neuropsychological test scores in older surgical patients presenting for elective spine operations. **Methods:** This was a prospective cohort study of 52 patients aged 65-89 years, having elective, inpatient spine surgery under general anesthesia. To determine the validity of cognitive screening using the Mini-Cog, we compared Mini-Cog scores with neuropsychological test scores. Neuropsychological tests included Digit Symbol Substitution to test attention and concentration, Animal Category Fluency and Trail Making Tests A & B to test executive function, and CERAD Word List Delayed Recall, Logical Memory Immediate & Delayed Recall to test Memory. Clinical Dementia Rating (CDR) and Instrumental Activities of Daily Living (IADL) were also assessed. **Results:** Of 52 patients enrolled, 9 patients scored between 0-2 (compatible with cognitive impairment) on the Mini-Cog, while 43 scored between 3-5. There were significant differences between the two groups in Digit Symbol Substitution Test scores (p=0.02), CERAD Word List Delayed Recall (p=0.05), Trail Making Test A (p<0.001), and Trail Making Test B (p<0.01). (See table) Of note, there was no difference between the two groups Mini-Mental State Examination scores. The two groups also had significantly different Clinical Dementia Ratings (p=0.02) and Instrumental Activities of Daily Living scores (p<0.01). **Conclusions:** These data support the validity of administering the Mini-Cog as a brief screening tool for cognitive impairment in older patients presenting for elective spine surgery.

Association of Mini-Cog Score with Neuropsychological Test Score

	Mini-Cog Score 0-2 (n=9)	Mini- Cog Score 3-5 (n=43)	
Digit Symbol Substitution Test Score	31.22	42.87	p= 0.02
Animal Category Fluency Score	15.67	17.74	p=0.23
CERAD Word List Delayed Recall	4.44	5.67	p=0.05
Logical Memory Immediate Recall	8.66	10.36	p=0.35
Logical Memory Delayed Recall	7.89	9.46	p=0.31
Trail Making Test A	67.75	35.09	p<0.001
Trail Making Test B	170.11	103.39	p<0.01
Mini-Mental State Examination	27.33	27.79	p=0.52
Clinical Dementia Rating	1	0.43	p=0.02
Instrumental Activities of Daily Living	7.33	2.79	p<0.01

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AN EHR-BASED COHORT DISCOVERY TOOL FOR IDENTIFYING PROBABLE AD

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Background: Electronic health records (EHRs) contain decades of longitudinal clinical data on hundreds of thousands of potentially at-risk individuals for Alzheimer's disease (AD). The ability to automatically identify probable AD patients within EHRs would facilitate downstream computational analyses on such large-scale datasets, by eliminating the need for labor intensive chart review. To this end, we developed and validated a cohort discovery tool that can be applied to EHR data for automatic classification of individuals with AD. **Methods:** We extracted EHR data from Michigan Medicine's Research Data Warehouse (RDW) pertaining to Michigan Alzheimer's Disease Center (MADC) participants with a consensus-based diagnosis ranging from cognitively normal to probable AD. We investigated the accuracy of different EHR-based rules for identifying patients with AD. Rules were based on combinations of criteria pertaining to ICD diagnoses, medications, laboratory results and encounter types. Applied to data from the RDW, these rules were evaluated against MADC diagnoses (Figure 1), in terms of sensitivity, specificity, and positive predicted value (PPV). To optimize for the probability that patients identified by the rule have AD, we prioritized PPV when ranking different rules. **Results:** MADC and RDW records overlapped in 624 patients 65 years and older. Though a diagnostic code for AD alone resulted in relatively low specificity, combination with an encounter involving medium/high complexity medical decision making resulted in increased specificity and the highest PPV (Figure 2). This rule yielded a PPV, specificity, and sensitivity of 0.82 (95% confidence interval (CI) 0.75-0.87), 0.95 (95%CI 0.93-0.97), and 0.65 (95%CI 0.60-0.68) respectively. For true positives, the first RDW diagnosis of probable AD occurred on average three years before the first MADC diagnosis (95% CI 2.3-3.7 years). Applied to the entire RDW, this rule identified 4,152 patients with probable AD. **Conclusions:** EHR-based criteria can automatically and accurately identify patients with probable AD. Applied to large longitudinal EHR datasets, these labels can be used for downstream analyses, e.g., modeling patient trajectories of disease progression.

