

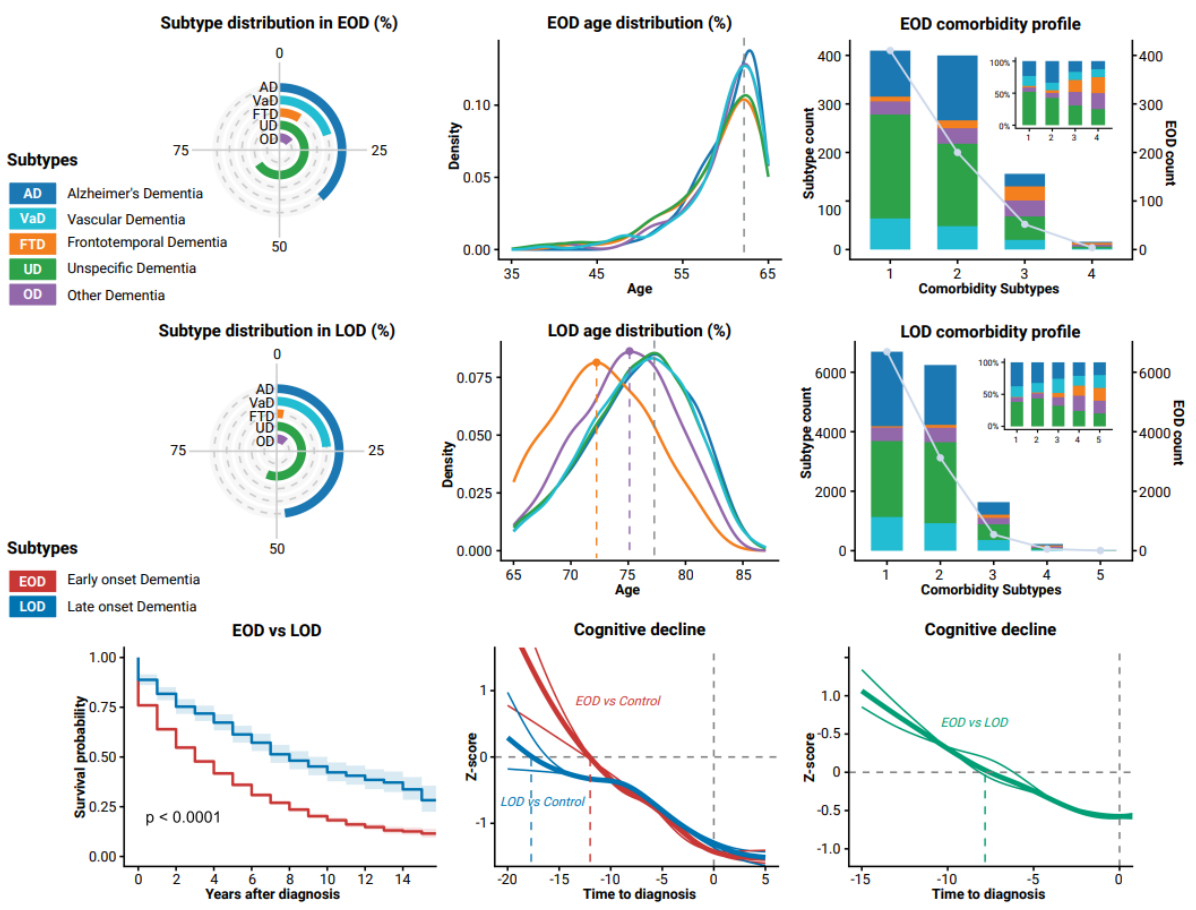
Longitudinal Analysis Of A Large-scale UK Dementia Population Reveals Clinical Heterogeneity Between Late-and Early Onset Dementia

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INTRODUCTION	METHODS	RESULTS	CONCLUSIONS	REFERENCES
Dementia is a growing global health burden characterized by significant heterogeneity between late-onset (LOD) and early-onset dementia (EOD). Despite its severe personal and economic impact, EOD remains under-recognized, often presenting with atypical clinical features that lead to frequent misdiagnosis and diagnostic delays. This study performs a systematic, large-scale comparative analysis to reveal critical differences in subtypes, prognosis, and cognitive decline between EOD and LOD.	The study identified over 10,000 dementia cases from the UK Biobank. Participants were stratified into EOD and LOD groups based on a 65 year age threshold. We first compared subtype distributions and age onset patterns to define clinical differences. Comorbidity profiles were assessed to evaluate the systemic health burden of each group. Pre-diagnostic cognitive trajectories were analyzed to map early disease progression. Kaplan Meier curves were employed to determine prognostic variations.	Alzheimer’s disease and vascular dementia are widely distributed across both EOD and LOD. EOD group shows a higher proportion of frontotemporal dementia (FTD) and unspecified dementia than LOD. FTD and other dementia subtypes in the LOD group exhibit a younger onset trend, whereas age distributions across EOD subtypes remain consistent. Multiple dementia diagnoses are prevalent across both groups, with FTD frequently presenting as a comorbidity. EOD carries a significantly better prognosis, likely due to age factors. The onset of pre-diagnostic cognitive decline in EOD occurs approximately six years later than in LOD. However, the rate of decline is more rapid in EOD, resulting in lower cognitive scores during the seven years preceding diagnosis compared to the LOD group.	This research clarifies the distinct clinical trajectories of EOD and LOD, providing a foundation for precision management. The discovery of more aggressive cognitive decline in EOD despite longer survival highlights a unique period for intervention and a prolonged need for specialized care. These findings challenge the current guidelines and resource allocation to reduce diagnostic delays and improve outcomes for younger patients. 	• Rong X, et al. <i>Alzheimers Dement</i>. 2025 Nov;21(11):e70921. • Dammer EB, et al. <i>Sci Transl Med</i>. 2024 Jun 26;16(753):eadn3504. • Shantaraman A, et al. <i>Mol Neurodegener</i>. 2024 Aug 6;19(1):60 • Erik J et al. <i>Nat Neurosci</i>. 2022 Feb;25(2):213-225. • Ray NR, et al. <i>Alzheimers Dement</i>. 2023 Sep;19(9):4187-4195. CONTACT Email:shulm@gzhmu.edu.cn 