Computational Phenotyping In CPAP Therapy

Using Interpretable Physiology-Based Machine Learning Models To Predict Therapeutic CPAP Pressures

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Introduction & Motivation

- With home sleep studies, there is a need to determine a therapeutic (AHI < 5) CPAP pressure with which to begin therapy.
- A common practice is to combine a predictive equation with the interpreting sleep physician's clinical judgement.
- This approach produces a therapeutic pressure recommendation to within ± 2 cmH_2O of the eventual therapeutic pressure in 85% of patients in our sample.
- We sought to determine if the use of a machine learning model, using readily available variables from a home sleep study, could integrate the predictive equation and the physician's judgement and produce a similarly accurate therapeutic CPAP pressure recommendation.

Methods & Study Sample

- We used cross-sectional analyses of patients (N = 7,794), ages 15–99 (M ± SD = 54 ± 13.9 years) who completed a diagnostic home sleep apnea test.
- In total, 30 interpretable physiological and clinical features were computationally derived from the dataset and used to predict the therapeutic CPAP pressure based on the therapeutic pressure settings prescribed by each subjects interpreting physician.
- Predictive performance was evaluated using a randomized 10-fold cross-validation of the sample.
- Machine learning techniques including Random Forests and Deep Neural Networks were trained, optimized, and evaluated to model the relationship between the interpretable features and optimal therapeutic CPAP pressures.

Optimal Therapeutic CPAP Pressure Validation

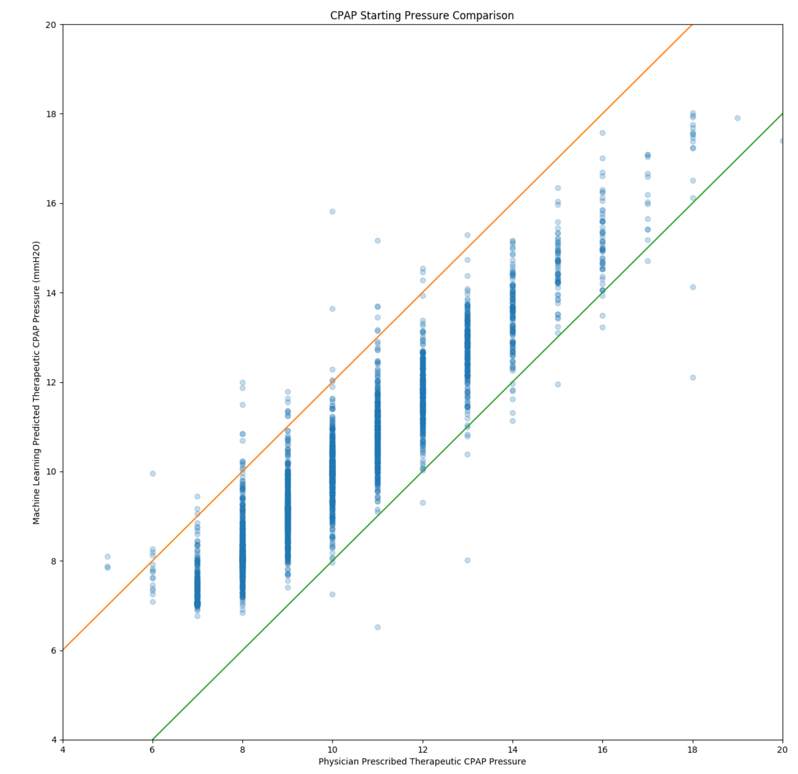
- To evaluate the effectives of the current practice, we compared the initially prescribed PAP pressure to the final therapeutic PAP pressure over the first 12 months of usage:
- 60% of patients have the same optimal therapeutic PAP pressure that was originally prescribed.
- 85% of patients have the same optimal therapeutic PAP pressure that was originally prescribed (± 2 cmH_20)
- 31% of patients have an eventual therapeutic pressure setting that is lower that the original prescription.
- 9% of patients have an eventual therapeutic pressure setting that is higher that the original prescription.
- Based on the patient's response to therapy, weight reduction, medications, and symptoms, the CPAP pressure may require further adjustment regardless of the method used to obtain a starting pressure.
- A repeat study to monitor response to therapy may be required, based on clinical response.

