Somnologie
Somnology – Current Sleep Research and Concepts

Somnologie
https://doi.org/10.1007/s11818-022-00349-5
Accepted: 14 April 2022

Partial update of the German S3 Guideline Sleep-Related Breathing Disorders in Adults

AWMF Registry No. 063-001—German Sleep Society (Deutsche Gesellschaft für Schlafforschung und Schlafmedizin – DGSM)

Boris A. Stuck[1] · Michael Arzt[2] · Ingo Fietze[3] · Wolfgang Galetke[4] · Holger Hein[5] · Clemens Heiser[5] · Simon D. Herkenrath[6] · Benedikt Hofauer[5,7] · Joachim T. Maurer[8] · Geert Mayer[9] · Maritta Orth[10] · Thomas Penzel[3] · Winfried Randerath[11] · J. Ulrich Sommer[12] · Armin Steffen[13] · Alfred Wiater[14]

[1] Department of Otorhinolaryngology, Head and Neck Surgery, University Hospital Marburg, Philipps-Universität Marburg, Marburg, Germany; [2] Centre for Sleep Medicine, Department of Internal Medicine II, University Hospital Regensburg, Regensburg, Germany; [3] Center of Sleep Medicine, Charité – Universitätsmedizin Berlin, Berlin, Germany; [4] Department of Pneumology, VAMED Hospital Hagen-Ambrock, Hagen-Ambrock, Germany; [5] Department of Otorhinolaryngology, Head and Neck Surgery, Klinikum rechts der Isar, Technical University of Munich, Munich, Germany; [6] Clinic of Pneumology and Allergology, Center for Sleep Medicine and Respiratory Care, Bethanien Hospital gGmbH, Solingen, Germany; [7] Department of Otorhinolaryngology, Head and Neck Surgery, Klinikum rechts der Isar, Technical University of Munich, Munich, Germany; [8] Division of Sleep Medicine, Dept. of Otorhinolaryngology, Head and Neck Surgery, University Hospital Mannheim, University Heidelberg, Mannheim, Germany; [9] Clinic for Sleep Medicine, Hephata-Kliniken, Schwalmstadt-Treysa, Germany; [10] Clinic for Pneumology, Sleep and Ventilation Medicine, Theresienkrankenhaus Mannheim, Mannheim, Germany; [11] Clinic of Pneumology and Allergology, Center for Sleep Medicine and Respiratory Care, Bethanien Hospital gGmbH, Solingen, Germany; [12] Department of Otorhinolaryngology, Head and Neck Surgery, Klinikum rechts der Isar, Technical University of Munich, Munich, Germany; [13] Department for Otorhinolaryngology, University of Luebeck, Luebeck, Germany; [14] Cologne, Germany

Steering Committee

- Prof. Dr. med. Boris A. Stuck, Marburg
- Dr. med. Alfred Wiater, Cologne

Supplementary Information

The online version of this article (https://doi.org/10.1007/s11818-022-00349-5) contains disclosures on the authors' conflict of interest.

The German version of this article can be found under https://doi.org/10.1007/s11818-020-00257-6.

Scan QR code & read article online

1 Abstract

A review of the recommendations in the currently applicable version of the chapter "Sleep-related breathing disorders in adults" in the guideline "Non-restorative sleep/sleep disorders" conducted by the guideline steering group identified a number of recommendations and chapters requiring revision or updating in the light of new scientific or clinical evidence. These included selected chapters on diagnosis (clinical examination, polysomnography, respiratory polygraphy, and diagnosis with reduced and alternative systems) and treatment (positional therapy, surgical procedures) of sleep-related breathing disorders, as well as the chapters on obstructive sleep apnea (OSA) and dementia and on sleep-related hypoventilation/sleep-related hypoxemia. These chapters were updated according to the methodology of an S3 guideline. The remaining recommendations and chapters, on the other hand, retain their validity for the time being.

With regard to the diagnosis of sleep apnea, a number of recommendations on clinical examinations, as well as on respiratory polygraphy and polysomnography, have been specified more precisely and modified. A chapter on diagnosis has been supplemented with alternative systems: tonometry-based diagnostics has been included as an alternative for the diagnosis of sleep apnea. Positional therapy for positional OSA and tonsillectomy with uvulopalatopharyngoplasty are given a higher level of recommendation based on new randomized trials. Recommendations

Published online: 22 June 2022

on OSA and dementia can no longer be made due to a lack of evidence; the recommendations on sleep-related hypoventilation/sleep-related hypoxemia have been specified with greater precision.

2 Concept of the update

The existing guideline "Non-restorative sleep/sleep disorders"—chapter "Sleep-related breathing disorders in adults"—became due for revision 3 years following its publication on 22.12.2019. After a review of the guideline content by members of the previous steering committee and the authors of the original guideline, it became evident that large parts of the guideline remain valid—thereby making a complete update unnecessary—and that its validity can instead be extended for a further 2 years. However, a number of chapters were identified as requiring revision due to new evidence. In view of the size and subject diversity of the guideline, the decision was taken not to update it in its entirety, but rather to revise only parts of the guideline. Therefore, the following update contains the revised guideline chapters. Accordingly, the unrevised chapters remain valid and can still be found under guideline Registry No. 063-001. A complete revision of the entire guideline is planned in the future. Details on the selection of chapters to be updated and the methodology used to this end can be found in the guideline protocol (see Appendix). It should be noted at this juncture that the guideline relates only to adults.

3 Diagnosis

3.1 Clinical examination

The aim of the clinical examination should be to identify anatomical changes in the upper respiratory tract or the region of the viscerocranium that could be (in part) responsible for the onset of obstructive sleep apnea (OSA). The clinical examination should include the nose, oral cavity, and pharynx, as well as craniofacial morphology. The clinical examination should be extended in cases where symptoms are reported or relevant pathologies are suspected in these regions [1, 2]. To this end, it may be necessary to consult relevant specialists (ear, nose, and throat specialists; oral and maxillofacial surgeons; orthodontists; specialized dentists). For the differential diagnostic planning of surgical interventions or the use of a mandibular advancement splint (mandibular advancement device, MAD), an examination of the pharynx under anesthesia (drug-induced sleep endoscopy [DISE]) is of particular importance in order to describe the collapse pattern, localization, and extent of relevant stenosis [3, 4].

