Defining and Monitoring Patients Clusters based on Therapy Adherence in Sleep Apnea Management

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***Abstract*—Obstructive Sleep Apnea (OSA) is a disorder in which breathing repeatedly stops and starts due to recurrent episodes of partial and complete airway obstructions during sleep. One of the common treatments for moderate and severe cases of OSA includes the use of Continuous Positive Airway Pressure (CPAP) devices that keep the airways open. Unfortunately, about 40% of the patients using CPAP devices abandon their therapy within 6 months. In this work, we propose a method to cluster and monitor patients according to their therapy usage behaviour aiming for a timely and appropriate intervention. Our work contrast with simple rule-based methods currently implemented in the sleep clinics today to identify non-adherent behavior. Our approach uses clustering techniques to group the patients into clusters based on the CPAP usage patterns and analyse the transition behavior between months using Markov Chain analysis. We also identify patient groups that are likely to abandon the therapy using Random forest models for each month. This approach improves on the current methods by predicting continuous adherence during all months as opposed to only the 6th month of therapy.**

***Index Terms*—Obstructive Sleep Apnea, Sleep Therapy, Markov Chains, Clustering, Therapy Adherence, Random Forest.**

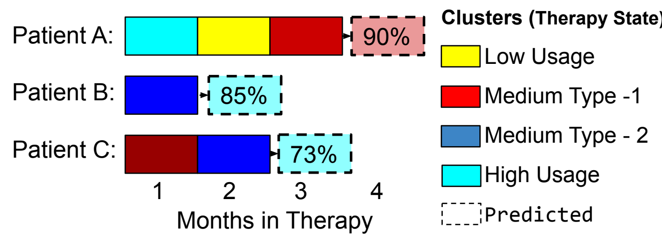

Fig. 1. CPAP Therapy adherence prediction using clustering Need to change color descriptions

I. Introduction

During sleep apnea events, the oxygen levels decrease, and the brain sends a reflex impulse to the pharyngeal muscle in the throat. The impulse causes a choking sensation, leading to interruption of sleep. The long-term effects of having multiple sleep apnea events per night are poor sleep quality, frequent awakenings, and daytime sleepiness. Currently, about 22 million Americans are diagnosed with Sleep Apnea, and thousands of new cases are identified every year [8].

In mild cases of sleep apnea, defined by having an Apnea-Hypopnea Index (AHI)[1] less than 15 but greater than 5, the treatment includes lifestyle changes such as a healthier diet and physical exercise. However, more invasive treatment such as Continuous Positive Airway Pressure (CPAP) therapy treatment is needed for more severe cases. The USA solely has 8 million CPAP users ADD reference, a population that grows 9% per year.

The CPAP is a mask connected to a pump that injects air into the patient's respiratory system to create positive air pressure and prevent the upper airways from collapsing. Since the therapy is not curative, patients should use the device constantly during the night for optimal effectiveness. Ensuring at least 4 hours of usage per night is essential to have significant outcomes from CPAP therapy [10], [11]. To be classified as long-term adherent, a patient should use the device for more than 4 hours for at least 70% of the days during a 30 days period (i.e. at least 21 days) [13], [14]. Owing to various social and psychological factors, the general adherence to CPAP therapy is as low as 60% of the patients [23]. The consequences of not treating sleep apnea can be devastating for an individual since its prevalence is highly associated with high blood pressure, chronic heart failure, stroke, type 2 diabetes, and depression ADD references.

Administrating early intervention on individuals who are likely to not adhere to their therapy is critical to revert non-adherent behavior ADD REFERENCE[2]. To perform a cost-effective early intervention, we need an accurate early identification of non-adherence to prioritize those individuals who need more attention.

