

INSOMNIA IN OLDER ADULTS LIVING WITH COGNITIVE IMPAIRMENT

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DISCLOSURES

None to disclose

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OBJECTIVES

1. Summarize the current evidence on the relationship between insomnia and cognitive impairment
2. Describe practical and clinical considerations to manage sleep concerns in older adults with cognitive concerns
3. Describe the use of technology to expand access to cognitive behavioral therapy for insomnia

TABLE OF CONTENTS

1. Relationship between insomnia and cognitive impairment
2. Insomnia management and treatment recommendations
3. Implications for treating older adults with insomnia and cognitive impairment
4. Use of technology to deliver an Internet-based insomnia intervention
5. Practical and clinical considerations

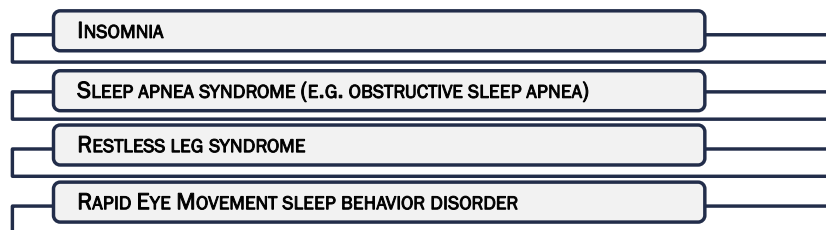
AGE-RELATED SLEEP CHANGES

- Decrease in total sleep time
- Increase in daytime napping
- Decreased sleep efficiency
- Decrease in ability to maintain sleep
- Decrease in slow-wave sleep
- Decrease in percentage of rapid eye movement (REM) sleep



<https://www.sleepfoundation.org/stages-of-sleep>

SLEEP DISORDERS & DISTURBANCES



- Sleep disorders and disturbances can cause poor sleep
- Poor sleep is associated with
 - Difficulty managing chronic conditions
 - Greater risk for cognitive decline, falls, and poorer quality of life

SLEEP & COGNITIVE IMPAIRMENT

- Individuals with cognitive impairment experience more sleep disorders than those without cognitive concerns
- The relationship between sleep and dementia is likely bidirectional
- Sleep quantity is associated with dementia risk
 - Inverted U-shaped association of sleep quantity with cognitive decline
 - Short sleep is associated with a greater p-tau/Ab42 ratio
- Sleep disturbances negatively impact survival time, and the deleterious impact of sleep disturbances on survival time is interrelated with cognition

SLEEP & COGNITIVE IMPAIRMENT

- Sleep disorders can lead to an increased vascular risk profile and vascular changes such as inflammation, endothelial dysfunction, and atherosclerosis
- Individuals with AD pathology have an increased inflammatory response, which increases beta-amyloid (A β) production, and insomnia symptoms can negatively impact the brain's ability to clear these plaques
- Sleep disturbances can increase levels of A β and tau
 - 'Glymphatic system' and the clearance A β and tau
 - Microglial reactivity and A β
 - Orexins as modulators of sleep and A β pathology

INSOMNIA MANAGEMENT & TREATMENT

PHARMACOLOGICAL OR BEHAVIORAL-BASED TREATMENT

PHARMACOLOGICAL TREATMENT

- Most common treatment for insomnia in older adults
- Short-term efficacy, but does not treat insomnia's underlying factors
- Older adults are poor candidates for common insomnia medications (e.g., sedative hypnotics, Zolpidem) due to increased susceptibility to the consequences of inappropriate medications
- Consider extended-release melatonin over the typical "Z-drugs"



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INSOMNIA MANAGEMENT & TREATMENT

BEHAVIORAL-BASED TREATMENT

- Cognitive behavioral therapy for insomnia (CBT-I) is recommended first-line treatment for insomnia
 - Replacing maladaptive thoughts and sleep habits to reduce sleep-related arousal
 - Restructuring the thoughts, feelings, and behaviors contributing to insomnia
 - Some techniques involve stimulus control, sleep restriction, and relaxation training
- CBT-I is considered effective for both short-term insomnia and chronic insomnia



<https://sleepwellbeing.co.uk/what-is-cbt-ib3f>



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ACCESS TO INSOMNIA TREATMENT

- Insomnia in older adults is often untreated because it is presumed to be an inevitable part of aging
- Less than 15% of all adults with chronic insomnia are estimated to get any treatment for insomnia
- CBT-I access is extremely limited because there are a limited number of certified specialists in Behavioral Sleep Medicine in the US
- Most accredited sleep centers do not have clinicians who specialize in behavioral insomnia treatment
- Need to improve access to efficacious insomnia treatment, especially in populations at risk for developing dementia



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ACCESS TO INSOMNIA TREATMENT

We propose that delivery of CBT-I using an empirically validated, Internet-delivered intervention for insomnia could address an unmet need for older adults living with mild cognitive impairment (MCI) by improving sleep and quality of life (QoL) and potentially slowing cognitive decline.



