Algorithm for automatic detection of self-similarity and prediction of residual central respiratory events during CPAP

Eline Oppersma¹, Wolfgang Ganglberger², Haoqi Sun², Robert J. Thomas³*, M. Brandon Westover²*

¹ Cardiovascular and Respiratory Physiology group, TechMed Centre, University of Twente, the Netherlands.
² Department of Neurology, Massachusetts General Hospital, Boston, MA, USA.
³ Division of Pulmonary, Critical care & Sleep Medicine, Department of Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA.

* Co-senior authors.

Corresponding author: E. Oppersma, CRPH group, University of Twente, Postal box 217, 7500 AE Enschede, the Netherlands, email: e.oppersma@utwente.nl
Abstract

Study objectives: Sleep disordered breathing is a significant risk factor for cardiometabolic and neurodegenerative diseases. High loop gain is a driving mechanism of central sleep apnea or periodic breathing. This study presents a computational approach that identifies “expressed/manifest” high loop gain via a cyclical self-similarity feature in effort-based respiration signals.

Methods: Working under the assumption that high loop gain increases the risk of residual central respiratory events during continuous positive airway pressure (CPAP), the full night similarity, computed during diagnostic non-CPAP polysomnography (PSG), was used to predict residual central events during CPAP (REC), which we defined as central apnea index (CAI)>10. Central apnea labels are obtained both from manual scoring by sleep technologists, and from an automated algorithm developed for this study. The Massachusetts General Hospital (MGH) sleep database was used, including 2466 PSG pairs of diagnostic and CPAP titration PSG recordings.

Results: Diagnostic CAI based on technologist labels predicted REC with an AUC of 0.82 ±0.03. Based on automatically generated labels, the combination of full night similarity and automatically generated CAI resulted in an AUC of 0.85 ±0.02. A subanalysis was performed on a population with technologist labeled diagnostic CAI>5. Full night similarity predicted REC with an AUC of 0.57 ±0.07 for manual and 0.65 ±0.06 for automated labels.

Conclusions: The proposed self-similarity feature, as a surrogate estimate of expressed respiratory high loop gain and computed from easily accessible effort signals, can detect periodic breathing regardless of admixed obstructive features such as flow-limitation, and can aid prediction of REC.

Keywords: Automatic detection, similarity, CPAP
Statement of significance:

This study shows that the proposed self-similarity feature, as a surrogate estimate for respiratory high loop gain and computed from easily accessible effort signals, can detect periodic breathing regardless of admixed obstructive features such as flow-limitation, and can aid prediction of residual central respiratory events during CPAP.
Introduction

The prevalence of sleep disordered breathing (SDB) among adults in the United States has increased substantially in recent years, in tandem with the prevalence of obesity. Among adults aged 30-70 years, approximately 13% of men and 6% of women have moderate to severe sleep disordered breathing (more than 15 obstructive events per hour of sleep)\(^1\). These sleep disorders are significant risk factors for cardiometabolic and neurodegenerative diseases, impaired performance, and decreased quality of life\(^2-5\). However, tolerance and efficacy of continuous positive airway pressure (CPAP), the primary form of therapy for moderate or greater severities of sleep apnea, is often poor. Among several reasons for CPAP intolerance, one area which stands to benefit from computational analysis is precision phenotyping of sleep-breathing patterns.

There is increasing awareness, supported by physiological phenotyping, that different endotypes can give rise to the same clinical apnea-hypopnea index (AHI).\(^6\) A key endotype-phenotype is high loop gain sleep apnea.\(^7-10\) This endotype can remain relatively silent (latent) until provoked by experimental methods or physiological challenges, such as arousals, overventilation with therapy targeting upper airway obstruction, or supine body positioning. The disorder may manifest as classic idiopathic central sleep apnea, periodic breathing, non-rapid eye movement dominant apnea, and treatment-emergent central sleep apnea (acute transient, emergent or persistent). Current definitions for central apnea and hypopnea are based on PSG data and are scored according to the American Academy of Sleep Medicine (AASM) scoring manual\(^11\). A central sleep apnea syndrome is defined when five or more central apneas and/or central hypopneas are present per hour of sleep with a central apnea-hypopnea index (CAHI) comprising more than 50% of all respiratory events.\(^12\)

