Machine Learning Prognostics for the Obstructive Sleep Apnea Disorder Following Long COVID

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***Abstract*—In the aftermath of the COVID-19 pandemic, the phenomenon of Long COVID has emerged as a profound health concern. It presents enduring symptoms that significantly overlap with those of Obstructive Sleep Apnea Disorder (OSAD), such as inconsistent breathing patterns, sleep disturbances, and cardiovascular complications. This paper presents an analysis of Long COVID using healthcare data from the Froedtert Health Medical System in Wisconsin. By leveraging advanced Machine Learning (ML) methodologies, we have formulated predictive models aimed at assessing the risk of OSAD onset in individuals diagnosed with Long COVID. Additionally, our study reveals critical factors influencing the incidence of OSAD. Considering recent research that underscores the increased risk of Long COVID in patients with pre-existing OSADs, this innovative research inversely investigates the likelihood of developing OSAD post-Long COVID diagnosis. We utilized the Recursive Feature Elimination (RFE) approach to extract salient features that substantially impact OSAD from our dataset. To counter the dataset's underlying imbalance, we implemented the Synthetic Minority Over-sampling Technique and Edited Nearest Neighbors (SMOTEEN) strategy. We experimented with multiple ML models and validated them using cross-validation techniques. The results indicate that the Gaussian Naive Bayes (GNB) classifier exhibits superior performance, with an area under the ROC curve (AUC) of 0.967, precision of 0.942, and recall of 0.929. Random Forest (RF) classifier also demonstrates robust predictive capabilities for OSAD risk prediction, achieving an AUC of 0.964, precision of 0.936, and recall of 0.918. The Support Vector Classifier (SVC) similarly achieves commendable results with an AUC of 0.969, precision of 0.947, and recall of 0.926. The pivotal features identified by our predictive models are instrumental in recognizing individuals at an elevated risk of OSAD post Long Covid diagnosis, thus paving the way for targeted preventive interventions and the allocation of essential healthcare resources.**

***Index Terms*—sleep apnea disorder, long COVID, electronic health records, machine learning**

I. Introduction

The aftermath of the COVID-19 pandemic has unveiled a complex network of health challenges, with Long COVID surfacing as a persistent and intricate issue [1] [2]. Beyond the initial resolution of the viral infection, Long COVID continues to affect a significant population with lasting symptoms and complications. Recent estimates indicate that approximately 65 million individuals globally are grappling with the persistent effects of Long COVID, underscoring the need for a deeper understanding of its diverse consequences [2]. While existing research has primarily focused on the health aspects of Long COVID, it is crucial to recognize its wider range of health implications. Among the numerous health issues linked to Long COVID, the association between Long COVID and OSAD emerges as a significant concern. Both conditions share similarities, including irregular breathing patterns, disrupted sleep, and increased cardiovascular risks [3].Understanding the relationship between Long COVID and OSAD is essential for comprehensive patient care and the development of effective intervention strategies. Given that individuals diagnosed with Long COVID are at an increased risk of developing OSAD, early detection and customized interventions are critical to alleviate potential health complications associated with this dual burden. ML techniques, which have proven effective in predicting COVID-19 outcomes and understanding the impact of Long COVID on mental health [4] , offer a promising approach to address the risk of OSAD in Long COVID patients. This study utilizes advanced ML algorithms to analyze Electronic Health Records (EHR) data, identify patterns, and pinpoint risk factors associated with OSAD in the context of Long COVID. The integration of diverse data sources from EHR forms the foundation of this research, with the aim of building predictive models with the highest accuracy. This research represents a significant shift in managing health outcomes related to Long COVID, with a focus on the complex relationship between Long COVID and OSAD. Through ML methodologies and sophisticated feature engineering, the goal is to uncover patterns and identify key variables that contribute to the development of OSAD in Long COVID survivors. By identifying patient subgroups with increased vulnerability, this research enables the development of customized treatment plans, facilitating timely interventions and ultimately improving patient outcomes. The general ML framework for predicting OSAD due to Long COVID is depicted in Figure 1. The subsequent sections of this paper explore related work, elaborate on the research methodology, present model evaluations, and conclude with a comprehensive summary and considerations for future research.

