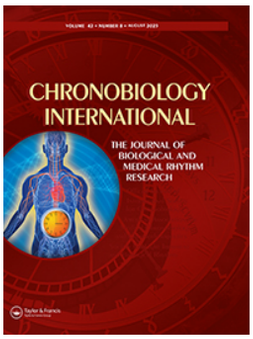

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ORIGINAL ARTICLE

Dynamic versus static LED-lighting for inpatients with major depression: Long-term antidepressant effects and short-term sleep improvement in a randomized controlled clinical trial

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ABSTRACT

Translational research has shown a profound impact of daylight and electrical lighting on circadian rhythms, sleep, mood, and alertness. Dynamic LED-lighting can mimic daily and seasonal changes in daylight by continuous changes in intensity and spectral distribution throughout the 24-hour day. The current study assessed the clinical effect of dynamic LED-lighting in a randomized controlled setup. In an affective disorders ward, 10 single patient rooms were fitted with a dynamic LED-lighting system, replacing the existing lighting, able to switch between a dynamic or a static mode. In the dynamic mode, daytime Melanopic Daylight Equivalent Illuminance (M-EDI) peaked at 10:30h with 576 lx M-EDI vs. 66 lx in the static mode. During the evening, the dynamic mode gradually reduced intensity to 0.3 lx M-EDI, with the static mode staying at 66 lx. Patients with major depression were randomly allocated to a static or a dynamic lighting mode in their room, lasting three weeks, with weekly assessments, and after 6 months. The primary outcome was the change in scores on the HAM-D6 scale from baseline to week 3. In all, 60 patients were included in the study with a 96.7% follow-up of the primary outcome. On the 6-item Hamilton Depression Rating Scale (HAM-D_6) scale, a significantly greater antidepressant effect of the dynamic light was seen at week 3 for females (71%) ($p = 0.02$), but not for the whole group ($p = 0.47$). At 6 months, a significantly greater effect of dynamic light was seen for the whole group ($p = 0.03$). Sleep diaries showed significantly longer sleep ($p = 0.02$), fewer awakenings ($p = 0.04$), and later sleep offset ($p = 0.03$) with dynamic light, for the whole group. The dynamic lighting system was well functioning. Participants were most satisfied with the dynamic light. These findings should be tested in larger studies with measurement of individual light exposure.

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Introduction

Depressive episodes, either as part of a major depressive disorder or a bipolar disorder, are prevalent and associated with a high level of personal suffering, disability, and societal burden (Friedrich 2017; Hasin et al. 2018; Kessler 2012). Patients suffering from severe depression have markedly reduced psychosocial functioning and often develop suicidal ideation and suicide attempts, causing admittance to inpatient psychiatric wards for treatment. Traditional treatment options in inpatient wards involve psychopharmacology, electroconvulsive treatment, physical therapies, relaxation therapies, supporting consultations with staff, and psychoeducation, all delivered in a typical 3–4 week stay (in Denmark). Even though patients improve during their inpatient stay, they are not in remission when discharged (Lauritsen et al. 2017), and we know residual symptoms are associated with increased risk of relapse and readmissions (Monroe and Harkness 2022; Tønning et al. 2021).

Thus, there is an unmet need for new treatment methods to support a faster and more complete recovery from depression, that would also reduce the likelihood of relapse

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and readmissions after discharge (Aggestrup, Martiny, et al. 2023; Martiny 2017).

Current treatment strategies mainly lie within the bio-psycho-social illness model (Borrell-CARRIÓ et al. 2004; Engel 1980), and the physical environment, including light, is often ignored (Volf et al. 2024) even though studies have shown that daytime and nighttime light exposure impact mental health significantly (Burns et al. 2021; Cajochen et al. 2011).

Light exposure, whether from daylight or from electrical lighting, is thus an important environmental factor for humans impacting mood, sleep, circadian rhythmicity, and wellbeing (Campbell et al. 2023; Fernandez et al. 2018; Münch et al. 2017, 2020; Sato and Sato 2023).

Following the seminal discovery of suppression of melatonin by light in humans (Lewy et al. 1980), came the first light therapy trials (Kripke 1981; Kripke et al. 1983), and the description of seasonal affective disorder (Rosenthal et al. 1984), and light has been used as a treatment option in mental health since. Seasonality of depressive episodes was later incorporated in the Diagnosis and Statistical Manual of Mental Disorders, version 5 (DSM-5) (DSM-5 2013) and the International Classification of Diseases, 10th revision (ICD-10), and now 11th revision (ICD-11), as course specifiers for depressive episodes (World Health Organization 2021).

Light has both visual and non-visual effects. The basic neurological pathways and mode of functioning of the non-visual effects are well described (Münch et al. 2017) including the intrinsically photoreceptive Retinal Ganglion Cell (ipRGC) system (Mure 2021). Since the discovery of the ipRGC (Berson et al. 2002; Hattar et al. 2002), a large amount of research on the function of the ipRGC and the connection to brain areas of interest in depression has been performed. Shortly described, the ipRGC are mainly nonvisual in their function with a peak sensitivity in the short-wavelength blue light spectrum (460–480 nm) (Munch and Kawasaki 2013), and with projections to several areas of interest in depression and to the circadian system (Fernandez et al. 2018; Legates et al. 2012). Specifically, the impact of light on the circadian system and the timing of sleep works through the phase response curve (PRC) for light eliciting a phase advance of sleep (and other rhythms) when a person is exposed to light in the first part of the subjective day and a delay when exposed in the later part of the subjective day and evening (Khalsa et al. 2003). A general alerting effect of light (Cajochen et al. 2011), and also an effect of prior light history during daytime on the timing of melatonin and alertness has been established (Chang et al. 2013; Hébert et al. 2002). The basic idea behind an antidepressant and sleep improving effect of dynamic lighting is based on the before mentioned physiological effects of light. By timing the intensity and spectral distribution of the light (blue light content), the circadian rhythms, e.g. sleep timing, can be adjusted forward or backwards. Patients with depression have a preponderance for a delayed sleep timing (eveningness) (Bauducco et al. 2020; Norbury 2019) and correctly timed dynamic light with adequate intensity and blue light content can work through the ipRGC system to provide a resetting, stabilization, and advance of the sleep/wake rhythm. Delaying of the sleep-phase cycle is associated with mood deterioration (Lauritsen et al. 2017) and advancing of the sleep-phase cycle with an antidepressant effect (Aggestrup, Svendsen, et al. 2023; Facer-Childs et al. 2019). Thus, correctly timed dynamic light should be able to reset the sleep-wake cycle by administering bright light in the morning in the phase advancing portion of the PRC for light, and in addition, administering low-intensity light with low blue light content in the afternoon/evening in the delaying part of the PCR for light. The dim blue content light can also be used for sleep induction by reducing the suppression of melatonin in the evening (Cajochen et al. 2011).

