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Functional–behavioral patterns associated with care-related risk in hospitalized patients with Alzheimer's disease: a real-world clustering analysis

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Abstract

Background

Alzheimer's disease (AD) exhibits substantial heterogeneity in functional impairment and behavioral symptoms beyond cognitive decline. However, clinically applicable multidimensional stratification approaches remain limited in real-world inpatient settings.

Methods

This retrospective cross-sectional study included 118 hospitalized patients with clinically diagnosed AD. Functional ability and behavioral symptoms were assessed using the Barthel Index (BI) and Nurses' Observation Scale for Inpatient Evaluation (NOSIE). Spearman correlation and K-means clustering were performed to identify functional–behavioral subtypes and characterize care-related risk profiles.

Results

Functional ability showed a weak correlation with behavioral burden (Spearman $\rho = -0.30$), indicating functional–behavioral dissociation. Three subtypes were identified: Subtype 1 with severe functional impairment and psychomotor retardation; Subtype 2 with preserved function and mild behavioral symptoms; Subtype 3 with intermediate impairment and prominent psychotic symptoms. Significant differences were observed in feeding, toileting, walking, irritability, and behavioral burden, while demographics and comorbidities did not differ.

Conclusions

Functional–behavioral subtypes can be identified in hospitalized AD patients, supporting multidimensional risk stratification and individualized care planning.

1. Introduction

Alzheimer's disease (AD) is a progressive neurodegenerative disorder and the most common form of dementia [1]. Current estimates indicate that more than 57 million people are living with dementia globally. This number is projected to double by 2060 as a result of population aging. Consequently, AD poses a significant economic burden, with the global societal cost of dementia reaching US $1313.4 billion in 2019. Informal care accounts for 50% of total costs, followed by social care costs (including long-term care) at 34%, underscoring the dominant role of caregiving demands [1, 2]. These challenges are further reflected in the substantial care burden associated with AD, highlighting the urgent need to better characterize care-related risk and develop more targeted and individualized care strategies [3].

Beyond cognitive decline, AD is characterized by a spectrum of neuropsychiatric symptoms (NPSs), functional impairment, and behavioral changes [4, 5]. These symptoms have a profound impact on the quality of life of both patients and caregivers [6–10]. Although their presentation and progression are inherently heterogeneous across individuals, most conventional analytic approaches in AD research rely on group-level comparisons between patients and healthy controls, implicitly treating AD populations as relatively homogeneous [11, 12]. This assumption may obscure clinically meaningful variability in symptom patterns and care needs, thereby limiting our understanding of the diverse behavioral and functional phenotypes observed in AD.

To address this issue, previous studies have described the frequency and types of NPSs, including agitation, depression, apathy, and psychosis, and their relationship with daily functioning, highlighting marked variability in both behavioral profiles and independence in activities of daily living (ADL) [13, 14]. Factor analysis of behavioral assessments has further shown that distinct behavioral symptom dimensions can be identified and are associated with functional status [15–18]. To date, such studies have been largely descriptive or correlational, lacking systematic classification of functional–behavioral subtypes, and insufficiently considering care-related risk stratification, limiting their applicability to individualized patient management.

More recent studies have used cluster and latent class analyses to identify latent subtypes by associating behavioral phenotypes with ADL, thereby quantifying variability in functional independence and behavioral profiles among patients [19–23]. Neuroimaging data have also been integrated to explore the neural correlates of these subtypes by linking distinct behavioral profiles to brain connectivity patterns or regional atrophy [19, 20, 22, 23]. These approaches have identified several reproducible subtypes, such as apathy-dominant, agitation-dominant, or mixed profiles [24]. Most of these studies, however, were conducted in community-based or electronic health record cohorts rather than real-world inpatient populations. In addition, functional and behavioral measures were not always jointly considered, and validation across independent inpatient datasets remains limited.

Here, we aimed to provide a framework for care-related risk stratification and individualized management in hospitalized patients with AD. To do so, we used k-means clustering to identify data-driven functional–behavioral subtypes of AD in a real-world inpatient setting. We analyzed measures of functional ability and behavioral symptoms in hospitalized patients with AD to define stable and clinically interpretable subtypes. We then characterized each subtype based on its functional and behavioral profile and examined differences in care complexity and risk-related outcomes across subtypes.

2. Methods

2.1 Study design and participants

This retrospective cross-sectional study was conducted in the Geriatric Psychiatry Unit of a tertiary psychiatric hospital. Electronic medical records of older adult inpatients admitted between January 1,

2023, and December 31, 2025, were retrospectively reviewed. This study was approved by the Medical Ethics Committee of Shenzhen Kangning Hospital and adhered to the principles of the Declaration of Helsinki (approval No. 2025-03-13-01). Anonymous and de-identified electronic medical record data were used for analysis, and, therefore, the requirement for written informed consent was waived.

Eligible participants met the following criteria: (1) age ≥ 60 years; (2) a clinical diagnosis of AD confirmed by attending neurologists or geriatric psychiatrists according to standard clinical criteria and comprehensive clinical evaluation; and (3) availability of baseline assessments of functional ability and behavioral symptoms, measured using the Nurses' Observation Scale for Inpatient Evaluation (NOSIE) and the Barthel Index (BI). Patients were excluded if data from either the NOSIE or the BI were missing.

A total of 118 patients with AD met the inclusion criteria and were included in the analysis. All study variables, including NOSIE and BI assessments, were extracted from electronic medical records. The proposed analytical framework for this study is illustrated in Fig. 1.

Overview of the study population, assessments, and analytical procedures. The study followed a two-path design: a correlation analysis to examine functional-behavioral dissociation, and a K-means clustering approach to identify functional-behavioral subtypes, followed by subtype comparisons and characterization using heatmap visualization. AD, Alzheimer's disease; BI, Barthel Index; NOSIE, Nurses' Observation Scale for Inpatient Evaluation.

