

# Temporal Progression of Sleep Microstructural EEG Alterations in Dementia Development

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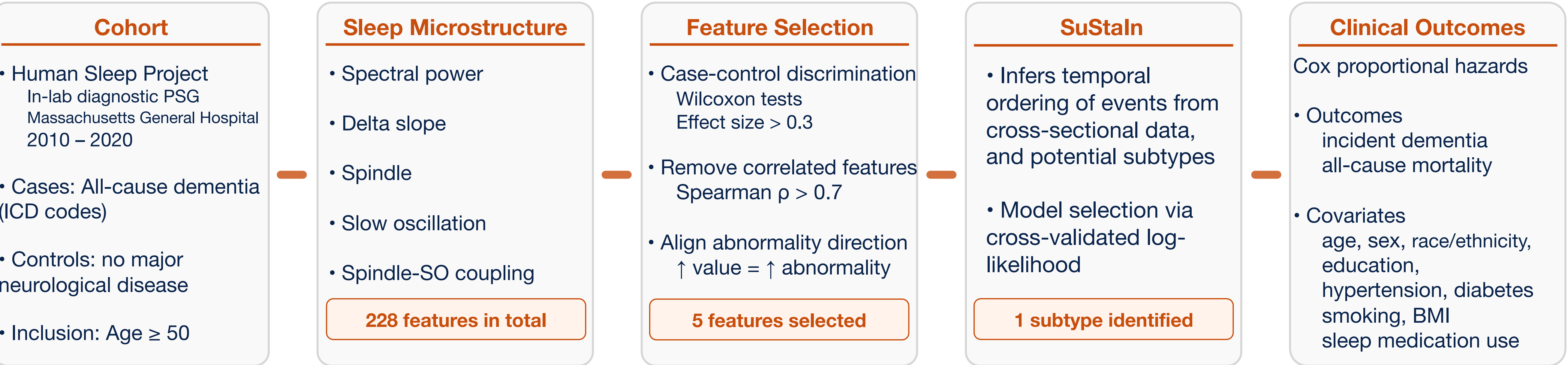
## Introduction

- Sleep EEG microstructure is altered in dementia, but the **temporal sequence** remains unknown.
- We applied the **SuStaln (Subtype and Stage Inference)** model to reconstruct the progression pattern of EEG microstructures from cross-sectional PSG data.
- We evaluated associations between inferred stages, incident dementia and mortality.

