

The effect of chronotherapy on depressive symptoms

Evidence-based practice

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ABSTRACT

النسبة العالمية للاكتئاب تتزايد، مع معدلات العجز المرتبط بالاكتئاب والوفيات، مما يجعل الاكتئاب قضية صحية عامة. علاج الساعة البيولوجية تشمل مجموعة متنوعة من الاستراتيجيات التي تتحكم في التعرض للمؤثرات البيئية التي تنظم الساعة البيولوجية، مثل الحرمان من النوم (SD) أو علاج الاستيقاظ (WT)، مرحلة النوم المتقدم (SPA)، و علاج الضوء و الظلام (LT, DT). الهدف من ورقة الممارسة القائمة على الأدلة هو الإجابة على أسئلة (PICOT) من خلال استعراض فعالية تدخلات علاجات الساعة البيولوجية على أعراض الاكتئاب عند الاكتئاب والاكتئاب ضمن الاضطراب الثنائي القطب. وتشير دراسات سابقة فعالية الحرمان من النوم أو علاج الاستيقاظ، مرحلة النوم المتقدم، و علاج الضوء أو الظلام، كشفت المزيد من البحوث التي أجريت مؤخراً الاختلافات في فعالية التدخلات المنفردة والمشاركة التي تنطوي على مكونات كل من علاجات الساعة البيولوجية والدوائية. هذا العلاج خفض مدة البقاء في المستشفى، تحسن التعافي، وخفض تغير في وصفات الدوائية.

The global prevalence of depression is increasing, along with rates of depression-associated disability and mortality, rendering depressive disorders a major public health issue. Chronotherapy involves a variety of strategies that control exposure to environmental stimuli that influence the biological clock, such as sleep deprivation (SD) or wake therapy (WT), sleep phase advance (SPA), and light and dark therapy (LT, DT). The purpose of this Evidence-Based Practice (EBP) paper is to answer PICOT questions by a review the effectiveness of chronotherapeutics interventions on depressive symptoms with depression and the depressive episode in the course of bipolar disorder. Early studies suggested the effectiveness of LT, SD, and SPA, more recent research has revealed differences in the efficacy of single and combined interventions involving both chronotherapeutic and pharmacological components. This therapy reduced duration of hospitalization, improvement recovery, and reduced for changes in drug prescriptions.

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Depression is a complex disorder involving the interaction of genetic, physiological, psychological, and environmental factors, resulting in clinical manifestations that include a variety of affective, cognitive, somatic, and behavioral symptoms.¹ As such, individuals experiencing depressive episodes exhibit variations in sleep/wake patterns (sleep architecture, sleep disturbances) and daily mood, in addition to abnormal levels of adrenocorticotrophic hormone and cortisol secretion. Such depressive episodes are also characterized by impaired attention, altered food intake, learning and memory dysfunction, psychological stress, and decreased psychomotor functioning. These alterations are collectively referred to as chronobiological disruption.¹⁻³

Major depressive disorder (MDD) is characterized by the presence of persistently depressed mood (low mood); loss of interest or pleasure; feelings of grief, guilt, or worthlessness; decreased energy, disturbed sleep or appetite; poor concentration; and hopelessness.^{4,5} According to the Fifth Edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), depression is diagnosed when the patient presents with substantial changes in functioning lasting at least 2 weeks (mood, pleasure, social, occupational, and psychomotor function).⁵

In 2010, the Global Burden of Disease Study concluded that depression was the second greatest cause of disability worldwide, affecting an estimated 300

million people globally.⁶ Similarly, the World Health Organization (WHO) reported depressive disorder as a leading cause of disability worldwide, and that the condition affects an estimated 350 million people worldwide.⁴ Furthermore, the global prevalence of depression is increasing, along with rates of depression-associated disability and mortality, rendering depressive disorders a major public health issue.^{4,7} Briley and Lépine⁸ reported that approximately 10-15% of people worldwide and 3-9% in Japan are affected by depression. Moreover, Samuels et al⁹ stated that depression is the most common psychiatric condition in the United States, with a prevalence as high as 18.9%. In addition, the symptoms of depression exert a substantial impact on occupational and social functioning, potentially increasing the economic burden. Indeed, a previous study estimated that the cost of treatment is approximately \$2000 per citizen.¹⁰

Although the fundamental treatment for depression involves pharmacotherapy,^{11,12} many people do not seek formal treatment with anti-depressive agents¹³ due to the high costs and risk of side effects, which can also prevent adherence once treatment has been initiated.¹⁴ Thus, individuals with depression may seek to decrease their symptoms via complementary and alternative medicine (CAM), which may be associated with fewer side effects. Samuels et al⁹ reported that the use of CAM is increasing, especially in patients diagnosed with anxiety and depression. However, there is no clear definition of what constitutes CAM.¹⁵ Furthermore, the National Health Service (NHS) has stated that there is no universally accepted definition of CAM,¹⁶ which often differs among various countries.¹⁷