The evidence for an antidepressant effect of light therapy now covers seasonal depression (Pjrek et al. 2020), non-seasonal depression (Tao et al. 2020), and bipolar depression (Dallaspezia and Benedetti 2020; Gottlieb et al. 2019). In addition, light has successfully been used as an augmentation strategy with antidepressants (Madsen et al. 2022; Martiny et al. 2005; Penders et al. 2016; Reis et al. 2023). Traditionally, light has been administered from a light box giving approximately 10.000 lux at 30 cm distance from the eye with a daily treatment duration of ½-1 h in the morning for 2–8 weeks or for the whole of winter (Terman and Terman 2005).

Development in architectural Light-Emitting Diode (LED) lighting has made it possible to replace conventional static indoor lighting with dynamic lighting based on high output LEDs that can change intensity and spectral distribution during the 24-h day. Many new buildings are provided with such dynamic lighting. Notably, a study in post-stroke patients showed an improvement in mood, fatigue, and circadian function in a ward with installed dynamic lighting compared to a similar ward with static lighting (West et al. 2019a, 2019b). However, any clinical effects of dynamic light systems have only been investigated in relatively few clinical trials in psychiatry (Canazei et al. 2022; Giménez et al. 2017; Lindskov et al. 2022). Evidence for a clinical effect of dynamic lighting is thus sparse and more RCT studies are needed.

Impact of light on mood and sleep depends on correct administration, like for a drug (Khalsa et al. 2003). The important characteristics of light administration include exposure time and timing, spectral distribution, intensity, and temporal distribution over the 24-h day.

The tolerability of a dynamic lighting scenario is highly important. Exposure to unpleasant bright light during the first part of the day will make participants turn off the light or leave the room to seek dimmer surroundings. Leaving the room in the bright part of the dynamic lighting cycle will thus reduce light exposure. Too dim evening room light will also make participants leave the room, exposing them to higher light intensity at the wrong time, risking a phase delay according to the PCR. Both scenarios will diminish the planned physiological effects of light (Boivin et al. 2022).

To assess these issues, we earlier conducted a feasibility trial, investigating a specific dynamic lighting installation in four patient rooms and found high levels of user satisfaction with good performance of the lighting system and with patients spending many hours in their room, based on Room Occupancy Diaries (Volf et al. 2020b).

The aim of this study was to investigate the clinical effects of dynamic LED-lighting versus standard LED-lighting in inpatients with depression, using a rigorous research design and using the light settings based upon our experiences from an earlier feasibility trial with a dynamic lighting system.

Materials and Methods

Design

The design of this study is described in the study protocol paper (Volf et al. 2020). In short, the study was a randomized controlled single-blinded (Hamilton assessment) parallel trial with a 1:1 balanced allocation ratio to either dynamic LED-lighting or static LED-lighting, with a 3-week inpatient phase and a 6-month follow-up. The project was a collaboration between the Technical University of Denmark, Department of Photonics Engineering, Copenhagen, Denmark, the lighting company Chromaviso A/S, Aarhus, Denmark, and Mental Health Center Copenhagen, Denmark.

Blinding

The HAM-D_{17} assessments which encompass the HAM-D_6 items were done by blinded raters, not knowing the patients' allocation. All Hamilton raters were trained for inter-rater reliability.

Population

Inpatients with a major depressive episode were consecutively recruited from specialized affective disorders open wards. Inclusion criteria were ≥18 y of age, current depressive episode either as part of major depressive disorder (MDD) or a bipolar disorder (BP) (DSM-5 2013), and patients with BP should be in mood stabilizing treatment for a minimum of 2 months before admission, written informed consent, able to speak and understand Danish. Exclusion criteria were suicidality assessed as >2 on the Hamilton Depression Rating Scale score item 3 or if the investigator was uncertain of the severity of suicidality, current psychotic features (last 2 weeks), abuse of alcohol or drugs, a Young Mania Rating Scale (YMRS) score >6 or a current hypomanic or manic episode, and coercive measure of any kind. Discontinuation criteria were Serious Adverse Reactions (SARs), Suspected Unexpected Serious Adverse Reactions (SUSARS), occurrence of all listed exclusion criteria during the study period, and if the patient wished to discontinue the study. We asked participants to be assessed for the primary outcome at endpoint (HAM-D_{17}/HAM-D_6 assessment), even if they dropped out of the study. All participants received standard concomitant care and treatment at the ward. Participants were assessed at the ward at baseline, and subsequently at week 1, week 2 and week 3 (endpoint) and with a final phone assessment at 6-month after endpoint. After signing the informed consent, patients were randomized by use of the OpenClinica system (Homepage for OpenClinica 2019).

Lighting System

General Description

Details of the lighting system are described in the protocol paper. All 10 single patient rooms at the inpatient ward had a dynamic LED-lighting system installed, replacing the existing room lighting.

The dynamic lighting system, provided by the lighting company Chromaviso, could work in either a 24-h dynamic mode or a static mode and the lighting setup was controlled by a central control unit in the head nurse's locked office.

The lighting design included a reading luminaire, two ceiling luminaires, and a large "sunlight" LED panel luminaire, built into the window jamb (see Supplemental Figure 1) to mimic incoming sunshine reflected on the jamb. Dimensions of the built-in light panel were 1950 × 310 * 60 mm (height, width, depth).

Dynamic LED-Lighting (Intervention)

When a participant was randomized to a dynamic setting, all luminaires in their room were set in

a dynamic 24-h schedule. During the night, the dynamic mode provided low-intensity light (if turned on) with 0.3 lx M-EDI/1800 K at location "Mh" (identified in Figure 1 as a horizontal point at 0.8 m height, just above the pillow of the patient bed) or 6.9 lx M-EDI/2100 K with the reading lamp turned on. Then, from 6:00h during spring-summer (15 February to 31 October) and from 7:00h during fall-winter (1 November to 14 February), the electrical light increased smoothly from the night levels to 576 lx M-EDI/5200 K at 10:30h , measured at location "Mh" and to 411 lx M-EDI/5200 K at "Mv" (identified in Figure 1 representing the gaze of a patient sitting on the bed). From 13:00h in spring-summer and from 12:30h in fall-winter, the intensity again smoothly decreased back to night level, which was introduced at 23:30h in spring-summer and 22:30h in fall-winter. The "sunlight" LED panel was permanently on from 06:00h to 18:00h in the period 15 February to 31 October (spring-summer) and from 07:00h to 17:00h during the period 1 November to 14 February (fall-winter) so it could not be turned off by the participants. All other luminaires could be switched off/on by the patients at any time of the day.