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BIG PICTURE



<https://gomohealth.com/2020/digital-therapeutics-what-are-they-and-why-do-they-matter/>

MILD COGNITIVE IMPAIRMENT

- Approximately 13.5 million adults over 65 live with MCI
- Of the 15-19% of adults with MCI, 8-15% of individuals with MCI progress to dementia each year
- Care is focused on prevention and symptom management

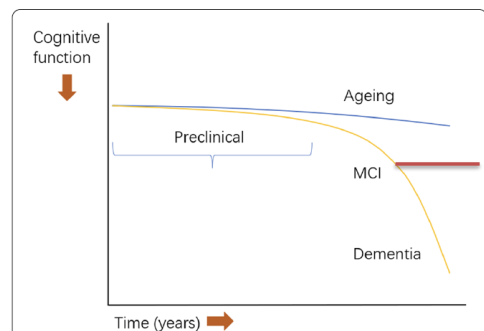


Fig. 1 Model of the cognitive function decline trajectory of Alzheimer's disease (AD) vs normal ageing. The stage of preclinical AD precedes with mild cognitive impairment (MCI), graph adapted from [10]

(Huang et al., 2023)

“SHUTI” IN MCI

To determine the feasibility, acceptability, and preliminary efficacy of Internet-delivered CBT-I for older adults with MCI and co-morbid insomnia



*This work has been presented previously at the 2020 and 2021 Alzheimer's Association International Congresses



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METHODS



- Single-arm intervention pilot study
- Intervention was an Internet-based CBT-I program called Sleep Healthy Using the Internet for Older Adult Sufferers of Insomnia and Sleeplessness (**SHUTi OASIS**)
 - Fully automated, interactive, and tailored program modeled on the primary tenets of face-to-face CBT-I
 - Relies on user-entered online sleep diaries to track progress and tailor treatment recommendations



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METHODS CONT.

Recruitment from the University of Virginia (UVA) Memory and Aging Care Clinic, UVA sleep clinics, and Carilion Clinic MCI clinic



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METHODS CONT.

Participant with MCI

- **Inclusion criteria:** >55 years old, MCI diagnosis; Internet and Email availability and use; sleep-onset insomnia and/or sleep maintenance insomnia; no more than 6.5 hours of sleep/ night
- **Exclusion criteria:** other untreated sleep disorders; current psychological treatment for insomnia; initiation of psychological or psychiatric treatment; current diagnosis of Huntington's or Parkinson's disease; current treatment for hyperthyroidism; currently undergoing chemotherapy; no presence of asthma or respiratory concerns with night treatment; opioid use; epilepsy

Care Partner

- **Inclusion criteria:** >=18 years of age, sleeps in the same home as the participant for at least 3 days/week
- No **exclusion criteria**



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MEASURES

Feasibility and acceptability

- Core completion
- Log-in count
- Qualitative interviews

Sleep and cognitive status

- Insomnia Severity Index (ISI)
- Sleep measures collected by sleep diary entry and actigraphy
- Montreal Cognitive Assessment

Exploratory

- Actiwatch wear
- Care partner data

ANALYSIS

- Quantitative
 - Descriptive statistics
 - Paired t-tests
- Qualitative
 - Analyzed using line-by-line coding and content analysis
 - Categories of shared or similar experiences organized findings
 - Category similarities, differences, and counter examples discussed until verified by consensus and convergence

RESULTS

- 10 of the 12 participants completed the study
 - Difficulties completing the Internet-delivered baseline survey citing it was “too hard to stay focused” (n=1)
 - Self-reported cognitive decline (n=1)
- 100% compliance with online sleep diary completion

Table 2. Preliminary Efficacy of SHUTi OASIS in Participants with MCI (n=10)

