SA45

A Cost-Effectiveness Analysis of Diagnostic Testing in Alzheimer's Disease

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BACKGROUND

- Alzheimer's disease (AD) is a form of dementia that progressively affects cognition, behavior, and functional status caused by accumulation of amyloid or tau protein in neuronal space.
- Early detection and diagnosis of AD enables earlier access to treatment leading to better clinical outcomes.
- Three commonly used amyloid-based AD diagnostic tests are amyloid blood test (ABT), cerebral spinal fluid tap (CSFt), and amyloid positron tomography (aPET).

OBJECTIVE

- This study aimed to identify the most cost-effective AD diagnostic strategy ABT, CSFt, and aPET from the US payer perspective set at a willingness-to-pay (WTP) threshold of $150,000.
- To identify the most sensitive inputs to the model.

METHODS

- **Study Platform:** TreeAge Pro Student Version R.20
- **Study Design:** Markov Model
- **Analyses Conducted:** Cost-effectiveness analysis (CEA) and sensitivity analysis (SA)
- **Assumptions:**
  - 70 years old patients with an AD diagnosis
  - Patient's movement is static, progressive or death (terminal state) (refer to Figure 1)
  - The cycle length was one year with a time horizon of 25 years
- **Inputs:** 25 inputs were included into the Markov Model including: rates of state transition, cost of each state, annual cost of the diagnostic, and specificity of diagnostic (refer to Table 1)
  - For specificity, the model leveraged true positive rates for each diagnostic
- A cost-effectiveness analysis (CEA) was conducted to assess the incremental cost-effectiveness ratio (ICER) and net monetary benefits (NMB) of the diagnostic strategies set at a WTP threshold of $150,000
- A sensitivity analysis (SA) was conducted with a standard ±10% variation to all model inputs (refer to Table 1)

Figure 1: State Transition Diagram

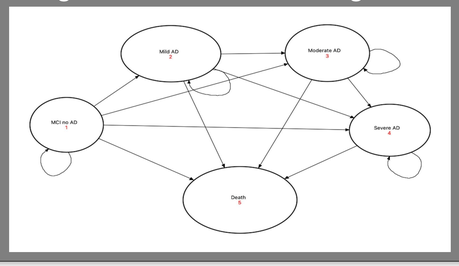

Table 1: Inputs and ± 10% SA Adjustment

Variable	Quantified	Low Value	High Value
Progress MCI no AD to MildAD	0.111	0.0999	0.1221
Progress MCI no AD to Moderate AD	0.014	0.0126	0.0154
Progress MCI no AD to Severe AD	0.0001	0.00009	0.00111
Progress Mild AD to Moderate AD	0.034	0.0306	0.0374
Progress Mild AD to Severe AD	0.0002	0.00018	0.00022
Progress Moderate AD to Severe AD	0.0098	0.00882	0.01078
Stay MCI no AD	0.811	0.7299	0.8921
Stay Mild AD	0.829	0.7461	0.9119
Stay Moderate AD	0.921	0.8289	1.0131
Stay Severe AD	0.995	0.8955	1.0945
Death from MCI no AD	0.031	0.0279	0.0341
Death from Mild AD	0.0095	0.00855	0.01045
Death from Moderate AD	0.021	0.0189	0.0231
Death from Severe AD	0.035	0.0315	0.0385
Yearly cost Amyloid blood testing	$575	517.842	632.918
Yearly cost Cerebral Spinal Fluid Tap	$900	810	990
Yearly cost Amyloid PET scan	$3,000	2,700	3,330
Specificity Amyloid blood testing	0.83	0.747	0.913
Specificity Cerebral Spinal Fluid Tap	0.86	0.774	0.946
Specificity Amyloid PET scan	0.9	0.81	0.99
Cost of stage: MCI no AD	$17,372	15,624.8	19,109.2
Cost of stage: Mild AD	$34,742	31,267.8	38,216.2
Cost of stage: Moderate AD	$41,134	37,020.6	45,247.4
Cost of stage: Severe AD	$52,834	47,550.6	58.117.4
Total Cycles	25	22.5	27.5

METHODS cont.

