The Beginning of the AI-Enabled Preventative PAP Therapy Era

by

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Abstract

Positive Airway Pressure (PAP) therapy is the most common and efficacious treatment for Obstructive Sleep Apnea (OSA). However, it suffers from poor patient adherence due to discomfort and may not fully alleviate all adverse consequences of OSA. Identifying abnormal respiratory events before they have occurred may allow for improved management of PAP levels, leading to improved adherence and better patient outcomes. Our previous work has resulted in the successful development of an Artificial Intelligence (AI) algorithm for the prediction of future apneic events using existing airflow and air pressure sensors available internally to PAP devices. Although researchers have studied the use of AI for the prediction of apneas, research to date has focused primarily on using external polysomnography sensors that add to patient discomfort and has not investigated the use of internal-to-PAP sensors such as air pressure and airflow to predict and prevent respiratory events. We hypothesized that by using our predictive software, OSA events could be proactively prevented while maintaining patients' sleep quality. An intervention protocol was developed and applied to all patients to prevent OSA events. Although the protocol's cool-down period limited the number of prevention attempts, analysis of 11 participants revealed that our system improved many sleep parameters, which included a statistically significant 31.6% reduction in Apnea-Hypopnea Index, while maintaining sleep quality. Most importantly, our findings indicate the feasibility of unobtrusive identification and unique prevention of each respiratory event as well as paving the path to future truly personalized PAP therapy by further training of AI models on individual patients.

List of Abbreviations Used

AI	artificial intelligence
APAP	automatic positive airway pressure
BMI	body mass index
CA	central apnea
CAI	central apnea index
CI	confidence interval
CNN	convolutional neural network
CPAP	continuous positive airway pressure
CVH	cardiovascular health
EEG	electroencephalogram
EMG	electromyogram
EOG	electrooculogram
HYI	hypopnea index
NREM	non-rapid eye movement
OA	obstructive apnea
OAI	obstructive apnea index
ODI	oxygen desaturation index
OSA	obstructive sleep apnea
PAP	positive airway pressure
PSG	polysomnography
RDI	respiratory distress index
REM	rapid eye movement
TST	total sleep time

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As one of my earliest childhood memories is being taught Archimedes' principle on the back of a napkin at the kitchen table, I would like to thank my dad for fostering my love for math, science, and engineering. Through him, I developed the belief that I could pursue anything.

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1 Introduction

Artificial Intelligence (AI) has revolutionized many health technologies, and the treatment of Obstructive Sleep Apnea (OSA) is no different. OSA is a common sleep disorder which causes frequent cessations in respiration, or apneas, throughout the night. This causes poor sleep quality which results daytime sleepiness, mood issues, and is linked to serious cardiovascular disease [1].

One cause of apneas is an obstruction of the airway due to the collapse of the pharyngeal muscles [2]. To treat OSA and prevent this collapse, a Positive Airway Pressure (PAP) device is most often prescribed, which applies pressure to the patient's airway through a mask worn during the night. This pressure on the airway prevents collapse and is effective in reducing the number of obstructive apneas [3]. However, PAP therapy's effectiveness is limited by low adherence as many find sleeping with such a device uncomfortable [4].

In some PAP devices, the amount of pressure applied automatically varies throughout the night. As the machine detects respiratory events, it responds by increasing pressure to prevent future events from occurring [5]. The motivation for doing so is to attempt to apply the lowest pressure needed throughout the night to give the wearer the most comfortable therapy possible. While this therapy is an improvement on a constant pressure therapy device, adherence to therapy remains low [5].

Alternatively, if abnormal breathing and apneic events could be anticipated before they occur, APAP pressure levels could be more personalized to the patient's needs, preventing upcoming apneas and likely improving treatment adherence and effectiveness. Rather than responding after an event has already occurred to prevent future events, the pressure could be adjusted pre-emptively and possibly stop the imminent event from occurring altogether. Further, increasing pressure only for the exact time period that it is required would allow the pressure to remain lower over the majority of the night, and therefore possibly increase patient comfort and subsequently improve adherence. This would lead to better treatment of the patient and further reduce the debilitating impact of OSA on quality of life. Overall, the goal of predicting the occurrence of harmful respiratory events is to establish a prophetic system that can be used to adjust the air pressure in PAP therapy targeted to the individual patient.

Some work towards predicting apneic events in advance has been previously explored in literature. Waxman et al. has shown that apnea and hypopnea events can be predicted in patients with OSA by looking at specific polysomnographic (PSG) measurements [6]. This study used Large Memory Storage And Retrieval (LAMSTAR) artificial neural networks and their method examined various physiological signals based on their potential association with apneas, as well as those commonly used in polysomnographic recordings [6]. They concluded that apnea prediction was possible with submental electromyography, which is commonly used in the investigation of swallowing disorders, whereas hypopnea prediction was possible with submental electromyography and heart rate variability [6]. Other studies have validated a framework for predicting apneas from single-lead electrocardiogram based on deep recurrent neural networks [7, 8].

Although the predictive performance demonstrated in recent studies [6–8] proves to be promising for enhancing the detection of OSA and for the prediction of apneas using artificial intelligence (AI) models input with PSG signals, integrating PSG equipment into modern PAP devices without compromising patient comfort and adherence will prove to be challenging. To seamlessly integrate a predictive model with home therapy PAP machines, the model input data would need to consist solely of patient signals which are currently measured during the night on these machines. This idea was explored in our previous work which resulted in successful development of a patent-pending proprietary Convolutional Neural Network (CNN). This model proved the concept of prediction and prevention of future apneic events using only pressure and airflow signals as recorded on conventional PAP machines [9].

Here, we develop a methodology to test the use of our AI-informed software that can monitor real-time air pressure and airflow data to anticipate future OSA events and intervene to prevent them from occurring. The intervention will involve directing the PAP device to gently ramp up the pressure to stabilize the patient's airway and treat the apnea before it occurs. The goal of the study is to determine if proactive airway management through prediction and intervention can be done to reduce occurrence of OSA events, and to investigate the changes in patients' sleep quality with use of the system.

2 Literature Review

2.1 Obstructive Sleep Apnea

2.1.1 Mechanism of Obstructive Sleep Apnea

Obstructive Sleep Apnea (OSA) is a sleep-related respiratory disorder characterized by repetitive bouts of complete cessation or transient reduction in breathing with maintained or increasing respiratory effort [2]. OSA occurs when there is recurrent collapse of the pharyngeal airway during sleep as a result of excessive pharyngeal muscle relaxation leading to pharyngeal collapse, subsequent blockage of the upper airway, and a pause in airflow [2]. These respiratory events are obstructive apneas. Obstructive hypopneas are another type of respiratory event seen in OSA patients, characterized by periods of shallow breathing which occur due to a partial airway blockage. These differ from apneas which are complete pauses in breathing due to full blockage of the airway [2, 10]. An even less severe blockage of the airway can result in a flow limitation or a snoring event [2, 10]. Central apneas, another type of respiratory event, are caused by a cessation in respiratory effort while the airway remains open [2]. A person afflicted with OSA can experience any of these event types multiple times throughout the night.

2.1.2 Impact on Quality of Life

The subsequent symptoms caused by OSA are wide ranging and can severely impact the quality of life for the person suffering from OSA. Snoring is one of the most common symptoms and is often reported by bed partners. This symptom can affect the sleep of the loved ones as well as the sufferer themselves [1]. Daytime sleepiness is reported in most OSA patients as their sleep is disrupted and adequate rest is difficult to obtain. Obstruction of the airway causes repetitive nighttime awakenings which causes the patient to awake feeling unrested. [1]. This results in lack of energy, poor mood, memory impairment, difficulty concentrating, and early morning headaches. These negative effects on the patient's mental capacity put the patient at an increased risk of a motor vehicle crash by two to three times [1]. These factors combined lead to a poorer quality of life for the typical OSA patient.

2.1.3 Impact on Health

OSA is linked to severe chronic health conditions such as obesity, diabetes, and an increased risk of cardiovascular disease, resulting in hypertension, coronary artery disease, stroke, heart failure, metabolic syndrome, and atrial fibrillation. [11, 12]. OSA can also cause a negative feedback loop with other conditions, where OSA worsens a coexisting condition, which then in turn worsens the OSA [12]. Multiple studies have shown that severe OSA is associated with increased all-cause mortality [12].

2.1.4 Epidemiology

OSA affects 12% of adults in the United States and is considered a serious illness with low rates of diagnosis [1]. A study by Young et al. (1993), showed an estimated 9% of women and 24% of men suffer from OSA, though the condition was only symptomatic in 2% of women and 4% of men. However, due to the rate of obesity increasing since the publication of that study, the current rates of OSA are likely higher [1].

Individuals who are at an increased risk of OSA include those with a body mass index (BMI) greater than 30 kg/m^2, which is the clinical criteria for obesity [13]. OSA is reported in around 70% of the morbidly obese [1]. Other characteristics which make an individual more likely to develop sleep apnea are those over the age of 35, males, and those with a neck circumference greater than 40 cm [13].

