

Prediction of 5-year Future Dementia Onset Using a Novel ADL Scale Designed by Mathematical Optimization

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A novel 12-item hybrid Activities of Daily Living (ADL) scale based on the most useful items from the Frequent Activities Questionnaire (FAQ) and the Everyday Cognition (ECog) scales based on data-driven recursive optimization, significantly improves on the 12-item ECog-12, the 39-item ECog, the 10-item FAQ, and the 20-item Mini-Mental State Examination (MMSE) in predicting 5-year future dementia onset (FDO). It displays an ROC-AUC value of 0.94, and a shorter 8-item version displays an ROC-AUC value of 0.93.

INTRODUCTION	METHODS	RESULTS	CONCLUSION
Activities of Daily living (ADL)¹ questions are often incorporated into patient interviews to help assess cognitive decline, but the specific questions asked and assessment of the responses are often <i>ad hoc</i>. Several quantitative ADL scales perform comparably to cognitive screens like the Mini-Mental State Examination (MMSE) for detecting dementia²⁻⁴, but are less widely used in clinical practice. Prior research on ADL scales has focused mainly on assessing diagnostic accuracy for dementia and MCI²⁻⁴. However, the ability to predict future dementia onset (FDO) would be best for assessing the potential efficacy of recently available disease modifying therapies^{5,6}. A 12-item shortened version of the Everyday Cognition (ECog) scale⁷, the ECog-12⁸, has been developed because the full 39-item scale is time-consuming to administer. Recently, the ECog-12 was shown to significantly predict future dementia onset compared to at-chance performance⁹, but it was not compared to any other ADL scales or cognitive tests. Here we used data-driven recursive optimization to design a 12-item and an 8-item hybrid ADL (hADL) scale for predicting 5-year future dementia onset based on extensive longitudinal data from the Alzheimer's Disease Neuroimaging Initiative (ADNI) dataset¹⁰. We incorporated the most useful items from the full ECog (administered to both patients and study partners), and Frequent Activities Questionnaire (FAQ – administered to study partners)¹¹ based on a greedy recursive build-up procedure for optimizing prediction of 5-year FDO. We rigorously evaluated predictive ability using Montecarlo cross-validation to compare our new 8-item and 12-item hADL scales to not only the ECog-12, but also full versions of the ECog, FAQ, and MMSE.	Step 0: We constructed an 89-item ADL question library by combining questions from the 39-item ECog-SP (administered to study partners), the 39-item ECog-PT (administered to patients), the 10-item FAQ (administered to study partners), and 1 general patient concern question. Data were compiled for cognitively unimpaired (CU, n = 404) and mild cognitive impairment (MCI, n = 377) participants who either converted to dementia within a 5-year window or survived dementia-free beyond that window. Step 1: Select the item from the library that has the highest ROC-AUC value for predicting 5-year FDO. Step 2: From the remaining ADL library items, select another item that, when combined with the first, yields the highest ROC–AUC for predicting 5-year FDO. Step 3: Repeat Step 2 recursively. At each iteration, add one item from the items remaining in the ADL library. Choose the item that, when combined with the currently selected set, yields the highest ROC–AUC for predicting 5-year FDO. Step 4: Compare the 8-item and 12-item sets generated in Step 3 as a novel hybrid ADL scale to the ECog-12, full ECog, full FAQ, and MMSE using cross-validated analyses.	<i>Optimally recursive item selection constructs a novel hybrid ADL (hADL) scale that can provide improved prognostic accuracy compared to current tools</i> <i>Statistical comparison of 8-item and 12-item versions of the optimal recursive hADL scale with current ADL scales and the MMSE for predicting 5-year future dementia onset.</i>	• Data-driven optimal recursive item selection from a library of 89 FAQ and ECog questions constructs a 12-item hybrid ADL scale that significantly outperforms current scales at predicting 5-year future dementia onset. • An 8-item version of our hADL scale performs nearly as well the 12-item version and nominally outperforms the the ECog 12, full ECog, and full FAQ scales as well as the MMSE. • Item-level data-driven design can improve the prognostic accuracy of cognitive assessment.
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