

Effects of Light Therapy on Mood and Sleep Disorders: A Systematic Review and Meta-analysis

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Abstract

Background: Light therapy (LT) had become a frequently-used treatment method for treating emotional disturbance and sleep disorders due to its convenience, safety and low cost.

Objective: To synthesize the research progress regarding the connections among light, sleep and mood, as well as evaluate the influencing factors of LT on depression improvement and impact of LT on the functional connectivity between multiple brain structures.

Methods: Relevant clinical trials were searched in 5 databases from January 1th 2020 to June 30th 2025. Quality of studies was assessed by Risk of Bias Tool 2 and GRADE. The primary outcome was depression improvement and secondary outcomes were anxiety improvement and sleep quality. The random effects model was applied, and heterogeneity was assessed by I² statistics. Meta-regression analysis was conducted to explore possible influencing factors. Sensitivity analysis was used to evaluate robustness.

Results: Depression improvement between two groups reached a significant level (SMD = 0.51, 95% CI [0.34, 0.68], p = 0.00, I² = 24.96%). Anxiety was tended to be significantly improved (MD = 1.95, 95% CI [-0.03, 3.94], p=0.05). Sleep efficiency (MD = 4.65, 95% CI [1.19, 8.11], p = 0.01), PSQI scores (MD = 1.60, 95% CI [0.71, 2.50], p = 0.00) and ISI score (MD = 3.45, 95% CI [2.00, 4.89], p = 0.00) significantly changed. There was positive correlation between treatment duration and depression improvement (? = 0.09, p = 0.037).

Conclusions: LT had a positive effect on depression, anxiety and sleep. Treatment duration and depression improvement was positively correlated.

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Original Manuscript

Effects of Light Therapy on Mood and Sleep Disorders:

A Systematic Review and Meta-Analysis

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Short Title: Effects of Light Therapy on Mood and Sleep Disorders

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Keywords: Light Therapy; Emotional disturbance; Sleep disorder; Systematic Review; Meta-Analysis

Abstract

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Conclusions: LT had a positive effect on depression, anxiety and sleep. Treatment duration and depression improvement was positively correlated.

Introduction

In 1925 at the Parkside Mental Hospital, researchers used ultraviolet radiation to conduct a clinical trial on 50 patients with mental illness, randomly dividing them into a carbon arc lamp group or a mercury arc lamp group [1]. The results showed that depression of all patients was improved [1]. Since then, many researchers have conducted studies on the effects of light therapy (LT) on mental diseases. In past years, lighting technology has been advanced continuously and mechanism of LT has been explored actively, so patients suffering from emotional disturbance (such as anxiety and depression) and sleep disorders can choose LT as auxiliary treatment or alternative treatment for their symptoms [2]. Previous studies often observe that those patients often experience significant improvement in their symptoms after being exposed to natural light or artificial light of specified illuminance, wavelength and treatment duration. Nowadays, owing to its safety, convenience, and low cost, LT has become an indispensable method for treating emotional disturbance and sleep disorders [3].

A systematic review [2] indicates that bright light therapy (BLT) can significantly improve non-seasonal depression. This review also conducted a regression analysis, finding that the relationship between the remission rate and the age of onset of major depressive disorder (MDD) was close to the threshold P value, which meant if more samples were included, there might be a correlation between the remission rate and the age of onset of MDD. Another systematic review [4] on LT and sleep problems found that effect size of improvement on sleep problems was small to moderate, and circadian rhythm and insomnia symptoms were the most sensitive to LT. In the meta-analysis of insomnia, it was discovered that light illuminance had positive effect on effect size [4]. However, there were no review that simultaneously summarize the therapeutic effects of LT on patients with emotional disturbance, sleep problems, or those with both problems concurrently.

Previous studies have shown that patients with emotional disturbance often experience insomnia at night and/or suffer from daytime sleepiness, and the probability of developing emotional disturbance among those with sleep problems is also higher than that of healthy individuals [5]. T.A. LeGates et al. [6] discovered that light, circadian rhythm, sleep and mood are closely related. Light regulates the circadian rhythm, thus effecting sleep and mood indirectly. Meanwhile, light can directly affect emotions by other pathways [6].

To synthesize the research progress made in recent years regarding the connections among light, sleep and mood, this review studied the results of randomized controlled trials from

January 2020 1th to June 30th 2025 on light therapy for patients with emotional disturbance (depression, anxiety), sleep disorders or comorbidities of both. This review outlined specific LT measures (light equipment, the time and duration of LT, illumination level, treatment duration, etc.) of included studies, as well as summarized the LT outcomes and conducts a meta-analysis. Meanwhile, we evaluated the influencing factors of LT on the improvement of depression (such as patient age, treatment duration, illumination level), and discussed the impact of LT on the functional connectivity between multiple brain structures.

Method

Search Strategy

The protocol was registered on PROSPERO (CRD420251116783) and the selection process of the studies followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [7] statement and the requirements of the Cochrane Handbook [8]. Relevant clinical trials were retrieved from the following databases: Cochrane library, Embase, EBSCO, PubMed and Web of Science. The following search terms were used: (“light therapy” OR “phototherapy” OR “bright light therapy” OR “BLT” OR “dawn simulation” OR “blue light” OR “red light” OR “near-infrared light” OR “low-level laser therapy” OR “LLLT”) AND (“depress*” OR “depressive disorder” OR “major depressive disorder” OR “bipolar disorder” OR “sleep disorder*” OR “insomnia” OR “anxiety”). Additional filtering criteria included “publication in English”, “publication date from January 1th 2020 to June 30th 2025” and “clinical trial”. Other studies listed in the reference sections of the relevant articles were reviewed to add missing literature to the search results.

Inclusion Criteria and Exclusion Criteria

Inclusion criteria were as follows: 1) The study was written in English; 2) The patients were adults (over 18 years old); 3) The study was a randomized controlled trial and involved at least 10 patients; 4) The patients must be clinically diagnosed with non-seasonal depression (DSM-5 [9] or ICD-10 [10]) or had a scale test result of subthreshold depression or had sleep disorders; 5) LT was the only differential treatment method between the intervention group and the control group; 7) LT must be used for treatment; 8) At least one sleep outcome or one depression scale was measured.

Exclusion criteria were as follows: 1) Not meeting the inclusion criteria; 2) Abstracts of conferences; 3) Participants were healthy individuals; 4) Main outcome was compliance or dropout rate; 5) Animal studies; 6) Mechanism studies or research plans without clinical

outcomes; 7) Repeated publications.

Starting from August 2nd 2025, relevant data from included studies was summarized by two independent researchers. In case of any disputes, the third researcher would make the judgment. For the included studies, the following information was collected: the authors of the study and the publication year, the number of patients (intervention group/control group), the number of females, the age of the patients (years), the diagnostic criteria, the LT characteristics of the control group and the intervention group, the medicine status, and outcomes.

Outcomes

The primary outcome was the improvement of depression in the intervention group and the control group before and after the intervention, which was determined by the changes in the scale scores. In the included studies, for those that reported multiple depression scale scores, the Hamilton Depression Scale (HAMD) [11] scores were given priority in the meta-analysis.