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DOI 10.1109/IRI62200.2024.00019

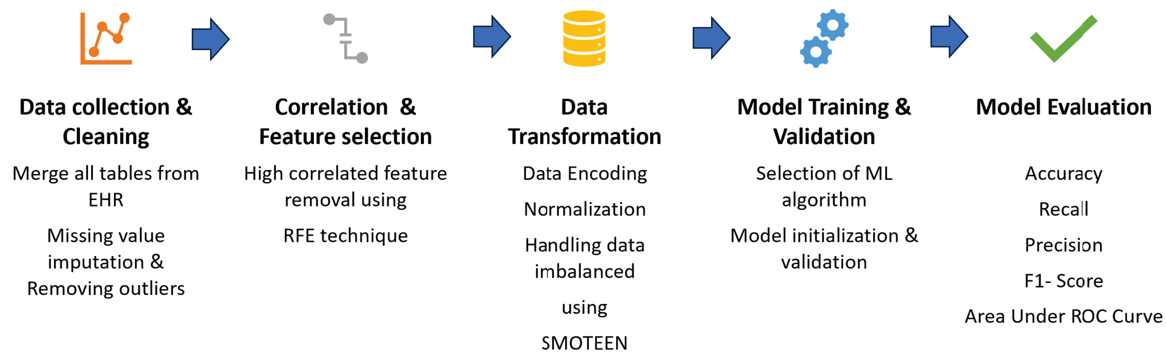

Figure 1. The The Machine Learning framework for predicting Sleep Apnea Disorders after diagnosis of Long COVID

II. Related work

Researchers are increasingly using ML, Deep Learning (DL), and Artificial Intelligence (AI) to predict and manage OSAD in COVID-19 patients. This section reviews key literature and methodologies related to OSAD prediction within the context of the COVID-19 pandemic.

A. Obstructive Sleep Apnea Disorder and its Implications in COVID-19: A Review of Recent Studies

The existing corpus of research has primarily focused on delineating the relationship between Obstructive Sleep Apnea (OSA) and the severity of Long COVID. However, the available research on the association between Long COVID and the risk of developing OSAD is limited. This literature review aims to highlight studies relevant to the severity of OSAD and Long COVID, with the goal of illuminating the current knowledge gap regarding the onset of OSAD thereby underscoring the need for further investigation in this area.

Recent academic inquiries have delved into the intricate relationship between persistent COVID-19 symptoms and the subsequent challenges associated with OSAD. A study conducted by Schwarzl et al. [5] investigated the prevalence of OSAD among 69 COVID-19 patients, highlighting correlations between Apnea-Hypopnea Index (AHI) scores, Body Mass Index (BMI), and age. This finding implies a potential role of OSAD in contributing to fatigue symptoms. Furthermore, Gao et al. [6] employed Mendelian randomization to explore causal relationships, suggesting a potential causal effect of severe COVID-19 on the risk of OSAD. In addition, Iannella et al. [7] found a correlation between severe COVID-19 and an increased risk of OSAD, emphasizing the need for further research. Moreover, Mandel et al. [8] analyzed EHR data, uncovering an increased risk of Post-Acute Sequelae of SARS-CoV-2 (PASC) among individuals with preexisting OSAD. Finally, Mashaqi et al. [9] investigated the relationship between OSAD and COVID-19 severity, suggesting that while OSAD may not independently contribute to worse COVID-19 outcomes, further research with larger sample sizes is necessary. This succinct review highlights the evolving understanding of Long COVID and OSAD, necessitating a comprehensive exploration to effectively guide clinical interventions.

