# High prevalence of major depression in US sleep clinics: the need for routine depression screening in sleep services.

Silvia Daccò[1,2,5], Psy.D., Daniela Caldirola[2,4,5], M.D., Ph.D., Massimiliano Grassi[1,2,5], Psy.D., Alessandra Alciati[3,5], M.D., Giampaolo Perna[1,2,4,5], M.D., Ph.D., Archie Defillo[1], M.D.

1. Research and Development Department, Medibio Limited, United States HQ, 8696 Eagle Creek Circle, Savage, MN 55378, USA
2. Department of Biomedical Sciences, Humanitas University, Via Rita Levi Montalcini 4, 20090 Pieve Emanuele, Milan, Italy
3. IRCCS Humanitas Research Hospital -, via Manzoni 56, 20089 Rozzano, Milan, Italy
4. Humanitas San Pio X, Personalized Medicine Center for Anxiety and Panic Disorders, Milan, Italy
5. Department of Clinical Neurosciences, Villa San Benedetto Menni Hospital, Hermanas Hospitalarias, Via Roma 16, 22032 Albese con Cassano, Como, Italy

**Corresponding author:**

Caldirola Daniela,

Department of Biomedical Sciences, Humanitas University, Via Rita Levi Montalcini 4, 20090 Pieve Emanuele, Milan, Italy

daniela.caldirola@hunimed.eu

This work has been performed at the Research and Development Department, Medibio Limited, United States HQ, 8696 Eagle Creek Circle, Savage, MN 55378, USA and Department of Biomedical Sciences, Humanitas University, Via Rita Levi Montalcini 4, 20090 Pieve Emanuele, Milan, Italy

The manuscript has been seen and approved by all authors.

We declare that none of the authors received financial support and has a conflict of interest related to this study.

Off-label or investigational use: not applicable

The manuscript does not report on a clinical trial.

Number of tables: 0

Number of figures: 0

Abstract word count: not applicable

Brief summary word count: not applicable

Manuscript word count: 812

Clinical practice and the available scientific literature indicate that major depression disorder (MDD) and sleep–wake disorders have a bidirectional relationship.

Sleep disturbances are one of the most common symptoms of MDD and are included in its diagnostic criteria. Around 90% of the individuals with MDD report disturbed sleep quality and about 66% experience insomnia, including difficulties in initiating, or maintaining sleep and early morning awakenings.[1] Residual sleep disturbances can also be an important symptom of inadequate MDD treatment, [2] representing a risk factor for the recurrence of depression[3] and suicidal thoughts and behaviors.[4]

Clinicians sometimes fail to recognize depression and might inappropriately refer patients to sleep clinics (SCs) for polysomnography to investigate the origin of sleep disturbances. Therefore, some authors have previously advocated the importance of routine depression screening in SCs.[5,6] However, current guidelines recommend psychological screening only for some sleep–wake disorders, such as insomnia,[7] but not as part of the routine clinical practice. Moreover, the lack of a systematic depression screening increases the risk of missing the diagnosis and adversely affects treatment choices and depression outcomes. The duration of untreated depression and the delay in antidepressant treatment have been correlated with worse outcomes,[8] as well as, the inappropriate use of hypnotics and sedatives to treat sleep disturbances in depressed patients has been associated with an increased incidence of depression exacerbations and recurrence.[3,9]

The failure to recognize and treat early depression can also be detrimental to the prognosis of sleep–wake disorders. Comorbidity between depression and sleep-wake disorders is frequent in general[1] and psychiatric[10] populations. Among the limited and heterogeneous studies in SCs,depression is overrepresented in patients with different sleep–awake disorders when compared with the 8.4% observed in the US general population.[11] Among patients with sleep–wake disorders, depressive symptoms have been found in up to 63% of patients using self-rating questionnaires and MDD has been reported in 20%–30% of patients by performing psychiatric interview.[5,12–14] Researchers have also reported similar rates of MDD diagnosed by performing psychiatric interviews among individuals suffering from restless leg syndrome (RLS)[15] and narcolepsy.[16] It is conceivable that untreated comorbid depression in these individuals maintains mechanisms like inflammation and autonomic hyperarousal shared by sleep–wake disorders,[2] thereby negatively affecting their course.

Previous studies[5] and international recommendations[17] indicate the need to rectify the lack of routine depression screening in SCs. We, therefore, aimed to expand the limited clinical data on the prevalence of depression in SCs, herein reporting these rates in a preliminary sample of 288 adults participant in our ongoing multicenter study involving 13 SCs around the US. Our investigation aims to collect data for the development of a polysomnography-based algorithm capable of screening individuals who may have current depression.

To maximize the specificity of identifying a current major depressive episode (MDE),[18] we used the Patient Health Questionnaire, 9 items (PHQ-9) and scored it according to the algorithm based on the Diagnostic and Statistical Manual of Mental Disorders, fourth editioncriteria (pooled sensitivity, 0.61; pooled specificity, 0.95).[19]

Our preliminary sample included participants (51% females, mean age 46.6 ± 14.8 years) with different sleep–wake disorders, as reported in their medical history, encompassing sleep-related breathing disorders (53%), insomnia (25%), RLS (8%), narcolepsy (2%), rapid eye movement sleep behavior disorder (2%), and mixed sleep-related complaints (10%). Approximately 21% of patients had current PHQ-based MDE, with about 4% reporting severe symptoms (i.e., PHQ-9 ≥ 20). Moreover, according to item 9 of the PHQ-9 (i.e., "Thoughts that you would be better off dead or of hurting yourself in some way"), 9% of patients with current MDE reported to have been bothered by those thoughts more than half the days in the last two weeks and 31% during several days, whereas none of those without MDE had those thoughts for more than half the days and only 2% for several days.

