"PREVALENCE OF RAPID EYE MOVEMENT SLEEP RELATED OBSTRUCTIVE SLEEP APNEA (REM RELATED OSA) IN PATIENTS WITH SLEEP DISORDERED BREATHING- A CROSS SECTIONAL STUDY"

By

REG NO.: BR0122002

Dissertation

Submitted to the

KLE University Belagavi, Karnataka

In partial fulfillment

Of the requirements for the degree of

DOCTOR OF MEDICINE (M.D)

In

RESPIRATORY MEDICINE

J. N. MEDICAL COLLEGE, NEHRU NAGAR

BELAGAVI-590010

SEPTEMBER/OCTOBER- 2025

KLE UNIVERSITY, BELAGAVI,

KARNATAKA

Endorsement By The Head of the Department, Principal/Head Of the Institution

This is to certify that the dissertation entitled **"PREVALENCE OF RAPID EYE MOVEMENT SLEEP RELATED OBSTRUCTIVE SLEEP APNEA (REM RELATED OSA) IN PATIENTS WITH SLEEP DISORDERED BREATHING - A CROSS SECTIONAL STUDY"** is a bonafide research work done by **REG NO.: BR0122002** in the Department of Respiratory Medicine, J. N. Medical College, Belagavi.

DR BHAGYASHRI PATIL MD,
Professor and Head,
Department of Respiratory Medicine,
J.N. Medical College,
Nehru Nagar, Belagavi- 590010

Date:
Place: Belagavi

Dr. N. S. MAHANTASHETTI MD
Principal,
J.N. Medical College,
Nehru Nagar,
Belagavi- 590010

PRINCIPAL
Jawaharlal Nehru Medical College
BELAGAVI

Date:
Place: Belagavi

KLE ACADEMY OF HIGHER EDUCATION AND RESEARCH

JAWAHARLAL NEHRU MEDICAL COLLEGE

(A constituent unit of KLE Academy of Higher Education & Research Deemed-to-be-University)

(Recognized by National Medical Commission, New Delhi)

Accredited 'A+' Grade by NAAC (3rd Cycle) **Placed in Category 'A' by MoE (GoI)**

Nehru Nagar, Belagavi- 590 010, Karnataka, INDIA

0831 - 2471350 0831 - 2470759 www.jnmc.edu principal@jnmc.edu

Ref No: MDC/PG/ Date: 11-04-2025

"ACCEPTANCE LETTER"

The softcopy of thesis entitled: **"PREVALENCE OF RAPID EYE MOVEMENT SLEEP RELATED OBSTRUCTIVE SLEEP APNEA (REM REALTED OSA) IN PATIENTS WITH SLEEP DISORDERED BREATHING A CROSS SECTIONAL STUDY"** has been submitted for anti-plagiarism check through Turnitin software. The scan has been carried out and the scanned output reveals a match percentage of 02% which is within the acceptable limits of 10% as per the guidelines given by UGC.

Guide.

KAHER BELAGAVI J.N. MEDICAL COLLEGE

Dr. (Mrs.) N.S. Mahantashetti.
Chairperson-Antiplagiarism Committee &
Principal,
J. N. Medical College, Belagavi.

To,
Reg. No. BR0122002
Postgraduate Student,
2022-23 Batch,
Department of Respiratory Medicine
J. N. Medical College, Belagavi.

K.L.E. ACADEMY OF HIGHER EDUCATION AND RESEARCH
(Deemed – to- be- University)
Accredited 'A+' Grade by NAAC in (3rd Cycle) Placed in Category 'A' by MHRD (GoI)

JNMC INSTITUTIONAL ETHICS COMMITTEE
JAWAHARLAL NEHRU MEDICAL COLLEGE,
NEHRU NAGAR, BELAGAVI-590010 (KARNATAKA-INDIA)

Website: http//www.jnmc.edu
E-Mail : dome@jnmc.edu
Phone: (+ 91-(0)831 Office : 2472550
Principal: 2471701
Fax No. +91 (0)831 – 2470759

Ref No.MDC/JNMCIEC/ 132 **Date: 30/03/2023**

To,
REG NO.: BR0122002
PG Student in Respiratory Medicine
J. N. Medical College,
BELAGAVI.

Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled **"PREVALENCE OF RAPID EYE MOVEMENT SLEEP RELATED OBSTRUCTIVE SLEEP APNOEA (REM RELATED OSA) IN PATIENTS WITH SLEEP DISORDERED BREATHING – A CROSS SECTIONAL STUDY"**, is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee.

(Dr. Smita Sonoli)
Member Secretary
JNMC Institutional Ethics Committee
J.N.Medical College, Belagavi.

(Dr. Harsha Hegde)
Chairman,
JNMC Institutional Ethics Committee
J.N.Medical College, Belagav

LIST OF ABBREVIATIONS

S.No	Abbreviation	Full Form
1	SDB	Sleep disordered breathing
2	OSA	Obstructive Sleep Apnea
3	PAP	Positive Airway Pressure
4	AASM	American Academy of Sleep Medicine
5	SRS	Sleep Research Society
6	NREM	Non Rapid Eye Movements
7	REM	Rapid Eye Movements
8	EEG	Electroencephalography
9	EMG	Electromyography
10	EOG	Electrooculography
11	RERA	Respiratory Effort Related Arousal
11	RDI	Respiratory Disturbance Index
12	AHI	Apnea Hypopnea Index
12	ODI	Oxygen Desaturation Index
13	ICSD	International Classification of Sleep Disorders
14	CSA	Central Sleep Apnea
15	SRBD	Sleep Related Breathing Disorders
16	OHS	Obesity Hypoventilation Syndrome
17	$PaCO_2$	Partial Pressure of Carbon dioxide in arterial blood
18	BMI	Body Mass Index
19	Pcrit,	Pharyngeal Critical Closing Pressure
20	ESS	Epworth Sleepiness Scale

21	PSG	Polysomnography
22	HSAT	Home Sleep Apnea Testing
23	CPAP	Continuous Positive Airway Pressure
24	APAP	Auto-adjusting Positive Airway Pressure
25	AVAPS	Average Volume Assured Pressure Support
26	MAD	Mandibular Advancement Devices
27	nEPAP	Nasal Expiratory Positive Airway Pressure
28	UA	Upper Airway
29	FDA	Food and Drug Administration
30	PDE5	Phosphodiesterase type 5
31	UPPP	Uvulopalatopharyngoplasty
32	GA	Genioglossus advancement
33	ERS	European Respiratory Society
34	HFpEF	Heart Failure with Preserved Ejection Fraction
35	HFrEF	Heart Failure with Reduced Ejection Fraction
36	ACC	American College of Cardiology
37	ECG	Electrocardiography
38	HTN	Hypertension
39	T2DM	Type 2 Diabetes Mellitus
41	NAFLD	Non Alcoholic Fatty Liver disease
42	PaO_2	Partial pressure of Oxygen in arterial blood
43	SpO_2	Saturation of peripheral Oxygen
44	IPAP	Inspiratory Positive airway Pressure
45	EPAP	Expiratory Positive Airway Pressure

46	IPAP	Inspiratory Positive Airway Pressure
47	BDI	Becks depression Inventory
48	CRP	C-reactive protein
49	IL-6	interleukin-6
50	EDS	Excessive Daytime Sleepiness
51	BDI	Beck’s depression Inventory
52	AF	Atrial Fibrillation
53	GABA	Gamma amino Butyric Acid

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

ABSTRACT

Background:

Rapid Eye Movement-related Obstructive Sleep Apnea (REM OSA) represents a distinct subtype of sleep-disordered breathing (SDB), often characterized by increased symptom burden and a unique clinical profile. While the global recognition of REM OSA is expanding, its prevalence, demographic correlations, and clinical manifestations remain understudied in Indian populations. Identifying reliable clinical predictors and validating the utility of commonly used screening tools is essential for early diagnosis and optimized management.

Objectives:

The primary objective of the study was to determine the prevalence of REM OSA among patients with sleep-disordered breathing, as per both strict and broad diagnostic criteria. The secondary Objective of the study is to assess the correlation of Epworth Sleepiness Scale (ESS), Beck Depression Inventory (BDI), Berlin Questionnaire, and STOP-BANG score with overall AHI and the diagnosis of REM OSA.

Materials and Methods:

A cross-sectional study was conducted over a one-year period at KLE's Dr. Prabhakar Kore Hospital, Belagavi. One hundred adult patients diagnosed with SDB via overnight attended polysomnography were included. REM OSA was classified using strict and broad American Academy of Sleep Medicine (AASM)-based definitions. Demographic variables, clinical symptoms, comorbidities, and polysomnographic indices were recorded. Screening tools (ESS, BDI, STOP-BANG, Berlin

Questionnaire) were administered and their correlations with apnea-hypopnea index (AHI) and REM OSA were analyzed using appropriate statistical tests.

Results:

The prevalence of REM OSA was 71% under broad criteria and 37% under strict criteria. No statistically significant correlation was observed between overall AHI and ESS ($r = 0.02$, $p = 0.81$), BDI ($r = 0.14$, $p = 0.17$), or STOP-BANG score ($r = –0.08$, $p = 0.38$). Similarly, these questionnaires did not show significant differences between REM OSA and non-REM OSA groups. The Berlin Questionnaire was also not significantly associated with REM OSA ($p = 0.51$). REM OSA was significantly more prevalent among males ($p = 0.03$) and older individuals ($p = 0.03$). Excessive daytime sleepiness ($p = 0.04$), fatigue ($p = 0.008$), and insomnia ($p = 0.02$) were more frequently reported in REM OSA. Hypertension (76.9%), cardiovascular disease (53.9%), and diabetes (50%) were the most common comorbidities. Patients with REM OSA had significantly lower minimum SpO_2 ($p < 0.001$).

Interpretation and Conclusion:

REM OSA was highly prevalent in this cohort, especially when applying the broad diagnostic criteria. Male gender, advancing age, and specific symptom profiles such as fatigue and insomnia were associated with REM OSA. However, standard screening tools like ESS, BDI, STOP-BANG, and Berlin Questionnaire demonstrated limited discriminative power for detecting REM-predominant OSA. The findings highlight the need for heightened clinical awareness and phenotype-specific diagnostic approaches to better identify and manage REM OSA in routine practice.

Keywords:

REM-related Obstructive Sleep Apnea, Sleep-Disordered Breathing, Prevalence,

Polysomnography, Epworth Sleepiness Scale, STOP-BANG, Beck Depression Inventory, Berlin Questionnaire, Gender Differences, Apnea- Hypopnea index

INTRODUCTION

Obstructive sleep apnea (OSA) represents a prevalent form of sleep-disordered breathing, characterized by repetitive episodes of partial or complete obstruction of the upper airway during sleep. These obstructive episodes lead to intermittent hypoxia, disrupted sleep architecture, and sleep fragmentation, significantly contributing to adverse health outcomes, including cardiovascular, metabolic, and neurocognitive morbidities [1,2]. Conventionally, the diagnosis and severity classification of OSA have been based on the apnea-hypopnea index (AHI), which measures respiratory events per hour of sleep without distinguishing events by specific sleep stages [3]. However, recent evidence increasingly emphasizes the clinical significance of rapid eye movement (REM)-predominant OSA, defined by the occurrence of respiratory disturbances predominantly during REM sleep [4,5].

Physiologically distinct from non-REM sleep, REM sleep is characterized by increased cerebral activity, vivid dreaming, rapid eye movements, and pronounced muscle atonia. These characteristics inherently elevate the risk of upper airway collapsibility and respiratory instability, rendering individuals particularly susceptible to respiratory events during REM sleep [6]. Consequently, REM-predominant OSA (REM OSA) presents specific diagnostic and clinical management challenges due to its atypical symptom presentation, complex diagnostic criteria, and potential for heightened cardiovascular and neurocognitive consequences compared to non-REM OSA [7,8.9]. Despite these significant implications, REM OSA remains considerably underdiagnosed, primarily due to inconsistent definitions across clinical guidelines, variability in polysomnographic scoring methodologies, and limited clinician awareness [10,11].

The primary objective of this dissertation is to ascertain the prevalence of REM OSA among patients diagnosed with sleep-disordered breathing, applying both strict and broad diagnostic criteria. Strict criteria typically necessitate a distinctly elevated REM AHI compared to non-REM AHI, highlighting a clear predominance of respiratory events within REM sleep. Conversely, broader criteria encompass cases exhibiting any notable excess of respiratory disturbances during REM sleep, irrespective of total AHI severity [5,12,13]. Comprehensive characterization and quantification of REM-predominant OSA are essential to refine epidemiological understanding, delineate risk factors, and enhance clinical recognition and therapeutic management of affected individuals.

Secondary objectives involve examining correlations between subjective symptom assessment tools like, the Epworth Sleepiness Scale (ESS), Beck's Depression Inventory (BDI), Berlin Questionnaire, and STOP-BANG questionnaire and objective polysomnographic indices pertinent to general and REM-specific OSA. While these tools are routinely employed in clinical practice to stratify risk and severity, their effectiveness in identifying REM OSA remains inadequately established, largely due to differential clinical presentations associated with REM-specific disturbances [14,15]. For example, the ESS primarily measures daytime sleepiness, a common yet non-specific symptom of OSA, potentially limiting its predictive validity for REM OSA. Alternatively, the STOP-BANG and Berlin questionnaires incorporate broader symptomatology and demographic variables, offering potentially enhanced predictive value, though still imperfectly aligned with REM-specific presentations [11,16]. Furthermore, the BDI, initially designed for depression assessment, has gained clinical relevance given emerging evidence linking

depressive symptoms with disturbed REM sleep patterns frequently observed in REM OSA patients [17,18].

A nuanced understanding of how these subjective screening tools correlate with objective polysomnographic metrics specific to REM OSA is crucial for improving diagnostic precision, enhancing patient identification, and facilitating individualized therapeutic strategies. By investigating these associations through a cross-sectional analytical framework, this study seeks to expand existing knowledge, inform clinical guidelines, and potentially improve diagnostic accuracy and treatment outcomes. Enhanced recognition and tailored management of REM-predominant OSA could ultimately lead to improved patient outcomes, optimized healthcare resource allocation, and a significant enhancement in overall patient care quality.

Need for This Study

The clinical importance of REM-predominant obstructive sleep apnea (OSA) has gained substantial attention in sleep medicine research; nevertheless, significant knowledge gaps remain concerning its epidemiology, precise diagnosis, and optimal therapeutic management. Although existing literature delineates distinct pathophysiological pathways, diverse clinical presentations, and specific risk profiles associated with REM-related respiratory disturbances, REM OSA continues to be frequently overlooked and inadequately managed in routine clinical practice. The urgency for this research stems from the notable scarcity of robust epidemiological studies investigating the prevalence of REM-predominant OSA using clearly defined strict and broad diagnostic criteria across diverse patient demographics.

Furthermore, subjective screening tools widely implemented in clinical practice—such as the Epworth Sleepiness Scale (ESS), Beck's Depression Inventory (BDI), Berlin Questionnaire, and STOP-BANG questionnaire—demonstrate inconsistent predictive accuracy specifically for REM-predominant OSA. These screening instruments, while generally effective for overall OSA risk assessment, may fail to capture accurately the nuanced clinical symptomatology and severity peculiar to REM-related disturbances. Thus, there is a critical need for systematic investigation into the correlation between these subjective measures and objective polysomnographic findings to improve diagnostic reliability and enhance clinical decision-making tailored explicitly for REM OSA.

By bridging these critical knowledge gaps, the present study seeks to generate robust evidence that will inform and refine clinical practice guidelines, enhance diagnostic precision, and optimize management strategies specifically for REM-

predominant OSA. Ultimately, the insights derived from this investigation are anticipated to improve clinical recognition, facilitate earlier and more targeted interventions, and positively influence patient outcomes, thereby significantly advancing the discipline of sleep medicine.

AIMS AND OBJECTIVES

Primary Objective:

- To determine the prevalence of REM related OSA in patients with sleep disordered breathing

Secondary objective:

- To determine the correlation of Epworth Sleepiness Scale (ESS), STOP-BANG, Becks Depression inventory and Berlin questionnaire in diagnosis of Obstructive sleep apnea and aREM OSA.

REVIEW OF LITERATURE

Sleep is defined as the intermediate state between wakefulness and death; wakefulness regarded as the active state of all animal and intellectual functions and death as that of their total suspension. [19] Sleep is conventionally defined behaviorally as a reversible state marked by reduced perceptual engagement and diminished responsiveness to external stimuli. Beyond this, it is increasingly recognized as a complex integration of physiological and behavioral phenomena. While commonly characterized by postural recumbence, behavioral quiescence, and eye closure, these features, although typical, are not universally requisite for the state to be classified as sleep. [20]

Throughout history, the conceptualization and comprehension of sleep and associated disorders have evolved extensively. Early civilizations frequently viewed sleep as an enigmatic state, heavily interwoven with dreams, spirituality, mysticism, and religious interpretations. Ancient Greek philosophers, including Aristotle and Hippocrates, speculated on the nature and functions of sleep, often linking it to physiological balance and overall health. Similarly, ancient Egyptian and Mesopotamian cultures documented dreams and sleep disturbances as manifestations of divine or supernatural communication, emphasizing their perceived mystical significance. [21] However, despite these early cultural acknowledgments, it was not until the late nineteenth and early twentieth centuries that systematic, scientific methods began to elucidate the physiological underpinnings and clinical implications of sleep and its disorders.

The foundational period of contemporary sleep medicine commenced notably with Hans Berger's groundbreaking introduction of electroencephalography (EEG) in

1929. Berger's innovation allowed researchers, for the first time, to objectively assess and document cerebral electrical activity during sleep. This methodological advancement provided an empirical basis for understanding the neurophysiology of sleep, fundamentally transforming sleep research from anecdotal and observational descriptions into an objective scientific discipline. [22] Subsequently, in 1937, Alfred Loomis and his colleagues further enriched the field by categorizing sleep into distinct electrophysiologically defined stages. Their work provided a structured analytical framework, enabling more precise investigation of sleep's complexities, including its architecture and cyclical nature. [22]

A pivotal advancement in sleep research occurred in 1953 with the groundbreaking discovery of rapid eye movement (REM) sleep by Nathaniel Kleitman and Eugene Aserinsky. [23] Their landmark identification of REM sleep as a distinct physiological state, characterized by heightened cortical activity, rapid ocular movements, vivid dreaming, and unique patterns of muscle atonia, significantly advanced scientific understanding of sleep. This discovery catalyzed an era of extensive research into the physiological functions, neurobiological underpinnings, and clinical significance of sleep stages, notably reshaping conceptions of sleep as an active, complex, and physiologically critical phenomenon.[23]

The clinical characterization and systematic study of obstructive sleep apnea syndrome (OSAS) gained significant momentum during the 1970s, primarily through the efforts of Christian Guilleminault, William Dement, and colleagues at Stanford University.[24] Their meticulous clinical descriptions, exploration of pathophysiological mechanisms, and elucidation of associated cardiovascular and metabolic risks significantly enhanced the understanding and clinical recognition of OSAS. As a

result, sleep apnea syndrome emerged as a central focus within sleep medicine research and clinical practice, influencing subsequent diagnostic methodologies and therapeutic interventions.[24]

The therapeutic landscape underwent a profound transformation in 1981 when Colin Sullivan and associates introduced continuous positive airway pressure (CPAP) therapy. This innovative non-invasive treatment modality represented a critical milestone in managing obstructive sleep apnea, effectively alleviating symptoms, reducing morbidity, and markedly improving patient outcomes and overall quality of life. [25]. Furthermore, REM-related obstructive sleep apnea (REM OSA) gained prominence as a distinct clinical phenotype in subsequent decades. REM OSA drew particular clinical attention due to its unique pathophysiological characteristics, diagnostic challenges, and specialized therapeutic considerations specifically associated with disturbances during REM sleep. [21]

Physiology and Importance of Sleep

Sleep constitutes an intricate physiological state critical for maintaining the homeostatic equilibrium across diverse biological systems essential for human health. At its foundation, sleep orchestrates crucial regulatory functions encompassing neurological, cognitive, metabolic, endocrine, immunological, and cardiovascular processes. The complexity of sleep is maintained through highly regulated neural circuitry, sophisticated neurochemical pathways, and coordinated systemic interactions, highlighting the essential nature of adequate sleep quality and duration for maintaining optimal physiological and psychological health. [26]

Neurobiologically, sleep plays a pivotal role in supporting synaptic plasticity, neuronal repair, and overall neural homeostasis. During non-rapid eye movement (NREM) sleep, especially the slow-wave sleep (SWS) phase, significant neuronal restructuring occurs, characterized by synaptic downscaling and strengthening, which facilitate efficient neural network function and memory consolidation processes. Conversely, rapid eye movement (REM) sleep is critically involved in the consolidation of procedural memories and the integration and regulation of emotional memories, thereby contributing substantially to emotional regulation, cognitive adaptability, and psychological resilience. [27] Distinct neurophysiological features of REM sleep, including elevated cortical activity, vivid dreaming, rapid ocular movements, and complete skeletal muscle atonia, further emphasize its integral role in maintaining optimal neurological and emotional health. Disruptions specifically within REM sleep have been shown to disproportionately affect emotional processing capabilities, increase vulnerability to mood disorders such as anxiety and depression, and impair overall cognitive and psychological functioning, underscoring the necessity for maintaining stable and uninterrupted sleep architecture.

In addition to cognitive and neurological functions, sleep exerts profound and widespread influences on systemic physiological processes, including cardiovascular regulation, immune response modulation, endocrine signalling, and metabolic control. Epidemiological and experimental studies consistently demonstrate robust associations between chronic sleep deprivation and adverse health outcomes - heightened risks for cardiovascular diseases, metabolic disorders such as impaired glucose tolerance and insulin resistance, obesity, and compromised immune defences. [28] Mechanistically, insufficient or disturbed sleep initiates inflammatory responses, elevates oxidative stress levels, and disrupts hormonal homeostasis, particularly

involving dysregulation of cortisol, leptin, and ghrelin concentrations. These pathophysiological disruptions collectively amplify susceptibility to chronic conditions and exacerbate underlying medical illnesses. Furthermore, sleep deprivation has been linked to increased sympathetic nervous system activation and diminished parasympathetic modulation, leading directly to heightened cardiovascular stress, increased blood pressure, and elevated cardiovascular morbidity risks. Disturbances in sleep quality and quantity significantly impact circadian rhythms, influencing genetic expression patterns crucial for regulating metabolic functions, immune efficiency, and stress adaptation mechanisms, thus profoundly affecting long-term physiological resilience and systemic health.

As per the guidelines issued by the American Academy of Sleep Medicine (AASM) and Sleep Research Society (SRS) , it is recommended that adults sleep at least 7 hours per night, with 7 to 9 hours being optimal. Extending sleep duration for those who consistently sleep insufficiently may lead to health improvements. Healthy sleep requires adequate sleep duration, regularity, appropriate timing, the absence of sleep disorders, and good sleep quality. [29]

STAGES OF SLEEP

As per the most recent American Academy of Sleep Medicine (AASM) guidelines, sleep is classified into two major types:[30]

1**.** Non-Rapid Eye Movement (NREM) Sleep

Divided into three stages (N1, N2, N3), which reflect progressively deeper sleep:

Stage N1 (NREM 1) – Light Sleep

- Transitional phase between wakefulness and sleep.
- Characterized by:
    - Low-voltage, mixed-frequency EEG activity.
    - Slow rolling eye movements.
    - Reduced muscle tone.
- Accounts for about 5–10% of total sleep time.

Stage N2 (NREM 2) – Intermediate Sleep

- Represents the largest proportion of total sleep time (~45–55%).
- EEG features:
    - Sleep spindles (11–16 Hz bursts).
    - K-complexes (high-amplitude biphasic waves).
- No eye movement; muscle tone continues to decline.

Stage N3 (NREM 3) – Deep Sleep / Slow Wave Sleep

- Also referred to as slow-wave sleep (SWS) or delta sleep.
- EEG shows:
    - High-amplitude, low-frequency delta waves (0.5–2 Hz, >75 μV).
- Most restorative stage of sleep.
- Comprises ~15–25% of total sleep time in young adults.
- Associated with memory consolidation, cellular repair, and immune function.

2**. Rapid Eye Movement (REM) Sleep**

- Characterized by:
    - Rapid eye movements.
    - Mixed-frequency, low-voltage EEG activity (similar to wakefulness).
    - Muscle atonia (paralysis of major voluntary muscles).

  - Vivid dreaming commonly occurs in this stage.
- Typically constitutes 20–25% of total sleep time.
- REM sleep cycles occur every ~90 minutes and lengthen in duration across the night.

Sleep Cycle Overview[30]

- A normal sleep cycle progresses from N1 → N2 → N3 → REM.
- In adults each sleep cycle lasts approximately 90–110 minutes.Adutlts typically go through 4-6 cycles per night
- With each successive cycle:
  - N3 decreases.
  - REM duration increases.
- The paediatric sleep cycle, especially in infants and young children, is shorter (about 50–60 minutes in infants). Newborns alternate mainly between active (REM-like) and quiet sleep, gradually developing distinct sleep stages with age. Children also spend more time in deep sleep compared to adults.

Standardized Terminology in Sleep-Disordered Breathing (According to AASM)

Approaching patients with sleep-related breathing disturbances requires standardized nomenclature, as outlined by the American Academy of Sleep Medicine (AASM) [30]. The core terms and their clinical meanings are summarized below:

- Apnea

  Refers to a near-total cessation of airflow, amounting to at least a 90% drop from baseline, lasting for a minimum of 10 seconds.

- Obstructive Apnea

  A form of apnea characterized by continued respiratory effort without effective airflow, indicative of upper airway obstruction.

- Central Apnea

  Represents a transient pause in breathing where there is no observable respiratory effort during the episode.

- Mixed Apnea

  A respiratory event beginning without any effort and ending with effortful breathing against a blocked airway.

- Hypopnea

  Defined as a partial decrease in airflow for at least 10 seconds, associated with a ≥3% drop in oxygen saturation or an arousal from sleep.

- Respiratory Effort-Related Arousal (RERA)

  A condition where increased respiratory effort causes sleep disruption, though it does not fulfill the criteria for apnea or hypopnea.

- Apnea–Hypopnea Index (AHI)

  A measurement indicating the average number of apneas and hypopneas occurring per hour of sleep.

- Respiratory Disturbance Index (RDI)

  A broader metric encompassing apneas, hypopneas, and RERAs per hour of sleep.

- Oxygen Desaturation Index (ODI)

  Describes the frequency per hour at which oxygen saturation drops by a set threshold (commonly ≥3% or 4%).

- Hypoventilation

  Describes a condition where elevated carbon dioxide levels persist during sleep due to inadequate ventilation.

- Cheyne–Stokes Breathing

  A pattern of rhythmic breathing fluctuations with periods of increased and decreased effort, typically ending in central apneas or hypopneas.

- Sleep-Disordered Breathing (SDB)

  A collective term for conditions marked by irregular or obstructed breathing patterns during sleep.

- Arousal

  A brief interruption of sleep characterized by a sudden shift in brain wave activity lasting at least 3 seconds, usually following stable sleep for 10 seconds or more.

Classification of sleep disorders according to ICSD 3 [31,32]

1. Insomnia Disorders:

   - Chronic Insomnia,

   – Short term insomnia

   – other insomnia

2. Sleep related Breathing disorders

   - Obstructive Sleep Apnea (OSA):

   - Central Sleep Apneas (CSA)

   - Central sleep apnea due to high Altitude Periodic breathing

   - Primary Central Sleep Apnea of Infancy

   - Primary Central sleep Apnea of prematurity

   - Treatment Emergent Central Sleep Apnea

3. Sleep Related Hypoventilation disorders
    - Congenital Central Alveolar Hypoventilation Syndrome
    - Sleep-Related Hypoxemia disorder
4. Central disorders of Hypersomnolence
    - Narcolepsy type 1
    - Idiopathic Hypersomnia
    - Kleine Levin syndrome
    - Hypersomnia due to a medical disorder
5. Circadian Rhythm Sleep-Wake disorders
    - Delayed Sleep-Wake Phase Disorder
    - Advanced Sleep-Wake Phase Disorder
    - Irregular Sleep-Wake Rhythm Disorder
    - Non-24-Hour Sleep-Wake Rhythm Disorder
    - Shift Work Disorder
    - Jet Lag Disorder
6. Parasomnias
    - NREM Parasomnias (Sleep walking, Confusional Arousals, Sleep Terrors)
    - REM sleep Behaviour disorder
    - Nightmare disorder
    - Sleep-Related eating disorder
    - Sleep related Urologic Dysfunction
        - Sleep Enuresis
        - Nocturia
        - Nocturnal Urinary Urge incontinence

7. Sleep-Related Movement Disorders
    - Nocturnal Muscle Cramps
    - Sleep related Bruxism
    - Restless Legs syndrome
    - Periodic Limb Movement disorder
    - Propriospinal Myoclonus at sleep Onset
8. Other sleep disorders
    - Isolated symptoms and Normal Variants
    - Unclassified Sleep Disorders

These changes reflect the AASM's effort to improve diagnostic specificity and harmonize sleep disorder classification with current clinical and research standards.

From the above mentioned sleep disorders, patients with sleep related breathing disorders are involved in this study.

Classification of Sleep-Related Breathing Disorders (According to ICSD-3):[31,32,33]

Sleep-Related Breathing Disorders (SRBDs) refer to a group of conditions characterized by abnormal respiration during sleep. These disorders are classified into the following categories based on the International Classification of Sleep Disorders – Third Edition (ICSD-3)

1. Obstructive Sleep Apnea Syndromes (Sleep disordered breathing)

    It is the most commonly diagnosed breathing disorder associated with sleep.It causes temporary cessation of breathing during sleep due to partial or complete blockage of the upper airway.These interruption are often accompanied by symptoms including snoring, night sweats, dry mouth or throat.Peoplle may awaken without realizing it resulting in

symptoms like excessive daytime fatigue, lack of focus and memory problems.

At this juncture it may be noted as per ICSD 3 guidelines obstructive sleep apnea is alternatively called sleep disordered breathing.

2. Central Sleep Apnea (CSA)

   It differs from obstructive sleep apnea syndrome (OSAS) in that it involves a cessation of breathing due to impaired neurological control rather than physical airway obstruction. The underlying mechanism involves dysfunction in the central nervous system (CNS) pathways that regulate respiratory drive. CSA can be precipitated by several etiological factors, including congestive heart failure, cerebrovascular events, and the use of opioids.

3. Sleep-Related Hypoxic Hypoventilation Disorders (SRHHD)

   These refer to a group of respiratory disturbances during sleep that result from neurological, cardiovascular, or pulmonary conditions, leading to inadequate oxygenation. These disorders generally emerge due to compromised ventilation stemming from an underlying disease.

Sleep related breathing disorders can significantly impair an individual's overall well-being, diminishing quality of life and limiting daily functional capacity. Timely identification and intervention with targeted therapies are essential to improving outcomes and minimizing the risk of further health deterioration.

Isolated Symptoms and Normal Variants, such as primary snoring, are characterized by repetitive upper airway noise during sleep without accompanying obstructive or central respiratory events. Although typically not linked to significant oxygen

desaturation, primary snoring may still disrupt sleep continuity and result in non-restorative sleep or daytime somnolence.

Among the spectrum of sleep-related breathing disorders, obstructive sleep apnea (OSA) remains the most prevalent. It is strongly associated with adverse cardiovascular outcomes. Current epidemiological evidence estimates the prevalence of OSA to range from approximately 9% to 38% in various populations.

OBSTRUCTIVE SLEEP APNEA

OSA is defined by recurrent episodes of partial or complete pharyngeal obstruction during sleep, resulting in apneas (≥90% airflow reduction) or hypopneas (≥30% airflow reduction with ≥3% desaturation or arousal), as per AASM scoring rules.[30,31] These events, detected via polysomnography or validated home sleep apnea testing, must occur at a frequency of ≥5 events/hour, with accompanying clinical symptoms or comorbidities, to satisfy diagnostic thresholds under the ICSD-3 framework [32].

These events induce intermittent hypoxemia, sleep fragmentation, and sympathetic activation, contributing to widespread end-organ effects. [34-38]

Severity is stratified based on the apnea-hypopnea index (AHI):

- Mild: 5–14 events/hour
- Moderate: 15–29 events/hour
- Severe: ≥30 events/hour [30]

Obstructive Sleep Apnea (OSA) is an established risk factor for multiple systemic diseases and adverse health outcomes due to its association with intermittent hypoxia, sympathetic activation, inflammation, and sleep fragmentation.

1**.** Hypertension (Especially Resistant Hypertension)

- Recurrent apneas increase sympathetic tone and endothelial dysfunction, leading to sustained hypertension.[34]

2. Coronary Artery Disease and Myocardial Infarction

- OSA contributes to atherosclerosis, endothelial dysfunction, and increased cardiac workload [35].

3. Stroke

- OSA increases the risk of both ischemic and haemorrhagic stroke through hemodynamic fluctuations and prothrombotic states [36].

4. Heart Failure (Especially HFpEF and HFrEF)

- OSA contributes to both systolic and diastolic dysfunction via hypoxia and intrathoracic pressure swings.[37]

5. Arrhythmias (e.g., Atrial Fibrillation)

- OSA is associated with increased atrial size, autonomic imbalance, and hypoxemia—predisposing to atrial fibrillation and other arrhythmias.[38]

6. Type 2 Diabetes Mellitus and Insulin Resistance

- Intermittent hypoxia promotes metabolic dysregulation and impairs glucose metabolism. [39]

7. Depression and Cognitive Impairment

- Fragmented sleep architecture and hypoxia contribute to mood disturbances and impaired executive function. [40]

8. Motor Vehicle Accidents

- Excessive daytime sleepiness in untreated OSA increases accident risk significantly. [41]

9. Nonalcoholic Fatty Liver Disease (NAFLD)

- OSA has been implicated in hepatic steatosis and fibrosis due to hypoxia-induced oxidative stress [45].

Epidemiology of OSA

Global Prevalence

- The global prevalence of OSA has seen a marked increase, largely driven by rising rates of obesity, aging populations, and improved awareness and diagnostic capability. According to the HypnoLaus study conducted in Switzerland, moderate-to-severe sleep-disordered breathing (AHI ≥15 events/hour) was present in 23.4% of women and 49.7% of men aged 40 to 85 years, suggesting that OSA may be more widespread than previously believed. [43]

A seminal model-based global estimate by Benjafield et al. (2019), which utilized data from 16 countries, projected that nearly 936 million adults aged 30–69 years g**lobally** may have OSA (AHI ≥5/h), with 425 million experiencing moderate-to-severe disease (AHI ≥15/h), signifying a major global health burden.[44] The prevalence is notably higher among males, older adults, and individuals with elevated

.**Prevalence in Asia**

Asia, with its diverse populations and rapid urbanization, is witnessing a rising prevalence of OSA. Despite differences in craniofacial structure and body habitus, studies from East and Southeast Asia report prevalence rates comparable to Western countries, particularly when using contemporary AHI thresholds.

In the Wisconsin Sleep Cohort adaptation in urban Chinese populations, prevalence of OSA (AHI ≥5) was estimated at 3.6% in women and 4.1% in men in

earlier studies, though more recent data reflect higher rates due to lifestyle transitions. [45]

A meta-analysis by Mirrakhimov et al. found pooled prevalence rates of OSA ranging from 9% to 38% in Asian males and 4% to 20% in Asian females, depending on the diagnostic criteria and age group.[46] East Asian populations often develop OSA at lower BMI due to craniofacial anatomical predispositions such as retrognathia and maxillary hypoplasia, despite lower obesity rates compared to Western counterparts [47].

Prevalence in India

OSA is increasingly recognized as a major health issue in India, with multiple population-based and hospital-based studies indicating substantial prevalence. A large community-based study by Udwadia et al. in Mumbai (2004) reported that OSA (AHI ≥5 plus symptoms) had a prevalence of 19.5% in males and 7.4% in females, with overall sleep-disordered breathing affecting 24.5% of the adult population. [48]

Subsequent studies from different regions of India have supported these findings, with prevalence estimates ranging from 13% to 33% depending on the urban or rural setting, population age, and BMI distribution [37,38]. A pan-Indian hospital-based study reported that moderate-to-severe OSA (AHI ≥15) was present in 19% to 21% of referred patients. [51] Despite these figures, under-recognition remains a major issue due to low public and physician awareness, limited sleep laboratories, and socio-cultural barriers.

Notably, Indian populations exhibit unique risk profiles with a combination of central obesity, craniofacial narrowing, and metabolic syndrome at lower BMI, contributing to OSA risk even in non-obese individuals [52].

OSA affects hundreds of millions of individuals worldwide, with similar prevalence patterns in Asian and Indian populations as in Western countries. Given its public health implications, especially in low- and middle-income countries, there is a pressing need for large-scale epidemiological surveillance, increased clinical awareness, and expansion of diagnostic infrastructure in India and across Asia.

Risk Factors for Sleep-Disordered Breathing (SDB)

Obstructive Sleep Apnea (OSA) is influenced by a range of interrelated risk factors.

Sex is a significant determinant, with men having a 2- to 4-fold higher prevalence of OSA than women. This disparity is attributed to anatomical differences such as longer pharyngeal length and greater upper airway fat deposition in men. However, the risk in women increases after menopause unless they are on hormone replacement therapy. Additionally, women with OSA tend to exhibit more hypopneas, shorter respiratory events, and less severe oxygen desaturation episodes compared to men. [53-55]

Advancing age is another established risk factor, with OSA prevalence rising due to reduced upper airway muscle tone and a greater burden of comorbid conditions such as cardiovascular, metabolic, and neurologic diseases [56].

