

Markov Modelling Of Assessment Of Hypothyroidism Progression

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Abstract

Hypothyroidism is a chronic endocrine disorder characterized by gradual transitions between clinically distinct states over time, making it well suited for stochastic state-transition modelling. This study proposes a discrete-time Markov modelling framework to analyze and quantify the progression dynamics of hypothyroidism using a finite number of clinically relevant disease states. A three-state Markov model comprising subclinical hypothyroidism, treated hypothyroidism, and overt hypothyroidism is developed to capture short-term disease evolution. Transition probability matrices are constructed, and probability mass functions are derived for one-day and two-day sequence lengths. Using these distributions, key statistical characteristics including mean, variance, skewness, and kurtosis are analytically obtained to describe the intensity, variability, and distributional behavior of each disease state.

Numerical illustrations based on secondary clinical data are employed to examine model behavior and to interpret disease dynamics in practical settings. The results indicate a higher likelihood and greater volatility associated with overt hypothyroidism compared with subclinical and treated states, while subclinical hypothyroidism exhibits relatively lower variability. Distributional properties further reveal state-specific asymmetry and tail behavior, offering insights into disease stability and progression risk.

This research focusses on applying markov modelling to the progression of Hypothyroidism. The Markov model is a useful way to assess/ extract the hidden information of hypothyroidism over time. In this article, we have illustrated the usefulness of Markov Models in the analysis of follow-up of Hypothyroidism. The valuable information provided by the Markov Model has rendered it as a reliable biomarker for the diagnosis and prognosis of Hypothyroidism. The main purpose of this study is to assess the importance and significance of Markov Model as a useful disease marker for Hypothyroidism by using a three stage Markov model.

Keywords: Hypothyroidism, Markov Model, Transition Probability Matrix, Disease Progression.

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I. Introduction:

Markov Modelling Framework for Hypothyroidism

The normal human thyroid is a homogeneous tissue mainly composed of two cell types: follicular cells and parafollicular cells. Thyroid follicular cells are epithelial cells responsible for the production, storage and secretion of thyroid hormone. Parafollicular cells (also known as C cells) account for only a relatively small proportion of the thyroid cells.

In Hypothyroidism, the thyroid gland secretes an inadequate amount of thyroid hormones. Hypothyroidism is a common non-communicable disease, especially in developing countries like India, posing a huge economic burden on the family and nation as a whole. In studies of many chronic medical conditions, the health status of a patient may be characterized using a finite number of disease states.

In the biomedical domain, we may predict Hypothyroidism patient using prediction algorithms. Such prediction can be done with the help of periodic clinical data. Machine learning approaches for prediction such as Markov Model can be used effectively in solving real time problems. Markov Model (MM) can be applied in many fields where the goal is to recover a data sequence that is not immediately observable and which is dependent on previous sequence. Thus, Markov Model can be used for detecting various diseases like thyroid, diabetes and heart problems. The prediction power of MM can be useful to address many problems in medical domain. we are proposing the idea to apply MM in predicting the risk of Hypothyroidism disease over a period of time.

Markov models provide a natural and transparent framework for representing the long-term progression of hypothyroidism as a stochastic process with discrete disease states and time-dependent transitions. Thyroid function evolves gradually over years, with individuals moving between euthyroid, subclinical, and overt disease states, making it well suited to state-transition modelling approaches.

In a typical hypothyroidism Markov model, mutually exclusive health states include euthyroidism, subclinical hypothyroidism, overt hypothyroidism, and treated hypothyroidism, with optional absorbing states such as death. Transitions between states occur at fixed time intervals (e.g., annual cycles) and are governed by probabilities estimated from longitudinal cohort studies and population-based surveys. Large epidemiological studies such as the Whickham Survey, HUNT Study, TEARS, and NHANES provide empirical estimates of incidence, remission, and progression rates across thyroid states in the general population and in elderly subgroups (Vanderpump et al.; Åsvold et al.; Vadiveloo et al.; Hollowell et al.).

