality suited to this vulnerable population.

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