

Identification of Persons Without Current Cognitive Decline Who Progress to Preclinical or Clinical Alzheimer's Disease

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A modified Psychometric Deterioration Score predicts future cognitive decline in cognitively normal individuals without subjective memory complaints, identifies a novel preclinical substage, Psychometric Cognitive Decline, and retains comparable predictive value to the original formula using routinely collected data.

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Introduction

- Alzheimer's disease causes substantial morbidity and mortality.
- Developing preventative strategies requires detection of **cognitively normal individuals (CNI)** at risk for future decline.
- We published an **original Psychometric Deterioration Score (oPDS)** formula that identified persons without cognitive decline at baseline who were future decliners and future non-decliners.¹

$$\text{oPDS} = (8 - (((\text{PARI}) + (\text{PARD}))/45 + ((\text{PRDI}) + (\text{PRDD}))/20 + ((\text{DESN})/10) + ((\text{WASV})/80) + ((\text{DSST})/75) + ((\text{WASDIGF}) + (\text{WASDIGB}))/17) \times 1.6)$$

- oPDS includes one measure, **WAIS vocabulary (WASV)**, that is not routinely collected in datasets.
- To further characterize and identify risk factors for cognitive decline in this Global Deterioration Scale Stage 1 substage, termed **Psychometric Cognitive Decline (PCD)**, we created a **modified PDS formula (modPDS)** removing WASV from oPDS.
- Herein we compared the validity and predictability of modPDS to oPDS, in the study cohort from our 2020 publication.

Methods

modPDS was created using the same dataset in a manner consistent with the development of oPDS. We computed oPDS and modPDS at baseline.

Discrimination of decliner status was tested and compared using slope of the oPDS versus modPDS score in logistic regression both with and without covariate adjustment (age, sex, education, follow-up time) and area-under-the-curve (AUC) of ROC curves.

Group differences were assessed with t-test and Wilcoxon Rank-Sum Test. Time-to-decline was modeled using Weibull regression.

In logistic models, $\beta > 0$ indicates higher odds of future decline with higher PDS. In Weibull models $\beta < 0$ indicates faster time-to-decline with higher PDS.

Chi-square (χ^2) statistic used to summarize model fit improvement over the intercept-only model in the Weibull analyses; larger χ^2 with small p-values indicates better improvement.

Results

Summary of statistical results for oPDS¹ and modPDS²

Analysis	Model	Statistics	oPDS	modPDS
Group comparison (t-test)	---	t, p	t = 2.80, p = 0.014	t = 2.85, p = 0.013
Group comparison (Wilcoxon Rank Sum Test)	---	p	p = 0.008	p = 0.006
Logistic regression	Unadjusted		$\beta = 0.177$, p = 0.008	$\beta = 0.181$, p = 0.005
Logistic regression	Fully adjusted ³		$\beta = 0.206$, p = 0.013	$\beta = 0.195$, p = 0.016
Logistic regression	Adjusted (no age) ⁴		$\beta = 0.250$, p = 0.002	$\beta = 0.239$, p = 0.002
Weibull time-to-decline	Unadjusted	β , p	$\beta = -0.230$, p = 0.002	$\beta = -0.254$, p = 0.001
Weibull time-to-decline	Adjusted (no age)	β , p	$\beta = -0.273$, p = 0.009	$\beta = -0.286$, p = 0.005
Weibull time-to-decline	Adjusted (with age) ⁵	β , p	$\beta = -0.127$, p = 0.298	$\beta = -0.148$, p = 0.222
AUC Discrimination ⁶	Unadjusted	AUC	0.776	0.782
	Fully adjusted		0.864	0.864
	Adjusted-no age		0.861	0.848
Model fit (Weibull)	Unadjusted	χ^2 , p	$\chi^2 = 8.78$, p = 0.003	$\chi^2 = 10.67$, p = 0.001

1. oPDS, Original Psychometric Deterioration Score formula. 2. modPDS, Modified Psychometric Deterioration Score formula. 3. Fully adjusted, includes all covariates (age, sex, education, and follow-up time). 4. Adjusted (no age), excludes age but includes sex, education, and follow-up time. 5. Adjusted (with age) is used for the Weibull time-to-decline models and includes all covariates. 6. AUC (Area Under the Receiver Operating Characteristic [ROC] Curve) quantifies discrimination between decliners and non-decliners (0.5=no discrimination; 0.7=fair; 0.8=good; 0.9=excellent). The reported AUCs indicate good-to-excellent discriminative performance of both oPDS and modPDS.

- Both oPDS and modPDS were higher at baseline, reflecting poorer performance in individuals who later declined versus non-decliners.
- Each score was significantly associated with decliner status across logistic models with different covariate specifications.
- In Weibull models, higher baseline scores predicted faster time-to-decline; adjustment for age attenuated these associations, while age itself predicted shorter time-to-decline.
- Discriminative performance (AUC) was good-to-excellent for both scales: oPDS AUCs were 0.776 (unadjusted) and 0.864 (fully adjusted); modPDS AUCs were 0.782 (unadjusted) and 0.864 (fully adjusted).

Reference

¹ Reisberg, B., et. al., Psychometric Cognitive Decline Precedes the Advent of Subjective Cognitive Decline in the Evolution of Alzheimer's Disease. *Dementia and Geriatric Cognitive Disorders*. 2020;49(1):16-21.



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Conclusions

Removing WASV did not diminish the predictive utility of oPDS.

modPDS performs comparably to oPDS for identifying future decliners and predicting progression, with AUCs indicating good-to-excellent discrimination.

These results support modPDS as a practical, valid tool for characterizing Psychometric Cognitive Decline and for risk stratification.