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# *Markov Chain Models in Clinical Performance and Decision Making*

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***Abstract.*** Within clinical research and healthcare decision-making, stochastic modeling methods are becoming increasingly more necessary due to the complexity of predicting the results of clinical processes, disease progression, and analyzing the effectiveness of various treatments. Markov chain models in particular present a good mix of accuracy and simplicity for modeling healthcare outcomes. This study presents a detailed overview of the theoretical foundations of Markov chain models while also discussing their application in patient risk stratification, clinical decision-making, and cost-effectiveness analysis of treatments. Both the advantages and disadvantages of Markov chain models like the memoryless assumption, data requirements needed, and state complexity particularly in healthcare contexts, are examined. Possible future directions for Markov chain modeling, namely hybrid modeling approaches and Markov decision processes (MDPs), are assessed to compare their ability to improve predictive accuracy and influence healthcare policies with regular Markov chain models. Combined all the elements, this study offers clinical researchers and policymakers a comprehensive reference on the strengths and weaknesses of Markov chain modeling specifically in healthcare applications.

***Keywords:*** Markov Chain Models, Health Economics, Markov Decision Processes

## 1. Introduction

Uncertainty, especially when examining disease progression and patient trajectories, is a major challenge in clinical research. The reason for the uncertainty is due to the wide variety of disease characteristics, treatment responses, data quality, and healthcare responses which often create situations that deterministic methods cannot capture properly [1]. As such, deterministic models which rely on fixed input-output relationships are oftentimes inadequate for representing the inherent uncertainty in patient outcomes [2]. Therefore, it is necessary to incorporate stochasticity and changing probabilities in modeling approaches to better capture the uncertainty of clinical processes and disease progression so that more informed healthcare decisions can be made [3].

One of the most widely applied stochastic modeling methods are Markov chain models [1]. These models work well for scenarios with recurring events, competing risks, and patient transitions over time as they represent clinical processes as transitions within a set of different health states where history has no effect on current transition probabilities [3]. By being able to capture real-world variation in disease progression and multiple sources of uncertainty, Markov chain models can be

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used to guide clinical decision-making and risk stratification [4]. For example, Markov models have been applied to oncology to simulate the effects of various treatments, cardiology for estimating patient transition probabilities regarding heart failure, and neurosurgery for modeling both recovery and complications [5,6]. They have also become a standard analytical tool for cost effectiveness, comparative effectiveness of research, clinical decision making, and guideline development across medical disciplines [1].

This study focuses on the application of Markov chain models in clinical decision-making, risk assessment, and cost-effectiveness analysis. The paper first introduces the theoretical foundations of Markov chain models. Afterwards, the paper discusses the wide application and advantages of Markov models in clinical research and decision-making. The paper then analyzes the future directions and the limitations of Markov modeling. Methodological issues such as model structure, transition probabilities, and their implications for outcome interpretation are also analyzed with regard to their implications for healthcare policy.

## 2. Theoretical foundations of Markov chain model

### 2.1. Basic concepts

A Markov chain is defined as a sequence of random variables taking values in a set of states and characterized by the Markov property. Formally, a stochastic process $\{X_n; n \in N\}$ with $n = 0,1,\ldots$ is called a discrete-time Markov chain if for all time indices $t_0 < t_1 < \cdots < t_n$ and states $j_0, j_1, \cdots, j_n \in S$, the conditional probability

$$P\left(X_n = j_n \mid X_{n-1} = j_{n-1},\ X_{n-2} = j_{n-2}, \ldots, X_0 = j_0\right) = P(X_n = j_n \mid X_{n-1} = j_{n-1}) \tag{1}$$

provided that $P(X_0 = j_0, \ldots, X_{n-1} = j_{n-1}) > 0$. Markov models are stochastic models where the system changes states ( $j_n \in S$ ) according to certain probabilities that are independent of history $(X_0, \cdots, X_{n-1})$ and given the current state $(X_{n-1})$. The state space $S$ is the collection of all possible transitions between clinical statuses or disease states. This provides a basis for modeling a patient's trajectory using transition probabilities. Markov state-transition models are useful in healthcare because events and outcomes involve heavy elements of uncertainty over time that most static deterministic approaches cannot capture [3].