The dim evening light contained little of the blue wavelengths and acted as sleep preparation and together with the higher morning and daytime intensity aimed at a slight sleep-phase advance intended to induce an antidepressant effect (Czeisler et al. 1999; Khalsa et al. 2003; Voderholzer et al. 2003). Also, the elevated light intensities during the morning and noon were supposed to reduce any alerting effects of evening light (Chang et al. 2013).

Static LED-Lighting (Control)

When a patient was randomized to a static setting, all the luminaires in their room were set in a static scenario and the window jamb light panel was inactive.

In static mode, the color temperature was set at 3000 K with an intensity of 66 lx M-EDI at location "Mh," and to 39 lx M-EDI vertically at 1.7 m height at location "Mv." The light intensities used in the static mode are in line with what is expected in a usual patient room and

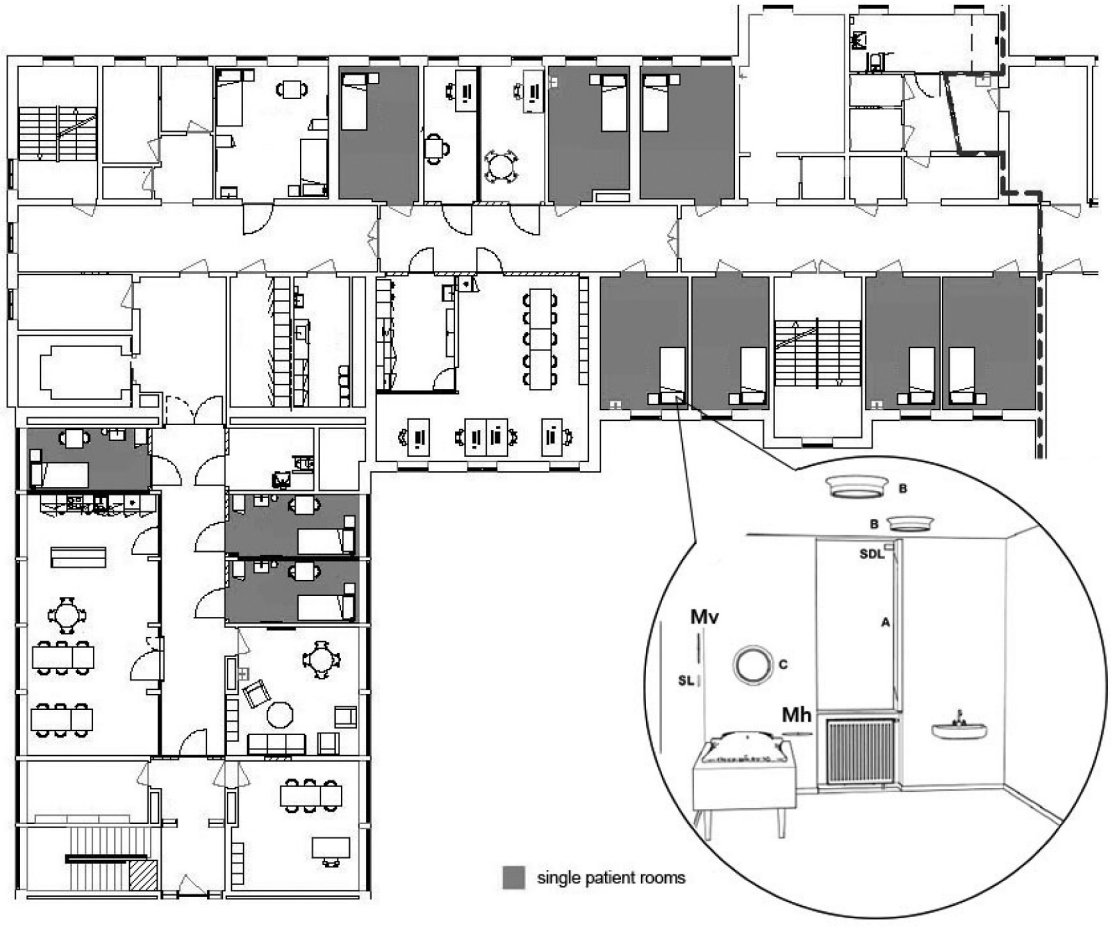

Figure 1. Plan of the ward and all 10 single patient rooms included in this study. Each single patient room had two ceiling luminaires (B), one wall luminaire (C) and one fixed "sunlight luminaire" with an LED-panel in the window jamb (A). Measuring points are also shown, "Mv" (vertical 1.7 m) and "Mh" (horizontal 0.8 m), respectively.

used in our earlier feasibility study (Volf et al. 2020b). All luminaires could be switched off/on throughout the 24-h day.

The exact settings of the lighting system in the two modes are given in the protocol paper in Figure 2 (Volf et al., 2020a), and described according to light intervention guidelines (Spitschan et al. 2019).

Light Measurements

A spectrometer GL Spectis 1.0 from GL Optic mounted on the upper part of the window glass facing outwards and connected to a power bank were used to collect at least 24 hr data of daylight in all four directions at four dates throughout the year, each representing a season. Data was collected for 5–62 h this way and documented the relationship between incident M-EDI, time of day, and time of year.

The output from the LED-lighting systems was measured both horizontally and vertically in one of the patient rooms with blackout blinds in the window to exclude all daylight, before the start of the study. The light measurements methods are described in the protocol paper.

Assessments and Outcomes

The diagnosis of a major depressive episode sampled from case reports was confirmed by use of the M.I.N.I. instrument (Sheehan et al. 1998). At baseline, participants filled in a rating scale for their expected outcome of the treatment (score 0–10, 0 = unchanged depression symptoms, 10 = total symptom remission). Participants were assessed weekly with the HAM-D_{17} scale containing the HAM-D_6 as a subscale (Bech et al. 2009), and the Young Mania Rating Scale (YMRS) (Lukasiewicz et al. 2013). In addition, patients were assessed with the Major Depression Inventory (MDI) (Bech et al. 2015), the Suicidal Ideation Attributes Scale (SIDAS) (VAN Spijker et al. 2014), the UKU side effects scale (Lingjaerde et al. 1987), a Room Occupancy Diary specifying number of hours spent in the bedroom (separated into 06:00h to 12:00h, 12:00h to 18:00h, 18:00h to 24:00h), a sleep diary covering last week sleep quality (0-10, 10 = best), wake-ups, naps, sleep onset and offset), and a newly developed Visual Comfort Scale enabling participants to evaluate their impression of their room light for the last week. Chronotypes were assessed by the Morningness Eveningness Questionnaire (MEQ) (Au and Reece 2017), and sleep quality by the Pittsburgh Sleep Quality Index (PSQI) (Buysse et al. 1989), both at baseline and endpoint. The WHOQOL-BREF (Skevington et al. 2004) was planned to assess quality of life, but was canceled early in the study because participants experienced difficulties with administration.