2.2. Measurements

2.2.1 Behavioral symptoms

Behavioral symptoms were assessed using the NOSIE, a standardized nurse-rated instrument for evaluating psychiatric and behavioral manifestations in inpatient settings [25]. The scale comprises 30 items scored on a 0–3 frequency scale (0 = none, 3 = almost always) and is aggregated into seven subscales: Social Competence, Social Interest, Personal Neatness, Irritability, Manifest Psychosis, Retardation, and Depression. Subscale scores were calculated by summing item scores within each subscale. Negative and positive factor scores were derived by summing the corresponding subscale scores. Higher scores on negative subscales (Irritability, Manifest Psychosis, Retardation, Depression) indicate more severe behavioral disturbances, whereas higher scores on positive subscales (Social Competence, Social Interest, Personal Neatness) reflect better behavioral status.

2.2.2 Functional ability

Functional ability was assessed using the BI, a standardized instrument for evaluating independence in ADL [26]. The BI assesses performance across ten basic tasks, including feeding, bathing, grooming, dressing, bowel and bladder control, toilet use, transfers, mobility, and stair climbing. Each task is scored from 0 to 10 or 0 to 15, depending on the item, with higher scores indicating greater independence. The total BI score ranges from 0 to 100, with higher scores reflecting better functional ability [27].

2.2.3. Baseline characteristics

Baseline demographic and clinical characteristics were extracted from electronic medical records. Demographic variables included age, sex, education level, and marital status, while clinical variables comprised laboratory measures (neutrophil-to-lymphocyte ratio [NLR], creatinine, hemoglobin, and sodium [Na]) and comorbidities (hypertension and diabetes mellitus).

2.3 Statistical analysis

Continuous variables were presented as mean ± standard deviation (SD) or median (interquartile range [IQR]), as appropriate, while categorical variables were summarized as frequencies and percentages. Spearman correlation analysis was used to examine the association between functional ability (Barthel Index) and behavioral symptoms (NOSIE) to assess functional–behavioral dissociation in AD.

To explore clinical heterogeneity, K-means clustering was performed to identify distinct functional–behavioral subtypes based on the Barthel Index total score and NOSIE subscales including Social Competence, Social Interest, Personal Neatness, Irritability, Manifest Psychosis, Retardation, and Depression and the total negative score. All clustering variables were standardized to z-scores (mean = 0, SD = 1) across the full cohort prior to analysis. Euclidean distance was used as the distance metric, and the algorithm was initialized with 25 random starting configurations to ensure stability. The optimal number of clusters was determined using the elbow method and silhouette analysis [28, 29].

Differences in demographic and clinical characteristics across subtypes were assessed using one-way analysis of variance (ANOVA) for normally distributed continuous variables and the Kruskal–Wallis test for non-normally distributed variables, followed by Dunn's post hoc test where appropriate. Categorical variables were compared using the chi-square test. All statistical analyses were performed using R software (version 4.4.3), and a two-tailed P value < 0.05 was considered statistically significant.

3. Results

3.1 Baseline characteristics

The baseline characteristics of the 118 hospitalized patients with AD are summarized in Table 1. The mean age was 72.09 ± 10.31 years, and females accounted for 65.0% of the cohort. Educational attainment was heterogeneous, with 26.0% of patients having a college education or above, whereas 14.0% were illiterate. Most patients were married (64.0%), and 26.0% were widowed.

The mean Barthel Index score was 58.73 ± 18.85, indicating moderate impairment in activities of daily living. The median NOSIE total negative score was 27.00 (IQR, 18.00–38.00), reflecting a substantial burden of neuropsychiatric symptoms with considerable inter-individual variability.

Regarding laboratory parameters, the median NLR was 2.22 (IQR, 1.49–3.24), creatinine was 69.00 μmol/L (IQR, 59.00–81.50), hemoglobin was 124.00 g/dL (IQR, 111.50–134.00), and sodium (Na) was 141.70 mmol/L (IQR, 140.20–143.20). Hypertension was present in 51.0% of patients, while diabetes mellitus was present in 6.3%.

Table 1
Baseline characteristics of hospitalized patients with AD

Variables	**N = 118[1]**
Age (years)	72.09 ± 10.31
Female, n (%)	
male	41 (35%)
female	77 (65%)
Education	
illiterate	16 (14%)
primary school	24 (21%)
middle school	18 (16%)
high school	28 (24%)
college or above	30 (26%)
Marital status	
married	75 (64%)
unmarried	1 (0.9%)
divorced	10 (8.5%)
widowed	31 (26%)
Barthel Index (total score)	58.73 ± 18.85
NOSIE – Total Negative Score	27.00 (18.00, 38.00)
NLR	2.22 (1.49, 3.24)
Creatinine (μmol/L)	69.00 (59.00, 81.50)
Hemoglobin (g/dL)	124.00 (111.50, 134.00)
Na (mmol/L)	141.70 (140.20, 143.20)
Hypertension	
Yes	59 (51%)
No	56 (49%)
Diabetes mellitus	

[1]Mean ± SD; n (%); Median (Q1, Q3)

Variables	N = 118[1]
Yes	7 (6.3%)
No	105 (94%)
[1]Mean ± SD; n (%); Median (Q1, Q3)	

3.2 Functional–behavioral dissociation

We performed Spearman correlation analysis to examine the relationship between functional status, measured by the Barthel Index, and behavioral outcomes, measured by the NOSIE total negative score and its subscales. The Barthel Index showed a weak negative correlation with the NOSIE total negative score ($r = -0.30$, $P < 0.05$), indicating that higher functional independence was modestly associated with fewer overall behavioral symptoms (Fig. 2A). Scatterplot visualization showed considerable variability, with patients exhibiting similar levels of functional impairment displaying a wide range of behavioral symptom severity.