Notably, 61% of those with current MDE according to the PHQ-9 were taking antidepressants. Despite the lack of information concerning treatment doses and durations, the finding that some participants receiving antidepressants may still have possible depression suggests that screening in SCs could help to identify poor responders to their pharmacotherapy requiring clinical reassessment, monitoring, or therapeutic regimen changes.

In our study, the lack of clinician-administered psychiatric interviews is one of the crucial limitations that may affect the true prevalence of MDD. However, our results highlight the considerable risk of prevalent depression among individuals that refer to SCs, supporting the limited existing data on this topic and confirming the need for routine depression screening in sleep services. This would reduce the risk of diagnostic and treatment errors and would improve therapeutic outcomes. Finally, implementing depression screening in clinical practice would also adhere to the accreditation requirements for sleep centres[20] suggesting the use of questionnaires or other screening assessments to include in the patient's medical records, which would represent a high-standard quality procedure toward a good-clinical practice in SCs.

**References**:


1. Franzen PL, Buysse DJ. Sleep disturbances and depression: risk relationships for subsequent depression and therapeutic implications. *Dialogues Clin Neurosci*. 2008;10:473.
2. Fang H, Tu S, Sheng J, Shao A. Depression in sleep disturbance: A review on a bidirectional relationship, mechanisms and treatment. *J Cell Mol Med*. 2019;23:2324-2332.
3. Inada K, Enomoto M, Yamato K, Marumoto T, Takeshima M, Mishima K. Effect of residual insomnia and use of hypnotics on relapse of depression: a retrospective cohort study using a health insurance claims database. *J Affect Disord*. 2021;281:539-546.
4. Harris LM, Huang X, Linthicum KP, Bryen CP, Ribeiro JD. Sleep disturbances as risk factors for suicidal thoughts and behaviours: a meta-analysis of longitudinal studies. *Sci Rep*. 2020;10.
5. Vandeputte M, de Weerd A. Sleep disorders and depressive feelings: a global survey with the Beck depression scale. *Sleep Med*. 2003;4:343-345.
6. Rosenberg RS. Depression in the sleep center: Are we treating the whole patient? *Sleep Med*. 2003;4:269.
7. Schutte-Rodin SL, Broch L, Buysee D, Dorsey C, Sateia M. Clinical Guideline for the Evaluation and Management of Chronic Insomnia in Adults. *J Clin Sleep Med*. 2008;4:487-504.
8. Kraus C, Kadriu B, Lanzenberger R, Zarate CA, Kasper S. Prognosis and improved outcomes in major depression: a review. *Transl Psychiatry 2019 91*. 2019;9:1-17.
9. Kripke DF. Greater incidence of depression with hypnotic use than with placebo. *BMC Psychiatry*. 2007;7.

10. Abad VC, Guilleminault C. Sleep and psychiatry. *Dialogues Clin Neurosci*. 2005;7:291-303.
11. NIMH » Major Depression. https://www.nimh.nih.gov/health/statistics/major-depression.
12. El-Sherbini AM, Bediwy AS, El-Mitwalli A. Association between obstructive sleep apnea (OSA) and depression and the effect of continuous positive airway pressure (CPAP) treatment. *Neuropsychiatr Dis Treat*. 2011;7:715-721.
13. Acker J, Richter K, Piehl A, Herold J, Ficker J, Niklewski G. Obstructive sleep apnea (OSA) and clinical depression—prevalence in a sleep center. *Sleep Breath 2016 212*. 2016;21:311-318.
14. Jackson ML, Tolson J, Bartlett D, Berlowitz DJ, Varma P, Barnes M. Clinical depression in untreated obstructive sleep apnea: examining predictors and a meta-analysis of prevalence rates. *Sleep Med*. 2019;62:22-28.
15. Becker P, Sharon D. Mood disorders in restless legs syndrome (Willis-Ekbom disease). *J Clin Psychiatry*. 2014;75.
16. Ohayon MM. Narcolepsy is complicated by high medical and psychiatric comorbidities: a comparison with the general population. *Sleep Med*. 2013;14:488-492.
17. Siu AL, (USPSTF)and the UPSTF, Bibbins-Domingo K, et al. Screening for Depression in Adults: US Preventive Services Task Force Recommendation Statement. *JAMA*. 2016;315:380-387.
18. Spitzer RL, Kroenke K, Williams JBW, and the Patient Health Questionnaire Primary Care Study Groupand the PHQPCSG. Validation and Utility of a Self-report Version of PRIME-MD: The PHQ Primary Care Study. *JAMA*. 1999;282:1737-1744.
19. He C, Levis B, Riehm KE, et al. The Accuracy of the Patient Health Questionnaire-9 Algorithm for Screening to Detect Major Depression: An Individual Participant Data Meta-Analysis. *Psychother Psychosom*. 2020;89:25-37.
20. American Academy of Sleep Medicine. Standards for Accreditation | Reference Materials. https://aasm.org/resources/standards-for-accreditation. Accessed October 5, 2022