B. Machine Learning, Deep Learning, and Artificial Intelligence in OSAD Prediction

The integration of ML, DL, and AI techniques has significantly advanced the field of OSAD prediction, enhancing both accuracy and understanding of its pathophysiology.

Ferreira et al. [10] conducted a systematic review assessing ML methods for OSAD screening in adults, noting logistic regression predictors achieved high accuracy (AUC = 0.98), yet lacked external validation and standardized criteria. Furthermore, Tasmi et al. [11] utilized ML to predict mortality in COVID-19 patients with OSAD, achieving promising results (precision = 100%) and advocating for integrating predictive models into treatment decisions to reduce mortality rates. Moreover, Rognvaldsson et al. [12] found OSAD associated with a twofold increase in severe COVID-19 risk, even after adjusting for demographics and comorbidities, based on a population-based study of Icelandic citizens. Finally, Ramesh et al. [13] used ML techniques on EHR to classify OSAD, emphasizing the significance of routine clinical data in prioritizing patient referrals for sleep studies. This study reveled that Support Vector Machines emerged as the most effective classifier, with key clinical features such as waist circumference, BMI, and self-reported symptoms contributing significantly to OSAD identification. In conclusion, these studies collectively underscore the growing importance and versatility of ML, DL, and AI in advancing OSAD prediction and management.

C. Innovative Approach and Contribution

Our research introduces a pioneering method for predicting the risk of OSAD by integrating a wide array of datasets, including social background, lifestyle factors, demographic information, health conditions, immunization history, medication prescriptions, vital signs, and diagnostic outcomes from EHR. This comprehensive integration provides a holistic view of an individual's health status, with a specific focus on patients diagnosed with Long COVID, addressing a critical gap in current research. We employ various ML algorithms for feature selection and prediction, significantly enhancing prediction accuracy. Our approach not only tackles the challenge of fragmented health data but also offers a targeted solution for a relevant patient subgroup, thereby contributing valuable insights and improving the effectiveness of OSAD risk assessments.

III. Methodology

In this section, we elaborate on our research methodology, as illustrated in Figure 1. Our process begins by identifying individuals diagnosed with Long COVID. We meticulously gather their medical records, adhering to stringent criteria aligned with established medical standards. Subsequently, we identify patients diagnosed with OSAD following their Long COVID diagnosis, utilizing comprehensive International Classification of Diseases (ICD-10) codes as shown in Table I. Our dataset undergoes thorough cleaning, including imputation for missing values and outlier elimination. Correlation analysis uncovers potential interrelationships among variables. We employ the RFE technique to systematically eliminate less impactful features, enhancing our model's predictive capacity. We utilize data transformation techniques to normalize variable ranges and mitigate the dataset imbalance, employing the SMOTEEN technique to ensure equitable representation of minority classes within our dataset. In the final stage, we fine-tune classification models and assess the predictive performance of the selected variables.

Table I
List of ICD Codes related to OSAD and Long COVID

ICD code	Description
G47.30	Sleep apnea, unspecified
G47.33	Obstructive sleep apnea; adult, pediatric
G47.39	Other sleep apnea
G47.31	Primary central sleep apnea
G47.37	Central sleep apnea
G47.9	Sleep disorder, unspecified
G47.8	Other sleep disorders
U09	Long COVID

A. Data Source

The present study leveraged de-identified data obtained from Froedtert Hospital (FH) in Milwaukee, WI, USA, spanning a three-year period from June 2021 to January 2023. Ethical approval was secured from the Institutional Review Board (IRB), ensuring compliance with privacy regulations.