Obesity plays a central role, with 40–60% of individuals with OSA being obese. Obesity contributes through fat accumulation in upper airway structures, decreased lung volumes, and heightened pro-inflammatory cytokines that impair ventilatory control and promote daytime sleepiness. Nevertheless, it is noteworthy that approximately 20% of OSA cases occur in non-obese individuals, underscoring the multifactorial nature of the disorder.[56]

Craniofacial abnormalities such as retrognathia, brachycephaly, a high-arched palate, and macroglossia are also recognized contributors, particularly in Asian populations where minor changes in BMI are associated with increased OSA risk due to structural predispositions.[57-59] **Systemic inflammation**, characterized by elevated levels of C-reactive protein (CRP), interleukin-6 (IL-6), insulin resistance, and leptin dysregulation, has been implicated in the pathogenesis of OSA by disrupting ventilatory drive and promoting adipose deposition in the upper airway .[60-63]

Genetics plays an important role, with first-degree relatives of OSA patients having approximately double the risk. This inherited susceptibility may be mediated through shared traits such as obesity, craniofacial architecture, ventilatory control instability, and common comorbidities.[64,65]

Pathogenesis Of OSA

The below illustration from Cowie et al. (2021) provides a comprehensive visual summary of the multifactorial pathophysiological mechanisms underlying sleep-disordered breathing (SDB), particularly obstructive sleep apnea (OSA). At the core of these abnormalities are repetitive apneic events that lead to sleep fragmentation, cyclical hypoxemia-reoxygenation, large intrathoracic pressure swings, and heightened sympathetic nervous system activation. These mechanisms contribute synergistically to systemic inflammation, oxidative stress, and neurohormonal dysregulation. Specifically, the negative intrathoracic pressures during obstructive events increase myocardial workload and preload, disrupt ventricular interactions, and predispose to arrhythmias and cardiac remodeling. Concurrently, intermittent hypoxia triggers pro-inflammatory and pro-thrombotic pathways, endothelial dysfunction, and insulin resistance, further linking SDB to cardiovascular

and metabolic disorders. The illustration underscores how these interconnected processes culminate in increased cardiovascular morbidity and systemic complications, reinforcing the need for early recognition and targeted management of SDB. [66]

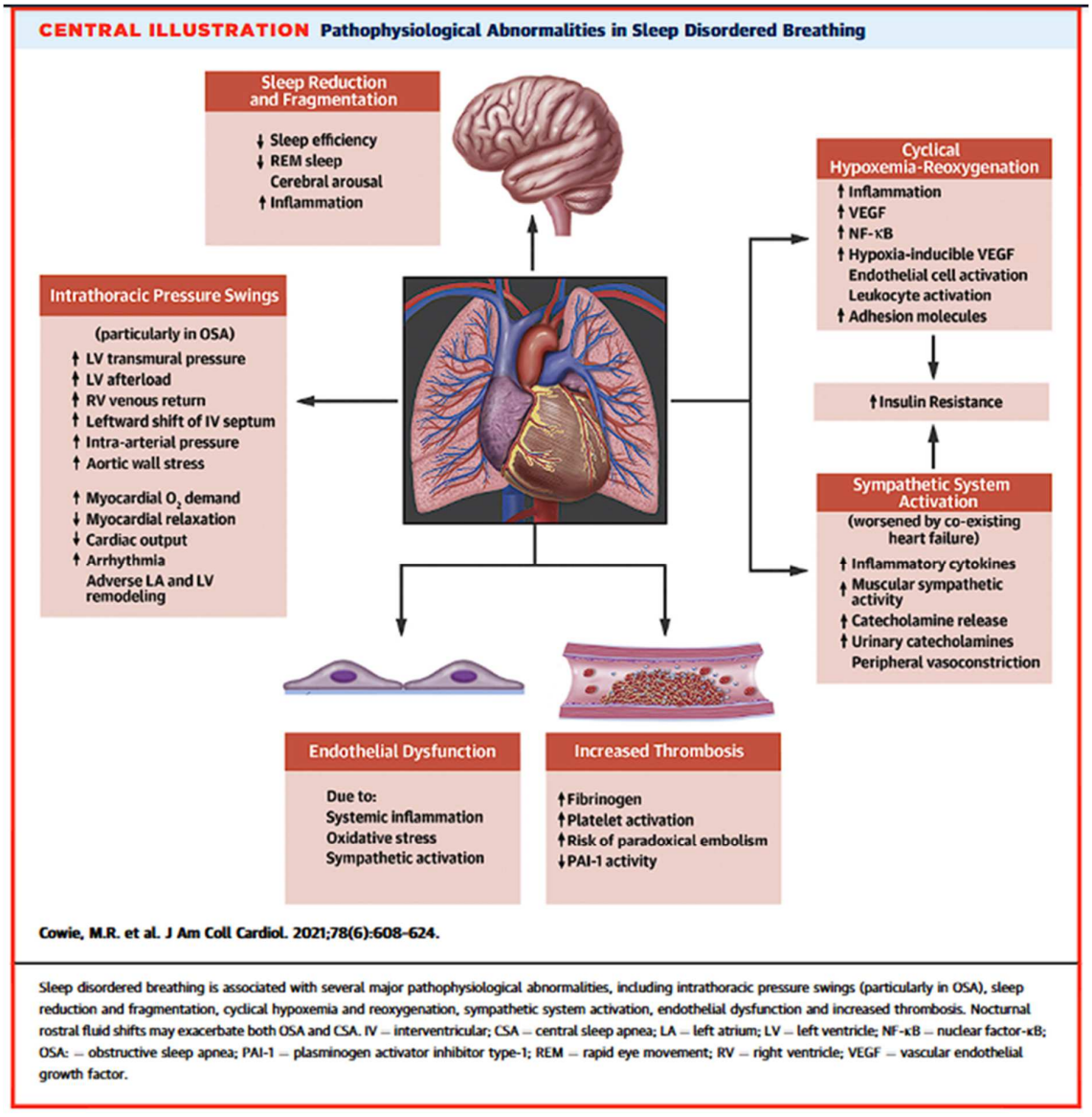


Fig 1: Pathophysiological abnormalities in Slep Disordered Breathing

Anatomical Considerations of the Upper Airway

A fundamental anatomical abnormality in OSA is increased pharyngeal collapsibility, which can be assessed by the pharyngeal critical closing pressure (Pcrit). In individuals with OSA, Pcrit is typically zero or positive, indicating a predisposition to airway collapse, while healthy individuals usually exhibit negative Pcrit values, though some overlap exists. [67] This increased collapsibility is often due to a narrower upper airway, as confirmed by imaging studies comparing OSA patients with healthy controls.[68-70] Obesity contributes to this abnormality through fat deposition around the airway, but other structural features such as increased airway length, greater tongue volume, and thicker lateral pharyngeal walls also play significant roles.[71,72]

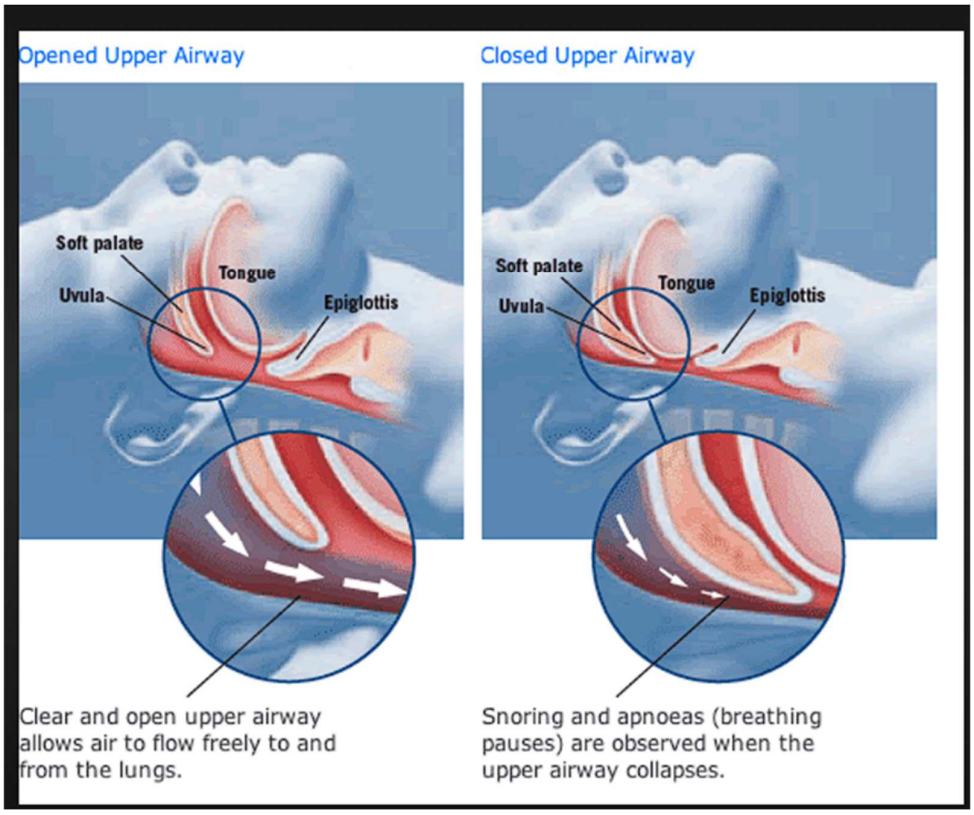


Fig 2: Demonstrates airflow in upper airway in Normal breathing Vs Sleep disordered breathing

Upper Airway Dilator Muscle Activity

If anatomical predisposition were the only factor, airway obstruction would occur during both wakefulness and sleep. However, OSA typically occurs during sleep, owing to reduced neuromuscular activity of upper airway dilator muscles. These muscles, which maintain airway patency, are active during wakefulness but become less responsive during sleep. [73,74] The genioglossus muscle, forming the bulk of the tongue, is the most studied among these muscles. It receives input from wakefulness centers as well as respiratory chemoreceptors and mechanoreceptors. [75-79] At sleep onset, genioglossus activity diminishes[72,80], but it may increase again later during sleep as airway resistance and end-tidal CO_2 rise. However, collapse still occurs, likely because other airway muscles remain less active due to their minimal input from respiratory control centers. Additional factors, such as reduced lung volume during sleep, may further predispose the airway to collapse.

Lung Volume and Airway Stability

Airway cross-sectional area is known to increase with rising lung volumes, from residual volume to total lung capacity. [81-83] Recent evidence indicates that increasing end-expiratory lung volume during sleep can reduce airway collapsibility and lower the severity of sleep-disordered breathing.[84-86] Healthy individuals generally experience a 200–400 mL reduction in lung volume upon falling asleep [87], which may exacerbate airway collapsibility. The mechanism may involve lung volume exerting a caudal traction effect, thereby stiffening and dilating the upper airway. [88] Lower lung volume may also contribute to rapid oxygen desaturation during apneic events.

Ventilatory Control Instability

Historically, periodic breathing patterns observed in tracheostomized OSA patients raised suspicions of abnormal central ventilatory control. [89] Modern studies confirm that individuals with OSA often have less stable ventilatory control compared to healthy controls. [90-92] Instability in central respiratory drive may cause waxing and waning patterns of muscle activation, affecting both the diaphragm and upper airway muscles like the genioglossus. This promotes upper airway hypotonia during hypoventilation and increases the risk of apnea in those with already vulnerable airways. The extent of this contribution to OSA pathogenesis varies between individuals and remains an active area of investigation. [93]

Role of Arousal in Respiratory Event Termination

Apneic episodes are frequently terminated by arousals from sleep, which reestablish airway patency. [94] While arousal is often necessary to restore ventilation, it may also induce excessive hyperventilation and resultant hypocapnia, which can precipitate subsequent airway collapse upon resumption of sleep. Interestingly, not all respiratory events require cortical arousal for resolution. When arousals occur at a low threshold and trigger exaggerated ventilatory responses, they may perpetuate the apneic cycle. Conversely, arousals that act as a final resort may be protective by preventing severe hypoxemia.

Signs and Symptoms of Obstructive Sleep Apnea (OSA)

Obstructive sleep apnea (OSA) is characterized by recurrent episodes of partial or complete upper airway obstruction during sleep, resulting in intermittent hypoxia and arousals from sleep. The clinical presentation of OSA is often heterogeneous, influenced by factors such as age, sex, body habitus, and comorbidities. It typically manifests through a constellation of nocturnal symptoms,

daytime features, and observed behaviors, some of which may be subtle or misattributed, especially in certain populations such as women and the elderly.

Nocturnal Symptoms

The hallmark symptom of OSA is loud, habitual snoring, often reported by bed partners. Snoring in OSA is typically irregular, punctuated by gasping, choking, or witnessed apneas, which are defined as episodes of complete cessation of airflow lasting ≥10 seconds. [13]

Nocturnal awakenings or restless sleep are also frequently reported, often due to arousals associated with respiratory effort or desaturation. Patients may experience nocturia (frequent nighttime urination), which has been linked to increased atrial natriuretic peptide levels resulting from negative intrathoracic pressure swings during apneic episodes. [95]

In some individuals, particularly those with severe OSA, insomnia symptoms, including difficulty initiating or maintaining sleep, may also be present and may obscure the diagnosis. [96]

Daytime Symptoms

Excessive daytime sleepiness (EDS) is one of the most prominent daytime symptoms of OSA. It results from fragmented sleep architecture and frequent arousals that prevent restorative sleep. EDS may manifest as an inability to stay awake in passive situations, such as reading, watching television, or driving, and is commonly assessed using tools such as the Epworth Sleepiness Scale (ESS).[97]

Other neurocognitive manifestations include morning headaches, difficulty concentrating, memory lapses, and irritability. These symptoms are primarily related to sleep fragmentation and intermittent nocturnal hypoxemia, which impair prefrontal cortex function and cerebral oxygenation.[98]

In contrast to the classic symptomatology seen in men, women with OSA may report more nonspecific symptoms, including fatigue, depression, anxiety, and insomnia, which may lead to underdiagnosis or misclassification. [99]

Observed Behaviors and Clinical Clues

Clinical suspicion is often raised by witnessed apneas, where the bed partner notices periods of silence during sleep followed by loud gasps. Patients themselves are frequently unaware of these events. Morning dry mouth or sore throat may also be noted due to mouth breathing during sleep. [100]

On examination, features such as obesity, increased neck circumference, retrognathia, high-arched palate, or macroglossia may provide anatomical clues to the likelihood of OSA. However, the absence of these findings does not exclude the diagnosis. [101]

Table 1: Signs and symptoms of OSA

Symptom Type	**Examples**
Nocturnal	Loud snoring, witnessed apneas, choking/gasping, nocturia, restless sleep
Daytime	Excessive sleepiness, fatigue, headaches, poor concentration, mood changes
Gender Differences	Females: insomnia, fatigue, depression; Males: snoring, witnessed apneas
Clinical Clues	Obesity, large neck circumference, craniofacial anomalies, dry mouth

Screening Tools and Questionnaires in the Evaluation of Sleep-Disordered Breathing

The deployment of standardized screening instruments for sleep-disordered breathing (SDB) represents an essential strategy in the early identification and clinical prioritization of individuals at heightened risk, particularly within primary care, outpatient specialty clinics, and perioperative contexts where access to comprehensive polysomnographic evaluation may be limited or logistically constrained. These tools, which have undergone rigorous empirical validation, provide a pragmatic, non-invasive, and cost-effective framework for risk stratification and serve as valuable adjuncts in guiding the allocation of diagnostic resources such as home sleep apnea testing or in-laboratory polysomnography.

Class 0: Ability to see any part of the epiglottis upon mouth opening and tongue protrusion

Class I: Soft palate, fauces, uvula, pillars visible

Class II: Soft palate, fauces, uvula visible

Class III: Soft palate, base of uvula visible

Class IV: Soft palate not visible at all

Figure. Modified Mallampati Score

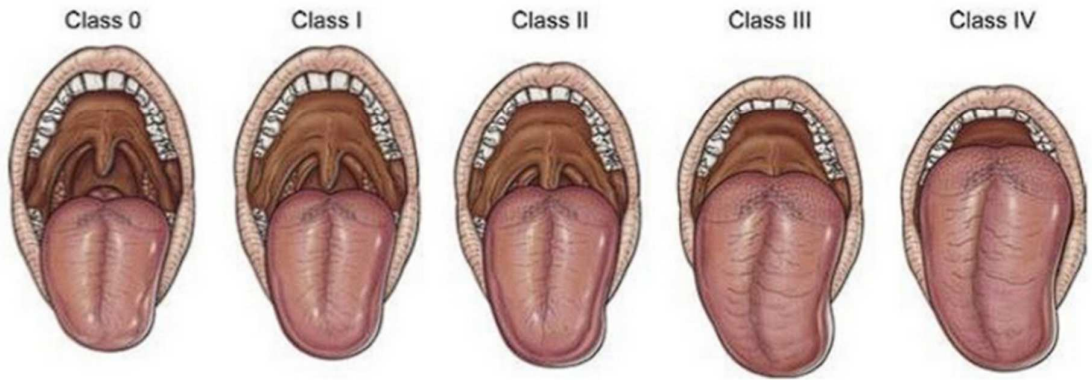


Fig 3 Modified Mallampati score

Among the most widely employed scales is the Epworth Sleepiness Scale (ESS), a self-administered questionnaire that quantifies subjective daytime sleepiness across eight real-life, sedentary contexts. Scores above the conventional threshold of 10 are suggestive of excessive daytime sleepiness, a cardinal symptom of SDB. The ESS has demonstrated high construct and criterion validity and is frequently employed not only for initial screening but also for monitoring treatment response, particularly in individuals managed with continuous positive airway pressure (CPAP) therapy. [97]

Epworth Sleepiness Scale

Name: _____

Date: _____

Your age: (Yr) _____ **Your sex**: ❑ Male ❑ Female

How likely are you to doze off or fall asleep in the situations described below, in contrast to feeling just tired?

This refers to your usual way of life in recent times.

Even if you haven't done some of these things recently try to work out how they would have affected you.

Use the following scale to choose the most appropriate number for each situation:-

0 = would never doze
1 = Slight chance of dozing
2 = Moderate chance of dozing
3 = High chance of dozing

Situation	Chance of dozing
Sitting and reading	
Watching TV	
Sitting, inactive in a public place (e.g. a theatre or a meeting)	
As a passenger in a car for an hour without a break	
Lying down to rest in the afternoon when circumstances permit	
Sitting and talking to someone	
Sitting quietly after a lunch without alcohol	
In a car, while stopped for a few minutes in the traffic	
Total	

Score:

0-10 Normal range
10-12 Borderline
12-24 Abnormal

Fig 4 Epworth Sleepiness scale

The Berlin Questionnaire adopts a multidimensional approach to risk stratification, capturing symptom clusters associated with OSA. Its three domains—snoring and witnessed apneas, daytime somnolence, and comorbid hypertension or elevated BMI—allow for the classification of patients into high- or low-risk categories. It has shown reasonable sensitivity and specificity in community-based and primary care settings, making it especially useful for front-line practitioners in identifying patients who require expedited sleep evaluation. [102]

Berlin Questionnaire

Attending MD_____

PCP_____

Patient Information
Height: Age:

Weight: Male/Female

Category 1

Do you snore?
- ☐ **Yes**
- ☐ No
- ☐ Don't Know

Your snoring is?
- ☐ Slightly louder than breathing
- ☐ As loud as talking
- ☐ **Louder than talking**
- ☐ **Can be hear in adjacent room**

Describe the snoring frequency
- ☐ **Nearly every day**
- ☐ **3-4 times a week**
- ☐ 1-2 times a week
- ☐ 1-2 times a month
- ☐ Never or nearly never

Has your snoring ever bothered other people?
- ☐ **Yes**
- ☐ No

Has anyone noticed that you quit breathing during your sleep?
- ☐ **Nearly every day**
- ☐ **3-4 time a week**
- ☐ 1-2 time a week
- ☐ 1-2 time a month
- ☐ Never or nearly never

Category 1 positive (≥2) ☐
Category 2 positive (≥2) ☐
Category 3 positive (1 or BMI>30) ☐

Category 2

How often do you feel tired or fatigued after you sleep?
- ☐ **Nearly every day**
- ☐ **3-4 times a week**
- ☐ 1-2 times a week
- ☐ 1-2 times a month
- ☐ Never or nearly never

During your wake time, do you feel tired, fatigued or not up to par?
- ☐ **Nearly every day**
- ☐ **3-4 times a week**
- ☐ 1-2 times a week
- ☐ 1-2 times a month
- ☐ Never or nearly never

Have you ever nodded off or fallen asleep while driving a vehicle?
- ☐ **Yes**
- ☐ No

If yes, how often does it occur?
- ☐ **Nearly every day**
- ☐ **3-4 times a week**
- ☐ 1-2 times a week
- ☐ 1-2 times a month
- ☐ Never or nearly never

Category 3

Do you have high blood pressure?
- ☐ **Yes**
- ☐ No

BMI= _____

Signature_____**Date**_____

Fig 5: Berlin Questionnaire

The STOP-BANG questionnaire, an eight-item screening tool, expands upon traditional models by combining subjective symptoms (snoring, fatigue, witnessed apneas) with objective clinical features (blood pressure, BMI >35 kg/m2, age >50, neck circumference >40 cm, male gender). Its ease of administration, high sensitivity for moderate-to-severe OSA, and applicability across multiple clinical domains have led to widespread adoption, especially in perioperative risk screening and sleep referral pathways (91). Modified versions of STOP-BANG have also been explored to improve specificity in targeted subpopulations. The mnemonic STOP- BANG includes the following:[103]

- S: “Do you snore loudly, loud enough to be heard through a closed door?”
- T: “Do you feel tired or fatigued during the daytime almost every day?”
- O: “Has anyone observed that you stop breathing during sleep?”
- P: “Do you have a history of high blood pressure with or without treatment?”
- B: BMI > 35 kg/m2
- A: Age > 50 years
- N: Neck circumference > 43 cm (17 in)
- G: Gender, male

When more than three items are positive, the sensitivity and specificity for OSA are 87% and 31%, Beyond the somatic manifestations of SDB, the psychiatric dimension warrants equal attention. The Beck Depression Inventory (BDI), a 21-item self-report instrument, provides a standardized method for evaluating depressive symptomatology. Given the strong bidirectional relationship between affective disorders and SDB—mediated by disrupted sleep architecture, inflammatory processes, and impaired emotional regulation—the BDI is frequently utilized in

multidisciplinary settings to support integrated care strategies.[104] Depression screening in SDB patients can also enhance adherence to therapy and reduce treatment attrition.

Taken together, these tools serve not only as diagnostic triage tools but also as important tools of healthcare equity and resource stewardship. Their systematic use enables more efficient identification of high-risk individuals, facilitates equitable distribution of diagnostic modalities, and ultimately contributes to the mitigation of disease burden associated with undiagnosed and untreated sleep-disordered breathing across various healthcare settings.

Diagnosis of OSA:

According to the American Academy of Sleep Medicine (AASM), the gold standard for diagnosis is polysomnography (PSG) conducted in a sleep laboratory, assessing airflow, oxygen saturation, respiratory effort, and EEG patterns. Home sleep apnea testing (HSAT) is recommended for high-risk OSA patients but not for those with suspected CSA or comorbidities like COPD or heart failure[93]. AASM criteria confirm OSA if AHI ≥5 with symptoms or AHI ≥15 regardless of symptoms.

Diagnostic Criteria for Obstructive Sleep Apnea (OSA) :

A diagnosis of OSA is established when either **(A and B)** or **C** is met:

A. At least one of the following symptoms is present:

1. The patient reports symptoms such as excessive daytime sleepiness, fatigue, insomnia, or other issues that impair sleep-related quality of life.
2. The patient experiences awakening episodes with breath-holding, gasping, or choking.
3. A bed partner or another observer notes habitual snoring or noticeable interruptions in breathing during the patient's sleep.[13]

B. Sleep study findings (via Polysomnography [PSG] or Home Sleep Apnea Testing [HSAT]) show:

1. Five or more predominantly obstructive respiratory events per hour of sleep (in PSG) or per hour of recording time (in HSAT). These events include obstructive apneas, mixed apneas, hypopneas, or respiratory effort-related arousals (RERAs).[13]

OR

C. Sleep study (PSG or HSAT) demonstrates:

1. Fifteen or more predominantly obstructive respiratory events (including obstructive and mixed apneas, hypopneas, or RERAs) per hour of sleep (PSG) or monitoring (HSAT), regardless of symptoms.[13]

Levels of Sleep Study

The evaluation of sleep-disordered breathing (SDB), including obstructive sleep apnea (OSA), relies on objective measurements of sleep and associated physiological parameters. The American Academy of Sleep Medicine (AASM) has categorized sleep studies into four diagnostic levels based on the number and type of monitored variables and the presence of technical supervision. These are commonly referred to as Level I to Level IV sleep studies.[106]

Level I: In-laboratory Polysomnography (PSG)

This is the gold standard for the diagnosis of OSA and other forms of SDB. It is conducted overnight in a sleep laboratory under direct supervision by trained technologists. Level I studies are fully attended and monitor a minimum of seven channels, including:

- Electroencephalogram (EEG)
- Electrooculogram (EOG)

- Electromyogram (EMG – chin and limb)
- Electrocardiogram (ECG) or heart rate
- Airflow (oronasal thermistor and nasal pressure transducer)
- Respiratory effort (thoracic and abdominal belts)
- Oxygen saturation (pulse oximetry)

This comprehensive monitoring enables differentiation of sleep stages, detection of arousals, and accurate classification of respiratory events, including apneas, hypopneas, and respiratory effort-related arousals (RERAs) [13,35,107].

Level II: Unattended Full PSG

This includes the same channels as Type I PSG, but are performed without a technologist present. These are typically used in research settings or in limited clinical applications where in-lab studies are not feasible. Though technically equivalent to Type I, data quality may be compromised due to the absence of real-time technician intervention. [108]

Level III: Limited Channel Monitoring (Portable Sleep Testing)

Level III studies are portable diagnostic devices used primarily in home sleep apnea testing (HSAT). These devices typically record a minimum of four parameters:

- Airflow
- Respiratory effort
- Heart rate or ECG
- Oxygen saturation

Type III devices do not include EEG, and therefore cannot determine sleep stages or arousals. As a result, they tend to underestimate the apnea-hypopnea index (AHI), as total recording time is used instead of total sleep time.[109] Despite this, Type

III testing is widely accepted for diagnosing moderate-to-severe OSA in patients with high pre-test probability, especially in resource-limited settings. [110]

Level IV: One or Two Parameter Monitoring

Level IV devices record one or two parameters, typically including pulse oximetry and/or airflow. They are the least comprehensive of all modalities and are not recommended as standalone diagnostic tools due to poor sensitivity and specificity. [106] These may serve as preliminary screening tools in high-volume or remote settings but require confirmation with higher-level testing.

Treatment of Obstructive Sleep Apnea (OSA)

Effective management of OSA necessitates a comprehensive, patient-centered approach that treats the condition as a chronic disorder. In addition to targeting upper airway obstruction, a successful treatment strategy also involves managing coexisting sleep disorders and systemic comorbidities. The primary goal is to optimize sleep quality and minimize OSA-related morbidity through a multimodal therapeutic framework.[111]

1. Positive Airway Pressure (PAP) Therapies

Continuous Positive Airway Pressure (CPAP)

CPAP remains the first-line treatment for moderate to severe OSA. It delivers a continuous stream of pressurized air via a mask interface to maintain upper airway patency during sleep. CPAP therapy has demonstrated robust efficacy in reducing the frequency of apneas and hypopneas, improving sleep continuity and quality of life [112,113].

Bilevel Positive Airway Pressure (BiPAP)

BiPAP provides two pressure settings—higher during inspiration (IPAP) and lower during expiration (EPAP)—and is generally reserved for individuals who are intolerant to CPAP or those with complex conditions such as obesity hypoventilation syndrome (OHS), central sleep apnea (CSA), or neuromuscular diseases [114].

Auto-adjusting Positive Airway Pressure (APAP)

APAP devices automatically modulate the delivered pressure based on real-time airflow and airway resistance. These devices enhance patient comfort and adherence by minimizing unnecessary pressure during sleep. However, they are not recommended in patients with significant cardiopulmonary comorbidities such as OHS, CSA, Cheyne–Stokes breathing (CSB), or COPD, due to insufficient validation in these populations.[106]

Average Volume-Assured Pressure Support (AVAPS)

AVAPS is a hybrid ventilatory modality that maintains a consistent tidal volume by adjusting inspiratory pressure within a preset range. It is particularly effective for patients with fluctuating respiratory effort, offering stable ventilation and improved long-term comfort. [6]

2. Oral Appliances

Mandibular Advancement Devices (MADs)

MADs function by repositioning the mandible and tongue anteriorly to expand the upper airway. These devices are primarily indicated for patients with mild to moderate OSA or those unable or unwilling to adhere to CPAP therapy. While not as effective as CPAP in reducing AHI, MADs can offer clinically significant improvements in symptoms and quality of life.[7]

3. Expiratory Positive Airway Pressure (EPAP) Devices

Nasal EPAP (nEPAP)

nEPAP utilizes a unidirectional valve that increases expiratory resistance, thereby elevating functional residual capacity and reducing upper airway collapsibility. Although trials have demonstrated reductions in AHI, issues related to long-term tolerability and adherence remain under investigation.[106]

4. Pharmacological Therapies

Although no pharmacologic agent has been approved as a standalone treatment for OSA, several medications are used adjunctively to alleviate symptoms such as excessive daytime sleepiness or to enhance upper airway stability.

- **Modafinil** and **Solriamfetol** are wake-promoting agents effective in reducing residual sleepiness despite adequate CPAP therapy [105,106].
- **Protriptyline**, a tricyclic antidepressant, has shown some potential in improving pharyngeal muscle tone during sleep [107].
- **Acetazolamide**, a carbonic anhydrase inhibitor, is beneficial in patients with central sleep apnea or altitude-induced periodic breathing by stimulating ventilation.[108]
- **Doxapram**, a respiratory stimulant, increases ventilation by activating peripheral chemoreceptors but is primarily used in acute settings.[109]
- **Orexin receptor antagonists** are under investigation for their role in enhancing sleep consolidation and reducing arousals in OSA.[110]
- **Sildenafil** has been studied for its effects on upper airway tone and pulmonary hemodynamics; however, its role in OSA management remains controversial.[111]

5. Surgical Interventions

Surgical therapy is considered in selected patients who do not respond to or tolerate conservative management and have identifiable anatomical contributors to upper airway collapse.

- **Uvulopalatopharyngoplasty (UPPP)** and **genioglossus advancement (GA)** are traditional surgical options aimed at enlarging the airway.[112]
- **Bariatric surgery** is effective in patients with morbid obesity and has been shown to significantly reduce OSA severity.[113]
- **Robotic-assisted upper airway surgeries** offer enhanced precision and reduced recovery time, representing a minimally invasive alternative in appropriate candidates.[114]

6. Hypoglossal Nerve Stimulation (Inspire Therapy)

- This surgically implanted device stimulates the hypoglossal nerve during inspiration, thereby activating upper airway dilator muscles and preventing airway collapse. It is indicated in patients with moderate to severe OSA who are CPAP-intolerant and meet specific anatomical and polysomnographic criteria.[115]

7. Telemedicine and Digital Health

- Advances in telemonitoring have improved CPAP adherence by allowing remote troubleshooting, device adjustment, and patient support. Real-time compliance tracking through telehealth platforms has shown efficacy in increasing treatment continuity and outcomes.[116]

8. Precision Medicine in OSA

- Emerging research on OSA phenotyping and genotyping holds promise for individualized therapy. Tailoring treatment based on endotypes, biomarkers, and patient characteristics may improve efficacy and reduce adverse outcomes in the future.[117]

Definition and Classification of REM-Related OSA

- REM-related Obstructive Sleep Apnea (REM OSA) refers to a phenotype of OSA in which the vast majority of apneas and hypopneas occur during rapid eye movement (REM) sleep, with relatively few events in non-REM (NREM) sleep. In practical terms, patients with REM-predominant OSA have minimal or no obstruction in NREM but significant worsening once they enter REM sleep. By contrast, NREM-predominant OSA, describes patients whose obstructive events occur mainly in NREM sleep with relatively spared REM periods. Clinically, the term "REM-related OSA" is applied when polysomnography (PSG) demonstrates a clear predominance of obstructive events in REM sleep.
- This stage-specific vulnerability is rooted in the unique physiology of REM sleep. REM is normally accompanied by nearly complete atonia of skeletal muscles (except the diaphragm and extraocular muscles) due to pontomedullary inhibitory circuits.[28] The upper airway dilator muscles (e.g. genioglossus) lose tone beyond what is seen in NREM, because REM sleep causes both tonic suppression of motor output and withdrawal of excitatory noradrenergic and serotonergic drive to upper airway motor neurons. As a result, individuals susceptible to airway collapse may have a patent airway during NREM sleep but experience obstruction once the REM-related atonia sets in. Apneas in REM tend to last longer and cause greater

oxygen desaturation compared to those in NREM, due to continued respiratory effort against an occluded airway and a higher arousal threshold during REM. In NREM, muscle tone is reduced relative to wake state but it is higher than in REM, and arousability is greater; thus some OSA patients experience significant events only in REM sleep, whereas others have events across all stages.

Diagnostic Criteria: There is no single universally adopted definition of REM-predominant OSA, and various operational criteria exist in the literature. The most commonly used criterion is a REM AHI at least double the NREM AHI (REM AHI / NREM AHI ≥ 2). This ratio-based definition labels a patient as REM-predominant if their obstructive event index in REM is disproportionately higher than in NREM. Broadly, this approach does not require a minimum amount of REM sleep during the study – it simply relies on the REM-to-NREM ratio.

More strict definitions are required to avoid missing diagnosis of sleep apnea in all stages. One strict definition is: overall AHI ≥5, REM/NREM AHI ≥2, and NREM AHI <5. This identifies patients whose breathing is essentially normal in NREM and disordered only in REM. A more moderate strict criterion allows NREM AHI up to 15 (to exclude moderate-to-severe NREM OSA) while still requiring REM/NREM AHI ≥2. Many studies also require a minimum REM sleep duration (commonly ≥20 or 30 minutes) to confidently label REM OSA. These stricter criteria yield a smaller, more specific subset of “true” REM-only OSA cases, whereas the broad definition captures a larger proportion but may include patients with some NREM disease. In research and clinical practice, both broad and strict definitions are employed. For consistency, some investigators apply both criteria to see how each affects prevalence and outcomes.

- It should be noted that the American Academy of Sleep Medicine (AASM) does not currently recognize "REM-related OSA" as a distinct diagnostic category in its nosology. However, the AASM Manual for the Scoring of Sleep and Associated Events recommends reporting stage-specific AHI values, which enables identification of REM-predominant patterns. Modern PSG reports typically list "REM AHI" and "NREM AHI" in addition to the total AHI.Therefore, REM OSA should be considered as a separate entity to enable further detailed study to understand the clinical significance.

Prevalence of REM-Related OSA

Overall Prevalence: Reported prevalence rates of REM-predominant OSA vary widely (approximately 10% to 50% of OSA cases) due to differences in definitions and populations studied. Early analyses suggested roughly 10–36% of OSA patients have REM-related OSA, with the lower end reflecting very strict criteria of pure REM-only OSA and the upper end reflecting broad criteria. For example, using a broad definition (REM/NREM AHI ≥2 with no minimum REM duration), many patients with overall mild OSA meet REM-predominant criteria, inflating prevalence. Under a strict definition (minimal NREM events required), only a subset of those patients, essentially those with isolated REM apnea, are counted.

One large U.S. clinical cohort by Koo et al.[118] (Cleveland Clinic, n=1,540) found about 14.4% of all OSA patients (AHI ≥5) met criteria for REM-related OSA when requiring REM/NREM AHI >2 and NREM AHI <15. In that sample, REM OSA was disproportionately common in women: 24.5% of female OSA patients had REM-predominant OSA versus 7.9% of male patients. Younger adults also had more REM OSA. Women under 55 had a 27.2% prevalence of REM OSA in OSA patients

compared to 18.6% in older women, and men under 55 had 9.9% versus 4.5% in older men. These data highlight that a younger, more female predominant subset of OSA patients often manifest the REM-predominant phenotype.

More recent studies in diverse populations corroborate these trends. For example, in a study conducted by Lee et al[119], the South Korean clinic cohort (n=692, mean age ~50) reported REM-predominant OSA in 20.2% of OSA patients (using criteria AHI >5, REM/NREM AHI ≥2, NREM AHI <15). In this study, 53.6% of the REM OSA group were female, even though women were only 28% of the total OSA sample . The REM-predominant pattern was present in nearly 70% of patients with mild overall OSA and ~30% of those with moderate OSA, but was uncommon in those with severe OSA. Similarly,in a study conducted by Sattaratpaijit N [120] et al, the Thai cohort (n≈400) found ~21–22% prevalence of REM-related OSA by similar criteria, with women about twice as likely as men to have REM-predominance (roughly 29% vs 16%). Another large study from Saudi Arabia (n=609) conducted by Qanash S[121] et al vividly demonstrated how prevalence depends on definition: using a very strict definition, ~26% had REM OSA (36% of women vs 18% of men), using a moderate definition 33% (48% of women vs 22% of men), and using a lenient ratio-only definition, fully 52% of OSA patients were classified as REM-predominant (almost 70% of female patients, ~35% of male). Thus, in some populations, particularly those with many mild cases or a high proportion of female patients, over half of OSA patients could be labelled REM-predominant if broad criteria are applied.

Notably, a recent study from India reported an especially high proportion of REM-related OSA. Nair et al. (2022)[120] found that 56.3% of patients with sleep-disordered breathing met criteria for REM-predominant OSA by broad definition.

Even using a strict definition, 25.3% of their sample had REM OSA. This high prevalence likely reflects a relatively young, non-obese referral population and inclusion of many mild OSA cases. It underscores that REM-predominant OSA is not a rare curiosity but rather a common phenotype, especially in cohorts with more women or milder disease. There may also be ethnic and anatomic factors: for instance, some evidence suggests African-Americans have higher REM OSA prevalence than Caucasians, and Asian patients develop OSA at lower BMI with relatively less anatomical compromise, manifesting more as stage-dependent OSA as demonstrated by Conwell et al[12]. However, further data are needed to confirm ethnic differences.

A major methodological factor in prevalence estimates is the type of sleep study. Many older studies did not account for stage-specific apnea burden because they used home sleep apnea tests (which lack EEG staging) or split-night studies (where REM sleep may be curtailed by early CPAP titration). These approaches can undercapture REM OSA. For example, REM episodes often occur in the later third of the night; in a split-night PSG, a patient might have only NREM-dominant sleep during the diagnostic portion, and then CPAP is started, effectively "missing" REM-related events. Koo et al.[118] and Appleton et al.[123] both found that split-night protocols missed a significant number of REM OSA cases – particularly in demographics prone to REM OSA such as younger individuals and women. Thus, full-night PSG is preferable when REM OSA is suspected. Going forward, large-scale population studies with full PSG and standardized definitions will be needed to accurately quantify REM OSA prevalence across different groups. In summary, depending on definition, REM-predominant OSA may comprise anywhere from about one-tenth to

over one-half of all OSA cases. Even with reasonably strict criteria, roughly 15–30% of OSA patients in many cohorts have a REM-OSA which warrants clinical attention.