2.1.5 Diagnosis

OSA can be suspected based on noted symptoms, such as snoring, witnessed apneas, and non-restorative sleep. Clinical testing is required for a diagnosis, usually performed in an overnight laboratory setting or as a home test [12]. Respiration and other physiological signals are monitored to determine the presence and frequency of disordered breathing events. The data collected can be analyzed and metrics relating to the severity of sleep disorder determined. The Apnea-Hypopnea Index (AHI) is the primary clinical measure of the severity of OSA and considers the frequency of hypopneas and apneas during each hour of sleep [1]. An AHI of at least 5 is required for a mild sleep apnea diagnosis [12].

2.1.6 Treatment

As the most common sleep-related respiratory disorder, it is imperative that tolerable and effective treatments are available for those diagnosed with OSA [14]. Treatment is aimed to reduce these adverse health consequences and reduce healthcare costs caused by untreated OSA. The most often prescribed and efficacious treatment for OSA is positive airway pressure therapy. This requires the patient to wear a mask connected to a PAP device via tubing while sleeping. The device delivers constant air pressure to the patient to support the airway and prevent collapse [3]. Other non-surgical treatments include the use of oral appliances, such as tongue-retaining devices and orthodontic or mandibular advancing appliances [15]. These devices work by adjusting the position of the airway structures to improve the airway of the patient. These devices are well-tolerated by patients, however they are associated with long term dental structure changes, such as a significant decrease in overbite [15].

Surgical options also are available for the treatment of OSA. These include the removal of tonsils, uvula, and posterior velum or the creation of a tracheostomy. These treatments are generally not recommended by physicians other than as a last resort when other treatment options have failed [15].

Finally, a neurostimulation treatment is also available to those suffering from OSA. Nerve stimulation can be utilized to stimulate tissue and prevent airway collapse via an implanted device in the airway muscles. This treatment can be effective in reducing AHI, though are associated with high costs, technical malfunctions, and moderate to sometimes severe negative health side effects [16].

2.2 Polysomnography in Observational Sleep Studies

2.2.1 Polysomnography Signals

To diagnose OSA, a patient will often attend a polysomnographic study in a laboratory setting. During this study, the patient will sleep as normal while physiologic data is collected and observed by a technologist [17]. The data is streamed real-time to a control room and also collected for post-analysis.

Data collected includes the airflow of the patient, monitored using a nasal pressure transducer and an oronasal thermal sensor, which tracks the breathing by the temperature changes of the breath. If a PAP device is used during the study, the pressure applied and leak of the device is also collected. Respiratory effort is monitored using respiratory inductance plethysmography belts on the thorax and abdomen of the patient [17]. Respiratory effort data is needed to determine between different types of respiratory events, especially distinguishing between central and obstructive events [2].

Electroencephalogram (EEG), electro-oculogram (EOG), and electromyogram (EMG) are performed using surface electrodes. These provide data on the electrical activity in the frontal, central, and occipital brain regions, as well as the eye and chin movements of the subject [17]. From this data, a trained technologist can determine the sleep stage the subject is in throughout the night. Any arousals from sleep are also determined with this data. Limb EMG is collected on the legs to monitor their movement [17].

Electrocardiogram is used to monitor the heart rate and rhythm. Pulse oximetry is used to report oxygen saturation, which is vital to determine the effect of possible disordered breathing. Finally, body position is recorded with either a position monitor on the patient or by visual monitoring via video [17].

2.2.2 Sleep Study Analysis and Metrics

A technologist can then take the recorded PSG data and provide a comprehensive evaluation of the patient's sleep. A diagnosis of sleep apnea can be obtained following the evaluation.

The AHI is determined along with statistics on quality of sleep, physiologic markers, and disordered breathing events. Other metrics reported include Respiratory Distress Index (RDI), which is the sum of apneas, hypopneas, and respiratory event related arousals per hour. Obstructive Apnea Index (OAI), Central Apnea Index (CAI), and Hypopnea Index (HYI) are determined by the average number of obstructive apneas, central apneas, and hyponpneas per hour, respectively. The arousal index is calculated by the average number of arousals per hour [18]. Oxygen Desaturation Index (ODI) is the average number of desaturation episodes per hour. Desaturation episodes are generally described as a decrease in the mean oxygen saturation of >=4% (over the last 120 seconds) that lasts for at least 10 seconds [17,18]. The oxygen saturation data is also analyzed to determine metrics such as the proportion of sleep time with oxygen saturation above 90% and the minimum oxygen saturation that was recorded.

Sleep study reports also can include proportion of time in each sleep stage (Stage 1, Stage 2, Stage 3, REM, Wake), proportion of time in each body position (supine, right side, left side, prone), time taken to fall asleep, proportion of night snoring, number of movements, total time in apnea, PAP pressure analysis, proportion of time in each range of heart rate, maximum and minimum heart rate, and other cardiac events.

2.3 Positive Airway Pressure Therapy

2.3.1 Continuous Positive Airway Pressure Therapy

Positive Airway Pressure (PAP) therapy is the most common and efficacious treatment for OSA [4]. Two main modes of PAP therapy are fixed Continuous Positive Airway Pressure (CPAP) and Auto-adjusting Positive Airway Pressure (APAP). CPAP therapy attempts to maintain airway patency by blowing air into the airway to maintain a fixed positive pressure that stents the airway open thereby preventing collapse [3].

2.3.2 Poor Adherence

Although efficacious, and the most common and conventional type of PAP therapy for OSA, CPAP therapy suffers from poor patient adherence due to discomfort and may not fully alleviate all adverse consequences of OSA [19], [20]. According to available data, PAP devices, when used as prescribed for at least six hours each night, can lead to reduced daytime drowsiness, improved daily functioning, and may even reduce cognitive impairment [4]. However, research has determined that 29% to 83% of patients use their machines for fewer than four hours per night [4]. Poor rates of adherence limit the effectiveness of the PAP therapy and OSA patients frequently seek alternate, and less effective, treatments [21].

2.3.3 Auto-adjusting Positive Airway Pressure Therapy

APAP, a more advanced type of PAP therapy used for those with OSA and especially for home titration [22], automatically adjusts the pressure with a goal of delivering the minimum necessary pressure to maintain airway patency over the night. It attempts to do this by relying on detection of respiratory events to determine when to react and apply the required positive pressures [5]. This technology allows for a lower overall mean pressure to be delivered, since pressure requirements vary through the night depending on factors such as body position and sleep stage. Although some patients might find APAP to be more tolerable, adherence remains low and it has only been shown to increase machine usage by about 13 minutes per night, which most deem not clinically meaningful [5].

Most PAP devices will record data each night, such as the airflow and pressure signals of the patient's respiration and any detected respiratory events. This data is stored on an SD card inserted into the PAP device.

2.4 Convolutional Neural Networks

Artificial neural networks are an AI structure which operates similar to the biological neural networks [23]. These networks can be trained to recognize patterns in data and classify samples based on known labels. Networks are trained by providing a set of data with known class labels and allowing the network to make class predictions for each sample, based on the input sample. Representative features are derived from the data by the network, and a class prediction is determined [23]. As the predicted and real class are compared, the network updates its internal parameters to reduce error between predicted and real class labels. This learning process continues and is stopped based on criteria for the accuracy for prediction [23]. The network is then tested on a data set that was not provided during training, and the real accuracy of the network is calculated based on its predictions [23].

Neural networks are developed with different layer types and structures, suited to each application. A Convolutional Neural Network (CNN) is a powerful artificial neural network capable of diverse tasks. This feed-forward network uses convolutional structures to derive features from the input data [24].

3 Methods

3.1 Subjects

Recruitment of patients for this study occurred at a commercial respiratory care company, The Snore Shop Inc. (Dartmouth, Nova Scotia, Canada), and in the community through study advertisements (Halifax, Nova Scotia, Canada). Recruited patients were included in the study if they were:

1. diagnosed with OSA
2. between 18 and 70 years old
3. were a current user of a ResMed AirSense^{TM} 10 PAP device
4. had used the ResMed PAP device for more than 4 months
5. were able to comply with all study requirements as outlined in the consent form
6. were able to follow directions of the study physician and research team
7. were able to understand English and provide written informed consent
8. were willing to provide their personal PAP device for all nights of the study
9. were willing to provide their PAP SD memory card for analysis of their historic 30 day data by OSCAR (an open-source software used for reviewing and exploring data produced by PAP machines)

10. had an Obstructive Apnea Index (OAI) on PAP of at least 0.8 events per hour.

This OAI threshold was chosen to ensure at least one obstructive apnea every two hours was observed so that researchers could adequately determine whether there was a difference in OAI during the treatment night compared to the control night. All participants were required to use the same model of PAP device so that the model of PAP device was not an uncontrolled variable that could influence our results. We chose the ResMed AirSense™ 10 device, specifically, because the majority of patients from The Snore Shop used this device. Exclusion criteria included:

1. actively using required oxygen therapy
2. history of severe cardiovascular or neurological issues
3. medically complicated or medically unstable
4. potential sleep apnea complications that may have affected the health and safety of the participant
5. any flu-like or upper airway tract infection symptoms at the time of assessment;
6. unable or unwilling to give written informed consent
7. pregnancy or breastfeeding.

The study was carried out on 11 patients who were undergoing PSG along with PAP titration due to obstructive sleep apnea. The protocol was approved by the Nova Scotia Health Authority Research Ethics Board (NSHA REB ROMEO File #1027088) and informed written consent was obtained from all subjects. Table 1 and Table 2 summarize subject demographics and baseline characteristics.