Predictive CPAP Pressure Results and Statistical Analysis

Performance and Significance of Machine Learning based CPAP Pressure

A randomized 10-fold cross-validation was applied to a dataset of N = 7,794 home sleep studies to predict optimal therapeutic PAP pressure based on computationally derived interpretable physiological variables from the home sleep studies using Random Forests and Deep Neural Network machine learning models:

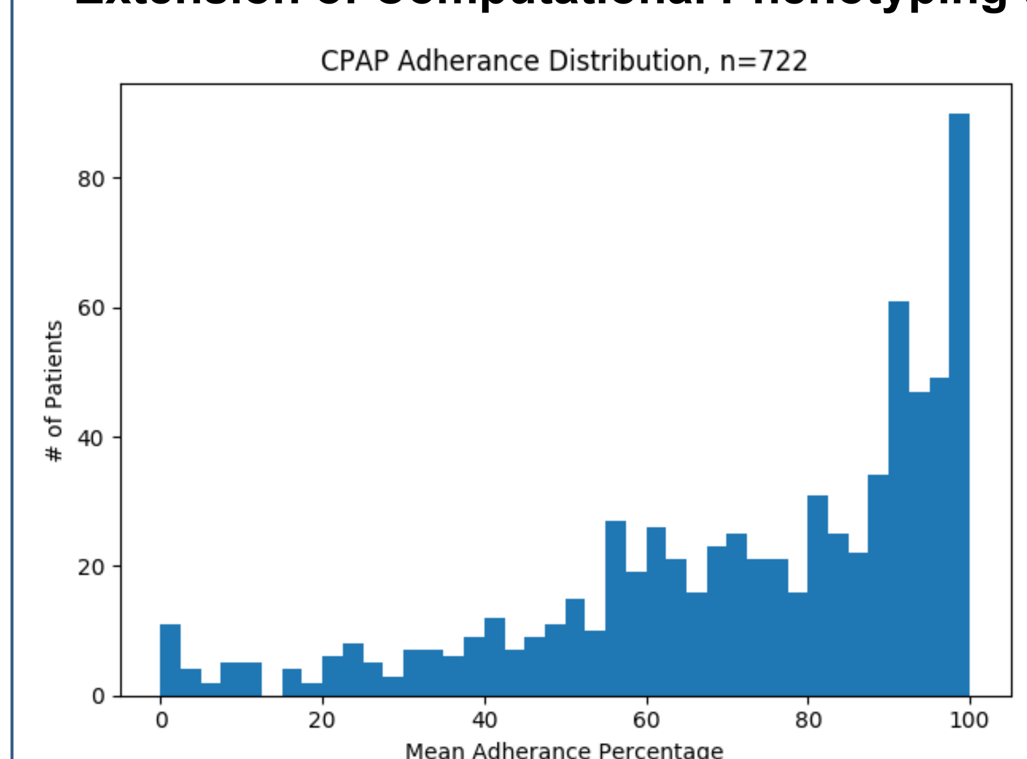
- Random Forests achieved the best performance for predicting the optimal therapeutic CPAP pressure ± 2 cmH_20, with an average accuracy of 97.8%.
- The top-10 variables ranked by Gini coefficient included BMI, AHI, neck circumference, ODI, longest apnea, age, snoring time, and others with established associations with sleep apnea in prior research studies.
- OLS regression was performed to estimate the strength of the relationship between the machine learning predicted CPAP pressure and the clinically prescribed CPAP pressure, resulting in an R-squared value of 0.888.
- The P-value for the F-test of overall significance of the regression analysis was observed to be < 0.05, confirming the R-squared estimate was statistically significant.