Variable	Pre-Intervention*	Post-Intervention*	Test statistic	p-value
Insomnia Severity Index (Range 0-28)	13.5 ± 4.8 (5-21)	8.3 ± 5.3 (0-19)	t(9)=4.0	<.01
Sleep efficiency, %	77.3 ± 18.8 (21-99)	86.5 ± 13.0 (31-99)	t(99)=4.8	<.001
Total sleep time, minutes	371.7 ± 114.9 (120-620)	396.8 ± 100.4 (120-695)	t(99)=-2.2	.03
Time in bed, minutes	478.9 ± 76.6 (280-665)	459.5 ± 91.6 (300-715)	t(99)= 2.2	.03
Total nap duration, minutes	10.6 ± 21.4 (0-90)	23.8 ± 61.8 (0-240)	t(99)= -2.5	.02
Sleep onset latency, minutes	36.0 ± 40.3 (5-180)	18.3 ± 26.3 (5-150)	t(99)=4.3	<.001
Wake after sleep onset,** minutes	71.2 ± 80.6 (0-360)	44.4 ± 54.5 (0-285)	t(99)=3.3	.001
Montreal Cognitive Assessment (Range 0-30), n=8	21.9 ± 2.8 (18-27)	21.3 ± 4.5 (14-28)	t(9)= 0.50	.63
Blind Montreal Cognitive Assessment (Range 0-22)	15.9 ± 2.3 (13-20)	15.6 ± 2.2 (13-20)	t(9)= 0.38	.71

* mean ± standard deviation (range)

** wake after sleep onset includes early morning awakening

RESULTS: USAGE

Table 3. Sleep Diary and Actiwatch Use in Older Adults, Baseline and Post-Intervention, N=11

Variable	Baseline (n=11)	Post Intervention (n=10)
Sleep diary completion, 10 entries over 14 days, #(%)	11 (100)	10 (100)
Actiwatch wear, number of nights, mean \pm standard deviation (SD, range, n= subjects with data)	11.1 \pm 4.3 (5-20, n=8)	10.1 \pm 6.4 (0-14, n=5)



DISCUSSION

- Participants with MCI and insomnia demonstrated feasibility of Internet-delivered CBT-I with consistent, frequent program use
- Care partners not needed for retention and participation
- Statistically and clinically meaningful changes in sleep efficiency, wake after sleep onset, sleep onset latency, and Insomnia Severity Index
- 40% of participants reported experiencing little to no insomnia symptoms at post-assessment

DISCUSSION

- Significant changes in sleep variables found in this trial are consistent with findings from other SHUTi studies
- Encouraging program adherence
- Interesting to find increased nap length
- Qualitative interview findings

CONCLUSIONS

- Demonstrated feasibility, acceptability, and preliminary efficacy of an Internet-delivered, CBT-I intervention in participants with MCI
- Older adults with MCI can independently complete CBT-I via the Internet and can clinically improve their sleep
- Behavioral interventions provide the opportunity to engage and include patients to improve their health without a pharmacological additive

LIMITATIONS

- Low enrollment rate of eligible patients
- Small sample with potential selection bias
- Single arm design
- Pre-post assessment
- Short study duration



NEXT STEPS

- Hypothesize a direct relationship between insomnia and cognition, whereby individuals with insomnia and cognitive impairment are at excess risk of dementia compared to older adults living with MCI without insomnia
- Posit that addressing insomnia symptoms in older adults with MCI and co-morbid insomnia will promote the maintenance of cognitive health
- Consider different recruitment approaches

SHUTi MIND

Sleep Healthy Using the Internet (SHUTi)

Mitigating Insomnia to Address Neurocognitive Difficulties (MIND)

- Randomized controlled trial
- Powered to detect change in sleep outcomes
- Internet-based recruitment
- Internet-based assessments
- Internet-based intervention

SHUTi OASIS



REDCap
Research Electronic Data Capture

qualtrics.^{XM}

**CAMBRIDGE
COGNITION**

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STUDY AIMS

AIM 1: To test the efficacy of SHUTi OASIS to improve sleep and daytime functioning in older adults with mild cognitive concerns

AIM 2: To examine the preliminary efficacy of SHUTi OASIS to maintain cognition in individuals with cognitive concerns and insomnia.