### 2.2. Transition structure

A Markov model transition matrix $P = [p_{ij}]_{i,j \in S}$ has probabilities which show the chances that a patient will move from one health state to another over a defined time step. Transition probabilities $p_{ij} = P\left(X_n = j \mid X_{n-1} = i\right),\ i, j \in S,$ are organized in a transition probability matrix, where each row represents a current state and each column represents a possible future state. The probabilities in each row must add up to one (Bishai et al., 2023), i.e., $\sum_{j \in S} p_{ij} = 1$ . Time-steps, usually corresponding to clinically meaningful intervals like months or years, define the simulation interval and are often tied to periods of risk, intervention, or outcome assessment. The matrix allows for the projection of disease progression or treatment effects over long periods of time, making it possible to compare alternative approaches in complex healthcare systems [3].

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## 2.3. State types

Within a Markov model, typically health states include transient states and absorbing states. The transient states refer to the cases always transit to other states over subsequent time steps. In the healthcare scenario, for example, stages of recovery, disease progression, and intermediate clinical conditions can be regarded as transient states. In contrast, absorbing states behaves like a terminal status that once the state is reached, it can never leave. Typical examples, as terminal health statuses, include death or permanent complications, where once a patient entered, he/she never leaves.

From a transient state $i$, multiple transition pathways to $j \in S^{'}$ are possible ( $0 < p_{ij} < 1, j \in S^{'}$ ), reflecting the range of clinical trajectories a patient may follow. From an absorbing state, however, the transition probability is defined such that the state transitions to itself with probability 1, i.e., $p_{ii} = 1$ . Once a patient enters an absorbing state, no further transitions occur, and the model effectively terminates further progression for that individual.

This distinction enables researchers to capture the full spectrum of possible health trajectories while identifying specific states as endpoints for long-term outcomes. By distinguishing between states that are modifiable through intervention and those that are not, models can more accurately estimate relative risks and disease progression patterns. The inclusion and appropriate classification of transient and absorbing states directly influence both the accuracy of trajectory models and their sensitivity to changes in clinical parameters [7].

## 2.4. Conceptual toy example

As an example, consider patients undergoing surgical treatment for cancer. A four-state model can be constructed, where the first health state is the post-surgical period without complications, the second state is postoperative adverse events, the third state is disease relapse, and the last is death, which acts as an absorbing state.

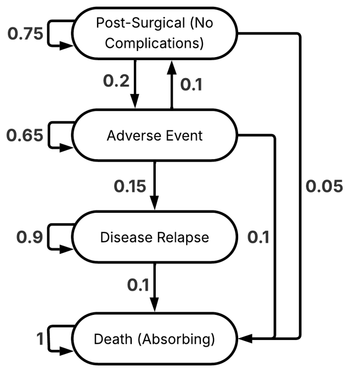


Figure 1. A transition diagram for a Markov model of patients experiencing the surgical treatment. Four nodes represent the four health states, the arrows indicate possible transitions between states, and labels indicates the corresponding probabilities

The state-transition diagram in Figure 1 shows each state as a node, with arrows connecting nodes to represent possible transitions labeled with the assigned probabilities, creating a visual representation of possible patient paths [4]. This diagram lets researchers quantitatively follow patient trajectories, estimate clinical outcome distributions, and support healthcare choices and policies.

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## 3. Applications to clinical performance

First of all, Markov chain models can be used to facilitate the dynamic risk stratification of patients. Dynamic risk stratification is a process where a patient's health risk is regularly updated throughout the course of a disease, taking in and accounting for new developments in their health. Compared to static risk stratification, dynamically risk stratification allows for more personalized patient management as medical practitioners can make use of up-to-date risk estimates instead of unchanging and potentially outdated risk estimates. In a study done by Kazmi et al. [5], a multistate Markov chain model was used in order to help facilitate dynamic risk stratification for patients with chronic heart failure. The Markov chain model was very accurate in predicting some of the longer-term results. Over a two-year period, the death and hospitalization rates that the model predicted closely matched actual observed outcomes. However, for other states, the inaccuracy was notably higher over the two-year period. This was, in large part, a result of the fact that their data only encompassed an 8-month period. Despite the inaccuracies caused by lack of data, the Markov chain model still did rather well at predicting patient risks especially when it came to the most important outcomes like death and hospitalization. As such, using Markov chain models for risk assessment can inform medical professionals about important risks to consider. However, it is important to note that the single-center design of the study does limit its generalizability, and further validation of the study's results are necessary [8].

Beyond dynamic risk stratification, Markov models have also been used to simulate and compare the effectiveness of different treatments with each other. In one review done by McCullum et al. [9], they examined how Markov models have been applied by other researchers in radiation oncology to compare various treatment options. They found that most available literature in the area focused on Monte Carlo simulations which compared several fixed treatment policies. While these papers do find the better policy between the ones selected, they are constrained by the requirement to define all policies in advance. There is no guarantee that the selected treatments for comparison will be the most optimal among all possible treatments [9-10]. Alternatively, the other papers they reviewed used Markov Decision Processes (MDPs). Unlike Monte Carlo simulations which were used to compare fixed policies, MDPs can determine the true optimal treatment policy by working to maximize their set goal over time. However, compared to Monte Carlo simulations of pre-selected treatment policies, MDPs require richer datasets and greater computational power. But as MDPs require far less computation than testing all possible treatment policies, there is significant value in exploring them further in order to find the most optimized policies [9].