The clinical implications of central sleep apnea with Hunter-Cheyne-Stokes respiration (HCSR) have been debated.\(^13,14\) Nevertheless, the features of classic HCSR are relatively non-controversial, with symmetric, self-similar, prolonged (over 60 seconds) waxing and waning patterns, free of obstructive features (snoring, flow-limitation), recognized as the key characteristic. Self-
similar breathing oscillations are the norm in idiopathic central sleep apnea, \(^{15,16}\) periodic breathing with shorter cycle lengths in the absence of cardiac dysfunction, \(^{17}\) high altitude periodic breathing and central sleep apnea, \(^{18}\) and high loop gain (HLG)/NREM-dominant obstructive sleep apnea.\(^{19}\) Moreover, obstructive pathophysiology can coexist in central apnea and at high altitude, thus making manual phenotyping laborious and inaccurate, especially for central hypopneas. In fact, central hypopneas are usually not scored\(^{11}\).

Currently, the gold standard for assessing loop gain requires administration of hypoxic or hypercapnic gas during a polysomnography (PSG) measurement\(^ {20}\). An alternative mathematical method has been proposed from routine polysomnography\(^{21}\); however, this model requires EEG information and does not make use of the cardinal feature of HCSR breathing, namely self-similarity.

The current study aimed to develop a computational approach to detect HLG based on self-similarity in respiratory oscillations during sleep solely using breathing patterns, as measured via Respiratory Inductance Plethysmography (RIP). RIP measures expansion of the thorax and abdomen using two sinusoid wire coils. A system based on RIP tracings could be useful for automated phenotyping during routine PSG recordings, and complementary to any manual approach to phenotyping. We developed a simple algorithm for detecting apneas as periods with reduced breathing effort, manifested in the RIP signal as low signal amplitude. Subsequently, our algorithm calculates self-similarity in breathing patterns between consecutive periods of apnea or hypopnea. The degree of self-similarity present over the entire night is summarized as the percentage of total sleep time during which high similarity was present. To quantify the potential clinical utility of this “full night similarity” metric, we developed an algorithm to predict, based on the diagnostic PSG, substantial (CAI >10) residual central respiratory events during the subsequent CPAP (REC) titration PSG.
Methods

Dataset

The dataset used in this study is from the Massachusetts General Hospital (MGH) sleep laboratory. The MGH Institutional Review Board approved retrospective analysis of clinically acquired PSG data without requiring additional consent. The dataset consists of in-lab PSG recordings which include electroencephalogram (EEG), respiratory signals (RIP) and electromyogram signals (EMG) and was scored as part of routine clinical practice by certified sleep technologists using the American Academy of Sleep Medicine (AASM) guidelines. Each PSG is scored by one technologist. There are seven technologists in total. The dataset consists of a mixture of diagnostic, split night, and CPAP titration protocols.

Data selection

A pair of diagnostic and CPAP PSG was only included in the study set when events were labeled and sleep was staged by the sleep technologists, and when both baseline and CPAP period was available. In cases with split night PSG, sleep time before and after the split was required and cases with multiple splits within one night were excluded. Full night diagnostic PSGs were included when there was a CPAP titration PSG available for the same patient within 2 years following the initial diagnostic PSG.

Data analysis

Data were analyzed using the MATLAB R2019a programming environment (The Mathworks, Natick, MA). Based on annotations from the PSG technologists, CAI and AHI in the diagnostic PSGs (both split night and full night) were calculated, as well as in the CPAP titration part of the PSG (split night and full night).

Scoring apneas and hypopneas

We used two complementary methods to label apnea and hypopnea events and to compute their total burden, measured by the central apnea index (CAI). The first method was standard manual/visual scoring by sleep technologists. Because inspection of the manually labeled data raised
concerns about possible “label noise” (inaccuracies in routine clinical annotations of apnea and hypopnea events), we also used an automated method to label events, and compared the results with those based on visual event scoring. Both methods are described below.