However, CAM has recently been defined to encompass therapies, interventions, and products that are regarded as equal in efficacy to conventional pharmacotherapy, with increased adherence and fewer side effects.¹⁸ Such treatments are often perceived as more natural, economical, and are available without the need for a prescription. According to the National Center for Complementary and Alternative Medicine (NCCAM), CAM includes a variety of medical and health care systems, interventions, and products not considered part of conventional medicine.¹⁹

Research has indicated that certain psychosocial therapies and interventions may be as effective as medication in treating symptoms of depression,²⁰ such as chronotherapy. Chronotherapy involves a variety

of strategies that control exposure to environmental stimuli that influence the biological clock, such as sleep deprivation (SD) or wake therapy (WT), sleep phase advance (SPA), and light and dark therapy (LT, DT).²¹ Several studies have reported that chronotherapy is effective in the treatment of mood and sleep disorders, including depression.²²

According to Wirz-Justice and Terman,²³ chronotherapeutics refers to nonpharmaceutical treatments designed to control exposure to external environmental stimuli that act on biological rhythms. Chronotherapy interventions are based on circadian rhythms, which direct a variety of biological processes on a near-24-hour cycle.²⁴ Circadian rhythms are responsible for generating biologic rhythms and variations in the function of physiological and biochemical processes, such as the activity of the sleep-wake cycle and emotional state.²⁵ These rhythms drive and synchronize neurotransmitter and hormone secretion, body temperature, and day-to-day stability according to pre-programmed patterns.^{26,27} The suprachiasmatic nucleus (SCN) is considered the circadian pacemaker.²⁸ and contains high concentrations of serotonin and melatonin receptors.²⁹ Chronotherapy aims to restore the balance of these neurotransmitter systems by resynchronizing circadian rhythms.³⁰⁻³² Indeed, research has indicated that such treatment exerts a positive impact on depressive symptoms.³³

Although the author was unable to find studies regarding the prevalence of depression in Jordan, Hamid³⁴ reported that the prevalence of depression was higher than 30% among 493 randomly selected female patients. Additional studies have reported that depression is a major public health concern in developing countries,³⁵ suggesting that the prevalence of depression may be high in Jordan.

Methodology. PICOT Question Structure. Recently, mental health research has focused on the use of evidence-based practice (EBP) for the development, promotion, and management of mental health treatment.³⁶ Cleary³⁷ defined EBP as the combined use of evidence from research and clinical experiences to aid in the clinical decision-making process. evidence-based practice provides clinicians with guidance regarding the most appropriate and effective treatment interventions,³⁸ also, the potential contribution of 4 types of evidence in the delivery of care: research, clinical experience, patient experience, and information from the local context.³⁹

Essential competency for nurses today is EBP to improve quality health care and increasing provider accountability, and PICOT question is one of the first EBP processes (P = population; I = intervention or area of interest; C = comparison; O = outcomes; T = timeframe in which to accomplish the first small tests of change).⁴⁰ The author concluded evidence question (PICOT), which is, P = depression patients and depressive episode in the course of bipolar disorder patients; I = chronotherapy; C = placebo or antidepressant; O = enhance and reduce depressive symptoms; T = 4 months of the start of the intervention. The nurse using the levels of evidence to determine the strength of research studies, assess the findings, and evaluate the evidence for potential implementation into best practice.⁴¹ The purpose of this EBP paper is to answer PICOT questions by reviewing the effectiveness of chronotherapeutic interventions.

Depression patients and depressive episode in the course of bipolar disorder patients, what is the effect of chronotherapy (SD, WT, SPA, LT, DT) in enhancing and reduce depressive symptoms compared with placebo within 4 months of start to intervention? Depression patients and depressive episode in the course of bipolar disorder patients, what is the effect of chronotherapy (SD, WT, SPA, LT, DT) in enhancing and reduce depressive symptoms compared with an antidepressant within 4 months of start to intervention?

Search strategy. The electronic databases that were searched were as follows: EBSCO, PUBMED, MEDLINE, CINAHL, the PILOTS database, the Cochrane Library and Ovid database from 2007 to 2015 and some websites, such as the World Health Organization, American Psychiatric Association, National Health Service, National Center for Complementary and Alternative Medicine, American Academy of Sleep Medicine, and Chicago Psychiatry Associates, with the following combination of keywords: major depression, depression, chronotherapy, light therapy, sleep deprivation, sleep phase advance, and triple chronotherapy.

