USING REAL WORLD DATA TO STRUCTURE AND POPULATE MARKOV MODELS – A CASE STUDY OF TELEMONITORING FOR HEART FAILURE

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OBJECTIVE

The objective is to present an alternative approach that uses routinely available hospitalisation data to define the states in the Markov model and estimate the transition probabilities for chronic heart failure patients. A case study of populating a heart failure model Markov using this real world data approach is provided.

BACKGROUND

Modelling is required to structure evidence on clinical and economic outcomes in a form that helps decision makers choose from among competing courses of action and allocate limited resources . A range of modelling techniques have been used for medical and economic decision modelling, but cohort-based Markov models are the most commonly used methods in HTA as they are relatively simple to develop, debug, communicate, and analyse using user-friendly software. Markov models are described in terms of the conditions that individuals can be in ("states"), how they can move among such states ("transitions"), and how likely such moves are ("transition probabilities).

Markov models typically contain states based on clinical/biological measures, such as, forced expiratory volume in one second (FEV1) which represents a measure of lung function. However, these measures are not always collected in the evaluation of non-pharmaceutical service developments. Likewise, detailed measures are not always available to allow locality specific transition probabilities to be generated. As a result, models based on clinical/biological measures are limited in their applicability to several decision making contexts.

METHODS

The severity measure chosen was based on the number of hospital admissions for the relevant condition (here, HF) over the past year. Thus an individual's state at any point in time was 0 if they had not been admitted to hospital for the condition over the past year, 1 if they had been admitted once, 2 if they had been admitted twice, and 3 if they had been admitted 3 or more times. This choice has the advantage that information on mortality and progression between states could be derived from hospital admissions statistics in the UK.

DATA

Hospitalisation data were accessed through a query run on national Hospital Episodes Statistics (HES). Data were obtained for individuals who suffered at least 1 admitted patient care (APC) event for heart failure (ICD10 code I50) between March 2005 and March 2010, including identifiers relating to x localities, or Primary Care Trusts (PCTs). Mortality data was obtained from Office for National Statistics with an anonymised identifier to allow linkage to HES data. Individuals' history of hospital use and mortality, was reconstructed and then categorized into states at each point of time according to the number of APC admissions for heart failure (HF) in the preceding year. The number of APC (HF & other cause) events, emergency department attendances (HF & other cause) events, outpatient attendances (HF & other cause), and deaths that occurred among individuals of a given severity state were then calculated .

ESTIMATION OF TRANSITION PROBABILITIES

Given the set of reconstructed individual histories, one can count the total number, $n_{a\varepsilon}$, of events of type ε occurring to individuals in a state a, and the total person-time spent in this state, T_a. The ratio of the count and the person time gives an estimate of the rate (hazard), $r_{a\varepsilon}$, at which event ε occurs to those in state a:

$$r_{a\varepsilon} = \frac{n_{a\varepsilon}}{T_a}$$

If the transitions between states are treated as continuous-time Markov process, then $\varepsilon = b$ for the event transition to state b, and with the convention that $r_{ab} = 0$ when $a = b$, the master equations (Kolmogorov forward equations) determining the probability, $P_a(t)$, of occupying state a at time t become

$$\frac{dP_a}{dt} = \sum_{b=0}^{4} (r_{ba}P_b - r_{ab}P_a).$$

Since the r_{ab} are constant in time the above equation can be solved using the matrix exponential of the transition rate matrix, M

$$M_{ab} = r_{ab} - \sum_{c=0}^{4} r_{bc}\delta_{ab}$$

where δ_{ab} is the Kronecker delta function (1 if $a = b$ and 0 otherwise). This gives

$$P_a(t) = \sum_{b=0}^{4} (e^{Mt})_{ba} P_b(0),$$

so that the usual Markov monthly transition matrix, Π, can be computed numerically in a software package supporting matrix exponentiation as $\Pi = \exp(M)$, if M is measured in units of events per person per month. Uncertainty in the rates is included by modelling event counts as Poisson distributions.

APPLYING EFFECTIVENESS PARAMETERS

The hazard ratio for hospitalisation, HR_{hosp}, is applied to upward transitions, i.e. states with $a \in \{0,1,2,3\}$ and $a < b$:

$$r'_{ab} = HR_{hosp} . r_{ab}$$

The hazard ratio for death, HR_{mort}, is applied to transitions to the dead state

$$r'_{a4} = HR_{mort} . r_{a4}$$

The effects of interventions are incorporated by computing new transition matrix via matrix exponentiation using new rates r'_{ab}. The resulting monthly transition matrix captures both the instantaneous direct reduction in mortality rates in each state, and also the indirect reductions due to slowed disease progression.

DISCUSSION

This paper presents an alternative approach to traditional economic modelling, making use of routinely available data to characterise the disease states based on hospitalisations in the previous year. This approach has a number of advantages over conventional Markov modelling approaches, especially in chronic disease areas where hospitalisation is a useful measure of both effectiveness and disease progression. Given the increasing emphasis on using real world evidence, it is likely that these approaches can prove a valuable addition to traditional approaches in cost-effectiveness modelling.

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