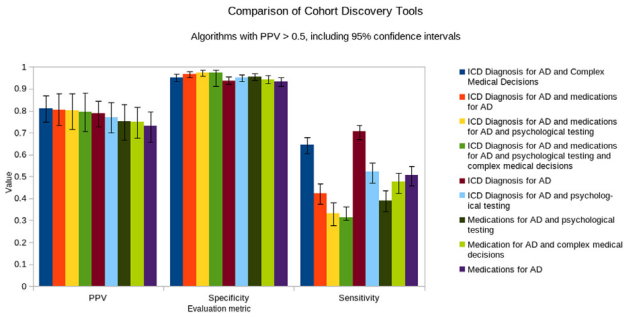

Figure 2: EHR-based rules with a PPV greater than 0.5 for identifying AD. Error bars correspond to 95% confidence intervals over 1,000 bootstrapped samples. Complexity in medical decisions is measured by the amount and variety of patient data examined by a physician, patient risk, and treatment options, as defined by CPT codes 99214 and 99215.

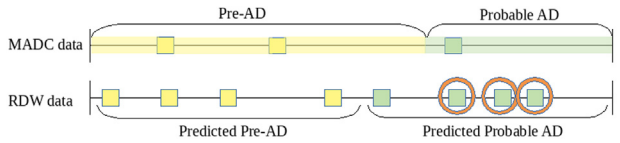

Figure 1: Comparing MADC and RDW encounters for a sample patient. Each row represents a timeline for the respective dataset, and encounters are indicated with squares. Shading along the MADC timeline indicates consensus-based diagnoses. A patient is considered to have probable AD six months prior to their first MADC encounter labeled as probable AD and anytime afterward. EHR-based criteria are applied to the RDW encounters. The encounters that occur on or after the first encounter that meets the criteria are labeled as probable AD. A true positive is counted if at least one predicted AD RDW encounter overlaps with the MADC defined probable AD window (e.g., the encounters in the orange circles).

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EHR-BASED PATIENT RISK STRATIFICATION TOOL FOR PROBABLE AD

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Background: To date, predictive modeling for Alzheimer's disease (AD) risk has focused on data not routinely collected in clinical care and is limited to short prediction horizons (e.g., 2-4 years). Given the limitations of existing datasets, we sought to leverage electronic health records (EHRs) that contain decades of longitudinal data for thousands of patients, with the goal of developing and validating a predictive model for AD onset with a 10-year prediction horizon. **Methods:** A retrospective study included patients aged 68-72 admitted to Michigan Medicine prior to 2008 with at least 10 years of follow-up. To control for age, we aligned patients between 68-72 years. Given EHR data up to and including the visit of alignment, we sought to predict the primary outcome: probable AD within the next 10 years (labeled by a previously validated cohort discovery tool). Patients were repeatedly randomly divided into a training and test sets. Using EHR-based covariates (e.g., demographics, diagnoses, procedures, vital signs, laboratory results, medications), we learned a linear model to predict AD. Predictive performance was measured on held-out test data using area under the receiver operating characteristics curve (AUROC). Covariates were ranked according to predictive power, using permutation importance. **Results:** After applying inclusion/exclusion criteria (Figure 1), patients in the final study population (n=8,416) had a median of 11 encounters prior to alignment (interquartile range (IQR)=4-25) and a median of 84 encounters during follow-up (IQR=36-172). The model achieved an AUROC of 0.708 (IQR=0.686-0.733). Important predictive factors included healthcare utilization, testing for secondary causes of AD, and cardiovascular factors (Figure 2). Identifying at-risk patients more than 6 years in advance was possible, though more difficult (Figure 3). **Conclusions:** Using longitudinal EHR data, we can predict AD in advance of clinical diagnosis with modest accuracy. Mining routinely collected data could shed light on AD progression, especially in the decades before clinical onset.