In this work, we propose a novel framework that uses clustering techniques to categorize patients into different groups based on their therapy behavior and then use it to identify patients who need intervention. Our approach defines the states in which a therapy trajectory for each individual can be mapped as illustrated in Figure 1. We show that these states depend on the level of adherence and how consistent the patients

[1]number of apnea or hypopnea events during one night, divided by the hours of sleep

[2]"Surveillance of medication use: Early identification of poor adherence," Journal of the American Medical Informatics Association

are in their therapy. By assuming that patients' behavior can change over time, we use Markov chain analysis calculate the transition probability of patients from one state to other states for any month in the therapy. Using the transition probabilities, we then compute the steady state probabilities of adherent and non-adherent groups, which serve as a metric to quantify the overall adherence of patients to the therapy(or we can say performance of patient monitoring method). Finally, we use a random forest model to predict each individual's therapy state for the next month based on past therapy information.

II. Related Work

Many attempts have been made to identify the key factors affecting CPAP adherence. In [15], the authors investigates device design, air humidity and psychological factors like claustrophobia. But none of them have been identified as predictive of adherence. Adherence is majorly affected by symptom amelioration, however significant symptom improvement might not occur until 6 months into therapy [16]. Alongside the adherence problem, most insurance plans require that patients are long-term adherents in the 6th month of therapy, or they will no longer cover the treatment ADD REFERENCE [3]. Thus, waiting till 6 months to intervene could be too late and might lead to permanent therapy abandonment by the patient.

As mentioned in [18] and [19], patients who receive real-time feedback are more likely to follow the therapy. Hence, continuous monitoring is important in effectively treating a patient. TAPC-CPAP tries to identify patients who are likely to drop the therapy much before the 6th month threshold and thereby helps in real-time intervention in such cases. This reduces the cost of telemedicine [20] and also impacts patients' lifestyle positively [21], [22].

Early intervention comes with the early identification of who are likely to abandon therapy within 6 months for intervention. According to [17], the adherence prediction for 30 days can be achieved using the first 3 days data of number of hours the patients are using the CPAP device along with their age and race. In [9], the authors propose two one-shot models: one for 13th day and the other for 30th day, which predict the adherence of the patient 5 months later. [23] proposes a continuous adherence prediction framework (CTAP-CPAP), in which, 150 models were trained - one of each day until the 150th day - and all of them predict the adherence of the patient between 150th to 180th day.

These studies prioritize patients but only consider predictions for the last 30 days of the 6th month of therapy. Therefore, we propose a novel approach that can be used to predict patients' adherence to therapy for each month starting from the 2nd month of the therapy. In contrast to previous work, we quantify the transition probability of a patient who was in an adherent state to change back to a non-adherent state and vice-versa. We are the first who define behavior therapy state and investigate how patients change their behavior over time since the first month of therapy.

[3]Positive airway pressure (pap) devices: Complying with documentation & coverage requirements

ADD REFERENCES ON PATIENT CLUSTERING TECHNIQUES

III. Methodology

In this section we discuss the the steps we followed to achieve the results for the proposed problem.

A. Data

The data we used for this study was collected and shared to us by the Fairview Sleep Clinic. The dataset contains the daily time on face (number of hours the machine detects breathing) from 1815 patients who used CPAP machines with nightly granularity. Every patient considered for this work has the data for at least the first 6-months of therapy.

For classification, we randomly divided patients into training(75%) and testing(25%) sets. The parameters of the Random Forest models used in this work were fit based on patients information from the training set. The prediction results are based on new patients from the test set.

B. Preprocessing

We reduced the granularity of the time-series daily data to monthly by aggregating the time on face signal by the mean and standard deviation (std) for each patient. The slope as aggregating metric was considered, but it did not incorporate significant information to the models and was disregarded. To define the clusters, the mean and standard deviation for all the 6 months of data is also computed for each patient.

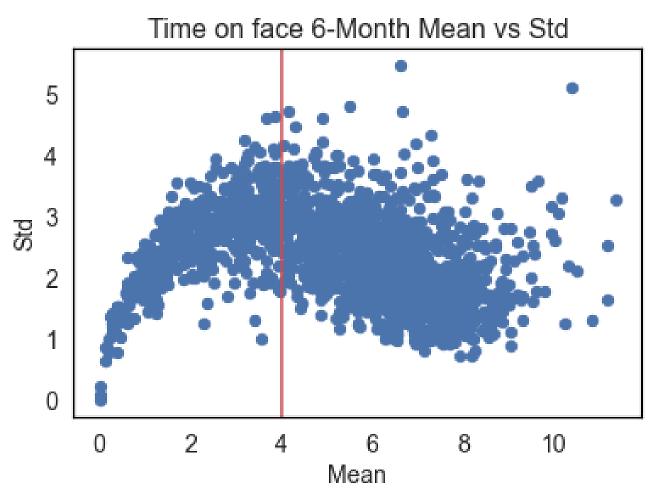

Fig. 2. Distribution of 6-month aggregate values.