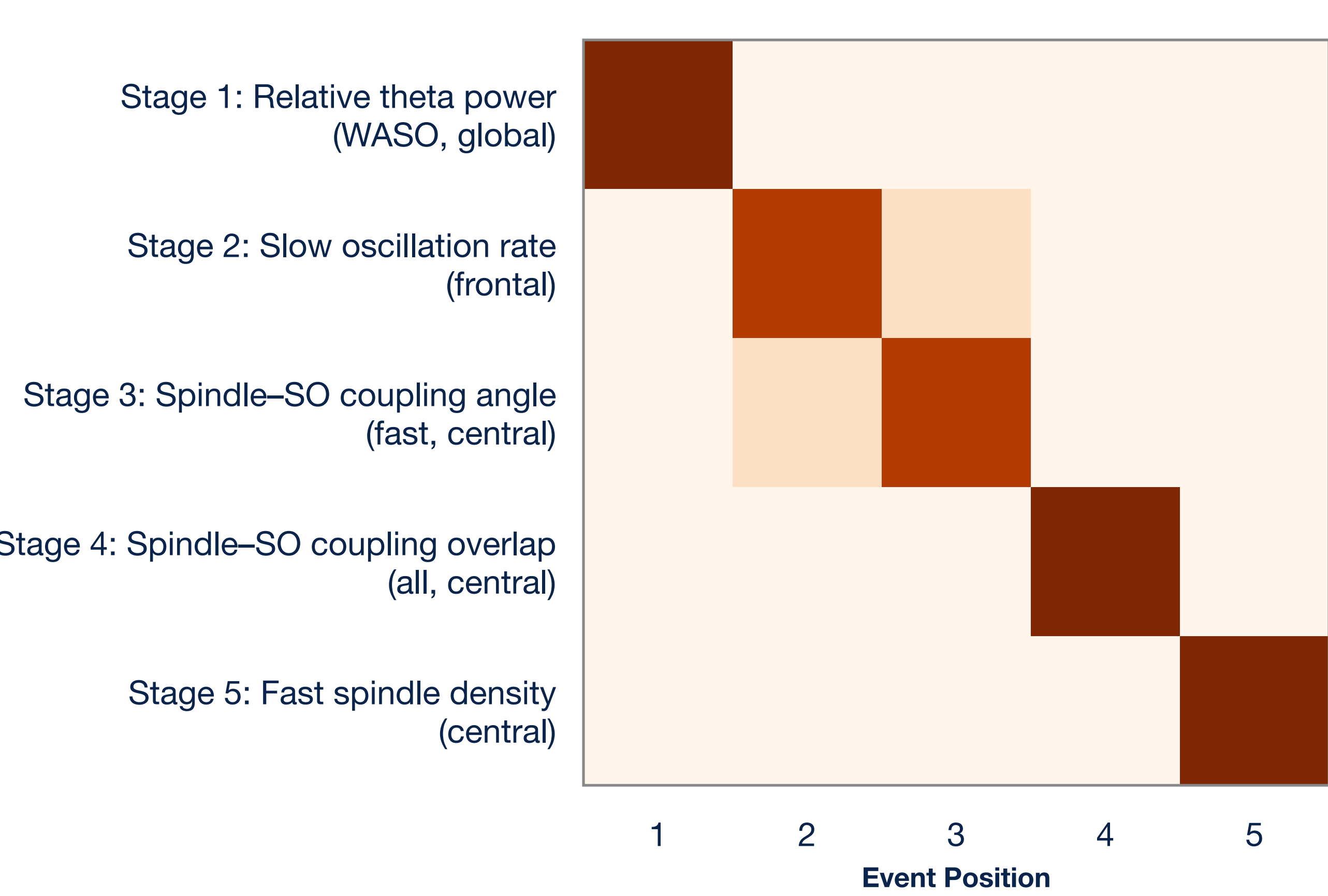
## Sample Characteristics

|                       | Dementia free<br>N = 2666 | Incident dementia<br>N = 168 | Prevalent dementia<br>N = 39 |
|-----------------------|---------------------------|------------------------------|------------------------------|
| Age                   | 61.3 ± 8.19               | 70.7 ± 8.94                  | 70.1 ± 10.6                  |
| Female                | 1421 (53.3%)              | 67 (39.9%)                   | 21 (53.8%)                   |
| Non-Hispanic White    | 2006 (75.2%)              | 136 (81.0%)                  | 29 (74.4%)                   |
| Hypertension          | 515 (19.3%)               | 62 (36.9%)                   | 20 (51.3%)                   |
| Diabetes              | 160 (6.0%)                | 25 (14.9%)                   | 9 (23.1%)                    |
| Benzodiazepine use    | 376 (14.1%)               | 25 (14.9%)                   | 8 (20.5%)                    |
| Follow-up time (days) | 3650 ± 1140               | 3390 ± 1130                  | 2390 ± 1310                  |
| Death                 | 53 (2.0%)                 | 32 (19.0%)                   | 7 (17.9%)                    |