Analysis of NOSIE subscales revealed heterogeneous patterns of association (Fig. 2B, Supplementary Table S1). The Barthel Index was positively correlated with Social Competence ($r = 0.39$, $P < 0.05$) and Personal Neatness ($r = 0.39$, $P < 0.05$), indicating that better functional ability was associated with higher competence in these domains. By contrast, Psychomotor retardation (Retardation) showed a strong negative correlation with functional status ($r = -0.52$, $P < 0.05$), indicating that greater functional impairment was associated with more severe retardation. Other subscales, including Social Interest, Irritability, Manifest Psychosis, and Depression, were not significantly correlated with the Barthel Index, highlighting a degree of dissociation between functional decline and specific behavioral symptoms.

3.3 Identification of functional–behavioral subtypes

K-means clustering based on standardized functional (Barthel Index) and behavioral (NOSIE) measures identified three distinct functional–behavioral subtypes among hospitalized patients with AD (Subtype 1: 29 participants; Subtype 2: 51 participants; Subtype 3: 38 participants). Clustering was performed using standardized scores of the Barthel Index and behavioral dimensions derived from the NOSIE, including Social Competence, Social Interest, Personal Neatness, Irritability, Manifest Psychosis, Retardation, and Depression. As illustrated by the two-dimensional distribution of functional ability and behavioral disturbance (NOSIE total negative score) (Fig. 3A), we found that the three subtypes occupied distinct regions of the functional–behavioral space. This distribution reflects heterogeneous combinations of functional impairment and behavioral symptom severity, rather than a single severity continuum.

ANOVA showed that the Barthel Index, Retardation, Manifest Psychosis, and Social Competence had the highest F-values, indicating that these variables contributed most strongly to subtype differentiation (all $P < 0.001$; Supplementary Table S2). These variables were therefore considered the most discriminative features. Clustering, however, was performed using the full set of functional and behavioral variables, while these four domains were selected for visualization to enhance interpretability.

The three subtypes demonstrated clearly distinct functional–behavioral profiles (Fig. 3B). Subtype 1 was characterized by marked functional impairment, elevated psychomotor retardation, and reduced social competence, with relatively lower levels of psychotic symptoms. Subtype 2 exhibited relatively preserved functional ability and generally mild behavioral disturbances across domains. By contrast, Subtype 3 showed intermediate functional impairment but was distinguished by prominent psychotic symptoms.

3.4 Comparison of demographic and clinical characteristics across subtypes

We found no significant differences among the three subtypes in demographic characteristics, including age, sex, education level, and marital status, or in clinical comorbidities such as hypertension and diabetes mellitus (all $P > 0.05$). These results indicate that the identified clusters were not driven by baseline demographic or clinical heterogeneity.

We did, however, detect significant inter-subtype differences in several key clinical indicators (all $P < 0.001$; Table 2). The three subtypes differed significantly in functional status measures, including feeding, toileting, and walking ability. Irritability scores also varied significantly across subtypes.

Table 2
Demographic and clinical characteristics of AD across three subtypes

Variables	Subtype 1	Subtype 2	Subtype 3	p-value
Age (years)	74.34 ± 9.70	70.18 ± 10.89	72.95 ± 9.75	0.183
Sex, n (%)				0.287
male	13(44.8%);	18(35.3%);	10(26.3%);	
female	16(55.2%)	33(64.7%)	28(73.7%)	
Education				0.483
illiterate	5(17.9%)	4(8.0%)	7(18.4%)	
primary school	3(10.7%)	10(20.0%)	11(28.9%)	
middle school	6(21.4%)	8(16.0%)	4(10.5%)	
high school	6(21.4%)	15(30.0%)	7(18.4%)	
college or above	8(28.6%)	13(26.0%)	9(23.7%)	
Marital status				0.269
married	19(65.5%)	34(66.7%)	22(59.5%)	
unmarried	0(0.0%)	1(2.0%)	0(0.0%)	
divorced	0(0.0%)	6(11.8%)	4(10.8%)	
widowed	10(34.5%)	10(19.6%)	11(29.7%)	
NLR	2.41 (1.68, 3.31)	1.95 (1.27, 3.01)	2.37 (1.94, 3.96)	0.116
Creatinine (μmol/L)	69.00 (58.25, 81.75)	69.00 (61.00, 80.00)	71.00 (57.00, 83.00)	0.948
Hemoglobin (g/dL)	121.00 (104.25, 130.75)	124.00 (114.00, 137.00)	125.00 (111.00, 132.00)	0.38
Na (mmol/L)	141.55 (139.05, 143.32)	141.50 (140.20, 142.50)	142.15 (140.53, 143.50)	0.206
Hypertension				
Yes	14(48.3%)	26(51.0%)	19(54.3%)	0.89
No	15(51.7%)	25(49.0%)	16(45.7%)	
Diabetes mellitus				0.135
Yes	4(15.4%)	2(3.9%)	1(2.9%)	
No	22(84.6%)	49(96.1%)	34(97.1%)	

Variables	Subtype 1	Subtype 2	Subtype 3	p-value
Feeding	5.00 (5.00, 5.00)	5.00 (5.00, 10.00)	5.00 (5.00, 5.00)	< 0.05
Toileting	5.00 (0.00, 5.00)	5.00 (5.00, 10.00)	5.00 (5.00, 5.00)	< 0.05
Walking	5.00 (5.00, 10.00)	15.00 (10.00, 15.00)	10.00 (10.00, 10.00)	< 0.05
Irritability	12.00 (6.00, 24.00)	10.00 (4.00, 15.00)	24.00 (20.00, 25.50)	< 0.05

ANOVA for normally distributed continuous data; Kruskal-Wallis for non-normally distributed data; Chi-square or Fisher's exact test for categorical data. P < 0.05 was considered statistically significant.