Pathophysiology of REM-Related OSA

REM-related OSA arises from a confluence of neurophysiological changes that make the upper airway uniquely vulnerable during REM sleep. REM sleep (also called "paradoxical sleep") is characterized by an activated EEG with dreaming, but also by almost complete skeletal muscle paralysis.[124] Several key REM-specific mechanisms contribute to airway collapse in susceptible individuals:

- **REM Atonia and Upper Airway Muscle Inhibition:** During REM, brainstem circuits in the pons, actively suppress motor output, causing near-total atonia of postural muscles.[124] This extends to upper airway dilators like the genioglossus. O'Donoghue and colleagues demonstrated that in REM sleep, the genioglossus shows markedly reduced responsiveness to negative pressure, failing to activate when the airway starts collapsing. In NREM, a negative airway pressure reflex triggers dilator activation to stent the airway; in REM, this protective reflex is blunted. The genioglossus and other pharyngeal muscles thus lose both tonic and reflexive tone in REM. The combination of withdrawal of excitatory drives (noradrenaline, serotonin) and active inhibition via glycine/GABA results in a highly collapsible airway during REM.[124] Essentially, REM "takes away" the usual muscle support that keeps the pharynx open, tipping the balance toward collapse.
- **Increased Upper Airway Collapsibility (Elevated Pcrit in REM):** The critical closing pressure of the pharynx (Pcrit) quantifies intrinsic airway collapsibility. A higher (less negative) Pcrit means the airway tends to collapse

more easily. Studies have shown Pcrit is significantly higher during REM sleep than NREM in OSA patients. Carberry et al. (2016)[6] found that REM sleep increased passive Pcrit by ~2–5 cm H_2O versus NREM, indicating a more collapsible airway. During REM, phasic activity of dilators like the tensor veli palatini and genioglossus is further reduced compared to NREM. For a person with a borderline anatomical airway (e.g. mild retrognathia or soft tissue crowding), this REM-induced loss of muscle support can push them from compensation to obstruction.

- **Ventilatory Drive Uncoupling (Neuromechanical Uncoupling):** Ordinarily, rising inspiratory effort during an apnea should recruit airway muscles or cause arousal to reopen the airway. In REM, this compensatory mechanism is blunted. Heinzer et al[84] described a phenomenon of "neuromechanical uncoupling" in REM OSA: the brain's respiratory centers drive the diaphragm harder as CO_2 rises, but the pharyngeal muscles do not respond due to REM atonia. Consequently, an individual can generate very large negative intrathoracic pressures during a REM apnea without breaking the apnea until an arousal finally occurs. The diaphragm and chest wall strain against a closed airway ("insufflation against a closed glottis"), but the tongue and soft palate remain flaccid. This uncoupling means that even strong ventilatory drive cannot compensate for the REM-related loss of muscle tone, prolonging the obstruction.
- **Altered Arousal Threshold and Chemoresponsiveness:** REM sleep has a higher arousal threshold for respiratory stimuli than NREM. The ventilatory responses to hypoxia and hypercapnia are also lowest in REM (only ~30% of the response seen in quiet wake). Thus, during an obstructive event in REM,

the body "tolerates" a longer apnea with deeper hypoxemia before arousal. Punjabi et al.[4] observed that apneas in REM are often prolonged and accompanied by severe oxygen desaturation. Esophageal pressure (a measure of effort) must drop more i.e. more negative intrathoracic pressure, to induce arousal in REM than in NREM. This delayed arousal contributes to longer apnea duration and greater oxyhemoglobin desaturation in REM. Additionally, functional residual capacity (FRC) is reduced in REM due to intercostal muscle relaxation and shallow breathing, so oxygen stores are smaller. The net effect is that REM apneas can last significantly longer (often 30–60 seconds or more) and cause larger O_2 drops than NREM apneas in the same patient.

- **Stable Loop Gain:** Ventilatory control stability (loop gain) is one contributing factor to OSA. A high loop gain means the respiratory control system tends to oscillate which predisposes to central apneas or periodic breathing. REM sleep is generally associated with a lower loop gain than NREM. This implies REM OSA is less about an unstable chemoreflex and more about mechanical collapse. In fact, REM OSA patients often have relatively stable breathing control; their primary issue is anatomical collapse under REM atonia. Treatments aimed at lowering loop gain (e.g. oxygen therapy, acetazolamide) may not fully resolve REM OSA, because the root problem is structural (airway patency) rather than respiratory overshoot/undershoot.

The profound atonia and inhibition of airway dilators, heightened collapsibility, failure of compensatory reflexes, and prolonged event durations all make REM a high-risk period for airway obstruction. In patients who have REM OSA, the usual defenses that keep the airway open during NREM are overwhelmed once REM sleep begins. REM sleep thus "unmasks" OSA in those who might

otherwise have no apnea in non-REM. Clinically, this explains why younger or premenopausal female patients with good muscle tone during NREM can still have significant OSA confined to REM. REM OSA should be viewed as more than an epiphenomenon of mild OSA which has unique mechanistic underpinnings with implications for diagnosis and therapy.

Polysomnographic Features of REM-Predominant OSA

PSG findings in REM-predominant OSA reflect the restriction of events to REM sleep and relative normalcy in NREM:

- **Sleep Architecture:** REM-predominant OSA patients typically maintain normal architecture during NREM, since breathing is unobstructed or only mildly disturbed outside REM. Total sleep time and sleep efficiency are often similar to those of non-stage-specific OSA patients. For instance, study conducted Bonsignore[10] et al found no significant difference in total sleep time (sleep efficiency (~88%) between REM-OSA and non-REM OSA patients. Sleep latency and REM latency are usually unaffected, indicating REM OSA patients do not generally have difficulty initiating sleep or entering REM. The key distinction is in the distribution and continuity of REM sleep. By definition, REM OSA patients may have normal amounts of REM (~20–25% of sleep) but that REM is fragmented by arousals. In some cases, if apneas repeatedly terminate REM, the overall REM percentage may be slightly reduced. However, many mild REM OSA patients still achieve a normal proportion of REM because their REM apneas, while present, are not so frequent as to drastically cut total REM time. Some individuals may even show a relatively high REM percentage—if NREM is very stable and OSA only manifests once in REM. Thus, it is not universally true that REM OSA

patients have less REM sleep; some have a normal REM quantity, but it may be broken into shorter episodes by respiratory arousals.

- **REM Fragmentation:** Each apnea/hypopnea in REM typically terminates with an arousal (a shift to lighter sleep or brief awakening) to reopen the airway. In REM OSA, REM sleep is thus repeatedly interrupted, leading to fragmented REM. Patients often cannot sustain long uninterrupted REM periods; instead, REM is broken into multiple brief episodes. This fragmentation can reduce the restorative value of REM and impair REM-dependent functions (memory consolidation, emotional regulation). In OSA patients , all stages maybe affected.In fact, the overall arousal index in REM-predominant OSA can be lower than in stage-independent OSA because of long stretches of undisturbed NREM. One analysis found the mean arousal index was ~18.5/hour in a REM-predominant group vs ~38.3/hour in those with NREM-predominant OSA.
- **Apnea/Hypopnea Characteristics:** Obstructive events during REM tend to be longer in duration and cause deeper oxygen desaturations than those in NREM. The higher arousal threshold in REM allows apneas to persist until more severe blood gas derangements accumulate. It's common to see REM apneas lasting 30–60 seconds or more, whereas the same patient's NREM apneas might terminate after 10–20 seconds. Findley et al.[126] first reported that apnea duration and oxyhemoglobin desaturation were significantly greater in REM sleep than NREM in OSA patients. Often the lowest oxygen saturation of the night occurs during a REM apnea. For example, a patient might only drop to 90% during NREM apneas but fall to 80% during a REM apnea. Punjabi and colleagues[7] similarly noted REM apneas are frequently

"prolonged and accompanied by severe desaturation". Another characteristic is the pronounced autonomic response at the end of REM apneas: the combination of hypoxia and sudden arousal from REM triggers large sympathetic surges, with heart rate and blood pressure spikes that are often larger for REM apneas than NREM events. On the PSG, one may see exaggerated tachycardia following a REM apnea termination. These physiologic stresses i.e greater hypoxemia and sympathetic activation underscore why REM OSA might carry specific cardiovascular risk despite an often mild overall AHI.

- **Stage-Specific Indices:** In REM-predominant OSA, the PSG report will show a high REM AHI and a low NREM AHI, sometimes with a dramatic ratio. The overall AHI of the REM-predominant patient would then be relatively low whereas NREM AHI is normal. This can underestimate true severity if one looks only at the total AHI. It is essential for clinicians to examine stage-specific indices. Many sleep labs now routinely report REM AHI and NREM AHI for this reason. Similarly, the oxygen desaturation index (ODI) i.e desaturations per hour, can be skewed low in REM OSA because desaturations occur only in REM (a quarter of the night) and are absent in NREM. For instance, one study noted overall ODI ~10/hour in a REM OSA group vs ~38/hour in a non-REM OSA group. Yet the severity of individual desaturation events can be high in REM OSA. A REM OSA patient might have a few desaturations to 75–80%, but if they occur only a couple times per hour and only during one phase of the night, the ODI and cumulative time <90% will appear modest. Thus, REM-predominant OSA often looks like "mild OSA with occasional large desaturations" on summary metrics.

REM OSA patients often have high-quality sleep during NREM, leading to near-normal sleep continuity and possibly fewer daytime symptoms. Their REM sleep, however, is repeatedly disrupted by prolonged apneas and deep desaturations. Recognizing this pattern on PSG is crucial. It requires that the study capture adequate REM sleep – if very little REM is recorded, one cannot exclude REM OSA. A minimum of 20–30 minutes of REM is often needed; otherwise a repeat PSG might be warranted if clinical suspicion for REM OSA is high. When interpreting the PSG, one should specifically note if significant desaturations or long events are confined to REM.

Clinical Correlates and Health Consequences of REM OSA

Daytime Sleepiness and Neurocognitive Effects

Usually, because REM OSA patients may have long stretches of normal breathing during NREM, one might expect less fragmentation of sleep and thus less daytime sleepiness. Evidence to date suggests that many REM OSA patients, especially if their overall AHI is low, indeed report less daytime sleepiness than patients with equivalent overall AHI who have events throughout all stages. Many REM OSA patients have an Epworth Sleepiness Scale (ESS) score in the normal range (≤10). In one cross-sectional study conducted by Oweidat et al[127], the average ESS in REM-predominant OSA patients was ~8.7, virtually identical to that of patients with NREM-predominant OSA (~9.7) – both indicating only mild subjective sleepiness. Large community studies such as the Sleep Heart Health Study also found that REM AHI by itself was not independently associated with excessive daytime sleepiness after controlling for total AHI and other factors.[8]

The overall AHI in REM OSA is often mild. Some patients do report specific complaints like unrefreshing sleep, morning headaches, or difficulty with morning

alertness, which may relate to the cluster of events in the early morning hours (when REM is concentrated). REM sleep is important for cognitive processes such as memory consolidation and emotional regulation. Repeated fragmentation of REM over time might lead to subtle deficits even if the person doesn't notice frank sleepiness. Taan et al[128] have linked REM OSA to neurocognitive changes like reduced attention, executive dysfunction, or memory impairment, even if patients do not report significant sleepiness. A recent critical review by Della Monica C[129] et al highlighted that REM sleep disruption could disproportionately affect mood and cognitive domains, given REM's role in emotional processing and brain restoration. Clinicians should therefore not equate "no daytime sleepiness" with "no impact" because a patient with REM OSA might still have cognitive or mood issues that are more subtle than overt sleepiness.

Mood and Psychiatric Correlates

REM sleep has strong links to mood regulation; it is the phase when most vivid dreaming occurs and is sometimes called "paradoxical sleep." Repeated arousals from REM and intermittent hypoxia can interfere with these processes. Some research suggests REM-predominant OSA is associated with higher rates of depressive and anxiety symptoms. For instance, one longitudinal cohort found untreated OSA was independently associated with depression in females but not in males – speculating that females (who more often exhibit REM-predominant OSA) might be particularly affected by OSA's impact on mood. Other work has shown that treating OSA can improve depression scores, implying a causal link. Krakow et al.[96] reported that REM-related OSA patients had significant alleviation of depression ratings after continuous positive airway pressure (CPAP) therapy, underscoring that disturbed REM sleep likely contributed to their mood symptoms. Clinically, it is reasonable to

inquire about mood disturbances in patients with REM OSA. While causality is not fully proven, the association is notable. Successful REM OSA treatment may confer mental health benefits – an aspect under active study.

Cardiovascular Risks

There is growing evidence that REM-specific OSA may carry unique **cardiovascular risk**. Two major longitudinal cohorts – the Wisconsin Sleep Cohort and the Sleep Heart Health Study[8] – found that apnea burden during REM sleep was significantly associated with hypertension, whereas apnea burden during NREM was not, after adjusting for confounders. In the Wisconsin cohort, individuals with OSA primarily during REM had higher odds of prevalent hypertension than those with equivalent overall AHI concentrated in NREM. Mokhlesi et al. (2014) analyzed the Wisconsin data and showed a dose-response: a REM AHI ≥15 was linked to significantly higher odds of hypertension, and in those with minimal NREM events (NREM AHI ≤5), each doubling of REM AHI raised the odds of hypertension by ~24%. [8] Non-REM AHI, in contrast, was not a significant predictor of hypertension in any model.[8] Similarly, Appleton et al. (2016)[9] reported that unrecognized OSA confined to REM sleep was associated with hypertension in a community sample of men; notably, men with overall AHI <10 still had greater prevalence of hypertension if their REM AHI was high (≥20)[9]. The proposed mechanism is that the episodic surges in blood pressure at the end of REM apneas (due to arousal and sympathetic discharge), night after night, promote sustained increases in sympathetic tone and vascular remodeling. Over years, this could lead to clinical hypertension even if the person's overall AHI is modest.

Beyond blood pressure, researchers have examined "hard" cardiovascular outcomes. A 2018 analysis of Sleep Heart Health Study data by Mokhlesi et al[8] found

that severe REM OSA (REM AHI ≥30) was associated with a ~2.5-fold increase in composite cardiovascular events (heart attack, stroke, revascularization, heart failure) in individuals who already had cardiovascular disease. Interestingly, in those without pre-existing heart disease, severe REM OSA did not significantly raise the incidence of new cardiac events over ~10 years. This suggests REM OSA may act as a factor which will be exacerbating underlying cardiovascular conditions and precipitating events, rather than solely causing disease in an otherwise healthy heart in the short-to-medium term. However, there are also indications of subclinical vascular effects: for example, patients with REM-predominant OSA have been found to have faster progression of carotid intima-media thickness (IMT), an early marker of atherosclerosis. In a cohort of middle-aged women, those with higher REM apnea burden showed greater carotid plaque buildup despite relatively mild overall OSA. A recent community-based study by Ljunggren et al. (2022) demonstrated that severe REM OSA was associated with a 9.9% thicker carotid intima compared to no REM OSA, and this association was significant in women but not in men.[130] These findings imply that selectively disrupting REM sleep (with its attendant hypoxemia and surges in blood pressure) can contribute to vascular endothelial dysfunction and atherogenesis.

While severe, multi-stage OSA is clearly linked to elevated cardiovascular risk, REM-predominant OSA presents a nuanced clinical picture. Patients with isolated REM OSA and a mild overall AHI may carry lower risk than those with severe, pan-sleep OSA, but potentially higher than those with minimal disease. This is particularly relevant in atrial fibrillation (AF), where events often occur during early morning REM sleep—frequently coinciding with periods of CPAP non-adherence. REM-specific fluctuations in blood pressure and intrathoracic pressure may promote

arrhythmogenesis. Although data delineating REM versus NREM contributions to arrhythmias are limited, some experts suggest that heart failure patients using CPAP for only part of the night may remain vulnerable to AF or premature ventricular contractions during untreated REM periods.[131] Further investigation is warranted to clarify these associations.

Metabolic and Endocrine Effects

REM sleep influences glucose metabolism and autonomic balance (through effects on sympathetic activity and hormones like cortisol, leptin, and ghrelin). Several studies have linked REM-predominant OSA with impaired glucose tolerance and insulin resistance. Chami et al. (2015)[131], analyzing the Sleep Heart Health Study[8], found that the severity of OSA during REM but not NREM, was associated with worse fasting and postprandial glucose levels and higher insulin resistance (HOMA-IR), after adjusting for BMI and waist circumference . In fully adjusted models, REM AHI remained significantly associated with elevated fasting glucose (~0.93 mg/dL per doubling of REM AHI) and 2-hour glucose (~3.0 mg/dL higher per doubling of REM AHI), whereas NREM AHI showed no such association . Chami et al concluded that REM-related OSA contributes to metabolic dysregulation, likely via sympathetic surges and intermittent hypoxemia during REM that adversely affect glucose homeostasis .

Similarly, Grimaldi et al. (2014)[133] studied diabetics and observed that those with more REM-related apnea had higher HbA1c levels despite similar overall OSA severity. Their model predicted that using CPAP only 4 hours/night (covering ~40% of REM) would yield minimal HbA1c improvement (~0.2–0.3%), whereas using it ~7 hours/night (covering >85% of REM) could reduce HbA1c by up to 1%). These data suggest REM OSA, by causing recurrent bursts of sympathetic activation, which

promote hepatic glucose release and peripheral insulin resistance and by fragmenting the REM sleep important for metabolic regulation, may hinder glycemic control. Treating OSA in patients with prediabetes or diabetes has shown modest improvements in glucose metabolism, with some analyses noting the improvement was greatest in those whose OSA was predominantly in REM.

REM OSA may also contribute to dyslipidemia and metabolic syndrome features, though data are less robust. Chronic intermittent hypoxia (especially if predominantly during REM) can induce oxidative stress and inflammation affecting the pancreas and adipose tissue. There is speculation that REM sleep loss and surges of catecholamines might alter cortisol rhythms, promoting visceral fat deposition and metabolic dysregulation. In addition, weight gain and increased fat, for example, with aging or menopause, can turn a formerly REM-specific OSA into a more generalized OSA – relationships are complex and bidirectional. In any case, given the links to insulin resistance and hypertension, REM OSA likely contributes to overall cardiometabolic risk.

Quality of Life and Functional Status

Many REM-predominant OSA patients have relatively preserved daytime function, especially if total sleep quantity is maintained. As noted, their Functional Outcomes of Sleep Questionnaire (FOSQ) scores or generic quality-of-life measures may be near-normal if they are not excessively sleepy. In large studies, after accounting for total AHI and sleepiness, REM AHI often does not show an independent effect on general quality of life. However, some patients report more subtle issues e.g. feeling less refreshed on waking, morning grogginess, or mild memory/concentration difficulties which they attribute to poor sleep. These may not severely impair daily function but can reduce one’s sense of well-being. There is also

concern about long-term neurocognitive consequences. One study[134] found older adults at risk for Alzheimer's disease had stronger associations between REM OSA severity and poorer memory performance, raising the possibility that untreated REM OSA in midlife could accelerate amyloid accumulation or neurodegeneration. REM sleep is believed to support the brain's lymphatic waste clearance; disrupting it repeatedly might have cumulative effects on brain health.

From a safety standpoint, because many REM OSA patients are not very sleepy, their risk of drowsy driving or work accidents is generally lower than that of all stage OSA. However, caution is still warranted: even mild OSA can degrade performance on subtler cognitive tasks. Early morning hours (5–6 AM) might be a period of vulnerability if a REM OSA patient had apneas toward morning and then drives shortly after awakening. There is no direct data showing increased car accidents specifically in REM OSA, but clinicians should individualize advice based on each patient's symptoms and occupation.

In summary, REM-predominant OSA can have significant clinical correlations which go unrecognised.

Clinical Significance and Diagnostic Considerations

Recognizing REM-related OSA as a distinct phenotype has important implications for patient management and risk assessment:

Symptom Discrepancy and Underdiagnosis

REM-predominant OSA is often underrecognized due to a deceptively low total AHI. Patients may be misclassified as having mild OSA despite significant respiratory events confined to REM sleep, leading to symptoms such as unrefreshing sleep, morning headaches, and daytime fatigue. For example, a patient with an AHI of 8 may have nearly all events during REM, resulting in substantial clinical impact

despite a “mild” diagnosis. Conversely, because NREM periods are unaffected, some REM OSA patients report less daytime sleepiness compared to those with similar AHI distributed across all stages. This highlights the limitation of total AHI as a sole measure of disease severity in REM-predominant phenotypes.

Therapeutic Implications and PAP Adherence

REM sleep predominates in the early morning, a period often missed in patients with suboptimal PAP adherence. In REM OSA, this pattern results in inadequate treatment of the most vulnerable sleep phase. Identifying REM-predominant OSA is thus essential to stress the need for full-night PAP use and to ensure pressures are adequate to treat REM-specific events. Without this recognition, patients may be falsely reassured by a low treated AHI, despite persistent REM-related apneas.

Cardiometabolic Considerations

REM-related apneas are typically longer, with greater desaturations and sympathetic surges compared to NREM, potentially increasing the risk for hypertension, insulin resistance, and other metabolic disorders. This raises the question of whether patients with mild but REM-predominant OSA warrant treatment akin to those with moderate OSA. While guidelines remain inconclusive, emerging evidence suggests that REM OSA is not a benign variant and requires individualized management strategies.

Gender and Hormonal Factors:

Identifying REM OSA can direct attention to underlying factors such as hormonal status. Premenopausal women are more likely to have REM-predominant OSA, possibly because progesterone and other factors maintain better airway tone during NREM, but in REM that protective effect wanes. Such patients might see OSA

worsen after menopause. Awareness of this pattern could prompt proactive monitoring around the menopausal transition or consideration of hormone effects on sleep.

Neuropsychiatric comorbidities

REM-predominant OSA is linked to increased rates of depression, anxiety, and mild cognitive impairments. Clinicians are advised to screen for these neuropsychiatric symptoms, as treating REM OSA with PAP therapy may improve mood in some patients.

Overall, recognizing REM-predominant OSA influences how we interpret a patient's sleep study, how we counsel them about therapy (and the importance of adherence), and how we consider their long-term health risks. This phenotype underscores the need to look beyond the aggregate AHI and appreciate sleep-stage specific pathology.

Diagnosis of REM-Related OSA

Accurate diagnosis of REM-related OSA requires careful analysis of stage-specific data during polysomnography:

- **Full-night Polysomnography with Stage-Specific Analysis:** An attended, overnight PSG is the gold standard for identifying REM-predominant OSA, because it provides EEG to distinguish REM from NREM sleep. During scoring, apneas and hypopneas are tallied for the whole night (total AHI), but it is imperative that the report also break down event counts or AHI in REM vs NREM. The latest AASM scoring manual (v2.6) encourages reporting stage-specific AHI. If the lab report does not explicitly list REM AHI, the interpreting physician should calculate it i.e events in REM divided by REM sleep hours. Accurate sleep staging is crucial: misclassifying an epoch as REM

when it was actually N1, or vice versa, can falsely alter the REM AHI. Strict adherence to scoring rules like only score REM when clear REM EEG/eye movement criteria are met, is needed to avoid over- or under-diagnosis.

A pitfall is that if a patient has very little REM during the study, one cannot reliably assess REM OSA. Some studies set a threshold (e.g. ≥30 min REM required) for inclusion in REM OSA analysis. Clinicians should be cautious: if a diagnostic PSG shows overall mild OSA with virtually no REM sleep recorded (perhaps due to first-night effect or insufficient total sleep), but the history is suggestive of REM OSA (e.g. the patient is a non-obese woman with morning headaches), a repeat PSG or further evaluation may be warranted rather than assuming no REM OSA occurred.

1. **Split-Night Studies:**

   Split-night protocols, dividing the night into diagnostic and CPAP titration phases, often fail to detect REM OSA because REM sleep predominantly occurs in the latter part of the night. Patients with REM OSA frequently show mild apnea in early (mostly NREM) sleep, potentially leading to missed diagnoses. Studies (e.g., Koo et al., Appleton et al.) have confirmed this limitation, particularly in younger and female populations. Moreover, split-night studies may induce REM rebound—excessive REM sleep after CPAP withdrawal—which artificially inflates REM apnea metrics, as noted by Jordan et al. Thus, a two-night PSG approach is preferable when REM OSA is suspected.

2. **Home Sleep Apnea Tests (HSAT):**

   HSAT devices, limited by the absence of EEG monitoring, cannot differentiate between sleep stages or accurately measure REM-specific apneas. This can result in falsely low overall AHI scores despite significant REM-

related events. Clinical guidelines (AASM) suggest that when HSAT results conflict with clinical suspicion, an attended PSG is recommended, especially for patients with characteristics suggestive of REM OSA, such as younger women or individuals with mood disturbances.

3. **Clinical Screening Tools:**

   Traditional screening questionnaires (Epworth Sleepiness Scale, STOP-Bang, Berlin Questionnaire) primarily detect classic OSA risk factors (obesity, male gender, daytime sleepiness) and thus underestimate REM OSA risk. REM OSA patients—often non-obese, female, and less sleepy—may score low on these questionnaires. Additionally, mood assessments (e.g., depression inventories) are hypothesized as potential adjunctive tools but lack validation. Therefore, clinicians should maintain vigilance for REM OSA in patients with atypical OSA profiles but suggestive clinical symptoms.

4. **Emerging Diagnostic Modalities:** Research is exploring ways to detect

   REM-predominant OSA without full PSG. For instance, wearables that estimate sleep stages via actigraphy or peripheral arterial tone might one day help screen for stage-specific phenomena. Some experimental approaches use heart rate variability or mandibular jaw movement to infer REM periods and then correlate with respiratory events. As of now, these are not accurate enough for clinical diagnosis. Therefore, a lab-based PSG remains the definitive test for REM-related OSA.

In summary, diagnosing REM OSA hinges on capturing sufficient REM sleep and doing a stage-specific analysis of respiratory events. Clinicians should choose diagnostic strategies that maximize REM sampling (avoid split-nights if possible, favor full-night studies) and be aware of the limitations of abbreviated studies and

HSAT in this context. Once a PSG is done, one must examine the REM AHI (and REM desaturations) rather than relying solely on aggregate AHI – especially in patients who meet only mild overall criteria but have clinical hints of REM concentration. Proper identification of REM-predominant OSA ensures this subgroup is not overlooked not mismanaged as in many cases their overall AHI may be mild.

Management of REM-Related OSA

Therapeutic interventions for REM-predominant OSA generally mirror those for OSA in general, but with some tailored considerations given its stage-specific nature. The goal is to eliminate obstructive events during REM sleep (as well as any in NREM) and mitigate associated symptoms or risks. Key aspects include:

Positive Airway Pressure (PAP) Therapy

Continuous Positive Airway Pressure (CPAP) is first-line treatment for significant OSA and is equally effective for REM-related OSA. CPAP delivers pressurized air to splint the airway open. In REM OSA patients, CPAP can virtually abolish apneas and hypopneas during REM, just as in NREM. In fact, titration of CPAP pressure often targets the worst-case scenario – for REM OSA patients this is usually during REM sleep (especially REM in supine position late in the night). If a patient's airway is kept patent in REM, it will almost always be patent in NREM (which is less demanding). Studies have shown CPAP improves symptoms and objective outcomes in REM-predominant OSA to a similar degree as in typical OSA. Su et al.[135] (2012) compared functional outcomes in REM-OSA vs non-stage-specific OSA treated with CPAP and found no significant difference in improvement – both groups had reduced daytime sleepiness and improved vigilance. This indicates that if REM OSA patients do have symptoms or neurocognitive deficits, they benefit from treatment comparably to other OSA patients. CPAP also addresses the physiologic

stresses of REM OSA by preventing oxygen desaturations and sympathetic surges. For example, one study focusing on mood in REM OSA found CPAP led to significant reduction in depressive symptoms.

A particular issue is ensuring the CPAP pressure is adequate during REM. Because upper airway collapsibility is highest in REM, the required pressure might be determined by what is needed in that phase. If a titration study does not capture REM, or if an auto-CPAP is set too low, there's a risk that pressure is sufficient for NREM but insufficient for REM. Technologists performing titrations should ideally continue until the patient cycles through REM on CPAP, to verify no apneas occur, adjusting pressure upward if needed. Auto-titrating CPAP (APAP) devices can be advantageous – they will increase pressure when flow limitation or apneas are detected, which in REM OSA typically happens in the early morning hours. The APAP will then lower pressure during NREM periods when fewer events occur. This capability suits REM OSA's pattern and can result in a lower mean pressure over the night without compromising REM control. Interestingly, REM-predominant OSA patients sometimes have overall lower pressure needs than equivalent-severity non-REM patients, since their airway is not collapsible in NREM (and they tend to be less obese). Regardless, titration should individualize pressure to eliminate REM events.

Adherence Challenges: A significant challenge in treating REM OSA is patient adherence to CPAP. Because many REM OSA patients have only mild daytime symptoms, their perceived benefit from CPAP may be limited. They might not feel dramatically better. As a result, motivation to use CPAP consistently can be low. In one large clinical review by Koo B et al [136] of REM OSA patients, a high proportion either declined CPAP or were non-adherent long-term. For instance, Conwell et al. (2012)[12] reported that although CPAP was recommended to 88% of

REM-predominant patients, only about 66% proceeded with an actual titration study, and merely ~27% had documented adherence at 30 days . A prospective study in Saudi Arabia by Almeneessier et al. 2017[137] similarly found that after 1 year, only 23% of REM-predominant OSA patients were using CPAP ≥4 hours per night on most nights, significantly lower than the adherence rate in non-REM OSA patients . Common reasons cited include: discomfort with the mask for a problem perceived as mild, and side effects like nasal congestion or pressure marks that outweigh subtle benefits in the patient's mind. To improve adherence, patient education is key. Patients should be counselled that treatment is not solely for symptom relief but also for long-term health protection, including cardiovascular and neuropsychological outcomes. Emphasizing data linking REM OSA to hypertension and cardiovascular morbidity may reframe the rationale for CPAP use, especially since some patients perceive "mild OSA" as low risk [29,30]. Additionally, addressing comfort-related barriers such as mask refitting, heated humidification for nasal congestion, or pressure desensitization protocols is critical, particularly for REM OSA patients who may not experience immediate symptomatic improvement due to minimal daytime sleepiness.[139]

Newer CPAP devices equipped with telemonitoring capabilities and patient-facing feedback applications (e.g., usage report cards, gamification) have shown promise in enhancing adherence by increasing patient engagement.[140,141] Another essential factor is the timing and continuity of CPAP use. In REM OSA, therapeutic efficacy hinges on consistent use throughout the entire sleep period. Discontinuation of CPAP after the initial 3–4 hours leaves the REM-rich later sleep periods untreated, reducing overall benefit.[142] In a secondary analysis of the APPLES study, CPAP usage of ≥6 hours per night was associated with significantly improved blood pressure

control, presumably due to more complete coverage of REM periods. [143] Clinicians should specifically inquire about CPAP usage duration and patterns, as some patients may unconsciously remove the device during the early morning hours.[143] Behavioral strategies such as setting early morning alarms to monitor mask use or using nasal insufflation devices may help reinforce adherence.[144]

Oral Appliances and Lifestyle Modifications

For patients with mild to moderate REM-predominant obstructive sleep apnea (OSA) who are unable to tolerate continuous positive airway pressure (CPAP), oral appliance therapy represents a reasonable alternative. Mandibular advancement devices (MADs), which function by anteriorly repositioning the mandible and tongue, serve to enlarge the upper airway and reduce its collapsibility.[145] These devices have established efficacy in the management of mild-to-moderate OSA, although therapeutic response can vary based on individual craniofacial and upper airway anatomy.[146]

In REM-predominant OSA, the potential benefit of oral appliances is theoretically plausible, particularly given their ability to address anatomic collapse during periods of profound muscular atonia characteristic of REM sleep. Although there is a paucity of published data specifically evaluating MAD efficacy in REM-predominant OSA, the pathophysiological rationale remains strong—if the device is capable of maintaining airway patency during REM, the most vulnerable sleep stage, it would be expected to be at least equally effective during non-REM sleep.[147]

Many individuals with REM-predominant OSA fall within the mild overall AHI category (<15 events/hour), a group for whom oral appliances are commonly indicated.[148] Thus, in cases where CPAP is declined or poorly tolerated, a trial of a custom-fabricated MAD fitted by a qualified dental sleep medicine provider is a rational therapeutic approach.[149] Compared to CPAP, oral appliances are often preferred for their comfort, portability, and minimal intrusion, potentially translating to better adherence in selected patients.[150] However, side effects such as temporomandibular joint discomfort and dental occlusal changes must be considered, and efficacy in moderate-to-severe OSA is generally inferior to CPAP.[151] Nevertheless, for a subset of patients with mild REM-predominant OSA, oral appliance therapy may be sufficient to normalize the AHI and improve clinical outcomes.

Weight loss and lifestyle measures Positional Therapy

Lifestyle interventions, including weight reduction, are integral to the management of all forms of obstructive sleep apnea (OSA), including REM-predominant OSA. Although many REM OSA patients are overweight rather than morbidly obese, even a modest weight loss of approximately 10% can significantly reduce the apnea–hypopnea index (AHI) and, in some cases, lead to resolution of OSA.[152] For patients with mild REM OSA, a 4.5–9 kg weight reduction may enhance upper airway stability during REM sleep, potentially obviating the need for immediate positive airway pressure therapy.

Avoidance of alcohol and sedatives before bedtime is particularly relevant in REM OSA. Alcohol consumption further diminishes upper airway muscle tone, increases apnea duration, and deepens oxygen desaturations, thereby exacerbating

REM-predominant events by suppressing arousals and prolonging airway collapse.[153] Similarly, benzodiazepines and non-benzodiazepine hypnotics (Z-drugs) increase arousal thresholds and reduce pharyngeal dilator activity during REM sleep, potentially worsening OSA severity.[154V]Such agents should be avoided unless clinically essential.

In select patients with isolated REM OSA, mild symptoms, and an overall AHI <15, a strategy of initial watchful waiting with lifestyle optimization may be appropriate. Interventions such as weight loss and positional therapy may yield sufficient improvement to defer or avoid continuous positive airway pressure (CPAP) initiation.[155] However, active treatment should be considered if there are comorbidities—such as hypertension, type 2 diabetes, or significant nocturnal desaturation—or if behavioral modifications are impractical or unsuccessful.[156]

Positional therapy (PT) involves preventing the patient from sleeping supine, because supine sleep can aggravate OSA due to gravity-related airway narrowing. Many OSA patients have fewer events when sleeping on their side. In REM OSA, positional effects can interact with stage effects. REM sleep in supine position is often the worst-case scenario for apneas. If a REM-predominant patient is also positional (meaning their REM apneas occur mainly supine and largely resolve when lateral), then positional therapy can be a very useful non-invasive approach.[157]

It appears a subset of REM OSA patients – particularly women and those with lower BMI – exhibit supine-dependent REM OSA. In these individuals, anatomical collapsibility is not very severe, so in lateral postures, even in REM, the airway may stay open; but when supine, the tongue and soft tissues fall back under REM atonia, causing obstruction. Lee et al. (2019)[158] showed that in REM OSA patients, the supine

position significantly increased REM AHI and worsened oxygen nadirs, whereas in lateral sleep the REM AHI was much lower. Avoiding the supine position markedly reduced the REM-related AHI burden in those patients.[159]

Common positional therapy techniques include wearable devices or specialty belts that vibrate or alarm when the patient rolls supine (prompting them to shift), as well as the old-fashioned tennis ball sewn into the back of pajamas. Newer devices like the NightBalance buzzer or smartphone apps provide gentle feedback to encourage side-sleeping. Ravesloot et al. [158] reviewed that such positional devices can significantly reduce AHI in position-dependent OSA, and noted partial benefit in REM-predominant patients with supine tendencies. One study by Eijsvogel MM[159] et al found that using a vibrotactile positional trainer increased the percentage of sleep spent laterally and decreased supine REM episodes, with modest improvements in subjective sleep quality and sleepiness.[160]

However, not all REM OSA patients are positional. Many will have apneas in REM regardless of posture (muscle atonia alone can collapse the airway even on the side). In such cases, positional therapy won't be effective. It's important to determine if a patient's REM OSA is truly posture-dependent. This can be seen on their PSG by examining REM AHI in supine vs lateral positions. If REM AHI is high supine but near-zero when lateral, that patient is an ideal candidate for PT. If REM AHI is high in all positions, PT is not beneficial.[161]

Clinical Recommendations: For a REM-predominant OSA patient who demonstrates supine-dependent REM apneas, positional therapy can be considered – especially if they are unwilling to use CPAP or as an adjunct to partial CPAP use. One approach is a trial of a positional device for a few weeks and then reassessment

with monitoring. If successful, it might be combined with other measures (like an oral appliance) to further improve outcomes. Generally, PT is most effective as part of a multimodal strategy rather than a standalone cure, unless the positional effect is very strong and consistent.[162]

Oxygen Therapy and Pharmacotherapy (Investigational)

In patients intolerant to CPAP or oral appliances and experiencing significant desaturations, supplemental nocturnal oxygen may be considered as a palliative adjunct. While it mitigates hypoxemia-related risks such as arrhythmias by preventing oxygen nadirs during apneas, it does not resolve airway obstruction or arousals. In fact, supplemental oxygen may prolong apneas by delaying arousal due to attenuated hypoxia, potentially increasing CO_2 retention [56]. Hence, its use should be restricted to select cases—e.g., REM OSA patients with severe desaturations rejecting CPAP—administered cautiously (e.g., 1–2 L/min to maintain SpO_2 >88%) under close monitoring. Importantly, oxygen therapy targets oxygenation metrics but not the underlying pathophysiology of OSA.[164]

Pharmacologic interventions for REM OSA remain investigational. Given REM-related upper airway hypotonia, agents enhancing pharyngeal dilator activity have shown potential. A notable combination—atomoxetine and oxybutynin—has demonstrated reductions in AHI by increasing genioglossus activity through noradrenergic and antimuscarinic mechanisms.[165] This combination may hold particular promise for REM OSA, although existing data primarily involve men with moderate OSA. Another approach targets arousal threshold modulation using sedatives like low-dose eszopiclone. However, since arousal thresholds are inherently higher in REM sleep, such strategies may exacerbate hypoxemia in REM OSA.[125] At

present, pharmacotherapy remains off-label and experimental, requiring further evidence before clinical implementation.[166]

Surgical options—including uvulopalatopharyngoplasty (UPPP), tonsillectomy, nasal surgeries, and hypoglossal nerve stimulation—are reserved for anatomically predisposed or CPAP-intolerant patients.[157] While no surgery specifically targets REM OSA, addressing identifiable structural contributors (e.g., tonsillar hypertrophy, retrognathia) may reduce global upper airway collapsibility, indirectly benefiting REM events.[167] In younger patients with enlarged tonsils and REM-predominant OSA, tonsillectomy may offer curative potential due to higher REM sleep proportions in this demographic.[156]

Management of REM-predominant OSA requires individualized strategies. While asymptomatic patients with mild REM OSA may be monitored with lifestyle modifications, those with comorbidities such as hypertension or excessive sleepiness may benefit from CPAP [65]. The absence of specific REM OSA guidelines necessitates clinical judgment, integrating REM AHI severity, symptom burden, desaturation depth, and patient preferences. Shared decision-making and trial therapies can assist in optimizing outcomes.[168]

Evidence Gaps and Future Directions

Despite growing recognition of REM-related obstructive sleep apnea (REM OSA) as a distinct phenotype within the spectrum of sleep-disordered breathing (SDB), several critical knowledge gaps and uncertainties persist. These limitations hinder consistent diagnosis, therapeutic strategies, and policy formulation. The following domains highlight key areas requiring further investigation:

1. Lack of Standardized Diagnostic Criteria

Current literature employs varying definitions of REM OSA, leading to inconsistencies in prevalence estimates and outcome data. Some studies use broad criteria (REM AHI ≥2× NREM AHI)[169], while others incorporate stricter thresholds (e.g. REM AHI ≥15, NREM AHI <15, REM duration ≥30 minutes).[170] The absence of a universally endorsed definition limits comparability across studies and hampers meta-analyses.[171] A formal consensus, ideally endorsed by the American Academy of Sleep Medicine (AASM) or European Respiratory Society (ERS), is necessary to standardize case identification and reporting. Routine inclusion of REM-specific metrics in polysomnographic reports, including REM and NREM AHI, would also enhance diagnostic clarity in both clinical and research contexts.[171]

2. Limited Epidemiological Data in Diverse Populations

Most REM OSA prevalence studies are based on North American, European, or East Asian cohorts. There is a dearth of large, population-based data in underrepresented ethnic groups, particularly South Asians, who may have increased susceptibility due to craniofacial morphology at lower BMI thresholds.[172] Early findings, such as higher REM OSA prevalence in African American populations [173], warrant replication in larger, multiethnic samples. Furthermore, pediatric and adolescent populations remain underexplored, despite the high proportion of REM sleep in early life stages and observations of REM-predominant patterns following adenotonsillectomy.[174] Comprehensive epidemiological studies spanning age groups and ethnicities are essential to inform targeted screening and management strategies.