Recommendations. Modified:

- An examination of the oral cavity and pharynx is of great importance and shall be performed (evidence level 5, grade A recommendation).
- If treatment with a mandibular advancement device is being considered, an assessment should be made of possible mandibular protrusion, and dental status should be recorded (evidence level 5, grade A recommendation).
- The diagnostic work-up of OSA should include a clinical assessment of craniofacial morphology for orientation (evidence level 5, grade A recommendation).
- To assess airflow-related nasal structures, a clinical examination of the nose should be performed (evidence level 5, grade B recommendation); this may also include an endoscopic assessment (evidence level 5, grade C recommendation).

New:

- To determine body mass index (BMI), both height and body weight should be obtained (evidence level 5, grade A recommendation).

The recommendations on clinical examination were adopted with strong consensus (18/18).

3.2 Diagnostic polysomnography

Supervised cardiorespiratory polysomnography (PSG) represents the most important instrument and reference in sleep medicine diagnostics in the sleep laboratory. It involves recording the physiological signals required for a quantitative assessment of sleep, sleep disorders, and diseases associated with sleep according to the International Classification of Sleep Disorders—Third Edition (ICSD-3; see ◘ **Table 1**).

Sleep stage classification largely corresponds to the older classification by Rechtschaffen und Kales [5, 6]. This reduces ambiguities and increases reliability [7]. A chapter on central nervous activation (arousals) adopts the definitions given in an earlier recommendation paper [8]. Other chapters define the recording and evaluation of electrocardiogram (ECG) parameters [9] and leg movements. Motor patterns, such as periodic leg movements, bruxism, and rapid eye movement (REM) sleep behavior disorders, are precisely defined [10]. With regard to nocturnal breathing disorders, definitions are given for various types of apnea and hypopnea. Esophageal pressure measurement is the reference method to determine increased respiratory effort in the case of obstruction and to differentiate obstructive from central respiratory disorders. However, it is not widely available. A PSG-based algorithm that includes flattening, respiratory effort, breathing patterns, arousal, and sleep stages is also highly accurate in the differentiation of respiratory disorders.

Inductance plethysmography is recognized as a noninvasive method yielding comparable results [11]. In order to detect hypoventilation during sleep, the CO_2 concentration needs to be continuously determined. The method most widely used to this end is transcutaneous measurement of the partial pressure of carbon dioxide ($tcPaCO_2$) [12]. PSG also includes recording body position and a finely synchronized video recording of the sleeping subject [13]. The American Academy of Sleep Medicine (AASM) Manual was updated to a limited extent in 2012 (version 2.0) and 2014 (version 2.1), as well as in 2015 (version 2.2) and again in 2016 (2.3), to take new findings into consideration [14–17]. Further changes followed in 2017 (version 2.4) and 2018 (2.5). In 2016, a chapter on the outpatient diagnosis of sleep apnea was included, setting out evidence-based parameters for recording and evaluation [18, 19]. This also includes a subchapter on outpatient diagnosis of sleep apnea us-

Table 1 Channels recommended for cardiorespiratory polysomnography. The table shows the function to be investigated, the associated biosignals, and the required technique as well as its technical specifications in relation to the optimal sampling rate and filter settings

Function	Parameter	Technique	Optimal sampling rate (Hz)	Filter (Hz)
Sleep	EEG, EOG	Electrodes	500	0.3–35
	EMG	Electrodes	500	10–100
Breathing	Respiratory flow	Nasal pressure, thermistor	100	0.1–15
	Respiratory effort	Inductance plethysmography	100	0.1–15
	Oxygen saturation	SaO_2	25	–
	Carbon dioxide	$tcPaCO_2$	25	–
	Snoring	Microphone	500	–
Cardiac	ECG	Electrodes	500	0.3–70
Movement	Tibial muscle EMG	Electrodes	500	10–100
	Body position	Position sensor	1	–
	Video	Video camera	5	–

EEG electroencephalogram, *EOG* electrooculogram, *EMG* electromyogram, *ECG* electrocardiogram, SaO_2 oxygen saturation, $tcPaCO_2$ transcutaneous measurement of partial pressure of carbon dioxide

ing peripheral arterial tonometry, together with the specific parameters of this technique [18, 19].

Monitored PSG makes it possible to investigate and quantitatively record sleep disorders involving changes in physiological parameters. With current computer-assisted technology, PSG sets manageable requirements in terms of equipment. It requires specially trained sleep medicine personnel to perform the measurements and evaluate the biosignals. Further training courses and qualifications in sleep medicine are established for medical technical personnel, psychologists, and natural scientists, as well as for physicians. Medical specialists in certain specialties have the opportunity to gain additional training in "sleep medicine" according to the relevant training regulations of the German State Chambers of Physicians. In addition, there is a defined further training program on the diagnosis and treatment of sleep-related breathing disorders (SRBD) according to the Fifth Book of the German Social Code. Physicians and natural scientists are able to obtain proof of qualification as a somnologist from the German Society for Sleep Research and Sleep Medicine (*Deutsche Gesellschaft für Schlafforschung und Schlafmedizin*, DGSM).

The AASM Scoring Manual [13, 14] enables classification into the following stages: awake, REM, N1, N2, and N3. There are national and international recommendations on the equipment and staffing of a sleep laboratory; compliance with these recommendations is a prerequisite for the accreditation of sleep laboratories by the sleep medicine societies [11].

Table 2 provides an overview of the evidence-based data on PSG. The validity and reliability of visual scoring has been demonstrated and fulfills the current requirements for the quality of visual scoring of biosignals [7, 20]. The report on sleep medicine findings must document whether the PSG was recorded and scored according to Rechtschaffen and Kales criteria [5] or AASM criteria [13, 14]. The AASM guidelines are revised approximately every 2 years, with the latest revision undertaken in 2018 (version 2.5) [21].

Recommendations. Reviewed and retained:

- PSG in the sleep laboratory monitored by personnel qualified in sleep medicine is recommended as the gold standard and reference method (evidence level 2a, grade A recommendation).
- PSG should be performed in line with current recommendations. This includes recording sleep electroencephalogram (EEG), electrooculogram (EOG), electromyogram (EMG), ECG, respiratory flow, snoring, respiratory effort, oxygen saturation, body position, and a video (evidence level 2a, grade A recommendation).

New:

- PSG should be performed in the case of inconclusive respiratory polygraphy results, persistent suspicion of SRBD despite normal respiratory polygraphy, in the differential diagnosis of disorders in sleep medicine, and/or in the case of suspected comorbid disorders relevant to sleep medicine (evidence level 2a, grade B recommendation).

The recommendations on diagnostic PSG were adopted with strong consensus (16/18).

3.3 Respiratory polygraphy for sleep-related breathing disorders

Simplified portable systems are available for the diagnosis of sleep-disordered breathing ([24–26]; see **Table 3**).