3.5 Functional and behavioral differences across subtypes

To assess differences in clinically interpretable functional and behavioral outcomes across subtypes, we compared BI scores and total negative behavioral symptoms (NOSIE total negative score).

Functional status, assessed by the Barthel Index, differed significantly among subtypes (ANOVA, $P < 0.05$). Subtype 2 exhibited the highest level of functional independence, whereas Subtype 1 showed the greatest functional impairment, with Subtype 3 demonstrating intermediate functional performance (Fig. 4A). Pairwise post hoc analyses confirmed significant differences between all subtype comparisons (all adjusted $P < 0.05$).

Similarly, overall behavioral symptom severity, measured by the NOSIE total negative score, varied significantly across subtypes (Kruskal–Wallis test, $P < 0.05$; Fig. 4B). Subtype 3 exhibited the highest burden of negative behavioral symptoms, Subtype 2 the lowest, and Subtype 1 an intermediate level. Pairwise post hoc analyses also confirmed significant differences between subtypes (all adjusted $P < 0.05$).

3.6 Care-related risk profiles across subtypes

To further characterize subtype-specific patterns, we visualized standardized care-related indicators using a heatmap (Fig. 5), which revealed distinct risk profiles across functional, behavioral, and biological domains. Subtype 1 showed the highest levels of functional dependency, particularly in feeding, toileting, and mobility, accompanied by a moderate behavioral burden and relatively preserved biological status. Subtype 2 showed consistently low levels across most functional and behavioral indicators, indicating a comparatively low care burden; however, reduced hemoglobin levels suggested potential underlying physiological vulnerability. By contrast, Subtype 3 was characterized by an elevated behavioral burden, particularly irritability and overall negative symptoms, along with increased inflammatory and metabolic risk markers, indicating a more complex and higher-risk care profile. These patterns highlight clear heterogeneity in care-related needs across subtypes, supporting the clinical relevance of subtype-specific risk characterization.

From a clinical perspective, these subtype-specific patterns may correspond to different care priorities. Subtype 1 may require intensified support for basic daily activities and prevention of physical complications, whereas Subtype 3 may benefit from closer behavioral monitoring and targeted management of neuropsychiatric symptoms. Although Subtype 2 appears to have a lower overall care burden, attention to underlying physiological status may still be warranted.

4. Discussion

Given the marked clinical heterogeneity of AD and the limited availability of clinically actionable stratification approaches, this study aimed to identify functional–behavioral subtypes using routinely collected clinical measures in a real-world inpatient setting [31–34]. We identified three distinct functional–behavioral subtypes based on integrated assessments of functional ability and behavioral symptoms. These subtypes were clearly separable and reflected distinct configurations of functional dependency and behavioral disturbance. Importantly, beyond statistical differentiation, they captured heterogeneous care-related risk profiles across functional, behavioral, and biological domains, underscoring their potential utility for risk stratification and individualized care.

A major contribution of this study is the extension of current AD subtyping strategies toward clinically implementable phenotyping. Previous studies have typically examined neuropsychiatric symptoms, functional impairment, or disease progression in isolation, or have relied on neuroimaging or biomarker-driven clustering approaches [19, 21, 23, 33, 34, 35, 36, 37]. Although informative, these strategies may be limited by reduced clinical interpretability and feasibility in routine care settings. In contrast, our framework integrates functional and behavioral dimensions—two domains that are directly observable, clinically meaningful, and closely linked to care needs. This multidimensional yet clinically accessible approach provides a complementary perspective to existing subtype models and may facilitate translation into real-world clinical decision-making.

Notably, the identified subtypes did not merely reflect disease severity, but rather distinct latent phenotypes characterized by different constellations of functional dependency and behavioral disturbance. This finding highlights the multidimensional nature of AD heterogeneity, in which functional decline and behavioral symptoms may evolve along partially independent yet interacting axes [38–42]. Baseline demographic and clinical characteristics were largely comparable across subtypes, suggesting that the observed heterogeneity is unlikely to be explained by conventional stratifiers such as age, sex, or comorbidity burden alone. Instead, these findings reinforce the notion that intrinsic variation in functional–behavioral manifestations represents an additional, clinically meaningful layer of AD heterogeneity.

The subtype-specific heatmap further enhanced the clinical interpretability of the classification by revealing distinct care-related risk profiles. Subtypes characterized by greater functional dependency—particularly in feeding, toileting, and mobility—are likely to require intensified nursing support and are at increased risk of complications such as malnutrition, incontinence, falls, and pressure injuries [43, 44]. In

contrast, subtypes with a higher behavioral burden, especially irritability and negative symptoms, may necessitate increased supervision, behavioral management strategies, and caregiver support [45]. These findings suggest that subtype classification may directly inform care prioritization, enabling clinicians to tailor interventions according to dominant risk domains rather than relying solely on global severity assessments.

In addition to functional and behavioral differences, variation in biological indicators, including neutrophil-to-lymphocyte ratio, creatinine, and hemoglobin, suggests that symptom profiles may co-occur with differing levels of physiological vulnerability [46, 47]. Although these markers are not disease-specific, their concordance with functional–behavioral patterns provides converging evidence supporting the robustness of the classification. The consistency of subtype-specific patterns across multiple domains further strengthens confidence in the internal coherence of the identified phenotypes despite the observational and cross-sectional nature of the data.