3. Prognostic Implications and Causal Relationships

While associations between REM OSA and adverse outcomes including hypertension, type 2 diabetes, and mood disorders—have been observed, causal inferences remain limited.[175] The therapeutic implications of treating isolated REM OSA, especially in patients with mild overall AHI, require further exploration. Short-term trials have indicated potential improvements in glycaemic control with CPAP therapy in REM-predominant OSA [176], but randomized controlled trials (RCTs) with long-term follow-up are needed to assess cardiovascular, metabolic, and neurocognitive outcomes. Ethical considerations pose challenges to withholding treatment, but carefully designed studies in asymptomatic or minimally symptomatic patients could offer clarity. Additionally, longitudinal cohorts could determine whether REM OSA serves as an early stage of generalized OSA progression, with implications for early intervention.[8]

4. Pathophysiological Mechanisms and Vulnerability Factors

Mechanistic studies of REM OSA are sparse. Animal models simulating REM-specific intermittent hypoxia could elucidate unique cardiovascular or neurocognitive sequelae.[177] Human neuroimaging might uncover REM OSA-specific patterns of neuronal injury or amyloid accumulation, potentially linking to neurodegenerative risk.[178]The disproportionate prevalence in females and younger individuals raises questions about hormonal modulation and neurophysiological vulnerability. Progesterone therapy trials in postmenopausal women have yielded mixed results[180]; future studies examining hormonal influences and ventilatory control in premenopausal women may clarify sex-specific mechanisms.[181]

5. Therapeutic Guidelines and Adherence Strategies

There is ongoing debate on the clinical significance of treating isolated REM-predominant OSA, particularly in patients with mild global AHI and minimal symptoms. Future trials should examine whether targeted treatment improves surrogate endpoints such as 24-hour ambulatory blood pressure, insulin sensitivity, and mood symptoms.[8] Innovations in therapy, such as smart positive airway pressure (PAP) devices that auto-adjust based on REM-onset physiology, could enhance adherence in this subgroup.[182] Behavioral interventions tailored to individuals with REM OSA and minimal daytime sleepiness may also prove effective in improving compliance.[183]

6. Integration with OSA Endotypes for Personalized Medicine

REM OSA likely coexists with other pathophysiological endotypes, such as low arousal threshold, high loop gain, or positional dependency.[184] Understanding these interactions can inform precision medicine strategies. For example, REM-predominant OSA with a low arousal threshold might benefit from pharmacologic agents that stabilize sleep architecture.[185] Similarly, individuals with REM OSA and positional OSA may respond better to combined positional therapy and CPAP.[186] Future research should incorporate REM OSA status into multidimensional phenotyping frameworks to individualize treatment.

7. Special Populations and Comorbid Conditions

The relevance of REM OSA in special populations remains underexplored. During pregnancy, rapid physiological changes may predispose women to REM-dominant patterns of SDB, with potential implications for maternal-fetal outcomes.[187]

Similarly, patients with post-traumatic stress disorder (PTSD) or nightmare disorder may experience REM-sleep disruption; the bidirectional interaction between REM OSA and these psychiatric conditions warrants evaluation. Furthermore, in central sleep apnea syndromes (e.g., Cheyne-Stokes respiration), resolution of central events may unmask underlying REM-predominant obstructive patterns.[189] Investigating REM OSA in such contexts could yield novel insights.

8. Health Economic Implications and Screening Policies

If REM OSA contributes independently to cardiometabolic risk, its early identification and management may prove cost-effective. However, health-economic analyses are lacking. Targeted screening strategies—for example, in women with refractory hypertension or individuals with metabolic syndrome and minimal symptoms—could be evaluated through prospective studies. Cost-benefit modelling could guide future screening guidelines and resource allocation.

Relevance to the Present Study

The current investigation is designed to address several of the aforementioned gaps. Specifically, it aims to:

- Assess the prevalence of REM-predominant OSA using both strict and broad diagnostic definitions.
- Characterize the clinical and polysomnographic profile of REM OSA patients versus non-REM OSA and mixed OSA cohorts.
- Evaluate the utility of standard symptom scales (Epworth Sleepiness Scale, STOP-Bang, Berlin Questionnaire, and Beck Depression Inventory) in identifying REM OSA.

- Examine the association between REM AHI and symptoms (e.g. fatigue, morning headaches) and comorbidities (e.g. hypertension, diabetes) independent of total AHI.

By focusing on an Indian clinical population, this study contributes to the limited literature from South Asia and supports global efforts to characterize REM OSA. The findings are expected to inform whether REM-specific phenotyping should influence screening, diagnosis, and therapeutic algorithms in routine sleep medicine practice.

MATERIALS AND METHODS

A one year hospital based prospective observational study was conducted from June 2023- May 2024 at KLE's Dr. Prabhakar Kore Hospital and Medical Research Centre, Belagavi

In this study, at the time of initial assessment, relevant socio demographic and anthropometric details were recorded in the structured proforma . A thorough clinical history including symptomatology, comorbidities were collected. Further more screening tools- Epworth Sleepiness Scale, STOP BANG, Berlin Questionnaire, Becks depression Inventory were applied to detect patients who were likely suspected to have obstructive sleep apnea.

Patient who fulfilled the inclusion and exclusion criteria were enrolled into the study after obtaining informed consent. These patients were then subjected to a polysomnography study done in the in-house, quality controlled level II sleep laboratory using the PSG system by Alice PDX device, Philips Respironics.

Data on polysomnographic variables were overall AHI, REM AHI, NREM AHI, REM AHI/NREM AHI ratio, supine AHI, longest recorded event in REM and NREM sleep, sleep latency and efficiency , snoring index, oxygen desaturation index, arousal index, lowest recorded oxygen desaturation (spO2), limb movement index, length of REM sleep as a percentage of total sleep duration and RDI.These were obtained from the PSG report data generated at the end of level II PSG.All the data were collected in a structured proforma and analyzed at the end of the study.

Statistical Analysis

The data was entered in Microsoft excel and analysis was done in SPSS version 17.0. Age was categorised into age categories and comparison and groups and gender with REM OSA were done with chi-square test. STRICT and BROAD criteria

was use to classify the REM OSA and the prevalence along with 95% CI was reported for each criterion. Association of symptoms and Berlin questionnaire risk with REM OSA was done with chi squared test. The association of continuous parameters like age, BMI, lowest SPO2, longest REM and NREM sleep and ESS sores, STOP BANG scores across strict and broad criteria was done with independent t-test. Correlation between the different parameters were done with Pearson correlation and correlation coefficient was reported. Bar diagrams, pie charts and scatter plots were used for graphical representation of data. A p-value of <0.05 was considered significant.

SAMPLE SIZE CALCULATION

The expected sample size was determined using the study conducted by Nair SC, Arjun P, Azeez AK, Nair S and average number of polysomnography studies being conducted in K.L.E's Dr. Prabhakar Kore Hospital, Belagavi per annum.

Considering p to be the prevalence if disease, q= 100-p. D is error precision.

p= 56%

q= 44%

d= error precision which is taken as 13% (around 20-25% of p)

Hence, $n = \frac{4 \times 56 \times 44}{13^2}$

$= 58.3 \sim 58$

Hence required sample size is 58.

After the allotted time, 100 participants were examined in total.

Inclusion Criteria

All consecutive in patients and out patients aged ≥18 years who underwent level II PSG in the timeframe of the study who were willing to give their consent were included in the study.

Exclusion Criteria

Age < 18 years

Failure to provide informed consent

RESULTS

This study presents a detailed analysis of the observational data on the prevalence of REM OSA and the correlation of the various scoring systems like the Epworth Sleepiness scale, STOP BANG score, Berlin questionnaire and Beck Depression Inventory with the diagnosis of obstructive sleep apnea and REM OSA. By examining demographic factors, presenting complaints clinical characteristics and associated comorbidities, this study aims to uncover patterns that may explain the critical significance of early diagnosis of REM OSA and also the phenotypic characteristics of such individuals.

It deserves special mention that none of the patients in this cohort met the criteria for central sleep apnea. The analysis of these findings not only quantifies the burden of REM OSA in this population but also identify key predictors that could point to an early diagnosis and targeted interventions.

This study aims to set a foundation that would help develop a deeper understanding of clinical parameters that can be used to diagnose REM OSA and how REM OSA impacts the cardio metabolic and neurognitive health of a patient, paving the way for improved patient management and future research directions.

We have included 100 patients for the purpose of the study.

Table-2: Prevalence of REM OSA strict and broad criteria

REM OSA (Broad criteria)	Number (n)	Percentage (%)
Yes	71	71.0
No	29	29.0
REM OSA (Strict criteria)		
Yes	37	37.0
No	63	63.0

The prevalence of REM OSA according to broad criteria was 71% with 95% CI (61-79.6) and prevalence of REM OSA according to strict criteria was 37% with 95% CI was (27.8-47.2)

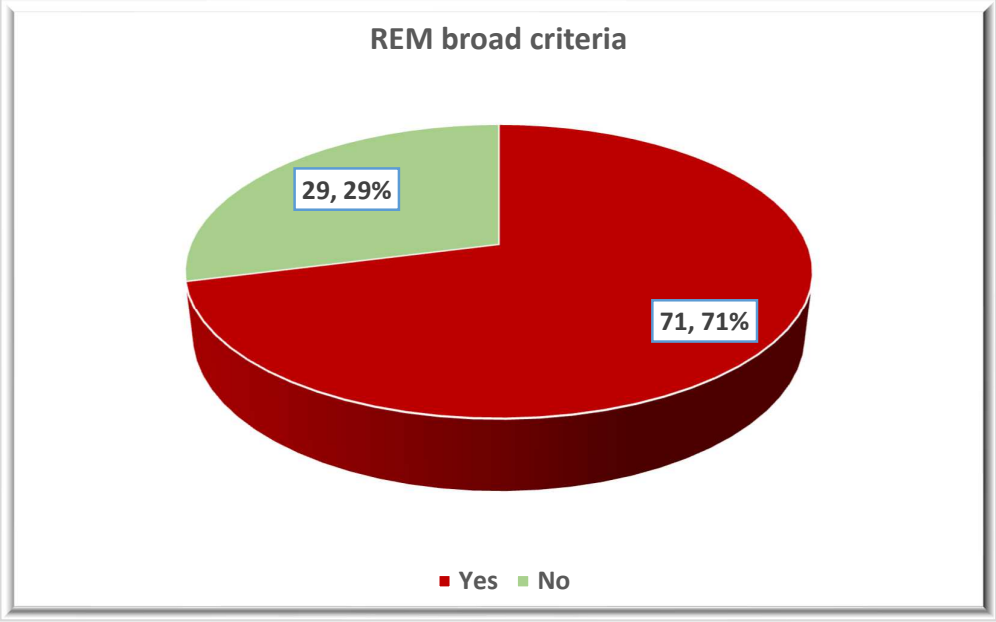


Fig 6: Prevalence of REM OSA (broad criteria)

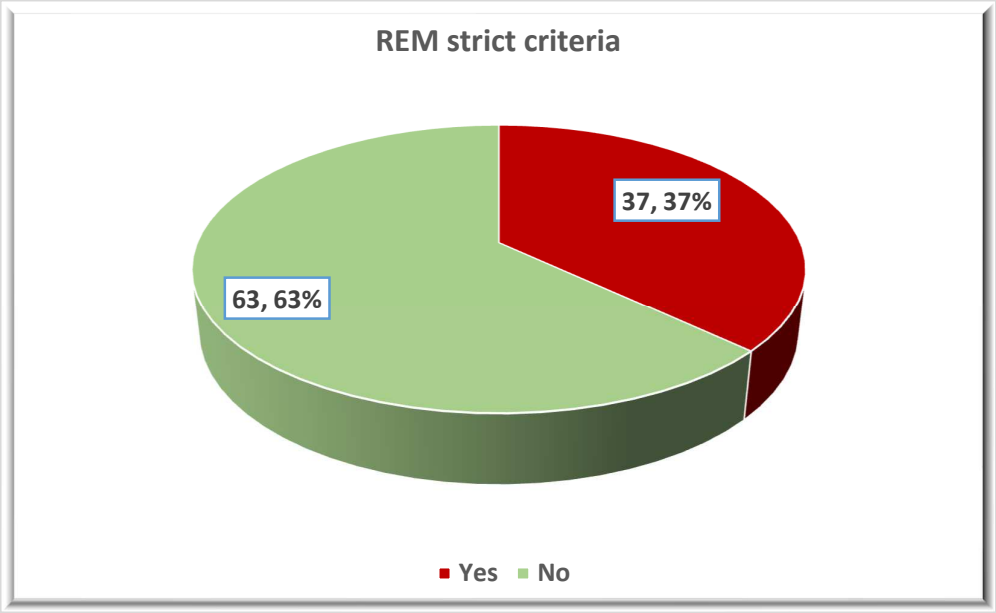


Fig 7: Prevalence of REM OSA (strict criteria)

Table 3: Correlation of few parameters with Overall AHI

Overall AHI	Correlation coefficient (r)	P value
ESS Scale	0.02	0.81
Becks's Depression inventory	0.14	0.17
Stopbang score	-0.08	0.38

The Epworth Sleepiness Scale (ESS) score showed a very weak positive correlation with AHI (r = 0.02, *p* = 0.81), indicating no meaningful relationship between daytime sleepiness and overall AHI. Similarly, Beck's Depression Inventory had a weak positive correlation with AHI (r = 0.14, *p* = 0.17), but this association was not statistically significant. The STOP-BANG score demonstrated a weak negative correlation with AHI (r = -0.08, *p* = 0.38), which was also not significant.

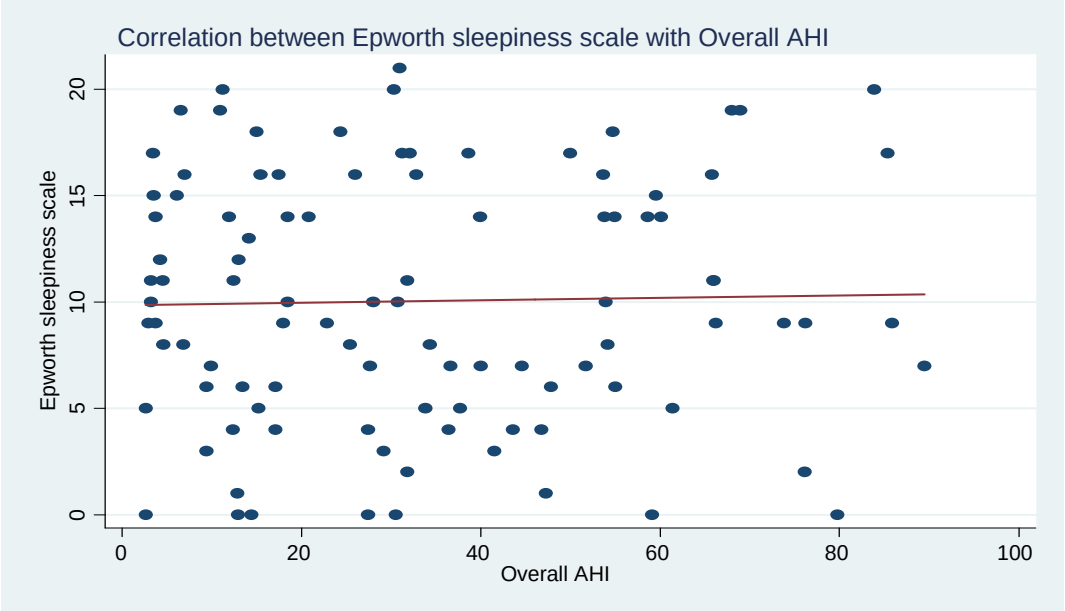


Fig 8: Correlation between Epworth Sleepiness scale and Overall AHI

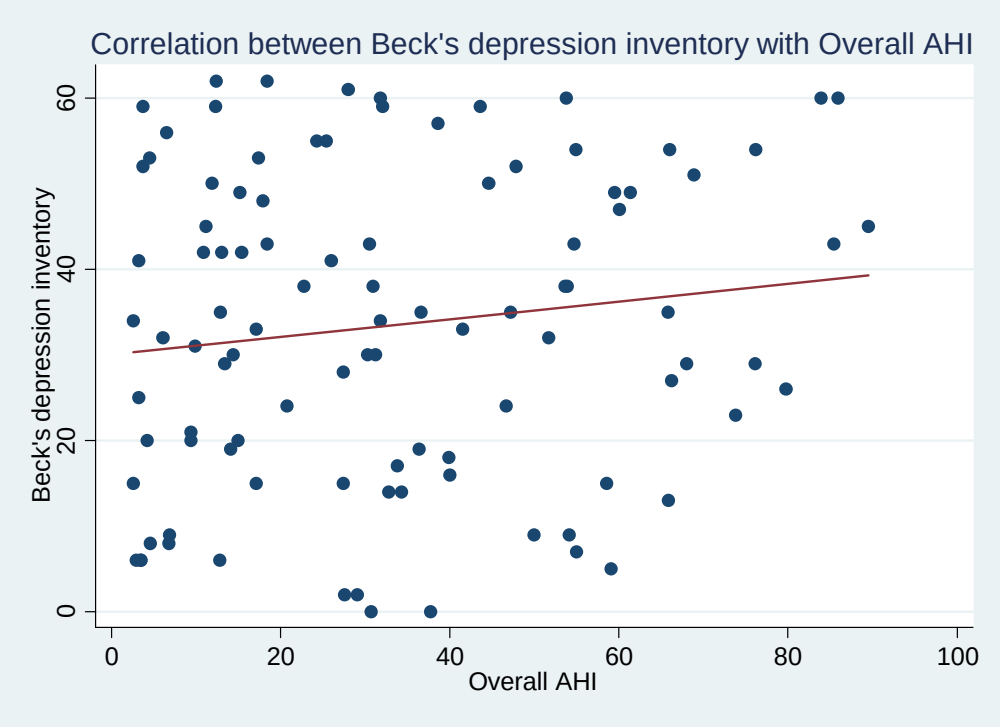


Fig 9: Correlatioo between Becks depression Inventory and Overall AHI

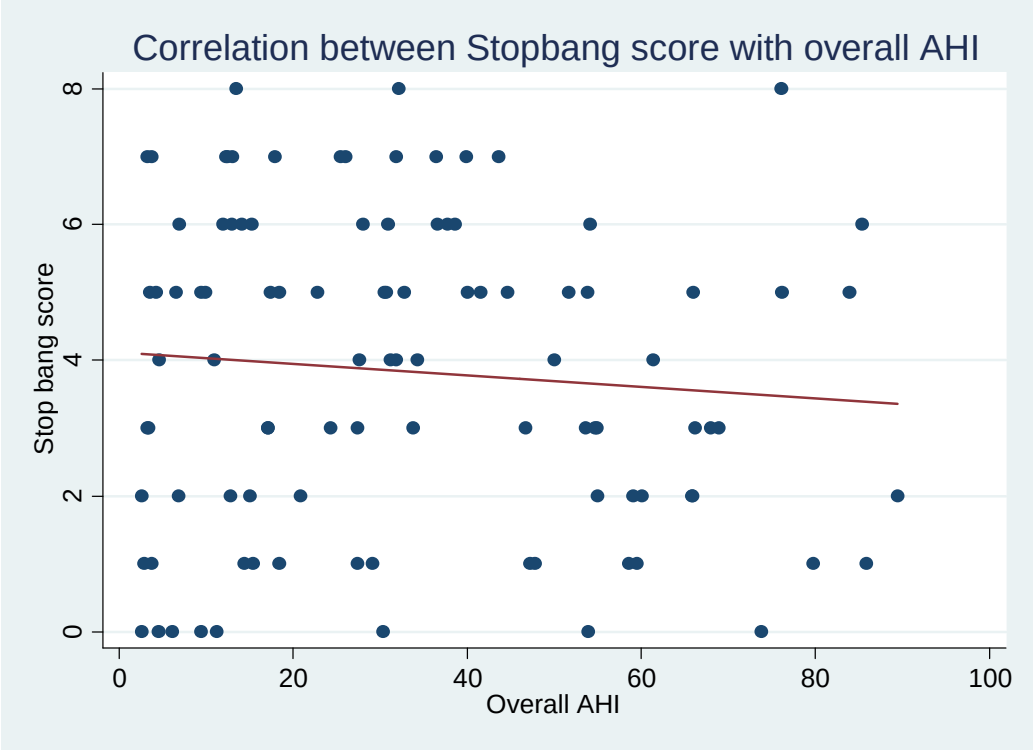


Fig 10: Correlation between STOP BANG score and overall AHI

Table-4: Comparison of parameters across REM OSA

	REM- OSA (Yes) N=78		REM-OSA (No) N=22		Mean difference	P value
	Mean	SD	Mean	SD		
Epworth sleepiness scale	10.0	5.9	10.1	5.9	0.07 (-2.8 to 3.0)	0.96
Beck's depression inventory	34.8	18.2	28.8	17.2	6.3 (-14.6 to 2.5)	0.16
Stopbang score	3.9	2.3	3.5	2.4	0.49 (-1.6 to 0.66)	0.39

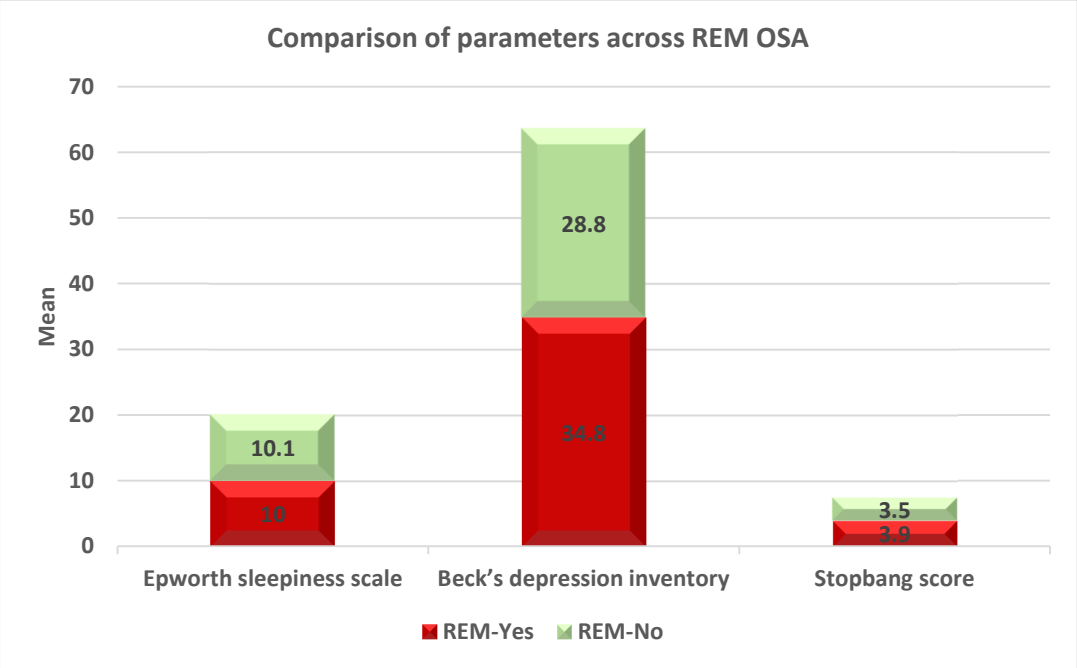


Fig 11: comparison of screening tools- ESS, BDI and STOP BANG score across REM OSA

The comparison of clinical parameters between individuals with REM OSA and those without REM OSA revealed no significant differences. The Epworth Sleepiness Scale (ESS) score was nearly identical between the two groups, with a mean of 10.0 (SD = 5.9) in the REM OSA group and 10.1 (SD = 5.9) in the non-REM OSA group, with a mean difference of 0.07 (95% CI: -2.8 to 3.0, $p = 0.96$). Similarly, Beck's Depression Inventory score was higher in the REM OSA group (34.8, SD = 18.2) compared to the non-REM OSA group (28.8, SD = 17.2), but the difference was not statistically significant (mean difference = 6.3, 95% CI: -14.6 to 2.5, $p = 0.16$). The STOP-BANG score also showed no significant difference between the groups, with a mean of 3.9 (SD = 2.3) in REM OSA and 3.5 (SD = 2.4) in non-REM OSA (mean difference = 0.49, 95% CI: -1.6 to 0.66, $p = 0.39$). These findings indicate that ESS, Beck's Depression Inventory, and STOP-BANG scores do not significantly differ between individuals with and without REM OSA.

Table-5: Association between Berlin Questionnaire and REM OSA

Berlin Questionnaire	REM OSA-Yes		REM OSA-NO	
	n	%	n	%
High Risk	43	55.1	14	63.6
Low Risk	35	44.9	8	36.4
Total	78	78	22	22
Chi square p value=0.51 (Not significant)				

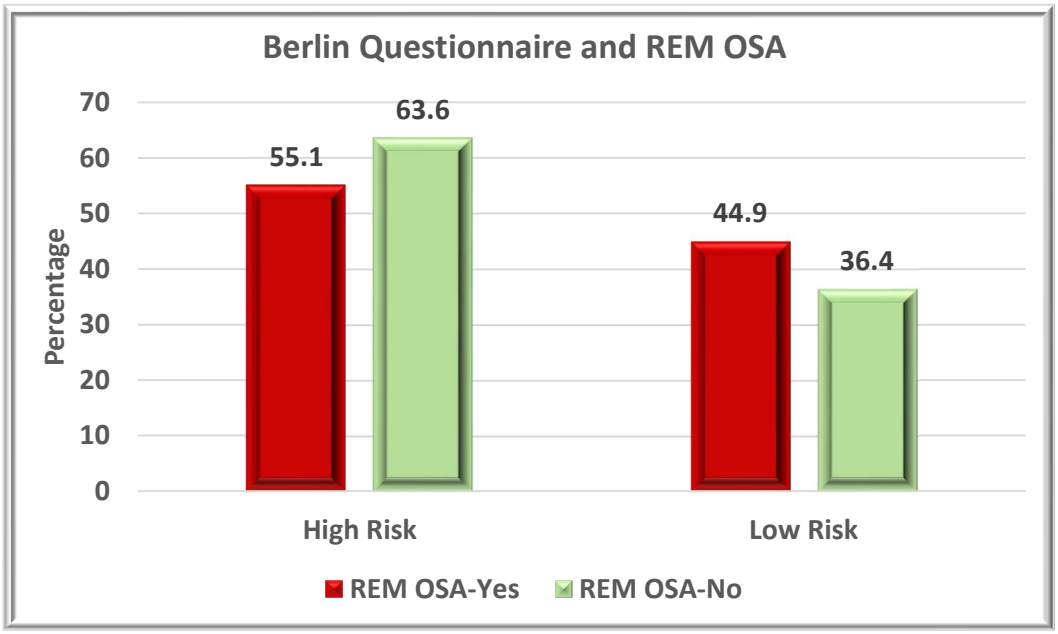


Fig 12: Association between Berlin questionnaire and REM OSA

Among individuals with REM OSA, 55.1% were classified as high risk, compared to 63.6% in the non-REM OSA group. Conversely, 44.9% of REM OSA individuals were classified as low risk, compared to 36.4% in the non-REM OSA group. The chi-square test yielded a *p*-value of 0.51.

Table-6: Gender wise prevalence of REM OSA

Gender	REM OSA-Yes		REM OSA-No	
	n	%	n	%
Female	33	68.8	15	31.2
Male	45	86.5	7	13.5
Total	78	78	22	22
Chi square p value=0.03 (Significant)				

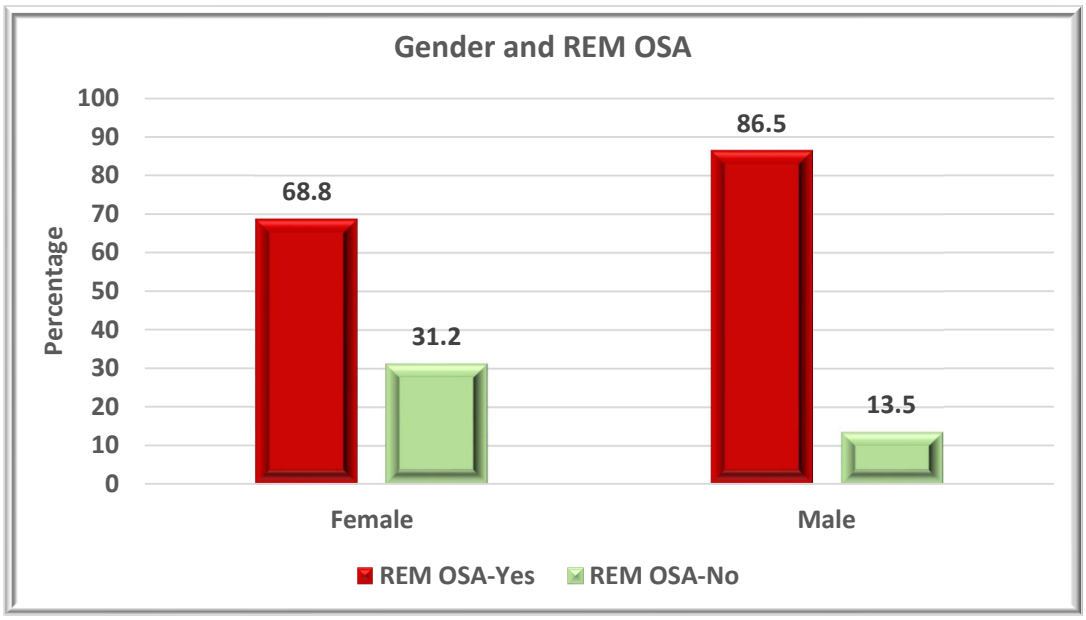


Fig 13: Gender prevalence in individuals with REM OSA

Among males, 45 had REM OSA (86.5%), while 7 did not have REM OSA (13.5%). Among females, 33 had REM OSA (68.8%), while 15 did not have REM OSA (31.2%). The prevalence of REM OSA was higher in males (86.5%) compared to females (68.8%), with a difference of 17.7%. This difference was statistically significant (p = 0.03).

Table-7: Age wise prevalence of REM OSA

Age categories (Years)	REM OSA-Yes		REM OSA-NO	
	n	%	n	%
0-40	3	8.1	34	91.9
41-50	5	21.7	18	78.3
>50	14	35	26	65
Total	78	78	22	22
Chi square p value=0.03 (Significant)				

Among individuals aged 0–40 years, 3 had REM OSA (8.1%), while 34 did not have REM OSA (91.9%). Among those aged 41–50 years, 5 had REM OSA (21.7%), while 18 did not have REM OSA (78.3%). In individuals older than 50 years, 14 had REM OSA (35.0%), while 26 did not have REM OSA (65.0%). The prevalence of REM OSA increased with age, from 8.1% in the 0–40 years group to 35.0% in those older than 50 years, showing a difference of 26.9%. This difference was statistically significant ($p = 0.03$).

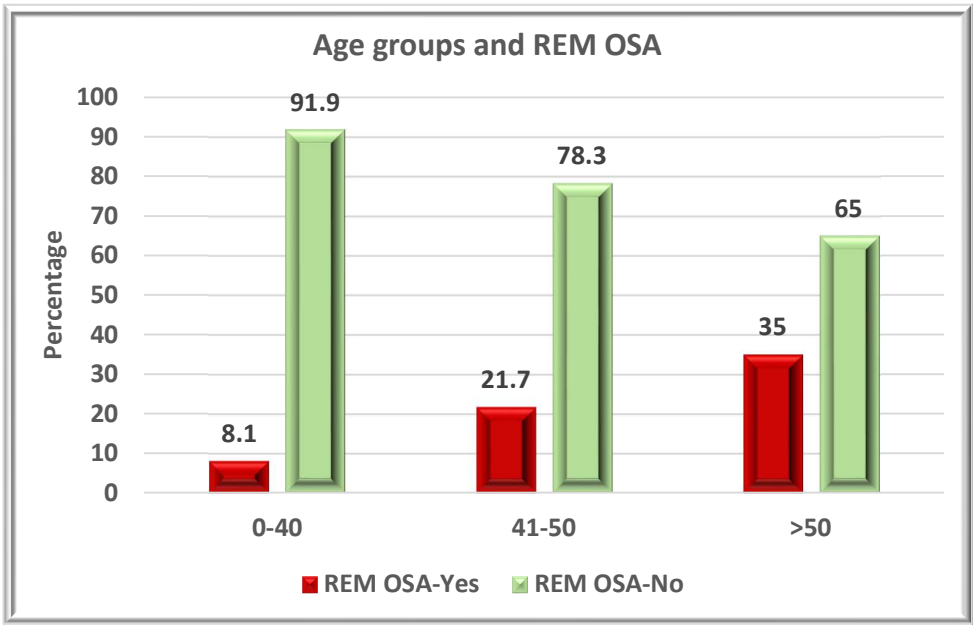


Fig 14: Distribution of Age in REM OSA

Table-8: Comparison of BMI across REM OSA

	REM OSA		Non REM OSA		P value
	Mean	SD	Mean	SD	
BMI	30.0	7.5	31.2	7.9	0.55
Independent t test P value not significant					

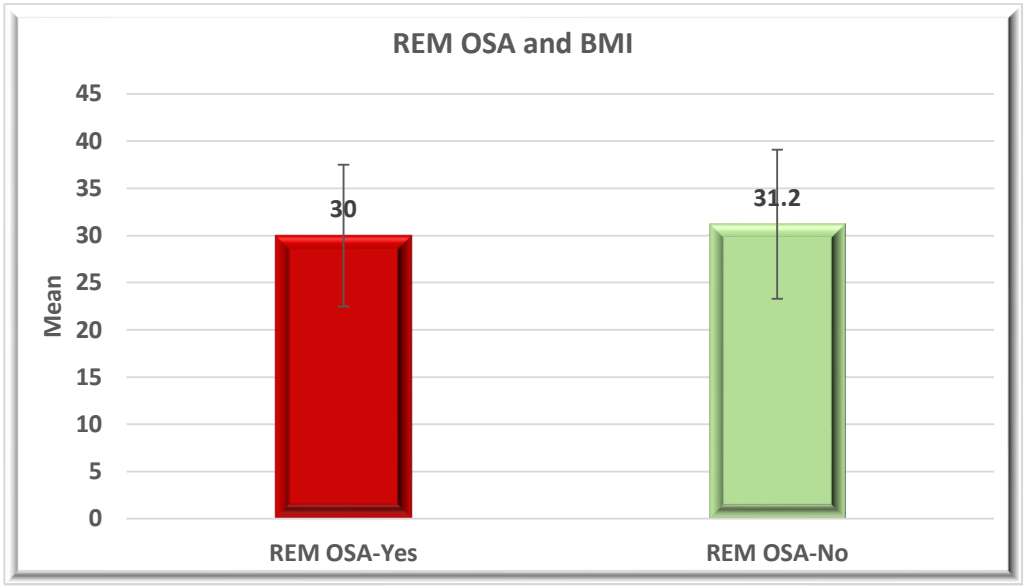


Fig 15: Comparison of REM OSA and BMI

The mean BMI was 30.0 (SD = 7.5) in the REM OSA group and 31.2 (SD = 7.9) in the non-REM OSA group. The difference between the two groups was not statistically significant (p = 0.55) based on the independent t-test, indicating that BMI did not differ significantly between individuals with and without REM OSA.