Natural history studies demonstrate that subclinical hypothyroidism is a dynamic and reversible condition, with transition probabilities strongly influenced by baseline TSH, thyroid autoantibody status, age, sex, and iodine status (Huber et al.; Diez and Iglesias; Imaizumi et al.; Somwaru et al.). These covariates can be incorporated into Markov models either by stratified transition matrices or by covariate-dependent transition functions, allowing heterogeneity in disease trajectories to be captured.

Recent modelling efforts have extended classical Markov structures by embedding them within biologically based and Bayesian frameworks. Lifetime thyroid status models integrate physiological constraints and exposure-related perturbations, enabling transitions to be informed by both mechanistic understanding and epidemiological data (Dzierlenga et al.; Lumen et al.; McLanahan et al.). Bayesian Markov models further allow uncertainty in transition probabilities to be formally quantified and propagated through long-term projections (Gelman et al.).

Overall, Markov modelling offers a coherent approach for synthesizing epidemiological evidence, clinical guidelines, and mechanistic insights to evaluate the long-term burden of hypothyroidism, assess progression risks, and simulate the population impact of screening and treatment strategies (Garber et al.; Biondi).

In 2017, Celia Siu et al., have described regarding epigenoms and transcriptome. The thyroid gland, necessary for normal human growth and development, functions as an essential regulator of metabolism by the production and secretion of appropriate levels of thyroid hormone. However, assessment of abnormal thyroid function may be challenging suggesting a more fundamental understanding of normal function is needed. Their study generated the first published reference epigenomes for human thyroid from four individuals using ChIP-seq and RNA-seq.

Dzierlenga MW et al., (2019) had developed a Markov chain model of functional thyroid disease status over the lifetime. Subjects were in one of seven thyroid disease states at any given point in their lives [normal, subclinical hypothyroidism, overt hypothyroidism, treated thyroid disease (ever), subclinical hyperthyroidism, overt hyperthyroidism, and reverted to normal thyroid status]. They used a Bayesian approach to fitting model parameters while a priori probabilities of changing from each disease state to another per unit time were based on published data and summarized using meta-analysis, when possible.

After reviewing the existing literature, it is felt that the MM has been used for hyperthyroidism mapping. However, in the context of hyperthyroidism progression research gap is existing in natural history evidence from longitudinal cohorts, physiological realism when linked to biologically based thyroid models and clinical thresholds used in practice guidelines, which will be addressed by Markov structure synthetization. The outcome has to be properly modelled with suitable Statistical tools and provides a robust platform for evaluating screening policies, treatment timing, and long-term disease burden of hypothyroidism.

Hence, the necessity of developing and predicting the parameters for the disease progression of Hypothyroidism motivated us to proceed with the work in this direction. This study has given focus on the development of constructing a Markov model based on transition probabilities. We have formulated the probability distributions for different states in the spans of 1 day ahead, 2 days ahead sequences. The study also derived the statistical characteristics based on the probability distributions. Mathematical formulae for all Karl-Pearson's measures were derived from the formulated probability distributions. Numerical data from sources of Wikipedia is collected and analysed for a better understanding of the model behaviour in a common man's perception. Indicators of intensity of states like *Subclinical hypothyroidism*, *Treated hypothyroidism* and *Overt hypothyroidism* are obtained from the data. Statistical summary reports are explored after writing the appropriate Python-code and its execution. Data interpretation/statistical inferences are carried out from the numerical illustration of real-time.

The proposed Markov framework provides a transparent and flexible approach for integrating longitudinal clinical observations with probabilistic disease modeling. By quantifying transition behavior and statistical properties of hypothyroidism states, the model offers a useful analytical tool for understanding hypothyroidism progression, supporting clinical monitoring, and informing decision-making in long-term

management strategies. The framework may be extended to incorporate covariates or Bayesian formulations for population-level policy evaluation and risk assessment.