2 shows the distribution of 6-month aggregate values for all the patients. The range for mean is almost twice as the range for std. But as most clustering methods are sensitive to the distance measure, both the features: standard deviation and the mean, for monthly aggregates as well as 6-month aggregates are scaled using a standard scaler that was fit on the 6-month aggregates. This is to normalize the features so that they will have a similar magnitude while clustering. Equation 1 denotes the transformation for the scaling process where z is the transformed feature, x is the original feature, and μ and

TABLE I
DESCRIPTION AND CATEGORIZATION OF THE CLUSTERS

Cluster	Colour	Description	adherence
0	Red	Low mean and low std dev	Non-adhering
1	Yellow	Low mean and high std dev	Non-adhering
2	Cyan	High mean and high std dev	Adhering
3	Blue	High mean and low std dev	Adhering

σ are the mean and the standard deviation of the feature from 6-month aggregates data.

$$z = \frac{(x-\mu)}{\sigma} \tag{1}$$

C. Clustering Patients

To define the clusters of patients in the CPAP therapy we analysed their usage pattern derived from the pre-processing step to cluster them into different groups that we call therapy states. We expect that the clusters would naturally be distributed according to their average therapy use, otherwise we would not be able to distinguish adherence patients from non-adherent patients solely by the clusters.

K-means (KM) and Gaussian Mixture Models (GMM) were both evaluated as potential clustering algorithm to be used in our work. The models were trained on the scaled 6-month aggregate data for each patient.

The most important parameter in a clustering algorithm is to choose K, the number of clusters, that we expect to be generated from the clustering algorithm. In Figure 3 we show the plots of AIC (Akaike Information Criterion) & BIC (Bayesian Information Criterion) for the GMM algorithm. In the same figure we show the SS (sum of squares) for the K-means. By using the elbow curve method in both plots, we decided that the number of clusters to be K=4. As shown in Figure 4, GMM formed clusters that are more dependent on the Mean value but not much explainability in terms of the standard deviation. Also, comparing to the threshold of 4 hours of mean usage, none of the clusters except the blue cluster can be categorized as adherent. On the other hand, K-Means provides a good clustering that can be explained well and can be divided into adhering and non-adhering groups. Although the yellow cluster has many values above the threshold, their high standard deviation indicates erratic usage and can be categorized as non-adherent. We provided a human interpretation of the clusters created by K-Means model in Table.I.

The same K-Means model that was fit using the 6-month aggregate data was used to cluster patients during 1st, 2nd, 3rd, 4th, 5th and 6th month separately using the monthly aggregate data. We used the same model as the underlying distribution is same and as the clusters are defined as adhering or non-adhering based on that model. to preserve uniformity across different time intervals while classifying patient therapy states The distribution of patients over the mean and std axes in each month and their clusters can be visualized in Figure 5. Even though the distributions look similar in all the months, the cluster compositions are different for each month. So, the usage pattern is shifting from one state to another from one month to another for many patients.