From a clinical implementation perspective, this framework has practical implications. Because it relies on routinely collected bedside assessments (NOSIE and BI), it can be feasibly applied in inpatient and potentially long-term care settings without additional resource burden [25, 48]. Subtype-based stratification may support early identification of high-risk patients, guide allocation of nursing and caregiving resources, and inform individualized care planning [49]. In resource-constrained healthcare systems, such an approach may improve efficiency by aligning care intensity with patient-specific risk profiles [50, 51].

The use of real-world inpatient data further enhances the translational relevance of our findings [52]. Compared with highly selected research cohorts, real-world populations better capture the complexity, comorbidity burden, and care demands encountered in clinical practice. This is particularly important in rapidly aging societies, where AD-related healthcare utilization and long-term care needs continue to increase [53, 54]. Our findings therefore provide a pragmatic framework that aligns with real-world clinical workflows.

Limitations

Several limitations should be considered. First, the cross-sectional design precludes causal inference regarding the relationships among functional impairment, behavioral symptoms, and biological indicators. Second, although key clinically relevant variables were included, additional factors—such as detailed comorbidity profiles, medication use, and biomarker data—were not available. Third, as an observational study based on electronic medical records, the potential for residual bias cannot be excluded, and external validation in independent cohorts is warranted. However, the consistency of subtype patterns across functional, behavioral, and biological domains, together with their clinical interpretability and alignment with established evidence, supports the robustness and validity of the findings.

Future research should extend this framework using longitudinal designs to examine subtype stability, transitions, and prognostic implications. Integration with multimodal data—including neuroimaging, fluid biomarkers, and digital health measures—may further refine subtype characterization and improve predictive accuracy. In addition, prospective studies evaluating subtype-guided care strategies are needed to determine whether this approach can improve clinical outcomes, reduce caregiver burden, and optimize healthcare resource utilization.

5. Conclusions

In conclusion, this study identifies clinically interpretable functional–behavioral subtypes of AD in a real-world setting and demonstrates their utility for stratifying care-related risk. By capturing the interplay between functional dependency, behavioral symptoms, and physiological vulnerability, this framework provides a practical basis for individualized care planning and resource allocation. Future studies should validate these subtypes in larger and longitudinal cohorts and integrate multimodal data to enhance their prognostic value. As the global burden of AD continues to increase, such multidimensional stratification approaches may support more efficient, targeted, and scalable care delivery.

Declarations

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Disclosure of conflict of interest

All authors report no disclosures.

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Data availability statement

The data that support the findings of this study are not publicly available because they contain confidential patient information derived from electronic medical records. De-identified data may be made available from the corresponding author upon reasonable request and with permission from the Medical Ethics Committee of Shenzhen Kangning Hospital, subject to institutional approval and applicable data protection regulations.

Ethics approval and consent to participate

This study was approved by the Medical Ethics Committee of Shenzhen Kangning Hospital and adhered to the principles of the Declaration of Helsinki (approval No. 2025-03-13-01). Anonymous and de-identified electronic medical record data were used for analysis and, therefore, the requirement for written informed consent was waived.

Consent for publication

Not applicable.

Author Contribution

J.W.Y. designed the study, collected data and drafted the original manuscript. Y.X., W.J.Y., X.Y.Y. and H.C.P. organized and analyzed the data. F.Y.T. prepared figures and tables. W.Y.J. and W.H.Q. supervised the research and revised the manuscript. All authors read and approved the final version of the manuscript.