Table-9: Prevalence of comorbidities in patients with REM OSA (N=78)

Comorbidities	Number (n)	Percentage (%)
Hypertension	60	76.9
Cardiovascular disease	42	53.9
Diabetes	39	50
Dyslipidemia	39	50
Cerebrovascular disease	22	28.2
No comorbid condition	2	2.6

Among patients with REM OSA (N = 78), hypertension was the most prevalent comorbidity, affecting 60 individuals (76.9%). Cardiovascular disease was present in 42 individuals (53.9%), followed by diabetes and dyslipidemia, each affecting 39 individuals (50.0%). Cerebrovascular disease was observed in 22 individuals (28.2%). Notably, only 2 individuals (2.6%) had no comorbid conditions.

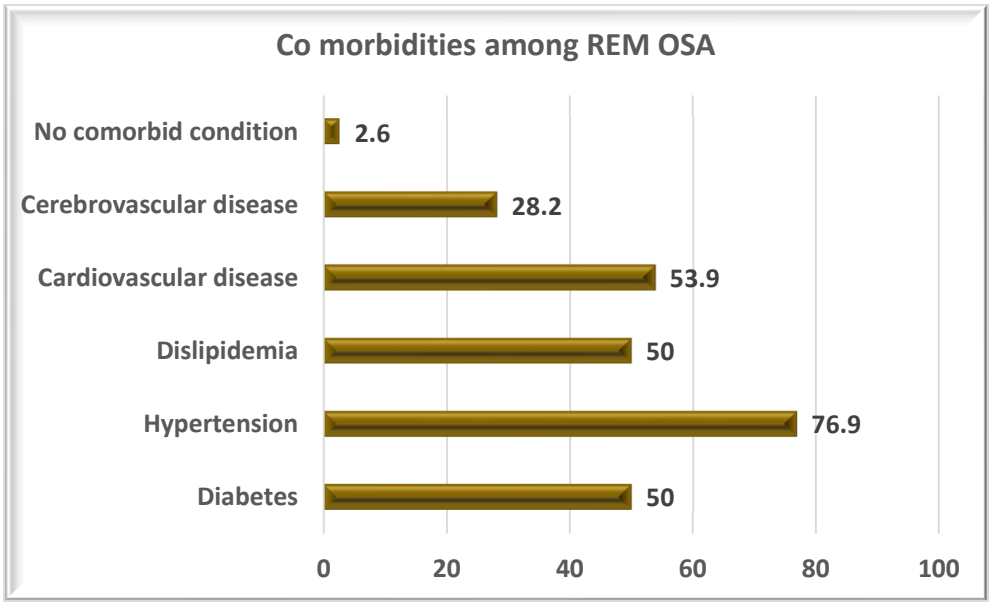


Fig 16: Comorbidities among REM OSA

Table-10: Prevalence of symptoms in REM OSA and Non REM OSA

Symptoms	REM OSA (N=78)		Non REM OSA (N=22)		P value
	n	%	n	%	
Excessive daytime sleepiness	44	56.4	7	31.8	0.04
Snoring	45	57.7	11	50	0.52
Fatigue	39	50	4	18.2	0.008
Non refreshing sleep	33	42.3	8	36.4	0.62
Morning headache	33	42.3	13	59.1	0.16
Mood changes	36	46.2	9	40.9	0.662
Neurocognitive repercussions	32	41	13	59.1	0.13
Insomnia	31	39.7	15	68.2	0.02
Increased dreams	38	48.7	12	54.5	0.63
Nightmares	39	50	11	50	1.0

Among individuals with REM OSA (N = 78), excessive daytime sleepiness was reported in 44 (56.4%) compared to 7 (31.8%) among those without REM OSA (N = 22), showing a significant difference (p = 0.04). Fatigue was also significantly more common in individuals with REM OSA (50.0%) than those without (18.2%) (p = 0.008). Insomnia was more prevalent in the REM OSA group (39.7%) than in the non-REM OSA group (68.2%), with a significant difference (p = 0.02).

Other symptoms, including snoring (57.7% vs. 50.0%, p = 0.52), non-refreshing sleep (42.3% vs. 36.4%, p = 0.62), morning headache (42.3% vs. 59.1%, p = 0.16), mood changes (46.2% vs. 40.9%, p = 0.66), neurocognitive repercussions (41.0% vs. 59.1%, p = 0.13), increased dreams (48.7% vs. 54.5%, p = 0.63), and nightmares (50.0% in both groups, p = 1.0), did not show significant differences between the groups.

Overall, excessive daytime sleepiness, fatigue, and insomnia were significantly more prevalent in individuals with REM OSA, suggesting these symptoms may be important indicators of the condition.

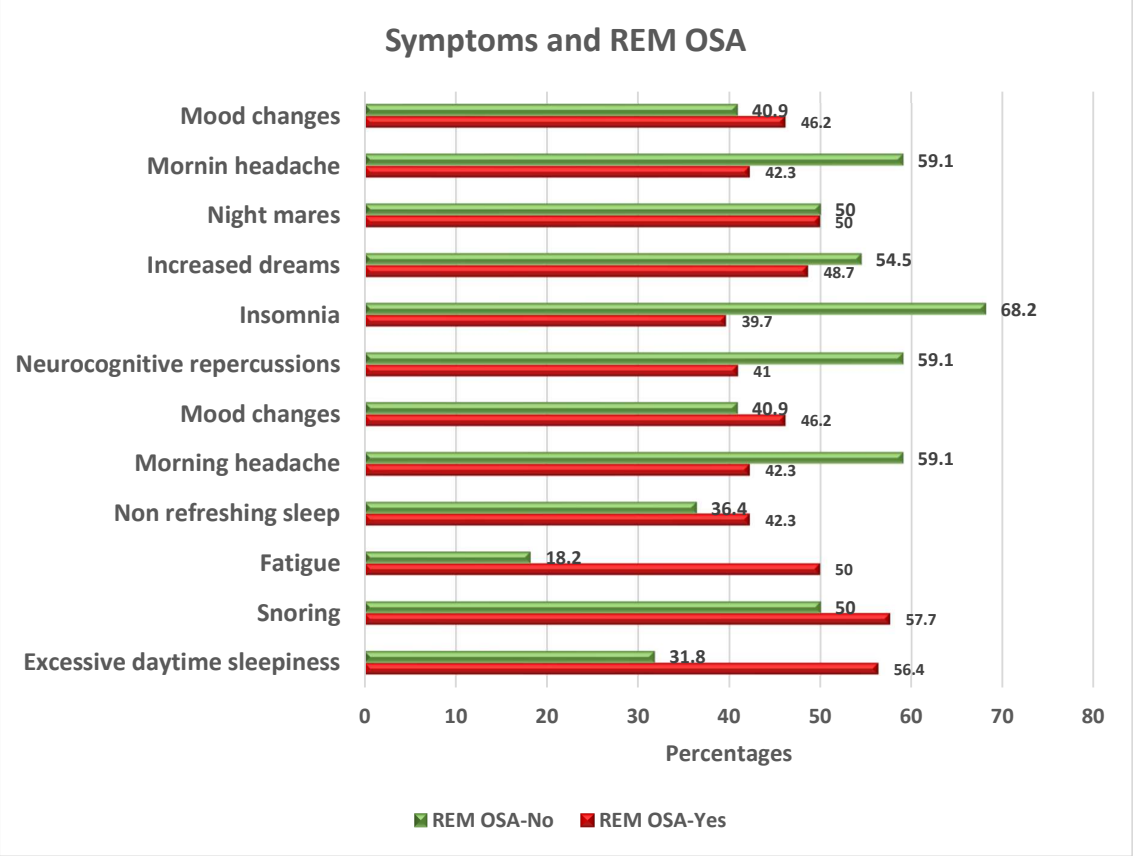


Fig 17: Symptoms in REM OSA

Table-11: Comparison of parameters across REM (Broad criteria)

Parameter	REM OSA-Yes (N=71)					REM OSA-No (N=29)					P value
	Mean	SD	Median	Q1	Q3	Mean	SD	Median	Q1	Q3	
Age	43.6	14.4	35	44	55	53.3	17	42	57	66	0.01
BMI	29.6	7.7	23	29.6	35.1	32	7.3	26.1	32.5	36.9	0.14
Neck Circumference	40.2	5.3	35.1	39.8	45	41	4.3	38.4	41.4	44.4	0.46
ESS	9.9	6	5	9	15	10.5	5.4	6	11	15	0.61
Supine AHI	46.6	32.8	18.6	39.5	67.1	37	32.6	6	20.6	65.4	0.19
Longest REM Event	8.9	4.1	5	9	12	9.8	3.5	7	9	13	0.24
Longest NREM Event	29.7	14.7	18	29	45	27.2	12.7	17	26	37	0.39
Snoring Index	21.5	15.5	7.9	18	35.7	24.7	14	14.4	21.1	33.6	0.32
Arousal Index	25.9	13.8	13.5	26	37.7	24.8	14.2	11.5	28.8	36.3	0.74
Desaturation Index	26.4	15.2	12.8	26.4	42.1	29.8	14.6	16.5	35.9	41.6	0.30
Sleep Efficiency (%)	75.1	15	61.2	77.1	88.7	75	13.5	66.5	72.1	84.7	0.97
Sleep Latency (min)	31.5	17.6	16	32	48	32.3	16.2	22	33	45	0.82
Lowest Spo2	76.6	17	58.3	80.1	93.3	87.1	10.2	81.4	89	95.5	<0.001
Limb Movement index	8.8	4.1	5.6	9.1	12.4	9.6	5	4.3	11	13.5	0.48
Stop Bang Score	4	2.3	2	4	6	3.4	2.3	2	3	5	0.24
Beck's Depression Inventory	34.9	18	20	35	50	30.1	18.3	15	30	41	0.24

Among individuals with REM OSA (N = 71), the mean age was 43.6 years (SD = 14.4), which was significantly lower than in those without REM OSA (53.3 years, SD = 17.0) (p = 0.01). The lowest SpO_2 was also significantly lower in the REM OSA group (76.6%, SD = 17.0) compared to the non-REM OSA group (87.1%, SD = 10.2) ($p < 0.001$).

Other parameters, including BMI (29.6 vs. 32.0, p = 0.14), neck circumference (40.2 cm vs. 41.0 cm, p = 0.46), Epworth Sleepiness Scale (ESS) score (9.9 vs. 10.5, p = 0.61), supine AHI (46.6 vs. 37.0, p = 0.19), longest REM event (8.9 min vs. 9.8 min, p = 0.24), longest NREM event (29.7 min vs. 27.2 min, p = 0.39), snoring index (21.5 vs. 24.7, p = 0.32), arousal index (25.9 vs. 24.8, p = 0.74), desaturation index (26.4 vs. 29.8, p = 0.30), sleep efficiency (75.1% vs. 75.0%, p = 0.97), sleep latency (31.5 min vs. 32.3 min, p = 0.82), limb movement index (8.8 vs. 9.6, p = 0.48), STOP-BANG score (4.0 vs. 3.4, p = 0.24), and Beck's Depression Inventory score (34.9 vs. 30.1, p = 0.24) did not show statistically significant differences between the groups.

Overall, individuals with REM OSA were significantly younger and had lower SpO_2 levels, while other sleep-related and physiological parameters did not differ significantly between the groups.

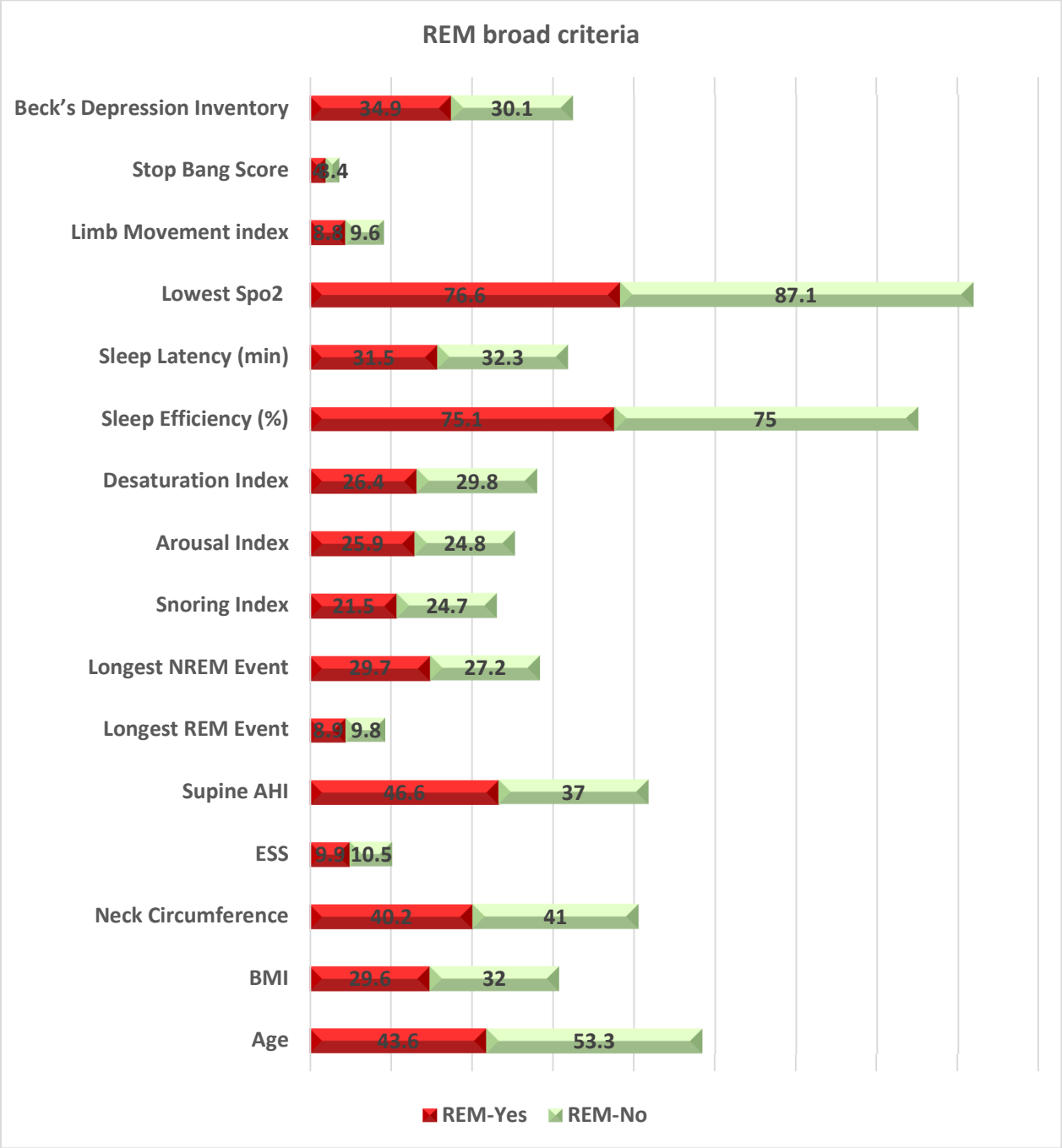


Fig 18: Comparison of parameters across REM OSA (broad criteria)

Table-12: Comparison of parameters across REM strict criteria

Parameter	REM OSA-Yes (N=37)					REM OSA-No (N=63)					P value
	Mean	SD	Median	Q1	Q3	Mean	SD	Median	Q1	Q3	
Age	43	14.6	36	41	51	48.4	16.1	37	50	61	0.09
BMI	31.2	6.6	27.1	31.1	35.1	29.7	8.1	22.4	29.8	36.9	0.33
Neck Circumference	40.1	5	34.8	40.4	44.4	40.6	5.1	36.7	40.3	44.9	0.64
ESS	11	5.2	7	11	15	9.5	6.1	4	9	15	0.18
Supine AHI	46.6	36.1	6.9	44.4	75.5	42.1	31	17.4	39.1	62.4	0.53
Longest REM Event	9.5	3.7	7	9	14	9	4.1	5	9	12	0.54
Longest NREM Event	29.8	14.2	20	28	43	28.5	14.1	16	28	42	0.65
Snoring Index	20	15.8	5.8	18.4	33	23.9	14.6	12.1	20.1	35.7	0.21
Arousal Index	26.7	15.1	11.5	28.1	40.8	24.9	13.2	12.8	25.4	36.3	0.54
Desaturation Index	29.4	15	14.6	32.3	43.7	26.2	15.1	12.5	25.5	40.6	0.30
Sleep Efficiency (%)	71.9	14.7	58.6	69.3	82.5	76.9	14.2	66.5	79.6	90	0.11
Sleep Latency (min)	29.4	16.9	14	31	45	33.1	17.2	18	36	49	0.30
Lowest Spo2	77	15.2	68.6	79.3	89	81.2	16.4	60.6	86.9	95.3	0.20
Limb Movement index	8.9	4.3	4.8	10	12.6	9.2	4.4	5.8	9.2	13.4	0.72
Stop Bang Score	3.8	2.4	2	4	6	3.9	2.3	2	4	6	0.92
Beck's Depression Inventory	32.3	18.4	17	38	48	34.2	18	19	33	50	0.62

Among individuals with REM OSA (N = 37), the mean age was 43.0 years (SD = 14.6), compared to 48.4 years (SD = 16.1) in those without REM OSA (N = 63), but the difference was not statistically significant (p = 0.09). Similarly, no significant differences were observed between the groups in BMI (31.2 (6.6) vs. 29.7 (8.1), p = 0.33), neck circumference (40.1 (5.0) cm vs. 40.6 (5.1) cm, p = 0.64), and Epworth Sleepiness Scale (ESS) score (11.0 (5.2) vs. 9.5 (6.1), p = 0.18).

Sleep-related parameters such as supine AHI (46.6 [36.1] vs. 42.1 [31.0], p = 0.53), longest REM event (9.5 [3.7] min vs. 9.0 [4.1] min, p = 0.54), longest NREM event (29.8 [14.2] min vs. 28.5 [14.1] min, p = 0.65), snoring index (20.0 [15.8] vs. 23.9 [14.6], p = 0.21), arousal index (26.7 [15.1] vs. 24.9 [13.2], p = 0.54), desaturation index (29.4 [15.0] vs. 26.2 [15.1], p = 0.30), sleep efficiency (71.9% [14.7] vs. 76.9% [14.2], p = 0.11), and sleep latency (29.4 [16.9] min vs. 33.1 [17.2] min, p = 0.30) did not show statistically significant differences between the groups.

The lowest SpO_2 levels were slightly lower in the REM OSA group (77.0% [15.2]) compared to the non-REM OSA group (81.2% [16.4]), but this difference was not significant (p = 0.20). Other parameters, including limb movement index (8.9 [4.3] vs. 9.2 [4.4], p = 0.72), STOP-BANG score (3.8 [2.4] vs. 3.9 [2.3], p = 0.92), and Beck's Depression Inventory score (32.3 [18.4] vs. 34.2 [18.0], p = 0.62), also showed no significant differences between the groups.

Overall, there were no statistically significant differences between the REM OSA and non-REM OSA groups based on the strict criteria, indicating that these parameters may not differ substantially between individuals with and without REM OSA when using a stricter classification.

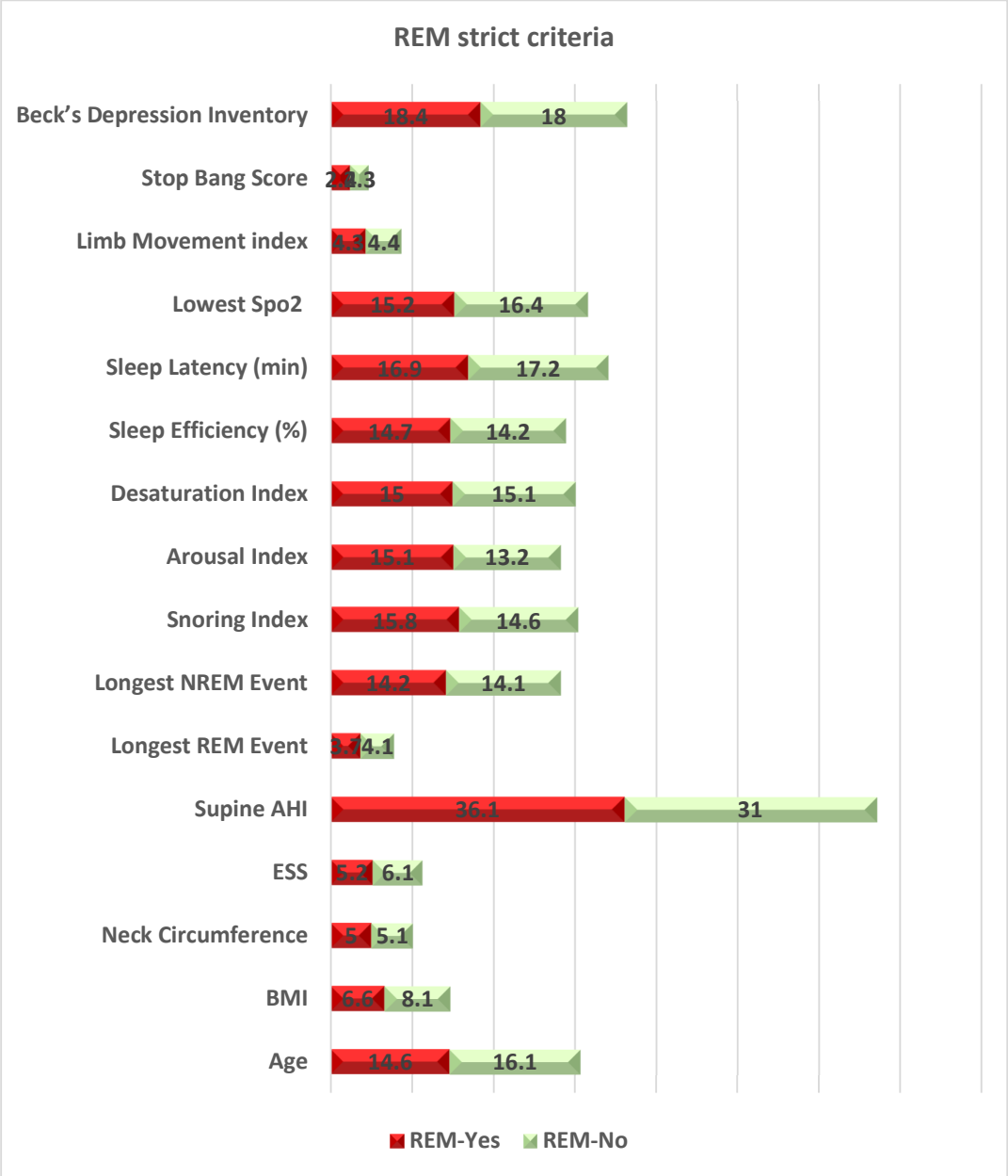


Fig 19: Comparison of parameters across REM OSA (strict criteria)

Table 13: Correlation between REM AHI and REM RDI

Comparison	Correlation coefficient (r)	P value
REM AHI and REM RDI	0.17	0.09

There was a weak positive correlation was observed between REM AHI and REM RDI with the Correlation coefficient (r) of 0.17.

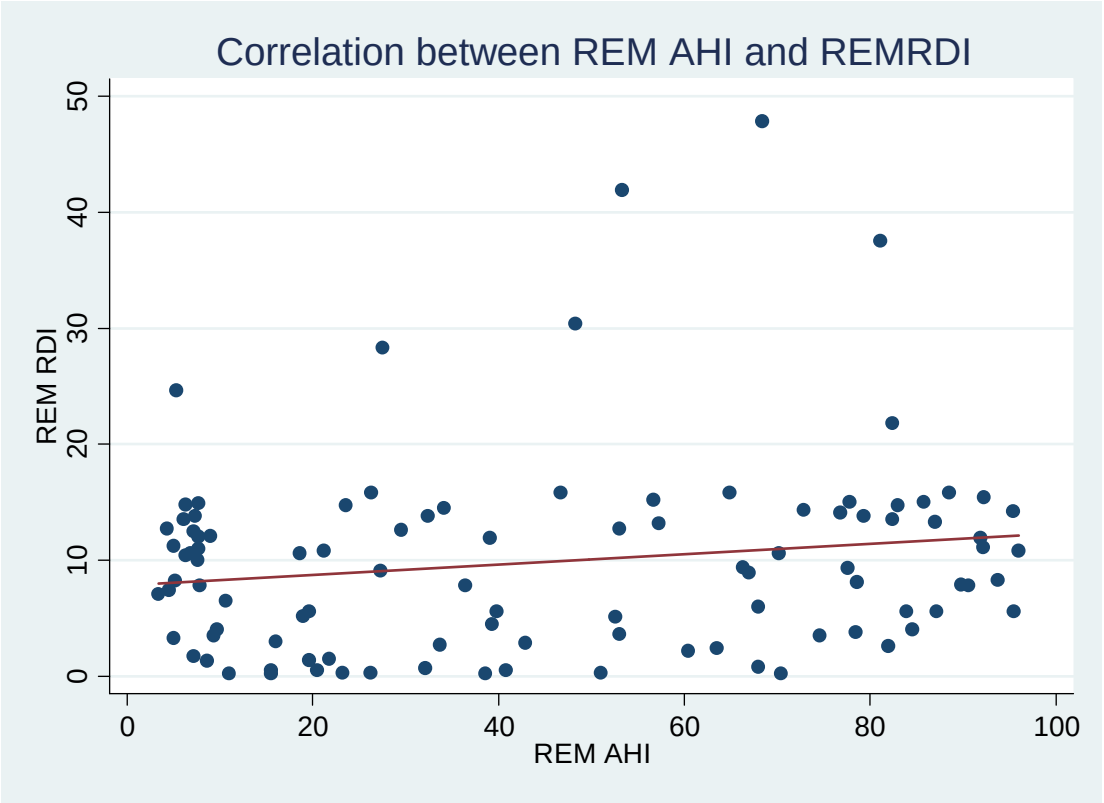


Fig 20: Correlation between REM AHI and REM RDI

DISCUSSION

A consistent observation across the literature is the substantial variability in the reported prevalence of REM-related obstructive sleep apnea (REM-OSA), significantly influenced by the diagnostic criteria employed. Broad definitions typically classify any OSA patient with a disproportionately higher apnea-hypopnea index (AHI) during REM sleep compared to non-REM (NREM) sleep (usually REM AHI/NREM AHI ≥ 2) as having REM-predominant OSA [191,127]. In contrast, strict definitions necessitate that obstructive events predominantly occur during REM sleep with minimal events during NREM sleep (typically overall AHI ≥ 5 with REM AHI >5 and NREM AHI <5).[127,192] Intermediate criteria often set thresholds between these extremes, such as requiring NREM AHI <15.[121] The absence of standardized definitions contributes significantly to the heterogeneity observed in estimates of prevalence.[191,192]

Reported prevalence rates distinctly reflect these definitional variations. In a study done by Conwell et al.[12], it was identified REM-OSA prevalence as 37% under broad criteria (REM/NREM AHI ≥ 2) in this large U.S. clinical sample, whereas stricter criteria (NREM AHI <8 and ≥10.5 min of REM sleep) reduced prevalence to 13.5% [4]. Similarly, Mano et al. reported broad and strict prevalence rates of 24.6% and 12.2%, respectively, in a Japanese cohort.[191]

Recent studies further highlight demographic and clinical factors influencing these variations. For instance, in Saudi Arabia, Qanash et al. reported prevalences of 52% (broad definition), 33% (intermediate definition), and 26% (strict definition), noting higher female representation and younger age in stricter criteria groups.[121] Conversely, a Jordanian study done by Oweidat et al reported significantly lower

prevalences (18% broad, 2.7% strict) due to a higher proportion of severe OSA cases, and notably highlighted a marked female predominance in REM-OSA prevalence.[127]

Population characteristics significantly impact REM-OSA prevalence estimates. Studies involving milder OSA cases consistently report higher REM-OSA prevalence under broad criteria. A cross-sectional Asian study found REM-OSA in 56.3% under broad criteria, dropping to 25.4% with strict criteria, predominantly among mild-to-moderate OSA patients.[122] This aligns with literature indicating REM-predominant OSA is notably more frequent in mild cases, becoming rare as overall disease severity increases.[175,193]

Table 14 summarizes key studies on REM-OSA prevalence by diagnostic criteria:

Study (Year, Location	Broad Criteria (%)	Strict Criteria (%)	Population Characteristics
Conwell et al., 2012 (USA)[12]	37	13.5	Mixed severity, 52% female
Al Oweidat et al., 2018 (Jordan)[127]	18	2.7	Severe cases predominant, 45% female
Mano et al., 2019 (Japan)[191]	24.6	12.2	Broad severity, 14.5% female
Nair et al., 2022 (Asia)[122]	56.3	25.4	Mild-moderate severity, 33% female
Qanash et al., 2023 (Saudi Arabia)[121]	52	26	Mixed severity, younger age, 42% female

REM-OSA prevalence varies significantly with diagnostic criteria, ranging from approximately 2.7% to over 50% depending on definitions and cohort characteristics. Such variability emphasizes the need for standardized criteria, especially when interpreting clinical implications or conducting comparative studies. Furthermore, recognizing subgroups with a higher REM-OSA prevalence (e.g., females, younger patients, mild OSA cases) is clinically important, potentially influencing diagnosis and treatment strategies.[121,122,127,175,191,192]

Prevalence in the current study vs literature

This study found a remarkably high prevalence of REM-related OSA in its sample, exceeding many prior reports. In this study, 56.3% of patients had REM-related OSA by a broad criterion (REM AHI at least double NREM AHI), and 25.4% met a strict definition (REM AHI >5, NREM AHI <5, with REM sleep >5% of total).This broad-criterion prevalence (~56%) is substantially higher than the ~10–36% range reported in most earlier clinic cohorts,and even the strict-criterion figure (25%) is at the upper end of what previous studies have observed for REM-predominant OSA. Even under the strict definition, this study's 25% prevalence notably exceeds the ~13% or lower strict-definition rates seen in some Western cohorts. In other words, the current study identified REM-related OSA in over half of its OSA patients with a broad definition, whereas the previous studies have found roughly one-quarter or less.

Several factors may explain why the present study's prevalence is higher. First, the study included patients across the OSA severity spectrum (including those with very low overall AHI), and it specifically looked for REM predominance even in cases that might otherwise be labelled "no OSA." In fact, the patients with AHI < 5

had more REM specific events. By counting such REM-predominant cases that conventional criteria might overlook, the broad-definition prevalence naturally increases. Many earlier studies, by contrast, have focused only on patients already meeting overall OSA criteria (AHI ≥5). Including those borderline cases (overall AHI <5 but REM AHI elevated) in the denominator can inflate the apparent proportion of REM-related OSA. Additionally, the cohort in this study had a preponderance of mild and moderate OSA cases and fewer severe cases, which is exactly the scenario in which REM-predominant OSA thrives.In severe OSA, breathing events occur so frequently in NREM sleep that few patients will have a REM/NREM ratio ≥2 ; hence studies with many severe patients tend to report lower REM-OSA percentages. The current study's population characteristics being skewed toward milder OSA and including some subclinical cases,likely contributed to the higher observed prevalence of REM-specific OSA.

Despite the numeric differences, many qualitative findings of the present study align with established literature.

Another point of alignment is that the symptom severity e.g. daytime sleepiness measured by Epworth score and body mass index were similar between REM-predominant OSA patients and those with non-stage-specific OSA in this study. Prior research has also found that patients with REM-predominant OSA can be just as sleepy and symptomatic as typical OSA patients despite having lower overall AHI. Thus, in terms of patient phenotype , female preponderance, moderate obesity, mild overall AHI but significant symptoms – the current study's findings corroborate existing knowledge. The major deviation lies in magnitude: this study emphasizes an even higher prevalence of REM-predominant OSA than most earlier

Correlation of Screening tools with diagnosis of OSA and REM OSA

In the present study, the correlation between the ESS score and the Apnea–Hypopnea Index (AHI) was extremely weak (r = 0.02, p = 0.81). This finding is consistent with previous research that has noted a limited association between self-reported daytime sleepiness and objective measures of sleep-disordered breathing. Johns MW, originally developed the ESS as a screening tool for subjective sleepiness; however, subsequent studies have demonstrated that while the ESS is clinically useful, it often fails to correlate strongly with AHI, suggesting that subjective perceptions of sleepiness may be influenced by other factors such as sleep quality, comorbid conditions, or interindividual variability in sleep physiology.[194,195]

Similarly, the weak positive correlation observed between BDI scores and AHI (r = 0.14, p = 0.17) aligns with literature indicating that depressive symptoms in patients with OSA are multifactorial. Several studies have reported that although depressive symptoms are more prevalent in patients with OSA, the severity of apnea as measured by the AHI does not consistently predict depression scores.[196] This inconsistency implies that while OSA may contribute to mood disturbances, other factors including the physiological stress of chronic sleep deprivation, underlying psychiatric vulnerabilities, or systemic inflammation could be playing a more decisive role in the manifestation of depressive symptoms.

The STOP-BANG score, designed primarily as a screening tool to identify individuals at high risk for OSA, demonstrated a weak negative correlation with AHI (r = –0.08, p = 0.38). Prior investigations have similarly highlighted that while STOP-BANG has high sensitivity for detecting OSA, its correlation with the severity of the disease as quantified by AHI is variable.[197] The tool's reliance on dichotomous items (e.g., gender, neck circumference, body mass index) may limit its precision in

capturing the nuanced continuum of OSA severity, particularly in heterogeneous populations.

Furthermore, when studying patients with REM-related OSA relative to those with non-REM OSA, the absence of statistically significant differences in the ESS, BDI, and STOP-BANG scores is noteworthy. The literature has reported similar findings; some studies indicate that REM-predominant OSA may not significantly alter subjective sleepiness or mood disturbance scores compared to non-REM OSA, even though the underlying pathophysiology might differ [12]. This suggests that the clinical impact of REM-specific events may be buffered by overlapping compensatory mechanisms in sleep architecture or by the patients' adaptive responses to sleep disruption.

The present study revealed a statistically significant higher prevalence of REM-related obstructive sleep apnea (REM OSA) among males (86.5%) compared to females (68.8%), with a difference of 17.7% ($p = 0.03$). While OSA overall is known to be more prevalent in males, findings regarding gender differences in REM-predominant OSA are more nuanced. Several studies, including work by O'Connor et al., have reported that females may exhibit a higher proportion of REM-predominant OSA, especially in milder forms of the disease and in younger age groups.[165] However, other data suggest that REM-related OSA remains prevalent across both sexes, and gender-related differences may reflect varying sleep architecture, hormonal influences, or craniofacial anatomy rather than distinct pathophysiological processes.[199] The discrepancy between our findings and those of prior studies may be attributed to differing definitions of REM OSA, sample size, or population-specific phenotypes.

Age-related trends observed in this study demonstrated a progressive increase in REM OSA prevalence with advancing age, rising from 8.1% in individuals aged 0–40 years to 35.0% in those older than 50 years. This trend was statistically significant (p = 0.03), supporting previous reports that OSA severity and REM sleep fragmentation tend to increase with age [15,16]. The loss of upper airway muscle tone and decreased ventilatory responsiveness during REM sleep with aging may partially explain the elevated prevalence in older adults.[202] However, contrasting studies have shown that REM OSA can also be disproportionately represented in younger adults and women, highlighting the heterogeneity of this phenotype and the potential influence of body composition, sleep stage duration, and comorbidities.[118]

Regarding body mass index (BMI), the current analysis found no statistically significant difference between individuals with REM OSA (mean BMI: 30.0 ± 7.5) and those without (31.2 ± 7.9; p = 0.55). These findings are in line with existing evidence that REM-predominant OSA is not consistently associated with higher BMI, unlike classic OSA, where obesity is a well-established risk factor [19]. Some studies have identified a non-obese phenotype in REM OSA, often linked with increased upper airway collapsibility during REM sleep rather than structural compromise from excess adipose tissue.[203] This could suggest a different mechanistic pathway for REM OSA, where ventilatory control instability and REM-specific neuromuscular inhibition play a more critical role than body structure alone.

The present study highlights a high burden of comorbidities and symptomatology among patients with REM-related obstructive sleep apnea (REM OSA), which is consistent with previous literature suggesting that this phenotype may carry distinct clinical implications. Among the REM OSA group, hypertension emerged as the most prevalent comorbidity, affecting 76.9% of individuals. This

aligns with findings by Appleton et al., who noted that REM OSA was significantly associated with nocturnal and early morning hypertension, likely due to heightened sympathetic activation during REM-related respiratory events.[204] Similarly, Mokhlesi et al. reported that REM OSA patients demonstrate higher nocturnal blood pressure variability and increased odds of developing systemic hypertension. [205]

Cardiovascular disease and metabolic dysfunction were also common in the REM OSA group in this study, with 53.9% reporting cardiovascular disease, and 50.0% each reporting diabetes and dyslipidemia. This reflects findings by Chervin and colleagues, who observed that REM-related apneas, due to their temporal clustering and deeper desaturations, may independently contribute to cardiovascular morbidity.[206] Moreover, the Sleep Heart Health Study found that REM AHI, independent of NREM AHI, was associated with incident hypertension and metabolic dysregulation.[207] The clustering of apneas during REM sleep, when ventilatory drive is diminished and upper airway tone is lowest, may predispose to longer apneas and greater hypoxic burden, potentiating end-organ effects.[208]

Cerebrovascular disease was present in 28.2% of individuals with REM OSA in this cohort. Although fewer studies have specifically addressed stroke or cerebrovascular disease in REM OSA, it is plausible that the intermittent hypoxia and autonomic fluctuations during REM events contribute to cerebrovascular risk. Research by Redline et al. supports the notion that REM sleep-related hypoxemia and arousals are linked with impaired cerebral autoregulation and increased risk of silent infarcts.[209]

Of note, only 2 individuals (2.6%) in the REM OSA group had no comorbid conditions, suggesting a strong association between REM OSA and co-morbidity. This aligns with findings by Punjabi et al., who emphasized that REM-predominant

OSA may be an under-recognized contributor to chronic disease burden in middle-aged and older adults.[210]

Symptomatically, excessive daytime sleepiness (EDS) was significantly more common in the REM OSA group (56.4%) compared to those without REM OSA (31.8%) ($p = 0.04$). This supports prior studies suggesting that EDS may correlate more strongly with REM-related respiratory events than with total AHI. Bianchi et al. demonstrated that REM AHI was independently associated with higher Epworth Sleepiness Scale (ESS) scores after adjusting for overall AHI and other sleep parameters.[211] The vulnerability of REM sleep to fragmentation and the cognitive-emotional importance of REM may partly explain the disproportionate daytime impairment observed in REM OSA.