Table 1: Subject Demographics and Baseline Characteristics

		Number of participants
Gender	Female	7
	Male	4
Highest education level	Bachelors	4
	College	5
	High school	1
	GED, technician	1
Lives independently	Yes	10
	No	1
Has a caregiver	No	11
Wears hearing aids	No	11
Wears glasses	Yes	11
Medical considerations	Apnea diagnosis	11
	Anxiety	1
	COPD/asthma	1
	Diabetes mellitus	1
	Head injury	1
	High cholesterol	1
	Insomnia	1
	Drinks alcohol	7
	Smokes	1
	Vapes nicotine	1
	Uses PAP machine	11
Severity of diagnosed OSA	Mild	1
	Moderate	2
	Severe	5
	Unknown	3

COPD: chronic obstructive pulmonary disorder; PAP: positive airway pressure.

Table 2: Subject Demographics and Baseline Characteristics cont.

	Mean ± Std. Dev.
Age (years)	54.2 ± 10.9
Height (cm)	169.7 ± 11.4
Weight (kg)	70.1 ± 6.8
Education (years)	14.7 ± 1.9
Duration of PAP therapy (days)	626 ± 238

PAP: positive airway pressure.

Based on the inclusion criteria from the most updated study protocol, 15 participants met the criteria and were recruited, but four of them were excluded due to insufficient data obtained as a result of the subject being unable to sleep. Subjects' ages ranged from 34 to 69 years, with seven female and four male participants. The average height of all participants was 169.7 cm, and the average weight was 70.1 kg. At the time of OSA diagnosis, one was diagnosed with mild sleep apnea, two with moderate sleep apnea, and five with severe sleep apnea. Three subjects were unable to retrieve their original sleep apnea diagnoses. AHI values were obtained from the analysis of each participant's 30-day historical PAP data on OSCAR, resulting in an average AHI of 3.6, and a range of 1.2 to 16.3. The average duration participants were on PAP therapy was 626 days, with a range of 244 days to 962 days. Relevant PAP device settings of the participants are summarized below in Table 3.

Table 3: Summary of Participant PAP Device Data

Device option	Setting	Number of participants
Therapy mode	APAP	8
	APAP for Her	2
	CPAP	1
EPR level	1 cmH_2O	1
	2 cmH_2O	2
	3 cmH_2O	6
	Off	2
Ramp Time	5 mins	1
	15 mins	1
	Automatic	4
	Off	5
Ramp start pressure	4 cmH_2O	4
	6 cmH_2O	2
	No ramp	5
Mask type	Full face	1
	Nasal	3
	Nasal cushions	1
	Nasal pillows	6
CPAP set pressure[1]	9 cmH_2O	1
APAP response[2]	Standard	10

	Mean ± Std. Dev.
APAP min pressure (cmH_2O)[2]	5.4 ± 0.7
APAP max pressure (cmH_2O)[2]	16.9 ± 1.2

APAP: auto-adjusting positive airway pressure; CPAP: continuous positive airway pressure; EPR: expiratory pressure relief.
[1]n=1, [2]n=10

Out of the 11 subjects, one used CPAP mode, two used AutoSet for Her, a premium auto-adjusting pressure mode for female patients, and eight used AutoSet.

The average minimum pressure was 5.4 cmH_2O and the average maximum pressure was 16.9 cmH_2O. Regarding mask type, most participants used nasal pillows (n = 6), followed by nasal masks (n = 3) and full-face masks and nasal cushions (n = 1 each).

3.2 Study Protocol

This study was a double-blind, randomised crossover study with the objective of comparing the efficacy of the intervention treatment. All subjects recruited underwent at least two nights at the sleep clinic and received one of two sleep treatments on each night:

1. The control treatment, in which the NovaResp cMAP™ Flow V2.0 system delivered therapy solely as its commercial counterpart,

2. The intervention treatment, in which the NovaResp cMAP™ Flow V2.0 system delivered therapy as its commercial counterpart, with the added intervention protocol.

All participants were to receive both treatments at least once. For both treatments, the NovaResp cMAP™ Flow V2.0 system's therapy settings were configured to be the same as the participant's preferred settings. The study design is illustrated in Fig. 1.

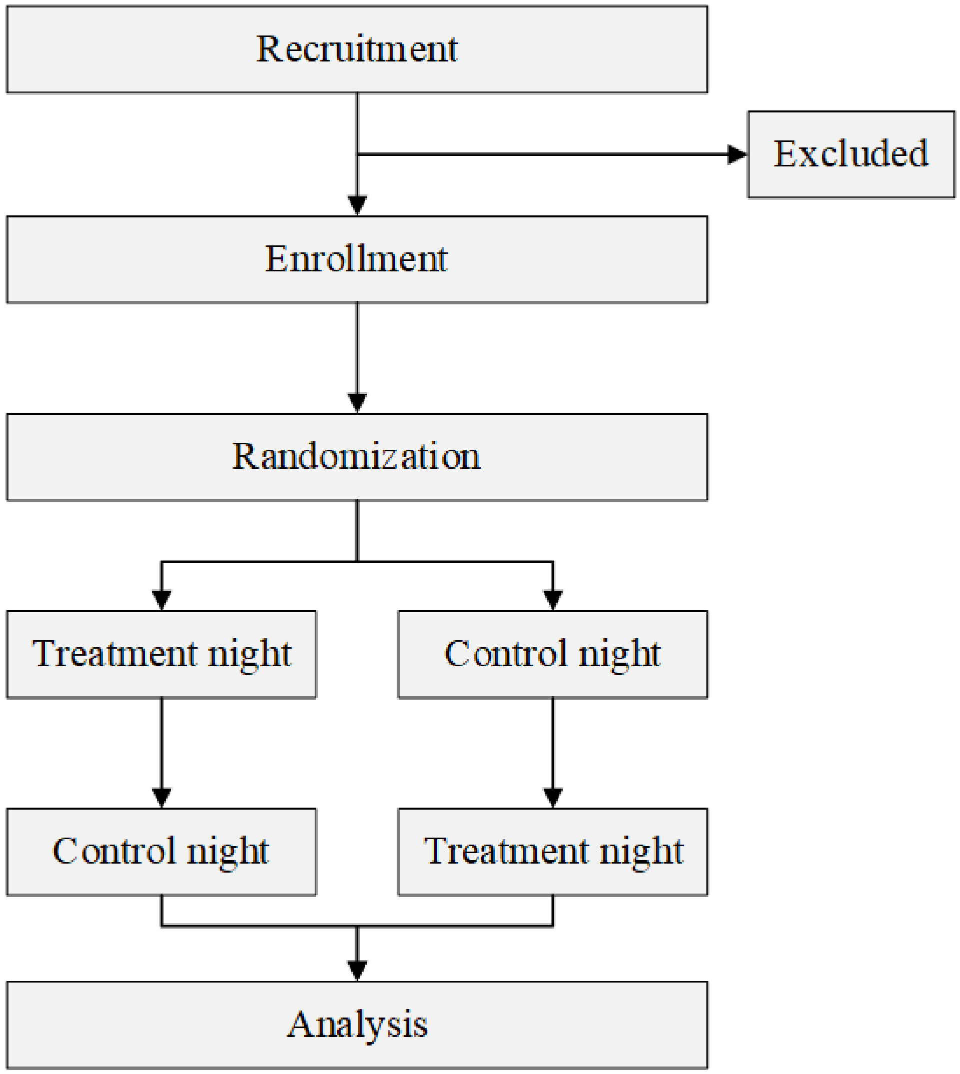

Figure 1: Study design flow chart.

3.3 Sleep Lab Set Up

The patient study was carried out during the standard 8 hours of sleep during PAP titration at the QEII health sciences centre sleep clinic. The NovaResp cMAP^{TM} Flow V2.0 system consists of a PAP device, that is interfaced by a laptop with company software. During the sleep study, the patient received PAP therapy during sleep from the NovaResp cMAP^{TM} Flow V2.0, which was monitored in the next room by the sleep technologist using a laptop. The laptop was running the company's software throughout the sleep trial to acquire data from the NovaResp cMAP^{TM} Flow V2.0 system and run the predictive computational model. The NovaResp cMAP^{TM} Flow V2.0 system was concealed from the patient to blind the treatment.

In order to integrate the respiratory data (pressure, flow and leak) read from the PAP machine onto the laptop to the PSG system for scoring and real time monitoring, a simple digital to analog converter board was developed. Proper functionality and calibration of the signals were validated. This board was attached to the Polysomnography (PSG) headbox and the NovaResp cMAP^{TM} Flow V2.0 system by USB port on the laptop. Once the subject was setup in the sleep clinic room with all standard PSG sensors, the NovaResp cMAP^{TM} Flow V2.0 system was turned on to ensure patient comfort. The subject then attempted to sleep throughout the night while being continuously monitored through PSG measurements and the NovaResp cMAP^{TM} Flow V2.0 computer software. This set up can be seen in Fig. 2.