Manual/visual event scoring

Standard AASM scoring rules were followed by the sleep technologists. Apneas were scored when flow was ≤ 10% of baseline regardless of oxygen desaturation, and hypopneas when flow was ≤ 70% of baseline (a 30% reduction) with a 3% oxygen desaturation or an arousal. Central apneas were scored when effort and flow were ≤ 10% of baseline regardless of oxygen desaturation.

Although the AASM scoring rules state that central hypopneas are defined as a concordant reduction of flow and effort by at least 30% in the absence of snoring and flow-limitation, these were not manually scored in the current dataset.

Automated labeling of central apneas and hypopneas

For automatic labeling, the envelope of the abdominal RIP band tracing (Figure 1A) was calculated automatically using the Matlab function ‘envelope’ (Figure 1B, for code see GitHub link at bottom of the paper). The envelope function returns the upper and lower envelopes of the signal, as the magnitude of its analytic signal (using its discrete Fourier transform). The difference between the upper and lower envelope was used to detect central events. When the difference between the upper and lower envelope fell to 20% or lower of the upper 90th percentile of amplitudes from the preceding 3 minutes, a central apnea was detected. A central hypopnea or hypoventilation event was defined as a period with RIP signal amplitude below 70% of the upper 90th percentile from the preceding 3 minutes. Subsequently, the same analysis was done for the RIP chest band. Only events detected in both chest and abdominal RIP signals were included for further analysis. According to AASM guidelines, a central apnea or hypopnea is defined only when an event lasts at least 10
seconds. As the envelope causes some signal smoothing, the algorithm used a minimum of 9 seconds to define central events.

**Definition of residual central respiratory events during CPAP (REC)**

Residual central respiratory events during CPAP (REC) were defined as substantial in case of a CAI during CPAP titration higher than 10/hour of sleep. CPAP success was defined as a CAI during CPAP titration lower than 5/hour of sleep. REC were analyzed in two ways, based on technologist labels and on our automatically generated labels as the basis for calculating CAI.

**Automated computation of self-similarity**

Within 2 minutes before and after the detected central events, similarity was calculated using the following procedure: Peaks in the envelope signal were detected, and 2 sequential envelope clusters containing a peak were cross-correlated with each other (Figure 1C). The maximum of these correlation values, between 0 and 1, indicates the similarity between successive clusters of waxing and waning breathing cycles. We then defined the ‘full night similarity’ as the ratio of time with high similarity (>0.8) events to total sleep time, i.e. the percentage of sleep time in which high similarity was present.

We defined detected hypopneas as “central” only when similarity during the hypopnea event was >0.8. From these automatically detected central events, CAI and CAHI (CAI including central hypopneas) were computed.

**REC prediction**

Logistic regression with 5-fold cross validation was used to create a model to predict REC vs. no REC. Means and standard deviations of the area under the receiver operating characteristic curve, and likelihood ratios (cut-off value defined as highest Youden index) for the 5 folds and were used to measure model performance.
Input features were the full night similarity and either the technologist-labeled CAI or the automatically generated CAI from the diagnostic night (split or full night), and the automatically generated CAHI.

**Analysis of data enriched with central events**

A sub analysis was performed on patients with a CAI higher than 5/hour of sleep labeled by the technologists in the diagnostic study. These patients were considered to be a subpopulation with possible more prominent high loop gain presentations in their respiratory tracings. The same prediction steps were performed as described above.

**Results**

The dataset included 8284 PSGs, of which 2466 pairs of diagnostic and CPAP PSGs met our inclusion criteria and were included in the training set. The pairs of diagnostic and CPAP PSG consisted of split night PSGs and full night diagnostic PSGs paired with CPAP titration PSGs, recorded from 2008 to 2016. Dataset characteristics and results of the automatically detected labels are provided in Table 1.

Figure 2 shows 15-minute tracings from 4 different patients with the corresponding similarity values for these tracings. The percentage shows how much of this 15-minute tracing similarity is higher than 0.8. These fragments show how similarity varies between patients.