II. Stochastic Model

This model intends to derive probability mass functions of the discrete distribution of a number of states. Let the states of transitions be of three categories, namely State – 1: *Subclinical hypothyroidism*; State-2: *Treated hypothyroidism*; State-3: *Overt hypothyroidism*. a_{ij} - the probability of transition from i^{th} state to j^{th} state.

$$a_{ij} : pr\{x_n = j / x_n = i\}; i, j = 1, 2, 3; a_{ij} \geq 0 \quad \forall i, j = 1, 2, 3 \quad \& \quad \sum_{j=1}^3 a_{ij} = 1; \forall i = 1, 2, 3$$

Let there be ‘i’ and ‘j’ states in which ‘i’ is the state of the previous trial and ‘j’ be the state of the current trial $i, j = 1, 2, 3$ where, 1, 2, 3 represents the identified positive cases in the states of *Subclinical hypothyroidism*, *Treated hypothyroidism*, *Overt hypothyroidism* respectively.

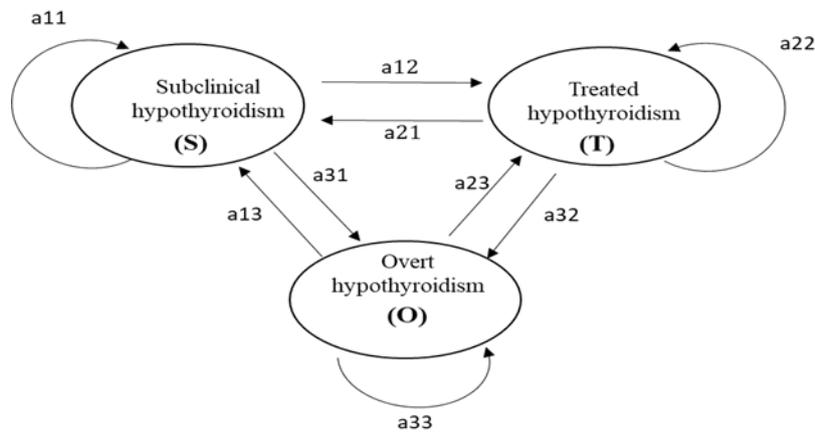


Figure 1. The schematic diagram for three state Markov model of Hypothyroidism progression.

III. Probability Distributions For One-Day Length Of A Sequence

$P[X(C)] = n$, Let C be a random variable, which denotes the number of times a specific state occurs in the study of one-day length. In this study, C can consist of three states namely, *Subclinical hypothyroidism*, *Treated hypothyroidism* and *Overt hypothyroidism* i.e., $C=S$ (or) T (or) O . ‘n’ will be the number of times the happening of the state, it can take values 0 to 1. Here, ‘0’ indicates the non-happening, and ‘1’ indicates the happening of the particular state under study.

Probability distribution of “Subclinical hypothyroidism”

$$P[X(S)] = \begin{cases} \sum_{j=2}^3 a(j) & ; X(S) = 0 \\ a(1) & ; X(S) = 1 \end{cases} \tag{3.1}$$

Characteristic function is

$$\phi_{[X(S)]}(t) = \sum_{j=2}^3 a(j) + e^{it} a(1) \tag{3.2}$$

Probability distribution of “Treated hypothyroidism”

$$P[X(T)] = \begin{cases} \sum_{j=2}^3 a(j) & ; X(T) = 0 \\ a(2) & ; X(T) = 1 \end{cases} \tag{3.3}$$

Characteristic function is

$$\phi_{[X(t)]}(t) = \sum_{\substack{j=1 \\ j \neq 2}}^3 a(j) + e^{it} a(2) \tag{3.4}$$

Probability distribution of “Overt hypothyroidism”

$$P[X(O)] = \begin{cases} \sum_{j=1}^2 a(j) & ; X(O) = 0 \\ a(3) & ; X(O) = 1 \end{cases} \tag{3.5}$$

Characteristic function is

$$\phi_{[X(o)]}(t) = \sum_{j=1}^2 a(j) + e^{it} a(3) \tag{3.6}$$

Statistical characteristics

In this section, some statistical characteristics are derived for the developed probability distributions given in the equations (3.1), (3.2) and (3.3) respectively. In this a(C) will be the probability for happening of the states where the values of ‘C’ will be ‘S’ which indicates the probability of "Subclinical hypothyroidism", ‘T’ which indicates the probability of “Treated hypothyroidism” and ‘O’ indicates the probability of " Overt hypothyroidism ".