The primary outcome was the baseline-adjusted mean score on the HAM-D_6 score at week 3. The secondary outcomes were the baseline-adjusted mean score on the SIDAS at week 3, and the baseline adjusted mean score on the HAM-D_{17} at week 3. Exploratory outcomes were HAM-D_6 and HAM-D_{17} scores at 6 months, sleep diary data, PSQI scores, Serious Adverse Events (SAEs), Visual Comfort Scale scores, and use of sedating drugs. The total use of electrical energy for lighting in the two groups was estimated based on calculations from the setup of the lighting controller, technical LED specifications, and user logs. Light sensor data and log data for the lighting system are reported.

Statistics

The sample size calculations were performed with the SAS V.9.4 software. Based on an expected difference in the primary HAM-D_6 outcome at the endpoint assessment of 2 points, a standard deviation (SD) of 3, a power of 90% and a α value of 0.05, a total number of 98 participants were needed. For other outcome calculations, please see the protocol paper (Volf et al. 2020). To allow for explorative analyzes, we aimed at a total number of 150 participants. All analyzes were performed by the primary investigator (KM) supervised by a trained statistician. Statistical analyzes described in the protocol paper were adhered to by using a linear regression model for continuous data employing the intention-to-treat method. Predicted endpoint values from the models are presented in the text. The dependent variables were the predefined outcomes. The independent variables were baseline values of the dependent variable, treatment allocation (dynamic/static), gender, length of actual episode, BP or MDD, MEQ scores, and calculated exposure time to the LED lighting based on the Room Occupancy Diaries. Exposure time was analyzed using the LOCF method because of some missing values in weeks 1 and 2. An interaction term between each independent variable and treatment allocation (dynamic/static) were inserted into the model one-by-one and only kept if significant. As an exploratory analysis we used a mixed model repeated measure method with sex as a covariate, using data from all visits.

The significance level was set at 5% two-tailed. No interim analysis was performed.

Data Collection and Management

Data was collected electronically using the OpenClinica system, provided by the Copenhagen Trial Unit. All

non-blinded data was entered in OpenClinica during sessions with the participants. The blinded data was first noted on a paper-and-pen Hamilton scoring sheet and later entered OpenClinica.

Ethics and Approvals

The trial was conducted under the Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Subjects. All participants received oral and written study information and provided their written informed consent prior to inclusion. The study was approved by the Regional Ethical Committee (approval number H-19004525) and the Danish Data Protection Agency (approval number VD-2018–515). We adhered to the Good Clinical Practice guidelines (Rock et al. 2010).

Results

In all, 252 inpatients were screened for participation from 24 May 2019 to 13 June 2022. Of these, 60 participants were included, with 30 allocated to the dynamic and 30 to the static group and 59 patients were evaluated for the primary outcome at baseline (98.3%) and 58 at endpoint (96.7%). The estimated sample size of 98 participants for the primary outcome was not reached, mainly because the Corona shutdown prohibited access to the wards but also because of non-eligible patients suffering from conditions outside the affective spectrum.

Two participants dropped out from the dynamic group (one because of a mixed state and one because of dissatisfaction with an earlier discharge date) and two from the static group (one because of worsening of depression and one because of relocation to a patient double room). According to rules, these were also evaluated for the primary outcome with a HAM-D_{17} assessment at expected endpoint and included in the analysis.

The study duration calculated from the baseline Hamilton assessment till the week 3 Hamilton assessment was 25.0 (SD = 9.6) days in the dynamic group and 27.0 (SD = 15.5) days in the static group ($p = 0.26$)

Sociodemographics

The sample consisted predominantly of participants with female gender (71.7%), recurrent unipolar depression, longstanding current episodes, and a high percentage with current and/or earlier suicide attempts, and most patients could point to an eliciting factor for the present episode. ECT was used frequently. The mean expectation rating was similar between group with 5.4 (SD = 2.2) in the dynamic group and 5.0 (SD = 2.9) in the static group, ($p = 0.58$). The frequency of light sensitivity was 40.7% in the dynamic and 42.9% in the static group. A marked difference for gender was found with 50% of females and only 20% of men categorizing themselves as photosensitive ($p = 0.04$). The sociodemographics are shown in Table 1.

Primary and Secondary Outcomes

The Primary and Secondary Outcomes are Shown in Table 2.

Table 1. Sociodemographics.

Parameter	Dynamic LED group	Static LED group
Age, years, mean (SD), [range]	40.1 (18.0) [18–79]	37.5 (14.4) [18–76]
Gender, female, percent (n)	66.7% (20/30)	76.7% (23/30)
Main diagnose		
Unipolar depression, percent (n)	73.3% (22/30)	76.7% (23/30)
Bipolar depression, percent (n)	26.7 % (8/30)	23.3% (7/30)
YMRS screening score, mean (SD), [range]	0.6 (1.4) [0–6]	0.7 (1.2) [0–3]
Duration of current episode:		
Month, mean (SD)	8.8 (13.3)	9.8 (11.6)
Month, median [IQR]	4.5 (6.0)	5.0 (5.0)
Recurrent episodes, percent (n)	66.7% (18/27)	73.1% (19/26)
Number of previous episodes:		
Mean (SD)	4.8 (6.9)	2.5 (2.6)
Median [IQR]	2.0 (8.0)	2.0 (3.0)
Suicide attempt in connection with actual admittance to inpatient ward, percent (n)	20.0% (6/30)	10.3% (3/29)
Suicide attempts earlier, percent (n)	35.7% (10/28)	37.0% (10/27)
Electroconvulsive treatment in current depressive episode, percent (n)	33.3% (10/30)	23.3% (7/30)
Experiencing an eliciting factor for actual episode, percent (n)	83.3% (25/30)	89.3% (25/28)
Smoking, percent	40.0% (12/30)	51.7% (15/29)
Number of cigarettes/day, mean (SD)	16.2 (4.5)	14.4 (7.7)
Drinking alcohol on a weekly basis, percent (n)	31.0% (9/29)	21.4% (6/28)
Drug abuse, percent (n)	3.4% (1/29)	0% 0/28)
Subjective feeling of being photosensitive, percentage (n)	40.7% (11/27)	42.9% (12/28)
Diagnosis of Migraine, percentage (n)	10.7%(3/28)	17.9% (5/28)
Expectation of improvement from the intervention (0–10, with 0 = unchanged and 10 = no depression) (SD)	5.4 (2.2)	5.0 (2.9)

Table 2. Hamilton and SIDAS outcomes.