Literature review. Somatic therapy for the treatment of depression includes both pharmacological and psychological interventions, or techniques designed to manipulate the stimuli received by the patient, such as chronotherapy.⁴² Chronotherapy encompasses a variety of interventions such as SD and SPA, which manipulate the sleep/wake rhythm and LT/DT which

alter exposure to the light/dark cycle.²² Research has increasingly focused on the use of these techniques in clinical practice as a result of their efficacy, rapidity of action, lack of side effects, low risk, and low cost. Furthermore, the combined use of multiple chronotherapeutic interventions or in conjunction with conventional psychiatric treatments may result long-lasting therapeutic effects.^{23,43} Moreover, increased use of these techniques in psychiatric settings may shorten hospitalization, increase the rate of recovery, and reduce the need for prescription changes.^{23,44,45} Here, we present an overview of the literature concerning light therapy, sleep deprivation, and triple chronotherapy.

Light therapy. In 2005, the American Psychiatric Association concluded that bright light therapy (BLT) can be used as a first-line treatment for seasonal affective disorder (SAD) and MDD. As this treatment is based on neurobiological principles, it has recently been established as the treatment of choice for SAD. Furthermore, studies have indicated that light exerts an anti-depressant effect in patients with non-seasonal depression.^{43,46} According to a report by the American Academy of Sleep Medicine (AASM), exposing the eyes to safe levels of intense, bright light for brief durations at strategic times of day synchronizes the body's internal clock.⁴⁷ Further research has indicated that the onset of depression can be prevented by modifying the color and intensity of light. The application of bright white light during the day has been shown to influence vision and the perception of the surrounding space.⁴⁸

Most studies utilizing BLT have involved exposure to white light with an intensity of 2,000-10,000 lux, with exposure time varying between 30-120 minutes per day. The duration of exposure is based on therapeutic responses at 2-4 weeks. Although exposure typically occurs in the morning, evening exposure is sometimes utilized to produce phase advances or phase delays.^{1,33,49} One randomized crossover study aimed to determine the efficacy of BLT in 28 adolescents (14-17 years old) with mild depressive disorder diagnosed based on DSM-IV criteria. In this study, the participants were divided into either a BLT (2,500 Lux) or placebo (50 lux) group. One group received placebo treatment for one hour each day for one week, followed by BLT for one week, while the opposite schedule was used for the other group. Beck's Depression Inventory (BDI) was used to assess depressive symptoms. The author reported significant improvements in BDI scores following BLT, with no

significant adverse reactions.⁵⁰ Additional studies have suggested that BLT is effective in the treatment of older adults with MDD. One study involving 89 patients age 60 or older sought to compare the efficacy of exposure to pale blue light (7500 lux) (BLT group) and dim red light (50 lux) (placebo group). The intervention consisted of 3 weeks of treatment for 1 hour each day in the early morning, following which the BLT group exhibited improvements in mood, sleep efficiency, and melatonin levels.⁵¹

Hizli et al⁵² further compared the effects of BLT monotherapy and combined BLT and fluoxetine-Selective Serotonin Reuptake Inhibitor (SSRI) therapy on symptoms of depression, circadian rhythms, and sleep quality in 15 participants with depression (age: 18-65 years). Participants of this study were diagnosed with depression using the Structured Clinical Interview for DSM-IV and subsequently divided into 2 groups. The first group of 7 patients received 10,000 lux of BLT for 30 minutes each day, for 7 days (drug-free patients). The second group of 8 patients received both BLT and fluoxetine therapy. Following BLT, patients of the drug-free group reported decreased severity of depressive symptoms on the Hamilton Depression Rating Scale (HAM-D), BDI, and Morningness-Eveningness Questionnaire (MEQ). Furthermore, positive effects on mood disturbance and sleep quality, as measured using the Profile of Mood States (POMS) and Pittsburgh Sleep Quality Index (PSQI), respectively, were observed in the drug-free group. However, no significant benefit of fluoxetine was observed in the combined-treatment group.

Sleep deprivation. Sleep deprivation (SD), also referred to as WT, is a chronotherapeutic intervention first described in the 1970s that involves remaining awake for long periods to reduce depressive symptoms. Responses are typically observed within 24-28 hours.^{30,53} Many studies on SD have supported its efficacy in quickly reducing depressive symptoms, with benefits observed in approximately 40-60% of patients.²³ Although the mechanism of action remains unknown, the effects of SD are likely associated with alterations in the circadian system.⁵⁴ Casher et al⁵⁵ further suggested that SD increases levels various neurotransmitters including serotonin, dopamine, and norepinephrine.

