PHYSICIANS' ASSESSMENT OF THE CLINICAL UTILITY OF A NOVEL TEST TO DIAGNOSE ALZHEIMER'S DISEASE (AD)

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Background and Objectives

The Problem

- Current standard of care (SOC) tests to diagnose AD have many limitations including lack of accuracy, subjectivity, limited coverage and high costs, and often a lack of a definitive diagnosis.[1,2,3] Only 48% of physicians are satisfied with current SOC tests to diagnose AD[4]
- The current diagnostic pathway may lead to frustration and anxiety for patients and caregivers and may also negatively impact patient management. A test providing an earlier, more definitive, and accurate diagnosis would help physicians to provide more supportive care, to prescribe appropriate treatments, and to enroll patients in clinical trials, where appropriate
- The indirect and direct cost burden of treating and managing AD and dementia is significant[5]

The Solution

- The DISCERN™ test was developed as an objective test for identifying early-stage AD (within 4 years of a diagnosis of dementia) and distinguishing AD from other forms of dementia, including in patients with mixed dementia
- The DISCERN test is comprised of three assays that assess several critical factors directly related to AD that regulate memory, the formation of synaptic connections among neurons, the levels of amyloid plaques and levels of neurofibrillary tangles in the brain; the sensitivity and specificity of these assays are each greater than 94%[6,7,8,9]
- Physicians can confidently diagnose a patient with AD based on DISCERN's results while avoiding other costly tests, allowing for optimized patient management

The objective of this study was to evaluate the decision-impact (clinical utility) of the DISCERN test and assess how physicians would use this test in the real-world to inform decision-making pertaining to patient diagnosis and management.

Methods

Figure 1. Sample Attrition (*n=402* physicians)

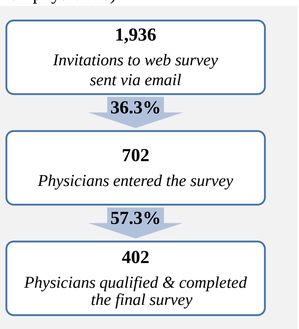

Figure 2. Approach to assessing decision-impact of DISCERN using conjoint analysis

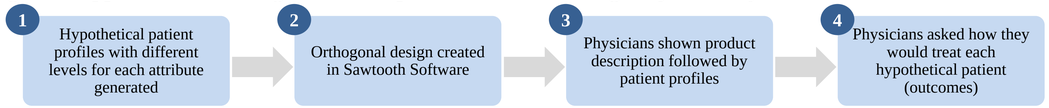

Table 1. Attributes and levels used in the generation of hypothetical patient profiles

Attribute	Level 1	Level 2	Level 3
DISCERN Result	No test	Negative for AD	Positive for AD
MRI/CT Scan	No presence of microhemorrhage, cerebral amyloid angiopathy, or atrophy	Presence of microhemorrhage, cerebral amyloid angiopathy, or atrophy	
MMSE Score	20-24 (mild dementia)	13-19 (moderate dementia)	<=12 (severe dementia)
Blood Test Results	No TSH, vitamin B12 or folate abnormalities, Lyme disease, or syphilis	TSH, vitamin B12 or folate abnormalities, Lyme disease, or syphilis present	
Age (years)	65	75	85

402 physicians (50 geriatricians, 102 neurologists, 250 PCPs) participated in a web-based survey (Figure 1). Conjoint analysis was used to assess decision-impact of DISCERN in a 4-step approach (Figure 2). The outcomes were evaluated per physicians' responses to the following questions: (1) Would you diagnose this patient as having AD?; (2) Would you prescribe medications indicated for cognitive impairment in AD to this patient?; (3) [PCPs and geriatricians only] Would you refer this patient to a neurologist?; (4) Would you prescribe a futuristic disease-modifying treatment (DMT) with a desirable safety and efficacy profile to this patient that slows the progression of AD?

Multivariable logit models were used to analyze the impact of the DISCERN test result and other attributes on these four outcomes. These models produced raw utilities for each level of each attribute. The impact of each attribute (relative importance) on physician decision-making (outcomes) was calculated as the mean difference in the minimum and maximum utility for each level and the proportion this makes up of all the attributes.