B. Patient Categorization: Sleep Apnea Disorder Diagnoses After Long COVID

The dataset contains ICD-10 codes covering a range of diagnoses, including those relevant to Long COVID, identified by codes starting with "U09". After initial data cleaning to remove duplicate encounters, comprising various encounter types like Ambulatory Visit (AV), Emergency Visit (ED), ED to Inpatient (EI), Inpatient Stay (IP), Other Ambulatory (OA), Observation Stay (OS), and Telehealth (TH), we refined it to 67,881 unique patient records from an initial 17 million encounters. We then filtered for Long COVID patients using code "U09" and categorized them based on the presence or absence of ongoing symptoms after the diagnosis of Long COVID, relying on specific ICD codes outlined in Table I. This meticulous process aimed at accurately identifying OSAD issues due to Long COVID. After merging additional EHR datasets by matching patient IDs and encounter identifiers, our final dataset comprised 998 rows and 34 columns. For a visual overview of our methodology, please refer to Figure 2. In our final dataset, we simplified the representation of OSAD presence into binary values, dividing patients into two distinct groups.

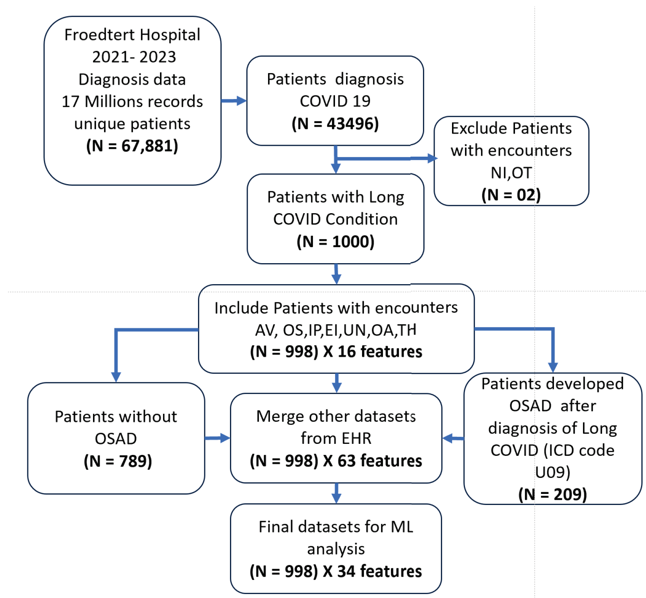

Figure 2. Flowchart illustrating the selection of the sample used in study .

C. Data Characteristics

The analysis of the final study population reveals significant class imbalances across various demographic and healthcare encounter variables. Overwhelmingly, the majority of patients are classified as non-Hispanic (94.99%) and predominantly White or Caucasian (75.85%). Notably, retired individuals comprise the largest occupational category at 32.46%, followed closely by those in full-time employment at 34.97%. Regarding insurance coverage, a substantial portion (43.39%) hold private insurance. Within the diagnosed OSAD group, there appears to be a higher representation of White patients, constituting 72.25% of this cohort. The median age of the population is 58 years, consistent across both non-OSAD and OSAD groups. Gender distribution indicates a higher proportion of females overall (64.03%), with a slightly lower representation within the OSAD group (53.11%).

Healthcare encounters highlight patterns in patient interactions with the healthcare system. AV comprise nearly half (48.7%)

of all encounters, with OA representing a significant portion of 24.2%. Notably, the non-OSAD group demonstrates a higher proportion of OA visits (26.5%) compared to the OSAD group (15.8%). These observations underscore the importance of understanding demographic and healthcare utilization patterns in informing healthcare delivery strategies and addressing potential disparities in access and care provision.

D. Correlation Analysis

The correlation analysis reveals interesting insights regarding the relationship between these top features and the presence of OSAD. In Table II, we showcase the 10 most correlated pairs within the dataset, accompanied by their respective correlation coefficients in association with the target variable. Notably, features such as sex, BMI, payor Medicare, employment status Disabled, and encounter type EI exhibit relatively strong, positive correlations with OSAD. This suggests that individuals with higher BMI, being male, covered by Medicare, disabled employment status, or encountering certain types of medical encounters (e.g., Emergency Department visits or inpatient visit) may be at a higher risk of developing OSAD. On the other hand, features like age at visit marital status Divorced, and employment status Retired show moderate positive correlations, indicating their potential role as risk factors for OSAD. The race Black variable also demonstrates a positive correlation with OSAD, suggesting a possible association between race and OSAD risk.