The secondary outcomes were the changes in anxiety and sleep quality before and after the intervention. The measurement tool for the former was the Hamilton Anxiety Rating Scale (HAMA) [12], while the measurement tools for the latter were divided into objective and subjective indicators. The objective outcome measures included sleep onset latency (SOL), total sleep time (TST), wake after sleep onset (WASO), sleep efficiency (SE), and sleep onset and offset times measured by a wrist actigraphy device. The subjective outcome measures included the Pittsburgh Sleep Quality Index (PSQI) [13] for measuring subjective sleep quality, the Insomnia Severity Index (ISI) [14] for measuring insomnia development, and the Epworth Sleepiness Scale (ESS) [15] for measuring daytime sleepiness.

Statistic Analysis

All statistical analyses were conducted by Stata 18.0 [16] and the extension package meta. When the data collected for one outcome were ≥ 3 , a meta-analysis would be performed for that outcome. The mean difference (MD) or standardized mean difference (SMD) was used to evaluate continuous variables, with the former used for data collected by the same outcome measure and the latter for the same outcome but with different measures. Both MD and SMD were assessed using a 95% confidence interval (CI) to reduce potential bias. SMD was measured by Hedge's g , and Hedge's g values of 0.2, 0.5, and 0.8 were considered small, medium, and large effects respectively [17]. The Hartung-Knapp-Sidik-Jonkman random effects model [18] was applied. Statistical significance was set at $P < 0.05$. The Q and I^2 statistics were used to evaluate heterogeneity, with 25%, 50%, and 75% I^2 values being

interpreted as low, moderate, and high heterogeneity, respectively [19]. Meta-regression analysis was conducted to evaluate the possible associations between age and the improvement of depression, treatment duration and the improvement of depression, as well as illuminance and the improvement of depression. Meanwhile, subgroup analyses were performed according to different scales, illuminance, disease subtypes, control measures, countries, age, treatment duration, and medication status. Funnel plots or egger test [20] were used to assess publication bias. Sensitivity analysis was used to determine the robustness of these results.

Risk of Bias and Quality of Evidence

The Cochrane Risk of Bias Tool 2 (ROB 2) [21] was used. Two assessors independently evaluated the risk of bias of the included studies in five fields: the randomization process, deviation from the intended intervention, missing outcome data, outcome measurement, and selection of reported results. The risk levels were classified as “low”, “some concerns” or “high”. When there was a disagreement, assessors would check and discuss to get same results. The quality of the outcomes was evaluated according to the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) [22], which was carried out independently by two researchers. The results of GRADE were divided to “very low”, “low”, “moderate” and “high”.

Results

Search Results

The search results are shown in the PRISMA flowchart (shown in Fig. 1). 6,848 results were generated from six databases. After searching based on the titles and authors to delete duplicate studies, a preliminary screening of the titles and abstracts was conducted for 4,666 articles. 4,602 studies were excluded in the initial screening, and a comprehensive review was conducted for the remaining 64 articles. Based on the various reasons shown in Figure 1, forty-five studies were excluded, and finally, 19 studies were included in meta-analysis.

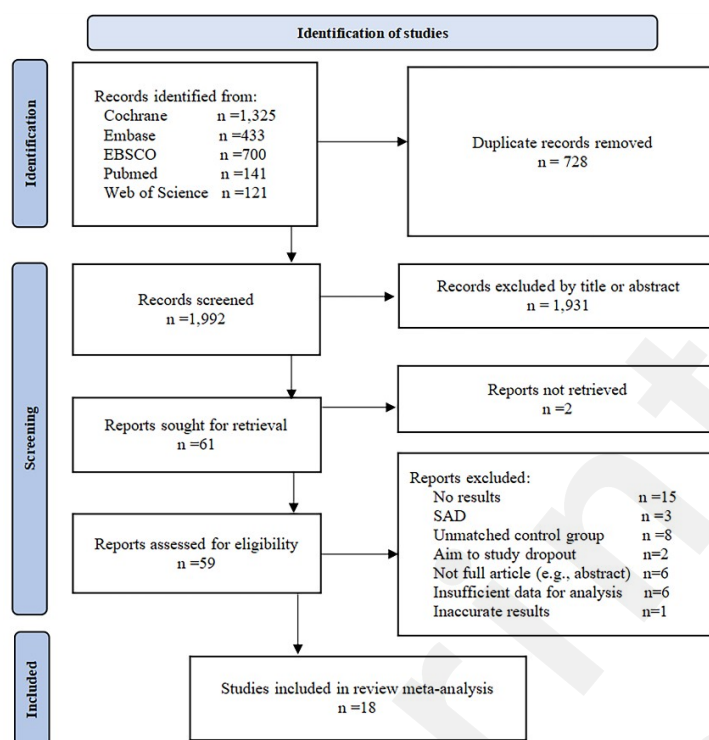


Figure 1 PRISMA flow chart of study selection process. SAD: seasonal affective disorder.

After analyzing the changes in depression scale scores of the LT group and the control group before and after the intervention in 12 studies [23-34], although it was found that compared with the control group, the improvement of depression in the LT group was better, and the difference between the two groups reached a significant level (SMD = 0.60, 95% CI [0.37, 0.82], $p = 0.00$), there was moderate heterogeneity among the studies ($I^2 = 59.96\%$, $Q(df = 11) = 25.59$, $p = 0.01$). Subgroup analyses were conducted based on different scales, illuminance, disease subtypes, control measures, countries, age, treatment duration, and medication status. Except for control measures ($p = 0.04$), age ($p = 0.03$), and medication status ($p = 0.01$), the P values for the differences between groups in the other subgroups did not reach a significant level. In the subgroup analysis of control measures, the heterogeneity within the WCL group was high ($I^2 = 81.83\%$); in the subgroup analysis of age, the heterogeneity within the 18-30 age group was moderate ($I^2 = 63.45\%$); in the medication status subgroup analysis, the heterogeneity within the non-medication group was also moderate ($I^2 = 55.80\%$). Through subgroup analysis, it can be seen that only the study by Lijun Jiang et al. [23] appeared in the three subgroups with high heterogeneity. Therefore, it is speculated that this study is the source of heterogeneity, so this study was re-evaluated.

The purpose of Lijun Jiang's study [23] was to compare the depression improvement between LT group and WLC group in patients with non-seasonal subthreshold depression. A three-arm randomized controlled trial was used, with the intervention group divided into 5,000 lux and

500 lux, and the control measure was the waiting list. The data included in this review was from the 5,000 lux group and the WLC group. Before the start of the three-arm trial, patients were informed of which group they were assigned to, so the expectations of the intervention group patients for the efficacy of LT might have a positive impact on the final results, while the control group might have a negative impact. Thus, it is speculated that the improvement effect of depression in the LT group in this study might have been exaggerated with a high effect size value, which ultimately led to high heterogeneity when this study and other studies were combined for meta-analysis. Therefore, this study by Lijun Jiang et al. [23] was excluded. Eventually, 18 studies (shown in Supplementary Table 1.) were included in this review.

Baseline Characteristics

The basic characteristics of included studies were shown in Supplementary Table 1. A total of 18 articles were included in this review, involving 1049 patients. Among them, 692 were female (66.0%), and 357 were male (34.0%). 544 patients (51.9%) received LT, while the remaining 505 patients (48.1%) formed the control group.