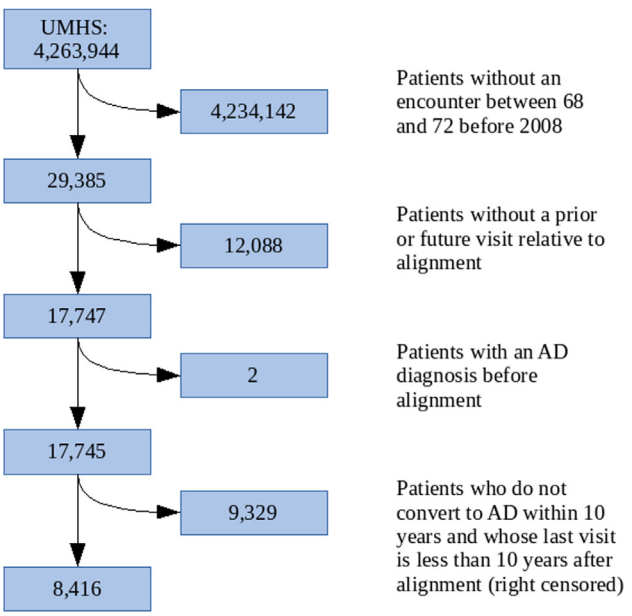

Figure 1: Applying Inclusion/Exclusion Criteria. We begin with all patients in Michigan Medicine's Research Data Warehouse (RDW). Numbers in each box correspond to the number of patients included/excluded. To simplify our analysis, we exclude censored patients and require that patients have at least 10 years of follow-up post alignment, unless they convert to probable AD sooner.

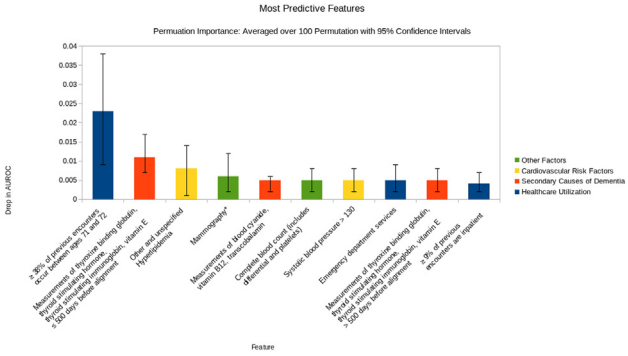

Figure 2: Top 10 most predictive features. We analyzed the predictive power of our features using permutation importance to identify which ones affected the AUROC the most. Results reported are averaged over 100 permutations, and error bars represent 95% confidence intervals. Risk factors correspond to features whose weights were positive, and protective factors (marked with an *) correspond to features whose weights were negative.

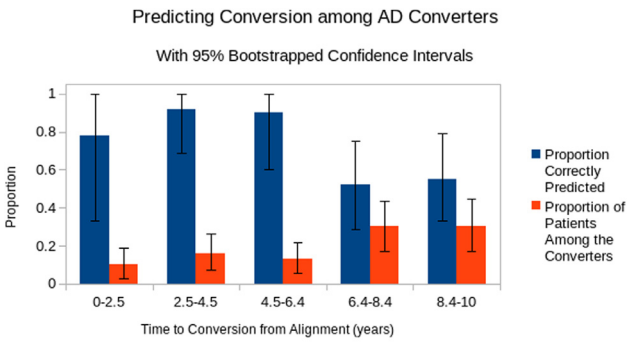

Figure 3: Model validation. Among those identified to convert to probable AD, we analyzed the model's ability to predict conversion relative to amount of time it took to convert starting from alignment. Patients were predicted to convert if the probability of conversion given by the model was above the 65th percentile. Our model was able to predict conversion on large time windows as well as small ones. Error bars represent 95% confidence intervals over 1,000 bootstrapped samples.