Portable diagnostic systems are classified according to the number of channels recorded. These are predominantly systems with between four and six channels that do not record sleep EEGs (synonym: respiratory polygraphy systems).

Respiratory polygraphy systems with an adequate selection of biosignals, very good signal acquisition, and very good signal processing can reduce the number of false-positive diagnoses [18, 19]. Preselecting patients by means of a targeted patient history can significantly increase pretest probability, as well as the number of false-positive diagnoses. Using respiratory polygraphy, it is possible to make a basic distinction between OSA and central sleep apnea (CSA). Validations are available for some systems, but these are not yet sufficient for a high level of evidence.

Respiratory polygraphy systems for the diagnosis of sleep apnea generally record airflow with a thermistor or nasal pressure transducer, respiratory effort by means of inductance plethysmography, oxygen saturation with appropriate pulse oximetry (averaging with sufficiently high temporal resolution), pulse rate, and body position [19]. With the method used in the SCOPER system, the num-

Table 2 Meta-analyses on cardiorespiratory polysomnography in the monitored sleep laboratory

Study name	Author	Year	Country	Study type	Outcome	EL
Diagnostic testing for obstructive sleep apnea in adults	Mokhlesi et al. (2017) [21]	2017	USA	Guideline of the American Medical Association	PSG or respiratory polygraphy should be used for diagnosis in uncomplicated cases involving moderate and severe sleep apnea. In complicated cases (with comorbidities), only PSG should be used	1
Sleep apnea: a review of diagnostic sensors, algorithms, and therapies	Shokoueinejad M et al. (2017) [22]	2017	USA	Methodology overview	Methodology overview of sensors, signals, and algorithms	1
Rules for scoring respiratory events in sleep: update of the 2007 AASM manual for the scoring of sleep and associated events	AASM (Berry et al. 2012) [14]	2012	USA	Update of Redline et al. 2007 meta-analysis with reference to sensors, recording, and scoring	Respiratory scoring	1a
The scoring of arousal in sleep	Bonnet et al. (2007) [8]	2007	USA	Meta-analysis of 122 studies following review of 2415 studies	Arousal scoring	1a
The scoring of cardiac events during sleep	Caples et al. (2007) [9]	2007	USA	Meta-analysis of 14 studies following review of 285 studies	ECG and circulation	1a
Digital analysis and technical specifications	Penzel et al. (2007) [23]	2007	USA	Meta-analysis of 119 studies following review of 154 studies	Technical specifications, automatic sleep scoring	1a
The scoring of respiratory events in sleep	Redline et al. (2007) [12]	2007	USA	Meta-analysis of 182 studies following review of 2298 studies	Respiratory scoring	1a
The visual scoring of sleep in adults	Silber et al. (2007) [6]	2007	USA	Meta-analysis of 26 studies following review of 1000 studies	Sleep stage scoring	1a
Movements in sleep	Walters et al. (2007) [10]	2007	USA	Meta-analysis of 44 studies following review of 81 studies	Scoring of movements	1a

EL evidence level, *PSG* polysomnography, *AASM* American Academy of Sleep Medicine, *ECG* electrocardiogram

ber of channels becomes irrelevant, with the focus being placed on measuring functions (S = sleep, C = cardiovascular, O = oximetry, P = position, E = effort, R = respiratory; [19]). There are several grades of quality for each function. Sleep can be assessed on the basis of actigraphy or other surrogate parameters, and, depending on the question being asked, does not need to be inferred from a sleep EEG. The SCOPER system is used today to grade respiratory polygraphy systems.

The respiratory polygraphy is evaluated according to the current rules of PSG [21] to allow visual scoring and processing of artifacts. It is essential to indicate in the documentation that visual scoring has been performed [31]. For the sampling rates and other technical specifications of polygraphy systems, the evidence-based recommendations for PSG are used (see ◘ **Table 1**).

Respiratory polygraphy systems for the diagnosis of SRBD should be used by medical specialists trained in sleep medicine who can record and evaluate pretest probability, symptomatology, and comorbidities [31]. In Germany, further training in sleep medicine according to the BUB guideline is a prerequisite for billing respiratory polygraphy according to a standardized evaluation scale (*einheitlicher Bewertungsmaßstab*, EBM). Respiratory polygraphy systems can be used to diagnose OSA, but not in the case of comorbid pulmonary, psychiatric, neurological, and neuromuscular disorders, nor in the case of other concomitant sleep disorders such as CSA, periodic limb movement disorder (PLMD), insomnia, circadian sleep–wake rhythm disorders, and narcolepsy [33, 34]. Respiratory polygraphy systems enable a distinction to be made between CSA and OSA. In cases where hypopneas predominate, polygraphy systems do not always enable a definitive differentiation to be made between CSA and OSA and are not validated for this purpose. Due to the absence of EEG channels (e.g., to measure sleep time and waking responses), respiratory polygraphy systems are inferior to PSG in that their assessment of the severity of SRBDs can be less accurate, they cannot reliably rule out an SRBD, and they are unable to diagnose possible differential diagnoses of an SRBD. Comparability of the number of hypopneas between respiratory polygraphy and PSG is most likely to be achieved if the following definition of hypopnea is chosen: a reduction in oronasal airflow of between 30 and 90% of baseline at an at least 4% drop in oxygen saturation [16, 35]. Physiological irregularities in breathing rhythm during the sleep–wake transition (also known as sleep-onset apneas) can be incorrectly classified as sleep apnea in the absence