Eight studies [24,26-28,31,37,38,40] conducted LT in patients' homes, while 5 studies [25,34,35,39,41] conducted LT during hospitalization or in clinics, and the remaining reports [29,30,32,33,36] didn't mention the locations of LT. The LED light box was the preferred light source in most studies, while 2 studies [35,41] chose to install light sources on the ceiling in their respective studies, and another 2 studies [25,38] selected light-activated glasses. 4 studies [24,26-28] used a light source with the illuminance of 5,000 lux and 8 studies [29-34,39,40] selected a light source with the illuminance of 10,000 lux. 2 studies [40,41] adopted an intervention measure where the illuminance fluctuated over time, and 1 study [24] did not report the illuminance. The remaining 3 studies used 16,500 lux [36], 1,250 lux [37], and 380 lux [38] respectively. Except for 1 study [25] that used violet light and 1 study [37] that used blue light, all other studies used devices that emitted full-spectrum or white light. Except for Yoshihiro Noda et al. [25], who conducted 3 hours of LT from 11:00 to 14:00, all other studies chose to conduct LT in the morning. Most studies conducted LT for 30 minutes, but 2 studies [35,41] adopted a 24-hour LT intervention, and another 2 studies [38,40] chose to conduct LT for 20 minutes each day. The intervention lasted from 2 weeks to 24 weeks, and 14 studies [24-34,36,38,40,41] lasted for 4 weeks or more. In most of included studies, the distance from the light source to patients ranged from 30 to 75 cm. In the studies that used luminous glasses, only 1 study [25] reported that the distance between the light source and the eye was 16.8 mm. The rest studies did not report the distance. 2 studies [35,41]

measured the actual illuminance at different distances because the light-emitting device was fixed on the ceiling and the patients could move around in the room. Only 1 study [34] chose drug treatment as the control measure, while the other control measures included dim red light [29,30,32], inactive equipment [24-28,39,40], standard light [31,35,36,41] and waiting list [33,37,38].

Primary Outcome

A total of 11 studies [24-34] were analyzed to regard the changes in depression scale scores of the LT group and the control group before and after the intervention. Except for 3 studies [25,30,33], the remaining studies all used the HAMD. The meta-analysis results (shown in Fig. 2 and Supplementary Table 2) showed that compared with the control group, the improvement of depression in the LT group was better, and the difference between the two groups reached a significant level ($SMD = 0.51$, 95% CI [0.34, 0.68], $p = 0.00$). There was low heterogeneity among the studies ($I^2 = 24.96\%$, $Q(df = 10) = 8.10$, $p = 0.62$). Subgroup analyses were conducted based on different scales, illuminance, disease subtypes, control measures, countries, age, treatment duration, and medication status (shown in Supplementary Table 9). Except for disease subtypes ($p = 0.04$), and medication status ($p = 0.02$), the P values for the differences between groups in the other subgroups did not reach a significant level. The egger test for the main outcome showed no publication bias ($p = 0.59$), which was consistent with the funnel plot (shown in Fig. 3). Sensitivity analysis (shown in Supplementary Fig. 8) using the sequential exclusion method was conducted to evaluate the sensitivity, and the combined effect size did not change significantly after sequentially excluding the included studies. The meta-analysis results of this outcome had good stability.

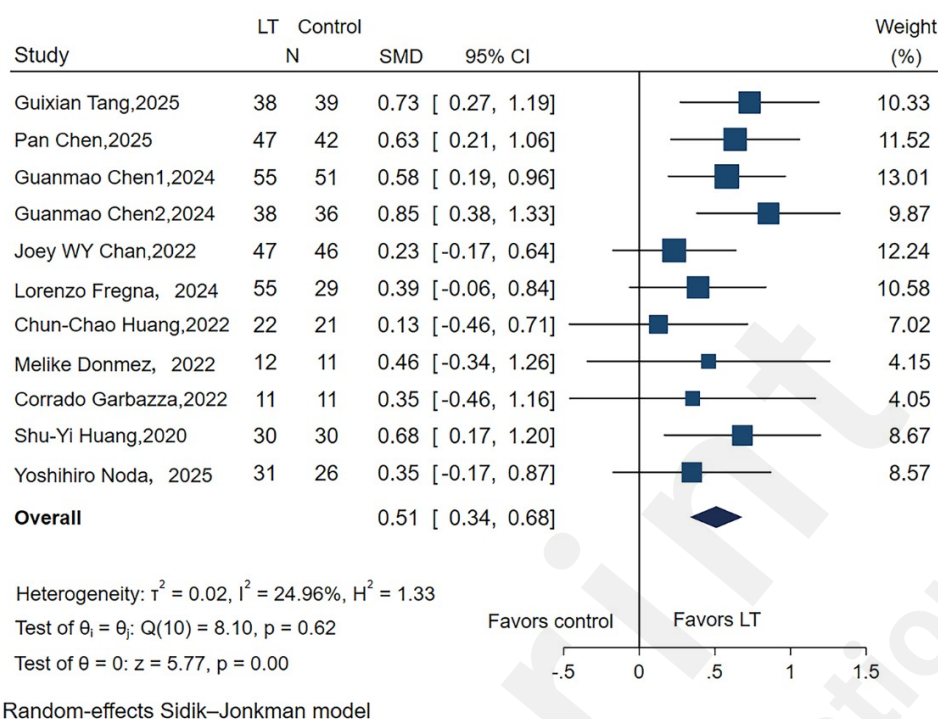


Figure 2 Forest plot for the changes in depression scale scores before and after the intervention.

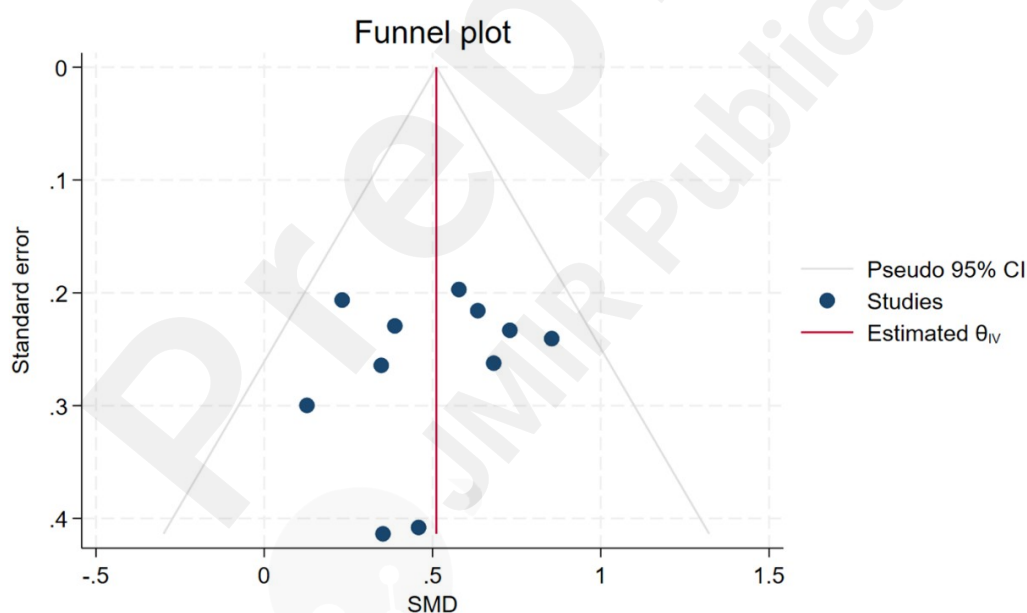


Figure 3 Funnel plot for depression.