Figure 2: Markov Model

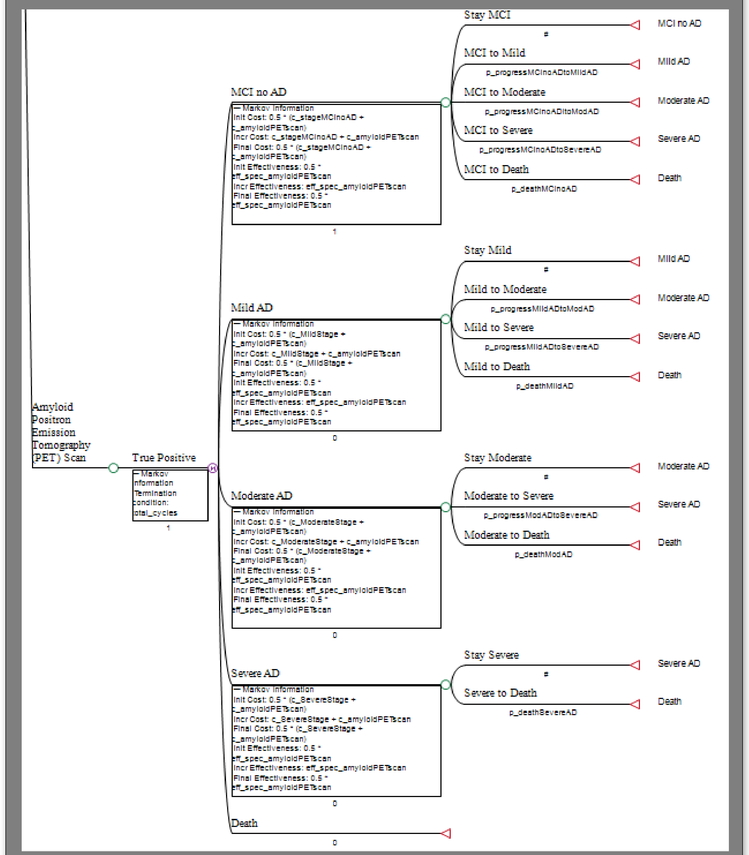

Figure 2: Displays an excerpt of the Markov Model displaying the aPET diagnostic test arm of the model.

- **Decision Node:** created three arms in the model: ABT, CSFt, and aPET
  - Outcome of each decision node immediately followed by a chance node assuming true positive rates of all diagnostic tests
- **Markov Nodes:** led to the state transitions described in Figure 1, ultimately resulting in terminal nodes
- **Costs and Utilities:** each state following the Markov node followed basic formula (refer to Table 2)
- **Probabilities:** rates of state transition in each phase of AD, rate of stay was determined to be the complement

Table 2: Cost and Utilities Formula

	Cost	Effectiveness
Initial	0.5 * (cost of stage + cost of diagnostic test)	0.5 * specificity of diagnostic test
Incremental	cost of stage + cost of diagnostic test	Specificity of diagnostic test
Final	0.5 * (cost of stage + cost of diagnostic test)	0.5 * specificity of diagnostic test

RESULTS

Figure 3: CEA

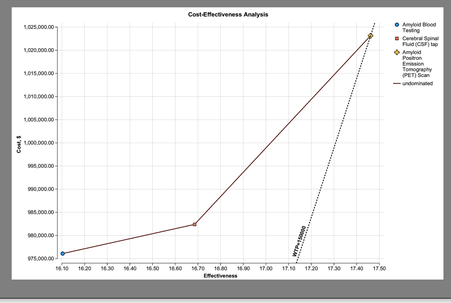

Table 3: NMB Report

Cost-Effectiveness Rankings Report

Category	Strategy	Cost	Incremental Cost	Effectiveness	Incremental Effectiveness	ICER (IC/IE)	NMB	C/E
All (no dominance)								
Undominated	Amyloid Blood Testing	$616,218.08		16.10			$1,799,293.13	38,266.31
Undominated	Cerebral Spinal Fluid (CSF) Tap	$622,516.26	$6,298.18	16.69	0.58	10,820.67	$1,880,302.58	37,308.91
Undominated	Amyloid Positron Emission Tomography (PET) Scan	$663,259.82	$40,743.56	17.46	0.78	52,500.00	$1,955,969.20	37,984.07
All referencing common baseline								
Undominated	Amyloid Blood Testing	$616,218.08		16.10			$1,799,293.13	38,266.31
Undominated	Cerebral Spinal Fluid (CSF) Tap	$622,516.26	$6,298.18	16.69	0.58	10,820.67	$1,880,302.58	37,308.91
Undominated	Amyloid Positron Emission Tomography (PET) Scan	$663,259.82	$47,041.74	17.46	1.36	34,637.43	$1,955,969.20	37,984.07
All by increasing effectiveness								
Undominated	Amyloid Blood Testing	$616,218.08		16.10			$1,799,293.13	38,266.31
Undominated	Cerebral Spinal Fluid (CSF) Tap	$622,516.26		16.69			$1,880,302.58	37,308.91
Undominated	Amyloid Positron Emission Tomography (PET) Scan	$663,259.82		17.46			$1,955,969.20	37,984.07

- CEA Results: aPET is the most cost-effective diagnostic test at a WTP threshold of $150,000.
  - The ICER for aPET ($52,500) was higher than for CSF ($14,821) but remained on the WTP threshold of $150,000.
  - Net monetary benefit (NMB) was highest for aPET ($1,955,969), followed by CSF ($1,880,303) and ABT ($1,799,293), making aPET the most cost-effective strategy.
- SA Results: Total cycles is the most sensitive input, followed by specificity across each diagnostic. See below for remaining top five sensitivity inputs for each diagnostic state
  - ABT: cost of mild state > probability of death in MCI state > cost of moderate state
  - CSFt: cost of mild state > probability of death in MCI state > cost of moderate state
  - aPET: probability of death in MCI state > cost of mild state > cost of moderate state

CONCLUSION

- Despite the higher cost, aPET provided the greatest effectiveness, making it the preferred diagnostic tool for Alzheimer's disease at a $150,000 WTP threshold.
- Payers should be prepared to continue to support amyloid blood testing as it is a central element to the standard of care.
- More research is needed to determine if earlier (pre-65 years old) screening would be further cost-effective due to improved outcomes associated with early diagnosis, and early access to treatment.

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