Fatigue was also significantly more prevalent among REM OSA individuals (50.0% vs. 18.2%, $p = 0.008$), which was comparable with a study by Lam et al., who found that fatigue and unrefreshing sleep were often underreported yet clinically relevant symptoms in REM-predominant OSA, potentially reflecting the disrupted consolidation of REM sleep.[212] In contrast, insomnia was significantly *less* common in REM OSA (39.7%) than in non-REM OSA (68.2%) ($p = 0.02$), a somewhat unexpected finding. While some studies report increased insomnia symptoms in OSA overall, literature differentiating REM OSA specifically is sparse. One possibility is that REM OSA patients may experience deeper sleep onset, with clustering of events during REM phases later in the night, thus escaping early-night sleep fragmentation associated with insomnia.[96]

Other symptoms such as snoring, non-refreshing sleep, morning headaches, mood changes, neurocognitive disturbances, and parasomnias (increased dreaming,

nightmares) did not show significant differences between REM and non-REM OSA groups.

Taken together, these findings reinforce that REM OSA is a clinically significant phenotype with distinct symptom clusters and associated comorbidities. Excessive daytime sleepiness and fatigue, in particular, may serve as clinical red flags prompting more detailed sleep evaluation. Furthermore, the strong association with cardiometabolic comorbidities underscores the importance of early recognition and targeted management strategies for REM-predominant OSA.

Oxygen Desaturation:

This study showed significantly lower nadir SpO_2 among REM OSA patients (76.6% vs. 87.1%) concurs with prior reports that REM-related OSA is characterized by more severe desaturations, likely due to increased upper airway collapsibility and reduced pharyngeal muscle tone during REM sleep.[7] Choi et al. similarly found REM-predominant events to be associated with greater oxygen desaturation indices.[213]

Polysomnographic Parameters:

This study found comparable values between REM and non-REM OSA groups in terms of supine AHI, arousal index, snoring index, sleep efficiency, and REM/NREM event durations. These findings observed minimal differences in polysomnographic metrics aside from those strictly related to REM phases . While REM OSA is often associated with increased vulnerability during REM periods, overall sleep architecture and event duration patterns may remain largely indistinguishable from non-REM OSA.

The greater oxygen desaturation and younger age profile associated with REM OSA underline its clinical relevance. These could be related to adverse cardiovascular consequences and neurocognitive impairments. These findings support the need for

heightened clinical awareness, comprehensive polysomnographic evaluation, and potentially tailored management strategies for individuals with REM OSA.

Prior studies have explored the relationship between AHI and RDI, particularly in the context of REM sleep. For instance, studies conducted by Moklesi et al[7] has demonstrated that OSA severity can differ between REM and non-REM (NREM) sleep stages, with some patients exhibiting more pronounced apneic events during REM sleep. This variability suggests that AHI and RDI may not always align perfectly, as they are influenced by the distribution and type of respiratory events across different sleep stages.Moreover, Koo and Nam emphasized that the diagnostic accuracy and clinical implications of REM-related respiratory events may differ based on the metric used, suggesting that RDI may provide a more sensitive assessment in some individuals with subtle but clinically relevant respiratory disturbances.[40].

Additionally, Eiseman et al. [214] further demonstrated that both body posture and sleep stage exert a substantial influence on sleep apnea metrics, with positional and stage-dependent variability affecting both AHI and RDI values. This reinforces the notion that AHI and RDI, while overlapping in scope, may be differentially influenced by sleep physiology and environmental factors.

This study showed a weak correlation between REM AHI and REM RDI. Relying solely on one index may not provide a complete picture of the patient's condition, potentially leading to underestimation or overestimation of disease severity. Therefore, clinicians should consider both AHI and RDI, along with other relevant parameters, to inform diagnosis and tailor treatment strategies effectively.

Implications for future research

The findings and limitations of this study point to several directions for future research. One crucial area is investigating the long-term outcomes associated with

REM-related OSA. Prospective studies or follow-ups of patients with REM-predominant OSA (especially those who otherwise have mild overall OSA) are needed to determine if this phenotype confers heightened risk for cardiovascular issues, metabolic syndrome, cognitive impairment, or other health consequences. From this study it is found that association of REM OSA and daytime sleepiness is more and association with hypertension is also more.Larger studies are required to support this evidence. In particular, it would be valuable to assess if untreated REM-predominant OSA leads to future hypertension or cardiovascular events, given preliminary data in that direction, and whether early intervention mitigates such risks.

Another priority is evaluating treatment strategies and their benefits for REM-related OSA. Since REM-predominant OSA patients often have overall mild OSA, there is debate about treating them with CPAP or other modalities. Randomized trials or targeted treatment studies could investigate if managing REM-specific OSA , using CPAP only during REM or employing therapies like REM-suppressant medications, though those are largely experimental, may show improvement in patient's outcomes such as daytime function, blood pressure, etc. Early evidence indicates these patients are as sleepy as others and can adhere to CPAP,but it remains to be proven whether treatment yields significant improvements. As Conwell et al. pointed out, "*further research is needed to establish whether these patients will derive any benefit from long-term CPAP therapy."*

Such studies would inform clinical guidelines on when to treat REM-predominant OSA versus observe. Additionally, future research should aim to standardize the definition of REM-related OSA or at least understand how different definitions impact outcomes. The current literature uses heterogeneous criteria like various REM/NREM AHI ratios, absolute cut-offs and minimum REM duration

requirements. Reaching a consensus definition would facilitate comparing studies and pooling data. In this study, multiple definitions are applied to see which best predicts clinical outcomes which may help in narrowing down the useful definition.

More studies should explore the pathophysiology and progression of REM-predominant OSA. For example, why do some population notably women and younger patients, manifest obstructive events mostly in REM sleep? Investigating hormonal influences, upper airway muscle responsiveness differences during REM, or neurochemical factors could shed light on this phenotype. Longitudinal studies could determine if REM-predominant OSA is an early stage of OSA that progresses with age or weight gain, or if it remains a stable phenotype in certain people. Cohort studies with polysomnography could identify how common this is in the aged population and whether those people have increased health risks over time. In summary, future research should focus on outcome associations to know clinical significance, treatment efficacy for REM-specific OSA, definition standardization, and pathophysiological mechanisms. Addressing these gaps will build upon the stronger evidence which will help determine how to incorporate REM-related OSA into the broader understanding and management of sleep apnea.

Strength of the study

The current study has several notable strengths. First, it employed two complementary definitions of REM-related OSA (a broad vs. strict criterion), which provides a more comprehensive assessment of this phenotype. By analyzing both, the study captures the full spectrum of REM-predominant breathing disturbances – from cases with any REM predominance to the most extreme REM-specific cases. This dual-definition approach also allowed direct comparison with prior studies that have used varying thresholds, enhancing the relevance of its findings across the literature. Second, the study stratified results by OSA severity subgroups (mild, moderate, severe), yielding granular insights – for example, quantifying how REM-predominant OSA virtually disappears in severe OSA. This level of detail helps confirm known patterns and adds to the exceptionally high fraction of REM OSA in the mildest group that advances understanding of disease spectrum.

Another strength is the characterization of clinical and polysomnographic differences between REM-related and NREM-related OSA groups. The study examined factors such as age, sex, BMI, neck circumference, sleepiness scores, oxygen desaturation index. The associations like lower desaturation index and longer event length in REM OSA were significant findings. While parameters like BMI and daytime sleepiness dis not show significant variations.

This comprehensive comparison reinforces the idea that REM-predominant OSA patients can look clinically similar to other OSA patients aside from their sleep stage distribution of events. It also externally validates prior research of insomnia and fatigue which strengthens in confidence in the findings.Finally, the study addresses a relatively under-reported problem in an Indian scenario.In that context, this study addsto the data in Indian population which can be compared with Western population.

These aspects make the study a valuable contribution, providing both breadth and depth in profiling REM-related OSA

Limitations of the Study

1. This investigation was conducted at a single tertiary care center using a cross-sectional methodology. As a result, the findings may not be generalizable to broader populations or primary care settings. Additionally, the study design precludes establishing temporal or causal relationships between REM OSA and associated demographic, clinical, and polysomnographic parameters.

2.The study enrolled a total of 100 participants, which, although adequate for prevalence estimation, may have limited statistical power for subgroup analyses—particularly when stratifying by strict vs. broad criteria or when analyzing symptom correlations. This limitation may have contributed to the absence of statistically significant findings in certain comparisons (e.g., STOP-BANG scores, BMI, and BDI).

3.The reliance on self-reported tools such as the Epworth Sleepiness Scale (ESS), STOP-BANG questionnaire, and Berlin Questionnaire may introduce response bias. These instruments are susceptible to under- or over-reporting of symptoms such as sleepiness and fatigue, which may not always correlate with objective indices like AHI or SpO_2.

4. The cross-sectional nature of the study precluded assessment of treatment outcomes, such as the response to CPAP or oral appliance therapy in REM OSA patients. As such, the clinical implications of identifying REM OSA subtypes remain speculative in the absence of outcome-based validation.

5.Despite adherence to AASM guidelines, variability in scoring respiratory events—particularly hypopneas and respiratory effort-related arousals (RERAs)—may affect REM AHI and RDI estimation. The use of REM-specific indices (REM AHI and REM RDI) further adds complexity due to their sensitivity to sleep stage transitions and scoring subjectivity.

6.The study did not incorporate endotype or phenotype classification (e.g., loop gain, arousal threshold, muscle responsiveness), which may offer deeper insight into pathophysiological mechanisms underlying REM-predominant OSA and explain inter-individual variability beyond conventional indices.

7. Although gender-based differences were noted, the study did not account for menopausal status or hormonal influences in females—factors known to significantly affect REM-related upper airway dynamics. This may have limited the interpretation of gender-related prevalence trends.

8. While the presence of comorbidities such as hypertension and diabetes was recorded, the study did not stratify them by severity or control status. As such, the influence of comorbidity burden on REM OSA expression and severity could not be fully delineated.

9. As participants were drawn from a sleep clinic population, they may represent individuals with more severe symptoms or higher health-seeking behavior, potentially inflating symptom and comorbidity prevalence compared to community-based cohorts.

.

CONCLUSION

This cross-sectional study highlights the substantial prevalence of REM-related obstructive sleep apnea (REM OSA) among patients diagnosed with sleep-disordered breathing, particularly when broad diagnostic criteria are employed. The findings reveal that REM OSA constitutes a distinct and clinically relevant phenotype with a unique demographic and symptomatic profile, predominantly affecting males and older individuals and associated with symptoms such as excessive daytime sleepiness, fatigue, and insomnia. Notably, conventional screening tools like the Epworth Sleepiness Scale, Berlin Questionnaire, STOP-BANG, and Beck Depression Inventory demonstrated limited utility in reliably detecting REM-predominant OSA, indicating a need for refined, stage-specific screening strategies.

Furthermore, the study underscores the association of REM OSA with significant comorbidities, especially hypertension, cardiovascular disease, and diabetes mellitus, as well as its potential to induce more profound nocturnal hypoxemia compared to non-REM OSA. These findings reinforce the need for clinicians to recognize REM OSA not merely as a sub-phenotype but as a condition warranting independent diagnostic attention and therapeutic consideration.

In conclusion, this study contributes meaningful insights into the prevalence, clinical characteristics, and diagnostic challenges of REM-related OSA in the Indian population. It emphasizes the necessity for heightened clinical vigilance, incorporation of sleep stage-specific indices in routine polysomnography reports, and the development of targeted screening tools. Future longitudinal and interventional studies are warranted to explore the long-term health outcomes, therapeutic responsiveness, and management strategies tailored to this often-underrecognized phenotype.

SUMMARY

- This cross-sectional study evaluated the prevalence and clinical correlates of REM-predominant obstructive sleep apnea (REM OSA) among 100 patients diagnosed with sleep-disordered breathing.
- The prevalence of REM OSA was 71% using broad diagnostic criteria and 37% using strict criteria, underscoring the heterogeneity in diagnostic thresholds and the impact of definitional variability on clinical prevalence estimates.
- In terms of screening tools, no significant associations were found between REM OSA diagnosis and the Epworth Sleepiness Scale (ESS), STOP-BANG score, or Beck Depression Inventory (BDI). The Berlin Questionnaire also failed to distinguish REM OSA patients from non-REM OSA, with a non-significant distribution between high- and low-risk categories ($p = 0.51$).
- Demographically, REM OSA was more prevalent in males (86.5%) than females (68.8%), and the condition showed a significant increase with age, particularly in individuals over 50 years.
- Comorbidities were highly prevalent in the REM OSA cohort, especially hypertension (76.9%), cardiovascular disease (53.9%), and diabetes (50%). Only 2.6% of patients with REM OSA had no comorbid conditions.
- Existing literature has shown excessive daytime sleepiness may not be a predominant symptom in patients with REM OSA .Contrary to this, our study noted that REM OSA patients more frequently reported excessive daytime sleepiness (56.4%), fatigue (50%), and insomnia (39.7%) compared to their non-REM OSA counterparts, with all differences reaching statistical significance.
- However, other symptoms, including snoring, morning headaches, mood changes, and neurocognitive complaints, did not significantly differ between groups.

- Polysomnographically, individuals with REM OSA were significantly younger
- Patients with REM OSA exhibited lower minimum oxygen saturation (SpO_2), indicating more pronounced nocturnal desaturation.
- However, other parameters such as BMI, neck circumference, AHI, arousal index, desaturation index, and sleep efficiency did not show statistically significant differences.
- Importantly, comparison using strict diagnostic criteria also yielded no significant differences across most demographic and polysomnographic variables, further highlighting the diagnostic subtlety of REM-predominant OSA.
- Finally, a weak, non-significant positive correlation ($r = 0.17$, $p = 0.09$) was observed between REM AHI and REM RDI, suggesting limited concordance between these two respiratory indices.

Collectively, these findings highlight the complexity of REM OSA as a clinical phenotype. The condition is associated with significant symptom burden and comorbidities but may not be effectively identified using commonly employed clinical screening tools or basic anthropometric data. These results advocate for more nuanced diagnostic protocols and raise the importance of full-night polysomnography in capturing the unique REM-specific manifestations of OSA.

Study Overview:

This study was a cross-sectional, hospital-based observational analysis conducted over one year (April 2023 to March 2024) at KLE's Dr. Prabhakar Kore Hospital, Belagavi. It aimed to assess the prevalence and clinical features of Rapid Eye Movement-related Obstructive Sleep Apnea (REM OSA) among individuals

diagnosed with sleep-disordered breathing (SDB), utilizing both broad and strict diagnostic criteria.

Objectives:

- **Primary**: Determine the prevalence of REM OSA using strict and broad criteria.
- **Secondary**: Evaluate correlations between subjective symptom scores (Epworth Sleepiness Scale [ESS], Beck Depression Inventory [BDI], Berlin Questionnaire, STOP-BANG) and objective polysomnographic indices, particularly the Apnea-Hypopnea Index (AHI).

Methodology:

- **Participants**: Included 100 adult patients who underwent attended overnight polysomnography.
- **Instruments**: Subjective assessments (ESS, BDI, STOP-BANG, Berlin Questionnaire) and comprehensive polysomnography were conducted.
- **Criteria**: REM OSA identified based on AASM-defined criteria, categorized as "strict" (distinct REM predominance, minimal NREM involvement) or "broad" (any notable REM predominance).

Results:

- **Prevalence**:
    - REM OSA (broad criteria): 71%
    - REM OSA (strict criteria): 37%

- **Correlations**:
    - No significant correlation found between overall AHI and subjective assessments (ESS, BDI, STOP-BANG).
    - Berlin Questionnaire showed no significant predictive value for REM OSA.
- **Clinical Features**:
    - Significant associations of REM OSA with male gender (86.5% prevalence in males vs. 68.8% in females) and increasing age (highest prevalence in age group >50 years).
    - BMI did not differ significantly between REM OSA and non-REM OSA groups.
- **Symptom Profiles**:
    - Excessive daytime sleepiness, fatigue, and insomnia were significantly more prevalent in REM OSA individuals.
- **Comorbidities**:
    - Hypertension (76.9%), cardiovascular disease (53.9%), diabetes (50%), and dyslipidemia (50%) were common in REM OSA patients.
- **Polysomnographic Parameters**:
    - REM OSA patients had significantly lower minimum oxygen saturation (SpO_2) compared to non-REM OSA patients.

Strengths:

- Comprehensive definition usage (strict and broad criteria) allowing a nuanced understanding of REM-predominant OSA.
- Detailed clinical and polysomnographic comparisons between REM and non-REM OSA subtypes.
- Contribution to limited Indian data on REM-related OSA.

Limitations:

- Single-center, cross-sectional design limiting generalizability and causality inference.
- Limited statistical power for subgroup analyses due to modest sample size.
- Subjective assessments prone to response bias.
- Lack of hormonal status considerations in females, detailed comorbidity stratifications, and absence of objective daytime sleepiness measures (MSLT or psychomotor vigilance tests).

Conclusion: The study identified a high prevalence of REM-related OSA, particularly with broader diagnostic criteria, with clear associations noted for male gender, age, and specific symptoms such as fatigue and insomnia. However, commonly employed screening tools had limited utility for discriminating REM-predominant OSA, underscoring the need for enhanced clinical awareness and tailored diagnostic strategies for better patient management

BIBLIOGRAPHY

1. Lévy P, Kohler M, McNicholas WT, Barbé F, McEvoy RD, Somers VK, Lavie L, Pépin JL. Obstructive sleep apnoea syndrome. Nature reviews Disease primers. 2015 Jun 25;1(1):1-21.
2. Peppard PE, Hagen EW. The last 25 years of obstructive sleep apnea epidemiology—and the next 25?. American journal of respiratory and critical care medicine. 2018 Feb 1;197(3):310-2.
3. Iber C. The AASM manual for the scoring of sleep and associated events: rules, terminology, and technical specification. (No Title). 2007.
4. Punjabi NM, Bandeen-Roche K, Marx JJ, Neubauer DN, Smith PL, Schwartz AR. The association between daytime sleepiness and sleep-disordered breathing in NREM and REM sleep. Sleep. 2002 May 1;25(3):307-14.
5. Aurora RN, Crainiceanu C, Gottlieb DJ, Kim JS, Punjabi NM. Obstructive sleep apnea during REM sleep and cardiovascular disease. American journal of respiratory and critical care medicine. 2018 Mar 1;197(5):653-60.
6. Kryger MH, Roth T, Dement WC, editors. Principles and Practice of Sleep Medicine. 7th ed. Philadelphia: Elsevier; 2022. p. 53–62, 1047–55.
7. Mokhlesi B, Punjabi NM. "REM-related" obstructive sleep apnea: an epiphenomenon or a clinically important entity?. Sleep. 2012 Jan 1;35(1):5-7.
8. Mokhlesi B, Finn LA, Hagen EW, Young T, Hla KM, Van Cauter E, Peppard PE. Obstructive sleep apnea during REM sleep and hypertension. results of the Wisconsin Sleep Cohort. American journal of respiratory and critical care medicine. 2014 Nov 15;190(10):1158-67.
9. Appleton SL, Vakulin A, Martin SA, Lang CJ, Wittert GA, Taylor AW, McEvoy RD, Antic NA, Catcheside PG, Adams RJ. Hypertension is associated with

undiagnosed OSA during rapid eye movement sleep. Chest. 2016 Sep 1;150(3):495-505.

10. Bonsignore MR, Mazzuca E, Baiamonte P, Bouckaert B, Verbeke W, Pevernagie DA. REM sleep obstructive sleep apnoea. European Respiratory Review. 2024 Feb 14;33(171).
11. Acosta-Castro P, Hirotsu C, Marti-Soler H, Marques-Vidal P, Tobback N, Andries D, Waeber G, Preisig M, Vollenweider P, Haba-Rubio J, Heinzer R. REM-associated sleep apnoea: prevalence and clinical significance in the HypnoLaus cohort. European Respiratory Journal. 2018 Aug 16;52(2).
12. Conwell W, Patel B, Doeing D, Pamidi S, Knutson KL, Ghods F, Mokhlesi B. Prevalence, clinical features, and CPAP adherence in REM-related sleep-disordered breathing: a cross-sectional analysis of a large clinical population. Sleep and Breathing. 2012 Jun;16:519-26.
13. Haba-Rubio J, Janssens JP, Rochat T, Sforza E. Rapid eye movement-related disordered breathing: clinical and polysomnographic features. Chest. 2005 Nov 1;128(5):3350-7.
14. Aurora RN, McGuffey EJ, Punjabi NM. Natural history of sleep-disordered breathing during rapid eye movement sleep. Relevance for incident cardiovascular disease. Annals of the American Thoracic Society. 2020 May;17(5):614-20.
15. Gupta MA, Simpson FC. Obstructive sleep apnea and psychiatric disorders: a systematic review. Journal of Clinical Sleep Medicine. 2015 Feb 15;11(2):165-75.
16. Chung F, Abdullah HR, Liao P. STOP-Bang questionnaire: a practical approach to screen for obstructive sleep apnea. Chest. 2016 Mar 1;149(3):631-8.
17. Baglioni C, Spiegelhalder K, Lombardo C, Riemann D. Sleep and emotions: a focus on insomnia. Sleep medicine reviews. 2010 Aug 1;14(4):227-38.

18. Reynolds CF, Kupfer DJ, McEachran AB, Taska LS, Sewitch DE, Coble PA. Depressive psychopathology in male sleep apneics. The Journal of clinical psychiatry. 1984 Jul.
19. Macnish R. The philosophy of sleep. D. Appleton; 1834..
20. Carskadon MA, Dement WC. Normal human sleep: an overview. Principles and practice of sleep medicine. 2005 Jan 1;4(1):13-23..
21. Kryger MH, Roth T, Dement WC (editors). Principles and Practice of Sleep Medicine. 7th ed. Elsevier; 2021
22. Shepard JW, Buysse DJ, Chesson AL, Dement WC, Goldberg R, Guilleminault C, Harris CD, Iber C, Mignot E, Mitler MM, Moore KE. History of the development of sleep medicine in the United States. Journal of clinical sleep medicine. 2005 Jan;1(01):61-82.
23. Aserinsky E, Kleitman N. Regularly occurring periods of eye motility, and concomitant phenomena, during sleep. Science. 1953 Sep 4;118(3062):273-4.
24. Guilleminault C, Tilkian A, Dement WC. The sleep apnea syndromes. Annual review of medicine. 1976..
25. Sullivan C, Berthon-Jones M, Issa F, Eves L. Reversal of obstructive sleep apnoea by continuous positive airway pressure applied through the nares. The Lancet. 1981 Apr 18;317(8225):862-5.
26. Walker M. Why we sleep: Unlocking the power of sleep and dreams. Simon and Schuster; 2017 Oct 3.
27. Stickgold R, Walker MP. Sleep-dependent memory triage: evolving generalization through selective processing. Nature neuroscience. 2013 Feb;16(2):139-45.

28. Knutson KL, Van Cauter E. Associations between sleep loss and increased risk of obesity and diabetes. Annals of the New York Academy of Sciences. 2008 May;1129(1):287-304.
29. Ramar K, Malhotra RK, Carden KA, Martin JL, Abbasi-Feinberg F, Aurora RN, Kapur VK, Olson EJ, Rosen CL, Rowley JA, Shelgikar AV. Sleep is essential to health: an American Academy of Sleep Medicine position statement. Journal of Clinical Sleep Medicine. 2021 Oct 1;17(10):2115-9.
30. Iber C. The AASM manual for the scoring of sleep and associated events: Rules. Terminology and Technical Specification. 2007.
31. American Academy of Sleep Medicine. International classification of sleep disorders: diagnostic and coding manual. 3rd ed. Darien (IL): American Academy of Sleep Medicine; 2014
32. American Academy of Sleep Medicine. International Classification of Sleep Disorders, 3rd ed. Text Revision (ICSD-3-TR): Supplemental Material. Darien, IL: AASM; 2023.
33. Feti CETİN YC. CLASSIFICATION OF SLEEP DISORDERS. Modern Medical and Health Sciences. 2023 Dec 24:57.
34. Peppard PE, Young T, Palta M, Skatrud J. Prospective study of the association between sleep-disordered breathing and hypertension. New England Journal of Medicine. 2000 May 11;342(19):1378-84.
35. Shahar E, Whitney CW, Redline S, Lee ET, Newman AB, Javier Nieto F, O'CONNOR GT, Boland LL, Schwartz JE, Samet JM. Sleep-disordered breathing and cardiovascular disease: cross-sectional results of the Sleep Heart Health Study. American journal of respiratory and critical care medicine. 2001 Jan 1;163(1):19-25.

36. Yaggi HK, Concato J, Kernan WN, Lichtman JH, Brass LM, Mohsenin V. Obstructive sleep apnea as a risk factor for stroke and death. New England Journal of Medicine. 2005 Nov 10;353(19):2034-41.
37. Oldenburg O, Lamp B, Faber L, Teschler H, Horstkotte D, Töpfer V. Sleep-disordered breathing in patients with symptomatic heart failure A contemporary study of prevalence in and characteristics of 700 patients. European journal of heart failure. 2007 Mar;9(3):251-7.
38. Gami AS, Hodge DO, Herges RM, Olson EJ, Nykodym J, Kara T, Somers VK. Obstructive sleep apnea, obesity, and the risk of incident atrial fibrillation. Journal of the American College of Cardiology. 2007 Feb 6;49(5):565-71.
39. Punjabi NM, Shahar E, Redline S, Gottlieb DJ, Givelber R, Resnick HE. Sleep-disordered breathing, glucose intolerance, and insulin resistance: the Sleep Heart Health Study. American journal of epidemiology. 2004 Sep 15;160(6):521-30.
40. Koo DL, Nam H. Clinical considerations of obstructive sleep apnea with little REM sleep. Sleep Med Res. 2016;7(2):57–61.
41. Tregear S, Reston J, Schoelles K, Phillips B. Obstructive sleep apnea and risk of motor vehicle crash: systematic review and meta-analysis. Journal of clinical sleep medicine. 2009 Dec 15;5(6):573-81.
42. Polotsky VY, Patil SP, Savransky V, Laffan A, Fonti S, Frame LA, Steele KE, Schweizter MA, Clark JM, Torbenson MS, Schwartz AR. Obstructive sleep apnea, insulin resistance, and steatohepatitis in severe obesity. American journal of respiratory and critical care medicine. 2009 Feb 1;179(3):228-34.
43. Heinzer R, Vat S, Marques-Vidal P, Marti-Soler H, Andries D, Tobback N, Mooser V, Preisig M, Malhotra A, Waeber G, Vollenweider P. Prevalence of

sleep-disordered breathing in the general population: the HypnoLaus study. The Lancet Respiratory Medicine. 2015 Apr 1;3(4):310-8.

44. Benjafield AV, Ayas NT, Eastwood PR, Heinzer R, Ip MS, Morrell MJ, Nunez CM, Patel SR, Penzel T, Pépin JL, Peppard PE. Estimation of the global prevalence and burden of obstructive sleep apnoea: a literature-based analysis. The Lancet respiratory medicine. 2019 Aug 1;7(8):687-98.
45. Ip MS, Lam B, Lauder IJ, Tsang KW, Chung KF, Mok YW, Lam WK. A community study of sleep-disordered breathing in middle-aged Chinese men in Hong Kong. Chest. 2001 Jan 1;119(1):62-9.
46. Mirrakhimov AE, Sooronbaev T, Mirrakhimov EM. Prevalence of obstructive sleep apnea in Asian adults: a systematic review of the literature. BMC pulmonary medicine. 2013 Dec;13:1-0.
47. Kryger MH, Roth T, Dement WC. Principles and Practice of Sleep Medicine. 7th ed. Philadelphia: Elsevier; 2022. p. 1132–1135.
48. Udwadia ZF, Doshi AV, Lonkar SG, Singh CI. Prevalence of sleep-disordered breathing and sleep apnea in middle-aged urban Indian men. American journal of respiratory and critical care medicine. 2004 Jan 15;169(2):168-73.
49. Reddy EV, Kadhiravan T, Mishra HK, Sreenivas V, Handa KK, Sinha S, Sharma SK. Prevalence and risk factors of obstructive sleep apnea among middle-aged urban Indians: a community-based study. Sleep medicine. 2009 Sep 1;10(8):913-8.
50. Sharma SK, Kumpawat S, Banga A, Goel A. Prevalence and risk factors of obstructive sleep apnea syndrome in a population of Delhi, India. Chest. 2006 Jul 1;130(1):149-56.

51. Utpat K, Bansal S, Desai U, Joshi J. Clinical profile of obstructive sleep apnea syndrome in a tertiary care hospital in Western India. Indian J Sleep Med. 2019 Jan;14:1-6.
52. Fishman AP, Grippi MA, Senior RM, Pack AI. Fishman's Pulmonary Diseases and Disorders. 6th ed. New York: McGraw Hill; 2023. p. 1564–6.
53. Young T. The occurrence of steep-disordered breathing among middle-aged adults. N Engl J Med. 1993;328:230-5.
54. Eo B. Prevalence of sleep-disordered breathing in women: effects of gender. Am J Respir Crit Care Med. 2001;163:608-13.
55. Jordan AS, McSharry DG, Malhotra A. Adult obstructive sleep apnoea. The Lancet. 2014 Feb 22;383(9918):736-47.
56. Kryger MH, Roth T, Dement WC. Principles and Practice of Sleep Medicine. 7th ed. Philadelphia: Elsevier; 2022. p. 1142–1150.
57. Schwab RJ, Pasirstein M, Pierson R, Mackley A, Hachadoorian R, Arens R, Maislin G, Pack AI. Identification of upper airway anatomic risk factors for obstructive sleep apnea with volumetric magnetic resonance imaging. American journal of respiratory and critical care medicine. 2003 Sep 1;168(5):522-30.
58. Veasey SC, Rosen IM. Obstructive sleep apnea in adults. New England Journal of Medicine. 2019 Apr 11;380(15):1442-9.
59. Malhotra A, Huang Y, Fogel RB, Pillar G, Edwards JK, Kikinis R, Loring SH, White DP. The male predisposition to pharyngeal collapse: importance of airway length. American journal of respiratory and critical care medicine. 2002 Nov 15;166(10):1388-95.

60. Ryan S, Taylor CT, McNicholas WT. Selective activation of inflammatory pathways by intermittent hypoxia in obstructive sleep apnea syndrome. Circulation. 2005 Oct 25;112(17):2660-7.
61. Vgontzas AN, Papanicolaou DA, Bixler EO, Hopper K, Lotsikas A, Lin HM, Kales A, Chrousos GP. Sleep apnea and daytime sleepiness and fatigue: relation to visceral obesity, insulin resistance, and hypercytokinemia. The Journal of Clinical Endocrinology & Metabolism. 2000 Mar 1;85(3):1151-8.
62. Polotsky VY, Li J, Punjabi NM, Rubin AE, Smith PL, Schwartz AR, O'Donnell CP. Intermittent hypoxia increases insulin resistance in genetically obese mice. The Journal of physiology. 2003 Oct;552(1):253-64.
63. Ip MS, Lam BI, Ng MM, Lam WK, Tsang KW, Lam KS. Obstructive sleep apnea is independently associated with insulin resistance. American journal of respiratory and critical care medicine. 2002 Mar 1;165(5):670-6.
64. Palmer LJ, Buxbaum SG, Larkin E, Patel SR, Elston RC, Tishler PV, Redline S. A whole-genome scan for obstructive sleep apnea and obesity. The American Journal of Human Genetics. 2003 Feb 1;72(2):340-50.
65. Redline S, Tishler PV, Tosteson TD, Williamson J, Kump K, Browner I, Ferrette V, Krejci P. The familial aggregation of obstructive sleep apnea. American journal of respiratory and critical care medicine. 1995 Mar;151(3):682-7.
66. Cowie MR. Sleep-disordered breathing: how should we judge its severity?. European Heart Journal. 2016 Jun 1;37(21):1704-6.
67. Patil SP, Schneider H, Marx JJ, Gladmon E, Schwartz AR, Smith PL. Neuromechanical control of upper airway patency during sleep. Journal of applied physiology. 2007 Feb;102(2):547-56.

68. Schwab RJ, Gupta KB, Gefter WB, Metzger LJ, Hoffman EA, Pack AI. Upper airway and soft tissue anatomy in normal subjects and patients with sleep-disordered breathing. Significance of the lateral pharyngeal walls. American journal of respiratory and critical care medicine. 1995 Nov;152(5):1673-89.
69. Haponik EF, Smith PL, Bohlman ME, Allen RP, Goldman SM, Bleecker ER. Computerized tomography in obstructive sleep apnea: correlation of airway size with physiology during sleep and wakefulness. American Review of Respiratory Disease. 1983 Feb;127(2):221-6.
70. Burger CD, Stanson AW, Sheedy PF, Daniels BK, Shepard JW. Fast-computed tomography evaluation of age-related changes in upper airway structure and function in normal men. Am Rev Respir Dis. 1992 Apr 1;145(4 Pt 1):846-52.
71. Malhotra A, Huang Y, Fogel RB, Pillar G, Edwards JK, Kikinis R, Loring SH, White DP. The male predisposition to pharyngeal collapse: importance of airway length. American journal of respiratory and critical care medicine. 2002 Nov 15;166(10):1388-95.
72. Schwab RJ, Pasirstein M, Pierson R, Mackley A, Hachadoorian R, Arens R, Maislin G, Pack AI. Identification of upper airway anatomic risk factors for obstructive sleep apnea with volumetric magnetic resonance imaging. American journal of respiratory and critical care medicine. 2003 Sep 1;168(5):522-30.
73. Ws M. Waking genioglossal EMG in sleep apnea patients versus normal controls (a neuromuscular compensatory mechanisms). J Clin Invest. 1992;89:1571-9.
74. Kubin LE, Davies RO. Mechanisms of airway hypotonia. Lung biology in health and disease. 2002;166:99-154.
75. Orem J. The wakefulness stimulus for breathing. Lung biology in health and disease. 1994;71:113-55.

76. Önal E, Lopata M, O'Connor TD. Diaphragmatic and genioglossal electromyogram responses to isocapnic hypoxia in humans. American Review of Respiratory Disease. 1981 Sep;124(3):215-7.
77. Horner RL, Innes JA, Holden HB, Guz A. Afferent pathway (s) for pharyngeal dilator reflex to negative pressure in man: a study using upper airway anaesthesia. The Journal of physiology. 1991 May 1;436(1):31-44.
78. Horner RL, Innes JA, Murphy K, Guz A. Evidence for reflex upper airway dilator muscle activation by sudden negative airway pressure in man. The Journal of physiology. 1991 May 1;436(1):15-29.
79. Worsnop C, Kay A, Pierce R, Kim Y, Trinder J. Activity of respiratory pump and upper airway muscles during sleep onset. Journal of applied physiology. 1998 Sep 1;85(3):908-20.
80. Lo YL, Jordan AS, Malhotra A, Wellman A, Heinzer RA, Eikermann M, Schory K, Dover L, White DP. Influence of wakefulness on pharyngeal airway muscle activity. Thorax. 2007 Sep 1;62(9):799-805.
81. Hoffstein V, Zamel N, Phillipson EA. Lung volume dependence of pharyngeal cross-sectional area in patients with obstructive sleep apnea. American Review of Respiratory Disease. 1984 Aug;130(2):175-8.
82. Bradley TD, Brown IG, Grossman RF, Zamel N, Martinez D, Phillipson EA, Hoffstein V. Pharyngeal size in snorers, nonsnorers, and patients with obstructive sleep apnea. New England Journal of Medicine. 1986 Nov 20;315(21):1327-31.
83. Brown IG, Zamel N, Hoffstein V. Pharyngeal cross-sectional area in normal men and women. Journal of Applied Physiology. 1986 Sep 1;61(3):890-5.
84. Heinzer RC, Stanchina ML, Malhotra A, Jordan AS, Patel SR, Lo YL, Wellman A, Schory K, Dover L, White DP. Effect of increased lung volume on sleep

disordered breathing in patients with sleep apnoea. Thorax. 2006 May 1;61(5):435-9.

85. Heinzer RC, Stanchina ML, Malhotra A, Fogel RB, Patel SR, Jordan AS, Schory K, White DP. Lung volume and continuous positive airway pressure requirements in obstructive sleep apnea. American journal of respiratory and critical care medicine. 2005 Jul 1;172(1):114-7.
86. Hudgel DW, Devadatta PR. Decrease in functional residual capacity during sleep in normal humans. Journal of Applied Physiology. 1984 Nov 1;57(5):1319-22.
87. Ballard RD, Irvin CG, Martin RJ, Pak JU, Pandey RA, White DP. Influence of sleep on lung volume in asthmatic patients and normal subjects. Journal of applied physiology. 1990 May 1;68(5):2034-41.
88. Van de Graaff WB. Thoracic influence on upper airway patency. Journal of applied physiology. 1988 Nov 1;65(5):2124-31.
89. Önal E, Lopata M. Periodic breathing and the pathogenesis of occlusive sleep apneas. American review of respiratory disease. 1982 Oct;126(4):676-80.
90. Younes M, Ostrowski M, Thompson W, Leslie C, Shewchuk W. Chemical control stability in patients with obstructive sleep apnea. American journal of respiratory and critical care medicine. 2001 Apr 1;163(5):1181-90.
91. Asyali MH, Berry RB, Khoo MC. Assessment of closed-loop ventilatory stability in obstructive sleep apnea. IEEE transactions on biomedical engineering. 2002 Mar;49(3):206-16.
92. Hudgel DW, Gordon EA, Thanakitcharu S, Bruce EN. Instability of ventilatory control in patients with obstructive sleep apnea. American journal of respiratory and critical care medicine. 1998 Oct 1;158(4):1142-9.