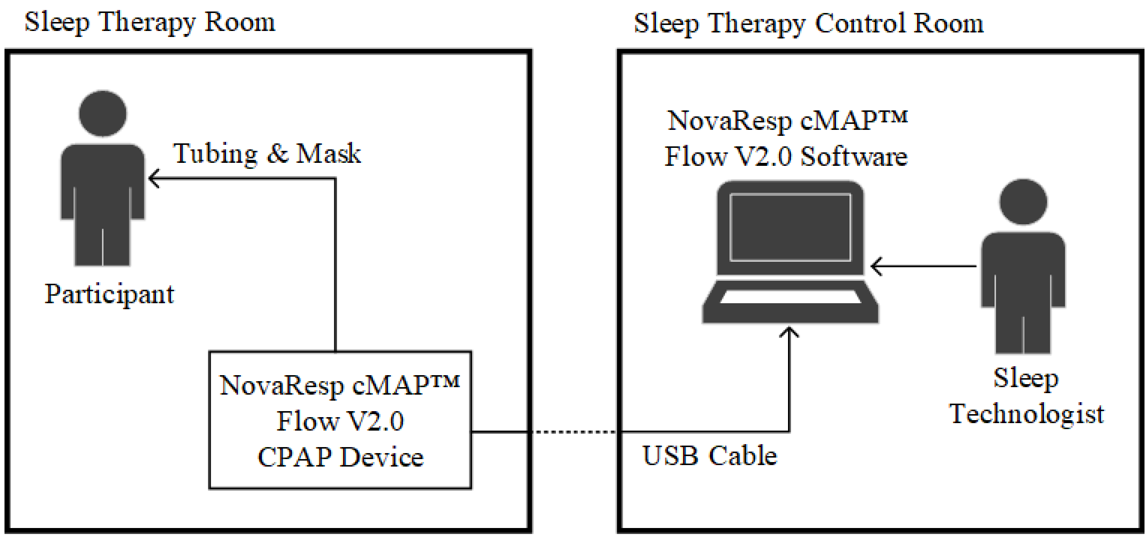

Figure 2: Study set-up at the QEII Health Sciences Centre sleep lab.

3.4 NovaResp cMAP™ Flow V2.0

The NovaResp cMAP™ Flow V2.0 system is a medical PAP device to be used during sleep therapy for patients who suffer from airway obstruction disorders, such as OSA. A modified version of ResMed AirSense™ 10 that was approved by Health Canada for research (Investigational Testing Authorization #329649) was used for this study. This device functions the same as a normal ResMed AirSense™ 10, with the addition of our NovaResp cMAP™ Flow V2.0 software. A communication interface has been added to a PAP device to enable the streaming of data between the PAP system and a computer running the company's software. Specifically, to the medical device's circuit board, we have connected a compact debugging board that enables input and output streams of data between the PAP system and a computer without alteration of the PAP system's hardware or firmware. Through this debugger, in conjunction with the software we developed, real-time measurements of airway pressure and flow obtained by ResMed's PAP device are fed into the deep learning model. The model then determines probabilities for the prediction of onset of obstructive apneas which informs the software's intervention decisions. The intervention involves ramping up the pressure to stabilize the patient's airway and treat the apnea before it occurs. Overall, this system was designed to be used in patients suffering from OSA during sleep therapy to monitor the patient's airway pressure and airflow, to predict the onset of obstructive apneas, and to intervene if an obstructive apnea is predicted. The system is depicted in Fig. 3.

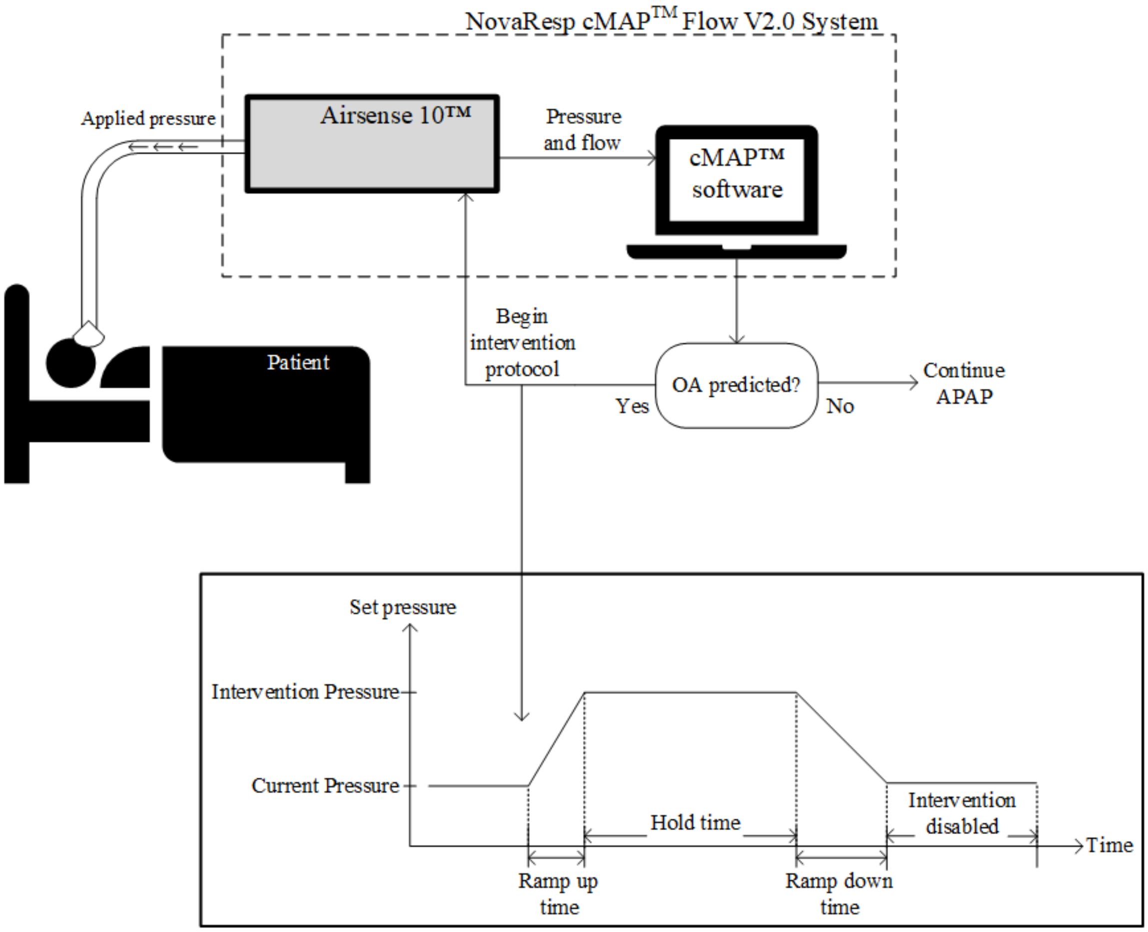

Figure 3: NovaResp cMAP™ Flow V2.0 System.
OA: obstructive apnea; APAP: auto-adjusting positive airway pressure.

During the cMAP™ intervention nights, model predictions are continuously generated and recorded, along with input pressure and flow data and any events tagged. Intervention is initially disabled to allow the subject to fall asleep (either the length of their normal device ramp up time, 5 minutes if no ramp used, or 30 minutes for auto ramp feature). Intervention is also disabled when any input data issues are detected (such as sampling frequency issues or when large leak is present) until the issue is resolved and the problematic data is cleared from the input data buffer.

If a central apnea or a hypopnea are predicted by the model, the predicted event is recorded, and interventions are disabled for 2 minutes. If an obstructive apnea is predicted and intervention is enabled, the following pressure increase protocol occurs: a ramp up of 3 seconds to +3 cmH_2O of pressure which is held for 6 minutes (i.e., hold time). The pressure then ramps over 2 minutes to the PAP's desired target pressure. Intervention is then disabled for 2 minutes, thus in total the minimum time between intervention initiations is 10 minutes. Fig. 3 illustrates this pressure protocol.

For APAP users, the normal APAP pressure upper limit is lowered by the intervention pressure increase amount (3 cmH_2O) to ensure that interventions can always take place without exceeding the normal pressure range of the subject. For CPAP users, their set pressure remains the same and the intervention increase is added on. The maximum pressure is never able to exceed 20 cmH_2O in either case.

3.5 cMAP™ Deep Learning Model

The software's deep learning model, a convolutional neural network, was trained on PAP respiratory data obtained from a previous study (NSHA REB ROMEO File #1024635) [9]. The final processed dataset was derived from 32 subjects and contained approximately 190 000 short temporal samples of air pressure and airflow, with a sampling frequency of 25 Hz. Each sample's class was labelled as baseline, which was defined as normal breathing, breathing preceding an obstructive apnea, breathing preceding a central apnea, or breathing preceding a hypopnea. The model output represents the predicted probabilities of each class. While central apneas and hypopneas were predicted, only obstructive apnea predictions were acted on, as the goal of the study was to predict and prevent obstructive apneas only. In future work, hypopnea and central apnea predictions could be used to adjust pressure proactively in addition to the obstructive apnea predictions.

70% of samples comprising the dataset were used for training, 15% were withheld as a validation set, which were used for tuning model parameters, and 15% of samples were withheld for testing. We report results on the testing set. The final model achieved an overall accuracy of 85% at the peak of the last breath before the event. The model achieves 81% accuracy 5 seconds before the peak of the last breath and 76% accuracy 10 seconds before. The prediction threshold was determined by processing full nights of patient data and selecting the ideal value to reduce false predictions, but still allow correct obstructive apnea predictions with enough time to intervene before the event begins. Two representative examples of obstructive apnea prediction using real patient data are shown in Fig. 4 and Fig. 5. The input flow and pressure signals and the corresponding output prediction probabilities are shown for each example. The figures show baseline prediction during normal breathing, followed by an increase in the prediction probability of obstructive apnea leading up to the apnea. When the obstructive apnea probability exceeds the defined threshold, such as illustrated by the dashed line at 80%, an upcoming obstructive apnea is predicted. A pause in breathing, the obstructive apnea, is then seen in the input data, thus, the event has been correctly predicted.