Table II
FEATURE CORRELATION WITH OSAD

Feature	Correlation Coefficient
OSAD	1.000000
age_at_visit_years	0.070080
sex	0.117088
ethnicity	0.005972
bmi	0.114592
payor_Medicare	0.111006
marital_status_Divorced	0.036169
employment_status_Disabled	0.108113
employment_status_Retired	0.079667
race_Black	0.054649
enc_type_EI	0.153634

E. Feature selection

In predictive model development, feature selection is crucial for managing computational complexity and enhancing model effectiveness. Our methodology began by evaluating feature correlations, removing pairs with coefficients exceeding 0.7 to address multicollinearity. We then utilized a RFE framework with RF classifier to systematically identify important features based on assigned weights. The analysis, depicted in Figure 3, identified 15 key features through RFE. Achieving a peak performance score of 0.96 with these features suggests minimal benefit from additional ones, underscoring RFE's effectiveness in capturing essential information for predictive modeling.

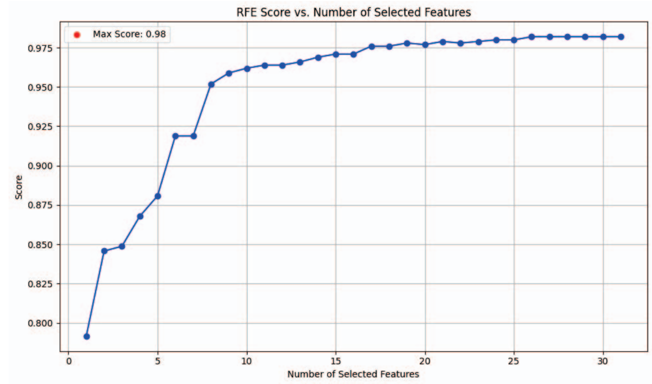

Figure 3. REF Score Vs Number of Selected Features (15)

F. Normalization and Data Balancing

In our research study, we analyzed an initial dataset containing 998 instances. As shown in Figure 2, among these, 789 represented patients without pre-existing OSADs, while 209 instances corresponded to patients who developed OSAD after their Long COVID diagnosis. To address the uneven data distribution, we strategically employed the SMOTEEN technique, which transformed the dataset to achieve a more balanced representation. This crucial rebalancing step occurred prior to involving ML algorithms. This equitable representation can help improve prediction accuracy and fairness in our research outcomes [14].

G. Exploring ML Approaches

After normalizing the data and ensuring balance, we used various ML models like random forest (RF), Gradient Boosting (GB), support vector classifier (SVC), XGBoost, k-nearest neighbors (KNN), Gaussian Naive Bayes (GNB), and Multi-Layer Perceptron. Each of these models has its own strengths. For example, RF combines multiple decision trees to make a strong and accurate model [15]. SVC is good at drawing lines to classify data points, especially in datasets with many different features [16]. Boosting algorithms like XGBoost combine weak learners to make a powerful model with fast and effective prediction [17]. We split the dataset into training and testing groups, with 70% for training and 30% for testing. This helps the models learn from most of the data while also testing their accuracy on the new data they haven't seen before.

IV. MODEL EVALUATION AND RESULTS

Our evaluation process for predicting OSAD involved a comprehensive set of performance metrics, including accuracy, precision, recall, F1-Score, and the area under the ROC curve (AUC). Special attention was given to precision and recall due to their crucial role in effectively classifying instances of the minority class, representing individuals with OSAD.

The study systematically assessed various classification methods for diagnosing OSADs. Table III provides a overview of evaluation metrics for each classifier used. Among these, GNB and RF emerged as the top performers.