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Figures

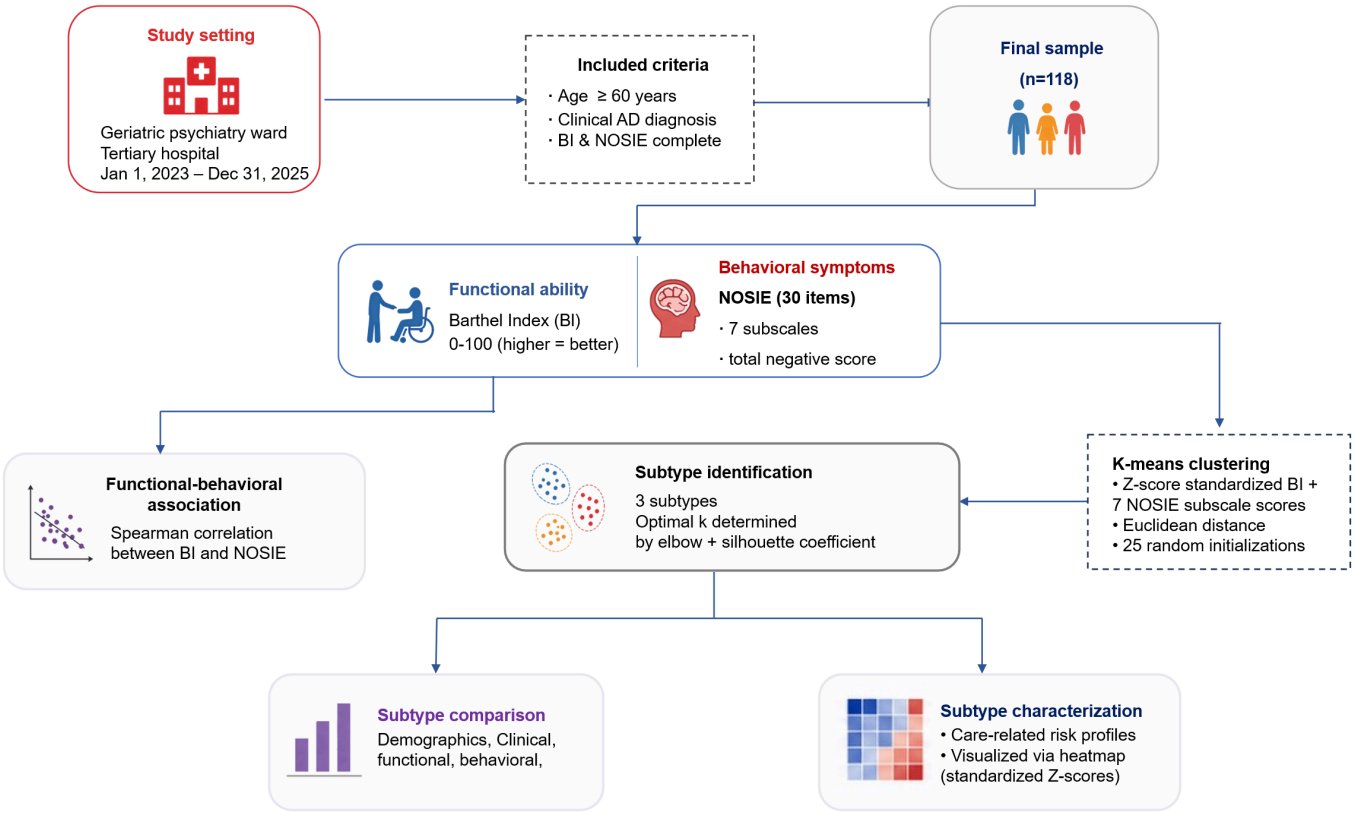

Figure 1

Study design and analytical workflow.

Overview of the study population, assessments, and analytical procedures. The study followed a two-path design: a correlation analysis to examine functional-behavioral dissociation, and a K-means clustering approach to identify functional-behavioral subtypes, followed by subtype comparisons and characterization using heatmap visualization. AD, Alzheimer's disease; BI, Barthel Index; NOSIE, Nurses' Observation Scale for Inpatient Evaluation.

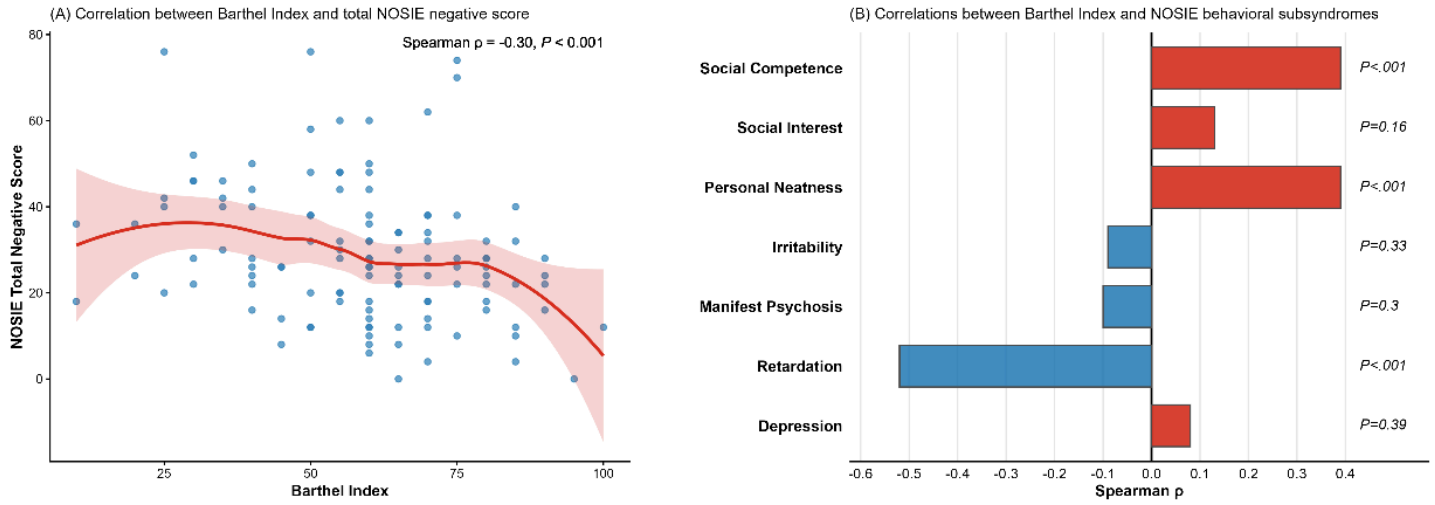

Figure 2

Functional–behavioral dissociation between Barthel Index and NOSIE measures

(A) Scatterplot showing the association between functional status (Barthel Index) and total NOSIE negative score. The solid line represents the fitted smoothing curve, and the shaded area indicates the 95% confidence interval. Each dot represents an individual participant. Spearman's ρ = -0.30, P < 0.001.

(B) Spearman correlation coefficients between the Barthel Index and NOSIE subscales. Bars represent correlation coefficients (ρ), with corresponding P values indicated. Positive correlations are shown in red and negative correlations in blue.