Previous studies regarding SD have often utilized a 3-day schedule, delaying bedtime by 2 hours and requiring participants to remain awake for up to 36

hours. Such studies have reported that this technique may be effective in preventing relapse.⁵⁶ Although the effects of SD are rapid, these effects are relatively short lasting, and relapse may occur following recovery of sleep.⁴² Vigilance (brain arousal) declines without stimulation from the external environment. Thus, this model provides a simple explanation for the effects of SD therapy in patients with affective disorders, as patients with depression often experience increased tiredness. Sleep deprivation (SD) may promote a state of hypervigilance, thereby reducing autoregulatory behavior.⁵⁷ Moreover, Hegerl et al⁵⁸ reported that affective disorders may have a pathogenetic role in the regulation of vigilance. Additional research has revealed that symptoms of withdrawal and sensation avoidance in MDD are autoregulatory reactions to a hyper stable regulation of vigilance and hyperarousal.⁵⁹

Martiny et al⁶⁰ studied the effects of a one-week intervention phase during 9 weeks of WT in individuals receiving inpatient treatment for MDD. The authors investigated combined use of WT, LT, and sleep time stabilization (36 patients) compared with exercise therapy (38 patients), reporting a significant antidepressant and mood-enhancing effective of WT combined with LT and sleep time stabilization relative to exercise therapy.

Triple chronotherapy. Early studies on triple chronotherapy involving combined use of BLT, SD, and SPA have suggested that such therapy may produce rapid improvements in depressive symptoms.⁶¹ Despite these encouraging results, few studies have examined the effects of triple chronotherapy, as this field has just begun to emerge.⁶² Moscovici and Kotler³³ examined the effects of a chronobiologic multistage intervention (CMI) in a study involving 12 patients with moderate-to-severe depression. The CMI was comprised of LT, SD, and SPA and was associated with significant improvements in depressive symptoms, which were maintained 30 days following the intervention. Furthermore, Sahlem et al⁶³ explored the impact of triple chronotherapy intervention in 10 patients with depression experiencing acute suicidal ideation. Patients underwent SD for 33-36 hours, followed by SPA for 3 nights, with 4 BLT sessions of 30 minutes each morning. The results of this study indicated that the CMI produced significant improvements in depressive symptoms and mood. Wu et al⁵⁶ further concluded that chronotherapy consisting of LT, SD, and SPA is effective

Table 1 - Summary of the literature review included in this study.

Authors & year of publication	Objective	Design & Intervention	Number of sample and setting	Results and tool	Level of evidence
Niederhofer & von Klitzing ⁵⁰	To show a major improvement in mood and sleep among volunteers receiving 1 week bright light in contrast to placebo	Randomized crossover trial BLT and Placebo	14, 14 Outpatient	A significant improvement of BDI scores between treatment and placebo groups. BDI	Level 2
Lieverse et al ⁵¹	To determine the effectiveness of BLT in elderly patients with MDD	Double blind, placebo controlled randomized control trial BLT and placebo	42, 47 Home based treatment	BLT group shown enhanced and improved in mood, sleep efficiency and increased melatonin level HAMD and cortisol and melatonin levels	Level 2
Hizli Sayar et al ⁵²	To compare the effects BLT alone or in conjunction with fluoxetine (SSRI), on the severity of depression, daily rhythm, the mood disorder, and the quality of sleep in patients who suffer from non-seasonal depression	Randomized control trial BLT and fluoxetine	7, 8 Outpatient	BLT is effective with regard to the severity of depression, circadian rhythms, mood disturbance, and sleep quality, in nonseasonal depression and not showed supportive results of used fluoxetine with BLT on any evaluation scale HAMD17, BDI, MEQ, POMS, and PSQI	Level 2
Martiny et al ⁶⁰	To inquiry into, if the combination of WT, LT, and sleep time stabilization effect and prevent deterioration of depressive symptoms between at the end of the series of WT	Posttest randomized controlled trials WT, LT, and exercise therapy	36, 38 Psychiatric inpatient wards	A significant impact in WT in conjunction with LT and a positive in mood from exercise therapy HAMD17	Level 2
Moscovici & Kotler ³³	To investigate the effectiveness of the CMI on depression	Quasi experimental (one group pretest and posttest design) LT, SD, and SPA	12 Peripheral psychiatric and family medicine outpatient clinics.	Affect dramatically improve symptoms of depression and maintain for a period of 30 days after the intervention of the study HAMD21, MADRS, SDS, and VAS	Level 3
Sahlem et al ⁶³	To identify the impact of triple chronotherapy intervention on depression patients with acute concurrent suicidality and on mood	Quasi experimental (one group pretest and posttest design) LT, SD, and SPA	10 Inpatient units at MUSC and IOP	The result was reduced and improved depressive symptoms and mood and the interventions were functional and accepted in suicidal and depressed patients. HAMD17, CSSRS, YMRS, IDSSR, PHQ9, ESS, PSQI, and SSI	Level 3
Wu et al ⁵⁶	To evaluate the effectiveness of the combination of three circadian-related treatments (SD, BL, SPA) as adjunctive treatment to lithium and antidepressants	Randomized controlled trials (pretestposttest equivalent group) SD, BL, and SPA.	32, 17 UCI and UCSD sites	Significant decreases in depression in the CAT versus medication patients over a 7-week period HAMD24	Level 2
Echizenya et al ⁶¹	To investigate the effect of combined chronotherapy on drug-resistant depression	Quasi experimental (one group pretestposttest design) SD, SPA, and BLT	13 Inpatients of Akita University Hospital	Significant improvements in depressive symptoms in HAMD17, SDS, and VAS HAMD17, SDS, and VAS	Level 3