Secondary Outcomes

HAMA

Three studies [24,28,32] analyzed the changes in HAMA scores of the LT group and the control group before and after the intervention. The results (shown in Supplementary Table 3 and Supplementary Fig. 2) showed that the difference between two groups tended to be significant ($MD = 1.95$, $95\% CI [-0.03, 3.94]$, $p=0.05$). There was no heterogeneity among the studies ($I^2 = 0.07\%$, $Q(df = 2) = 0.07$, $p = 0.97$). The egger test showed no publication bias (p

= 0.86). Sensitivity analysis (shown in Supplementary Fig. 9) showed that the combined effect size of this outcome did not change significantly after eliminating each included study, and the robustness was good.

TST and SE

Five [35,36,39-41] and four [36,39-41] studies respectively analyzed TST and SE in the LT group and the control group before and after the intervention. The meta-analysis (shown in Supplement Table 4, Supplement Fig. 3, Supplement Table 5 and Supplement Fig. 4) showed that compared with the control group, the improvement of TST in the LT group was not significant (MD = 6.79, 95% CI [-11.54, 25.11], $p = 0.47$), and the heterogeneity among the studies was very low ($I^2 = 12.64\%$, $Q(df = 4) = 1.36$, $p = 0.85$). However, SE of the LT group significantly improved (MD = 4.65, 95% CI [1.19, 8.11], $p = 0.01$) and the heterogeneity was very low ($I^2 = 6.24\%$, $Q(df = 3) = 1.08$, $p = 0.78$). The P value of egger test was 0.52 and 0.51 respectively in analyses on TST and SE, which showed no publication bias of two objective outcome measures. Sensitivity analysis (shown in Supplementary Fig. 10 and Supplementary Fig. 11) indicated that results of two meta-analysis had good stability.

SOL, WASO, Sleep Onset and Offset time

The data collected of these three measures did not able to conduct meta-analysis. However, it can be observed that compared with the control group, the SOL in the LT group was shortened, the number of WASO decreased, and the patients in the LT group started sleep earlier at night and woke up earlier in the morning.

PSQI, ISI and ESS

The PSQT scores, ISI scores and ESS scores are subjective indicators related to sleep. Five [31,34,36,39,40], three [32,38,39] and four [36,37,39,40] studies respectively analyzed the changes in PSQI scores, the changes in ISI scores as well as the changes in ESS scores of the LT group and the control group before and after the intervention. The results showed that compared with the control group, the PSQI scores of the LT group was significantly reduced (MD = 1.60, 95% CI [0.71, 2.50], $p = 0.00$, shown in Supplementary Table 6 and Supplementary Fig. 5), and the heterogeneity among the studies was low ($I^2 = 22.83\%$, $Q(df = 4) = 3.49$, $p = 0.48$). ISI scores of the LT group were significantly lower (MD = 3.45, 95% CI [2.00, 4.89], $p = 0.00$, shown in Supplementary Table 7 and Supplementary Fig. 6), so the improvement of insomnia was better. The heterogeneity among the studies was very low ($I^2 = 3.17\%$, $Q(df = 2) = 0.41$, $p = 0.81$). The improvement of ESS scores in the LT group was not significant (MD = 0.91, 95% CI [-0.26, 2.08], $p = 0.13$, shown in Supplementary Table 8 and

Supplementary Fig. 7), and there was no heterogeneity among these studies ($I^2 = 0.32\%$, $Q(df = 3) = 0.18$, $p = 0.98$). The P value of egger test was 0.23, 0.79 and 0.99 respectively, which showed no publication bias of three subjective outcome measures. Sensitivity analysis (shown in Supplementary Fig. 12-14) showed that the combined effect size of three outcome measures did not change significantly after eliminating each included study, and the robustness was good.

Meta-regression analysis

A meta-regression analysis of 11 studies [24-34] on the relationship between age, treatment duration and changes in depression scale scores was conducted. However, due to the absence of illuminance in the study by Yoshihiro Noda et al. [25], the regression analysis of the relationship between illuminance and changes in depression scale scores only included 10 studies [24,26-34]. The illuminance in these studies was 5,000 lux or 10,000 lux.

Results of meta-regression (shown in Supplementary Table 10) for the relationship between age and changes in depression scale scores showed p -value of 0.173. The regression analysis results of the relationship between treatment duration and depression improvement remained positively correlated ($\beta = 0.09$, $p = 0.037$, shown in Fig. 4), but there was no correlation between light intensity and depression improvement ($p = 0.062$).

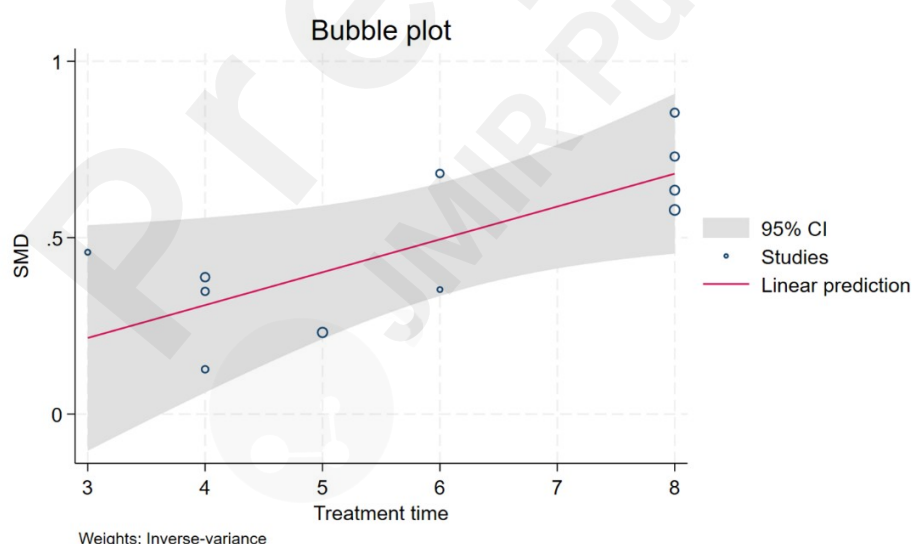


Figure 4 Meta-regression of treatment time vs improvement of depression.

Study Quality

The results of the bias risk assessment from RoB 2 was shown in Supplement Figure 1. Eight studies [24,26-29,32,36,39] had low risk of bias, and four studies [30,34,37,41] had a high risk of bias, and the remaining studies [25,31,33,35,38,40] was “some concerns”. Among the five aspects of bias assessment, the aspects of randomization and result analysis had very low

risks. However, since most studies did not mention the plans to correct for patients' non-compliance or deviations from the established intervention measures, the bias caused by intervention deviations was relatively high in this aspect.