GNB demonstrated an accuracy of 89.7%, a recall of 92.8%, and a precision of 94.2%, indicating its capability to accurately classify instances of OSAD while minimizing false positives. RF exhibited competitive performance with an accuracy of 88.8%, a recall of 91.8%, and a precision of 93.6%, highlighting its ability to accurately identify positive OSAD cases while maintaining a high precision rate.

Additionally, the F1-score and AUC values further confirmed the robust performance of both classifiers. The mean ROC AUC of 0.96, depicted in Figure 4, underscores the significance of employing ensemble methods in medical diagnostic tasks, combining the strengths of multiple models to achieve enhanced predictive performance.

Table III
THE PERFORMANCE MEASURE OF ALL CLASSIFICATION METHODS

Classifier	*Accuracy*	*Recall*	*Precision*	*F1-score*	*AUC*
GB	0.865	0.884	0.915	0.898	0.945
GNB	0.897	0.928	0.942	0.934	0.967
KNN	0.861	0.880	0.911	0.894	0.942
MLP	0.878	0.912	0.932	0.921	0.963
RF	0.888	0.918	0.936	0.926	0.964
SVC	0.895	0.926	0.947	0.936	0.968
XGBoost	0.871	0.888	0.920	0.902	0.945

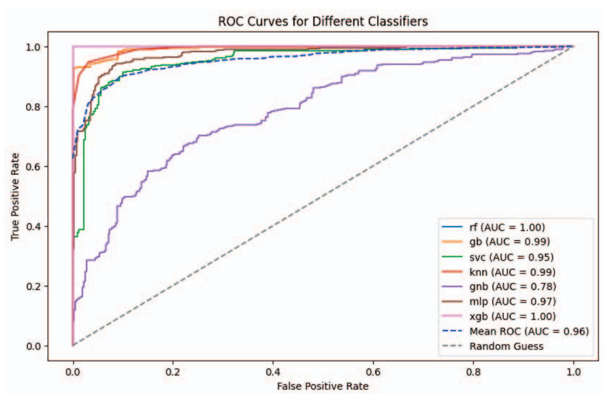

Figure 4. Average Receiver Operating Characteristic (ROC) curves for different classifiers

In our analysis, we employed the feature importance attribute method to identify the top 10 features for both the RF algorithm (Figure 6) and the GNB classifier (Figure 5). This approach was adapted to assess feature relevance for RF, utilizing the frequency of each feature's usage in node splitting within the constructed trees. However, for GNB, feature importance is typically evaluated through statistical measures such as the significance of feature distributions. These values are computed during the training process of models and are based on the log probabilities of the features within each class. The attribute quantifies the contribution of each feature to enhancing the model's predictive performance, and these values are normalized to ensure their sum equals 1, allowing for a relative comparison of feature importance. In our comprehensive investigation, we conducted a detailed analysis of the top 10 features associated with OSADs. These features encompass a diverse range of attributes, including the type of encounter (specifically TH, EI, AV, or ED), employment status denoting "disabled," BMI, marital status (both "divorced" and "married"), insurance payer (such as "Medicare" or "private"), racial category ("Black"), age at the visit, and sex. The compilation of these significant attributes underscores their pivotal role in shaping the predictive capabilities of our models. This facilitates targeted interventions and enables effective risk identification for OSADs.