BDI - beck depression inventory, BLT - bright light therapy, MDD - major depression disorder, HAM-D - hamilton depression scale, SSRI - selective serotonin reuptake inhibitors, MEQ - morningness-eveningness questionnaire, POMS - profile of mood states survey, PSQI - pittsburgh sleep quality index, WT - wake therapy, LT - light therapy, CMI - chronobiologic multistage intervention, SD - sleep deprivation, SPA - sleep phase advance, MADRS - montgomery-asberg depression rating scale, VAS - visual analogue scale, MUSC - Medical University of South Carolina, IOP - Institute of Psychiatry, CSSRS - Columbia Suicide Severity Rating Scale, YMRS - Young Mania Rating Scale, IDSSR - inventory of depressive symptoms-self report, PHQ-9 - Patient Health Questionnaire-9, ESS - Epworth Sleepiness scale, SSI - Scale for Suicidal Ideation, UCI - University of California Irvine, UCSD - University of San Diego, CAT - chronotherapeutic augmentation treatments, SDS - Zung Self-Rating Depression Scale, BL - bright light

when combined with pharmacological treatment (sertraline and lithium) in patients with bipolar disorder experiencing depressive episodes. In this study, 49 patients were divided into a chronotherapeutic augmentation treatment (CAT) group (32 patients) and a medication-only group (17 patients). Patients of the CAT group exhibited significant responses by day 2 of treatment, as well as improvements in depressive symptoms, over the 7-week intervention. Echizenya et al⁶¹ conducted a study involving 13 participants receiving inpatient treatment for drug-resistant major depressive episodes. A 6-day combined chronotherapy protocol including one day of total SD followed by SPA and LT for 5 days was employed. Significant and rapid improvement in depressive symptoms and increases in mood were maintained over 3 weeks, without evidence of relapse or side effects.

Discussion. Several studies have concluded that chronotherapy exerts a positive effect on depressive symptoms. The studies discussed in this literature review are summarized in Table 1. Most studies in this literature review were double-blind RCTs, which are considered to provide level 2 evidence. Most of these studies recruited and divided patients randomly into 2 groups. The results of these studies provide satisfactory answers to the PICOT questions for SD or WT, SPA, LT, and DT.

The effect of chronotherapy in enhancing and reducing depressive symptoms compared with placebo treatments within 4 months of initiation is addressed by the first PICOT question. Our review revealed that LT is effective at reducing depressive symptoms, improving mood, and enhancing sleep efficiency in patients with depression when compared with placebo treatment. Furthermore, enhancements in these effects are observed when WT is combined with LT, and when triple chronotherapy (LT, SD, SPA) is utilized. The effect of chronotherapy in enhancing and reducing depressive symptoms compared with an antidepressant within 4 months of initiation is addressed by the second PICOT question. Our review revealed that BLT monotherapy more significantly improved the severity of depression, mood disturbance, and sleep quality than fluoxetine combined with BLT. Furthermore, we observed that CAT involving LT, SD, and SPA with medication resulted in improvements in depressive symptoms relative to chronotherapy alone.

Recommendations and implications. Recent guidelines provided by the American Psychiatric Association, World Health Organization, National Health Service, National Center for Complementary and Alternative Medicine, American Academy of Sleep Medicine, and Chicago Psychiatry Associates recommend the use of chronotherapy as a first-line treatment for depressive disorders in patients who refuse, resist, or cannot tolerate medication, or for whom medications may be contraindicated, as in a case of antepartum depression. Based on the present literature review, the author recommends the use of chronotherapy for the treatment of depressive symptoms, which appear to be effective and associated with few adverse effects relative to other treatments. However, future studies on chronotherapy should increase sample size, use new light devices, and more thoroughly compare combined use of SD and SPA to triple chronotherapy. Furthermore, as no studies regarding the use of chronotherapy in Jordan were identified, the author recommends that future studies focus on the use of such treatment in Jordan, given the global prevalence of depression. Our findings indicate that chronotherapy should be emphasized at the educational, research, and clinical levels. Educational and research systems should focus on the integration of chronotherapy methods. Although early studies have been published, further studies regarding chronotherapy in Jordan are required. In the clinical field, the use of this therapy may improve the quality of care, decrease hospitalization, and increase social functioning. As such, chronotherapy should be applied in psychiatric hospitals and clinics throughout Jordan.