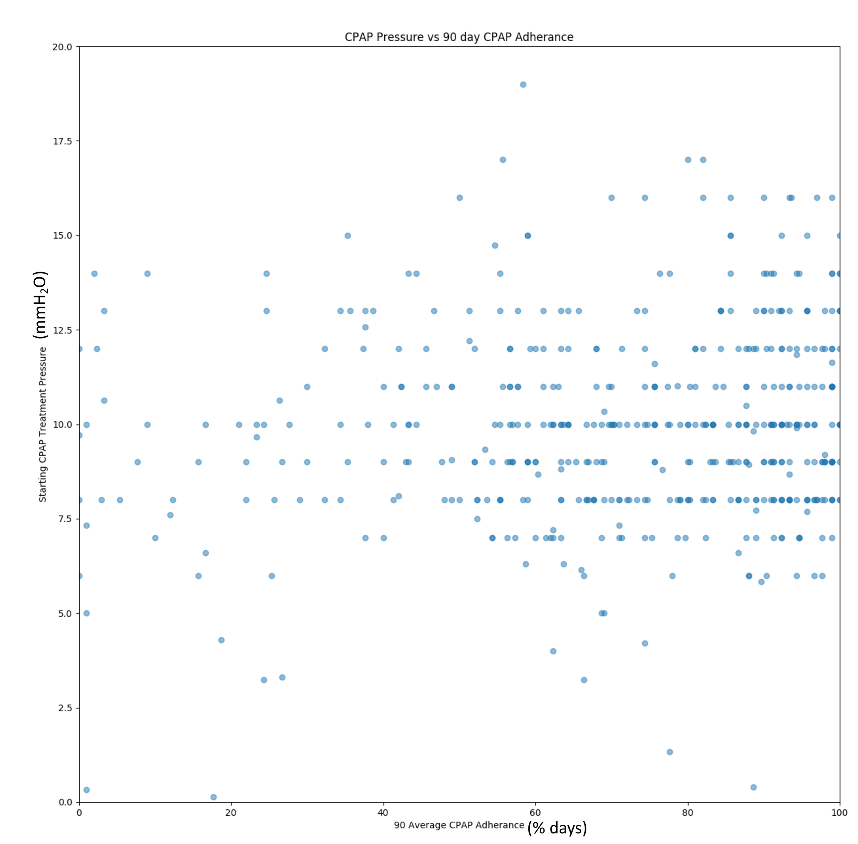


Feature Rank	Gini Coefficient	Physiological Variable
1	0.31	Body Mass Index (BMI)
2	0.28	Oxygen Desaturation Index (ODI)
3	0.17	Apnea-Hypopnea Index (AHI)
4	0.14	Neck Circumfrence
5	0.02	Obstructive Apneas per Hour
6	0.02	Longest Apnea (seconds)
7	0.01	Snoring time (% of scored time)
8	0.01	Percent Time SpO2 < 90%
9	0.01	Hypopneas per Hour
10	0.01	Age
11	0.01	Highest Heart Rate (HR)

Left: Scatterplot of Prescribed CPAP Pressure vs. Machine Learning CPAP Pressure
Right: Top-10 Predictive Physiological Variables Ranked by Gini Coefficient Value

Extension of Computational Phenotyping to 90-day CPAP Compliance Prediction





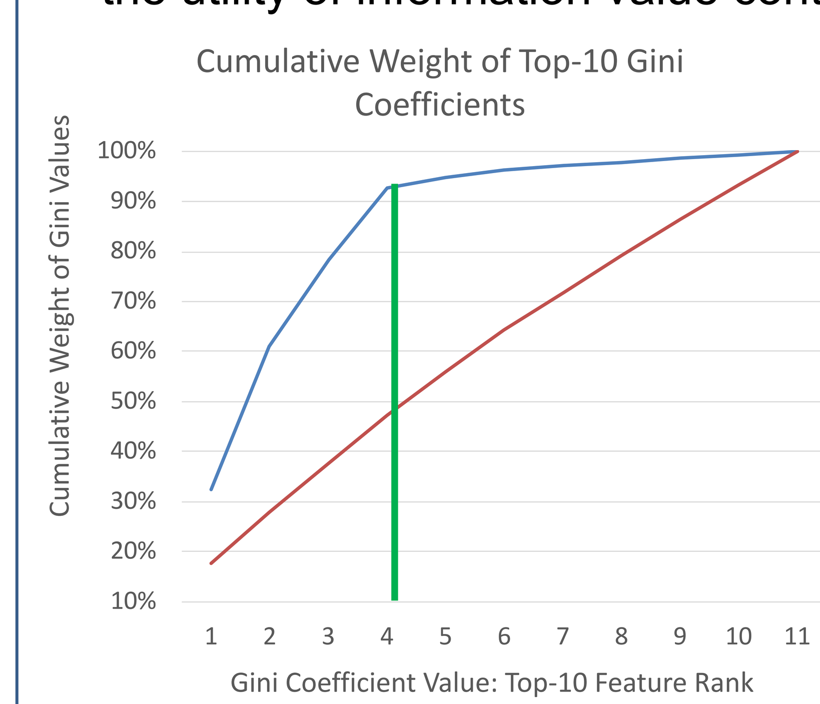
Left: Distribution of Compliance Over the First 90-days of CPAP Therapy (% of days)
Right: Scatterplot of 90-day CPAP Compliance vs. Prescribed CPAP Pressure

