STOCHASTIC PROCESS MODEL FOR MEDICAL DECISION-MAKING

Takashi Namatame* and Yumi Asahi†

ABSTRACT

In this paper, we describe various stochastic process models, mainly the Markov model, for medical decision-making. Particular attention is given to modeling, the Markov cohort model and the Markov decision process model for computation and limitation in stochastic models. We also discuss the current problems: how to collect the required data and the relation between the model solution and the actual decision.

1. Introduction

EBM (evidence-based medicine) and pharmaco-economics have recently received increasing attention in Japan because of the increasing focus on the patient side as a check on the medical system (Petitti, 2000). Another reason for the increased interest is that patient medical expenses, which up to now have been very light in Japan because of the medical insurance system, will soon increase sharply owing to changes to be made in the system. The emergence of various new medicines and cures increases the number of choices available to the doctor and the patient, but also makes it more difficult to choose the best treatment for the patient from the many treatment plans available. It is important to offer treatment choices that the patients can understand. Patients with a chronic disease need to be made aware of the effect of the medical treatment and how much it will cost.

Stochastic process models, including the Markov model, are highly useful techniques for measuring the effects of the future of medical treatment. The value of a treatment is measured based on the patient’s health condition, transition between health conditions, the utility for each condition, and cost.

2. Markov model for medical decision-making

In this paper, we describe stochastic models for medical analyses, focusing especially on Markov model, which plays a central role in medical decision-making. Beck and Pauker (1983) were the first to publish a paper on application of the Markov model in medical decision-making. They introduced the use of a discrete-time Markov model for determining medical prognosis. Markov models are particularly useful when a decision involves risk that is ongoing over time, when the times at which important events will occur are uncertain, and when those events may happen repeatedly (Sonnenberg and Beck, 1993). Various medical decision-making methods using the Markov model have since been discussed in many papers

*School of Commerce, Senshu University, 2-1-1, Higashimita, Tama-ku, Kawasaki, Kanagawa 214-8580, Japan E-mail: takashi@isc.senshu-u.ac.jp
†Graduate School of Social Relations, Rikkyo (St. Paul’s) University, 3-34-1, Nishi-ikebukuro, Toshima, Tokyo 173-8501, Japan

Key words: Evidence-based medicine; Markov model; Stochastic process
2.1. The Markov model

Markov models used in medical decision-making fall in two general categories:

1. Markov cohort simulation,

2. Markov decision process.

The former, generally called the “Markov model,” is the major method. Cohort simulation is widely used to compare different medical treatments and in cost benefit analysis. The analysis procedure is: 1) formulate the model, and 2) forwardly calculate the state transition from the present state under the prescribed treatments. The present value of the patient’s utility or cost is then calculated. The algorithm for this is as follows.

Let $t$ be time ($t \in \{0, 1, \ldots, N\}$), where $N$ is the terminal time), $s$ be state ($s = 1, 2, \ldots, K$, where state $K$ is usually the absolute state, that is, the death state), $A = [a_0, \ldots, a_t, \ldots, a_N]$ be the treatment sequence matrix (where $a_t = [a_t(s)]$, $a$ is treatment), $P^{a_t}(t) = [p_{s_j}^{a_t}(t)]$ be the Markov transition probability matrix (where $p_{s_j}^{a_t}(t) = Pr[X_{t+1} = j|X_t = s, a_t(s) = a]$) and $r^a_t = [r^a_t(s)]$ is the utility vector at time $t$ with treatment $a$. Then, the discounted present value of utility with respect to the treatment sequence $A$ is calculated as:

$$u^{A}_{t_0} = \sum_{t=t_0}^{N} \delta^{t-t_0} h^T_{t_0} \prod_{\xi=t_0}^{t} P^{a_\xi}(\xi) r^a_{\xi},$$

where $N$ and $t_0$ are the terminal and present time, respectively, $u^{A}_{t_0}$ is the net present utility at $t_0$ under treatment sequence $A$, $\delta$ is the discount factor ($0 < \delta \leq 1$) and $h^T_t = [0, \ldots, 0, 1, 0, \ldots, 0]$ is the stay vector at time $t$.

In the Markov decision process case, when the transition probabilities are constant over time, i.e., the Markov decision process is time-homogeneous, there are several methods for optimally solving the problem. The setting of most medical cases is non-homogeneous, however, and no analytically tractable result is available other than in certain asymptotic cases. Still, in a medical case, the death probability increases exponentially with age, so the state of all patients in the distant future can be considered to be the death state. The optimal action (treatment) sequence can therefore be derived by going up the time stream from a terminal time (e.g. the age when the survival rate is less than 0.01% or when the age reached 120). This method is called the backward induction algorithm.

The backward induction algorithm can be described as follows:

1. Set $t = N$ and $u^*_N(s) = r^*_N(s)$.

2. Substitute $t - 1$ for $t$ and calculate $u^*_t(s)$ by

$$u^*_t(s) = \max_a \left\{ r^a_t(s) + \delta \sum_j p^a_{s_j}(t) u^*_{t+1}(j) \right\}.$$  

3. Set the optimal action at state $s$ and at time $t$ as $a^*_t(s) = a^*$, where

$$u^*_t(s) = r^a_t(s) + \delta \sum_j p^a_{s_j}(t) u^*_{t+1}(j).$$
\(a_t(s)\) is the element of the vector \(a_t\) for state \(s\) and \(u_t(s)\) is the net present utility at time \(t\) and state \(s\). Using this algorithm, we can obtain the present value (of quality-adjusted life years) for each time and each state in the case of the optimal treatment. Clearly, the optimality of this algorithm is validated by Bellman's principal of optimality (see Puterman (1994) for the theoretical property of the Markov decision process, and Schmee et al. (1979) and Mogi et al. (1999) for the applications to medical problems).