Table 3 Studies on respiratory polygraphy for sleep apnea

Study name	Author	Year	Country	Study type	No. of patients	Outcome	EL
Executive summary on the systematic review and practice parameters for portable monitoring in the investigation of suspected sleep apnea in adults	Am. Thoracic Soc. (2004) [24]	2004	USA	Meta-analysis of 51 studies	–	Under certain conditions, portable monitoring can increase or reduce the pretest probability of sleep apnea	1
Practice parameters for the use of portable monitoring devices in the investigation of suspected obstructive sleep apnea in adults	Chesson et al. (2003) [25]	2003	USA	No formal meta-analysis due to excessive study heterogeneity. Formal analysis of study evidence	–	Under certain conditions, portable monitoring can increase or reduce the pretest probability of sleep apnea	1
Clinical guidelines for the use of unattended portable monitors in the diagnosis of obstructive sleep apnea in adult patients	Collop et al. (2007) [18]	2007	USA	Meta-analysis of 291 studies	–	Portable monitoring for sleep apnea is possible with four to six channels, performed by sleep medicine specialists	1a
Obstructive sleep apnea devices for out-of-center (OOC) testing: technology evaluation	Collop et al. (2011) [19]	2011	USA	Evaluation of respiratory polygraphy devices and systematic literature review	–	SCOPER criteria to evaluate respiratory polygraphy devices	1
Home diagnosis of sleep apnea: a systematic review of the literature	Flemmons et al. (2003) [26]	2003	USA	Meta-analysis of 35 high-quality studies	–	Portable monitoring for sleep apnea possible, not in the case of comorbidities and other sleep disorders	1a
Systematic review and meta-analysis of the literature regarding the diagnosis of sleep apnea	Ross et al. (2000) [27]	2000	USA	Meta-analysis of 71 studies following review of 937 studies, HTA report	7572	Up to 17% false-negative findings and up to 31% false-positive findings	1a
Diagnosis of obstructive sleep apnea by peripheral arterial tonometry: meta-analysis	Yalamanchali et al. (2013) [28]	2013	USA	Meta-analysis of 14 studies	909	Portables monitoring with WatchPAT device enables diagnosis of obstructive sleep apnea in the case of high pretest probability	1a
Screening for obstructive sleep apnea in adults	Bibbins-Domingo et al. (2017) [29], Jonas et al. (2017) [30]	2017	USA	Recommendation of US Preventive Services	–	Asymptomatic adults do not need to be screened for sleep apnea since evidence for the need for this is inadequate	1
Clinical use of a home sleep apnea test: an American Academy of Sleep Medicine Position Statement	Rosen et al. (2017) [31]	2017	USA	Position paper	–	Only physicians can carry out sleep apnea diagnosis. A clinical examination and risk assessment is required. Respiratory polygraphy can be used in symptomatic patients with moderate and severe sleep apnea. Visual scoring of respiratory polygraphy is required. Screening in patients without symptoms is not indicated	1
Classification methods to detect sleep apnea in adults based on respiratory and oximetry signals: a systematic review	Uddin et al. (2018) [32]	2018	USA	Systematic review	–	In all, 62 studies reviewed. If quality and algorithms are good, the combination of respiratory signals and SaO_2 is sufficient to reliably diagnose sleep apnea	1

EL evidence level, *SCOPER* sleep, cardiovascular, oximetry, position, effort, and respiratory parameters, *HTA* health technology assessment
WatchPAT is a product of Itamar Medical Caesarea, Israel

of EEG analysis and lead to false-positive results.

It has been shown in patients with chronic cardiovascular disease that medical history is not sufficient to detect sleep-related disorders. This group of patients requires respiratory measurement parameters to be recorded. There are no data as yet on whether systematic screening has an effect on long-term prognosis [29, 30].

Recommendations. Modified:
- Respiratory polygraphy systems should be used to diagnose OSA if pretest probability is high (evidence level 2a, grade A recommendation).
- Respiratory polygraphy should not be used as the sole mode of detection and exclusion of OSA in the case of low pretest probability, nor in suspected concomitant sleep disorders or sleep-related comorbidities (evidence level 5, grade A recommendation).
- Respiratory polygraphy for the diagnosis of SRBDs should be performed by specialists qualified in sleep medicine who are able to record and evaluate pretest probability, symptoms, and comorbidities (evidence level 5, grade A recommendation).
- The recorded signals should be visually scored by trained personnel. Scoring by automatic scoring alone is currently not recommended (evidence level 2a, grade A recommendation).
- Cardiorespiratory PSG should be performed as the diagnostic method to exclude SRBDs; respiratory polygraphy is not sufficient for this purpose (evidence level 2a, grade A recommendation).
- Respiratory polygraphy is not sufficient for the diagnostic work-up of ventilatory failure, hypoventilation during sleep, or obesity hypoventilation syndrome; daytime blood gas parameters ($paCO_2$ and HCO_{3-}) as well as CO_2 during sleep are needed for this (evidence level 2a, statement).
- Disease course and treatment follow-up can be performed using respiratory polygraphy. In patients with questionable treatment success, as well as in patients at cardiovascular risk and patients with other disorders that impair sleep, PSG follow-up can be performed without prior respiratory polygraphy (evidence level 2b, grade C recommendation).

The recommendations on respiratory polygraphy for SRBDs were accepted with strong consensus (the recommendation on the diagnostic work-up of ventilatory failure by 10/11, and the remaining recommendations by 10/10).

3.4 Diagnosis of sleep-related breathing disorders with reduced systems

Systems that record only between one and three channels (pulse oximetry, long-term ECG, actigraphy, oronasal airflow measurement) yield up to 17% false-negative and up to 31% false-positive findings [27]; this explains why their use is not recommended for the definitive diagnosis or exclusion of SRBDs.

Recommendations. Reviewed and retained:
- Respiratory polygraphs that meet fewer than all the abovementioned criteria can provide an indication of whether an SRBD is present. They should not be used as the sole method to diagnose SRBDs (evidence level 2b, grade A recommendation).

Modified:
- In the case of cardiovascular diseases that increase the risk of SRBDs (e.g., arterial hypertension, heart failure, atrial fibrillation, cerebrovascular disease) in the absence of all typical symptoms, single- or dual-channel registration is possible as a screening test. If this registration prompts suspicion of OSA, further diagnostic evaluation with respiratory polygraphy or PSG should be carried out (evidence level 2b, grade A recommendation).

The recommendations on the diagnosis of SRBDs with reduced systems were adopted with strong consensus (14/17).

3.5 Diagnosis of sleep-related breathing disorders using alternative systems

Recent studies of varying quality point to possibilities for monitoring SRBDs using alternative systems that cannot be classified as classic PSG, respiratory polygraphy, or reduced-signal systems. These alternative systems are based on the SCOPER criteria [19], which specify that the physiological entities of sleep, cardiovascular parameters, oxygen saturation, position, respiratory effort, and airflow are recorded, either directly or indirectly, in varying quality. Systems with new sensor technology, such as peripheral arterial tonometry [28], breathing sound/snoring sound analysis [36, 37], noncontact high-resolution detection of body motion using radar technology [38, 39], and bed sensor technology [40, 41], are able to extract multiple entities from one signal by means of advanced biosignal analysis. A prominent example that has been published with high evidence is the successful extraction of airflow and respiratory effort from a modified finger pulse (peripheral arterial tonometry) for the diagnosis of sleep apnea [28]. Smartphone- and smartwatch-based systems are picking up on these technical developments and are generally not approved as medical devices.

Recommendations. New:
- Systems using peripheral arterial tonometry demonstrate good evidence for the diagnosis of sleep apnea and should be used analogously to respiratory polygraphy in the case of high pretest probability in order to confirm the diagnosis and determine the severity of SRBDs (evidence level 2a, grade B recommendation).
- Systems based on smartphone and smartwatch technology with internal and external sensors are not yet approved as medical devices; moreover, validation studies are lacking or only available in exceptional cases, meaning that these devices are not currently recommended (evidence level 5).