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PRACTICAL & CLINICAL CONSIDERATIONS TO MANAGE SLEEP CONCERNS

- More longitudinal studies and rigorous clinical trials examining the underlying pathophysiological mechanisms are necessary
- CBTi > pharmacological treatment
- If treating with medication, consider extended-release melatonin over “Z-drugs”
- Need to examine the role of sleep in efficacious behavioral interventions to improve brain health
- Use of new wearable devices to understand and implement sleep interventions



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TAKE AWAY MESSAGES: TECHNOLOGY

- Older adults use the Internet
- Older adults demonstrate interest in research studies using Internet-based recruitment
- Older adults can stay engaged in a research study using a behavioral intervention delivered via the Internet
- Older adults can complete complicated and lengthy study activities when provided with the appropriate resources and time



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NEXT STEPS

- Efficacy trial with a clinically-based cohort examining long-term cognitive outcomes
- Pharmacological + non-pharmacological combination therapy
- Non-pharmacological combination therapy
- Use of new wearable devices for clinical data collection



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A large photograph of a classical building with a portico of white columns, set against a backdrop of trees with vibrant autumn foliage. The sun is shining brightly, creating a lens flare effect. In the foreground, a few people are sitting on the grass.

Clinical Trial Registry:
NCT05565833; <https://clinicaltrials.gov>

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REFERENCES

- Almond, K. M. de, Costa, M. V., Malloy-Diniz, L. F., & Diniz, B. S. (2016). Insomnia and risk of dementia in older adults: Systematic review and meta-analysis. *Journal of Psychiatric Research*, *77*, 109–115. <https://doi.org/10.1016/j.jpsychires.2016.02.021>
- Benca, R., Joseph Herring, W., Khandker, R., & Qureshi, Z. P. (2022). Burden of Insomnia and Sleep Disturbances and the Impact of Sleep Treatments in Patients with Probable or Possible Alzheimer's Disease: A Structured Literature Review. *Journal of Alzheimer's Disease*, *86*(1), 83–109. <https://doi.org/10.3233/JAD-215324>
- Beyer, J. L., Dix, E., Husain-Krautter, S., & Kyomen, H. H. (2024). Enhancing Brain Health and Well-Being in Older Adults: Innovations in Lifestyle Interventions. In *Current Psychiatry Reports* (Vol. 26, Issue 8, pp. 405–412). Springer. <https://doi.org/10.1007/s11920-024-01513-4>
- Brewster, G. S., Riegel, B., & Gehrman, P. R. (2022). Insomnia in the Older Adult. In *Sleep Medicine Clinics* (Vol. 17, Issue 2, pp. 233–239). W.B. Saunders. <https://doi.org/10.1016/j.jsmc.2022.03.004>
- Cummings, J. (2021). New approaches to symptomatic treatments for Alzheimer's disease. In *Molecular Neurodegeneration* (Vol. 16, Issue 1). BioMed Central Ltd. <https://doi.org/10.1186/s13024-021-00424-9>
- Dzierzewski, J. M., Dautovich, N., & Ravyts, S. (2018). Sleep and Cognition in Older Adults. In *Sleep Medicine Clinics* (Vol. 13, Issue 1, pp. 93–106). W.B. Saunders. <https://doi.org/10.1016/j.jsmc.2017.09.009>



SCHOOL of NURSING

37

REFERENCES

- Edinoff, A. N., Wu, N., Ghaffar, Y. T., Prejean, R., Gremillion, R., Cogburn, M., Chami, A. A., Kaye, A. M., & Kaye, A. D. (2021). Zolpidem: Efficacy and side effects for insomnia. *Health Psychology Research*, *9*(1). <https://doi.org/10.52965/001c.24927>
- Emert, S. E., Taylor, D. J., Gartenberg, D., Schade, M. M., Roberts, D. M., Nagy, S. M., Russell, M., Huskey, A., Mueller, M., Gamaldo, A., & Buxton, O. M. (2023). A non-pharmacological multi-modal therapy to improve sleep and cognition and reduce mild cognitive impairment risk: Design and methodology of a randomized clinical trial. *Contemporary Clinical Trials*, *132*. <https://doi.org/10.1016/j.cct.2023.107275>
- Fernandes, M., Chiaravalloti, A., Nuccetelli, M., Placidi, F., Izzi, F., Camedda, R., & Bernardini, S. (2023). Sleep Dysregulation Is Associated with 18F-FDG PET and Cerebrospinal Fluid Biomarkers in Alzheimer's Disease. *Journal of Alzheimer's Disease Reports*.
- Jaqua, E. E., Hanna, M., Labib, W., Moore, C., & Matossian, V. (2022). *Common Sleep Disorders Affecting Older Adults*.
- Kong, J., Zhou, L., Li, X., & Ren, Q. (2023a). Sleep disorders affect cognitive function in adults: an overview of systematic reviews and meta-analyses. In *Sleep and Biological Rhythms* (Vol. 21, Issue 2, pp. 133–142). Springer. <https://doi.org/10.1007/s41105-022-00439-9>
- Kong, J., Zhou, L., Li, X., & Ren, Q. (2023b). Sleep disorders affect cognitive function in adults: an overview of systematic reviews and meta-analyses. In *Sleep and Biological Rhythms* (Vol. 21, Issue 2, pp. 133–142). Springer. <https://doi.org/10.1007/s41105-022-00439-9>