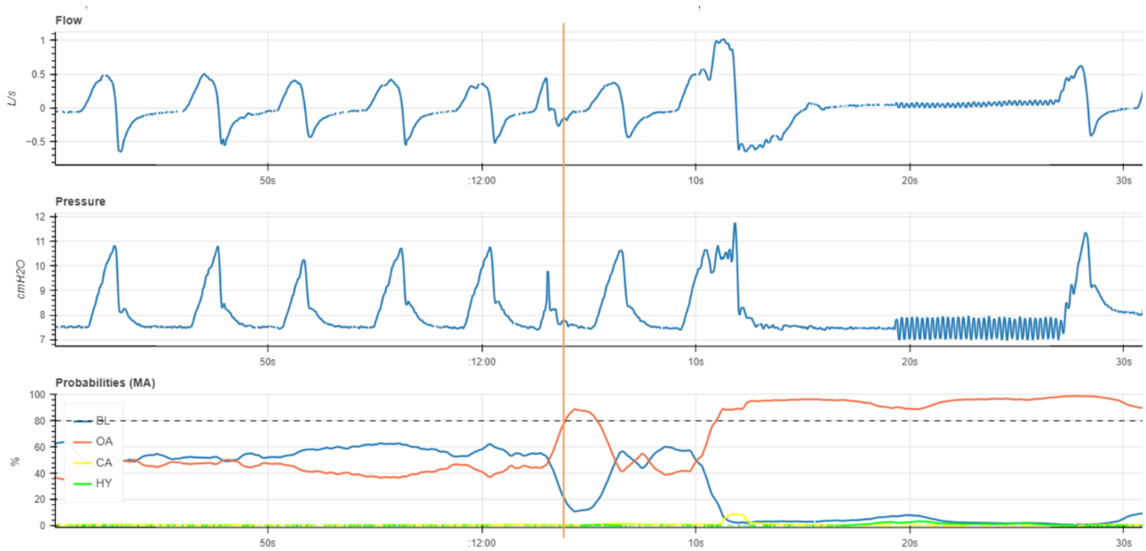

Figure 4: Example 1 of input data and output model probabilities of respiration leading up to and including an obstructive apnea.

The orange vertical line indicates where the OA prediction probability crosses the threshold and an upcoming OA has been predicted. BL: baseline/normal breathing; OA: obstructive apnea: CA: central apnea; HY: hypopnea; MA: moving averaged.

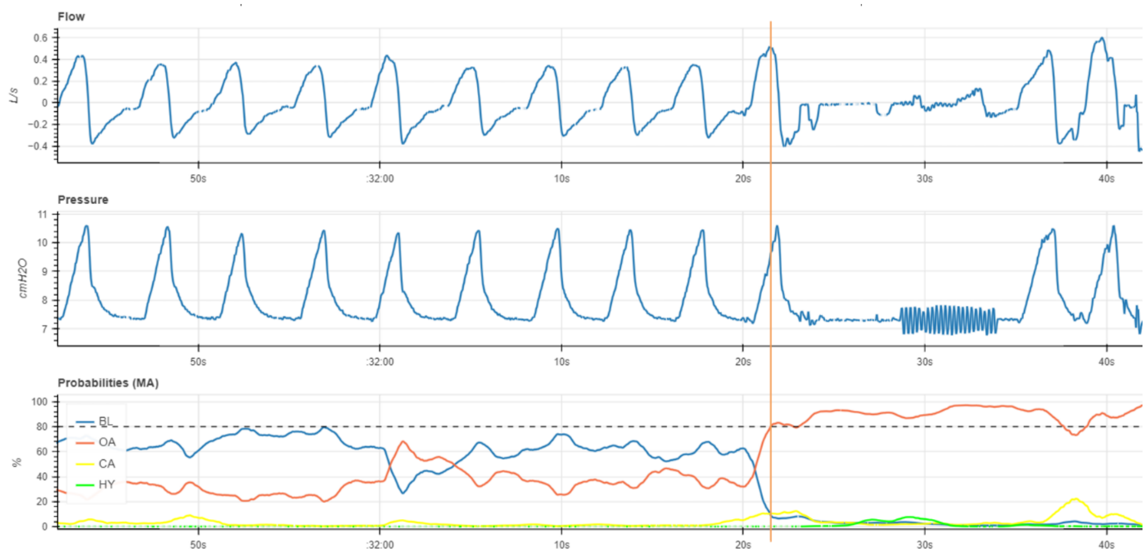

Figure 5: Example 2 of input data and output model probabilities of respiration leading up to and including an obstructive apnea.

The orange vertical line indicates where the OA prediction probability crosses the threshold and an upcoming OA has been predicted. BL: baseline/normal breathing; OA: obstructive apnea: CA: central apnea; HY: hypopnea; MA: moving averaged.

3.6 Polysomnography

During the study, standard polysomnography (PSG) data were collected using either the Sandman$^{\text{TM}}$ (Embla N 7000) or SleepWorks$^{\text{TM}}$ (Natus Embla NDx) data collection software. The PSG included a recording of EEG (F3, F4, C3, C4, O1, and O2 for SleepWorks$^{\text{TM}}$ and Sandman$^{\text{TM}}$), EOG (LOC/E1 and ROC/E2 for SleepWorks$^{\text{TM}}$ and LOC and ROC for Sandman$^{\text{TM}}$), EMG (Chin 1, Chin 2, Chin z, RLEG-, RLEG+, LLEG-, and LLEG+ for SleepWorks$^{\text{TM}}$ and X2, X3, X4, -2/+2 and -3/+3 for Sandman$^{\text{TM}}$), and ECG (LA/ECGL and RA/ECGR for SleepWorks$^{\text{TM}}$ and -1/+1 for Sandman$^{\text{TM}}$) that were used for identifying sleep stages and sleep events.

The PSG recordings were annotated by Registered Polysomnographic Technologists with over 10 years of experience, indicating different sleep events (i.e., arousal, obstructive hypopnea, obstructive apnea, respiratory effort related arousal, and central apnea) as well as different sleep stages (i.e., wake, stages 1-3, and REM). To score respiratory events, CPAP flow, abdomen and chest respiratory inductance plethysmography for effort, and pulse oximetry (Nonin Medical) were used. The averaging time for the pulse oximeter was 3 seconds or faster for pulse rates of 60 bpm or greater. Scoring was done in accordance with the AASM Manual for the Scoring of Sleep and Associated Events, version 2.6. An apnea was defined as cessation of airflow (>90% decrease in apnea sensor excursions compared to baseline) of a minimum duration of 10 seconds; a hypopnea was defined as a 30% reduction in airflow from baseline for a minimum duration of 10 seconds, and this must be accompanied by a >3% desaturation or an arousal; oxygen desaturation index (ODI) was defined as the number of oxygen desaturations of >3% multiplied by 60 divided by the total sleep time; OAI was defined as the total number of obstructive apnea events per hour of sleep; respiratory effort-related arousal (RERA) was defined as a sequence of breaths characterized by increasing respiratory effort, or inspiratory flattening in the nasal pressure or PAP device flow channel, for a minimum duration of >10 seconds; RDI was defined as the total number of apneas, hypopneas, and RERAs per hour of sleep; and arousal index was defined as the total number of arousals per hour of sleep [18]. Other relevant definitions can be found in the AASM Manual, version 2.6. After the sleep clinic technologist scored each patient's sleep study, sleep reports and analyses were subsequently generated for each patient by the Sandman™ or SleepWorks™

softwares.

3.7 Statistical Analysis

The primary objective of this study was to evaluate the potential of using our software to effectively predict, intervene, and prevent the occurrence of obstructive apneas before they occur during sleep therapy, using existing pressure and flow sensors in a conventional PAP machine. This experiment was carried out during both non-REM and REM sleep and standard PSG measurements were obtained to assess quality of sleep. This study was expected to assess the effectiveness of proactive management and treatment of OSA using real-time monitoring of air pressure and airflow and deep learning predictive models. Sleep metrics collected through PSG, such as AHI, OAI, RDI and ODI and arousal indices were analyzed to determine whether quality of sleep improved during the nights in which patients underwent the interventional treatment as compared to the control treatment The treatment was considered effective if patients' quality of sleep, as indicated by AHI, OAI, RDI, ODI and other sleep parameters, is improved compared to standard sleep therapies. Accurate prediction and prevention of these events could improve clinical treatment of people suffering from obstructive sleep apnea (OSA) syndrome.

Our secondary objective was to investigate whether proactive management and treatment of OSA had an effect in patient's overall sleep quality as determined by an adherence/satisfaction questionnaire. This questionnaire was adapted with slight changes from a questionnaire developed by McArdle and colleagues at the University of Western Australia [25]. Participant's subjective ratings to each therapy were compared to assess whether the use of our system had a greater positive effect on their sleep. Participant satisfaction after each night of sleep was assessed in the morning using a Likert scale to determine whether the use of our system had a positive, negative, or neutral effect on their sleep.