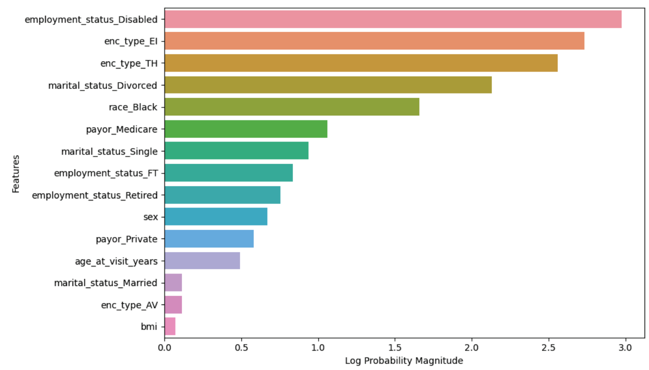

Figure 5. Feature Importance of GNB Classifiers (Feature Importance Attribute)

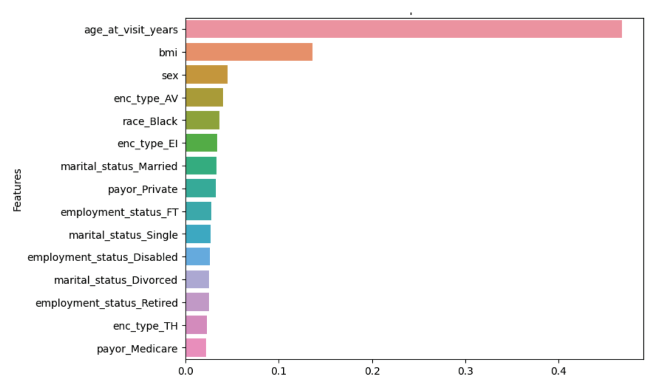

Figure 6. Feature Importance of RF Classifiers (Feature Importance Attribute)

The confusion matrix for the GNB and RF classifiers is presented in Table IV. The GNB classifier correctly identified 201 instances of OSAD as true positives (TP), but it missed 32 cases (false negatives, FN) and misclassified 48 cases as OSAD when they were not (false positives, FP). Simultaneously, the RF classifier exhibited higher true positive predictions (TP = 217) but also had a greater number of false positives (FP = 58). Notably, false negatives in medical records can have significant implications, potentially leading to undiagnosed health issues.

Table IV
CONFUSION MATRIX FOR RF AND GNB CLASSIFIERS

Actual/Predicted	GNB Classifier	RF Classifier
Positive	201 TP	217 TP
	32 FN	16 FN
Negative	19 TN	9 TN
	48 FP	58 FP

CONCLUSION

In this comprehensive study, we leveraged advanced ML techniques to explore the intricate relationship between Long COVID and the subsequent development of OSAD. Our investigation involved rigorous assessment of diverse ML algorithms, specifically focusing on their predictive capabilities in identifying OSAD cases following exposure to Long COVID. By scrutinizing a range of features, we successfully identified crucial predictors that illuminate the trajectory of OSAD in the post-Long COVID phase. The significance of these predictors extends beyond theoretical insights. Healthcare practitioners now have access to a potent predictive tool—one that proactively identifies individuals at risk of OSAD. Targeted interventions can be initiated promptly, potentially alleviating the burden of this sleep-related disorder. Moreover, our findings underscore the transformative potential of technology in healthcare paradigms, offering hope to those navigating the aftermath of Long COVID.

A. Limitation and Future Work

The present investigation, focusing on Long COVID patients within a specific healthcare system, faces limitations due to selection bias and limited generalizability. Despite their potential, ML models, dependent on retrospective data, may not fully capture the diverse factors influencing OSAD outcomes. The heterogeneity among Long COVID patients, in terms of demographics, clinical manifestations, and comorbidities, presents challenges for accurate predictive models. Future work will explore the use of DNNs to capture complex, non-linear relationships in the data, potentially improving prediction accuracy, while integrating Explainable Artificial Intelligence (XAI) techniques to enhance model transparency and provide insights into the most influential factors affecting OSAD risk. To enhance robustness, prospective data collection from resources such as National Institutes of Health (NIH) All of Us or National COVID Cohort Collaborative (N3C) datasets is advocated.

ACKNOWLEDGMENT

This work was supported by the Northwestern Mutual Data Science Institute through the NMDSI Research Scholars Program Award, granted in February 2024. We extend our sincere appreciation for their financial support.

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