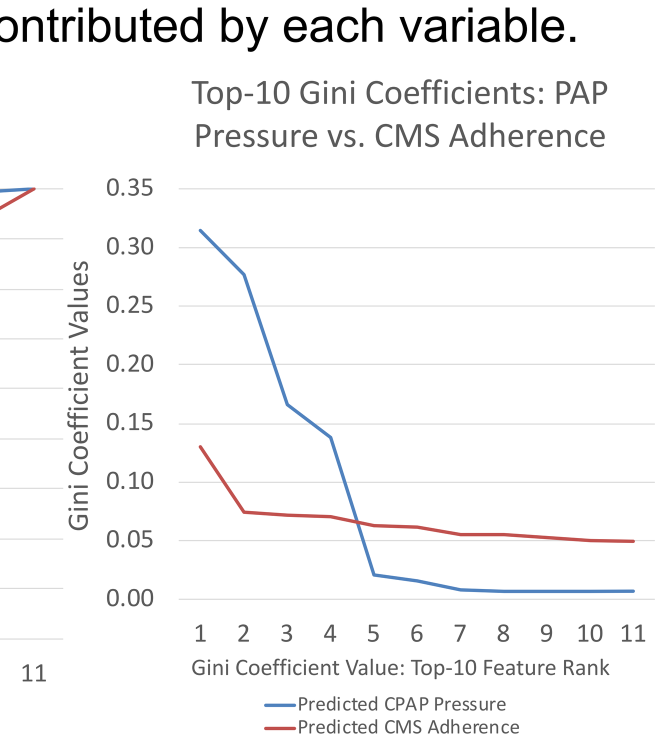
Predictive Phenotyping of PAP Compliance

Significance of Machine Learning based CPAP Compliance

A randomized 10-fold cross-validation was applied to a dataset of N = 580 cloud based CPAP utilization data collected over the first 90-days of CPAP Therapy to predict CPAP compliance according to the CSM Adherence Criteria using computationally derived interpretable physiological variables from CPAP usage data with Random Forests and Neural Network machine learning models:

- CMS Adherence to CPAP is defined as usage >= 4 hours per night on 70% of nights during a consecutive 30 days anytime during the first 3 months of initial usage.
- Precision-Recall was used to analyze performance given the class imbalance of complaint (83%) vs. noncompliant (17%).
- The best performance for predicting CMS Adherence was RF model with an aggregate F1-score of 74% (R: 71%, P: 81%).
- The top-6 variables ranked by Gini coefficient included snoring time, heart rate, longest apnea, ESS score, percent time under SpO2 of 85%, and number of apneas per hour.
- The cumulative weight of the predicted CPAP Pressure versus predicted CMS Adherence demonstrated relative differences in the utility of information value contributed by each variable.





Discussion & Conclusions

- Interpretable machine learning models show promise as another means for determining therapeutic CPAP pressures.
- Following the initial prescription, this approach enables novel applications for AI to assist with monitoring and refining PAP pressure settings on a longitudinal basis to optimize outcomes.
- Based on the variations in performance for the CPAP Pressure and CMS Adherence tasks, we hypothesize that the incorporation of digitized behavioral phenotypes in addition to physiological phenotypes would be the greatest contributor to improve performance, shown in terms of increased Gini Coefficient Weight Value convergence and PRC-AUC statistics.
- Further deep learning model optimization beyond grid-search and random-search techniques shows promise with larger data.
- Future work will be dedicated to identifying and extracting behavioral phenotypes from several sources including EMRs, consumer wearables, and questionnaires and AI optimization.