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38

REFERENCES

- Kyle, S. D., Siriwardena, A. N., Espie, C. A., Yang, Y., Petrou, S., Ogburn, E., Begum, N., Maurer, L. F., Robinson, B., Gardner, C., Lee, V., Armstrong, S., Pattinson, J., Mort, S., Temple, E., Harris, V., Yu, L. M., Bower, P., & Aveyard, P. (2023). Clinical and cost-effectiveness of nurse-delivered sleep restriction therapy for insomnia in primary care (HABIT): a pragmatic, superiority, open-label, randomised controlled trial. *The Lancet*, *402*(10406), 975–987. [https://doi.org/10.1016/S0140-6736\(23\)00683-9](https://doi.org/10.1016/S0140-6736(23)00683-9)
- Lam, A., Kong, S., & Naismith, S. L. (2024). Recent advances in understanding of sleep disorders and disturbances for dementia risk and prevention. In *Current Opinion in Psychiatry* (Vol. 37, Issue 2, pp. 94–100). Lippincott Williams and Wilkins. <https://doi.org/10.1097/YCO.0000000000000921>
- Li, J., Vitiello, M. V., & Gooneratne, N. S. (2018). Sleep in Normal Aging. *Sleep Medicine Clinics*, *13*(1), 1–11. <https://doi.org/10.1016/j.jsmc.2017.09.001>
- Louzada, L. L., Machado, F. V., Quintas, J. L., Ribeiro, G. A., Silva, M. V., Mendonça-Silva, D. L., Gonçalves, B. S. B., Nóbrega, O. T., & Camargos, E. F. (2022). The efficacy and safety of zolpidem and zopiclone to treat insomnia in Alzheimer's disease: a randomized, triple-blind, placebo-controlled trial. *Neuropsychopharmacology*, *47*(2), 570–579. <https://doi.org/10.1038/s41386-021-01191-3>
- Madari, S., Golebiowski, R., Mansukhani, M. P., & Prakash Kolla, B. (n.d.). *Pharmacological Management of Insomnia*. <https://doi.org/10.1007/s13311-021-01010-z>/Published



SCHOOL of NURSING

39

REFERENCES

- Mattos, M. K., Barnes, L., Davis, E. M., Manning, C. M., Quigg, M., & Ritterband, L. M. (2020). Feasibility of Technology Use in an Internet-Delivered Intervention. *The Gerontologist*.
- Mattos, M. K., Chang, A., Pitcher, K., Whitt, C., Ritterband, L. M., & Quigg, M. S. (2021). A review of insomnia treatments for patients with mild cognitive impairment. In *Ageing and Disease* (Vol. 12, Issue 4, pp. 1036–1042). International Society on Ageing and Disease. <https://doi.org/10.14336/AD.2021.0423>
- Mattos, M., Manning, C., You, W., MacDonnell, K., & Ritterband, L. (2023, October 25). *Internet-based insomnia intervention to prevent cognitive decline: Use of Internet-based recruitment, intervention, and assessment methods*. .
- Mayer, G., Frohnhofen, H., Jokisch, M., Hermann, D. M., & Gronewold, J. (2024). Associations of sleep disorders with all-cause MCI/dementia and different types of dementia – clinical evidence, potential pathomechanisms and treatment options: A narrative review. In *Frontiers in Neuroscience* (Vol. 18). Frontiers Media SA. <https://doi.org/10.3389/fnins.2024.1372326>
- Mukherjee, U., Sehar, U., Brownell, M., & Reddy, P. H. (2024). Mechanisms, consequences and role of interventions for sleep deprivation: Focus on mild cognitive impairment and Alzheimer's disease in elderly. In *Ageing Research Reviews* (Vol. 100). Elsevier Ireland Ltd. <https://doi.org/10.1016/j.arr.2024.102457>
- Nielson, S. A., Kay, D. B., & Dzierzewski, J. M. (2023). Sleep and Depression in Older Adults: A Narrative Review. In *Current Psychiatry Reports* (Vol. 25, Issue 11, pp. 643–658). Springer. <https://doi.org/10.1007/s11920-023-01455-3>