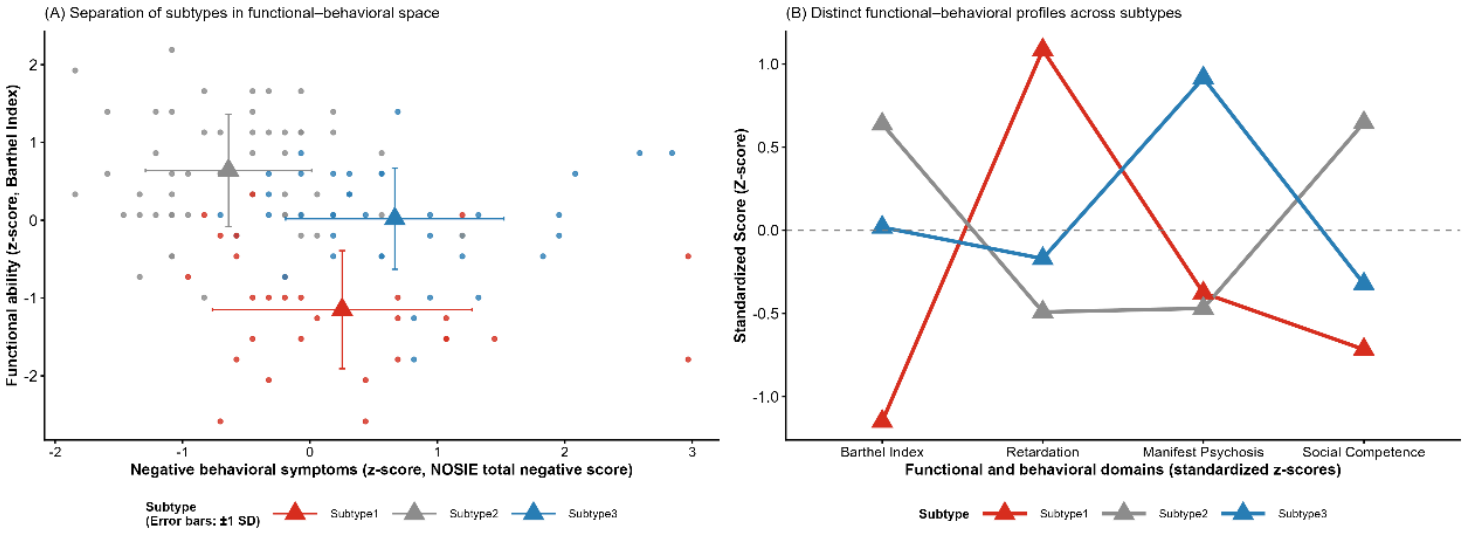

Figure 3

Functional–behavioral subtypes of AD characterized by distribution and standardized profiles.

(A) Two-dimensional distribution of functional ability (z-scored Barthel Index) and behavioral burden (z-scored NOSIE total negative score), illustrating the separation of three subtypes in functional–behavioral space. Each point represents an individual participant. Triangles indicate subtype centroids, and error bars represent ±1 standard deviation.

(B) Standardized profiles of selected functional and behavioral domains across subtypes. Values are presented as z-scores (mean = 0, standard deviation = 1). The four most discriminative variables identified by one-way ANOVA (Barthel Index, Retardation, Manifest Psychosis, and Social Competence) are shown to highlight subtype-specific patterns.