The recommendations on the diagnosis of SRBDs with alternative systems were adopted with strong consensus (14/15).

4 Obstructive sleep apnea syndrome

4.1 Obstructive sleep apnea and dementia

Two prospective cohort studies with 2636 older men and 298 older women, respectively, without cognitive impairment at *baseline* investigated the effect of OSA on brain performance. In the men, a significantly greater loss of cognitive performance was found after a mean of 3.4 years in the presence of OSA with additional hypoxemia [42]. Among the women with OSA and hypoxemia, the risk of developing mild cognitive impairment (MCI) or dementia was increased by a factor of 1.85 (95% confidence interval [CI] 1.11–3.08) over a mean of 4.7 years after adjustment for other risk factors [43]. The risk for sleep apnea patients to develop dementia is increased if the apolipoprotein E ε4 allele is absent [44]. Furthermore, a significant decline in instrumental activities of daily living has been demonstrated in older women with untreated sleep-disordered breathing [45].

4.1.1 Treatment of obstructive sleep apnea in individuals with dementia

In a small randomized controlled trial, individuals with mild or moderate dementia and OSA (apnea–hypopnea index [AHI] > 10/h) were treated with continuous positive airway pressure (CPAP) or subtherapeutic CPAP therapy. Although acceptance of CPAP therapy was initially high, 25% of patients dropped out of the study after randomization [46, 47]; the dropout rate after the randomized study was also high [48].

After 3 weeks of treatment, patients receiving CPAP therapy showed a clinically nonrelevant improvement in daytime sleepiness compared with patients receiving subtherapeutic CPAP therapy (Δ Epworth Sleepiness Scale [ESS] CPAP versus subtherapeutic CPAP: −1.6) [47]. A significant improvement was seen in various neuropsychological test scores [46].

CPAP therapy can improve daytime sleepiness [47], sleep profile [49], and cognitive performance [48] only in selected patients with mild or moderate dementia in nonrandomized trials. Long-term CPAP therapy is possible in selected patients with mild or moderate dementia and OSA [46–49].

The randomized studies conducted to date have not been able to demonstrate that CPAP therapy relevantly improves symptoms and cognitive performance in patients with mild to moderate dementia. The studies were too small to demonstrate effects of this kind (◘ **Table 4**). Therefore, it is currently not possible to make specific recommendations on the treatment of sleep apnea in dementia patients.

Pharmacological treatment of dementia using donepezil can lead to a relevant improvement in obstructive sleep apnea [50].

4.1.2 Nocturnal positive-pressure ventilation

The recommendations in the existing chapter on nocturnal positive-pressure ventilation remain valid. This section merely specifies with greater precision the statement on CPAP/APAP initiation without PSG monitoring, which is now as follows: "With regard to managing therapy initiation, there is a growing body of RCTs (randomized controlled trials) showing that in certain subgroups of patients, CPAP/APAP discontinuation can be carried out on an outpatient basis at a sleep medicine center without PSG monitoring in a sleep laboratory."

4.2 Non-CPAP methods in obstructive sleep apnea

4.2.1 Positional therapy

The term "position-dependent" or "positional" OSA is usually used when the AHI is at least twice as high in a supine position compared to other positions [51]. The prevalence of positional sleep apnea is estimated to be 25–30% of all patients with OSA. The probability that a patient has positional sleep apnea diminishes with increasing severity of sleep apnea and obesity [51].

In principle, positional therapy (preventing a supine position) has therapeutic potential especially in patients whose respiratory disorders manifest only in the supine position or whose AHI in other body positions is lower or does not require treatment. The methods or devices used for positional therapy differ significantly in terms of design and the reliability with which the supine position is prevented. A distinction can be made in positional therapy between passive methods (e.g., the so-called tennis ball technique, as well as special pillows and backpacks) and active methods (positional trainer, vibration alarm devices controlled by a special algorithm) [52]. Here, as with other devices for sleep apnea treatment, the problem of compliance and adherence also arises.

A recent meta-analysis includes three randomized studies comparing active procedures using a positional trainer versus CPAP therapy. However, it is important to note that these meta-analyses investigated primarily only one system. Two of these studies showed that CPAP resulted in a greater reduction in AHI, with a mean difference of 6.4 events per hour (95% CI 3.00–9.79) compared to positional therapy [52]. Positive effects on daytime sleepiness were comparable under positional therapy and CPAP [52]. It was not possible to draw conclusions regarding adverse events, quality of life, or long-term effect [52]. In a recent randomized crossover study in which each treatment lasted 6 weeks, the mean nocturnal duration of use was approximately 1 h longer with a positional trainer than with CPAP therapy [51]. No severe adverse events occurred in either group. The rate of adverse events was lower under positional therapy compared to automatic CPAP therapy (4.2% versus 18.8%) [51]. Patients receiving positional therapy reported pain in the back, shoulder, and neck (3.4%, 4/117), as well as abdominal skin irritation (< 1%, 1/117). While both treatments significantly improved daytime sleepiness, neither achieved a relevant improvement in sleep-related quality of life (as measured with the Functional Outcomes of Sleep Questionnaire, FOSQ) [51].

In another randomized trial, active positional therapy was equivalent to treatment with a mandibular advancement device (MAD) for positional OSA [53], while in yet another study, a combination of the two therapies was shown to be significantly more effective than the individual therapies [54].

Although active positional therapy was equal to passive positional therapy in terms

Table 4 Treatment of patients with OSA and dementia

Author	Year	Country	Study type	Population	Patients	Intervention	Design/endpoints	Effects	EL
Chong [47]	2006	USA	Randomized, placebo-controlled, double-blind	Moderate to severe OSA, mild to moderate dementia	$N = 37$	CPAP versus subtherapeutic CPAP Observation period: 6 weeks	Change in subjective daytime sleepiness	CPAP versus subtherapeutic CPAP: Δ ESS: at 3 weeks −2.3 versus −0.7; at 6 weeks −3.4 versus −1.8 Intergroup comparisons not analyzed	2b
Ancoli-Israel et al. [46] and Cooke et al. [49]	2008 and 2009	USA	Randomized, placebo-controlled, double-blind	Moderate to severe OSA, mild to moderate dementia	$N = 52$	CPAP versus subtherapeutic CPAP Observation period: 3 weeks	Change in composite neurophysiological score (CNS), deep sleep and waking responses	No significant change in CNS score or other neurophysiological tests in either treatment group Deep sleep increased and waking response declined in the CPAP group	2b
Cooke et al. [48]	2009	USA	Case series	Moderate to severe OSA, mild to moderate dementia	$N = 10$	CPAP versus discontinuation of initiated CPAP therapy	CNS scores and other neuropsychological tests, subjective daytime sleepiness (ESS score)	Numerically better cognitive performance, less daytime sleepiness and fewer symptoms of depression in the CPAP group compared to the CPAP-discontinuation group	4
Moraes et al. [50]	2008	Brazil	Randomized, placebo-controlled, double-blind	Moderate to severe OSA, mild to moderate dementia	$N = 23$	Donepezil (drug to treat cognitive symptoms in dementia) versus placebo for 3 months	Apnea-hypopnea index, SaO_2, REM sleep	Donepezil significantly improved AHI, oxygen saturation, and REM sleep	2b