TABLE II
TRANSITION PROBABILITIES BETWEEN THE CLUSTERS

Clusters	0	1	2	3
0	0.79	0.11	0.07	0.04
1	0.17	0.48	0.26	0.09
2	0.07	0.19	0.44	0.30
3	0.02	0.03	0.19	0.76

TABLE III
STEADY STATE PROBABILITIES FOR THE CLUSTER TRANSITIONS

Clusters	0	1	2	3
Probability	0.23	0.16	0.23	0.38

D. Cluster Transition Probabilities

We analysed how patients change from one state to another over time starting from 1st month to the 6th month of therapy. The heatmap in Figure 6 shows these transitions for a random stratified sample of 100 patients where each column is a month, and each thin line is a patient. We show the first month ordered by cluster from the one with lowest adherence (red) to the one with highest adherence (blue) and the subsequent columns are the clusters that patients changed to in the subsequent months. From the heatmap we observe that patients in the extreme clusters (red & blue) tend to remain in the same cluster throughout the course of the therapy. The patients in the other two clusters (yellow & cyan) keep shifting between the clusters. Hence, considering the process as Markov chain where the clusters are the states, we computed the state transition probabilities (p_{ij}) between the states using 2 and the steady state probabilities (π_j) for each state using using 3 and using 4, which are shown in II and III respectively. The fact that the extreme clusters are relatively stable is also evident from the transition probabilities where the first and last elements on the diagonal are much higher compared to the other two diagonal elements.

$$p_{ij} = \frac{\sum_{t=1}^{t=5} Count(i \rightarrow j)}{\sum_{j=0}^{j=3} \sum_{t=1}^{t=5} Count(i \rightarrow j)} \tag{2}$$

$$\pi_j = \sum_{k=0}^{k=3} \pi_k p_{kj} \tag{3}$$

$$\sum_{j=0}^{j=3} \pi_j = 1 \tag{4}$$

E. Therapy State Prediction using Machine Learning

After analysing the state transitions of the patients from one month to another using K-Means model, we evaluated if we can predict the next state for any patient using the current

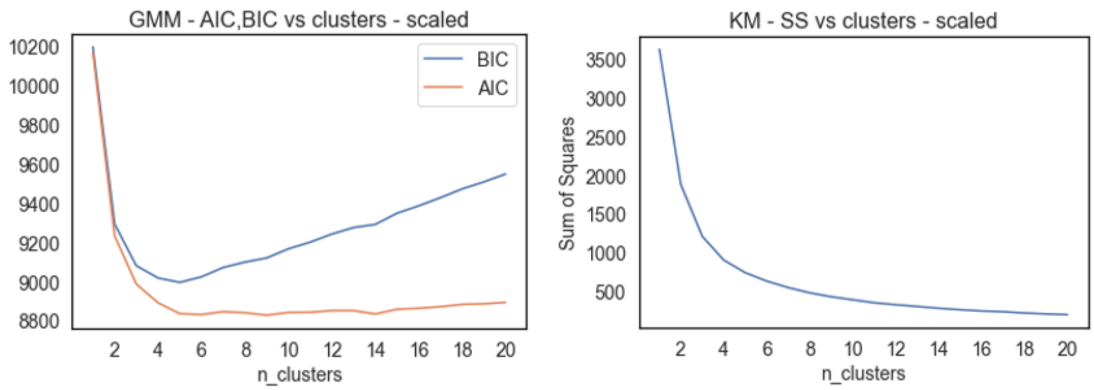

Fig. 3. Both the plots -Sum of Squares and AIC,BIC plot- have a sudden change of slope(elbow) at n=4. Hence, 4 is the optimum number of clusters for both K-Means and the GMM models