**REC prediction**

Based on technologist labels, 13% (n = 313) of patients had REC (CAI>10/hour of sleep), 75% (n=1850) of patients had no REC (CAI<5/hour of sleep), and 12% (n=303) were excluded from the prediction analysis because of indeterminate outcomes (CAI between 5 and 10/hour of sleep).

Based on automatically generated labels, 10% (n=244) of patients had REC, 81% (n=2018) had no REC and 10% (n=244) were excluded from the prediction analysis because of indeterminate outcomes (CAI between 5 and 10/hour of sleep).
The left graph in Figure 3 shows the AUC values resulting from REC prediction in mean ± standard deviation of the 5fold cross validation prediction. Our proposed full night similarity as input for a logistic regression model resulted in a (mean ±SD) AUC-value of 0.70 ±0.02 to predict REC based on technologist labels. In case of automatically generated labels to calculate CAI, full night similarity resulted in an AUC of 0.78 ±0.02. The most accurate prediction of REC based on technologist labels resulted from the diagnostic CAI based on technologist labels (AUC=0.82 ±0.03). However, based on automatically generated labels, the combination of the full night similarity and the automatically generated CAI resulted in an AUC for prediction of REC of 0.85 ±0.02.

To find a clinical threshold to predict REC, the positive predictive value (PPV) was plotted for both input variables in Figure 4. The red dot shows a PPV of 30%, implying that when similarity is ≥17% or auto CAI ≥ 3 events per hour of sleep, the probability of REC was 30%.

Figure 5 shows the positive and negative likelihood ratios resulting from the REC prediction in mean ± standard deviation of the 5-fold cross validation prediction.

The highest positive likelihood ratio to predict REC based on technologist labels was 3.44 ±1.20 with the technologist labeled CAI as input. The highest positive likelihood ratio to predict REC based on automatically generated labels was 4.06 ±1.16 also with the technologist labeled CAI as input.

The best (smallest) negative likelihood ratio to predict REC based on technologist labels was 0.28 ±0.03 with the automatically generated CAHI and full night similarity as input. The best (smallest) negative likelihood ratio to predict REC based on automatically generated labels was 0.16 ±0.04 with the automatically generated CAI and full night similarity as input.
Subanalysis

Based on technologist labels, a subpopulation was defined consisting of 515 patients with CAI higher than 5/hour of sleep in the diagnostic PSG. Dataset characteristics are shown in Table 2.

Based on technologist labels, 35% (n=182) of patients had REC (CAI>10/hour of sleep), 42% (n=220) of patients had no REC (CAI<5/hour of sleep), and 22% (n=113) of patients had indeterminate results (CAI during CPAP between 5 and 10/hour of sleep).

Based on automatically generated labels, 29% (n=150) of patients had REC, 55% (n=285) of patients had no REC, and 10% (n=80) of patients had indeterminate outcomes (CAI during CPAP between 5 and 10/hour of sleep).

The right graph in Figure 3 shows the AUC values resulting from the REC prediction in mean ± standard deviation of the 5-fold cross validation prediction. In this subpopulation, our proposed full night similarity as input for a logistic regression model resulted in an AUC-value of 0.57 ± 0.07 to predict REC based on technologist labels, near chance performance. However, using automatically generated labels to calculate CAI, the full night similarity resulted in an AUC of 0.65 ± 0.06, moderately better than chance. Similar performance was obtained based on the CAI from technologist labels (AUC 0.67 ± 0.05). CAI based on automatically predicted labels resulted in an AUC to predict REC (based on automatically generated labels) of 0.75 ± 0.05.

Figure 6 shows the positive and negative likelihood ratios resulting from the REC prediction in mean ± standard deviation of the 5-fold cross validation for the subpopulation.

The highest positive likelihood ratio to predict REC based on technologist labels was 3.13 ± 3.73 with the full night similarity and the automatically generated CAI as input. The highest positive likelihood ratio to predict REC based on automatically generated labels was 3.55 ± 2.55 also with the full night similarity and the automatically generated CAI as input.
The best (smallest) negative likelihood ratio to predict REC based on technologist labels was $0.45 \pm 0.07$ with the automatically generated CAHI and full night similarity as input. The best (smallest) negative likelihood ratio to predict REC based on automatically generated labels was $0.32 \pm 0.05$ with the full night similarity as input.