The studies reviewed in this paper consist of randomized clinical trials and quasi-experimental studies involving 2 to 3 variables published from 2007 to 2015. These studies have several notable strengths, as follows: manipulation present, ethical implication available;^{33,50-52,56-58,60} high power and credibility, low selection bias, clearly identified control group and interventions;^{50-52,56,60} appropriate experimental design for evaluating the hypothesis;^{50-52,60} conducted in a natural setting, high external validity;^{33,61,63} clear conceptual framework;^{33,63} operationally and conceptually defined for dependent and independent variables, adequate background information;^{51,52} mention of the instrument's reliability, and validity.⁵¹ However, several limitations were also noted as follows: small sample size;^{33,50-52,56-58,63} no mention of the instrument's

reliability and validity;^{33,50,52,56-58} operationally and conceptually undefined dependent and independent variables;^{33,50,56,61} lack of clear theoretical and conceptual framework;^{50,52,56,60} non-random assignment, low internal validity, no inference regarding cause and effect;^{33,61,63} no control group;^{33,61} unclear application of theoretical framework;⁵¹ focus on an open study rather than a placebo-controlled study, unequal duration of treatment among patients;⁵² bias towards lower scores in “last hour” time window relative to those from longer time windows,⁶⁰ lack of a control group,⁶³ inclusion of patients with both unipolar and bipolar depression, and lack of standardized therapeutic drug regimens.⁶¹

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References

- Soria V, Urretavizcaya M. Circadian rhythms and depression. *Actas Españolas De Psiquiatría* 2009; 37: 222-232.
- Kondratova A, Kondratov R. The circadian clock and pathology of the ageing brain. *Nat Rev Neurosci* 2012; 13: 325-335.
- Wulff K, Gatti S, Wettstein J, Foster R. Sleep and circadian rhythm disruption in psychiatric and neurodegenerative disease. *Nat Rev Neurosci* 2010; 11: 589-599.
- World Health Organization. Depression [Internet]. 2012 [cited 4 November 2015]. Available from: http://www.who.int/mental_health/management/depression/en/
- American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5th ed. Arlington (VA): American Psychiatric Publishing; 2013.
- Vos T, Flaxman A, Naghavi M, Lozano R, Michaud C, Ezzati M et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. *The Lancet* 2012; 380 (9859): 2163-2196.
- Fitzpatrick J, Tusaie K. Advanced practice psychiatric nursing: Integrating psychotherapy, psychopharmacology, and complementary and alternative approaches. New York (NY): Springer Pub; 2013.
- Lépine JP, Briley M. The increasing burden of depression. *Neuropsychiatr Dis Treat* 2011; 7 (Suppl 1): 3-7.
- Samuels N, Gropp C, Singer S, Oberbaum M. Acupuncture for Psychiatric Illness: A Literature Review. *Behav Med* 2008; 34: 55-64.
- Goetzl R, Pei X, Tabrizi M, Henke R, Kowlessar N, Nelson C, et al. Ten modifiable health risk factors are linked to more than one-fifth of employer-employee health care spending. *Health Aff (Millwood)* 2012; 31: 2474-2484.
- American Psychiatric Association. Depression [Internet]. 2010 [cited 12 October 2015]. Available from: <http://apa.org/topics/depress/index.aspx>
- Gertsik L, Poland R, Bresee C, Rapaport M. Omega-3 fatty acid augmentation of citalopram treatment for patients with major depressive disorder. *J Clin Psychopharmacol* 2012; 32: 61-64.
- Linden M, Wurzendorf K, Ploch M, Schaefer M. Self medication with St. John's wort in depressive disorders: An observational study in community pharmacies. *J Affect Disord* 2008; 107: 205-210.
- Sajatovic M, Levin J, Fuentes-Casiano E, Cassidy K, Tatsuoka C, Jenkins J. Illness experience and reasons for nonadherence among individuals with bipolar disorder who are poorly adherent with medication. *Compr Psychiatry* 2011; 52: 280-287.
- Freeman M. Complementary and Alternative Medicine for Psychiatrists. *Can J Psychiatry* 2012; 57: 395-396.
- National Health Service. About complementary medicines - Live Well - NHS Choices [Internet]. 2012 [cited 6 November 2015]. Available from: <http://www.nhs.uk/Livewell/complementary-alternative-medicine/Pages/complementary-alternative-medicines.aspx>
- Smith G, Wu S. Nurses' beliefs, experiences and practice regarding complementary and alternative medicine in Taiwan. *J Clin Nurs* 2012; 21: 2659-2667.
- Ravindran A, Lam R, Filteau M, Lespérance F, Kennedy S, Parikh S, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) Clinical guidelines for the management of major depressive disorder in adults. *J Affect Disord* 2009; 117 Suppl 1: S54-S64.
- National Center for Complementary and Alternative Medicine. Complementary, Alternative, or Integrative Health: What's In a Name? [Internet]. [Updated 2008; cited 2015 November 3]. Available from: <http://nccam.nih.gov/health/whatiscam>
- Wirz-Justice A. Temporal organization as a therapeutic target. *Dialogues Clin Neurosci* 2012; 14: 335-337.
- Ohdo S. Chronotherapeutic strategy: Rhythm monitoring, manipulation and disruption. *Adv Drug Deliv Rev* 2010; 62: 859-875.
- Dallaspezia S, Benedetti F. Chronobiological therapy for mood disorders. *Expert Rev Neurother* 2011; 11: 961-970.
- Wirz-Justice A, Terman M. Chronotherapeutics (light and wake therapy) as a class of interventions for affective disorders. *Handb Clin Neurol* 2012; 106: 697-713.
- Cagampan F, Bruce K. The role of the circadian clock system in nutrition and metabolism. *Br J Nutr* 2012; 108: 381-392.
- Valdez P, Ramírez, García A. Circadian rhythms in cognitive performance: implications for neuropsychological assessment. *Chrono Physiology and Therapy* 2012; 2: 81-92.
- Hasler B, Buysse D, Kupfer D, Germain A. Phase relationships between core body temperature, melatonin, and sleep are associated with depression severity: Further evidence for circadian misalignment in non-seasonal depression. *Psychiatry Res* 2010; 178: 205-207.
- O'Brien P, Kennedy W, Ballared k. Psychiatric Mental Health Nursing: An Introduction to theory and practice. Sudbury (MA): Jones and Bartlett Publishers; 2008.
- Reppert S, Weaver D. Coordination of circadian timing in mammals. *Nature* 2002; 418: 935-941.
- Lambert G, Reid C, Kaye D, Jennings G, Esler M. Effect of sunlight and season on serotonin turnover in the brain. *The Lancet* 2002; 360 (9348):1840-1842.
- Benedetti F, Barbini B, Colombo C, Smeraldi E. Chronotherapeutics in a psychiatric ward. *Sleep Med Rev* 2007; 11: 509-522.