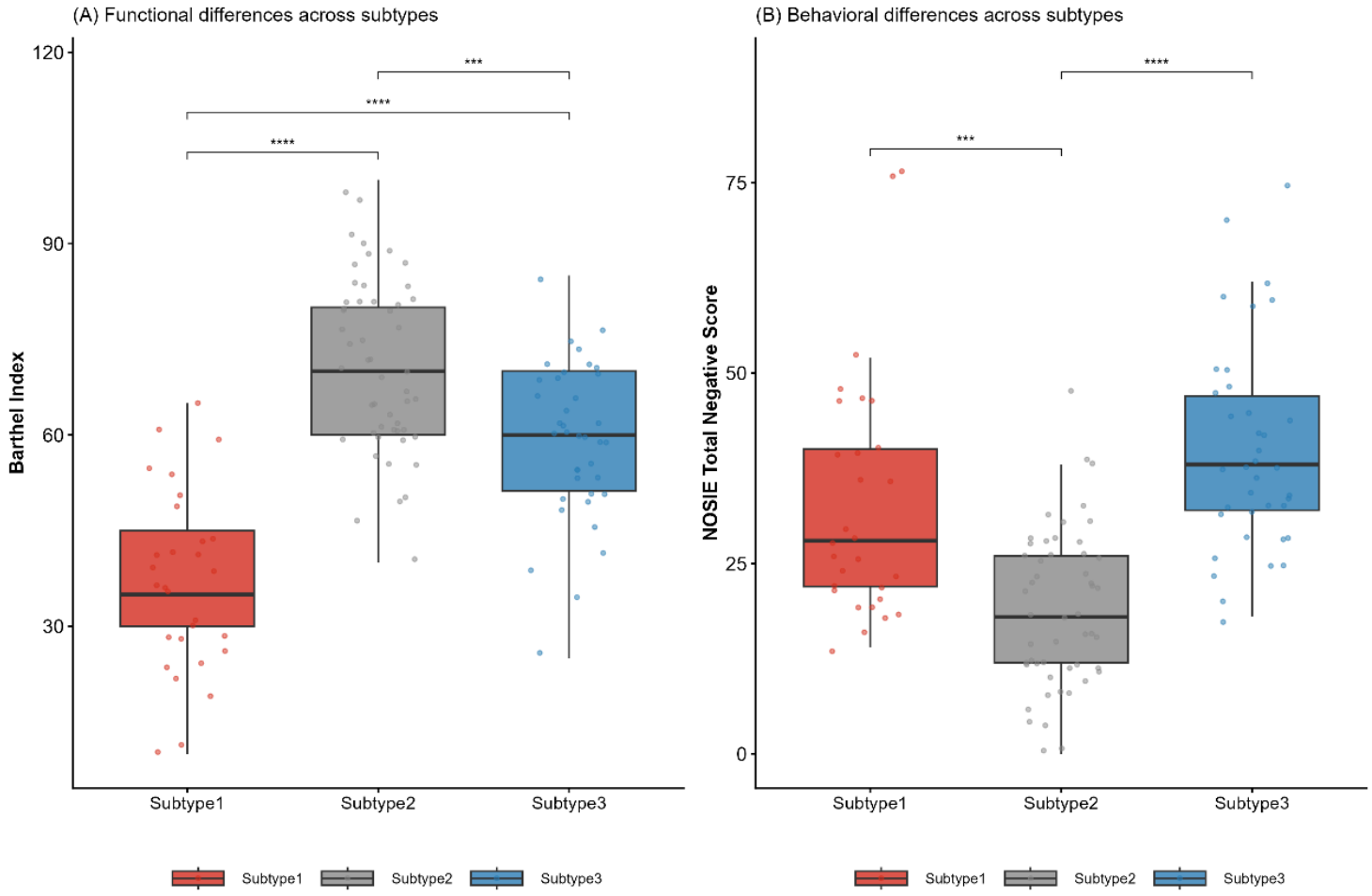

Figure 4

Functional and behavioral differences across AD subtypes.

(A) Functional ability measured by the Barthel Index across subtypes.

(B) Behavioral burden measured by the NOSIE total negative score across subtypes.

Data are presented as boxplots showing the median, interquartile range, and range, with individual data points overlaid. Group differences were assessed using one-way ANOVA (A) or Kruskal–Wallis test (B)

with post hoc comparisons. Statistical significance is indicated as ***: $P < 0.001$ and ****: $P < 0.0001$.

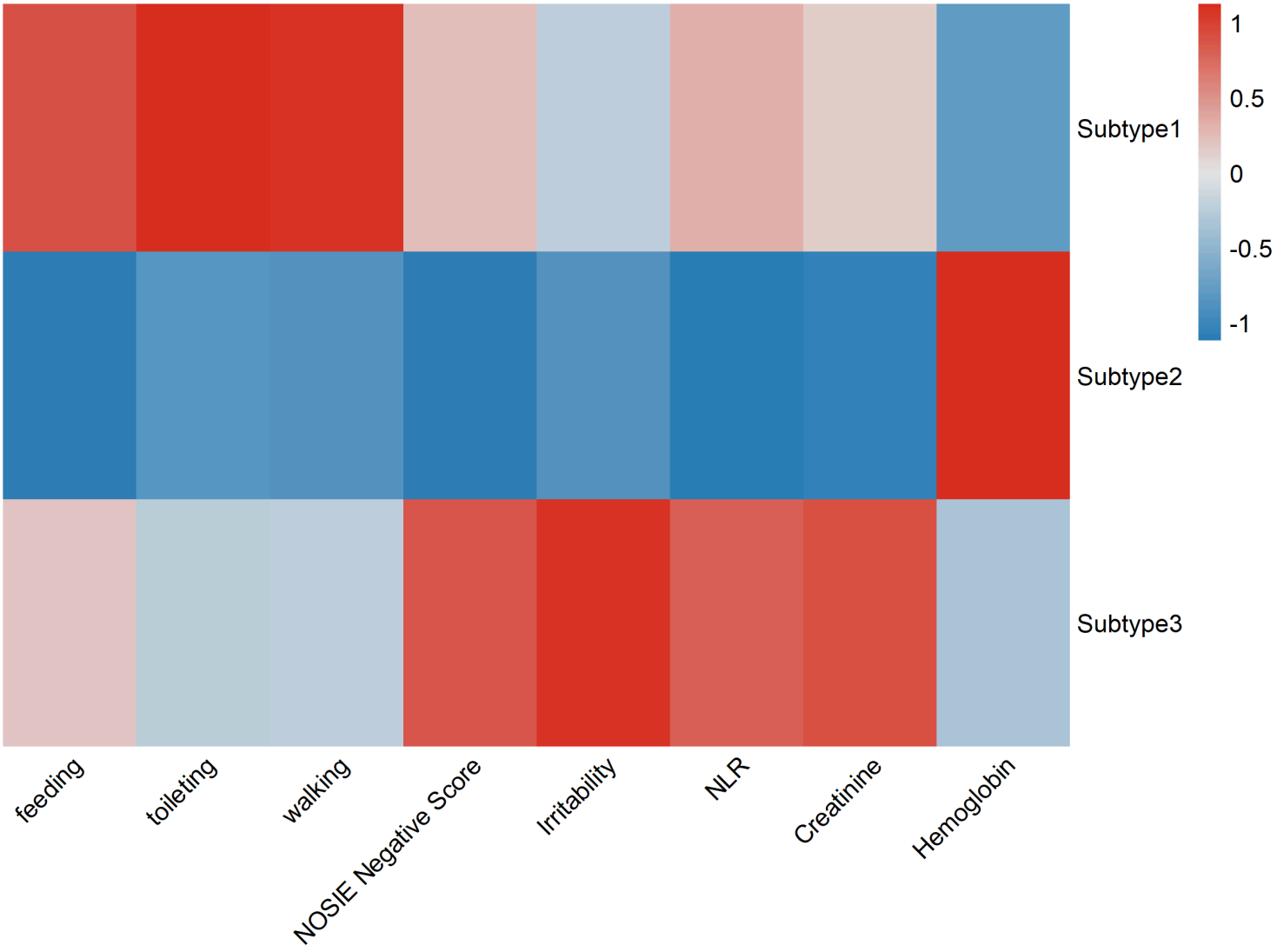

Figure 5

Care-related risk profiles across AD subtypes.

Heatmap illustrating standardized care-related indicators across three AD subtypes. Variables include functional measures (feeding, toileting, walking), behavioral measures (NOSIE total negative score, irritability), and biological markers (neutrophil-to-lymphocyte ratio [NLR], creatinine, hemoglobin). Values are presented as z-scores. Warmer colors indicate higher values,and cooler colors indicate lower values relative to the overall mean.

Supplementary Files

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