**Discussion**

The current study provides a measure for cyclical self-similarity of breathing patterns during sleep. Our study makes two main contributions. First, our results show that breathing pattern self-similarity as an indicator of manifest (expressed) high loop gain predicts REC. Second, central apnea labels were derived in an automated way and we showed that short-term REC (acute treatment-emergent central sleep apnea) is predicted at least as well based on labels generated by automated analysis as by manual scoring. Our results show that computational estimation of central apneas, hypopneas and self-similarity is feasible and may have clinical value to complement other methods of disease phenotyping. Though we used a laboratory polysomnographic dataset, our method should work as well on home-study data and in other conditions where breathing pattern estimation may be informative.

Although automatically generated CAI and full night similarity were highly correlated (Pearson Rho = 69%), we believe that similarity provides additional useful information not captured by CAI alone, as it reflects more directly high loop gain. We showed that either a high auto CAI or a high full night similarity means that the risk of REC is high. Choosing a probability of REC $>30\%$ as a clinically meaningful trigger warranting further investigation, we find that this condition is met when either full night similarity is $\geq 17\%$ or auto CAI $\geq 3$ events per hour of sleep, as shown in figure 4. It should be noted in figure 4 that PPV appears to worsen as similarity increases; however, this is likely due to limitations of data. Sufficient data was not available to calculate statistically reliable estimates of PPV above full night similarity values of $\sim 25\%$ (396 of 2466 PSGs).
Automation of event scoring

The most important advantage of automated event scoring in polysomnography is the saving of time, compared to manual labeling. It is already shown that integrated analysis of polysomnography (PSG) features can improve identification of central hypopneas. Predominance during non-rapid eye movement (NREM) rather than rapid eye movement (REM) sleep, lack of inspiratory airflow curve flattening or thoracoabdominal paradoxical breathing (chest wall moving inward with inspiration) during hypopnea, arousals in the middle of the recovery breath sequence, and gradual flow restoration pattern at hypopnea termination can help classify hypopneas as central. Automation of hypopnea phenotyping (obstructive vs. central) is possible, but accuracy in comparison to electromyography is limited (69%). “Mixed” events are more problematic, as how much “mixture” of obstructive and central components is required to differentiate from obstructive and central events suffers from visual bias and inaccuracies. Moreover, insurance coverage of treatments do not consider mixed events as equivalent to high loop gain.

Phenotyping of sleep disorders could be done more quickly, more objectively, and in a technologist-independent manner using computational methods. Automated detection of apneas and hypopneas may be especially useful in situations where central events are frequent but obstructive features may coexist, for example in heart failure, atrial fibrillation and stroke. The presented automated labelling method is agnostic to the presence of flow-limitation, mild degrees of which are frequently seen in central hypopneas. Lastly, our method is relatively insensitive to cycle length. AASM scoring rules state a minimum central hypopnea/periodic breathing cycle time of 40 seconds, but this is not likely a biologically valid cut-off; short (< 30 seconds) cycle respiratory events are seen at high altitude and in non-REM dominant and high loop gain OSA, and in idiopathic central sleep apnea.

A more detailed example of correlation between the automated and tech scored central apneas and hypopneas is provided in the supplemental material.
**Therapeutic implications of autoscorer central events**

The diagnosis of central apnea syndromes has used arbitrary thresholds, such as ≥5/hour of sleep and ≥ 50% of events scored as central. In addition, manual scoring of central hypopneas is difficult and imprecise, considered “optional”, and consequently is rarely performed. Current diagnostic criteria can pose a challenge to investigators and clinicians because reliably differentiating hypopneas as central versus obstructive is difficult. Evidence of upper airway obstruction on polysomnography, including flow-limitation, does not rule out central apneas/hypopneas, and esophageal manometry is rarely used in practice. Unclassified hypopneas are thus summed into the overall AHI, biasing metrics towards obstructive sleep apnea.