Mean

$$E[X(C)] = a(C) \tag{3.7}$$

Variance

$$V[X(C)] = a(C)[1 - a(C)] \tag{3.8}$$

Third central moment

$$\mu_3[X(C)] = a(C)(1 - a(C))(1 - 2a(C)) \tag{3.9}$$

Skewness

$$\beta_1[X(C)] = [a(C)(1 - a(C))(1 - 2a(C))]^2 [a(C)(1 - a(C))]^{-3} \tag{3.10}$$

Kurtosis =

$$\beta_2[X(C)] = [[a(C)(1 - a(C))]^2 (1 - a(C))(1 - 3a(C))(1 - a(C))] [a(C)(1 - a(C))]^{-2} \tag{3.11}$$

IV. Probability Distributions For Two-Day Length Of Sequence

On similar lines of one-day length in section 3, the sequence of two-day length is considered in this section. The occurrence of non-happening of the state in two-days length, happening of the state once in two days, and happening of the state twice in two-days length are to be modelled for the derivation of the probability distribution. The possibility of taking the value of ‘n’ is 0, 1, 2.

Probability distribution of "Subclinical hypothyroidism"

$$P[X(S)] = \begin{cases} \sum_{j=2}^3 [\sum_{i=2}^3 a(i) a_{ij}^{(2)}]; & X(S) = 0 \\ \sum_{i=2}^3 a(i) a_{i1}^{(2)} + a(1) \sum_{j=2}^3 a_{1j}^{(2)}; & X(S) = 1 \\ a(1) a_{11}^{(2)}; & X(S) = 2 \end{cases} \tag{4.1}$$

Characteristic function is

$$\phi_{X(S)} = \sum_{j=2}^3 [\sum_{i=2}^3 a(i) a_{ij}^{(2)}] + e^{it} \left[\sum_{i=2}^3 a(i) a_{i1}^{(2)} + a(1) \sum_{j=2}^3 a_{1j}^{(2)} \right] + e^{2it} [a(1) a_{11}^{(2)}] \tag{4.2}$$

Probability distribution of "Treated hypothyroidism"

$$P[X(T)] = \begin{cases} \sum_{j=1}^3 [\sum_{i=1, i \neq 2}^3 a(i)a_{ij}^{(2)}]; & X(T) = 0 \\ \sum_{i=1, i \neq 2}^3 a(i)a_{i2}^{(2)} + a(2)\sum_{j=1, j \neq 2}^3 a_{2j}^{(2)}; & X(T) = 1 \\ a(2)a_{22}^{(2)}; & X(T) = 2 \end{cases} \quad (4.3)$$

Characteristic function is

$$\phi_{X(T)} = \sum_{j=1}^3 [\sum_{i=1, i \neq 2}^3 a(i)a_{ij}^{(2)}] + e^{it} \left[\sum_{i=1, i \neq 2}^3 a(i)a_{i2}^{(2)} + a(2)\sum_{j=1, j \neq 2}^3 a_{2j}^{(2)} \right] + e^{2it} [a(2)a_{22}^{(2)}] \quad (4.4)$$

Probability distribution of "Overt hypothyroidism"

$$P[X(O)] = \begin{cases} \sum_{j=1}^2 [\sum_{i=1}^2 a(i)a_{ij}^{(2)}]; & X(O) = 0 \\ \sum_{i=1}^2 a(i)a_{i3}^{(2)} + a(3)\sum_{j=1}^2 a_{3j}^{(2)}; & X(O) = 1 \\ a(3)a_{33}^{(2)}; & X(O) = 2 \end{cases} \quad (4.5)$$

