

Clinical-Biological Stage Concordance in Sporadic Alzheimer Disease

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Objective & Background

- **Apply** the revised AA–2024 biological-clinical staging framework within an active, well-characterized, research cohort from the Knight Alzheimer Disease Research Center (Knight-ADRC).
- **Identify** patterns of agreement (concordance) and disagreement (discordance) between biological and clinical stages.
- **Characterize** how these patterns impact sporadic Alzheimer's disease-staging heterogeneity.

Cohort & Biomarkers

- **Cohort:** 4,099 Knight-ADRC participants.
- **Amyloid (A β) PET:** 1,935 ¹¹C-Pittsburgh Compound-B (PiB) and 811 ¹⁸F-Florbetapir (FBP) scans.
- **Tau PET:** 907 ¹⁸F-Flortaucipir (FTP) scans.
- **Inclusion Criteria:** Any participants with Clinical Dementia Rating[®] (CDR[®]) assessment, A β PET and Tau PET within one year.

Biological Staging by PET

Classified by spatial extent using validated PET Standardized Uptake Value Ratio (SUVR) thresholds.

Scan Type / Metric	A+T- (Stage A)	A+T ⁺ _{MTL+} (Stage B)	A+T ⁺ _{MOD+} (Stage C)	A+T ⁺ _{HIGH+} (Stage D)
Amyloid PET (Centiloid > 18.42)	+	+	+	+
Medial Temporal Tau (SUVR > 1.28)	-	+	+	+
Moderate Neocortical Tau (SUVR 1.23 - 1.42)	-	-	+	+
High Neocortical Tau (SUVR >1.42)	-	-	-	+

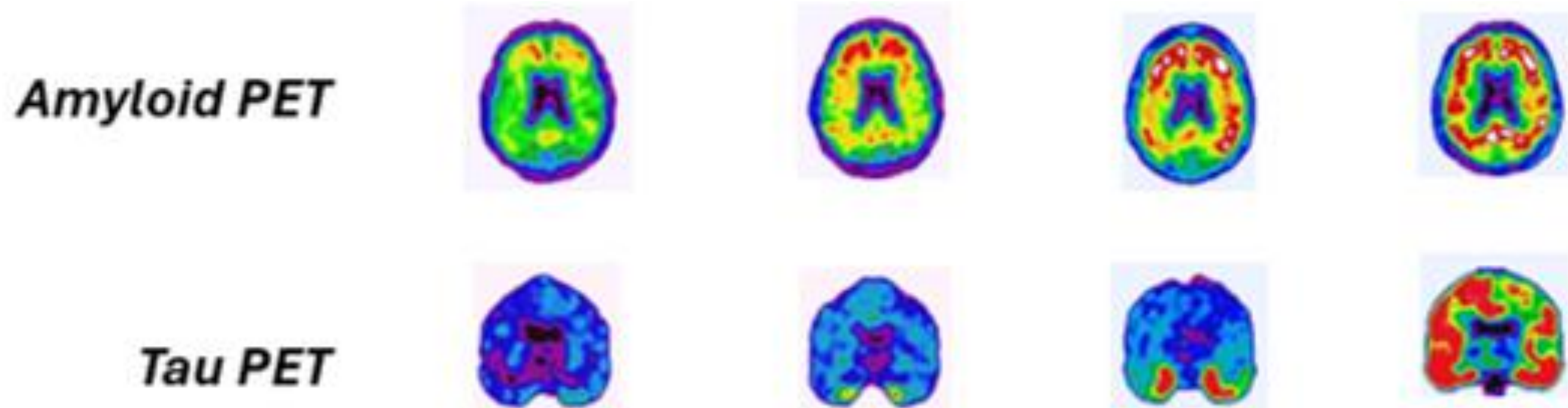


Figure 1. PET-Based Biological Staging Framework. Classification of Alzheimer's disease into four progressive biological stages using amyloid-beta (A+) and spatial tau (T+) PET biomarkers:

- **Stage A** (A+T-; regional tau negative, SUVR <1.28)
- **Stage B** (A+T⁺_{MTL+}; limited to medial temporal lobe, SUVR >1.28)
- **Stage C** (A+T⁺_{MOD+}; moderate neocortical uptake, SUVR 1.23-1.42)
- **Stage D** (A+T⁺_{HIGH+}; extensive neocortical uptake, SUVR >1.42)

Scans embedded below the table display representative amyloid and tau PET scans for each respective stage.

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Clinical Staging

Defined using CDR scale & Subjective Cognitive Decline (SCD) criteria.