This practice of lumping all hypopneas as obstructive has translated to scoring central apneas alone, underestimating the component of central events when hypopneas are significant. Thus, a CAHI/CAI of 4.9/hour of sleep and 49% central events is considered obstructive. There are real clinical implications of such arbitrariness, including insurance coverage of therapies such as oxygen and adaptive ventilation. Such thresholds also confound research studies and interpretation. Decision making about the expressed phenotype is especially relevant to heart failure, where adaptive ventilation is contraindicated in those with systolic heart failure (ejection fraction ≤ 45%) and central sleep apnea. Therapy may be withheld when indicated, or the inappropriate therapy chosen, based on central event count errors.

Accurately classifying SDB as predominantly central or obstructive has implications for treatment, as targeting high loop gain is possible with body positioning, low dose acetazolamide, adaptive ventilation, oxygen, and sedatives. Moreover, although providing continuous positive airway pressure (CPAP) might resolve obstructive apneas, it can induce complex sleep apnea (CompSA): a condition defined by the emergence of problematic central sleep apnea and Hunter-Cheyne-Stokes respiration (HCSR) in the absence of obstructive events. Patients who develop CompSA have a higher prevalence of coronary artery disease, a higher diagnostic central apnea index (CAI, central apneas per hour of sleep) and more pre-existing periodic breathing.
Limitations of the presented automated labeling method

The presented method for automated labelling of central apneas is based on two major assumptions. First, high loop gain is a driver of central apneas. Second, high loop gain results in cyclical self-similar behavior of breathing patterns. However, we did not calculate or estimate high loop gain directly in our patients. Instead, we used the presence of high similarity as a surrogate for high loop gain. While this assumption is reasonable, and our method is thus likely to detect high loop gain effects on sleep-breathing, we do not provide a direct loop gain estimate. Although the AASM provides rules to score central hypopnea, the database in our study did not provide labels for central hypopneas, as these were usually not scored by the sleep technologists. This is mainly because scoring of central hypopneas is difficult, considered “optional”, and some of the components of the rules have been shown to be unsupported by research. In general, central hypopneas are not scored by clinical sleep services or are scored only when there is overt periodic breathing or Hunter-Cheyne-Stokes respiration. For these reasons we could not compare manual/visual and the proposed automated detection of central hypopneas.

It should be noted that our data is cross-sectional, so the long-term impact of self-similarity and central event detection cannot be estimated from the present data. Features of respiratory control instability may decrease, persist or emerge during long-term treatment with CPAP in apnea patients, dependent on an interaction of genetic and acquired factors, such as degree of hypoxia, associated disorders such as heart failure or atrial fibrillation, and gender. However, a high central apnea index does predict high residual AHI on CPAP, and a high degree of self-similarity could help risk-stratify patients. Lastly, we did not have enough patients on opiates to estimate accuracy in detection of opiate-induced CSA, though inter-breath variability would be expected to decrease self-similarity. A subanalysis of 496 patients with high CAHI (>10) and low similarity (<20%) the algorithm predicted 70% of patient not to have REC versus 16% with REC. Another subgroup of 10 patient with high CAHI and high similarity (>70%), the algorithm predicted that 0% of the patient would have REC.
and 40% would have not. Although these are not enough patients to base firm conclusions on, it is speculative but possible that CSA detection without self-similarity may suggest ataxic breathing, as can be seen with opiates and high spinal/brain stem disorders.

**Conclusion**

This study presents an algorithm to automatically label central apneas and central hypopneas, based on envelope features in respiratory tracings. Our proposed full night similarity measure was able to predict REC based on automatically generated labels at least as well as manually scored labels by sleep technologists.
**Financial disclosure**

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**Non-financial disclosure**

Dr. Thomas declares the following “conflicts” 1) Patent and license for the ECG-spectrogram to MyCardio, LLC, through the Beth Israel Deaconess Medical Center; 2) patent and license to DeVilbiss-Drive for an auto-CPAP algorithm; 3) consultant to Jazz Pharmaceuticals, Guidepoint Global and GLC Councils; 4) Unlicensed patent for a device to regulate carbon dioxide in the positive airway pressure circuit. Dr. Westover is a co-founder of Beacon Biosignals, Inc. Other authors report no conflicts of interest. None of the entities listed played any role in the present study.