The results of quality assessment (shown in Supplement Table 12) on the depression scale scores was "high". The quality assessment of anxiety scale scores was "moderate" because of low imprecision. After evaluating sleep-related outcome indicators, it was found that the evidence quality of TST and ISI score was "moderate". Quality of PSQI score, SE and ESS score was rated as "low" due to the high risk of bias and the small simple size.

Discussion

This review included a total of 18 studies [24-41], and the outcomes of these studies were summarized through meta-analysis. The main outcome was the difference in depression scores before and after the intervention. Compared with the control group, the depression scores of patients in the LT group decreased more after the intervention, and the depressive symptoms improved significantly. Further subgroup analysis revealed that except for the disease subtypes and medication status, the differences between the groups in other subgroups did not reach a significant level. Regression analysis indicated a positive correlation between treatment duration and depression improvement.

Through a meta-analysis of the differences in HAMA scores before and after the intervention, it was found that the difference between light groups and control groups tended to be significant. There was no heterogeneity among the included studies, and the egger test showed no publication bias.

The sleep disorders included in this review are insomnia and sleep problems after neurological damage. Through a comprehensive analysis, it can be seen that all the outcome measures included in the meta-analysis, except for TST and ESS, were found to have significant effects, which meant LT significantly improved these outcomes of sleep. For the three outcome measures (SOL, sleep onset and offset times and WASO) that were not included in the meta-analysis, although Markus Canazei et al. [35] did not observe the effect of dynamic environmental bedroom lighting (DD-N) on sleep latency, they reported that patients under DD-N lighting had earlier sleep onset and offset times. Won-Hyoung Kim et al. [39] found that compared with the placebo control group, bright light therapy improved the SOL of patients with mild to moderate post-stroke insomnia, which is the same as the finding of Riccardo Cremascoli et al. [40]. Jihyun Yoon et al. [37] found that using bright blue light in

the morning, sleepiness and fatigue in the daytime were improved, and this point was also mentioned by another study [39]. Jihyun Yoon et al. [37] also found a downward trend in cortisol levels in the LT group, but there was no significant difference in the expression levels of clock genes between the LT group and the control group. Shu-Yi Huang et al. [33] also found that the salivary cortisol level in the LT group decreased significantly after three weeks of intervention, and it remained significantly decreased six weeks after the intervention began, which is consistent with the finding that LT can regulate cortisol secretion through the HPA axis as mentioned earlier.

Abnormalities in Brain Region Structure and Dynamic Functional Connectivity (dFc) Analysis

When exposed to strong light, the light signal is received and converted into electrical signals by ipRGCs, and ipRGCs directly transmit these signals to the amygdala, as well as indirectly transmitting them through the superior colliculus (SC), posterior pulvinar complex (Pul-LP), brainstem nuclei and hypothalamic region to the amygdala, thus reducing the reactivity of amygdala to negative stimuli and thereby improving depressive symptoms [42]. LT can also significantly enhance the connection between the amygdala and the medial prefrontal cortex (mPFC) in a dose-dependent manner to reduce anxiety symptoms [43]. Moreover, a previous experiment [44] on mice indicated that functional connection between the temporal lobe cortex, the amygdala and the hypothalamus could be strengthened by blue light, thereby contributing to the response to negative emotion in voice-sensitive areas in temporal lobe cortex and the hippocampus. In previous studies [45], it was found that through two pathways, light therapy might affect the function of the anterior cingulate cortex (ACC). The first circuit is composed of the direct connection between ACC and the brainstem, including dopaminergic input from VTA and the connection with the blue nucleus (LC), and LC releases norepinephrine in response to light therapy. The second circuit includes functional connections with the amygdala and the frontal cortex [45]. However, there are few studies on how light regulates the ACC and its functional connections with other regions. Therefore, it is difficult to further clarify the specific mechanisms.

Among these studies included in this review, 5 studies [24,26-29] on subthreshold depression in college students all conducted static functional connectivity (sFC) or dynamic functional connectivity (dFC) analyses by using resting-state functional magnetic resonance imaging (rs-fMRI). The dFC analysis employed a sliding window method with a window size of 50 TRs (100 seconds).

Chun-Chao Huang et al. [29] found that the internal network functional connections in the

default mode network (DMN), frontal-parietal network (FPN), salience network (SN) and somatomotor network (SMN) of the patients in the LT group increased. In previous studies [46], it had been proven that the functional connections of the DMN in patients with major depressive disorders (MDD) were abnormal, which led to the memory dysfunction and repetitive reflection. The FPN function in depression patients also became disordered, inhibiting the activation of the dorsolateral prefrontal cortex and posterior parietal cortex [46]. Anxiety disorders were usually comorbid with depression, and were related to the excessive activity of the autonomic neuron nodes in the SN [46]. SMN governs sensory-motor functions, and MDD disrupts this processing process [46]. The findings of Chun-Chao Huang et al. [29] provide new ideas and targets for LT in treating depression.

Another study [28] on subthreshold depression found that LT enhanced the functional connections between the dorsal raphe nucleus (DRN) and the prefrontal cortex (PFC), as well as between the dopaminergic ventral tegmental area (VTA) and the superior frontal gyrus (SFG) during the subthreshold depressive state, thereby improving depression.

The significant reduction in Center for Epidemiological Studies-Depression Scale (CES-D) and HAMD scores was positively correlated with the variability of dFC between the right supracallosal anterior cingulate cortex (supACC) and the right temporal pole (TP), and BLT increased this variability [24]. The changes in dFC between the left middle cingulate cortex (MCC) and the right insula (BLT increased this variability), between the right supACC and the right TP (BLT increased this variability), as well as between the right supACC and the right middle frontal gyrus (MFG) (BLT decreased this variability) were significantly correlated with the activity of depression-related hormones (such as dopamine, serotonin, norepinephrine, etc.) [24].

The improvement of depressive symptoms was also related to the changes in sFC between the right basal lateral amygdala (BLA) and the right middle temporal gyrus (MTG), and bright light therapy enhanced these changes [26]. BLT weakened the sFC between the right amygdala-striatal transition or central medial amygdala (AStr/CMA) and the left thalamus, while enhancing the sFC between the right basal lateral amygdala or superficial amygdala (BLA/SFA) and the right MTG. BLT also strengthened the dFC between the right CMA and the right inferior lateral frontal gyrus (IOFG), and weakened the dFC between the right superficial amygdala (SFA) and the right medial prefrontal cortex (mPFC) [26]. This enhancing or weakening effect of BLT was related to the secretion of 5-HT.

In another study [27], it was found that LT enhanced the sFC between the right cerebellar

lobule IX and the left TP, thus improving attention and alertness. LT also improved negative emotions by reducing the short-range functional connectivity within the posterior cerebellum, and LT also decreased the dFC between the right cerebellar lobule IX and the left mPFC.

Special intervention

The intervention measures adopted by Beatrix Feigl et al. [36] involved enhanced lighting that would increase the secretion of melatonin, and the control measures adopted were the Day Mel condition, which provided light similar to natural light. Markus Canazei et al. [35] used a dynamic bedroom lighting, including dawn simulation, dusk simulation, and non-blue light nighttime lighting. The study showed that patients under DD-N lighting usually woke up earlier in the morning, and had longer total sleep time, higher sleep efficiency as well as shorter nighttime wake time. Another study [41] on sleep disorders in dementia patients also used dynamic bedroom lighting as an intervention measure. The control group was given standard lighting (150 - 300 lux). The results showed that the objective sleep quality assessed by the wrist actigraphy device did not significantly improve, but the sleep disorder scale (SDI) evaluated by the caregiver indicated that the patients' sleep quality significantly improved.