Characteristic function is

$$\phi_{X(O)} = \sum_{j=1}^2 [\sum_{i=1}^2 a(i)a_{ij}^{(2)}] + e^{it} \left[\sum_{i=1}^2 a(i)a_{i3}^{(2)} + a(3)\sum_{j=1}^2 a_{3j}^{(2)} \right] + e^{2it} [a(3)a_{33}^{(2)}] \quad (4.6)$$

Statistical characteristics

Some statistical characteristics are explored for the probability distributions shown in the above equations (4.1), (4.2), (4.3). Let us consider, γ_R is the probability of non-happening of the state, α_R is the probability of happening of the state once, β_R is the probability of happening of the state twice. Here, $C = S, T, O$.

Mean =

$$E[X(C)] = \alpha_R + 2\beta_R \quad (4.7)$$

Variance

$$V[X(C)] = \alpha_R(1 - \alpha_R) + 4\beta_R(1 - \alpha_R - \beta_R) \quad (4.8)$$

Third central moment

$$\mu_3[X(C)] = 2\alpha_R^3 + 16\beta_R^3 - 3\alpha_R^2(1 - 4\beta_R) - 24\beta_R^2(1 - \alpha_R) + \alpha_R(1 - 8\beta_R) + 8\beta_R \quad (4.9)$$

Skewness =

$$\beta_1[X(C)] = \frac{[2\alpha_R^3 + 16\beta_R^3 - 3\alpha_R^2(1 - 4\beta_R) - 24\beta_R^2(1 - \alpha_R) + \alpha_R(1 - 8\beta_R) + 8\beta_R]^2}{[\alpha_R(1 - \alpha_R) + 4\beta_R(1 - \alpha_R - \beta_R)]^3} \quad (4.10)$$

Kurtosis =

$$\beta_2[X(C)] = \frac{[\alpha_R + 4\beta_R(4 - 10\alpha_R) - 4\alpha_R^2(1 - 12\beta_R) - 8\beta_R^2(8 - 15\alpha_R + 9\alpha_R^2) + 6\alpha_R^3(1 - 4\beta_R) + 96\beta_R^3(1 - \alpha_R) - 3\alpha_R^4 - 48\beta_R^4][\alpha_R(1 - \alpha_R) + 4\beta_R(1 - \alpha_R - \beta_R)]^2}{[\alpha_R(1 - \alpha_R) + 4\beta_R(1 - \alpha_R - \beta_R)]^3} \quad (4.11)$$

V. Description Of Methodology

The current study is on developing Markov model for three (*Subclinical hypothyroidism, Treated hypothyroidism, Overt hypothyroidism*) states of hypothyroidism. Separate probability distribution developed for each state (*Subclinical hypothyroidism, Treated hypothyroidism, Overt hypothyroidism*). Statistical measures like mean, variance, coefficient variation, and Pearson’s coefficients are derived for each state using corresponding developed probability distribution. For understanding the behaviour of developed model numerical data set is considered for this study.

Subclinical and Overt hypothyroidism are classified by thyroid-stimulating hormone (TSH) and free thyroxine (fT_4) levels. Overt hypothyroidism is defined by elevated TSH and low (fT_4) with symptoms, while subclinical hypothyroidism presents with elevated TSH but normal (fT_4) levels, often with few or no symptoms. Treated hypothyroidism is generally classified based on the status of thyroid hormone levels (specifically TSH and Free T_4) while on medication, reflecting whether the patient is in a stable, under-treated, or over-treated state.

The secondary data on hypothyroidism of procured from the internet sources which consists of 230 observations/records of 46 patients. The observations have been recorded at regular intervals from the patients. The number of incidences per 6 weeks is categorised as three transitions: *Subclinical hypothyroidism, Treated hypothyroidism, and Overt hypothyroidism*.

VI. Results And Discussion

Probability distribution for *Subclinical hypothyroidism* state

The probability distribution for one and two-days length of *Subclinical hypothyroidism* state is placed in table-1 and table-2 respectively.