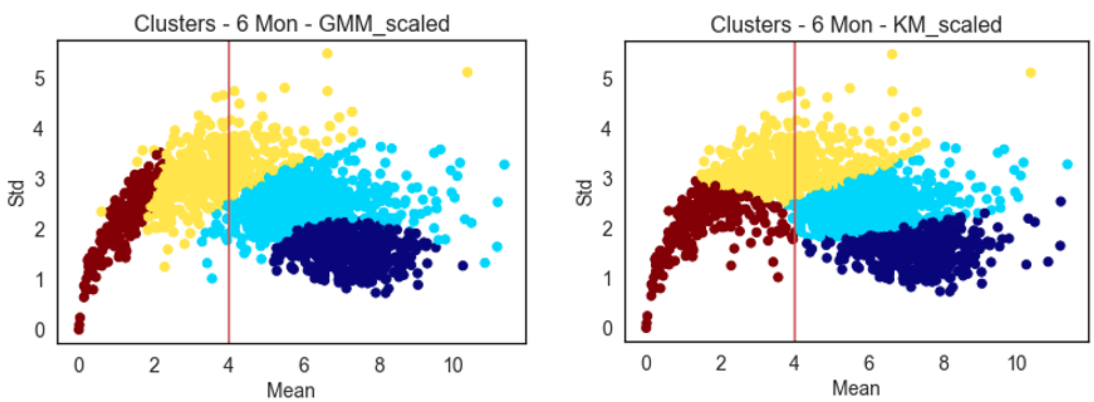

Fig. 4. Of the two algorithms, K-Means gives clusters that are more explainable and can be categorized as adherent(blue, cyan) and non-adherent(red, yellow)

and preceding months' aggregate data. We used 5 Random Forrest models, one for each month starting from 2nd to the 6th, each trained on separate training sets (75% of the patients) created from previous months' aggregate data as shown in the 'Model' column of IV, to predict the clusters of a separated test set of patients (25% of the patients). We followed a binary classification approach for this step as we only need to classify the patients as adhering and non-adhering. For this, we combined the clusters 0,1 into class-0 (non-adhering) and clusters 2,3 into class-1 (adhering). The trained models are then tested on the separate test sets created for each of them and the results for this prediction are given in Table.IV. We used accuracy and ROC_AUC score as the metric to compare it with the baseline model of classifying all patients as adhering.

It is noticeable that the performance of the models increase as we move along the timeline, with more accurate predictions and low false positive rates (as indicated by high ROC_AUC score). This indicates that the approach of categorizing patients into clusters and using it for adherence prediction is an efficient way for continuous prediction of adherence in Sleep Apnea therapy.

IV. Results & Discussion

As the transition probabilities suggest, the patients in red cluster (cluster 0) have the highest tendency (79%+11%) to remain non-adherent more than the patients in yellow cluster(17%+48%). Hence, this approach not only predicts the adherence of patients, but also gives an estimate of the severity of non-adherence. The final steady state probabilities shown in

TABLE IV
Classification accuracy & ROC-AUC score for proposed models

Model	Accuracy	ROC-AUC
RF1: 1→2	82.38%	0.84
RF2: 1+2→3	81.94%	0.88
RF3: 1+2+3→4	84.14%	0.90
RF4: 1+2+3+4→5	84.36%	0.92
RF5: 1+2+3+4+5→6	88.32%	0.94

TABLE V
Baseline model accuracy & ROC-AUC score Let me know how to show this better

Month	Accuracy	ROC-AUC
1→2	75.56%	0.5
2→3	70.92%	0.5
3→4	66.08%	0.5
4→5	63.66%	0.5
5→6	62.56%	0.5