Placebo Effect

In previous studies [47], it has been found that placebo treatment can activate the eprefrontal-subcortical systems to participate in effecting emotions, learning and cognitive functions. Guanmao Chen et al. [28] found that placebo effect is contrary effects of BLT by VTA-IFG and VTA-occipital lobe connectivity. In one study [31], the illuminance for the control group was set to less than 500 lux because there was no definite evidence suggesting that using this light intensity alone could improve depression. However, depression symptoms of the control group patients still showed improvement at the early stage, but the improvement effect disappeared later, so researchers attributed this phenomenon to the placebo effect [31]. Therefore, to reduce the influence of the placebo effect, it is very important to blind both the patients and the researchers.

Acceptability, Compliance and Safety

The research conducted by Markus Canazei et al. [35] had a relatively high dropout rate. The main reason was that patients' acceptance of the wrist actigraphy device was not high, and some patients' nighttime sleep was negatively affected by the actigraphy. In a study by Corrado Garbazza et al. [30] on postpartum depression, patients all recognized and accepted LT as treatment method. However, when patients were required to sit in front of a light box

for half an hour and were told the trial would last for six weeks, some patients withdrew from the trial due to the long duration and limited space [30]. In the study by Jihyun Yoon et al. [37], one person reported mild dazzle, but no serious adverse events occurred. Riccardo Cremascoli et al. [40] used LT glasses as an intervention measure, and only one patient withdrew from the trial due to eye irritation and burns. Melike Donmez et al. [31] stated that mild headache was the most common side effect during LT. Yoshihiro Noda et al. [25] used 40 Hz VL irradiation goggles with low illumination, indicating that light glasses had more portability and comfort, which could improve patient compliance and trial safety. From above studies, it could be concluded that patients generally have a good acceptance of this LT, but due to the fixed position of the light equipment and long treatment duration, patient compliance still needed to be improved.

Limitations and Future Research

This review had some limitations. Firstly, the diseases included in the study are diverse and not all studies were diagnosed according to the ICD-10 or DSM-5, which may cause diagnostic differences. Therefore, subgroup analysis was conducted based on disease classification. Meanwhile, the diagnostic methods for each disease were similar and usually used in clinical practice, thus these methods were likely to be reliable. Future studies should preferably specify the standard diagnostic methods when including studies. Secondly, this study only included studies on adults and lacked studies on children or adolescents. Therefore, the conclusions did not have universal applicability to all age. More studies on the impact of LT on depression and sleep disorders in children and adolescents need to be conducted in the future. Thirdly, in some of the studies included in this review, patients had been taking psychotropic drugs before the trial. Although the types and dosages of drugs did not change during the research period, the different types of drugs might be a potential bias. Future research can investigate the interactions between different psychotropic drugs and LT. Fourthly, in the meta-regression analysis, only a positive correlation was found between the treatment duration and the improvement of depression. No other influencing factors were found, and no regulatory effects among various factors were explored. Future research can further explore other influencing factors on efficacy of LT, such as patients' occupation and degree of education, light wavelength and color temperature, etc.

Conclusion

LT had a positive effect on improvement of depression, anxiety and sleep quality. Treatment

duration and depression improvement was positively correlated. LT also affected the functional connections between multiple brain structures. Therefore, changes in depressive symptoms and the therapeutic effect of light therapy might be predicted through the combination of sFC and dFC.



Statement of Ethics

This study is a review and analysis based on previously published literature, and all included studies had been approved by Ethics Committee.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

The concept and design of this systematic review was conducted by all authors (X.-Y. Wang, W.-H. Jiang, and Y.-G. Yuan). Selecting articles and evaluating the quality of studies was conducted by X.-Y. Wang and W.-H. Jiang. X.-Y. Wang extracted as well as analyzed the data, and wrote first draft of the manuscript. All authors contributed to the writing of the final version of the manuscript.

Data Availability Statement

All data were from previously published literature, and detailed information can be found in Table 1.

Abbreviations

ACC: anterior cingulate cortex

AStr/CMA: amygdala-striatal transition or central medial amygdala

BLA: basal lateral amygdala

BLT: bright light therapy

CES-D: Center for Epidemiological Studies-Depression Scale

CI: confidence interval

DD-N : dynamic environmental bedroom lighting

dFc: dynamic functional connectivity

DMN: default mode network

DRN: dorsal raphe nucleus

ESS: Epworth Sleepiness Scale

FPN: frontal-parietal network

GRADE: the Grading of Recommendations Assessment, Development, and Evaluation

HAMA: Hamilton Anxiety Rating Scale
HAMD: Hamilton Depression Scale
IOFG: inferior lateral frontal gyrus
ISI: Insomnia Severity Index
LC: blue nucleus
LLLT: low-level laser therapy
LT: light therapy
MCC: middle cingulate cortex
MD: mean difference
MDD: major depressive disorder
MFG: middle frontal gyrus
mPFC: medial prefrontal cortex
MTG: middle temporal gyrus
PFC: prefrontal cortex
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PSQI: Pittsburgh Sleep Quality Index
Pul-LP: posterior pulvinar comple
ROB 2: the Cochrane Risk of Bias Tool 2
rs-fMRI: resting-state functional magnetic resonance imaging
SC: superior colliculus
SE: sleep efficiency
SFA: superficial amygdala
sFC: static functional connectivity
SFG: superior frontal gyrus
SMD: standardized mean difference
SMN somatomotor network
SN: salience network
SOL: sleep onset latency
supACC: supracallosal anterior cingulate cortex
TP: temporal pole
TST: total sleep time
VTA: ventral tegmental area
WASO: wake after sleep onset

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Supplementary Files

Figures

Fig.1 Flow Chart.