93. Eckert DJ, Wellman A. Physiological phenotypes. Obstructive Sleep Apnoea (ERS Monograph). Sheffield, European Respiratory Society. 2015 Mar 1;67:9-31.
94. Eckert DJ, Younes MK. Arousal from sleep: implications for obstructive sleep apnea pathogenesis and treatment. Journal of Applied Physiology. 2014 Feb 1;116(3):302-13.
95. Gami AS, Somers VK. Obstructive sleep apnoea, metabolic syndrome, and cardiovascular outcomes. European heart journal. 2004 May 1;25(9):709-11.
96. Krakow B, Melendrez D, Ferreira E, Clark J, Warner TD, Sisley B, Sklar D. Prevalence of insomnia symptoms in patients with sleep-disordered breathing. Chest. 2001 Dec 1;120(6):1923-9.
97. Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. sleep. 1991 Nov 1;14(6):540-5.
98. Beebe DW, Groesz L, Wells C, Nichols A, McGee K. The neuropsychological effects of obstructive sleep apnea: a meta-analysis of norm-referenced and case-controlled data. Sleep. 2003 May 1;26(3):298-307.
99. Ye L, Pien GW, Weaver TE. Gender differences in the clinical manifestation of obstructive sleep apnea. Sleep medicine. 2009 Dec 1;10(10):1075-84.
100. Kryger MH, Roth T, Dement WC. Principles and Practice of Sleep Medicine. 7th ed. Philadelphia: Elsevier; 2022. p. 1123–1126
101. Adult Obstructive Sleep Apnea Task Force of the American Academy of Sleep Medicine. Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. Journal of clinical sleep medicine. 2009 Jun 15;5(3):263-76.

102. Netzer NC, Stoohs RA, Netzer CM, Clark K, Strohl KP. Using the Berlin Questionnaire to identify patients at risk for the sleep apnea syndrome. Annals of internal medicine. 1999 Oct 5;131(7):485-91.

103. Chung F, Abdullah HR, Liao P. STOP-Bang questionnaire: a practical approach to screen for obstructive sleep apnea. Chest. 2016 Mar 1;149(3):631-8.

104. Beck AT, Steer RA, Brown GK. Beck depression inventory.

105. Rosen IM, Kirsch DB, Chervin RD, Carden KA, Ramar K, Aurora RN, Kristo DA, Malhotra RK, Martin JL, Olson EJ, Rosen CL. Clinical use of a home sleep apnea test: an American Academy of Sleep Medicine position statement. Journal of Clinical Sleep Medicine. 2017 Oct 15;13(10):1205-7.

106. Kapur VK, Auckley DH, Chowdhuri S, Kuhlmann DC, Mehra R, Ramar K, Harrod CG. Clinical practice guideline for diagnostic testing for adult obstructive sleep apnea: an American Academy of Sleep Medicine clinical practice guideline. Journal of clinical sleep medicine. 2017 Mar 15;13(3):479-504.

107. Kushida CA, Littner MR, Morgenthaler T, Alessi CA, Bailey D, Coleman Jr J, Friedman L, Hirshkowitz M, Kapen S, Kramer M, Lee-Chiong T. Practice parameters for the indications for polysomnography and related procedures: an update for 2005. Sleep. 2005 Apr 1;28(4):499-523.

108. Iber C. The AASM manual for the scoring of sleep and associated events: Rules. Terminology and Technical Specification. 2007.

109. Collop NA, Anderson WM, Boehlecke B, Claman D, Goldberg R, Gottlieb DJ, Hudgel D, Sateia M, Schwab R. Clinical guidelines for the use of unattended portable monitors in the diagnosis of obstructive sleep apnea in adult patients. Journal of Clinical Sleep Medicine-JCSM. 2007;3(7):737-47.

110. Malhotra RK, Kirsch DB, Kristo DA, Olson EJ, Aurora RN, Carden KA, Chervin RD, Martin JL, Ramar K, Rosen CL, Rowley JA. Polysomnography for obstructive sleep apnea should include arousal-based scoring: an American Academy of Sleep Medicine position statement. Journal of clinical sleep medicine. 2018 Jul 15;14(7):1245-7.
111. Adult Obstructive Sleep Apnea Task Force of the American Academy of Sleep Medicine. Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. Journal of clinical sleep medicine. 2009 Jun 15;5(3):263-76.
112. Kushida CA, Littner MR, Hirshkowitz M, Morgenthaler TI, Alessi CA, Bailey D, Boehlecke B, Brown TM, Coleman Jr J, Friedman L, Kapen S. Practice parameters for the use of continuous and bilevel positive airway pressure devices to treat adult patients with sleep-related breathing disorders. Sleep. 2006 Mar 1;29(3):375-80.
113. Kryger MH, Roth T, Dement WC. Principles and Practice of Sleep Medicine. 7th ed. Philadelphia: Elsevier; 2022. p. 1175–1179.
114. Gay P, Weaver T, Loube D, Iber C. Evaluation of positive airway pressure treatment for sleep related breathing disorders in adults. Sleep. 2006 Mar 1;29(3):381-401.
115. Morgan TD. Novel approaches to the management of sleep-disordered breathing. Sleep medicine clinics. 2016 Jun 1;11(2):173-87.
116. Ramar K, Dort LC, Katz SG, Lettieri CJ, Harrod CG, Thomas SM, Chervin RD. Clinical practice guideline for the treatment of obstructive sleep apnea and snoring with oral appliance therapy: an update for 2015: an American Academy of Sleep

Medicine and American Academy of Dental Sleep Medicine clinical practice guideline. Journal of clinical sleep medicine. 2015 Jul 15;11(7):773-827.

117. Black JE, Hirshkowitz M. Modafinil for treatment of residual excessive sleepiness in nasal continuous positive airway pressure-treated obstructive sleep apnea/hypopnea syndrome. Sleep. 2005 Apr 1;28(4):464-71.

118. Koo BB, Patel SR, Strohl KP. Gender differences in REM-related obstructive sleep apnea. Sleep Breath. 2008;12(3):259–264.

119. Lee M, Oh J, Um YH, Kim YC, Kim TW, Seo HJ, Jeong JH, Hong SC. Obstructive Sleep Apnea and Medical Comorbidities in the Asian Population: Evidence From a Nationwide Healthcare System Data in South Korea. Psychiatry Investigation. 2024 Aug 20;21(9):987.

120. Sattaratpaijit N, Kulalert P, Wongpradit W. Characteristics of rapid eye movement-related obstructive sleep apnea in Thai patients. Scientific Reports. 2022 Jul 5;12(1):11360.

121. Qanash S, Alkhaldi H, Alotaibi O, et al. The prevalence of rapid eye movement-related obstructive sleep apnea in a sample of Saudi population. Healthcare (Basel). 2023;11(10):1421.

122. Nair D, Kumar R, Hegde S. Proportion of rapid eye movement sleep related obstructive sleep apnea (REM related OSA) in patients with sleep disordered breathing: A cross sectional study. Sleep Sci Pract. 2022;6:5.

123. Appleton SL, Vakulin A, McEvoy RD, Martin SA, Grant JF, Taylor AW, et al. Nocturnal hypoxaemia and severe obstructive sleep apnoea are associated with incident cardiovascular disease events: The Men Androgens Inflammation Lifestyle Environment and Stress (MAILES) study. Eur Respir J. 2016;48(2):589–97.

124. O'Donoghue FJ, Catcheside PG, Eckert DJ, McEvoy RD. Changes in respiration in NREM sleep in hypercapnic chronic obstructive pulmonary disease. The Journal of physiology. 2004 Sep;559(2):663-73.

125. Carberry JC, Jordan AS, White DP, Wellman A, Eckert DJ. Upper Airway Collapsibility (Pcrit) and Pharyngeal Dilator Muscle Activity are Sleep Stage Dependent. SLEEP [Internet]. 2016 Feb 29;39(3):511–21. Available from: https://doi.org/10.5665/sleep.5516

126. Findley LJ, Wilhoit SC, Suratt PM. Apnea Duration and Hypoxemia During REM Sleep in Patients with Obstructive Sleep Apnea. CHEST Journal [Internet]. 1985 Apr 1;87(4):432–6. Available from: https://pubmed.ncbi.nlm.nih.gov/3979129

127. Al Oweidat K, AlRyalat SA, Al-Essa M, Obeidat N. Comparing REM- and NREM-related obstructive sleep apnea in Jordan: a cross-sectional study. Can Respir J. 2018;2018:9270329.

128. Tan X, Ljunggren M, Kilander L, Benedict C, Lindberg E. Obstructive sleep apnea during rapid eye movement sleep and cognitive performance in adults. Sleep Medicine [Internet]. 2023 Nov 12;113:34–40. Available from: https://doi.org/10.1016/j.sleep.2023.11.017

129. Della Monica C, Johnsen S, Atzori G, Groeger JA, Dijk DJ. Rapid eye movement sleep, sleep continuity and slow wave sleep as predictors of cognition, mood, and subjective sleep quality in healthy men and women, aged 20–84 years. Frontiers in Psychiatry [Internet]. 2018 Jun 22;9. Available from: https://doi.org/10.3389/fpsyt.2018.00255

130. Ljunggren M, Naessén T, Theorell-Haglöw J, Franklin KA, Lindberg E. Rapid eye movement sleep apnea and carotid intima thickness in men and women: a

SHE-MUSTACHE cohort study. Journal of Sleep Research [Internet]. 2022 Apr 12;31(5).

131. Neilan TG, Farhad H, Dodson JA, Shah RV, Abbasi SA, Bakker JP, et al. Effect of sleep apnea and continuous positive airway pressure on cardiac structure and recurrence of atrial fibrillation. Journal of the American Heart Association [Internet]. 2013 Nov 18;2(6).
132. Chami HA, Gottlieb DJ, Redline S, Punjabi NM. Association between Glucose Metabolism and Sleep-disordered Breathing during REM Sleep. American Journal of Respiratory and Critical Care Medicine [Internet]. 2015 Jul 22;192(9):1118–26.
133. Grimaldi D, Beccuti G, Touma C, Van Cauter E, Mokhlesi B. Association of obstructive sleep apnea in rapid eye movement sleep with reduced glycemic control in Type 2 diabetes: therapeutic implications. Diabetes Care [Internet]. 2013 Oct 8;37(2):355–63.
134. Lui KK, Dave A, Sprecher KE, Chappel-Farley MG, Riedner BA, Heston MB, et al. Older adults at greater risk for Alzheimer's disease show stronger associations between sleep apnea severity in REM sleep and verbal memory. Alzheimer S Research & Therapy. 2024 May 9;16(1).
135. Su CS, Liu KT, Panjapornpon K, Andrews N, Foldvary-Schaefer N. Functional Outcomes in Patients with REM-Related Obstructive Sleep Apnea Treated with Positive Airway Pressure Therapy. Journal of Clinical Sleep Medicine [Internet]. 2012 Jun 14;08(03):243–7.
136. Koo BB, Wiggins R, Molina C. REM rebound and CPAP compliance. Sleep Medicine. 2012 Jun 15;13(7):864–8.
137. Almeneessier AS, Almousa Y, Hammad O, Olaish AH, ALAnbay ET, BaHammam AS. Long-term adherence to continuous positive airway pressure in

patients with rapid eye movement-only obstructive sleep apnea: a prospective cohort study. Journal of Thoracic Disease. 2017 Oct 1;9(10):3755–65. Mokhlesi B, Finn LA, Hagen EW, Young T, Hla KM, Van Cauter E, et al. Obstructive sleep apnea during REM sleep and hypertension: results of the Wisconsin Sleep Cohort. Am J Respir Crit Care Med. 2014;190(10):1158–67.

138. .Weaver TE, Grunstein RR. Adherence to continuous positive airway pressure therapy: the challenge to effective treatment. Proceedings of the American Thoracic Society. 2008 Feb 15;5(2):173-8.
139. Kuna ST, Gurubhagavatula I, Maislin G, Hin S, Hartwig KC, McCloskey S, Hachadoorian R, Hurley S, Gupta R, Staley B, Atwood CW. Noninferiority of functional outcome in ambulatory management of obstructive sleep apnea. American journal of respiratory and critical care medicine. 2011 May 1;183(9):1238-44.
140. Murase K, Tabata H, Saito M, et al. Telemonitoring-based strategy improves adherence to CPAP in obstructive sleep apnea. Eur Respir J. 2015;45(5):1232–1239.
141. Antic NA, Catcheside P, Buchan C, et al. The effect of CPAP in normalizing daytime sleepiness, quality of life, and neurocognitive function in moderate to severe OSA. Sleep. 2011;34(1):111–119.
142. Weaver TE, Sawyer AM. Adherence to continuous positive airway pressure treatment for obstructive sleep apnea: implications for future interventions. Indian J Med Res. 2010;131:245–258.
143. Pépin JL, Bailly S, Tamisier R. CPAP therapy: adherence and maintenance. Eur Respir Rev. 2019;28(151):190065.

144. Sutherland K, Vanderveken OM, Tsuda H, Marklund M, Gagnadoux F, Kushida CA, Cistulli PA. Oral appliance treatment for obstructive sleep apnea: an update. Journal of Clinical Sleep Medicine. 2014 Feb 15;10(2):215-27.

145. Marklund M. Long-term efficacy of an oral appliance in early treated patients with obstructive sleep apnea. Sleep and Breathing. 2016 May;20:689-94.

146. Ogawa T, Long J, Sutherland K, Chan AS, Sasaki K, Cistulli PA. Effect of mandibular advancement splint treatment on tongue shape in obstructive sleep apnea. Sleep and Breathing. 2015 Sep;19:857-63.

147. Positive Airway Pressure Titration Task Force of the American Academy of Sleep Medicine. Clinical guidelines for the manual titration of positive airway pressure in patients with obstructive sleep apnea. Journal of Clinical Sleep Medicine. 2008 Apr 15;4(2):157-71.

148. Ferguson KA, Cartwright R, Rogers R, Schmidt-Nowara W. Oral appliances for snoring and obstructive sleep apnea: a review. Sleep. 2006 Feb 1;29(2):244-62.

149. Phillips CL, Grunstein RR, Darendeliler MA, Mihailidou AS, Srinivasan VK, Yee BJ, Marks GB, Cistulli PA. Health outcomes of continuous positive airway pressure versus oral appliance treatment for obstructive sleep apnea: a randomized controlled trial. American journal of respiratory and critical care medicine. 2013 Apr 15;187(8):879-87.

150. Giannasi LC, Almeida FR, Nacif SR, de Oliveira LV. Efficacy of an oral appliance for the treatment of obstructive sleep apnea. International Journal of Prosthodontics. 2013 Jul 1;26(4).

151. Tuomilehto HP, Seppa JM, Partinen MM, Peltonen M, Gylling H, Tuomilehto JO, Vanninen EJ, Kokkarinen J, Sahlman JK, Martikainen T, Soini EJ. Lifestyle intervention with weight reduction: first-line treatment in mild obstructive sleep

apnea. American journal of respiratory and critical care medicine. 2009 Feb 15;179(4):320-7.

152. Miyamoto K, Ozbek MM, Hira HS, et al. Alcohol and sleep apnea. In: Kryger MH, Roth T, Dement WC, editors. Principles and Practice of Sleep Medicine. 7th ed. Philadelphia: Elsevier; 2023. p. 1345–1349
153. Carter SG, Carberry JC, Cho G, Fisher LP, Rollo CM, Stevens DJ, D'Rozario AL, McKenzie DK, Grunstein RR, Eckert DJ. Effect of 1 month of zopiclone on obstructive sleep apnoea severity and symptoms: a randomised controlled trial. European Respiratory Journal. 2018 Jul 19;52(1).
154. Adult Obstructive Sleep Apnea Task Force of the American Academy of Sleep Medicine. Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. Journal of clinical sleep medicine. 2009 Jun 15;5(3):263-76.
155. Rishi AR, Rishi MA. Rapid eye movement related obstructive sleep apnea: where do we stand?. Respiratory Investigation. 2021 Sep 1;59(5):589-95.
156. Ravesloot MJ, Van Maanen JP, Dun L, De Vries N. The undervalued potential of positional therapy in position-dependent snoring and obstructive sleep apnea—a review of the literature. Sleep and Breathing. 2013 Mar;17:39-49.
157. Jo S, Kim HW, Jeon JY, Lee SA. Protective effects of REM sleep without atonia against obstructive sleep apnea in patients with idiopathic REM sleep behavior disorder. Sleep Medicine. 2019 Feb 1;54:116-20.
158. Radwan H. Positional vs Nonpositional Obstructive Sleep Apnea Patients. Chest. 1997 Sep 3;112:629-39.

159. van Maanen JP, Meester KA, Dun LN, Koutsourelakis I, Witte BI, Laman DM, Hilgevoord AA, de Vries N. The sleep position trainer: a new treatment for positional obstructive sleep apnoea. Sleep and breathing. 2013 May;17:771-9.

160. Cartwright RD. Effect of sleep position on sleep apnea severity. Sleep. 1984 Sep 1;7(2):110-4.

161. De Vries GE, Hoekema A, Doff MH, Kerstjens HA, Meijer PM, van der Hoeven JH, Wijkstra PJ. Usage of positional therapy in adults with obstructive sleep apnea. Journal of Clinical Sleep Medicine. 2015 Feb 15;11(2):131-7.

162. Mehta V, Vasu TS, Phillips B, Chung F. Obstructive sleep apnea and oxygen therapy: a systematic review of the literature and meta-analysis. Journal of Clinical Sleep Medicine. 2013 Mar 15;9(3):271-9.

163. Javaheri S, Barbe F, Campos-Rodriguez F, Dempsey JA, Khayat R, Javaheri S, Malhotra A, Martinez-Garcia MA, Mehra R, Pack AI, Polotsky VY. Sleep apnea: types, mechanisms, and clinical cardiovascular consequences. Journal of the American College of Cardiology. 2017 Feb 21;69(7):841-58.

164. Taranto-Montemurro L, Messineo L, Sands SA, Azarbarzin A, Marques M, Edwards BA, Eckert DJ, White DP, Wellman A. The combination of atomoxetine and oxybutynin greatly reduces obstructive sleep apnea severity. A randomized, placebo-controlled, double-blind crossover trial. American journal of respiratory and critical care medicine. 2019 May 15;199(10):1267-76.

165. Caples SM, Rowley JA, Prinsell JR, Pallanch JF, Elamin MB, Katz SG, Harwick JD. Surgical modifications of the upper airway for obstructive sleep apnea in adults: a systematic review and meta-analysis. Sleep. 2010 Oct 1;33(10):1396-407.

166. Bhattacharjee R, Kheirandish-Gozal L, Spruyt K, Mitchell RB, Promchiarak J, Simakajornboon N, Kaditis AG, Splaingard D, Splaingard M, Brooks LJ, Marcus CL. Adenotonsillectomy outcomes in treatment of obstructive sleep apnea in children: a multicenter retrospective study. American journal of respiratory and critical care medicine. 2010 Sep 1;182(5):676-83.

167. Mokhlesi, B. (2012). REM-Related Obstructive Sleep Apnea: To Treat or Not to Treat? Journal of Clinical Sleep Medicine, 8(5), 597–598.

168. O'Connor, C., Thornley, K. S., Hanly, P. J. (2008). Gender differences in the polysomnographic features of obstructive sleep apnea. American Journal of Respiratory and Critical Care Medicine, 158(2), 461–465.

169. Adams, C., Fenton, M. E., Herckes, A., et al. (2016). The impact of differing definitions of REM-related obstructive sleep apnea on clinical characteristics and outcomes. Sleep and Breathing, 20(2), 625–632.

170. Zinchuk, A., & Yaggi, H. K. (2020). Phenotyping obstructive sleep apnea: Beyond severity metrics. Sleep, 43(7), zsz306.

171. Sasidaran, V., Kumar, S., Reddy, R., & Menon, P. (2024). Clinical profile of REM-related obstructive sleep apnea in a South Indian cohort. Indian Journal of Sleep Medicine, 19(1), 15–21.

172. Johnson, D. A., Billings, M. E., & Hale, L. (2018). Circadian disruption and human health: A bidirectional relationship. Sleep Health, 4(6), 444–453.

173. Katz, E. S., Mitchell, R. B., & D'Ambrosio, C. M. (2015). Obstructive sleep apnea in infants. American Journal of Respiratory and Critical Care Medicine, 191(12), 1385–1395.

174. Aurora, R. N., Crainiceanu, C., Gottlieb, D. J., Kim, J. S., Punjabi, N. M., & Redline, S. (2015). Obstructive sleep apnea during REM sleep and hypertension:

Results of the Wisconsin Sleep Cohort. American Journal of Respiratory and Critical Care Medicine, 191(10), 1150–1157.

175. Martinez-Ceron, E., Barquiel, B., Bezos, A. M., et al. (2016). Effect of continuous positive airway pressure on glycemic control in patients with obstructive sleep apnea and type 2 diabetes. A randomized clinical trial. American Journal of Respiratory and Critical Care Medicine, 194(4), 476–485.
176. Gozal D, Daniel JM, Dohanich GP. Behavioral and anatomical correlates of chronic episodic hypoxia during sleep in the rat. J Neurosci. 2001;21(7):2442–50.
177. Morrell MJ, McRobbie DW, Quest RA, Cummin AR, Ghiassi R, Corfield DR. Changes in brain morphology associated with obstructive sleep apnea. Sleep Med. 2003;4(5):451–4
178. Kalkbrenner M, Dossow V von, Steffen A, Penzel T, Fietze I, Glos M. Sex differences in REM-predominant obstructive sleep apnea: a retrospective analysis of a large clinical cohort. J Clin Sleep Med. 2022;18(1):77–86.
179. Popovic RM, White DP. Upper airway muscle activity in normal women: influence of hormonal status. J Appl Physiol (1985). 1998;84(6):2227–32.
180. AS, McSharry DG, Malhotra A. Adult obstructive sleep apnoea. Lancet. 2014;383(9918):736–47.
181. Popovic RM, White DP. Influence of gender on waking genioglossal electromyogram and upper airway resistance. American journal of respiratory and critical care medicine. 1995 Aug;152(2):725-31.
182. Berry RB, Kryger MH, Massie CA. A novel auto-adjusting CPAP device for the treatment of obstructive sleep apnea. Sleep. 2002;25(2):148–53
183. Stepnowsky CJ, Marler MR, Ancoli-Israel S. Determinants of CPAP adherence in sleep apnea patients. Sleep Med. 2002;3(3):239–47.

184. Edwards BA, Eckert DJ, McSharry DG, et al. Clinical predictors of the respiratory arousal threshold in patients with obstructive sleep apnea. Am J Respir Crit Care Med. 2014;190(11):1293–1300.

185. Eckert DJ, Malhotra A, Wellman A, et al. The influence of obstructive sleep apnea and gender on genioglossus activity during rapid eye movement sleep. Chest. 2009;135(4):957–964.

186. Oksenberg A, Silverberg DS, Arons E, Radwan H. Positional vs nonpositional obstructive sleep apnea patients: anthropomorphic, nocturnal polysomnographic, and multiple sleep latency test data. Chest. 1997;112(3):629–639.

187. Facco FL, Ouyang DW, Zee PC, Grobman WA. Sleep disordered breathing in a high-risk cohort prevalence and severity across pregnancy. Am J Perinatol. 2014;31(10):899–904.

188. Germain A, Buysse DJ, Nofzinger EA. Sleep-specific mechanisms underlying posttraumatic stress disorder: integrative review and neurobiological hypotheses. Sleep Med Rev. 2008;12(3):185–95.

189. Naughton MT, Benard DC, Liu PP, Rutherford R, Rankin F, Bradley TD. Effects of nasal CPAP on sympathetic activity in patients with heart failure and central sleep apnea. Am J Respir Crit Care Med. 1995;152(2):473–9.

190. Mano M, Hoshino T, Sasanabe R, et al. Impact of gender and age on rapid eye movement-related obstructive sleep apnea: a clinical study of 3234 Japanese OSA patients. Int J Environ Res Public Health. 2019;16(6):1068.

191. Berry RB, Brooks R, Gamaldo CE, et al. The AASM manual for the scoring of sleep and associated events: rules, terminology and technical specifications. Version 2.6. Darien, IL: American Academy of Sleep Medicine; 2020.

192. Haba-Rubio J, Janssens JP, Rochat T, Sforza E. REM sleep obstructive sleep apnea: clinical and polysomnographic characteristics. Chest. 2005;128(5):3350-3357.

193. Johns MW. A new method for measuring daytime sleepiness: the Epworth Sleepiness Scale. Sleep. 1991;14(4):540-5.

194. Chervin RD, Aldrich MS, Pickett R, Guilleminault C. Prevalence of sleep-disordered breathing in 10-year-old children: results from the Tucson Children's Assessment of Sleep Apnea Study (TuCASA). Sleep. 2002;25(2):186-91.

195. Budhiraja R, Auckley D, et al. Diagnosis and management of obstructive sleep apnea. Clin Chest Med. 2011;32(4):663-75.

196. Chung F, Yegneswaran B, Liao P, et al. Stop-bang questionnaire: a practical approach to screen for obstructive sleep apnea. Chest. 2008;134(5):1380-8.

197. Berry RB, Budhiraja R, Gottlieb DJ, et al. Rules for scoring respiratory events in sleep: update of the 2007 AASM Manual for the Scoring of Sleep and Associated Events. J Clin Sleep Med. 2012;8(5):597-619.

198. Bixler EO, Vgontzas AN, Lin HM, et al. Prevalence of sleep-disordered breathing in women: effects of gender. Am J Respir Crit Care Med. 2001;163(3 Pt 1):608–613.

199. Young T, Peppard PE, Gottlieb DJ. Epidemiology of obstructive sleep apnea: a population health perspective. Am J Respir Crit Care Med. 2002;165(9):1217–1239.

200. Ancoli-Israel S, Kripke DF, Klauber MR, et al. Sleep-disordered breathing in community-dwelling elderly. Sleep. 1991;14(6):486–495.

201. Malhotra A, White DP. Obstructive sleep apnoea. Lancet. 2002;360(9328):237–245.

202. Mokhlesi B, Mazzotti DR, Ortega SP, et al. Unstandardized definitions of REM-related OSA lead to variations in prevalence and associated clinical characteristics. Sleep Med. 2018;47:33–40.

203. Appleton SL, Vakulin A, McEvoy RD, Martin SA, Grant JF, Taylor AW, et al. Nocturnal hypoxaemia and severe obstructive sleep apnoea are associated with incident cardiovascular disease events: The Men Androgens Inflammation Lifestyle Environment and Stress (MAILES) study. Eur Respir J. 2016;48(2):589–97.

204. Mokhlesi B, Finn LA, Hagen EW, Young T, Hla KM, Van Cauter E, et al. Obstructive sleep apnea during REM sleep and hypertension: results of the Wisconsin Sleep Cohort. Am J Respir Crit Care Med. 2014;190(10):1158–67.

205. Chervin RD, Hedger K, Dillon JE, Pituch KJ. Pediatric sleep apnea syndrome: prevalence of snoring, diagnosis, and behavioral correlates. Arch Pediatr Adolesc Med. 2000;154(3):251–6.

206. Shahar E, Whitney CW, Redline S, Lee ET, Newman AB, Javier Nieto F, et al. Sleep-disordered breathing and cardiovascular disease: Cross-sectional results of the Sleep Heart Health Study. Am J Respir Crit Care Med. 2001;163(1):19–25.

207. Azarbarzin A, Sands SA, Stone KL, Taranto-Montemurro L, Messineo L, Terrill PI, et al. The hypoxic burden of sleep apnoea predicts cardiovascular disease-related mortality: the Osteoporotic Fractures in Men Study and the Sleep Heart Health Study. Eur Heart J. 2019;40(14):1149–57

208. Redline S, Yenokyan G, Gottlieb DJ, Shahar E, O'Connor GT, Resnick HE, et al. Obstructive sleep apnea–hypopnea and incident stroke: the Sleep Heart Health Study. Am J Respir Crit Care Med. 2010;182(2):269–77.

209. Punjabi NM, Caffo BS, Goodwin JL, Gottlieb DJ, Newman AB, O'Connor GT, et al. Sleep-disordered breathing and mortality: a prospective cohort study. PLoS Med. 2009;6(8):e1000132.

210. Bianchi MT, Thomas RJ, Westover MB. An open request to epidemiologists: please stop reporting AHI as the sole metric of sleep apnea severity. J Clin Sleep Med. 2012;8(5):577–82.

211. Loo MH, Wong J, Khoo SM, Narayanaswamy V, Ayas N, Fleetham JA, et al. REM-related obstructive sleep apnea and its association with adherence to CPAP. Chest. 2011;140(4):AB269.

212. Choi H, Cho JH, Kim SW, Kim TH. REM-related obstructive sleep apnea is associated with greater subjective sleepiness and depressive symptoms. Psychiatry Investig. 2017;14(4):559–565. doi:10.4306/pi.2017.14.4.559

213. Eiseman NA, Westover MB, Ellenbogen JM, Bianchi MT. The impact of body posture and sleep stages on sleep apnea severity in adults. J Clin Sleep Med. 2012;8(6):655–66.

ANNEXURES – I

KAHERs JNMC
BELAGAVI
INFORMED CONSENT FORM

"Prevalence of rapid eye movement sleep related obstructive sleep apnoea (REM related OSA) in patients with sleep disordered breathing – a cross sectional study done in 1 year"

Name of Student/Principal Investigator: **REG NO.: BR0122002**

Name of Guide/Co Investigators:

Introduction:

Polysomnography, also known as sleep study is a test used to identify sleep disorders.This study records the brain waves,the oxygen levels in the blood,heart rate during sleep.It also assesses the breathing pattern and eye and leg,movements during sleep.
In addition to diagnosis, Polysomnography can also aid in devising a treatment plan to promote the quality of life in such individuals.

The measurements recorded during a sleep study provide a great deal of information about your sleep patterns
For example,

- Brain waves and eye movements- this helps assess the sleep stages
  This helps identify any disruption in stages
  Disruptions can occur due to sleep disorders like narcolepsy, REM sleep behaviour disorder
- Heart and breathing rate changes- atypical changes maybe suggestive of sleep apnoea
- Frequent leg movements- that disrupt your sleep may indicate periodic limb movement disorder
- Unusual movements or behaviours during sleep may be suggestive of REM sleep behaviour disorder or other sleep disorders
- Using PAP or oxygen can indicate which device settings work best for you

Explanation of procedure:

The patient will be admitted for sleep study.

The study is conducted usually during the night.
Once the patient is ready to go to bed,the technologist will place the sensors on the scalp, chest, temples and legs.The sensors are then connected to a computer.A small clip is placed on your finger or ear which monitors the level of oxygen in the blood.
While the patient sleeps , the technologist monitors in the patient

- Brain waves
- Eye movements
- Heart rate
- Breathing pattern
- Blood oxygen level
- Body position
- Chest and abdominal movement
- Limb movement
- Snoring and other noises

The technologist monitor the patient during the night .If the patient needs any help he/she can communicate with the technologist through the monitoring equipment.They can come into the room to free up the wires if you need to get up

Withdrawal from participation in the study: Participation in this study in voluntary. You will be free to decide whether to participate in this study or continue participation once enrolled. In case you decide to withdraw your participation, you are free to do so. However, please convey the decision to the principal investigator.

Possible benefits from participating in the study: You will/will not have nor get any benefits by participating in this study. The data gathered will help population at large.

Possible risks from participating in the study: There are no risks involved in participating in this study.

Privacy and confidentiality: The information collected from you will be coded, to prevent any person to identify you. Your identity will never be revealed. The data collected from you will be kept confidential and only processed or aggregated data will be used for publication.

Financial incentives: You will not receive any payment for participating in this study.

Authorization for publication of aggregated data: Results obtained after processing of the aggregated data will be published for scientific purpose and or presented to scientific groups.
However, your identity will never be revealed.

Questions:
In case of any questions with regard to this study, you are free to contact:
REG NO.: BR0122002
If you have any question or complaints with regard to your right as study participant you may contact Dr Harsha Hegde, Chairperson, Ethical committee of JNMC, 0831-2473777 Extension 4052.

Legal rights: By signing this consent form, we are not waving any of your legal rights

CONSENT STATEMENT

I am making a voluntary decision to participate in the study "Proportion of rapid eye movement sleep related obstructive sleep apnoea (REM related OSA) in patients with sleep disordered breathing – a cross sectional study done in 1 year". My signature below indicates that I have decided to participate and I have read the information provided above or the information provided above has been read to me in the language that I understand best. I was given the opportunity to ask questions and that they have been answered to my satisfaction.

Name of the participant:

Signature or left thumb impression of the participant:

Name of the witness:

Signature or left thumb impression of the witness:

Name of the investigator:

Signature of the investigator:

PROFORMA

Demographic information

1. Patient ID:
2. Age:
3. Gender:
4. Height (cm):
5. Weight (kg):
6. Body mass index (BMI)
7. Neck circumference (cm):
8. Waist-Hip Ratio:

Medical history

Comorbidities

- Hypertension
- Diabetes mellitus
- Cardiovascular diseases
- Hypothyroidism
- Dyslipidemia
- Cerebrovascular diseases

Family history of OSA

Smoking status

Alcohol use

Sedative/Hypnotic use

Symptoms

1. Daytime sleepiness : (Epworth sleepiness scale score):	
2. Snoring:	
3. Witnessed apnoea:	
4. Morning headaches	
5. Non restorative sleep, fatigue:	
6. Mood changes: Neurocognitive repercussions	
7. insomnia	
8. increased dreams, nightmares	
9. STOP BANG score	

10.BERLIN questionnaire	
11.Beck depression inventory	
12.Mallampati score	

POLYSOMNOGRAPHY (PSG) DATA

1. Total sleep time:
2. Apnoea- Hypopnoea index:
    - REM AHI
    - NREM AHI
3. REM sleep duration (minutes)
4. Sleep efficiency
5. sleep latency (minutes)
6. Oxygen desaturation index (ODI)
7. Lowest recorded oxygen saturation (%)
8. Supine AHI
9. Non supine AHI
10. Longest REM event
11. Longest NREM event

12. Snoring index
13. Arousal index
14. Limb movement index
15. REM RDI
16. Total sleep duration

REM OSA definition and classification

1. REM OSA present: Yes/No

2. Severity Classification (Based on overall AHI)

- MILD (AHI 5-14)
- MODERATE (AHI 15-29)
- SEVERE (AHI ≥ 30)

Beck's Depression Inventory

This depression inventory can be self-scored. The scoring scale is at the end of the questionnaire.

1.
- 0 I do not feel sad.
- 1 I feel sad
- 2 I am sad all the time and I can't snap out of it.
- 3 I am so sad and unhappy that I can't stand it.

2.
- 0 I am not particularly discouraged about the future.
- 1 I feel discouraged about the future.
- 2 I feel I have nothing to look forward to.
- 3 I feel the future is hopeless and that things cannot improve.

3.
- 0 I do not feel like a failure.
- 1 I feel I have failed more than the average person.
- 2 As I look back on my life, all I can see is a lot of failures.
- 3 I feel I am a complete failure as a person.

4.
- 0 I get as much satisfaction out of things as I used to.
- 1 I don't enjoy things the way I used to.
- 2 I don't get real satisfaction out of anything anymore.
- 3 I am dissatisfied or bored with everything.

5.
- 0 I don't feel particularly guilty
- 1 I feel guilty a good part of the time.
- 2 I feel quite guilty most of the time.
- 3 I feel guilty all of the time.

6.
- 0 I don't feel I am being punished.
- 1 I feel I may be punished.
- 2 I expect to be punished.
- 3 I feel I am being punished.

7.
- 0 I don't feel disappointed in myself.
- 1 I am disappointed in myself.
- 2 I am disgusted with myself.
- 3 I hate myself.

8.
- 0 I don't feel I am any worse than anybody else.
- 1 I am critical of myself for my weaknesses or mistakes.
- 2 I blame myself all the time for my faults.
- 3 I blame myself for everything bad that happens.

9.
- 0 I don't have any thoughts of killing myself.
- 1 I have thoughts of killing myself, but I would not carry them out.
- 2 I would like to kill myself.
- 3 I would kill myself if I had the chance.

10.
- 0 I don't cry any more than usual.
- 1 I cry more now than I used to.
- 2 I cry all the time now.
- 3 I used to be able to cry, but now I can't cry even though I want to.

11.
- 0 I am no more irritated by things than I ever was.
- 1 I am slightly more irritated now than usual.
- 2 I am quite annoyed or irritated a good deal of the time.
- 3 I feel irritated all the time.

12.
- 0 I have not lost interest in other people.
- 1 I am less interested in other people than I used to be.
- 2 I have lost most of my interest in other people.
- 3 I have lost all of my interest in other people.

13.
- 0 I make decisions about as well as I ever could.
- 1 I put off making decisions more than I used to.
- 2 I have greater difficulty in making decisions more than I used to.
- 3 I can't make decisions at all anymore.

14.
- 0 I don't feel that I look any worse than I used to.
- 1 I am worried that I am looking old or unattractive.
- 2 I feel there are permanent changes in my appearance that make me look unattractive
- 3 I believe that I look ugly.

15.
- 0 I can work about as well as before.
- 1 It takes an extra effort to get started at doing something.
- 2 I have to push myself very hard to do anything.
- 3 I can't do any work at all.

16.
- 0 I can sleep as well as usual.
- 1 I don't sleep as well as I used to.
- 2 I wake up 1-2 hours earlier than usual and find it hard to get back to sleep.
- 3 I wake up several hours earlier than I used to and cannot get back to sleep.

17.
- 0 I don't get more tired than usual.
- 1 I get tired more easily than I used to.
- 2 I get tired from doing almost anything.
- 3 I am too tired to do anything.

18.
- 0 My appetite is no worse than usual.
- 1 My appetite is not as good as it used to be.
- 2 My appetite is much worse now.
- 3 I have no appetite at all anymore.

19.
- 0 I haven't lost much weight, if any, lately.
- 1 I have lost more than five pounds.
- 2 I have lost more than ten pounds.
- 3 I have lost more than fifteen pounds.

20.

0 I am no more worried about my health than usual.
1 I am worried about physical problems like aches, pains, upset stomach, or constipation.
2 I am very worried about physical problems and it's hard to think of much else.
3 I am so worried about my physical problems that I cannot think of anything else.

21.

0 I have not noticed any recent change in my interest in sex.
1 I am less interested in sex than I used to be.
2 I have almost no interest in sex.
3 I have lost interest in sex completely.

INTERPRETING THE BECK DEPRESSION INVENTORY

Now that you have completed the questionnaire, add up the score for each of the twenty-one questions by counting the number to the right of each question you marked. The highest possible total for the whole test would be sixty-three. This would mean you circled number three on all twenty-one questions. Since the lowest possible score for each question is zero, the lowest possible score for the test would be zero. This would mean you circles zero on each question. You can evaluate your depression according to the Table below.