Means, mean difference, and 95% confidence intervals are reported for each metric of the study results. Paired two-tailed t-test was used for the statistical analysis on the difference between control and treatment values. A t-test p-value of < 0.05 was considered to indicate a statistically significant result. SciPy's statistical functions library was used for the analysis. AHI and mean mask pressure are also displayed in box and whisker plot showing median, interquartile range, and full data range.

4 Results

4.1 Polysomnography Results

Polysomnography and standard scoring criteria were used to determine AHI values, resulting in an average AHI without cMAP^{TM} (i.e., control nights) of 6.3 events per hour, while it decreased to 4.3 events per hour when cMAP^{TM} was used (i.e., intervention nights); this reduction of 2.0 events per hour was statistically significant ($p = 0.02$). This can be visualized in Fig. 6.

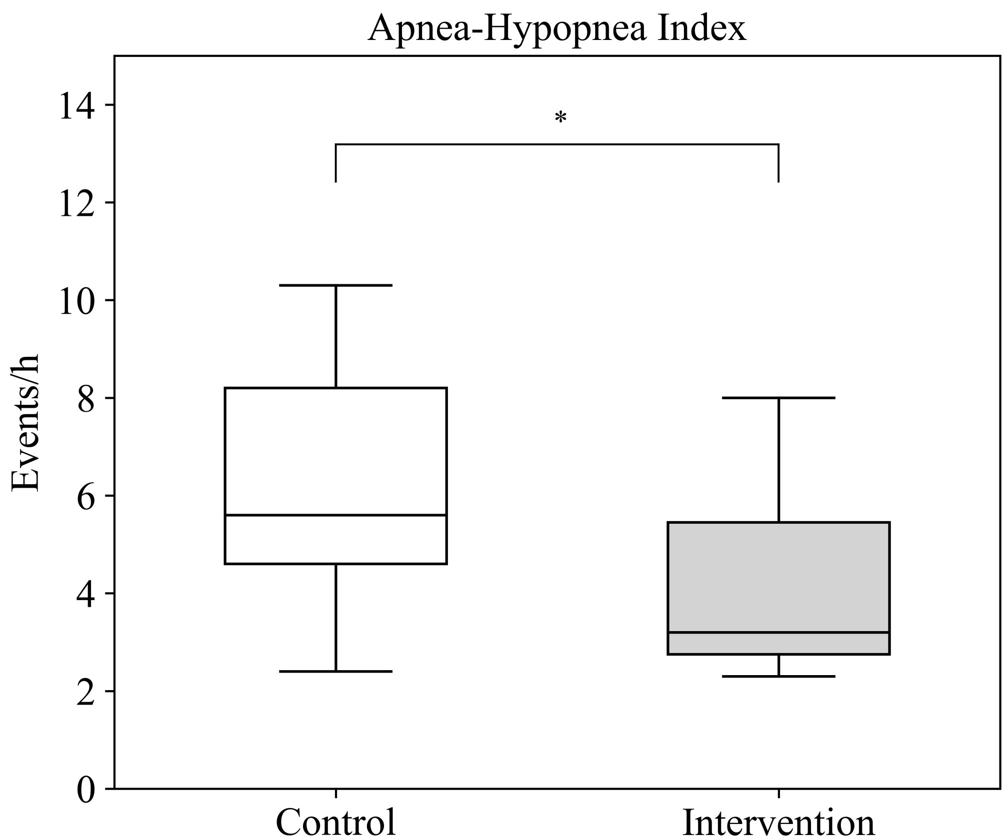

Figure 6: AHI box plot displaying the median, lower and upper quartile, and range for the control nights and the intervention nights.
An asterisk is displayed to indicate significance.

Average total sleep time (TST) above 90% oxygen saturation (SpO_2) without cMAP^{TM} was 98.2 minutes, while it increased to 99.4 minutes with cMAP^{TM}; this result approached statistical significance ($p = 0.05$). The average minimum SpO_2 during REM sleep without cMAP^{TM} was 88.5%, while it increased to 90.3% with cMAP^{TM}; this was a non-statistically significant increase in SpO_2 of 1.8% (p =

0.06). There was an issue with data collection for one subject, so the results refer to the remaining 10 subjects for these metrics.

The number of arousals per hour during REM sleep and NREM sleep (arousal indices) and the RDI were all non-significantly reduced during the cMAP^{TM} treatment nights compared to the control nights, with a 3.0 point reduction in the arousal index during REM sleep, a 0.7 point reduction in the arousal index during NREM sleep, and a 3.0 point reduction in RDI. Average arousals per hour on the control nights was 19.9 while average arousals per hour over the intervention nights was 19.2. This is an average mean difference of -0.7 arousals per hour of total sleep time without statistical significance ($p = 0.66$). During the intervention nights, pressure increases did not result in an increase in arousals.

There was no statistical significance of cMAP^{TM} for the total sleep time and proportions of total sleep time in each sleep stage, and sleep efficiency metrics. Proportion of sleep time in each sleep position (prone, supine, left side, right side) was also not significantly affected by the intervention protocol.

During cMAP^{TM} treatment nights, non-REM sleep heart rate ranges trended more in the 40-60 bpm range than the 60-80 bpm range when compared to non-cMAP^{TM} nights with findings which were not statistically significant. Other metrics derived from PSG data and scoring are shown below in Table 4 and Table 5.

Table 4: Participant Sleep Metrics From PSG Data and Scoring

Metric		Mean	95% CI	P-value
AHI (events/h)	Control	6.26	(4.59, 7.94)	
	Intervention	4.28	(2.97, 5.59)	
	Difference	-1.98	(-3.53, -0.44)	0.02
OAI (events/h)	Control	0.70	(-0.05, 1.46)	
	Intervention	0.49	(0.00, 0.98)	
	Difference	-0.21	(-0.64, 0.22)	0.30
CAI (events/h)	Control	0.82	(0.18, 1.45)	
	Intervention	0.55	(0.19, 0.92)	
	Difference	-0.26	(-0.65, 0.12)	0.15
HYI (events/h)	Control	4.58	(3.22, 5.94)	
	Intervention	3.15	(2.18, 4.11)	
	Difference	-1.44	(-2.98, 0.11)	0.07
Mixed apnea index (events/h)	Control	0.17	(0.00, 0.35)	
	Intervention	0.15	(0.02, 0.27)	
	Difference	-0.03	(-0.21, 0.16)	0.75
RDI (events/h)	Control	8.51	(4.43, 12.58)	
	Intervention	5.51	(3.69, 7.33)	
	Difference	-3.00	(-7.00, 1.00)	0.13
Arousal index REM (events/h)	Control	10.97	(5.14, 16.81)	
	Intervention	8.01	(5.61, 10.41)	
	Difference	-2.96	(-8.98, 3.05)	0.30
ODI (events/h)	Control	5.10	(2.80, 7.40)	
	Intervention	4.33	(1.24, 7.41)	
	Difference	-0.77	(-2.88, 1.34)	0.43

PSG: polysomnography; CI: confidence interval; AHI: apnea-hypopnea index; OAI: obstructive apnea index; CAI: central apnea index; HYI: hypopnea index; RDI: respiratory disturbance index; ODI: oxygen desaturation index; REM: rapid eye movement;

Table 5: Participant Sleep Metrics From PSG Data and Scoring cont.

Metric		Mean	95% CI	P-value
	Control	98.2	(97.2, 99.3)	
SaO_2 above 90% TST (%)[1]	Intervention	99.4	(98.6, 100.3)	
	Difference	1.2	(0.0, 2.4)	0.05
	Control	86.5	(84.1, 88.9)	
Min SaO_2 TST (%)[1]	Intervention	88.2	(86.5, 89.9)	
	Difference	1.7	(-0.5, 3.9)	0.11
	Control	88.5	(86.0, 91.0)	
Min SaO_2 REM (%)[1]	Intervention	90.3	(88.2, 92.4)	
	Difference	1.8	(-0.1, 3.4)	0.06
	Control	372.2	(330.2, 414.2)	
Total sleep time (mins)	Intervention	357.4	(322.4, 392.4)	
	Difference	-14.8	(-39.8, 10.2)	0.22

PSG: polysomnography; CI: confidence interval; TST: total sleep time; REM: rapid eye movement; NREM: non-rapid eye movement; SaO_2: oxygen saturation.
[1]n=10

4.2 cMAP™ Results

The average number of interventions per treatment night was 14.1 with a range of 6 to 26. The average number of interventions per hour of sleep was 2.4 with a range of 1.1 to 4.2.

4.3 PAP Tagging Results

Analysis of the PAP data for the intervention and control nights on the computer software OSCAR yielded an average OAI without cMAP™ of 1.9, while it decreased to 1.3 with cMAP™; this reduction of 0.6 was statistically significant ($p = 0.03$).

Total AHI was reduced from 3.2 events per hour to 2.5, with a non-significant p-value of 0.19. Central apnea and hypopnea indices were slightly decreased and not statistically significant.

4.4 Pressure Level Results

Pressure comparison of nine APAP users' data show mean mask pressure was raised from 8.6 cmH_2O to 9.1 cmH_2O on average with intervention ($p = 0.32$), which can be seen in Fig. 7. Note that one APAP user was excluded from this comparison as their APAP range was limited by the intervention protocol to essentially operate as CPAP.