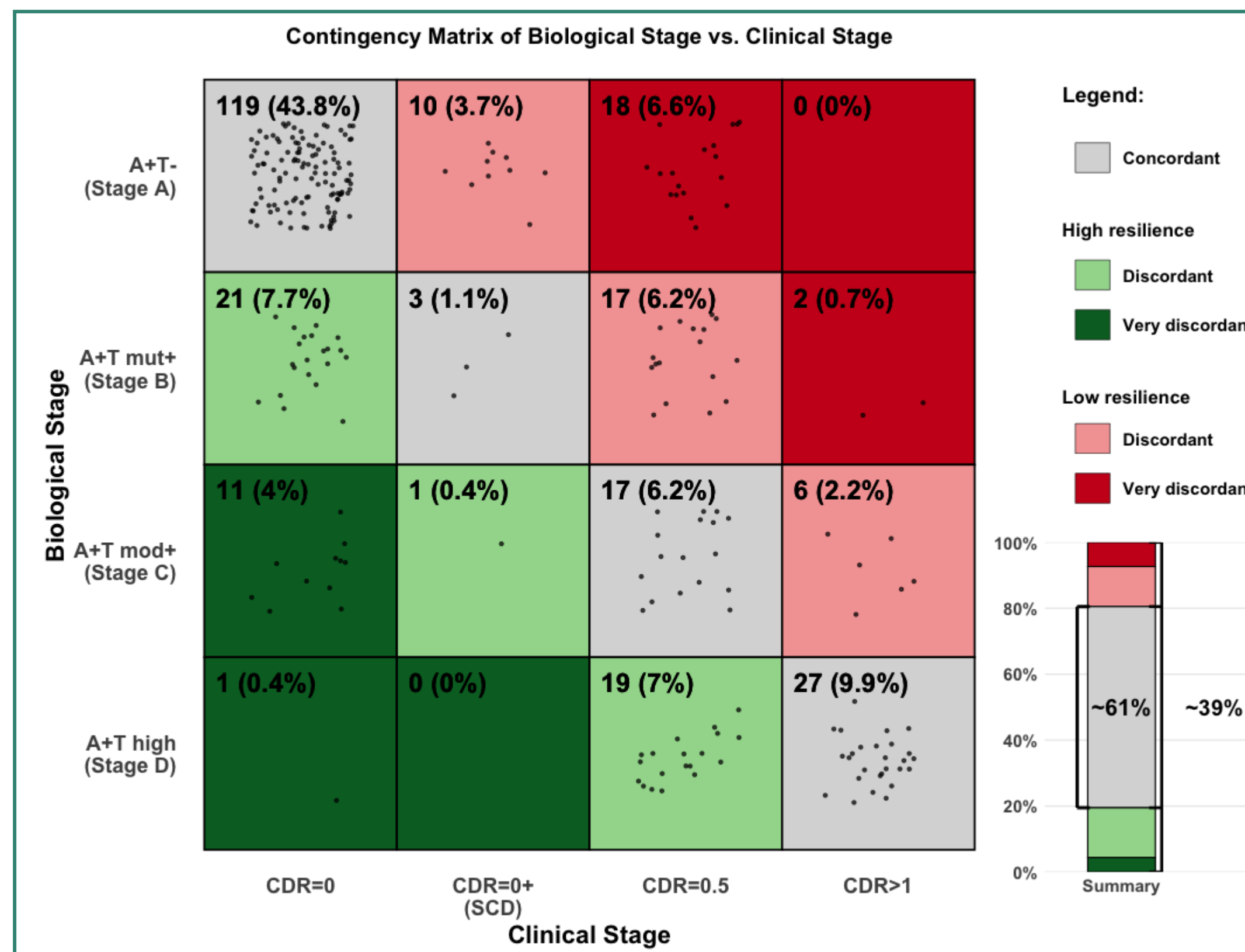
CDR=0	CDR=0 & SCD	CDR=0.5	CDR≥1		
CDR=0	CDR=0	CDR=0.5	CDR=1	CDR=2	CDR≥3
Cognitively Unimpaired	Subjective Cognitive Decline (SCD)	Cognitive Impairment with Mild Functional Impact	Dementia with Mild Functional Impairment	Dementia with Moderate Functional Impairment	Dementia with Severe Functional Impairment

Table 1. CDR staging, utilizing granular scores (0 to ≥3) and detailed clinical descriptors.

Results

- **Cohort:** 869 of 4,099 Knight-ADRC participants met full inclusion criteria; **272** were amyloid-positive (A+).
- **Concordance:** 61% (n=166) were "**Concordant**", directly matching clinical impairment to biological stage.
- **Discordance:** 39% (n=106) were "**Discordant**", split evenly between:
 - **Low Resilience:** 19.5% (n=53)
 - **High Resilience:** 19.5% (n=53)
- **Statistics:** “Concordant” cases were significantly more frequent than combined “Discordant” groups ($\chi^2=12.06$, $p=0.0005$). Post-hoc pairwise comparisons confirmed significant proportional differences across categories ($p < 0.05$).

Selected Participant Demographics by CDR Scores					
Variable	Totals	CDR = 0	CDR = 0.5	CDR ≥ 1	P-value
Sex					0.064
Woman (%)	478 (55.01%)	418 (56.87%)	40 (43.96%)	20 (46.51%)	
Man (%)	391 (44.99%)	317 (43.13%)	51 (56.04%)	23 (53.49%)	
APOE					<0.001
ε4-positive (%)	348 (40.23%)	265 (36.15%)	56 (62.92%)	27 (62.79%)	
ε4-negative (%)	517 (59.77%)	468 (63.85%)	33 (37.08%)	16 (37.21%)	



Conclusion

- **Key Finding:** The AA–2024 framework confirms a 39.0% discordance between biological and clinical stages within the Knight-ADRC cohort.
- **Future Directions:** Future research must characterize these discordant profiles by identifying non-AD co-pathologies or specific resilience factors.

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