Alzheimer's Disease ACE[1] Simulator Q&A

What Is It?

- A multi-application simulator of Alzheimer's Disease (AD) designed to: support commercial strategy development, inform clinical trial designs, and meet HTA agency requirements for formal submissions

Why Is It Better Than Other Models?

- Covers the full spectrum of AD: from prodromal to severe AD, as well as the transition from normal cognitive function
- Can evaluate the impact of disease-modifying agents on disease progression
- Built on multiple components of AD, such as cognition, behavior, biomarkers, function, and their interactions, to properly capture the multi-dimensional nature and adapt to the evolving definitions of AD
- Multiple applications, including: health economics, epidemiology, early decision making, and support for RCT design, labeling strategy development, and HTA submissions
- Programmed in MS Excel®, providing transparency for HTA bodies, decision makers, and internal stakeholders
- Extensively documented, flexible and yet transparent and easy to use

What Is Its Scope?

- Includes interrelations between components of AD pathology and their impact on disease progression
- Captures heterogeneity by modeling individual profiles separately
- Goes from MCI or prodromal AD to severe disease
- Disease progression incorporates multiple components of AD, including:
  - Patient Characteristics – Baseline Age, Sex, ApoE4 status
  - Biomarkers – Hippocampus MRI, FDG-PET, PIB-PET, CSF Aβ42, CSF t-tau
  - Cognition – MMSE, ADAS-cog, CDR-SB
  - Behavior – Neuropsychiatric Inventory (NPI)
  - Function – Disability Assessment for Dementia (DAD)
  - Dependence – Dependence Scale (DS)
- New measures are easily integrated

[1] Archimedes Condition Event simulator

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How Can I Use It?

HTA submissions

- Estimate cost-effectiveness of a new treatment, with flexibility to focus on specific sub-groups
- Features that favor HTA submission include:
  - Highly transparent
  - Implemented in MS Excel
  - Calculates ICERs
  - Full uncertainty analyses, including PSA, built-in
  - Efficiency frontiers can be produced
  - Inputs can be adapted for any jurisdiction

Early decision making

- Valuation and testing of target product profile(s)
- Economically justifiable pricing / early economic evaluation
- Evidence gap analysis to understand uncertainty in the value of a treatment
- Support for partnership and in-licensing discussions
- Prioritization of pipeline compounds based on likelihood of success, size of addressable market, etc.

Epidemiology

- Burden of illness, market size, and budget impact forecasting
- Public health impact
- Identifying target patient populations based on risk

Inform labeling strategies

- Risk stratification approaches
- Implications for value of TPP

Support RCT design

- Optimization of study population admissibility criteria
- Outcome measures
- Comparators
- Timing of measurements and duration of follow-up
- Other features

Will It Be Relevant For My Product?

- May be used with disease-modifying treatments, symptomatic treatments, prevention, diagnostics, and other interventions

What Data Is It Based On?

- Individual patient data from the Alzheimer's Disease Neuroimaging Initiative (ADNI) and aggregate information from both primary and secondary literature, including substantial components of the Assessment of Health Economics in Alzheimer's Disease (AHEAD) II model

What Software is Needed?

- Microsoft Excel; no additional software

How Has It Been Validated?

- Continuous process of internal and external validation, including testing against ADNI data, published literature, and peer review

Can It Be Modified?

- Yes, modifications such as adding new treatments or measures of disease progression can be performed directly in the Excel spreadsheet. More extensive modifications may be completed in collaboration with an Evidera scientist.

What Countries Is It Available For?

- U.S. is the base case, but designed for very simple adaptation to any market with appropriate data availability

What Perspectives Can Be Handled?

- Payer and societal perspectives, including caregiver burden

How Often Will It Be Updated?

- Periodic updates as needed; driven by new data, diagnostic or treatment paradigms, and clinical trials

How Do I Get Access?

- Contact info@evidera.com to speak with an Evidera scientist about your specific needs

For more information, including publications, white papers, and a webinar on the AD ACE model, please visit: evidera.com/ACE.