EL evidence level, *OSA* obstructive sleep apnea, *CPAP* continuous positive airway pressure, *REM* rapid eye movement, *AHI* apnea–hypopnea index, *ESS* Epworth Sleepiness Scale, *CNS* composite neurophysiological score

of preventing a supine position, it showed significantly better compliance, mean disease alleviation, sleep quality, and quality of life [55]. In a long-term study on active positional therapy (positional trainer), the discontinuation rate within 1 year was 16% (9/58) [56]. Active positional therapy, therefore, appears to represent a realistic long-term treatment method for positional OSA. This was not the case for most passive positional therapies (e.g., tennis ball method). ◘ **Table 5** provides an overview of the studies presented here.

Recommendation. Modified:

In patients with mild to moderate positional OSA, positional therapy with validated systems should be considered (evidence level 1b, grade B recommendation).

The recommendation on positional therapy was adopted with strong consensus (9/11).

4.2.2 Surgical treatment methods

In terms of surgical treatment, a distinction is made between resective and nonresective surgical methods and procedures that modify the facial skeleton (osteotomies). Resective methods include all surgical procedures aiming to remove or correct anatomical obstructions which are diminishing the airflow. This goal is achieved by resection or by modifying the upper airway with different kinds of surgical techniques. Overall, resective procedures carry a peri- and postoperative risk, but this risk is described as low in more recent studies and depends on the procedure [62]. Tracheotomy is another procedure that reliably eliminates OSA [63] but should be seen as a last choice. In general, surgical treatment forms are more difficult to evaluate to a high level of evidence, since surgical techniques are individually selected depending on the anatomy and function of the upper airway. This makes standardization challenging. Moreover, only a few surgical centers master the entire spectrum of the different surgical approaches [64]. Due to the nature of many surgical techniques, blinding is not feasible. Nevertheless, an ever-growing number of controlled and randomized studies comparing surgical treatment methods with CPAP, placebo, or waiting are available. Data on long-

Table 5 Positional therapy in patients with OSA

Author	Year	Country	Study type	Population	Patient number	Intervention	Endpoint	Effect	EL
Benoist et al. [53]	2017	International	RCT	POSA	99 randomized (81 completed the study)	SPT vs. MAD	AHI, ODI, sleep time in supine position, ESS, FOSQ, MDA (mean disease alleviation)	MAD and SPT equivalent in AHI/ODI reduction; no effect on ESS and FOSQ	1b
Berry et al. [51]	2019	USA	Crossover RCT	POSA	117	SPT and automatic CPAP therapy	AHI, mean nighttime use	AHI 3.58/h ($p < 0.001$) higher under SPT. SPT use 58 min/night longer than CPAP use ($p < 0.0001$)	1b
Dieltjens et al. [54]	2015	International	RCT	POSA	20 (all with residual POSA under OA therapy)	SPT vs. SPT and MAD	Primary: AHI Secondary: ODI, positional change, sleep stages	OA and SPT equivalent in AHI and ODI reduction; combination significantly better than single therapies. No subjective parameters recorded	1b
Eijsvogel et al. [55]	2015	The Netherlands	Parallel for 1 month	POSA	55	SPT vs. TBT	Primary: sleep time in supine position Secondary: AHI, ESS, FOSQ, SASQ, neuropsychological test battery, blood pressure	TBT and SPT equivalent in reducing a supine position. Compliance, MAD, sleep quality, and quality of life significantly better with SPT than with TBT	1b
Jackson et al. [57]	2015	Australia	Parallel for 4 weeks	POSA	86	Modified tennis ball technique (TBT) vs. lifestyle plan	Primary: sleep time in supine position Secondary: AHI, ESS, FOSQ, SASQ, neuropsychological test battery, blood pressure	TBT reduces sleep time in a supine position significantly more than does a lifestyle plan	1b
Ha et al. [58]	2010	International	Meta-analysis	OSA	71	Positional therapy vs. CPAP	AHI, ESS, O_2 saturation, subjective test methods/questionnaires	Superiority of CPAP therapy only in relation to AHI and O_2 saturation, recommended for positional OSA in the case of CPAP non-compliance/intolerance	1b
Laub et al. [59]	2017	International	RCT	POSA	101	SPT vs. no therapy	AHI, sleep time in a supine position, ESS	SPT reduces AHI and sleep time in a supine position compared to no therapy Significant ESS reduction under SPT	1b
De Ruiter et al. [60]	2018	International	Randomized over 12 months	POSA	99 included (completed by 58)	SPT vs. MAD	AHI, ODI, ESS, FOSQ-30, adherence	AHI, ODI significantly reduced in both groups. No difference between the two groups	1b
Skinner et al. [61]	2008	New Zealand	Parallel for 4 months	OSA	20	Thoracic anti-supine band (modified tennis ball technique) versus CPAP	AHI (mean and successful reduction) and mean O_2 saturation ESS, FOSQ, SF-35 Compliance, side effects	CPAP > positional therapy Significantly better than control n.s. Positional therapy > CPAP	1b
Srijithesh et al. [52]	2019	India	Meta-analysis of 5 RCTs	POSA	251	3 RCT on active positional therapy (SPT); 2 on passive positional therapy (similar to tennis ball technique, positional sleeping pillow)	AHI and ESS	Positional therapy significantly improves AHI (−7.38/h, 95% CI −10.06–−4.7) and daytime sleepiness (ESS −1.58, 95% CI −2.89–−0.29) compared to the control intervention	1a

Table 5 (Continued)