31. Martiny K. Chronotherapeutics for affective disorders. A clinician's manual for light and wake therapy. *Acta Psychiatr Scand* 2013; 129: 160.
32. Bódizs R, Purebl G, Rihmer Z. [Mood, mood fluctuations and depression: role of the circadian rhythms]. *Neuropsychopharmacol Hung* 2010; 12: 277-287. Hungarian
33. Moscovici L, Kotler M. A multistage chronobiologic intervention for the treatment of depression: A pilot study. *J Affect Disord* 2009; 116: 201-207.
34. Hamid H. A Primary Care Study of the Correlates of Depressive Symptoms Among Jordanian Women. *Transcult Psychiatry* 2004; 41: 487-496.
35. Taqui A, Itrat A, Qidwai W, Qadri Z. Depression in the elderly: Does family system play a role? A cross-sectional study. *BMC Psychiatry* 2007; 7: 57.
36. Corcoran K. From the scientific revolution to evidence-based practice: Teaching the short history with a long past. *Research on Social Work Practice* 2007; 17: 548-552.
37. Cleary M. The "Buzz" About Evidence-Based Practice in Psychiatric-Mental Health Nursing. *J Psychosoc Nurs Ment Health Serv* 2014; 52: 3-4.
38. Rice M. Evidence-Based Practice Principles: Using the highest level when evidence is limited. *J Am Psychiatr Nurses Assoc* 2011; 17: 445-448.
39. Rycroft-Malone J, Seers K, Titchen A, Harvey G, Kitson A, McCormack B. What counts as evidence in evidence-based practice? *J Adv Nurs* 2004; 47: 81-90.
40. Levin R, Chang A. Tactics for teaching evidenced-based practice: determining the level of evidence of a study. *Worldviews Evid Based Nurs* 2014; 11: 75-78.
41. Peterson M, Barnason S, Donnelly B, Hill K, Miley H, Riggs L, et al. Choosing the best evidence to guide clinical practice: Application of AACN levels of evidence. *Crit Care Nurse* 2014; 34: 58-68.
42. Calandra C, Luca M, Luca A. Sleep disorders and depression: brief review of the literature, case report, and nonpharmacologic interventions for depression. *Clin Interv Aging* 2013; 8: 1033-1039.
43. American Psychiatric Association. Practice guideline for the treatment of patients with major depressive disorder. 3rd ed. Arlington (VA): American Psychiatric Publishing; 2010.
44. Bauer M, Glenn T, Whybrow P, Grof P, Rasgon N, Alda M, et al. Changes in self-reported sleep duration predict mood changes in bipolar disorder. *Psychol Med* 2008; 38: 1069-1071.
45. Bauer M, Pfennig A, Linden M, Smolka M, Neu P, Adli M. Efficacy of an algorithm-guided treatment compared with treatment as usual. *J Clin Psychopharmacol* 2009; 29: 327-333.
46. Even C, Schröder C, Friedman S, Rouillon F. Efficacy of light therapy in nonseasonal depression: A systematic review. *J Affect Disord* 2008; 108: 11-23.
47. American Academy of Sleep Medicine. American Academy of Sleep Medicine-Association for Sleep Clinicians and Researchers [Internet]. [Updated 2008; cited 10 November 2016]. Available from: <http://www.aasmnet.org/>
48. Howland R. Somatic therapies for seasonal affective disorder. *J Psychosoc Nurs Ment Health Serv* 2009; 47: 17-20.