Total Score_____Levels of Depression

1-10_____These ups and downs are considered normal
11-16_____ Mild mood disturbance
17-20_____Borderline clinical depression
21-30_____Moderate depression
31-40_____Severe depression
over 40_____Extreme depression

Class 0: Ability to see any part of the epiglottis upon mouth opening and tongue protrusion

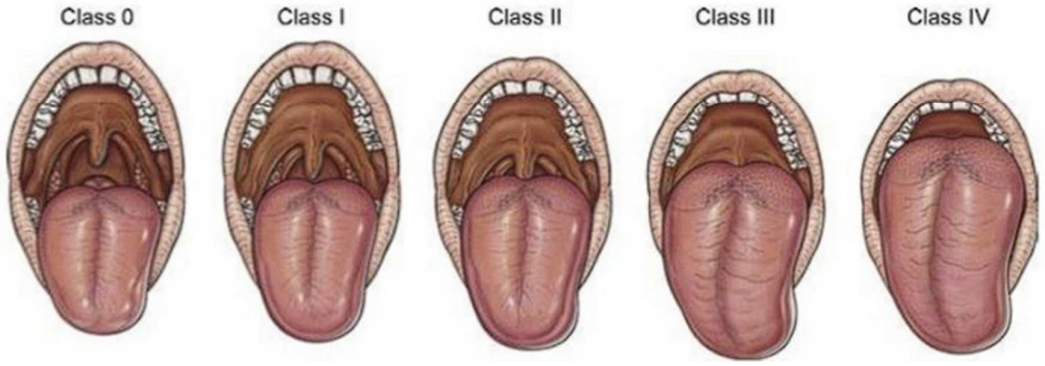
Class I: Soft palate, fauces, uvula, pillars visible

Class II: Soft palate, fauces, uvula visible

Class III: Soft palate, base of uvula visible

Class IV: Soft palate not visible at all

Figure. Modified Mallampati Score



Epworth Sleepiness Scale

Name: _____

Date: _____

Your age: (Yr) _____ **Your sex:** ❑ Male ❑ Female

How likely are you to doze off or fall asleep in the situations described below, in contrast to feeling just tired?

This refers to your usual way of life in recent times.

Even if you haven't done some of these things recently try to work out how they would have affected you.

Use the following scale to choose the most appropriate number for each situation:-

0 = would never doze
1 = Slight chance of dozing
2 = Moderate chance of dozing
3 = High chance of dozing

Situation	**Chance of dozing**
Sitting and reading	
Watching TV	
Sitting, inactive in a public place (e.g. a theatre or a meeting)	
As a passenger in a car for an hour without a break	
Lying down to rest in the afternoon when circumstances permit	
Sitting and talking to someone	
Sitting quietly after a lunch without alcohol	
In a car, while stopped for a few minutes in the traffic	
Total	

Score:	
0-10	Normal range
10-12	Borderline
12-24	Abnormal

Berlin Questionnaire

Attending MD_____

PCP_____

Patient Information

Height: Age:

Weight: Male/Female

Category 1

Do you snore?
- ☐ **Yes**
- ☐ No
- ☐ Don't Know

Your snoring is?
- ☐ Slightly louder than breathing
- ☐ As loud as talking
- ☐ **Louder than talking**
- ☐ **Can be hear in adjacent room**

Describe the snoring frequency
- ☐ **Nearly every day**
- ☐ **3-4 times a week**
- ☐ 1-2 times a week
- ☐ 1-2 times a month
- ☐ Never or nearly never

Has your snoring ever bothered other people?
- ☐ **Yes**
- ☐ No

Has anyone noticed that you quit breathing during your sleep?
- ☐ **Nearly every day**
- ☐ **3-4 time a week**
- ☐ 1-2 time a week
- ☐ 1-2 time a month
- ☐ Never or nearly never

Category 1 positive (≥2) ☐
Category 2 positive (≥2) ☐
Category 3 positive (1 or BMI>30) ☐

Category 2

How often do you feel tired or fatigued after you sleep?
- ☐ **Nearly every day**
- ☐ **3-4 times a week**
- ☐ 1-2 times a week
- ☐ 1-2 times a month
- ☐ Never or nearly never

During your wake time, do you feel tired, fatigued or not up to par?
- ☐ **Nearly every day**
- ☐ **3-4 times a week**
- ☐ 1-2 times a week
- ☐ 1-2 times a month
- ☐ Never or nearly never

Have you ever nodded off or fallen asleep while driving a vehicle?
- ☐ **Yes**
- ☐ No

If yes, how often does it occur?
- ☐ **Nearly every day**
- ☐ **3-4 times a week**
- ☐ 1-2 times a week
- ☐ 1-2 times a month
- ☐ Never or nearly never

Category 3

Do you have high blood pressure?
- ☐ **Yes**
- ☐ No

BMI= _____

Signature_____**Date**_____

ANNEXURES – III

PHOTOGRAPHS

ALICE PDX system, Philips Respironics system available in the ingouse level II sleep lab

S.No	Age	Gender	BMI	Neck Circumference	Waist Hip Ratio	Daytime Sleepiness	Snoring	Fatigue	Non-refreshing Sleep	Morning Headache	Mood Changes	Neurocognitive Repercussions	Insomnia	Increased Dreams	Nightmares	Mallampati Score	Epworth Sleepiness Scale	Berlin Questionnaire	Beck's Depression Inventory	STOP BANG SCORE	Diabetes	Hypertension	Dyslipidemia	Cardiovascular Diseases	Cerebrovascular Diseases	No Comorbidities	Hypothyroidism	Overall AHI	REM AHI	NREM AHI	REM AHI/NREM AHI	SUPINE AHI	NON SUPINE AHI	Longest Recorded REM Event	Longest Recorded NREM Event	Sleep Latency	Sleep Efficiency	Snoring Index	Oxygen Desaturation Index	Arousal Index	Lowest Recorded Oxygen Saturation	Limb Movement Index	Length of REM Sleep (mins)	REM RDI	Total Sleep Time (mins)	Criteria for REM OSA Diagnosis	REM OSA
1	60	Female	35.46	45	0.73	1	1	0	1	1	1	1	0	0	0	4	11	High Risk	54	5	1	1	0	1	1	0	0	66	74.6	2.9	25.72	75.5	32.4	14	47	7	80.6	3.2	13.6	33.4	71.1	4.6	97	3.5	339	Both	Yes
2	49	Female	17.71	48.2	0.73	1	1	1	0	0	0	0	0	0	1	4	4	Low Risk	59	7	0	1	1	1	0	0	0	43.6	96	1.8	53.33	78.9	37	9	37	51	52.2	2.8	45.6	40.8	94	2.5	38	10.8	249	Both	Yes
3	62	Female	24.78	31.8	0.73	0	0	1	0	0	1	1	0	0	1	4	9	Low Risk	48	7	1	1	0	0	1	0	1	17.9	39.8	1	39.8	23.3	10.5	9	8	7	88.7	40.6	32.4	36.8	70.1	9.1	132	5.6	258	Both	Yes
4	44	Male	30.52	45.3	0.94	0	0	1	0	0	0	0	0	1	1	3	8	High Risk	9	6	0	1	1	1	0	0	1	54.1	57.3	3.7	15.49	57.1	24.2	6	5	45	69.9	33	32.3	3.3	87.5	9.4	136	13.2	449	Both	Yes
5	40	Male	27.35	43.5	1.16	1	1	0	0	1	1	0	0	1	1	4	18	Low Risk	43	3	1	1	0	1	1	0	0	54.7	95.5	3.4	28.09	64.9	52.7	11	30	31	55.9	4	36.6	46.1	51.2	2.7	142	5.6	255	Both	Yes
6	39	Female	27.22	47.7	0.72	1	0	1	1	0	0	0	1	0	0	3	14	High Risk	18	7	1	1	0	1	0	0	1	39.9	92.3	3	30.77	59.9	41.7	6	25	21	64.3	17.9	44.8	27.9	99.8	14.6	36	15.4	349	Both	Yes
7	62	Female	20.16	37.7	0.73	0	1	0	0	0	0	0	0	1	0	4	5	High Risk	17	3	1	1	0	0	0	0	0	33.8	64.9	3.1	20.94	47.5	26.8	15	46	28	95.3	9.8	19.7	4.1	96.6	12.6	49	15.8	214	Both	Yes
8	50	Male	28.38	39.5	0.89	1	0	1	0	0	0	0	0	1	0	3	10	Low Risk	0	5	0	1	0	0	1	0	0	30.7	78.6	2.3	34.17	44.4	21.5	7	30	32	52.3	6	46.7	25.3	80.6	3.2	131	8.1	257	Both	Yes
9	41	Male	27.11	34.4	0.9	1	0	0	0	0	0	0	0	1	1	3	6	High Risk	52	1	1	1	0	0	0	0	0	47.8	87	2.5	34.8	78.4	42.4	6	49	10	67.4	42.9	7.1	41.8	55	4.8	58	13.3	368	Both	Yes
10	20	Female	42.13	37.1	0.7	0	0	1	1	1	0	0	0	1	1	1	5	Low Risk	49	4	1	1	1	1	0	0	0	61.4	84.6	3.9	21.69	91.7	36.1	12	48	4	69.3	43.6	2.8	27.5	52.2	10	120	4	296	Both	Yes
11	39	Male	22.99	39.5	0.89	0	1	1	0	1	0	0	1	0	0	1	6	High Risk	21	5	0	1	1	0	0	0	0	9.4	19	1.4	13.57	12.6	8.9	7	47	48	78.1	1.1	8.2	18.2	84.2	3.8	36	5.2	258	Both	Yes
12	38	Male	31.13	34.8	0.91	1	1	1	1	1	0	0	0	0	0	3	17	High Risk	9	4	1	1	1	1	0	0	0	50	72.9	4.4	16.57	59.4	29.6	5	35	32	93.5	7.2	5.6	10.5	55.7	5.3	36	14.3	312	Both	Yes
13	50	Female	33.18	33.2	0.74	1	1	0	0	0	0	1	0	0	1	4	15	High Risk	32	0	0	1	0	0	0	0	0	6.1	9.3	2.9	3.21	6.9	2.2	5	6	51	56.7	46	14.4	47.6	85.8	11	140	3.5	497	Both	Yes
14	47	Male	37.03	34.7	0.85	1	1	1	1	1	0	0	0	0	0	4	17	Low Risk	43	6	1	1	0	1	1	0	0	85.4	90.6	2.9	31.24	130.9	48.3	15	40	31	64.3	11	49.5	14.7	72.3	9.1	43	7.8	362	Both	Yes
15	38	Male	29.58	47.3	0.95	1	1	1	0	0	1	0	1	1	0	2	14	Low Risk	47	2	1	1	0	1	0	0	0	60.1	83	4.7	17.66	101.5	60.3	10	16	34	96	1	24	6.7	57.8	8.5	146	14.7	299	Both	Yes
16	54	Male	22.17	34.4	0.84	1	1	0	0	0	0	0	0	0	1	4	10	High Risk	25	7	0	1	0	0	0	0	0	3.2	7.6	0.6	12.67	4.8	3.2	11	53	27	99	28	28	35.2	65.1	10.5	173	10	473	Both	Yes
17	40	Male	33.71	35.1	0.85	0	1	0	1	1	0	0	0	1	0	3	0	High Risk	26	1	1	1	1	0	0	0	1	79.8	95.4	3	31.8	101.7	52.8	7	49	29	77.2	3.4	26.5	42.7	94.9	13.6	119	14.2	316	Both	Yes
18	18	Female	34.12	33.8	0.85	1	1	0	1	0	0	0	1	0	1	1	7	High Risk	2	4	0	1	0	0	1	0	0	27.6	40.8	4.8	8.5	34.1	19.4	14	11	56	53.1	11.2	17.8	34	81.8	10.4	168	0.5	532	Both	Yes
19	36	Female	43.69	44.5	0.72	1	0	0	0	0	1	1	0	0	0	3	12	High Risk	42	7	1	1	1	1	0	0	0	13	36.4	2.5	14.56	33.1	19.8	9	35	57	53.8	21.1	33.1	6.4	79.3	10.8	86	7.8	296	Both	Yes
20	47	Male	30.02	46.9	0.93	1	0	0	0	0	1	0	0	1	1	3	8	Low Risk	55	7	0	1	0	1	0	0	0	25.4	53	1.9	27.89	64.7	37.7	15	6	36	94.2	9.3	31.9	10.2	56.7	14.1	93	3.6	292	Both	Yes
21	67	Male	23.87	46.7	1.04	1	0	0	1	0	0	0	0	0	0	1	6	High Risk	7	2	1	1	1	1	0	0	0	55	77.8	4.2	18.52	95.7	42.6	8	45	22	79.2	23.5	47.4	7.9	85	12.4	135	15	354	Both	Yes
22	66	Male	43.2	44.1	0.99	1	1	1	1	1	1	0	0	1	1	3	14	High Risk	15	1	1	1	0	1	1	0	0	58.6	60.4	1.6	37.75	92.8	30.9	14	9	12	55.7	18.4	26.6	14.2	98.5	10.8	111	2.2	224	Both	Yes
23	68	Male	18.12	42.6	0.95	1	1	0	1	0	1	1	0	1	0	4	19	Low Risk	51	3	1	1	1	0	0	0	1	68.9	78.5	2.5	31.4	72.4	37.9	8	40	19	80.9	39.9	43.7	2.9	98.9	14.7	78	3.8	421	Both	Yes
24	18	Male	38.55	40.4	1	1	1	1	1	0	1	0	1	1	1	4	2	Low Risk	34	4	1	1	0	0	0	0	0	31.8	42.9	4.8	8.94	32.6	24.7	7	31	6	50.7	0.1	40	53.9	90.8	4.3	132	2.9	555	Both	Yes
25	50	Male	26.11	41.2	1.18	0	1	1	0	0	0	1	1	1	1	1	7	High Risk	45	2	0	1	1	1	0	0	0	89.5	81.1	68.7	2.4	26.7	59.9	9	27	6	79.1	8.2	10.6	11.5	69.7	2.1	111	37.5	296	Both	Yes
26	36	Female	29.52	42.9	1.19	0	1	0	0	1	1	0	0	1	0	1	21	High Risk	38	6	0	1	1	0	0	0	1	30.9	68.4	70.3	0.85	81.2	55.8	14	22	0	51.1	23.7	10.4	26	54	12.6	39	47.8	508	Both	Yes
27	41	Male	35.1	44.4	0.94	1	0	0	1	0	1	1	0	0	1	2	20	Low Risk	45	0	0	1	1	1	0	0	0	11.2	27.5	96.7	0.28	18.6	5	11	20	14	68.4	2.2	37	28.1	73.8	7.5	45	28.3	371	Both	Yes
28	24	Female	33.05	45.4	1.02	0	0	0	0	1	0	0	1	1	0	3	16	High Risk	9	6	1	1	1	0	0	0	1	6.9	82.4	41	2.01	5.6	68.4	15	18	31	76.7	44.9	43.8	29.4	52.9	10.7	141	21.8	311	Both	Yes
29	22	Male	34.8	35.1	1.16	0	0	0	0	0	1	1	1	0	0	2	16	Low Risk	38	3	0	1	1	1	1	0	0	53.6	11	62.4	0.18	67.1	79.2	5	28	45	61.8	41.3	14.6	32.4	85.4	8.6	98	0.2	364	Both	Yes
30	45	Female	31.05	42	1.1	0	1	0	1	0	1	1	0	0	0	4	9	High Risk	23	0	1	1	1	1	1	0	0	73.8	48.3	41.8	1.16	25.9	98.6	7	19	55	91.3	48.8	43.9	45.4	68.6	0.5	70	30.4	281	Both	Yes
31	44	Female	20.4	31.8	0.7	1	0	1	0	0	0	1	1	1	1	4	5	Low Risk	0	6	1	1	1	1	0	0	0	37.7	93.8	17.3	5.42	40.7	22.4	12	27	57	81	3.4	25	41.6	98.4	8.1	138	8.3	517	Broad Onl	Yes
32	40	Female	23.8	47.9	0.72	0	0	1	0	1	1	0	0	0	1	3	4	High Risk	59	7	0	1	0	1	1	0	0	12.3	4.5	84.6	1.41	18.4	5.8	1	46	36	50.7	13.4	23.9	11.4	56.2	13.9	106	7.4	544	Broad Onl	Yes
33	64	Male	22.33	48.4	1.02	1	0	0	0	0	1	1	0	1	1	2	8	Low Risk	8	2	0	1	1	1	0	0	0	6.8	56.7	29.2	1.94	9.9	4.3	12	5	50	96.9	49.1	34.4	30.1	59.3	8.6	85	15.2	216	Broad Onl	Yes
34	55	Male	29.77	45.7	1.04	1	1	1	1	0	1	1	1	0	0	4	14	High Risk	50	6	0	1	0	1	0	0	0	11.9	3.4	37	0.09	5.2	9.6	1	5	55	92.8	8.6	5.4	26.4	53.4	13.8	81	7.1	530	Broad Onl	Yes
35	48	Male	38.53	46.7	1.02	0	0	0	0	0	0	0	0	1	1	4	20	High Risk	60	5	0	1	1	1	0	0	0	83.9	85.8	41.8	2.05	125.9	45.7	4	26	12	90	9.8	18.7	24.2	50.7	14	73	15	458	Broad Onl	Yes
36	33	Male	21.5	31.9	0.84	1	0	0	1	0	0	1	1	0	0	2	9	Low Risk	6	1	0	1	0	0	0	0	0	2.9	4.3	1.9	2.26	2.9	2.1	2	41	21	93.1	31.8	6.6	3	90.8	14.6	80	12.7	320	Broad Onl	Yes
37	57	Female	27.07	39.5	0.85	1	1	1	1	1	0	1	1	1	1	2	17	High Risk	57	6	1	1	1	0	0	0	0	38.6	70.2	5	14.04	44.3	19.2	15	13	16	98.6	4.5	20.2	47.7	92.8	1.4	101	10.6	567	Broad Onl	Yes
38	43	Male	37.64	35.1	0.84	1	1	1	0	1	1	1	0	0	0	3	0	High Risk	34	2	0	1	1	1	0	0	0	2.6	5.3	2.5	2.12	3.2	1.5	4	29	35	80.7	38.8	24.9	32.2	50.7	8.4	17	24.6	442	Broad Onl	Yes
39	18	Female	43.38	49	0.73	1	0	1	1	0	0	1	0	1	0	4	4	High Risk	28	1	0	1	1	1	0	0	0	27.4	91.9	47.6	1.93	13.5	18.8	4	29	22	98.7	31.7	33.9	35.7	96.8	9	147	11.9	403	Broad Onl	Yes
40	18	Female	18.58	37.8	0.77	0	1	0	0	0	1	0	0	0	1	1	19	High Risk	42	4	0	1	0	0	0	0	0	10.9	7.3	34.3	0.21	14.2	7.3	11	41	38	77.1	12.8	6.3	40.8	91.4	11.8	145	13.8	425	Broad Onl	Yes

41	39	Male	42.98	41.3	0.95	0	0	1	1	1	1	0	0	0	0	1	7	High Risk	32	5	0	1	1	0	0	0	1	51.7	83.9	26.1	3.21	59.4	21.5	4	7	10	90.6	45.8	7.9	22.3	58.3	10.1	99	5.6	495	Broad Onl	Yes
42	34	Female	36.5	47.2	0.72	0	0	0	0	1	0	0	0	1	0	1	9	Low Risk	60	1	0	1	0	1	1	0	0	85.9	9.7	58.6	0.17	86	14.7	15	47	48	84.9	13.4	43.7	29	98	2.4	59	4	521	Broad Onl	Yes
43	64	Female	25.92	36.1	0.72	1	1	0	1	0	1	0	0	1	1	4	11	Low Risk	62	7	1	1	0	0	0	0	0	12.4	29.5	14.3	2.06	14.3	10.8	13	50	10	80.7	41.2	26.4	11.9	57.5	11.1	116	12.6	372	Broad Onl	Yes
44	53	Female	33.67	44.8	0.8	1	1	1	1	1	1	1	0	0	1	4	10	Low Risk	43	5	0	1	0	1	1	0	0	18.4	46.7	7.7	6.06	21.1	12.4	2	29	23	53.7	7.9	37.6	17.6	80.8	13.4	173	15.8	399	Broad Onl	Yes
45	59	Male	16.72	44.3	0.93	0	1	1	1	1	0	0	1	0	0	1	18	High Risk	20	2	0	1	1	0	0	0	0	15	6.3	80.6	0.08	19.5	1.5	5	49	43	62.8	18	45.8	8.4	95.3	7.8	141	10.4	377	Broad Onl	Yes
46	58	Male	31.66	36.9	0.82	1	1	0	1	1	0	0	1	1	0	2	7	Low Risk	50	5	1	1	0	0	0	0	0	44.6	23.2	38.4	0.6	55.3	32.7	1	31	53	74.8	32	15.8	21.6	96.4	0.9	73	0.3	546	Broad Onl	Yes
47	23	Male	24.99	36.9	0.89	1	1	1	0	0	0	0	1	0	1	1	7	Low Risk	35	6	0	1	1	0	0	0	0	36.6	92.2	45.3	2.03	52.7	28.6	12	25	40	68.8	3.8	7	43	54.8	12	42	11.1	413	Broad Onl	Yes
48	19	Female	17.91	46.1	0.72	0	0	1	0	1	1	0	0	1	1	2	7	Low Risk	16	5	0	1	0	1	0	0	0	40	39.1	6.3	6.21	40.9	33	14	11	3	58.4	29.8	43.7	39.5	60.1	7.7	73	11.9	357	Broad Onl	Yes
49	30	Female	30.05	33.4	0.78	0	0	1	0	1	0	0	1	1	1	4	4	High Risk	19	7	1	1	1	0	0	0	1	36.4	51	42.5	1.2	49.5	19.8	8	45	10	77	20.1	38.8	6.5	59.3	5.8	75	0.3	565	Broad Onl	Yes
50	26	Male	28.53	34.5	0.81	1	1	0	0	0	1	0	1	0	0	2	20	High Risk	30	0	0	1	0	1	0	0	0	30.3	26.3	31.8	0.83	30.6	15.4	9	31	56	61.2	6.3	45.7	38.4	94.9	9.4	77	15.8	435	Broad Onl	Yes
51	56	Male	22.44	39	0.93	1	0	1	1	0	0	0	0	1	0	4	0	Low Risk	15	3	1	1	1	1	0	0	0	27.4	66.3	10.4	6.37	39.5	21	8	18	18	51.9	9.8	49.6	41.6	98.5	9.1	145	9.4	411	Broad Onl	Yes
52	50	Female	18.23	46	0.71	0	0	1	0	0	1	0	1	0	1	1	14	Low Risk	24	2	0	0	0	0	0	0	0	20.8	10.6	51.7	0.2	25.6	11.4	11	43	59	81.1	35.8	44.3	25.9	84.7	9.4	147	6.5	501	Broad Onl	Yes
53	55	Female	21.12	31.9	0.7	1	1	0	0	1	1	0	0	0	0	3	8	Low Risk	14	4	1	0	1	0	0	0	0	34.3	52.6	6.5	8.09	39.1	31.1	2	42	40	85.7	48.2	25.4	17	70.1	6.9	43	5.1	550	Broad Onl	Yes
54	58	Male	23.97	33.4	0.83	0	1	0	1	1	1	0	0	1	1	2	5	High Risk	49	6	1	1	0	1	0	0	0	15.2	38.6	31.7	1.22	21.5	16.7	14	20	33	59.9	13.2	26.1	31.6	59.1	10.8	95	0.2	441	Broad Onl	Yes
55	28	Female	32.62	33.5	0.71	0	1	1	1	1	0	0	0	1	1	4	18	High Risk	55	3	1	1	0	1	1	0	1	24.3	15.5	30.9	0.5	17.1	16.4	8	9	49	74.7	4.1	6.9	25.4	51.8	13	133	0.5	488	Broad Onl	Yes
56	35	Male	23.66	42.9	0.9	0	1	0	1	0	0	1	0	0	0	2	3	Low Risk	33	5	1	0	0	1	1	0	0	41.5	39.3	22.3	1.76	47.5	17.1	5	13	36	98.4	41.3	18.2	13.5	75.4	15.9	104	4.5	539	Broad Onl	Yes
57	64	Male	40.63	36.7	0.86	1	1	0	1	0	1	1	1	1	1	3	9	High Risk	27	3	0	0	1	1	0	0	0	66.2	67	31.6	2.12	104.6	47	5	45	22	79.6	39.8	5.4	44.8	87.3	5.4	89	8.9	455	Broad Onl	Yes
58	53	Male	23.02	46.6	0.92	0	0	1	0	1	0	1	1	1	1	3	16	Low Risk	41	7	1	0	0	0	0	0	1	26	32.4	43.7	0.74	27.6	23.7	14	45	10	81.1	20.5	36.4	16.2	92	10.9	95	13.8	343	Broad Onl	Yes
59	40	Male	28.47	42.5	0.89	1	1	0	0	1	1	1	0	0	0	1	19	High Risk	56	5	1	1	1	0	0	0	1	6.5	20.5	10.6	1.94	7.5	3.7	5	28	36	90.4	31.4	48.8	49.2	76.8	2.1	142	0.5	294	Broad Onl	Yes
60	45	Male	19.2	38.4	0.9	1	1	0	0	1	1	0	0	0	0	2	1	Low Risk	6	2	1	0	1	1	0	0	0	12.8	23.6	8.4	2.81	17.4	4.2	6	60	50	92.6	32.4	5.8	36.4	93.3	15.7	18	14.7	438	Broad Onl	Yes
61	44	Male	34.52	39.9	0.88	0	0	1	0	0	0	1	1	0	0	4	2	High Risk	29	8	0	0	1	1	1	0	0	76.1	63.5	38.5	1.65	115.6	57	12	29	55	74.7	34	16.1	11.1	95.7	8.1	112	2.4	430	Broad Onl	Yes
62	64	Female	36.46	34.6	0.75	1	0	0	0	0	0	0	1	1	1	2	15	High Risk	49	1	1	0	0	0	0	0	0	59.5	15.5	40	0.39	67	29.7	11	28	16	77	13.4	2.7	15.9	57.6	14.8	45	0.2	456	Broad Onl	Yes
63	42	Female	18.73	37	0.7	1	0	1	0	0	0	0	1	1	0	1	0	Low Risk	35	6	1	0	1	0	0	0	0	12.9	16	26.5	0.6	17.4	7.7	5	16	56	70.8	3.2	26.8	8.7	95.2	5.8	127	3	528	Broad Onl	Yes
64	53	Male	40.03	39.5	0.87	1	1	0	1	0	0	0	1	0	1	4	9	High Risk	54	5	1	1	1	1	1	0	0	76.2	82.4	47.4	1.74	94.2	43.2	13	16	20	95	4.3	31.4	18.2	83.8	5.5	131	13.5	391	Broad Onl	Yes
65	45	Male	18.75	35.2	0.92	0	1	0	1	1	0	1	0	1	0	3	4	Low Risk	24	3	0	0	0	0	0	1	0	46.7	21.8	39	0.56	51.2	21.8	11	36	56	77.5	31	48.8	23	99.2	13.5	107	1.5	363	Broad Onl	Yes
66	60	Female	35.06	32.4	1.07	1	0	1	1	0	0	1	1	0	0	2	10	High Risk	61	6	1	0	1	1	1	0	1	28	53.3	42.7	1.25	80.9	56.1	12	31	39	80.5	12.1	42.1	37.7	60.6	13.3	45	41.9	308	Broad Onl	Yes
67	61	Female	36.92	45	0.73	0	0	1	0	1	1	0	1	0	1	2	0	High Risk	30	1	1	1	0	1	1	0	0	14.4	7.2	6.4	1.13	18.5	9.2	6	16	10	58.9	14.3	20.1	11.1	68.2	9.5	108	12.5	276	Broad Onl	Yes
68	19	Female	43.11	34.2	0.73	0	0	1	0	0	1	1	0	1	1	2	14	High Risk	62	1	1	0	1	0	1	0	1	18.4	5	22.3	0.22	22.1	9.2	13	20	5	57.8	30.2	12.8	17	80.1	6	63	11.2	565	Broad Onl	Yes
69	28	Female	39.8	48.8	0.75	0	0	0	1	0	1	0	0	0	0	4	16	Low Risk	42	1	0	1	1	1	0	0	0	15.4	21.2	48.2	0.44	21.4	10.4	12	50	41	68.5	45.1	48.2	42.1	94	7.2	123	10.8	352	Broad Onl	Yes
70	21	Female	34.22	44	0.73	1	1	1	0	1	1	1	1	1	1	4	0	Low Risk	43	5	0	1	0	1	0	0	0	30.5	7.8	80.6	0.1	39.4	14.9	5	49	45	55.9	13.5	4.8	35.2	93	0.8	83	7.8	539	Broad Onl	Yes
71	37	Male	25.26	39.8	0.81	1	1	1	1	1	0	1	1	0	0	3	11	High Risk	60	7	0	0	1	1	1	0	0	31.8	19.6	18.4	1.07	32.9	23.3	12	26	52	88.4	35.7	2.2	19.9	55	5.6	61	1.4	535	Broad Onl	Yes
72	64	Female	19.02	46.9	1.1	1	1	0	1	1	1	1	0	0	1	2	14	High Risk	54	3	0	0	0	0	0	1	0	54.9	7.7	83.5	0.09	65.4	40.1	9	17	26	85.3	13.7	12.5	44.5	81	4.3	166	12	440	o REM OS	No
73	48	Female	25.1	39.4	0.72	0	0	0	0	1	1	0	0	0	1	4	3	High Risk	20	0	0	0	0	0	0	1	0	9.4	68	86.1	0.79	74.1	31.9	13	19	22	66.5	28.4	21.4	36.1	94	3	128	0.8	554	o REM OS	No
74	42	Male	36.86	44.9	1.17	1	0	1	0	0	0	1	1	1	0	4	5	Low Risk	15	0	1	0	1	0	1	0	1	2.6	26.2	8.4	3.12	3	1.3	7	32	57	83.2	15.5	7.9	35.1	77.2	15.1	62	0.3	491	o REM OS	No
75	49	Female	31.09	34	0.73	0	0	0	0	1	0	1	1	0	0	4	16	Low Risk	53	5	0	0	0	0	0	1	0	17.4	9	15.5	0.58	20.6	11.9	12	25	33	87.3	27.4	9.2	28.8	56.2	15.4	98	12.1	350	o REM OS	No
76	53	Female	41.71	46.8	0.72	0	1	1	0	1	0	1	1	1	0	4	15	High Risk	6	5	1	1	0	0	0	0	0	3.5	7.7	83.5	0.09	10.5	3.3	15	15	33	93	49.2	39.9	12.8	96	11.8	50	14.9	349	o REM OS	No
77	43	Male	30.4	41.4	0.9	1	1	1	1	0	1	1	1	1	1	4	13	High Risk	19	6	1	1	1	0	0	0	0	14.1	18.6	6.6	2.82	15.3	8.7	5	20	13	71.6	47.2	45.8	3.2	86.1	15.4	104	10.6	342	o REM OS	No
78	60	Female	37.14	41.8	0.75	0	1	0	0	1	0	1	0	1	0	1	6	Low Risk	15	3	0	0	1	1	1	0	1	17.1	76.8	55.8	1.38	17.3	8.9	15	21	27	55.6	25.3	35.1	3.4	96.2	8.6	88	14.1	302	o REM OS	No
79	37	Male	32.45	46.5	0.9	1	0	0	1	0	1	1	1	1	1	4	9	Low Risk	38	5	0	0	0	0	1	0	0	22.8	68	86.1	0.79	44.4	18.9	14	49	57	66.5	19.4	8.1	9.9	87	9.2	41	6	328	o REM OS	No
80	50	Female	23.43	47.7	0.71	1	0	0	0	1	0	1	1	1	0	4	1	Low Risk	35	1	1	0	0	1	0	0	0	47.2	32.1	15.6	2.06	62.4	27	6	43	59	93.8	46.8	42.9	16.5	73.7	11	40	0.7	372	o REM OS	No
81	33	Female	28.24	37.8	0.74	0	1	0	0	1	0	1	1	0	1	3	3	High Risk	2	1	0	0	0	0	0	1	0	29.1	89.8	64.6	1.39	40.4	20.9	10	34	45	83.4	18.4	40.6	11.5	98.7	15.4	60	7.9	472	o REM OS	No
82	25	Female	25.52	42	0.72	0	0	0	1	1	0	0	0	0	1	4	7	Low Risk	31	5	0	0	1	0	1	0	0	9.9	88.5	75.2	1.18	9.9	4.5	9	15	4	90	42.6	13	11.2	86.9	7.6	50	15.8	534	o REM OS	No
83	64	Male	26.12	44.4	0.91	0	1	0	0	1	0	0	0	1	1	3	4	High Risk	33	3	1	0	0	0	0	0	1	17.1	87.2	11.3	7.72	20.1	9.2	11	37	36	68	17.9	41.8	42	94.4	15.8	74	5.6	331	o REM OS	No

84	57	Female	19.5	40.3	0.71	0	1	0	0	1	1	1	0	0	1	1	10	High Risk	38	0	0	0	0	0	0	1	0	53.9	34.1	89	0.38	65.5	49.4	8	13	30	57.5	14.4	38.3	28	98.8	3	135	14.5	444	REM OS	No
85	72	Male	32.32	44.1	0.9	0	1	0	0	0	1	0	1	0	0	4	16	High Risk	35	2	1	0	0	0	0	0	0	65.8	77.6	44.5	1.74	96.4	52.8	7	43	49	84.7	34.8	7.7	36.3	97.3	2	101	9.3	391	REM OS	No
86	75	Female	41.39	44.6	0.71	0	0	0	1	0	1	1	1	0	0	4	0	Low Risk	5	2	1	0	0	0	1	0	1	59.1	53	50.6	1.05	98	52	15	10	40	57.2	49.8	29.5	32.7	82.8	9.9	137	12.7	431	REM OS	No
87	64	Female	22.33	39.5	0.75	0	0	0	0	0	1	0	0	1	0	4	6	High Risk	29	8	0	0	1	0	0	0	0	13.4	70.4	78.3	0.9	16.8	7.6	9	13	11	72.1	2.9	16.5	19	81.4	15.4	126	0.2	442	REM OS	No
88	66	Female	20.9	37	0.75	1	0	0	0	1	0	0	1	1	0	4	14	Low Risk	60	5	0	1	1	0	0	0	0	53.8	79.3	48.6	1.63	74.5	37.4	12	42	22	93.4	19.2	44.7	16.8	97.2	11	69	13.8	475	REM OS	No
89	72	Female	42.26	44.2	0.75	0	1	0	1	1	0	0	1	0	1	4	17	High Risk	30	4	1	0	0	0	1	0	0	31.2	7.2	10.2	0.71	34.9	21.9	13	32	19	81.6	32.2	35.9	32.9	95.5	13.5	134	1.7	327	REM OS	No
90	69	Male	41.87	39.7	0.84	1	1	0	0	0	0	1	1	1	0	4	17	High Risk	59	8	1	0	0	1	1	0	0	32.1	27.3	44.9	0.61	48.5	23.6	9	9	44	50.3	10.7	25.5	30.5	86.5	2.5	103	9.1	387	REM OS	No
91	77	Female	43.16	44.7	0.72	0	0	0	1	0	1	1	1	1	1	4	19	High Risk	29	3	0	1	0	0	0	0	0	68	33.7	37.5	0.9	100	40.1	10	21	49	59.1	38.8	36.4	37.4	91	4.1	48	2.7	344	REM OS	No
92	72	Female	34.77	41.3	0.76	0	0	1	1	1	0	0	1	1	0	4	11	High Risk	13	2	1	0	0	0	1	0	0	65.9	19.6	80.2	0.24	76.7	34.4	8	48	13	98.4	6.7	43.4	2	92.2	7.7	128	5.6	408	REM OS	No
93	74	Male	30.33	33.6	0.87	0	1	0	0	0	0	0	1	0	1	3	16	High Risk	14	5	0	0	0	1	0	0	0	32.8	82	73.3	1.12	44.1	27.8	9	9	8	70.4	11.8	17.1	6.3	97.2	3.4	130	2.6	509	REM OS	No
94	20	Male	35.36	34.7	0.88	1	1	1	0	1	0	1	0	1	1	4	12	Low Risk	20	5	1	0	0	0	0	0	0	4.2	5	2.6	1.92	4.9	2.2	6	22	24	63.2	18.9	41.6	12.6	73.6	12.9	85	3.3	424	Strict Only	Yes
95	21	Male	40.83	41.4	0.84	0	0	1	1	1	1	1	1	0	1	4	9	High Risk	52	1	0	0	1	0	0	0	0	3.7	6.1	3.3	1.85	4.4	2.4	6	43	53	82.8	21.1	49.5	42	86	13.3	63	13.5	473	Strict Only	Yes
96	51	Female	26.65	38.4	0.84	0	1	0	0	0	0	1	0	0	1	2	14	High Risk	59	7	0	1	0	1	1	0	0	3.7	5.2	3.5	1.49	4.3	3.5	2	28	50	82.9	5.8	31.1	40.8	76.2	13.3	69	8.2	574	Strict Only	Yes
97	57	Male	34.8	33.9	0.9	1	1	0	0	0	1	1	1	1	0	4	17	High Risk	6	3	1	0	1	0	0	0	0	3.4	6.8	3.8	1.79	4	2.8	9	26	36	68	32	39.2	11.5	89	6.1	45	10.6	525	Strict Only	Yes
98	62	Male	34.39	39.5	0.92	0	1	0	0	0	0	1	0	1	0	4	11	Low Risk	41	3	0	0	0	0	1	0	0	3.2	6.3	3.4	1.85	4.9	2.4	15	26	43	66.9	33.6	3.4	45.7	70.8	11.3	92	14.8	457	Strict Only	Yes
99	40	Male	36.91	44.1	0.92	0	1	0	0	0	0	0	0	0	1	4	8	Low Risk	8	4	0	0	0	0	0	1	0	4.6	8.6	4.2	2.04	6	2.9	14	28	22	82.5	5.5	36	37.5	91.8	15.4	65	1.3	468	Strict Only	Yes
100	29	Male	33.71	33.7	0.85	0	1	1	0	1	1	0	1	0	0	3	11	Low Risk	53	0	0	1	0	0	0	0	0	4.5	7.7	3.2	2.41	5.9	3.6	7	48	12	58.6	27.3	49	33.4	92.5	0.8	47	11	400	Strict Only	Yes