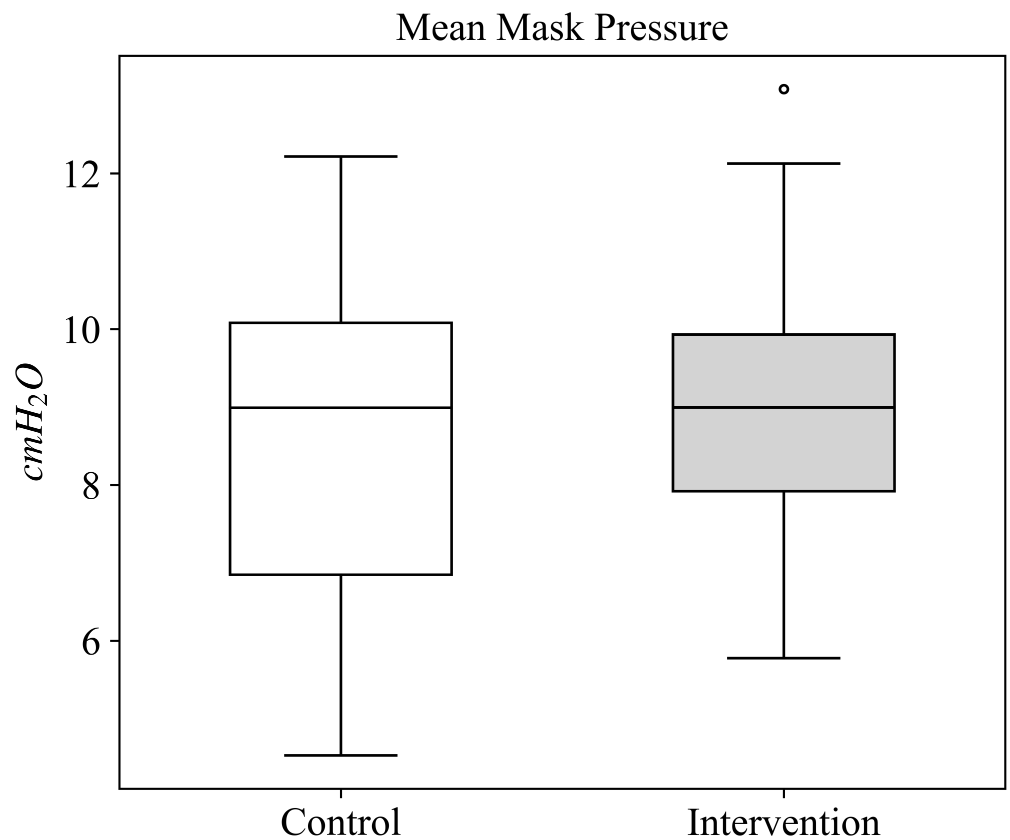

Figure 7: Box plot displaying the median, lower and upper quartile, and range for the mean mask pressure on the control nights and the intervention nights of the APAP users.

4.5 Subjective Ratings

The subjective ratings gathered from the post-study questionnaire show no statistically significant changes in the comfort, ease of falling asleep, disturbances, and feeling refreshed of the subjects when comparing the control nights to the intervention nights. Results are displayed in Table 6.

Table 6: Post-Study Questionnaire

Metric		Mean	95% CI	P-value
	Control	8.09	(6.18, 10.00)	
Comfort	Intervention	9.00	(7.96, 10.04)	
	Difference	0.91	(-1.45, 3.26)	0.41
	Control	6.09	(4.07, 8.12)	
Ease of falling asleep	Intervention	7.82	(6.23, 9.40)	
	Difference	1.73	(-0.38, 3.83)	0.10
	Control	8.91	(7.31, 10.50)	
Disturbances	Intervention	7.82	(5.97, 9.67)	
	Difference	-1.09	(-3.52, 1.34)	0.34
	Control	6.91	(5.85, 7.97)	
Feeling refreshed	Intervention	7.00	(5.59, 8.41)	
	Difference	0.09	(-0.88, 1.06)	0.84

CI: confidence interval.

5 Discussion

In this first-in-human study, we have tested the feasibility of preventing apneas and hypopneas by utilizing our previously developed deep learning model [9]. By intervening and increasing air pressure when an obstructive apnea is predicted, we were able to improve patients' objective sleep parameters. The findings of this study overall support the hypothesis that our software can proactively prevent OSA events and maintain patients' sleep quality.

Our findings show that our cMAP^{TM} system can decrease AHI in OSA patients, with a statistically significant reduction based on PSG scoring, and a non-significant reduction by PAP tagging. Since AHI is used to assess the severity of sleep apnea, and a reduction of AHI is a primary indicator of success with PAP therapy, the difference in AHI reduction between that from the PAP device tagging and that from professional sleep technologist standard scoring is concerning and points to a need for better developments in this area, including better algorithms to detect sleep-related events (i.e., AHI, OAI, etc.). As AHI tends to differ depending on the method of collection and sleep scoring, our results also indicate the importance of considering patient sleep quality when evaluating the performance and success of PAP therapy, rather than solely focusing on keeping the airway open, which is currently measured by AHI and oftentimes the only metric used in the evaluation of sleep apnea severity. This idea is consistent with Tam and colleagues, concluding that measures of therapy outcomes should go beyond the sole use of AHI and rather should also include general measurements around quality of life, OSA-specific quality of life, sleepiness, performance, and those that are physiological such as blood pressure, and our current results also concluded that these additional outcome measures don't often correlate with AHI [26]. Therefore, although AHI can be beneficial as a basic measure of PAP therapy success, it is not always reliable and often differs depending on the method of collection, so ultimately should be supplemented with additional measures, specifically those that are more patient-centred.

Our findings also show that cMAP^{TM} can decrease OAI, with a statistically significant reduction by PAP tagging, and a non-statistically significant reduction by PSG scoring. It is important to note that PAP devices use outdated criteria in tagging hypopneas, so they tend to over-account for obstructive apneas and under account for hypopneas. Since our model is based on PAP device tagging, we speculate that some of the obstructive apneas that our model predicts and prevents are, by more updated tagging criteria, considered hypopneas. Therefore, when looking deeper at the PAP device tags, there was a reduction in OAI by using our system, with statistical significance, and when looking at PSG scoring, OAI was reduced, but hypopneas were reduced even more. The non-statistically significant reduction of OAI by PSG scoring could be explained by the cMAP^{TM} model having been trained based on the OA definitions from the device tagging, rather than PSG scoring, and therefore, the model yielded a moderately better performance when analyzing the results from the device tagging compared to those by PSG scoring. The non-significant reduction in AHI by PAP tagging in the previous section can also potentially be explained by this concept.

We have additionally shown that our cMAP^{TM} system resulted in a significant increase in the TST above 90% SaO_2 and an increase in the minimum SpO_2 during

REM sleep. Hausler and colleagues found that those with a greater TST spent under 90% oxygen saturation were significantly less likely to have intermediate and ideal cardiovascular health (CVH) compared to poor CVH [27]. Oksenberg et al. also concluded that sleepy patients have a lower minimum SpO_2 during REM sleep compared to nonsleepy patients, which suggests that this outcome measure may be indicative of excessive daytime sleepiness [28]. Therefore, since our results show that our system increased the TST above 90% SpO_2 and the minimum SpO_2 during REM sleep, this indicates the potential to lead to better overall health of OSA patients by improved CVH and decreased daytime sleepiness. Longer term studies will be necessary to confirm these hypotheses.

While this paper demonstrated the feasibility of using machine learning to predict and prevent individual apneic events, most importantly the outcome of our work may pave the way for true personalized therapy. Given that a) individual patients have their unique breathing pattern, and b) the breathing pattern of each individual could alter each night, our work establishes the foundation to develop future individualized PAP therapy that is adaptable to individual patients and the nightly variations in their breathing patterns.

In order to demonstrate accurate prevention of true OSA events, it would have to be proven that an apnea was predicted correctly in the first place, before intervening. However, this is difficult to prove, as the prediction of false positives would yield the same result as the prediction of true positives, being an intervention that attempts to prevent a sleep event. Therefore, we decided that a reduction in AHI is the most reasonable metric that would be able to demonstrate proof of our hypothesis. As a result, in this study, we repeated the same intervention protocol for every subject, so we did not try to intervene and prevent every single apneic event. The average number of interventions per treatment night was 14.1 with a range of 6 to 26. The goal of future work will be to personalize the intervention protocol in order to deliver tailored treatment to each individual, which should result in more interventions per night and therefore more a significant reduction in apneic events.

Although our results show a slight increase in mean mask pressure of APAP users with cMAP™ compared to without cMAP™, this increase was non-significant. The difference in mean mask pressure between the control and intervention night was not measured for the one fixed CPAP user as an increase in pressure would be expected in fixed CPAP users. This is because the intervention pressure increase is added onto CPAP users' normal set pressures, whereas for APAP users, their set pressure upper limit is lowered by the intervention pressure increase amount to ensure that we do not exceed their normal set upper limit during interventions. It is also of note that one participant on APAP was considered a CPAP user, as their APAP range was too small, and they spent most of their sleep time at their upper limit. Therefore, this patient was also not accounted for in our calculations of the mean mask pressure. Finally, while our study showed no statistically significant changes in subjective ratings of participant sleep quality, this is still important to report on. As we have revealed that our intervention can reduce AHI and OAI, with no statistically significant increase in pressure levels, it is significant to note that we have done so without worsening patient sleep quality. Somiah and colleagues demonstrated that better sleep quality was related to better CPAP adherence [29], and Yang and colleagues concluded that CPAP treatment had beneficial effects on sleep quality in subjects with high CPAP adherence [30]. Additionally, Salepci et al. found that higher CPAP adherence led to an improvement in satisfactory sleep, and decreased chest discomfort, difficulty falling asleep, and sleep disturbances [31]. Thus, as quality of sleep is one important metric that correlates strongly with PAP device adherence, and vice versa, we suspect that there should not be any reduction in PAP adherence with our device. Adherence is a critical marker of PAP therapy success and proves to be the most challenging part of therapy to achieve [4].