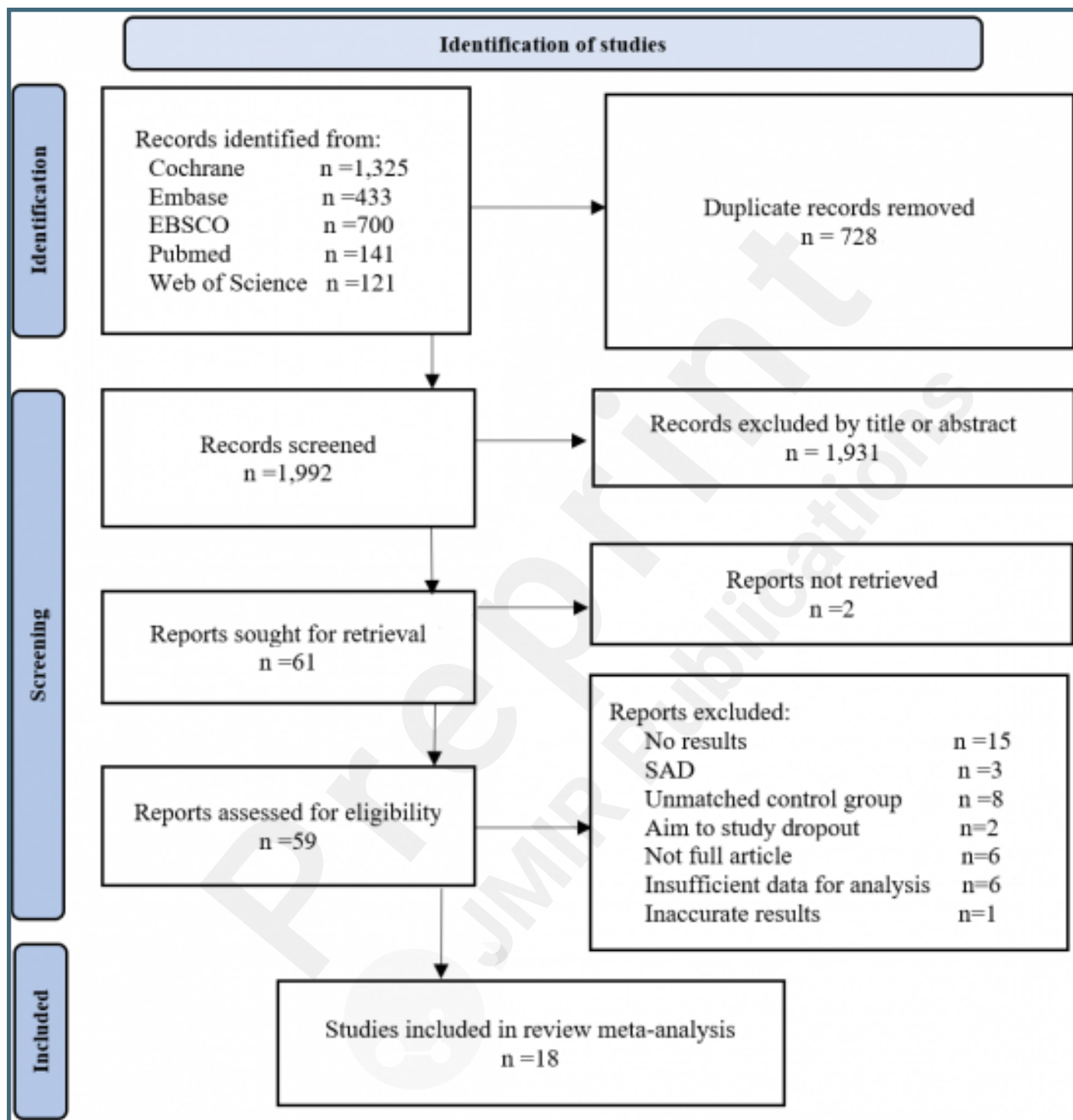


Fig.2 Forest plot for the changes in depression scale scores before and after the intervention.

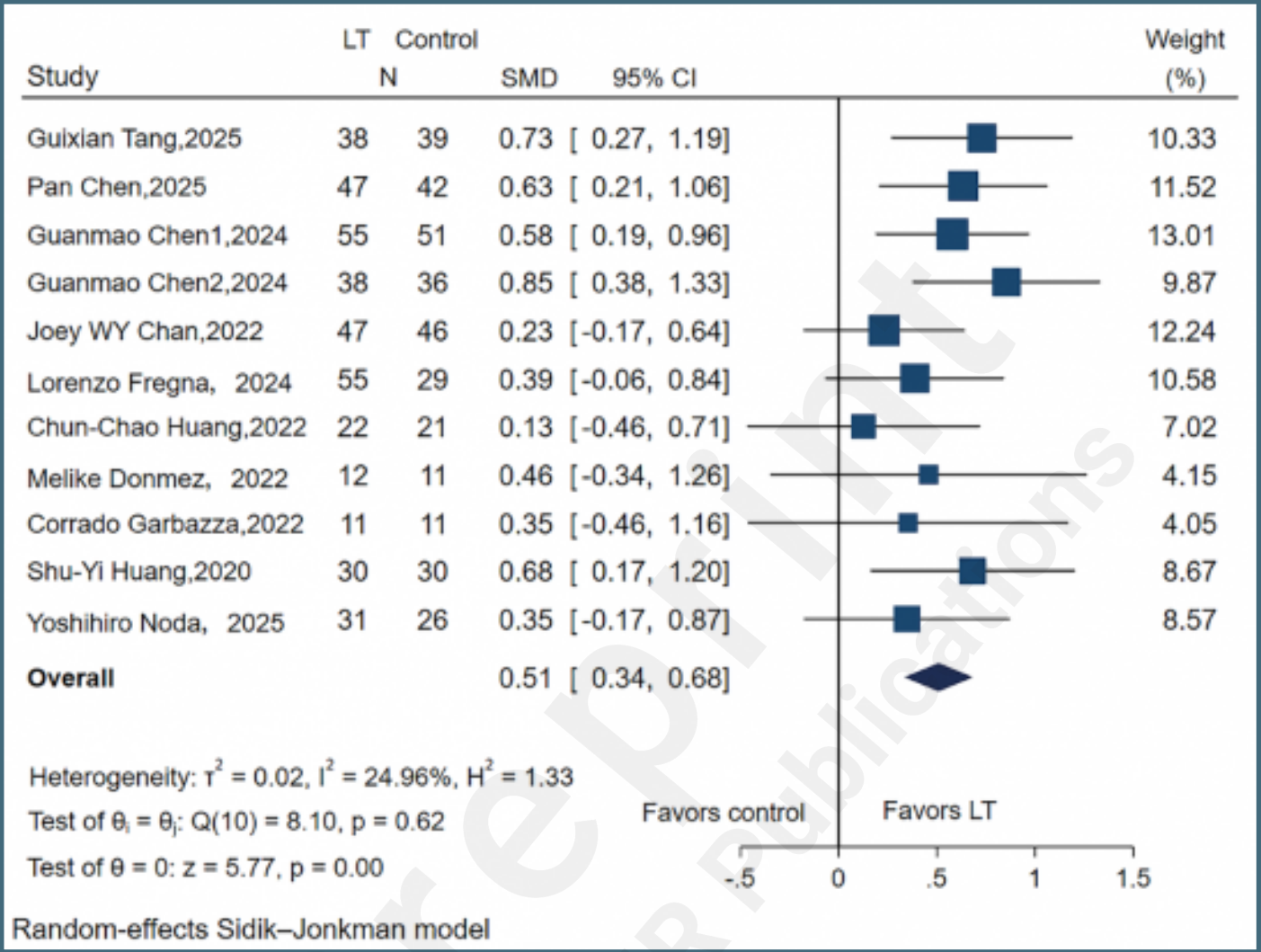


Fig.3 Funnel plot for depression.