## Methodology

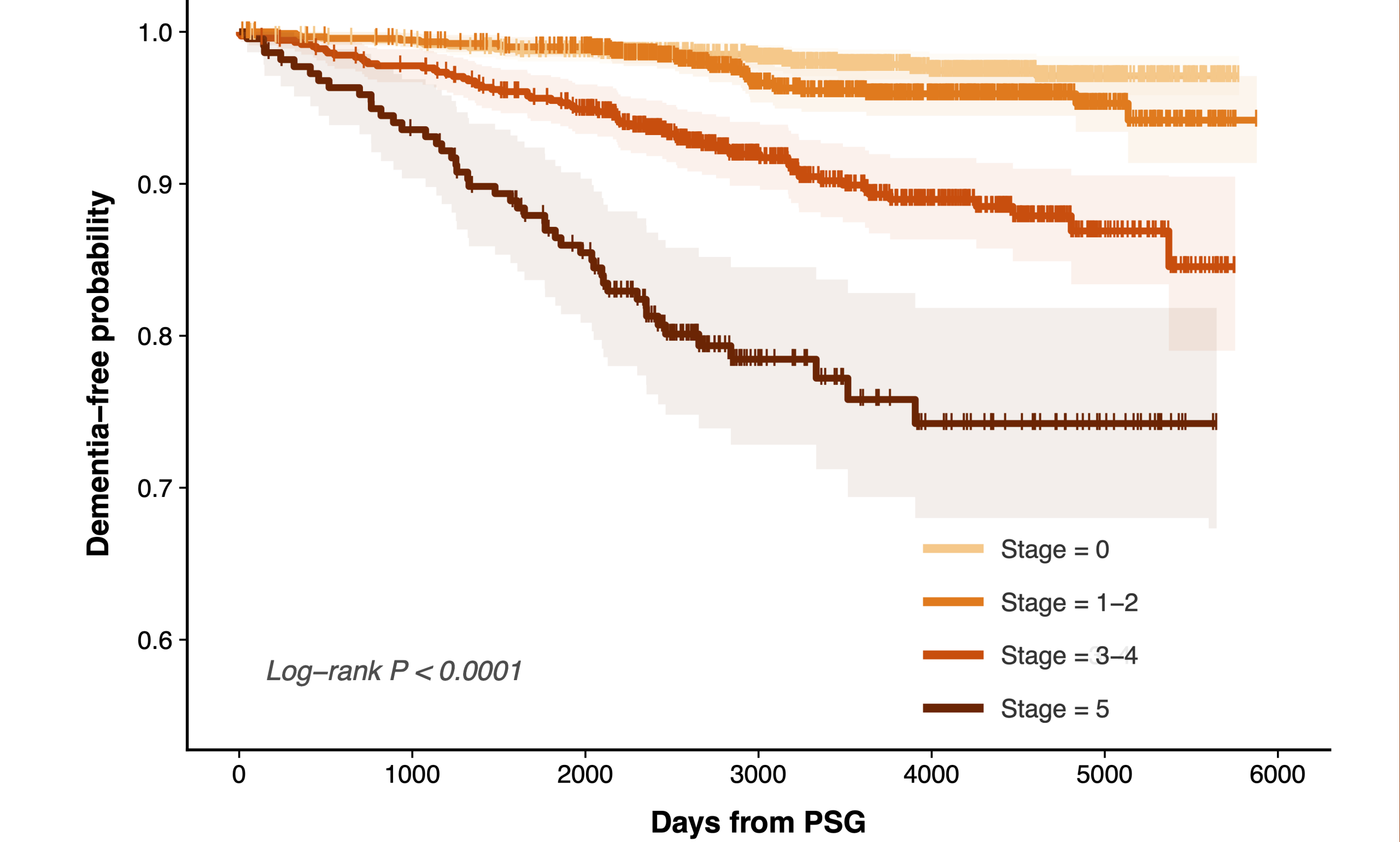


## Inferred Temporal Progression of Sleep EEG Abnormalities



**Positional variance diagram**  
Darker colors indicate higher probability of event ordering.  
Log-likelihood ratio test supported one pattern instead of ≥2 subtypes.  
Ten-fold cross-validation confirmed the robustness of the inferred event ordering.

## Late stage: 4× Dementia Risk, 3x Mortality Risk



|               | Incident Dementia<br>N (%) | Dementia free<br>N (%) | Dementia Risk<br>HR (95% CI) | Death Risk<br>HR (95% CI) |
|---------------|----------------------------|------------------------|------------------------------|---------------------------|
| Stage 0 (ref) | 38 (22.6%)                 | 1414 (53.0%)           | 1.00                         | 1.00                      |
| Stage 1-2     | 17 (10.1%)                 | 385 (14.5%)            | 1.06 (0.59, 1.92)            | 1.09 (0.49, 2.42)         |
| Stage 3-4     | 26 (15.5%)                 | 423 (15.9%)            | 2.11 (1.23, 3.61)            | 1.52 (0.72, 3.22)         |
| Stage 5       | 87 (51.8%)                 | 444 (16.7%)            | 4.13 (2.27, 7.52)            | 2.93 (1.30, 6.61)         |

## Conclusion

- We applied a novel disease progression model to resolve the temporal sequence of sleep microstructural decline in dementia development.
- Early alterations involve theta activity and slow oscillations, followed by spindle–SO coupling disruption and spindle loss, consistent with **evolving dysfunction in arousal regulation, slow-wave generation, and thalamocortical network**.
- Advanced stages were independently associated with **2x to 4x dementia risks and 3x mortality risk**.
- Sleep EEG represent promising biomarkers for dementia risk stratification and progression monitoring.



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