49. Pail G, Huf W, Pjrek E, Winkler D, Willeit M, Praschak-Rieder N, et al. Bright-light therapy in the treatment of mood disorders. *Neuropsychobiology* 2011; 64: 152-162.
50. Niederhofer H, von Klitzing K. Bright light treatment as monotherapy of non-seasonal depression for 28 adolescents. *Int J Psychiatry Clin Pract* 2012; 16: 233-237.
51. Lieveise R, Van Someren E, Nielen M, Uitdehaag B, Smit J, Hoogendijk W. Bright light treatment in elderly patients with nonseasonal major depressive disorder: a randomized placebo-controlled trial. *Arch Gen Psychiatry* 2011; 68: 61-70.
52. Hizli Sayar G, Agargun, Tan, Bulut. Comparison of effects of bright light therapy alone or combined with fluoxetine on severity of depression, circadian rhythms, mood disturbance, and sleep quality, in patients with non-seasonal depression. *ChronoPhysiology and Therapy* 2013; 3: 53-59.
53. Chicago Psychiatry Associates. Chicago Psychiatry Associates' Program in Psychiatric Chronotherapy [Internet]. 2011 [cited 11 November 2016]. Available from: <http://www.chicagochronotherapy.com/waketherapy.html>
54. Bunney B, Bunney W. Mechanisms of Rapid Antidepressant Effects of Sleep Deprivation Therapy: Clock Genes and Circadian Rhythms. *Biol Psychiatry* 2013; 73: 1164-1171.
55. Casher M, Schuldt S, Haq A, Burkhead-Weiner D. Chronotherapy in Treatment-Resistant Depression. *Psychiatr Ann* 2012; 42: 166-169.
56. Wu J, Kelson J, Schachat C, Bunney B, DeModena A, Golshan S, et al. Rapid and Sustained Antidepressant Response with Sleep Deprivation and Chronotherapy in Bipolar Disorder. *Biol Psychiatry* 2009; 66: 298-301.
57. Hegerl U, Hensch T. The vigilance regulation model of affective disorders and ADHD. *Neurosci Biobehav Rev* 2014; 44: 45-57.
58. Hegerl U, Sander C, Olbrich S, Schoenknecht P. Are Psychostimulants a Treatment Option in Mania?. *Pharmacopsychiatry* 2009; 42: 169-174.
59. Hegerl U, Wilk K, Olbrich S, Schoenknecht P, Sander C. Hyperstable regulation of vigilance in patients with major depressive disorder. *World J Biol Psychiatry* 2012; 13: 436-446.
60. Martiny K, Refsgaard E, Lund V, Lunde M, Sørensen L, Thougard B et al. The Day-to-Day Acute Effect of Wake Therapy in Patients with Major Depression Using the HAM-D6 as Primary Outcome Measure: Results from a Randomised Controlled Trial. *PLoS One* 2013; 8: e67264.
61. Echizenya M, Suda H, Takeshima M, Inomata Y, Shimizu T. Total sleep deprivation followed by sleep phase advance and bright light therapy in drug-resistant mood disorders. *J Affect Disord* 2013; 144: 28-33.
62. Benedetti F, Riccaboni R, Locatelli C, Poletti S, Dallaspesza S, Colombo C. Rapid Treatment Response of Suicidal Symptoms to Lithium, Sleep Deprivation, and Light Therapy (Chronotherapeutics) in Drug-Resistant Bipolar Depression. *J Clin Psychiatry* 2013; 75: 133-140.
63. Sahlem G, Kalivas B, Fox J, Lamb K, Roper A, Williams E et al. Adjunctive triple chronotherapy (combined total sleep deprivation, sleep phase advance, and bright light therapy) rapidly improves mood and suicidality in suicidal depressed inpatients: An open label pilot study. *J Psychiatr Res* 2014; 59: 101-1017.