Author	Year	Country	Study type	Population	Patient number	Intervention	Endpoint	Effect	EL
Srijithesh et al. [52]	2019	India	Meta-analysis of 3 crossover RCTs	POSA	72	1 RCT on active positional therapy (SPT), 2 RCTs on passive positional therapy (TBT, modification of the TBT)	AHI, ESS, subjective night-time usage time	Similar treatment effects in terms of ESS score. AHI reduction greater under CPAP than with positional therapy (6.4/h, 95% CI 3.00–9.79). Subjective nighttime usage time of positional therapy was 2.5 h/night (95% CI 1.41–3.59) longer than with CPAP therapy	1a

AHI apnea–hypopnea index, *CI* confidence interval, *CPAP* continuous positive airway pressure, *EL* evidence level, *ESS* Epworth Sleepiness Scale, *FOSQ* Functional Outcome of Sleep Questionnaire, *OA* oral appliance therapy, *ODI* oxygen desaturation index, *OSA* obstructive sleep apnea, *POSA* positional OSA, *RCT* randomized clinical study, *SASQ* Subjective Apnea Severity Questionnaire, *SPT* sleep position trainer, *TBT* tennis ball technique/passive positional therapy, *MAD* mandibular advancement device

term effects are not available for all the procedures presented in this manuscript.

A sleep diagnosis is needed if surgical procedures are used in OSA patients. The predictors of surgical success—and thus the selection criteria for selecting the appropriate surgical procedure in OSA patients—need to be elaborated separately for each intervention. They can differ significantly and are not available for all surgical procedures. Obesity is a negative predictor but has different and to some extent as yet unknown threshold values, depending on the intervention.

Surgeries to improve nasal breathing need to be considered in a different context since they generally do not improve the breathing disorder, but they do reduce daytime sleepiness, snoring, as well as the required CPAP pressure, and improve general acceptance of CPAP therapy [65]. Since the underlying studies were conducted in patients with existing nasal airway impairment—so due to an existing rhinological indication—surgical procedures to improve nasal airway function are limited to this population.

Tonsillectomy, uvulopalatopharyngoplasty, and modifications. Two randomized studies evaluated the combination of tonsillectomy (TE) and uvulopalatopharyngoplasty (UPPP) in groups of patients that had exclusively or predominantly tonsils which were obstructing the oropharynx. In these groups, surgery was highly significantly superior to a 6-month waiting period in terms of reduction in respiratory events. For example, an AHI reduction was seen in 60% (surgery group) versus 11% (waiting group). Furthermore, treatment success (Sher criteria: reduction of AHI > 50% to an AHI < 20) was shown in 59% (surgery group) vs. 6% (waiting group) [66]. The AHI was reduced from 35.7 ± 19.4 to 28.6 ± 19.3 in the control group and 33.7 ± 14.5 to 15.4 ± 14.1 in the surgical group [67]. Accordingly, a systematic review of these studies also demonstrated significant superiority of TE with UPPP in terms of AHI, snoring, and daytime sleepiness compared to an untreated control group of patients with clinically diagnosed isolated oropharyngeal obstruction [68].

Positive predictors of treatment success include defined anatomic factors (e.g., tonsil size), clinical scoring systems derived from these, BMI, and severity of sleep apnea [68, 69]. For patients with very large tonsils, TE alone can be helpful and effective [70]. For *unselected* patients, the efficacy of TE combined with UPPP has been shown only with a lower level of evidence to date [68]. A significant and long-term improvement in daytime sleepiness, physical and mental wellbeing, and quality of sleep has recently been demonstrated for TE-UPPP in randomized controlled trials [71–74]. Cohort studies achieved normalization 3 months after successful UPPP of serum leptin and nitric oxide levels, as well as endothelium-dependent vasodilation [75, 76]. Furthermore, tumor necrosis factor-α (TNF-α) and interleukin-6 (IL-6), as inflammatory markers, were also significantly reduced 3 months after UPPP with septoplasty compared to a healthy control group [77]. In an epidemiological cohort study of 444 patients, OSA mortality was significantly reduced by UPPP compared to mortality in an untreated control group. This result of mortality was comparable to that of CPAP therapy [78].

Whether the initial effect of surgery diminishes over time is the subject of debate due to inconsistent data [79, 80]. However, in contrast to previous published data, the results of more recent 24-month data do not support an attenuation of the effect over time, at least in the case of TE-UPPP [81].

Persistent side effects, such as voice changes, foreign body sensation, and difficulty in swallowing, are possible depending on the surgical procedure [62, 68]. Therefore, relevant reviews recommend TE-UPPP in patients with mild to moderate OSA, especially if they do not tolerate CPAP therapy and have suitable anatomy (tonsillar hyperplasia with clinically suspected oropharyngeal obstructions), since it is superior to "no therapy" and has acceptable side effects [70]. Whether UPPP offers a benefit compared to TE alone cannot be determined on the basis of the currently available data.

The value of the numerous modifications of UPPP (e.g., uvulopalatal flap, Z-palatoplasty, relocation pharyngoplasty, Han's UPPP, lateral pharyngoplasty) has

not yet been elucidated. Hence, corresponding studies should be performed [82]. A systematic review was able to show superiority over UPPP only for expansion sphincter pharyngoplasty in the case of suitable anatomy [83]. A meta-analysis showed that anterior palatoplasty significantly improves AHI, snoring, and daytime sleepiness in patients with mild OSA [84].

Laser-assisted uvulopalatoplasty (LAUP) reduces AHI to below 10/h in 50% of cases, while postoperative side effects are seen in up to 60% of cases [85]. Similar results were seen in the long-term over a period of 11 years on average [86]. Therefore, LAUP is also not recommended in international publications.

Hypoglossal nerve stimulation. In the past decade, stimulation of the hypoglossal nerve (HN) has become firmly established in the treatment of OSA. Stimulation of the nerve fibers generates a contraction of the genioglossus muscle, which results in an active opening of the upper airway [87]. There are currently different methods of hypoglossal nerve stimulation (HNS), which, due to their clinical results, also need to be considered in a differentiated manner [88, 89]. The largest amount of evidence is available for the method of selective breathing cycle-controlled HNS. Extensive clinical data are available from a controlled multicenter study with randomized treatment withdrawal and also from a 5-year follow-up period. Many other controlled studies as well as routine care studies exist [90–95]. All studies show sustained effects with selective breathing cycle-controlled HNS in reducing respiratory events in patients with moderate to severe OSA. A high usage time could be detected and led to a significant improvement in health-related quality of life. Patient age and previous upper airway surgery have an impact on the efficacy of HNS. Procedure-related morbidity can be described as low [88]. The rate of revision surgery over a period of 5 years in the first clinical trials was 6% [89, 90] and could be reduced to 1% according to the data of the subsequent large registry study (ADHERE registry) [88].