Overall, the success of our prediction and prevention system is important and has many benefits. First, the use of existing airflow and air pressure sensors already built into conventional PAP devices makes the idea of prediction and prevention more practical, rather than utilizing PSG sensors to predict sleep events, which is what some other researchers have focused on to date. Integration of PSG equipment into conventional PAP devices would be challenging without compromising patient comfort and adherence, which is why we have focused on using the existing PAP data, so that we would not have to add any additional components to PAP devices. Furthermore, our software works by detecting a pre-apnea pattern of airflow and pressure in order to make apnea event predictions and subsequently prevent their occurrence. The original apnea definition originated from a study in 1975 where the 10-second rule for scoring respiratory events was based on the average amount of time that would lapse if two regular breaths were skipped with the subject breathing at their usual respiratory rate [32]. However, not all patients meet this criterion but still experience multiple pauses in their breathing every hour of sleep. Even though this may not have substantial effects on their oxygen levels, it might still result in sleep fragmentation and adverse cardiovascular consequences [33], [34]. Therefore, a potential benefit of this software could be in the prevention of sleep-related breathing events that don't last 10 seconds, as it relies solely on the patient's pre-apnea pattern to predict when the patient's airway is going to close, which is more personalized than the standard definition for the requirement of all apneas being at least 10 seconds long.

Much research has been conducted on inspiratory flow limitation, which is characterized by the flattening of the flow-time curve on inhale and is caused by a partial obstruction of the upper airway [35]. This prevents the full amplitude of inspiratory flow which should have been achieved based on the respiratory effort of the patient [35]. Inspiratory flow limitation has been recognized as an important parameter for identifying sleep breathing disorders and current technology can identify flow limitation [35]. However, since our machine learning algorithm takes many different breathing patterns into account, with flow limitation being one of them, it is more comprehensive, which is another advantage of our algorithm.

We believe our system has the potential to lead to the use of lower PAP device pressures for patients, and consequently, increased comfort and therapy adherence. By predicting apneas and hypopneas before they occur, we believe this could allow for the application of lower pressures throughout the night until the system predicts the occurrence of a sleep event, in which pressure will then be increased. Although some studies have concluded that higher CPAP pressure is indicative of higher long-term adherence [36], this likely primarily reflects greater symptom relief in those with more severe OSA, where higher pressures would be necessary and expected for these patients. One study that indicated the relationship between higher pressures and greater adherence analyzed results from a large international CPAP trial, where they only included those with moderate-to-severe OSA, so it could be expected that higher pressures would lead to higher adherence by achieving better apnea relief in these more severe cases of OSA [36]. This likely does not reflect comfort of the device nor less severe cases of OSA. On the contrary, many studies have reported that CPAP nonadherence can be due to pressure intolerance, and one of the main reasons for poor adherence reported by participants in a study by Barratta and colleagues was pressure-related side effects [37]. Therefore, if we can achieve the same symptom relief and reduction in AHI with lower pressures, we suspect this will improve patient adherence.

While this study explored the important topic of improving PAP therapy, and points to new avenues of future research, it is not without limitations. While our results are promising, we only included a sample size of eleven patients. This is primarily due to the difficulty of finding individuals who met the inclusion criteria, including having a high enough AHI on PAP to determine the efficacy of our treatment. Nonetheless, having a larger sample size would have added more value to our results and potentially would have enabled us to see significant results in more of the sleep parameters we measured. Furthermore, most of our patients had a low AHI, due to the difficulty of finding participants with higher AHIs who were willing to participate in this study. Including a subset of patients with higher degree of sleep apnea burden would have also added more value to this study, as we could have tested the ability of our treatment to improve higher AHIs, in addition to improving respiratory events that were already in the low to medium range upon enrolment. Finally, based on our knowledge, we were the first to develop a method to predict and prevent OSA during sleep therapy using existing pressure and flow sensors in conventional PAP machines. Therefore, to keep everything standardized and to limit the influence of any uncontrolled variables on our results, we used a protocol with a long cool down period and hold time, and repeated the same intervention protocol for everyone. However, the long cool down period for every participant meant that our attempts to prevent obstructive apnea were limited to only a specific number of times a night. In future work, we will be focused on developing a more personalized intervention protocol for each individual subject, based on the data collected before their night of therapy, which should result in further reductions of AHI and improved sleep quality. We also used the same model of PAP device for every patient, being the ResMed AirSense$^{\text{TM}}$ 10, to also limit additional uncontrolled variables. Although this may be considered a limitation, every CPAP machine has an air pressure and airflow sensor, and our algorithm is sensitive to breathing patterns that should be the same on every machine, so we expect the performance to be similar on other commercial machines.

6 Conclusion

6.1 Summary

In summary, the presented work provides evidence to the effectiveness of the use of our previously developed AI network in the treatment of OSA. In the present work, we utilized a deep learning software to monitor real-time air pressure and airflow data to predict respiratory events during sleep therapy. The software was used to monitor real-time sleep therapy data provided by the PAP device, generate predictions of upcoming obstructive apneas, and intervene when predicted. The intervention involved directing the PAP device to gently ramp up the pressure to stabilize the patient's airway and treat the apnea before it occurred. Our results showed that our software can significantly decrease AHI, OAI, and minimum SpO_2 during REM sleep.

Our findings are of clinical significance as, based on our knowledge, they were the first to report the success of preventing the occurrence of obstructive apneas during sleep therapy by using existing air pressure and airflow sensors in conventional PAP machines in conjunction with a machine learning algorithm. Therefore, we speculate that the integration of machine learning in next generation PAP machines will help personalize PAP therapy and tailor prescriptions to each patient's individual breathing patterns, resulting in a more effective therapy and superior management of their sleep apnea. This may result in numerous health benefits for patients with sleep apnea. Furthermore, we believe that the prediction of apneic events has the potential to lead to overall PAP pressure reductions throughout the night and the ability of only increasing pressure when an apnea is predicted. Although the ability to reduce pressure was not directly evaluated in this study, this could lead to an improvement in patient care.

6.2 Future Work

The work presented provides a basis for future exploration in many exciting directions. First, further work should be done to develop the AI network used to predict respiratory events in order to increase its practicality. As the current network was trained on 30-50 different subjects, better data set diversity should be achieved by gathering data from as many different subjects as possible. This would allow better generalization and better performance on new subjects.

Further, networks which are trained to be focused on a specific person's data may result in better accuracy for that individual. This would give a personalized therapy option to PAP device users. Considering the future deployment of the network and intervention method in available PAP devices, the network could be set up to learn continuously on a person's nightly sleep, thus improving performance over time.

Although the current algorithm was focused on prediction and prevention of obstructive apneas only, prediction of other types of events such as flow limitation and snoring should also be explored in future work, as these events could possibly also benefit from pressure intervention. The impact of pressure increase intervention on a predicted hypopnea should be investigated as well as the effect of a pressure decrease intervention on a central apnea. Additionally, a model could be developed to classify both the current breathing state as well as the future breathing state. This could lead to more intelligent decision making on the intervention protocol and prevent interventions at inopportune times. As this work relied on the APAP mode of the PAP device when not intervening, in the future a nowcasting algorithm could also inform decisions for all pressure adjustments throughout the night. Overall, future work should include the development of a complete pressure control system based on a predictive AI network.

Additionally, as the goal of the current work is to provide a better algorithm for PAP devices, next steps should include the development of an embedded solution. This could be implemented with the network and cMAP control logic on-board a PAP device.

More trials should be performed with the cMAP protocol and more data collected on the impact of the interventions on sleep and apnea occurrence. A long term study where a subject would use the device at home for a period of time would provide better information on the impact on AHI, as AHI varies night to night. Different parameters for the pressure intervention could be further tested to determine the ideal settings and how they may vary based on a person's characteristics. The threshold of parameters which can prevent an apnea effectively while not disturbing the user would be beneficial to determine. The ideal intervention parameters including ramp up rate, pressure increase, hold time, and ramp down time should be investigated via extensive testing.

Finally, as a predictive algorithm can allow pressure intervention only when necessary, it should be tested whether lowering the overall pressure of therapy is possible. With a reduced baseline pressure and pressure increases only for the periods where it is required, this could be achieved. Lower overall pressure would make therapy more comfortable to users and likely improve adherence, reducing a major roadblock in PAP therapy and improving the treatment outcomes for many patients. Further, if lower pressure therapy was feasible, PAP devices could be developed to be smaller and possibly battery powered, as the size and power demand of the pressure blower would be lower. This could lead to devices which are more portable, discrete, quiet, and possibly wearable. This could eliminate the need for the patient to be tethered to their bedside via tubing and further increase comfort and adherence, and reduce the overall negative image of PAP therapy.

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