In practice, the Markov model with discrete-time, discrete-state and time-heterogeneity is broadly utilized in various medical decision-making problems, because of the availability of data discussed in a later section.

*State, transition probability and utility value* are needed to build a Markov model. Moreover, *sensitivity analysis* is also often performed. We explain these items in order.

### 2.1.1. State

To build a Markov model, first, we need to enumerate the all-important states of the treated disease of the patient.

For example, if a treatment greatly affects a complication, we need to distinguish between the health states with and without the complication.

We can consider that the continuous state as a continuous index value represents the health state. But, most models treat discrete states (e.g. to match the condition of patient), because the distinctions of the state must be related with the transition probability, and it is actually very difficult to get the appropriately continuous transition probability.

### 2.1.2. Transition probability

We need to get the transition probability between states mentioned in the previous section. In fact, the transition probability changes continuously over time. So the transition of state also occurs continuously according to the transition probability. However, the discrete model is more popular than the continuous one because of ease of data collection and observation.

In medical decision analysis, the transition probability is often obtained by meta-analysis. We often treat *age* as discrete time. This is because the stochastic process model is not used in a large number of medical institutions yet. Therefore, broad meta-analyses are required to obtain the data for analysis. To accomplish this, we may need many related papers, and we should confirm many kinds of data through interviews conducted by a specialist.

In most models, there is the *death* state as the absorbing state. Death is caused by various factors. In the medical model, we should distinguish between deaths that are and are not related to disease considered in the model. The death probability is also related to the patient's age. The death probability increases exponentially as the patient grows older. In calculating the transition probability taking age into account, a specific translating function such as the Gompertz function (Gompertz, 1825) should be used. Especially in the treatment of chronic diseases, we need to translate the probability in terms of age using meta-analysis.
2.1.3. Utility for each state

Next, we set the utility value for each state. When we discriminate between survival and death, the utility value of the death state is 0 and that of other states is 1 (or a specific positive value). However, there is a difference in the degree of satisfaction between survival states associated with the degree of the physical or disease condition. Furthermore, the degree of satisfaction may change as the patient grows older or with treatment. So we need to obtain the utility value for each patient according to his or her condition or from the viewpoint of QOL (quality of life). We can obtain the utility values using, for example, the basic reference gamble method (Llewellyn-Thomas et al., 1984) or multi-attribute utility theory (Torrance et al., 1982) through interviews with the patient, but in most cases, we are obliged to rely on meta-analysis to obtain the utility values.

When we consider cost-effectiveness, the utility value for each state is equal to the cost for each state and treatment. In this case, the point of interest is the lost utility, which is converted into cost, by the treatment.

2.1.4. Sensitivity analysis

Using the foregoing kinds of data, we first calculate the present utility value. The analytical calculation is carried out using representative values, and for this reason is called baseline analysis. However, the analysis using the representative values cannot take into account the difference between individuals and the error of the utility value. Therefore, some sensitivity (post-optimality) analyses are carried out to the measure the data error (e.g., of the transition probability or utility value). Through these analyses, the robustness of the treatment is ascertained.

2.2. Software

Broad use of the Markov model in a real clinical setting requires appropriate software. A few programs for Markov model analysis have been made publicly available, such as DATA, SMLTree or Decision Maker (Pauker and Kassirer, 1981; Lau et al., 1983, Treeage Software Inc., 1999). Among these tools, the most popular is DATATM (Treeage Software Inc., 1999). We found over 14,000 papers related to DATA on MEDLINE and over 100 downloadable papers on the subject on OVID.

DATA can perform various medical decision-making analyses involved in the Markov model, and can be used to verify the analyzing model in many papers. Figure 1 shows the Markov model of Sonnenberg and Beck (1993). As shown in the figure, DATA can process a considerably large model. However, it is very difficult to operate when many states related to the Markov model are complexly involved. Another shortcoming of DATA is that it cannot work with the Markov decision process model.

2.3. Limitations

In this section, we point out the limitations of the present theoretical model.

The transition of the health state and the appearance of the effect of treatment arise continuously over time. But it is impossible to observe continuously the transition of the all-important disease condition. So we are forced to accept various data approximated into discrete values. As pointed out earlier, the general practice is to use meta-analysis. However, the data from meta-analysis often differ depending on the method used to collect the data. In many cases, moreover, sex, age and race differ from paper to paper. When differences in data strongly affect the analysis, we must remove the causes.
It is said that published papers include academic bias. So care must be used when collecting data from various papers.

The medical treatment must be decided for each patient. So each medical decision-making model is also tailored for the individual patient. This enables the stochastic process model to validate the transition probability and utility for each patient. However, the transition probability and utility value data are obtained through meta-analyses, so they often restrict the consideration of differences between patients. Care must therefore be taken when utilizing a model in a real clinical setting.

3. Concluding remarks

EBM will become a very important element in the future medical system. In particular, the Markov model and more general stochastic models will become powerful tools. But at present the Markov model is not being used widely in clinical practice. Researchers are using the Markov model only for verification.

Our opinion is therefore that the stochastic process model is only used to obtain information for evaluating the medical treatment.

For the Markov model to become a practical judgment element in medical decision-making, common knowledge of the theory in actual treatment, easy-to-use analysis tools, and the establishment of a method for proper data collection are necessary. Moreover, there is a trade-off relationship between utility and cost, so a method that treats these simultaneously must be developed.
REFERENCES