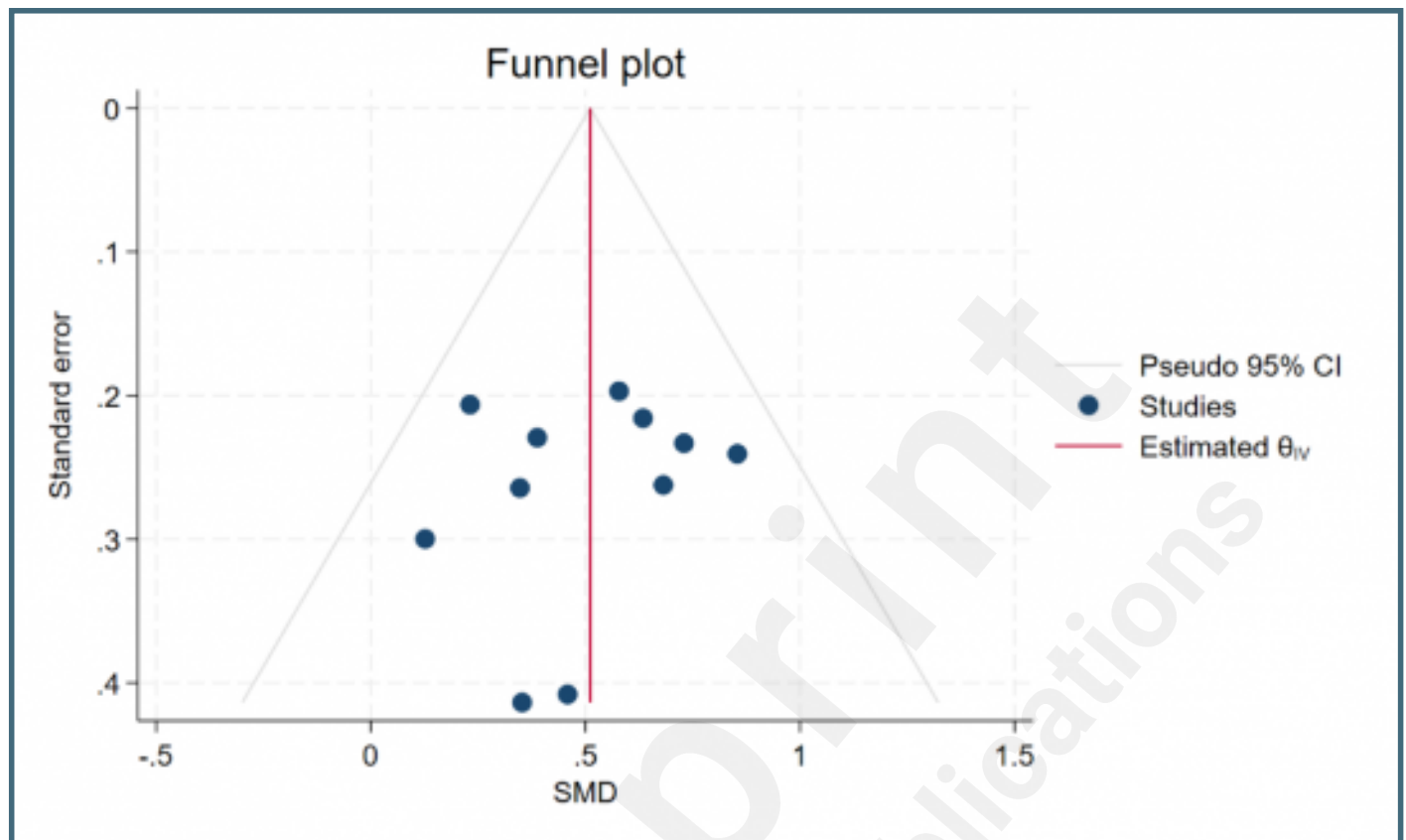
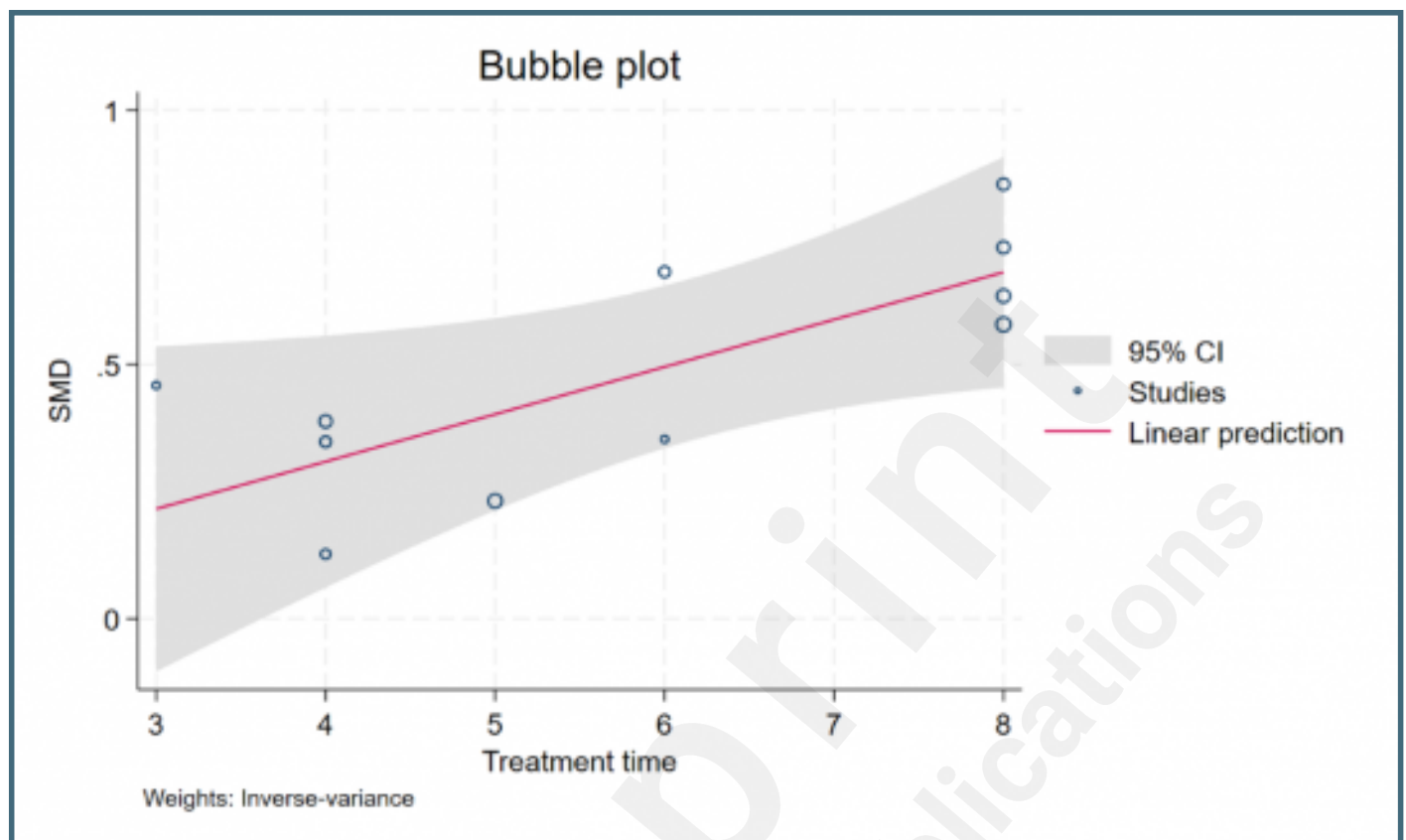


Fig.4 Meta-regression of treatment time vs improvement of depression.



Multimedia Appendixes

This is supplement material.

URL: <http://asset.jmir.pub/assets/fad29745855040b1e55aebca795a95ed.docx>