Lastly, Markov chain models have been heavily utilized in health economics and cost-effectiveness analysis for long-term resource allocation and policy development [1]. Markov models allow for comparisons of healthcare interventions as they model outcomes which can be paired with costs to calculate Quality-Adjusted Life Years (QALYs) and other utility-based measures. These measurements are essential for analyzing cost-effectiveness [4]. In neurosurgery, a high-cost specialty, Markov models were applied to compare expected lifetime costs and QALYs for patients undergoing one of three common surgical procedures. It captured not only the immediate costs of care but also projections of expected outcomes over time in alternative interventions [6]. The structured nature of Markov models also supports one-way, two-way, and probabilistic sensitivity analyses, further making it easier to assess assumptions about transition probabilities and state-associated costs [6]. At a broader level, Franklin & Hunter [11] used a five-state stratified cohort model to evaluate fall-risk screening in older adults, finding that preventive interventions were substantially more cost-effective in older patients as they were more likely to have falls that injured them. In another case, Li et al. [12] combined a decision tree for initial patient allocation with a

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Markov model using real-world Dutch data. They found that fracture liaison services achieved an ICER of €409 per QALY, a cost well below the Dutch threshold of €20,000 per QALY. Together, these studies illustrate how Markov modeling can support evidence-based resource allocation under conditions of clinical uncertainty.

## 4. Limitations and future directions

Despite the usefulness of Markov models, there are still several major limitations tht must be considered in their usage. The first of these limitations is the Markovian assumption, also known as the memoryless property. This property refers to how the transition probabilities of a Markov chain model are determined by the current state and not by their previous states. In the pharmacoeconomic modeling of Dengue vaccination, the memoryless property prevented the model from accounting for prior infection status when it came to estimating transition probabilities. As a result, cost-effectiveness estimates were meaningfully distorted [2]. The second major limitation is state aggregation, where the wide range of patient characteristics, clinical events, and more must be collapsed into a limited number of distinct states. However, aggregating states often results in a model losing valuable details related to the characteristics of a disease characteristics or the effects of different treatments. Townsley et al. [7] demonstrated the issue of state aggregation within colorectal cancer screening. They showed that aggregating patient risk profiles into broad states obscured important differences in disease trajectory and that more refined model specifications were needed to capture these differences. The third major limitation is the data requirements of Markov models. Specifically, the long-term follow-up data often necessary when it comes to estimating transition probabilities that take time into consideration, is both expensive to collect and frequently unavailable. As obtaining the long-term data is sparse, the transition probability estimates that require it can often carry uncertainties and inaccuracies [7].

Fortunately, there are solutions being developed to address the limitations of traditional Markov models. One of these solutions is hybrid modeling, which integrates Markov frameworks with machine learning algorithms, which can improve the prediction of state transitions even when the data for the models are sparse or partially unobserved by analysing the non-linear interactions between clinical variables [13]. Nicora et al. [14] demonstrated the utility in using machine learning algorithms with Markov models by incorporating matrix tri-factorization into a continuous-time Markov model for myelodysplastic syndrome progression to extrapolate data from the sparsely available existing genomic data. The use of Markov Decision Processes also offers a promising direction. While MDPs do require both greater datasets and greater computational demands than the simulation of pre-specified policies, they can find the most optimal treatment policy and are still more efficient than simulating all possible treatment options [9]. MDP's potential to perfect treatment policies make them highly valuable for future clinical research.

Beyond the medical fields, Hidden Markov Models have demonstrated their usefulness when it comes to financial modeling, stock market analysis, and bioinformatics [13]. Clinical fields can benefit greatly by using the advancements in Markov modeling from these non-medical fields.

## 5. Conclusions

This paper summarizes the role of Markov chain models in the development of clinical research methodology as they provide a structured approach to managing uncertainty and to the temporal dynamics of patient care. Markov models have proven effective when it comes to risk stratification, clinical decision-making, and cost-effectiveness analysis across a range of clinical contexts and

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fields. However, the accuracy of Markov chain models continues to suffer from the limitations of the memoryless principle and state aggregation. The limitations of Markov chain models are being addressed through hybrid modeling and the use of Markov Decision Processes.

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