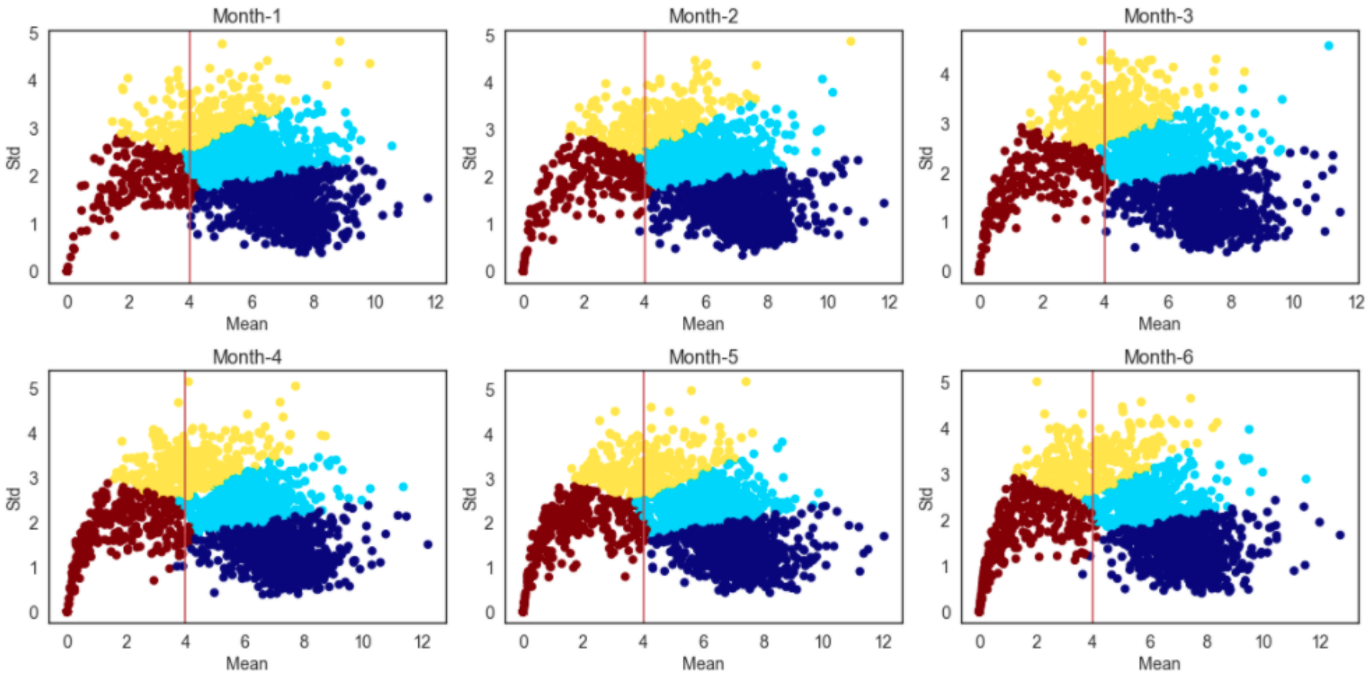

Fig. 5. Standardized monthly aggregates clustered using K-Means model

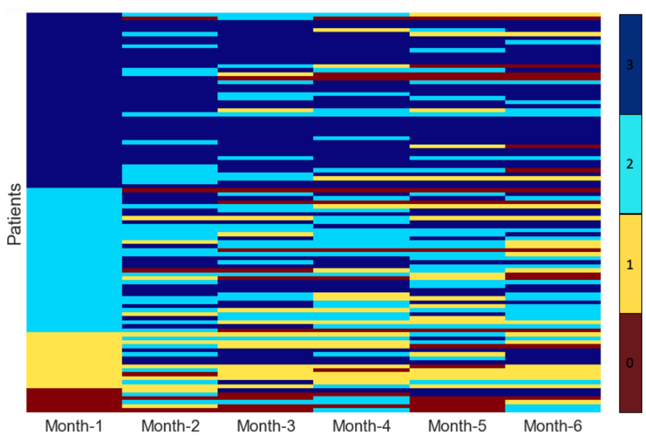

Fig. 6. Transition Heatmap for a random sample of 100 patients

Table.III indicate that about 39% (23+16) of the patients will eventually not adhere to the therapy and the rest will continue to more or less adhere to the therapy in the long term. This is also supported by [23] which mentions the adherence rate is as low as 60%. Hence, this metric can be used to monitor the performance of the therapy management in the long run.

The classifiers trained on the previous months' aggregate data outperforms the baseline model and can be used in the sleep clinics to identify non-adherent patients from the initial stages of therapy. more comments can be added if you can think of any

V. Conclusion and Future Work

The goal of this work is to establish a framework that can monitor adherence of patients to therapy in each month following the first month of therapy. Though the existing models like one-shot models [9] and CTAP-CPAP [23] models perform a good job at prediction of adherence to CPAP therapy for sleep apnea, they do so only for a specific time period in the treatment i.e. (6th month). The framework proposed in this work provides a novel approach for continuous prediction of adherence to CPAP therapy right from the 2nd month of the therapy and thereby helps in identifying the patients who are likely to drop from the therapy much earlier than 6 months. The performance of the proposed models is significantly better than the baseline model of classifying everyone as adherent. This performance can further be improved by extracting time series features from the CPAP signal data and using them for clustering and classification as they provide much richer information compared to aggregation. Further, other sophisticated classification models can also be used to improvise on the performance of the current framework.

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