X(S)	0	1
P[X(S)]	0.228	0.772

Table 1. Probability distribution for one-day length of sequence

From table 1, it is observed that the non-happening of the state has a chance of 0.228 and the happening of the condition has a chance of 0.772. Hence, it is inferred that the happening of the *Subclinical hypothyroidism* is more likely than the non-happening in the *Subclinical hypothyroidism* state.

X(S)	0	1	2
P[X(S)]	0.15634	0.17689	0.66677

Table 2. Probability distribution for two-day length of sequence

From table 2, it is observed that the non-happening of the state has a chance of 0.15634 and happening of the state once in two days is 0.17689 and the occurrence of the condition twice in two days has a chance of 0.66677. Hence, we may interpret the result of occurrence of the *Subclinical hypothyroidism* state as more likely when compared to others.

Statistical measures for *Subclinical hypothyroidism* state

The statistical characteristics for the *Subclinical hypothyroidism* state are placed in the table-3 for understanding the behaviour of the developed model.

Statistical measures	1 day	2 days
Mean	0.772	1.51043
Variance	0.176016	0.562571
3 rd central moment	-0.09575	-0.48402
Beta 1	1.681302	1.315794
Beta 2	2.681302	2.730057

Table 3. Statistical results for sequence of *Subclinical hypothyroidism* State

Probability distribution for *Treated hypothyroidism* state

The probability distribution for one and two-days length of *Treated hypothyroidism* state is placed in table-4 and table-5 respectively.

X(T)	0	1
P[X(T)]	0.61245318	0.38754682

Table 4. Probability distribution for one-day length of sequence

From table 4, it is observed that the non-happening of the state is having a chance of 0.61245318 and the happening of the state has a chance of 0.38754682. Hence, it may be inferred that the non-happening of the *Treated hypothyroidism* has more likely than the happening of the *Treated hypothyroidism state*.

X(T)	0	1	2
P[X(T)]	0.528895342	0.25336795	0.217736708

Table 5. Probability distribution for two-day length of sequence

From table 5, it is observed that the non-happening of the state has a chance of 0.528895342 and happening of the state once is 0.25336795 and the occurrence of the state twice in a run has a chance of 0.217736708. Hence, we may interpret the result of non-occurrence of the *Treated hypothyroidism* state as more likely when compared to others.

Statistical measures for *Treated hypothyroidism* state

The statistical characteristics for the *Treated hypothyroidism* state are placed in the table-6 for understanding the behaviour of the developed model.

Statistical measures	1 day	2 days
Mean	0.387547	0.688841
Variance	0.237354	0.649812
3 rd central moment	0.053382	0.325552
Beta 1	0.213111	0.386257
Beta 2	1.213111	1.81161

Table 6. Statistical results for sequence of *Treated hypothyroidism* State

Probability distribution for *Overt hypothyroidism* state

The probability distribution for one and two-days length of the *Overt hypothyroidism* state is placed in table-7 and table-8 respectively.

X(O)	0	1
P[X(O)]	0.561723	0.438277

Table 7. Probability distribution for one-day length of sequence

From table 7, it is observed that the non-happening of the state is having a chance of 0.561723 and the happening of the state has a chance of 0.438277. Hence, it may be inferred that the non-happening of the *Overt hypothyroidism* is more likely than the happening of the *Overt hypothyroidism state*.

X(O)	0	1	2
P[X(O)]	0.5199619	0.283482	0.1965561

Table 8. Probability distribution for two-day length of sequence

From table 8, it is observed that the non-happening of the state has a chance of 0.5199619 and happening of the state once is 0.283482 and the occurrence of the state twice in a run has a chance of 0.1965561. Hence, it interprets the result that the non-occurrence of the *Overt hypothyroidism* state is more likely when compared to other states.

