

Wearables-and Blood-based Biomarkers-incorporated Care For Circadian Rhythm Disruption In Alzheimer’s Dementia - A Protocol

Ta-Wei Guu^{1,2}, Dag Aarsland², Wan-Jing Li^{3,4}, Wei-Fen Ma^{4,5} and Li-Jung Chen⁶



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- 1 Division of Psychiatry, Departments of Internal Medicine, China Medical University Beigang Hospital, Yunlin, Taiwan
- 2 Centre for Healthy Brain Ageing, Institute of Psychiatry, Psychology and Neuroscience, King's College London, UK
- 3 Department of Nursing, Asia University, Taichung, Taiwan
- 4 School of Nursing, China Medical University, Taichung, Taiwan
- 5 Departments of Nursing, China Medical University Hospital, Taichung, Taiwan
- 6 Department of Exercise Health Science, National Taiwan University of Sport, Taichung, Taiwan

- 1. Current assessment and treatment of sleep and circadian disturbances in dementia are limited by subjective caregiver-reported measures and reliance on medications with potential safety concerns, highlighting the need for objective monitoring and non-pharmacological interventions.
- 2. This project evaluates the feasibility of actigraphy application in Taiwanese patients with Alzheimer's disease (AD) and conduct a double-blind randomised trial to determine if wearable transcranial photobiomodulation (tPBM) can improve sleep, circadian rhythms, and other behavioural and psychological symptoms of dementia (BPSD).
- 3. By integrating wearable-device data, clinical assessments, and blood-based AD biomarkers, the study aims to develop a comprehensive, three-dimensional dementia care model and identify digital phenotypes linked to disease progression and circadian dysfunction.

INTRODUCTION	METHODS: Year 1	METHODS: Year 2-4	EXPECTED IMPACT	REFERENCES
Taiwan became a super-aged society in 2025, with more than 20% of its population aged over 65 years, leading to a growing prevalence of dementia and increasing caregiving demands. Behavioural and psychological symptoms of dementia (BPSD), particularly sleep disturbances and circadian rhythm disruption, are major contributors to caregiver burden and healthcare utilisation. Current assessment relies on caregiver-reported questionnaires, which are subjective and often cross-sectional. Treatments are also limited, often relying on sedative-hypnotics or antipsychotics that carry significant safety risks. Wearable technologies offer a promising alternative by enabling objective, continuous monitoring of sleep, activity, and environmental factors, while generating novel digital phenotypes. Emerging non-pharmacological interventions, such as wearable transcranial photobiomodulation (tPBM), may improve circadian regulation and sleep. By integrating wearable-device data, blood-based Alzheimer's disease (AD) biomarkers, and clinical assessments, this study aims to develop more precise, personalised, and safer approaches to dementia care.	This four-year project investigates the feasibility, effectiveness, and clinical utility of wearable technologies for assessing and managing sleep and circadian rhythm disturbances in AD (Figure 1). Figure 1. Study objectives by project year.	In Year 2-3 (RCT phase), this study employs a double-blind randomised controlled trial to evaluate the efficacy and feasibility of a home-based wearable near-infrared transcranial photobiomodulation (tPBM, Figure 2) for improving sleep and other BPSD in patients with dementia. A total of 132 participants will be recruited and randomly assigned (1:1) to active or sham groups. Continuous actigraphy will be used over 12 weeks to objectively assess sleep, activity, and light exposure. The intervention consists of daily tPBM use (30–90 minutes) over 8 weeks. Outcomes include questionnaire-based measures (PSQI, NPI) and actigraphy-derived metrics. Cognitive tests and blood biomarkers will be collected. Quantitative analyses involve mixed-model ANOVA and correlation methods, while qualitative interviews explore user experiences. Safety monitoring and longitudinal follow-up are included to assess feasibility, acceptability, and long-term effects. Year 4 examines tPBM effects across dementia subgroups using wearable-derived digital phenotypes and biomarkers, extends collaboration with the RADAR-AD consortium, integrates ongitudinal data.	Figure 2. The study devices. Left: Wearable tPBM headband. Right: Research-grade actigraphy. This project is expected to have impact at three key levels. First, it addresses a major gap in Asia by establishing a research platform for dementia using research-grade wearable devices. This platform will expand both in sample size and longitudinal depth, and through collaboration with UK and European cohorts, enable cross-cultural comparisons of digital phenotypes between Asian and Western populations. Second, the project aims to develop safe, home-based, non-pharmacological intervention models. By incorporating lifestyle and environmental factors such as circadian rhythms and light exposure, these approaches seek to improve sleep disturbances and other BPSD while reducing caregiver burden, particularly in underserved ageing communities. Finally, integrating wearable data, clinical assessments, and blood-based biomarkers will enhance understanding of interactions among circadian disruption, cognitive decline, and AD pathology, supporting personalised therapeutic strategies.	Guu, T.-W., Brem, A.-K., Albertyn, C. P., Kandangwa, P., Aarsland, D., & ffytche, D. (2024). Wrist-worn actigraphy in agitated late-stage dementia patients: A feasibility study on digital inclusion. <i>Alzheimer's & Dementia</i>, 20(5), 3211-3218. https://doi.org/https://doi.org/10.1002/alz.13772 Guu, T.-W., Cassano, P., Li, W.-J., Tseng, Y.-H., Ho, W.-Y., Lin, Y.-T., Lin, S.-Y., Chang, J. P.-C., Mischoulon, D., & Su, K.-P. (2024). Wearable, self-administered transcranial photobiomodulation for major depressive disorder and sleep: A randomized, double blind, sham-controlled trial. <i>Journal of Affective Disorders</i>. https://doi.org/https://doi.org/10.1016/j.jad.2024.12.065 Guu, T.-W., Li, W.-J., Lee, S.-H., Hsu, C.-S., Chou, C.-N., Lack, L., & Ma, W.-F. (2026). Facilitating the measurement and treatment of Behavioral and Psychological Symptoms of Dementia (BPSD) and understanding caregiver burden using wearable devices in Rural Taiwan—Protocol for a dyadic feasibility pilot study. <i>PLoS One</i>, 21(5), e0342136. https://doi.org/10.1371/journal.pone.0342136 Guu, T.-W., Muurling, M., Khan, Z., Kalafatis, C., Aarsland, D., ffytche, D., & Brem, A. K. (2023). Wearable devices: underrepresentation in the ageing society. <i>The Lancet Digital Health</i>, 5(6), e336-e337. https://doi.org/https://doi.org/10.1016/S2589-7500(23)00069-9
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