Parameter	Dynamic LED group		Static LED group	
Hamilton Depression Rating Scale 6-item version (HAM-D_6) whole group	Value	n	Value	n
Baseline, mean (SD), [range], n	11.0 (3.1) [5–16]	29	11.4 (2.8) [5–15]	30
Week 1, mean (SD), [range], n	9.2 (2.9) [1–14]	26	10.0 (3.0) [1–16]	26
Week 2, mean (SD), [range], n	6.9 (4.0) [0–14]	24	8.5 (2.9) [1–13]	24
Week 3, mean (SD), [range], n	7.4 (3.8) [0–15]	28	8.4 (3.2) [0–15]	30
Month 6, mean (SD), [range], n	4.5 (3.4) [0–11]*	26	6.6 (3.9) [0–13]	27
Hamilton Depression Rating Scale 6-item version (HAM-D_6) females	Value	n	Value	n
Baseline, mean (SD), [range], n	11.5 (3.3) [5–16]	20	11.4 (2.8) [5–15]	23
Week 1, mean (SD), [range], n	9.9 (3.0) [1–14]	20	10.4 (3.2) [1–16]	20
Week 2, mean (SD), [range], n	7.1 (4.2) [0–14]	18	8.8 (3.0) [1–13]	19
Week 3, mean (SD), [range], n	7.0 (3.8) [0–15]*	20	8.7 (3.4) [0–15)]	23
Month 6, mean (SD), [range], n	4.8 (3.7) [0–11]	18	6.3 (3.7) [1–13]	22
Hamilton Depression Rating Scale 6-item version (HAM-D_6) men	Value	n	Value	n
Baseline, mean (SD), [range], n	10.0 (2.6) [6–13]	9	11.4 (2.9) [7–15)]	7
Week 1, mean (SD), [range], n	7.2 (1.0) [6–9)]	6	9.0 (2.4) [6–13]	6
Week 2, mean (SD), [range], n	6.3 (3.8) [0–10]	6	7.6 (2.7) [5–12]	5
Week 3, mean (SD), [range], n	8.5 (3.9) [4–14]	8	7.6 (2.6) [5–12]	7
Month 6, mean (SD), [range], n	3.8 (2.7) [1–8]	8	8.0 (4.6) [0–12]	5
Suicidal Ideation Attributes Scale (SIDAS)	Value	n	Value	n
Baseline, mean (SD), [range], n	10.5 (10.7) [0–33]	29	14.1 (14.6) [0–44]	28
Week 1, mean (SD), [range], n	9.0 (9.2) [0–30]	27	9.9 (12.5) [0–34]	24
Week 2, mean (SD), [range], n	7.1 (11.4) [0–37]	22	9.1 (10.0) [0–30]	20
Week 3, mean (SD), [range], n	10.1 (11.8) [0–43]	23	8.9 (10.9) [0–35]	26
Hamilton Depression Rating Scale 17-item (HAM-D_{17}) whole group	Value	n	Value	n
Baseline, mean (SD), [range], n	21.4 (5.9) [9–33]	29	22.4 (5.0) [14–32]	30
Week 1, mean (SD), [range], n	17.5 (4.9) [7–27]	26	19.2 (6.7) [5–32]	26
Week 2, mean (SD), [range], n	13.7 (6.6) [2–26]	24	18.0 (6.0) [1–28]	24
Week 3, mean (SD), [range], n	14.1 (6.4) [0–26](*)	28	17.6 (7.0) [1–34]	30
Month 6, mean (SD), [range], n	9.5 (6.9) [0–24]*	26	14.3 (7.5) [2–26]	27
Hamilton Depression Rating Scale 17-item (HAM-D_{17}) females	Value	n	Value	n
Baseline, mean (SD), [range], n	21.9 (6.0) [9–33]	20	22.6 (5.0) [14–32]	23
Week 1, mean (SD), [range], n	18.6 (4.6) [7–27]	20	19.5 (6.9) [5–32]	20
Week 2, mean (SD), [range], n	13.1 (7.1) [2–26]	18	18.1 (6.0) [1–26]	19
Week 3, mean (SD), [range], n	12.5 (6.2) [0–24]*	20	17.7 (7.3) [1–34]	23
Month 6, mean (SD), [range], n	9.6 (7.4) [0–24]	18	13.2 (6.9) [2–26]	22
Hamilton Depression Rating Scale 17-item (HAM-D_{17}) men	Value	n	Value	n
Baseline, mean (SD), [range], n	20.4 (6.0) [11–30]	9	21.6 (5.3) [15–30]	7
Week 1, mean (SD), [range], n	13.8 (4.3) [9–20]	6	18.3 (6.4) [12–30]	6
Week 2, mean (SD), [range], n	15.7 (4.4) [10–23]	6	17.8 (6.6) [12–28]	5
Week 3, mean (SD), [range], n	18.3 (5.3) [13–26]	8	17.1 (6.1) [8–25]	7
Month 6, mean (SD), [range], n	9.4 (6.2) [1–21]	8	19.0 (8.9) [4–26]	5

*$p < 0.05$,(*) $p = 0.07$.

The HAM-D_6 baseline scores were balanced between groups. There was no significant difference between groups at week 3 with predicted HAM-D_6 values of 7.2 (SD = 1.8) in the dynamic group and 8.6 (SD = 1.1) in the static group ($p = 0.47$). However, in females (71.7%) a statistically significant superior effect of dynamic versus static light was found at week 3 (parameter estimate 2.7; CL 0.48 to 4.96; $p = 0.02$). At 6 months, a significantly better effect of dynamic light was found for the whole group, with predicted HAM-D_6 scores of 4.4 (SD = 0.4) in the dynamic group and 6.6 (SD = 0.3) in the static group (parameter estimate 2.2; CL 0.16 to 4.20; $p = 0.03$).

There was no significant difference in SIDAS scores between groups at the endpoint (t-value = 1.0; $p = 0.33$).