Statistical measures for *Overt hypothyroidism* state

The statistical characteristics for the *Overt hypothyroidism* state are placed in the table-9 for understanding the behaviour of the developed model

Statistical measures	1 day	2 days
Mean	0.438277	0.676594
Variance	0.24619	0.611927
3 rd central moment	0.030391	0.304122
Beta 1	0.061899	0.403642
Beta 2	1.061899	1.909403

Table 9. Statistical results for sequence of *Overt hypothyroidism* State

Recommendations

From table 3, 6 and 9 it is observed that the average occurrence of one-day length for *Subclinical hypothyroidism*, *Treated hypothyroidism* and *Overt hypothyroidism* states are 0.772, 0.387547 and 0.438277 respectively. Hence, it reveals that the average occurrence of an *Overt hypothyroidism* state in one day is more

likely than other states (*Subclinical hypothyroidism*, and *Treated hypothyroidism*). Similarly, in the sequence of two days the average occurrence for *Subclinical hypothyroidism*, *Treated hypothyroidism* and *Overt hypothyroidism* states are 1.511043, 0.688841 and 0.676594 respectively. Hence, it reveals that the occurrence of Subclinical hypothyroidism state (1.511043) in two days is more likely than other states (*Overt hypothyroidism* and *Treated hypothyroidism*). Healthcare professionals may find these findings useful in controlling and monitoring patient hypothyroidism states.

The variance of one-day length for *Subclinical hypothyroidism*, *Treated hypothyroidism* and *Overt hypothyroidism* states are 0.176016, 0.237354 and 0.24619 respectively. In two-days length for *Subclinical hypothyroidism*, *Treated hypothyroidism* and *Overt hypothyroidism* states are 0.562571, 0.649812 and 0.611927 respectively. Hence, it is observed that there is less volatility observed in the *Subclinical hypothyroidism*, more in the *Overt hypothyroidism* state of one-day sequence length and more in the *Treated hypothyroidism* state of two-days sequence length. It is indicating that there are fluctuations in thyroid-stimulating hormone levels. These results may be helpful to the healthcare professionals giving good treatment and assessing thyroid-stimulating hormone (TSH) and free thyroxine (fT_4) levels' stability.

Regarding Skewness, the third central in both days sequence length of *Treated hypothyroidism* and *Overt hypothyroidism* states are non-negative and positive and while for the *Subclinical hypothyroidism* state is negative. It is interpreted that the distribution is positively skewed in *Treated hypothyroidism* and *Overt hypothyroidism* states and negatively skewed in *Subclinical hypothyroidism* state. These results may help doctors in giving optimal treatment to patients in controlling hypothyroidism levels.

The coefficient of Kurtosis in both days sequence length of *Subclinical hypothyroidism*, *Treated hypothyroidism* and *Overt hypothyroidism* states is less than 3. It reveals that the distribution is platykurtic in Subclinical hypothyroidism, Treated hypothyroidism and Overt hypothyroidism states. These are helpful to healthcare professionals in managing thyroid-stimulating hormone (TSH) and free thyroxine (fT_4) levels' incidents.

VII. Conclusion

The provided analysis delves into the probabilities of *Subclinical hypothyroidism*, *Treated hypothyroidism*, and *Overt hypothyroidism* states, revealing that the occurrence of *Subclinical hypothyroidism* states is more likely than *Treated hypothyroidism* and *Overt hypothyroidism*. This trend persists across both one day and two-days sequences, where the other state's occurrence stands out. The data highlights the *Subclinical hypothyroidism* state's prevalence, indicating its significance in hypothyroidism management.

Moreover, the examination of variance underscores the volatility in thyroid-stimulating hormone (TSH) and free thyroxine (fT_4) levels across these states. Notably, the *Subclinical hypothyroidism* state showcases lower volatility, while the *Treated hypothyroidism* and *Overt hypothyroidism* states demonstrates higher fluctuations. This insight into variability can guide healthcare professionals in devising strategies for stable thyroid-stimulating hormone (TSH) and free thyroxine (fT_4) levels' control.

Skewness and Kurtosis analyses offer further insights. *Treated hypothyroidism* and *Overt hypothyroidism* states exhibit positive skewness and platykurtic distribution, signifying their distribution shape. In contrast, the *Subclinical hypothyroidism* state displays negative skewness and platykurtic distribution, revealing its distinct distribution characteristics.