Conclusion

The DISCERN test addresses several unmet needs identified in AD diagnosis and management. The results from our study indicate that physicians see value in the information from the DISCERN test and would order this test to make clinical decisions compared to current SOC tests. This study provides evidence demonstrating the clinical utility of the DISCERN test and has implications for clinicians considering adoption of this test and payers evaluating coverage of the test.

References

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Results

Figure 3. Likelihood of ordering DISCERN test (*n=402* physicians)

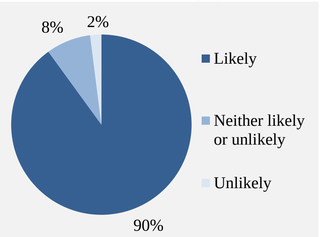


Figure 4. Current diagnostic challenges pertaining to AD (*n=402* physicians)

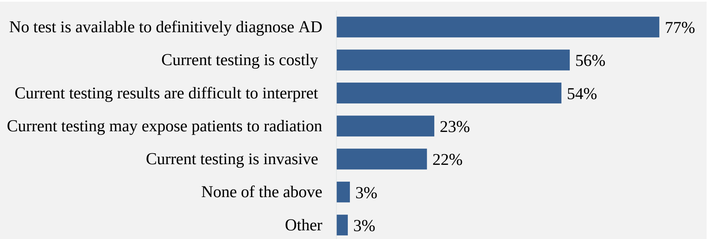
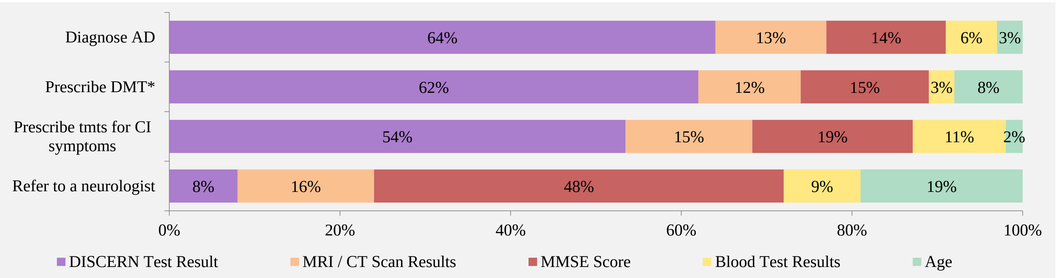


Figure 5. Relative Importance of DISCERN Results Compared to SOC Tests and Clinical Variables (*n=388* physicians)



*Physicians were asked to imagine a hypothetical scenario where a disease modifying treatment (DMT) with a good safety and efficacy profile was approved by the FDA for use in AD patients

The DISCERN test result was the most important attribute in 3 out of 4 physician decision-making outcomes, as presented in Figure 5.

Table 2. Impact of DISCERN Test Results on Physician Decision-Making (*n=388* physicians)

Outcome	DISCERN Test Result	Odds Ratio	95% Confidence Interval	
			Lower Bound	Upper Bound
Definitively diagnose AD	**No Test**	**REF**	-	-
	Negative for AD	0.39*	0.32	0.48
	Positive for AD	6.45*	5.09	8.17
Prescribe treatments for symptoms of cognitive impairment	**No Test**	**REF**	-	-
	Negative for AD	0.58*	0.48	0.70
	Positive for AD	2.98*	2.40	3.68
Refer to a neurologist	**No Test**	**REF**	-	-
	Negative for AD	1.07	0.86	1.33
	Positive for AD	0.97	0.78	1.20
Prescribe DMT**	**No Test**	**REF**	-	-
	Negative for AD	0.57*	0.47	0.70
	Positive for AD	4.12*	3.36	5.04

*Significant at α =0.05; **Physicians were asked to imagine a hypothetical scenario where a disease modifying treatment (DMT) with a good safety and efficacy profile was approved by the FDA for use in AD patients

Clinicians were significantly more likely to definitively diagnose patients with AD and appropriately treat AD with symptomatic treatments or DMTs, when relying on the DISCERN test result (Table 2).

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