The HAM-D_{17} baseline scores were balanced between groups. There was a borderline significant better effect in the dynamic group at week 3 with predicted endpoint HAM-D_{17} values of 14.0 (SD = 2.6) in the dynamic group and 17.6 (SD = 2.1) in the static group (parameter estimate 3.1; CL −0.23 to 6.49; $p = 0.07$). In females, a significantly better effect was found in the dynamic versus static group (parameter estimate 4.9; CL 1.12 to 8.7; $p = 0.01$). At the 6 months evaluation, the predicted HAM-D_{17} scores were significantly lower in the dynamic group, with a score of 9.4 (SD = 0.9) versus 14.3 (SD = 0.8) in the static group, for the whole group (parameter estimate 4.7; CL 0.75 to 8.73; $p = 0.02$). Time course for individual patients' HAM-D_{17} scores and group means are shown in Supplemental Figure 2.

There was no significant difference in the primary outcome, neither at week 3 or at 6 months evaluations, between patients having a depressive episode as part of a bipolar disorder or patients having a depressive episode due to a major depressive disorder.

Using the mixed model repeated measure model with sex as a covariate using all time points, we found comparable results as with the linear model with a significantly better effect in the dynamic group for

females at week 3 on the HAM-D_6 ($p = 0.05$) and at 6 months ($p = 0.03$) for the whole group. On the HAM-D17, we found a significantly better effect in the dynamic group for females at week 3 ($p = 0.03$) and for the whole group at 6 months ($p = 0.03$).

The administration of sedating pro re nata medication was equal in the two groups with a mean of 18.7 (SD = 15.4) administrations per participants in the dynamic group and 17.4 (SD = 16.3) administrations in the static group, for the 3 weeks period. Medications are listed in supplemental Table 1.

Serious Adverse Events

No serious adverse events were reported.

Chronotype and Sleep Measures

Data for chronotype based on the MEQ and sleep quality based on the PSQI are shown in Table 3 and sleep diary data in Table 4. Categorization according to accepted cutoff scores for the MEQ showed that 21.7% were evening chronotypes (MEQ score below 42), 60.0% percent were intermediate types (MEQ score from 42 to 58), and 18.3% were morning chronotypes (MEQ score above 58). Mean baseline MEQ scores for participants with a unipolar depression were 52.8 (SD = 9.3) and 48.2 (SD = 6.6) for bipolar depression (t-value = 1.9; $p = 0.07$).

There was a borderline significantly better effect for sleep quality on PSQI scores at week 3 in the dynamic group, with a predicted score of 9.2 (SD = 1.2) compared to 11.4 (SD = 1.3) in the static group (parameter estimate 2.5; CL − 0.19 to 5.23; $p = 0.068$). For females, a significantly lower PSQI score (better sleep quality) was found for dynamic versus static light at week 3 (parameter estimate 4.1; CL 0.89 to 7.24; $p = 0.01$).

The predicted number of nightly awakenings at endpoint was significantly lower in the dynamic group, with 1.3 (SD = 0.9) awakening per night compared to 2.0 (SD = 0.8) in the static group (parameter estimate 0.7; CL 0.05 to 1.37; $p = 0.04$). Estimated sleep offset was significantly later in the dynamic group with 07:13h (SD = 0:58) versus 06:48h (SD = 1:06) in the static group (parameter estimate 38.9 min; CL 0.06 min to 1.24 min; $p = 0.03$). Estimated duration from sleep onset to sleep offset was significantly longer in the dynamic group with 8.4 h (SD = 0.8) versus 7.7 h (SD = 1.1) in the static group (parameter estimate 1.0; CL 0.13 to 1.85; $p = 0.03$).

The frequency of naps, endpoint sleep onset and sleep quality from the sleep diaries data did not differ significantly between groups.

Use of Room and Curtains

The results from the Room Occupancy Diaries (covering the whole day from 06:00h till 24:00h) and curtain diaries are shown in Table 5. The mean daily number of room occupancy hours was 10.1 h (SD = 4.2 h) in the dynamic group and 8.6 h (SD = 3.0 h) in the static group, without any significant difference between female and male sex. Data from the curtains diary showed that most of the participants used the curtain and, for different reasons, mostly to avoid exposure to neighboring buildings. As no increase in curtain use was observed from baseline, we assume that the light panel used in the dynamic group did not increase the use of curtains (curtains could be drawn to shield the light panel in the window jamb).

Lighting Comfort

Results from the lighting comfort diaries covering "last week" are shown in supplemental Table 2. Overall, the user satisfaction ratings were high in both groups, with

Table 3. Morningness-eveningness questionnaire (MEQ), Pittsburgh sleep quality Index (PSQI), and sleep efficiency from PSQI.

	Dynamic LED group		Static LED group	
Parameter	Value	n	Value	n
MEQ				
Baseline, mean (SD), [range], n	53.0 (8.6) [41–75]	30	50.8 (9.4) [29–67]	30
Week 3, mean (SD), [range], n	52.4 (8.0) [39–66]	23	51.3 (8.7) [30–64]	23
PSQI				
Baseline, mean (SD), [range], n	12.3 (4.3) [3–19]	27	11.3 (4.5) [1–19]	29
Week 3, mean (SD), [range], n	9.2 (3.7) [3–18](*)	24	11.6 (5.1) [3–20]	25
Sleep efficiency				
Baseline, mean percent (SD), n	75.9 % (20.2)	27	80.7 % (17.8)	29
Week 3, mean percent (SD), n	86.2 % (10.8)	24	78.2 % (18.1)	25

*$p < 0.07$.

Table 4. Sleep outcomes from sleep diaries.