In summation, this multifaceted analysis provides comprehensive insights crucial for healthcare practitioners managing hypothyroidism. The probabilities, average occurrences, volatility, and distribution properties of different states collectively contribute to an enhanced understanding of thyroid-stimulating hormone (TSH) and free thyroxine (fT_4) levels' dynamics, fostering more effective and personalized patient care approaches.

VIII. Future Scope

Future research may extend this framework to the following analysis:

Mathematical Formulation of a Markov Model for Hypothyroidism in extended way:

Let thyroid disease progression be represented as a discrete-time, finite-state Markov process observed over equally spaced time intervals (e.g., annual cycles). At any time (t), an individual occupies exactly one thyroid health state.

Health States

Define the state space
 $S = \{E, SH, OH, TH, D\}$

where

- E: Euthyroid
- SH: Subclinical hypothyroidism
- OH: Overt hypothyroidism
- TH: Treated hypothyroidism
- D: Death (absorbing state)

This structure reflects the clinically recognized continuum of thyroid dysfunction described in population-based and longitudinal studies (Vanderpump et al.; Huber et al.; Somwaru et al.).

State Occupancy Vector

Let $\pi_t = [\pi_{E,t} \ \pi_{SH,t} \ \pi_{OH,t} \ \pi_{TH,t} \ \pi_{D,t}]$

denote the proportion of the cohort in each state at time t.

Transition Probability Matrix

Disease progression is governed by a **time-homogeneous transition matrix P**:

$$P = \begin{bmatrix} p_{EE} & p_{ESH} & 0 & 0 & p_{ED} \\ p_{SHE} & p_{SHSH} & p_{SHOH} & 0 & p_{SHD} \\ 0 & 0 & p_{OHOH} & p_{OHTH} & p_{OHD} \\ 0 & 0 & 0 & p_{THTH} & p_{THD} \\ 0 & 0 & 0 & 0 & 1 \end{bmatrix}$$

With

$$\sum_j p_{ij} = 1 \quad \forall i$$

Transitions are restricted based on clinical plausibility and empirical evidence. For example:

- Progression from (SH → OH) reflects risk estimates reported in longitudinal cohorts (Díez & Iglesias; Imaizumi et al.).
- Regression (SH → E) captures spontaneous normalization observed in population studies (Huber et al.; Rosario et al.).
- Transition (OH → TH) represents initiation of treatment, consistent with clinical guidelines (Garber et al.).

State Evolution

The cohort distribution evolves according to:

$$\pi_{t+1} = \pi_t P$$

Over a lifetime horizon T, the distribution becomes:

$$\pi_T = \pi_0 P^T$$

This formulation allows estimation of **lifetime prevalence, expected duration in each thyroid state, and cumulative incidence of overt hypothyroidism.**

Covariate-Dependent Transitions

To account for heterogeneity, transition probabilities may depend on individual-level covariates such as age, sex, baseline TSH, thyroid autoantibody status, or iodine exposure:

$$\text{logit}(p_{ij}) = \alpha_{ij} + \beta_{ij} \cdot X$$

This approach is supported by evidence that baseline TSH and thyroid antibodies strongly predict progression risk (Huber et al.; Åsvold et al.; Effraimidis et al.).

Bayesian Specification (Optional Extension)

In a Bayesian framework, transition probabilities are treated as random variables:

$$p_{ij} \sim \text{Beta}(\alpha_{ij}, \beta_{ij})$$

or, for each row,

$$p_i \sim \text{Dirichlet}(\alpha_i)$$

allowing uncertainty from epidemiological estimates (NHANES, Whickham, HUNT) to propagate through long-term projections (Gelman et al.; Dzierlenga et al.).

Compliance with Ethical Standards

Conflict of Interest

The author(s) declares that there is no conflict of interest.

Disclaimer

The views expressed in this paper are purely personal views and not the views of the institution to which the author(s) is affiliated i.e., Government of India.

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