Feasibility of Simplifying Complex Decision Trees via Linear Regression Analysis: An Application to Cost-Effectiveness Analysis of Hormone Therapy for Menopausal Symptoms

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Objectives

- Outputs of published models cannot be easily modified by end users, who typically have neither direct access to the model nor the willingness or ability to reprogram it without considerable time, effort, and risk of error.
- We explored whether second-order Monte-Carlo simulation (MCS) and regression techniques could satisfactorily replicate and simplify complex decision trees and facilitate their understanding and use by end users.

Methods

Overview

- We developed a one-year, four-cycle Markov chain to compare the cost and quality-adjusted survival of two hypothetical cohorts of women receiving either continuous combined hormone replacement therapy (CCHRT) or no CCHRT for the management of vasomotor symptoms (Figure 1).
- The target treatment population consisted of women aged 45-55 years with an intact uterus, experiencing vasomotor symptoms, and considered candidates for CCHRT.
- Only direct medical costs were included. Qualitatively adjusted life years (QALYs) were used as the main effectiveness measure.

Epidemiological and Clinical Inputs

- Data on breakthrough bleeding and/or spotting were obtained from a randomized clinical trial (RCT) that showed that the incidence of cumulative amenorrhea for patients on CCHRT or placebo was 88% and 91%, respectively, at one year postbaseline. Assuming bleeding resumes immediately after initiation of therapy, the cumulative proportion of CCHRT patients who are amenorrheic would increase by 41% each three-month cycle to reach the 99% rate at one year. For simplicity, all patients not receiving CCHRT were presumed to have reached amenorrhea.
- Transition probabilities for the menopausal symptom states were taken from a 12-week RCT that demonstrated that 10% and 34% (P<0.05) of patients on placebo and CCHRT, respectively, experienced complete elimination of hot flashes after three months.

Economic and Quality of Life (QOL) Inputs

The economic and QOL inputs for the model are summarized in Table 1. Costs were derived either based on the valuation of defined treatment protocols or directly from published estimates in the literature. QOL was included in the model via QALY weights derived from the literature.

Results

Traditional Model Results

The results of the traditional model are presented in Table 2. Costs were derived either based on the valuation of defined treatment protocols or directly from published estimates in the literature. QOL was included in the model via QALY weights derived from the literature.

Monte-Carlo and Regression Analyses

A sample of the output of the MCS is presented in Tables 3,4.

- Second-Order Monte-Carlo Simulation and Regression Analyses
  - We ran 1,000 MCS of the Markov model to simulate the effect of uncertainty in probability, utilities, and costs in estimating incremental QALYs, incremental costs, and net monetary benefit (NMB; using a willingness-to-pay threshold of $5,000 per QALY gained) associated with CCHRT.
  - We arbitrarily used uniform distributions for each input included in the MCS. Each variable was varied by ±50% except utility weights (Table 1).
  - We fitted the output data (incremental QALY and costs) from the 1,000 individual MCS using two separate ordinary least-squares (OLS) regressions.
  - The predictive regression equations (net QALY and net cost) were then used to back-predict the NMB of CCHRT. This was accomplished by taking the sum of the products of predictor values and their coefficients from the regression.
  - Multiple tests were conducted to determine the predictive abilities of the regression against the results of the traditional model.

Conclusions

- MCS and regression techniques can be combined to simplify complex decision treas into more easily interpretable empirical forms.
- The regression representation may be more suited for universal adoption by end users, who could use basic algebra to readily adapt the original decision tree to calculate results for their own settings.
- This use of regression representation could expand the appreciation of cost-effectiveness analyses by end users and further its responsible use.

References