Application of Discrete-Event Simulation in Health Technology Assessment: A Cost-Effectiveness Analysis of Alzheimer's Disease Treatment Using Real-World Evidence in Thailand

Authors : Khachen Kongpakwattana, Nathorn Chaiyakunapruk

Abstract : Background: Decision-analytic models for Alzheimer's disease (AD) have been advanced to discrete-event simulation (DES), in which individual-level modelling of disease progression across continuous severity spectra and incorporation of key parameters such as treatment persistence into the model become feasible. This study aimed to apply the DES to perform a cost-effectiveness analysis of treatment for AD in Thailand. Methods: A dataset of Thai patients with AD, representing unique demographic and clinical characteristics, was bootstrapped to generate a baseline cohort of patients. Each patient was cloned and assigned to donepezil, galantamine, rivastigmine, memantine or no treatment. Throughout the simulation period, the model randomly assigned each patient to discrete events including hospital visits, treatment discontinuation and death. Correlated changes in cognitive and behavioral status over time were developed using patient-level data. Treatment effects were obtained from the most recent network meta-analysis. Treatment persistence, mortality and predictive equations for functional status, costs (Thai baht (THB) in 2017) and quality-adjusted life year (QALY) were derived from country-specific real-world data. The time horizon was 10 years, with a discount rate of 3% per annum. Cost-effectiveness was evaluated based on the willingness-to-pay (WTP) threshold of 160,000 THB/QALY gained (4,994 US$/QALY gained) in Thailand. Results: Under a societal perspective, only was the prescription of donepezil to AD patients with all disease-severity levels found to be cost-effective. Compared to untreated patients, although the patients receiving donepezil incurred a discounted additional costs of 2,161 THB, they experienced a discounted gain in QALY of 0.021, resulting in an incremental cost-effectiveness ratio (ICER) of 138,524 THB/QALY (4,062 US$/QALY). Besides, providing early treatment with donepezil to mild AD patients further reduced the ICER to 61,652 THB/QALY (1,808 US$/QALY). However, the dominance of donepezil appeared to wane when delayed treatment was given to a subgroup of moderate and severe AD patients [ICER: 284,388 THB/QALY (8,340 US$/QALY)]. Introduction of a treatment stopping rule when the Mini-Mental State Exam (MMSE) score goes below 10 to a mild AD cohort did not deteriorate the cost-effectiveness of donepezil at the current treatment persistence level. On the other hand, none of the AD medications was cost-effective when being considered under a healthcare perspective. Conclusions: The DES greatly enhances real-world representativeness of decision-analytic models for AD. Under a societal perspective, treatment with donepezil improves patient's quality of life and is considered cost-effective when used to treat AD patients with all disease-severity levels in Thailand. The optimal treatment benefits are observed when donepezil is prescribed since the early course of AD. With healthcare budget constraints in Thailand, the implementation of donepezil coverage may be most likely possible when being considered starting with mild AD patients, along with the stopping rule introduced.

Keywords : Alzheimer's disease, cost-effectiveness analysis, discrete event simulation, health technology assessment
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