**Preprint repositories**

This manuscript is not preprinted or published prior to submitting to *Sleep*.

**Code Availability**

Code for the algorithm is open source with no restrictions and is available from https://github.com/mghcdac/self_similarity
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Figure captions

Figure 1 A: Line of 5-minute respiratory tracing (abdominal RIP band). B: Upper and lower envelope. C: peaks detected (*) and convolution applied

Figure 2 Examples of 15-minute respiratory tracings from 4 different patients, similarity values indicate the percentage during which similarity values were higher than 0.8 for these fragments

Figure 3 Area under the curve as outcome of logistic regression to predict REC for the whole population (left) and the sub population (right) as mean and standard deviation of 5-fold cross validation

Figure 4 Positive predictive values for full night similarity and auto CAI to find a clinical threshold to predict high probability of CPAP failure, based on automatically generated labels.

Figure 5 Negative likelihood ratio (left) and positive likelihood ratio (right) as model performance measure to predict REC

Figure 6 Negative likelihood ratio (left) and positive likelihood ratio (right) as model performance measure to predict REC for the subpopulation
**Table 1. Dataset characteristics (mean ± SD)**

| Characteristic                                      | Value          |
|-----------------------------------------------------|----------------|
| Sex (Male/Female)                                   | 1683/783       |
| Age (years)                                         | 55 ±14         |
| BMI                                                 | 34.0 ±7.6      |
| Type of diagnostic PSG (n, Split night/full night)  | 1923/543       |

| CAI technologist labels                             |                |
|-----------------------------------------------------|----------------|
| **Diagnostic**                                      | 4.5 ±9.8       |
| **CPAP titration**                                  | 4.7 ±9.1       |

| AHI technologist labels                             |                |
|-----------------------------------------------------|----------------|
| **Diagnostic**                                      | 42.3 ±30.2     |
| **CPAP titration**                                  | 12.9 ±15.1     |

| CAI auto labels                                     |                |
|-----------------------------------------------------|----------------|
| **Diagnostic**                                      | 4.8 ±8.7       |
| **CPAP titration**                                  | 3.6 ±8.0       |

| CAHI auto labels                                     |                |
|------------------------------------------------------|----------------|
| **Diagnostic**                                       | 13.2 ±15.9     |
| **CPAP titration**                                   | 6.6 ±12.1      |

**Legend:** CAI, Central Apnea Index. AHI, Apnea Hypopnea Index. CAHI, Central Apnea Hypopnea Index. CAHI was calculated only via the automated method, because technologist-scored central hypopneas were not available. AHI is calculated only based on technologist labels.
Table 2. Dataset characteristics of subpopulation, technologist labeled diagnostic CAI>5 (mean ± SD)

|                         |                          |                  |
|-------------------------|--------------------------|-----------------|
| Sex (Male/Female)       |                          | 433/82          |
| Age (years)             |                          | 57 ±14          |
| BMI                     |                          | 33.9 ±7.7       |
| Type of diagnostic PSG (n, Split night/full night) | | 452/63 |
| CAI technologist labels | [ ] Diagnostic           | 17.8 ±15.2      |
|                         | [ ] CPAP titration       | 12.0 ±15.4      |
| AHI technologist labels | [ ] Diagnostic           | 61.3 ±28.7      |
|                         | [ ] CPAP titration       | 21.4 ±20.3      |
| CAI auto labels         | [ ] Diagnostic           | 12.2 ±13.1      |
|                         | [ ] CPAP titration       | 8.7 ±12.3       |
| CAHI auto labels        | [ ] Diagnostic           | 26.1 ±19.6      |
|                         | [ ] CPAP titration       | 15.1 ±17.6      |

Legend: CAI, Central Apnea Index. AHI, Apnea Hypopnea Index. CAHI, Central Apnea Hypopnea Index. CAHI was calculated only via the automated method, because technologist-scored central hypopneas were not available. AHI is calculated only based on technologist labels.
The graph shows the relationship between the positive predictive value and the threshold for full night similarity and auto CAI. The positive predictive value increases as the threshold increases. The red circles indicate specific thresholds where the positive predictive value is significantly higher.