Parameter	Dynamic LED group		Static LED group	
Mean for last week				
Sleep quality				
Baseline, mean (SD)	5.8 (2.3)	28	5.4 (2.4)	29
Week1, mean (SD)	6.2 (2.2)	26	5.4 (2.8)	25
Week2, mean (SD)	6.7 (2.6)	22	5.6 (2.4)	20
Week3, mean (SD)	6.5 (2.6)	25	5.5 (3.0)	26
Wake-ups				
Baseline, mean (SD)	1.7 (1.6)	28	1.7 (1.4)	29
Week1, mean (SD)	1.7 (1.6)	25	1.9 (1.9)	26
Week2, mean (SD)	1.8 (1.4)	22	1.6 (1.4)	20
Week3, mean (SD)	1.4 (1.6)*	25	1.9 (1.3)	26
Naps				
Baseline %	32.1 %	9/28	31.0 %	9/29
Week1 %	20.0 %	5/25	32.0 %	8/25
Week2 %	13.6 %	3/22	15.0 %	3/20
Week3 %	28.0 %	7/25	15.4 %	4/26
Sleep onset (SO)				
Baseline, mean (SD)	23:13h (1:04h)	28	23:07h (1:16h)	29
Week1, mean (SD)	23:02h (1:10h)	26	23:11h (1:15h)	25
Week2, mean (SD)	22:48h (0:42h)	22	23:03h (1:07h)	20
Week3, mean (SD)	22:49h (0:51h)	25	23:03h (1:05h)	26
Sleep offset (SOFF)				
Baseline (SD)	6:51h (1:28h)	28	7:11h (1:39h)	29
Week1, mean (SD)	6:54h (1:14h)	25	7:00h (1:27h)	25
Week2, mean (SD)	6:57h (1:19h)	22	6:50h (1:24h)	20
Week3, mean (SD)	7:16h (1:19h)*	25	6:46h (1:38h)	26
Sleep period (Sleep Onset to Sleep Offset)				
Baseline (SD)	7.6 h (1.4 h)	28	8.1 h (2.0 h)	29
Week1, mean (SD)	7.9 h (1.7 h)	25	7.8 h (1.9 h)	25
Week2, mean (SD)	8.1 h (1.5 h)	22	7.8 h (1.6 h)	20
Week3, mean (SD)	8.5 h (1.5 h)*	25	7.7 h (2.0 h)	26
Hours of sleep (minus awakenings)				
Baseline (SD)	6.8 h (1.8 h)	28	7.1 h (2.2 h)	29
Week1, mean (SD)	7.5 h (1.6 h)	25	6.8 h (2.5 h)	25
Week2, mean (SD)	7.6 h (1.8 h)	22	7.4 h (1.8 h)	20
Week3, mean (SD)	7.9 h (1.9 h)	25	7. 1h (2.1 h)	26

*$p < 0.05$.

Table 5. Room occupancy and use of curtains.

Parameter	Dynamic LED group		Static LED group	
Time spent in room per day	Mean (SD)	n	Mean (SD)	n
Baseline, mean (SD)				
6:00h till 12:00h, hours decimal time, mean (SD)	3.7 (1.7)	28	3.1 (1.5)	29
12:00h till 18:00h, hours decimal time, mean (SD)	3.5 (1.7)	28	2.9 (1.4)	29
18:00h till 24:00h, hours decimal time, mean (SD)	3.8 (1.6)	28	3.6 (1.6)	29
Total in room from 6:00h till 24:00h, hours decimal time, mean (SD)	11.0 (4.6)	28	9.7 (3.8)	29
Week1, mean (SD)				
6:00h till 12:00h, hours decimal time, mean (SD)	3.3 (1.8)	26	2.6 (1.5)	24
12:00h till 18:00h, hours decimal time, mean (SD)	2.9 (1.9)	26	2.4 (1.3)	24
18:00h till 24:00h hours decimal time, mean (SD)	3.7 (1.8)	26	3.3 (1.6)	24
Total in room from 6:00h till 24:00h, hours decimal time mean (SD)	9.9 (5.1)	26	8.3 (3.5)	24
Week2, mean (SD)				
6:00h till 12:00h, hours decimal time, mean (SD)	3.4 (1.6)	22	2.3 (1.4)	20
12:00h till 18:00h hours decimal time, mean (SD)	3.1 (1.4)	22	2.3 (1.2)	20
18:00h till 24:00h, hours decimal time, mean (SD)	3.3 (1.4)	22	3.3 (1.6)	20
Total in room from 6:00h till 24:00h, hours decimal time mean (SD)	9.8 (3.6)	22	8.0 (3.5)	20
Week3, mean (SD)				
6:00h till 12:00h, hours decimal time, mean (SD)	3.7 (1.6)	15	2.4 (1.4)	17
12:00h till 18:00h, hours decimal time, mean (SD)	3.2 (1.4)	15	2.4 (1.5)	17
18:00h till 24:00h, hours decimal time, mean (SD)	3.8 (1.8)	15	3.0 (1.6)	17
Total in room from 6:00h till 24:00h hours decimal time, mean (SD)	10.7 (4.3)	15	7.8 (3.8)	17
Total in room from 6:00h to 24:00h decimal time all weeks, LOCF, means (SD)	10.1 (4.2)	28	8.6 (3.0)	29
Time spent in room for whole study period				
Hours in room from 6:00h till 24:00h, all days in study, hours decimal time mean (SD), LOCF	189.5 (94.4)	28	154.8 (74.8)	29
Use of curtains at some time of day				
Baseline: Percentage using curtains (n)	78.6 %	(22/28)	86.7 %	(26/30)
Week 1: Percentage using curtains (n)	84.6 %	22/26	87.5 %	21/24
Week 2: Percentage using curtains (n)	90.9 %	20/22	95.2 %	20/21
Week 3: Percentage using curtains (n)	87.5 %	14/16	90.5 %	19/21

low levels of reported glare for all luminaires for all parts of the day.

Participants were significantly more satisfied with the color of the lighting in the dynamic group compared to the static group in week 3 (morning, $p = 0.07$; evening, $p = 0.02$). The same was found for intensity of the evening light with satisfaction ratings of 77.3%/38.9% in week 2 and 81.3%/37.5% in week 3 in the dynamic/static groups (evening, $p = 0.01$). There was higher satisfaction when evaluating lighting on the item "homely and comforting" in the dynamic group with significant differences at several assessments and time-points, especially at week 3 (morning, $p = 0.05$, evening, $p = 0.005$). The satisfaction with the window jamb light panel was above 95% and low levels of glare were reported.

Safety Outcomes

Results from the YMRS and the UKU side effect scales are shown in supplemental Table 3. No participants developed hypomania or mania and YMRS scores were low. The UKU side effect scale showed a low grade of side effects, with no difference between groups and no development over the 3 weeks of exposure to the lighting system.

Light Sensor and Dynamic System Log Data

It was not possible to establish a long-term stable sensor data flow from light loggers.

The retrieved daylight sensor data is shown in supplemental material 1 where the figure illustrates the vast differences in daylight exposure in each room depending on time of day, season, and direction.

The log data for the dynamic system are shown in supplemental material 2. The table shows more use of lighting in the dynamic setting through all periods of the day compared to static lighting.

Other Results

Information on data for energy consumption is found in supplemental material 3.

Discussion

This is the first study to find a sustained 6-month antidepressant effect (HAM-D_6 and HAM-D_{17}) of dynamic lighting.