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40

REFERENCES

- Parhizkar, S., Gent, G., Chen, Y., Rensing, N., Gratuze, M., Strout, G., Sviben, S., Tycksen, E., Zhang, Q., Gilmore, P. E., Sprung, R., Malone, J., Chen, W., Serrano, J. R., Bao, X., Lee, C., Wang, C., Landsness, E., Fitzpatrick, J., ... Holtzman, D. M. (2023). Sleep deprivation exacerbates microglial reactivity and A β deposition in a TREM2-dependent manner in mice. *Science Translational Medicine*, 15(693). <https://doi.org/10.1126/scitranslmed.ade6285>
- Sikkes, S. A. M., Tang, Y., Jutten, R. J., Wesselman, L. M. P., Turkstra, L. S., Brodaty, H., Clare, L., Cassidy-Eagle, E., Cox, K. L., Chélat, G., Dautricourt, S., Dhana, K., Dodge, H., Dröes, R. M., Hampstead, B. M., Holland, T., Lampit, A., Laver, K., Lutz, A., ... Bahar-Fuchs, A. (2021). Toward a theory-based specification of non-pharmacological treatments in aging and dementia: Focused reviews and methodological recommendations. *Alzheimer's and Dementia*, 17(2), 255–270. <https://doi.org/10.1002/alz.12188>
- Wang, S., Zheng, X., Huang, J., Liu, J., Li, C., & Shang, H. (2024). Sleep characteristics and risk of Alzheimer's disease: a systematic review and meta-analysis of longitudinal studies. In *Journal of Neurology* (Vol. 271, Issue 7, pp. 3782–3793). Springer Science and Business Media Deutschland GmbH. <https://doi.org/10.1007/s00415-024-12380-7>
- Winer, J. R., Deters, K. D., Kennedy, G., Jin, M., Goldstein-Piekarski, A., Poston, K. L., & Mormino, E. C. (2021). Association of Short and Long Sleep Duration With Amyloid- β Burden and Cognition in Aging. *JAMA Neurology*, 78(10), 1187. <https://doi.org/10.1001/jamaneurol.2021.2876>



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41

REFERENCES

- Xu, W., Tan, C.-C., Zou, J.-J., Cao, X.-P., & Tan, L. (2020). Sleep problems and risk of all-cause cognitive decline or dementia: an updated systematic review and meta-analysis. *Journal of Neurology, Neurosurgery & Psychiatry*, 91(3), 236–244. <https://doi.org/10.1136/jnnp-2019-321896>
- Yuan, M., Hong, B., Zhang, W., Liu, A., Wang, J., Liu, Y., Yan, F., Xiao, S., Xu, H., & Wang, T. (2023). Late-life sleep duration associated with amnesic mild cognitive impairment. *International Psychogeriatrics*, 35(8), 439–448. <https://doi.org/10.1017/S1041610221000466>
- Zawar, I., Mattos, M. K., Manning, C., & Quigg, M. (2022). Sleep Disturbances, Cognitive Status, and Biomarkers of Dementia. *Journal of Alzheimer's Disease*, 89(4), 1367–1374. <https://doi.org/10.3233/JAD-220664>
- Zawar, I., Mattos, M. K., Manning, C., & Quigg, M. (2023). Sleep disturbances predict cognitive decline. *Journal of Alzheimer's Disease*.



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REFERENCES

Graphic references:

- <https://www.medicalnewstoday.com/articles/318827#who-needs-an-iron-infusion>
- https://www.google.com/imgres?imgurl=https%3A%2F%2Fwww.freepnglogos.com%2Fuploads%2Fdollar-sign-png%2Fdollar-sign-won-and-dollar-signs-comd-19.png&imgrefurl=https%3A%2F%2Fwww.freepnglogos.com%2Fpics%2Fdollar-sign&tbnid=N-QMlzyCc0h1DM&vet=12ahUKEwi-n67etKnyAhXrgHIEHb28CMkQMyg3egQIARBg..i&docid=v752j_HWSW5wiM&w=620&h=1014&q=dollar%20sign&client=safari&ved=2ahUKEwi-n67etKnyAhXrgHIEHb28CMkQMyg3egQIARBg
- Associated Press
- <https://gomohealth.com/2020/digital-therapeutics-what-are-they-and-why-do-they-matter/>



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