At week 3, we found a borderline significant effect of dynamic lighting on the HAM-D_{17} scale, and a significant effect for the large subgroup of female participants (71.7%) both on the HAM-D_6 and HAM-D_{17} scale. No serious adverse events and no treatment-emergent side-effects were seen. The dynamic system was well tolerated and there was very high satisfaction with the built-in window jamb panel.

Subjective sleep outcomes were better under the dynamic light conditions compared to the static lighting with significantly longer sleep, later sleep offset, and fewer awakenings. This is in accordance with findings in recent studies in similar settings, using artificial dawn-dusk and blue depleted nighttime lighting, showing longer sleep with shorter awakenings (Canazei et al. 2022; Vethe et al. 2021). Our finding of improved sleep is adding to the evidence for beneficial effects of 24-hour dynamic lighting in inpatient wards for affective disorders. We found a significantly better effect on sleep quality (PSQI) for females that also reported significantly more sensitivity to light. It can be speculated that the larger effect of light on both depression and sleep quality in females is mediated through sex-specific light sensitivity (Chellappa 2021). The MEQ results confirm that patients with a bipolar disorder usually exhibit later chronotypes than patients with a unipolar depression (Melo et al. 2017).

During the study, participants would receive an unknown amount of daylight both from the windows in the room, in the ward, and also from going outside. As we do not have any data on the extent of this, we cannot know how much this influenced results. Patients in the dynamic group might be more aware of the beneficial effects of daylight. However, room occupancy diaries showed that participants in the dynamic group spend more time in their room compared to participants in the static group. The effect of daylight on depression and sleep also depends on the time of exposure. Late night daylight during the summer potentially delays sleep and early light exposure advances sleep, probably improving depression. This exposure to daylight is linked to seasons and expected to have more influence in summer, but even on cloudy days in November, daylight exposure can have an influence on sleep and mood as the intensity can reach the threshold for an effect of the circadian system.

The sustained antidepressant effect of patients in the dynamic group compared to the static group at the 6-month follow-up might be explained by patient in the dynamic group replicating light patterns from their inpatient room after discharge by using dim light in the evening and getting more daylight during daytime. This is plausible since these patients were aware from the participant information that this was thought to be beneficial for mood and sleep and as the experienced it in

their rooms. Another possible explanation is that the better sleep obtained in the dynamic group sustained improvement from depression.

The overall findings are important, as many new hospitals are now equipped with dynamic lighting but without evidence on how to set an optimal lighting scenario. From the theoretical and empirical backgrounds that we used to create the dynamic lighting scenario, we had expected a slight phase advance of the sleep-wake cycle from the use of a brighter morning light and a dimmer evening light. There might be a signal in the sleep onset data (see Table 4), but this was not significant, which could be a question of lack of power in the study. Another possibility for the lack of a sleep phase advance is that patients, if wanting higher light intensities in the evening, would leave the room for part of the evening, thus receiving the brighter light outside the patient room. Also, some participants, if finding the light too bright, could have turned off the light in the morning or left the room, exposing themselves to the lower morning/noon intensities.

Whether any specific luminaire or setting were causal for the effect on depression and sleep measures is uncertain. We assume that the dim light with low blue content provided by the ceiling and reading luminaires functioned as "sleep preparation" by allowing melatonin to rise unimpeded by bright light, providing a higher sleep pressure. This could be reinforced by the mechanism of prior light history where exposure to high-intensity daytime light reduces the alerting effect of bedtime light and thus contributes to sleep preparation (Chang et al. 2013).

Limitations of the Study

The main limitation is that the study did not reach the planned sample size, thus reducing the power to find significant differences. There are several challenges when trying to evaluate the effect of dynamic lighting. First, patients do not stay in their room for the entire day but enter other lighting scenarios in the ward and receive daylight outside or in courtsides or from windows. Another limitation is that the study did not have the power to correct for daylight exposure, with the 10 patient rooms having differences in daylight availability because of the architectural design, with different sizes, windows, and orientation of rooms (see Figure 1). The exposure to daylight from windows depends very much on the geographical location of the window, as was shown in our prior measurements in a 1:1 rotatable mock-up of a patient bedroom (Volf et al. 2022). We could have applied wearable light sensors to assess participant-specific light exposure. Instead, we had to rely on the Room Occupancy Diaries that were not fine-grained enough to assess whether participants sought brighter evening light or dimmer morning light outside their rooms.

Even if patients reported staying in their rooms for most of the day (8–10 h), their exposure to bright, blue-enriched light in their room would vary depending on whether they turned off the ceiling luminaires and the reading lamp.

An objective sleep assessment would have been a strong improvement in the design. However, sleep diaries are a validated measure of sleep (Fabbri et al. 2021; Ibáñez et al. 2018) and a full actigraphy or polysomnographic evaluation was beyond the scope of this study.

Our problem with continuous logging of daylight and LED-lighting makes replication more difficult regarding daylight, but the LED-lighting scenarios are described in the protocol paper as they were used in the study.

Conclusions

The results show a short-term antidepressant effect in females and a sleep-promoting effect for the whole group and a long-term antidepressant effect for the whole group. These results are of high clinical relevance since current inpatient treatment is often insufficient for patients to achieve remission. The 1-h increase in sleep duration in the dynamic group is also of major clinical importance. The dynamic lighting condition was found more satisfactory and comforting than the static light.

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Author Contribution Statement

All authors contributed substantially to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; and drafted the work or revised it critically for important intellectual content; and made a final approval of the version to be published; and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

In addition:

Carlo Volf and Klaus Martiny were primary in the design's conception. Carlo Volf was primarily responsible for project leader tasks and for measuring procedures.

Anne Sofie Aggestrup was primary in the inclusion and assessment of participants and collaborated with the staff.

Paul Michael Petersen was involved in the measurement design of the study and planning of technical and onsite measurements.

Carsten Dam-Hansen was involved in the measurement design of the study and the planning of technical and onsite measurements.

Ulla Knorr was involved in the study's conception and practicalities around communication with the ward.

Janus Engstrøm was primarily on the building of the OpenClinica database and data management.

Torben Skov Hansen was the primary in creating lighting scenarios and onsite measurements.

Helle Østergaard Madsen was involved in design of the study and blinded Hamilton assessments.

Ida Hageman was involved in the study's design and support regarding the use of facilities and installation of the dynamic light system.

Klaus Martiny and Carlo Volf were primary in the study's design, and responsible for the overall conduct of the trial.

All authors read and accepted the final manuscript.

Data Availability Statement

Authors agree to make data and materials supporting the results or analyzes presented in their paper available upon reasonable request. Data should only be shared if it is ethically correct to do so, where this does not violate the protection of human subjects, or other valid ethical, privacy, or security concerns.

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