Selective breathing cycle-controlled HNS is only beneficial in patients without tonsillar hypertrophy and moderate to severe OSA. Since previous studies showed that complete concentric collapse at the level of the soft palate during drug-induced sleep endoscopy (DISE) was associated with a much higher nonresponder rate, patients showing this obstruction pattern at the velum need to be excluded [96]. Former studies showed that treatment response was dependent on BMI and AHI. Although the STAR study primarily included patients with a BMI < 32 kg/m^2 and an AHI between 20 and 50/h, results of cohort studies and the international registry study (ADHERE) suggest that the indication criteria could be broader (BMI of 35 kg/m^2 instead of 32 and AHI of between 15 and 65/h instead of 20 and 50/h) [87, 88, 90, 97, 98].

Targeted hypoglossal neurostimulation (continuous non-breathing-dependent stimulation of the hypoglossal nerve) consists primarily of upper airway stabilization and not—in contrast to breathing-controlled selective stimulation—active opening [89, 99]. Targeted hypoglossal neurostimulation can be considered in patients with an AHI of 20–65/h and a BMI of up to 35 kg/m^2, as well as in patients with concentric collapse of the upper airways.

A success rate according to Sher criteria (≥ 50% reduction in AHI and AHI < 20/h under treatment) was achieved at 12 months for the individual systems in 72% of 211 patients receiving selective breathing cycle-controlled HNS and in 77% of 13 patients receiving targeted hypoglossal neurostimulation [89]. There are no randomized comparative studies addressing the different stimulation methods or comparing with other therapies (e.g., MAD) [89].

Osteotomies. Osteotomies to advance the maxilla and mandible (maxillomandibular advancement) enlarge the pharyngeal airway and increase the pharyngeal muscle tone. Both effects synergistically reduce the collapsibility of the upper airway. Osteotomies can be highly effective in the treatment of OSA, not only in the case of congenital malformations (e.g., Pierre Robin sequence, Crouzon syndrome, Apert syndrome), but also for specific anatomical features of the pharyngeal airway such as microgenia (small mandible), mandibular retrognathia (retroposition of the mandible in relation to the anterior skull base), or the associated narrow sagittal craniofacial structures. Osteotomies can also be performed in normognathic patients. Advancement by 10 mm is considered necessary. In a meta-analysis of 627 patients, a substantial improvement in AHI of 86% was reported, and an AHI < 5 was achieved in 43.2% [100]. The treatment effect was stable for more than 2 years in the series of long-term data. In cohort studies and in a randomized study, no difference in effectiveness compared to ventilation therapy could be detected [101, 102]. A meta-analysis in 2016 showed an overall reduction in AHI by 47.8/h (±4.7) [103]. The preoperative ESS of 13.5 (±2.8) was reduced to 3.2 (±3.2) postoperatively (median minimum follow-up time of 6 months, range 2–6 months). In terms of adverse effects, transient paresthesia (altered perception of sensation) of the second and/or third trigeminal branch is often reported [99]. This can be found in 14% of patients at 12 months. More than 90% of patients report positive or neutral aesthetic effects [100].

Other surgical procedures. Radiofrequency ablation (RFTA) and soft palate implants, which are minimally invasive surgeries, are better tolerated than resective procedures. However, both surgeries appear to be significantly inferior to the latter in terms of efficacy [104–106]. To date, RFTA has been shown to result in only 31%—and only short-term—reduction in sleepiness measured by the ESS [106]. For example, a placebo-controlled study showed RFTA as single procedure to have no effects on OSA [107]. With regard to RFTA tongue base reduction, robust evidence of an effect is lacking to date, apart from isolated studies [108]. Radiofrequency surgery of the soft palate, at least in OSA patients, appears to have no effect on AHI, daytime sleepiness, and subjective snoring [109]. With a high level of evidence, soft palate implants have been shown to reduce snoring and OSA with a low to moderate effectiveness. Furthermore, extrusion was reported in nearly 10% of patients [105, 110].

Table 6 Surgical treatment in patients with OSA

Author	Year	Country	Study type	Population	Patient number	Intervention	Endpoint	Effect	EL
Amali et al. [104]	2017	Iran	Randomized clinical trial	OSA	40	RFTA of the soft palate vs. UPPP	AHI, ESS	TE-UPPP superior compared to radiofrequency ablation of the soft palate. No difference in ESS	1b
Bäck et al. [107]	2009	International	Review	Snoring	30 (number of studies)	RFTA of the soft palate vs. placebo	Snoring, adverse effects	Snoring becomes moderate, but is significantly reduced with lower morbidity compared to LAUP or injection snoreplasty. Decline in effect after more than 12 months	1a
Babademez et al. [114]	2011	Turkey	Randomized clinical trial	OSA	45	Open transoral radiofrequency tongue base resection vs. submucosal minimally invasive tongue excision with radiofrequency vs. ultrasonic scalpel (all combined with UPPP)	AHI, ESS, tongue volume (magnetic resonance imaging), pain	No relevant difference between the groups	1b
Bäck et al. [107]	2009	Finland	Randomized clinical trial	OSA	32	RFTA of the soft palate vs. placebo surgery	Primary: AHI, ESS, SF-36 Secondary: Snoring, cephalometric parameters, adverse events	No difference between the groups, but only one treatment as opposed to the standard of two or more treatments	1b
Browaldh et al. [66]	2013	Sweden	Randomized clinical trial	OSA	65 (BMI < 36, Friedman stage I or II)	UPPP vs. 7-month wait	Primary: AHI Secondary: further PSG parameters	UPPP highly significantly superior to waiting with regard to AHI and all respiratory parameters irrespective of BMI, tonsil size, and Friedman stage. Of sleep parameters, only arousal index significantly reduced	1b
Browaldh et al. [66]	2016	Sweden	Randomized clinical trial	OSA	65	TE-UPPP	ESS, SF36	ESS significantly improved from 12.5 to 6.8; SF23 "physically" significantly improved from 47.8 (8.3) to 51.2 (8.8); SF36 "mentally" significantly improved from 42.1 (10.6) to 48.1 (9.7)	1b
Camacho et al. [63]	2014	International	Review	OSA	18 (number of studies)	Tracheostomy	AI, AHI, ODI, daytime sleepiness	Tracheotomy reliably eliminates OSA with regard to disordered breathing and daytime sleepiness; central apnea > 14 weeks post tracheotomy no longer detectable; from BMI 45, OHS possible cause of persistently elevated ODI	1a
Caples et al. [62]	2010	International	Review (meta-analysis)	OSA	36 (number of studies)	MMA (9), UPPP (15), LAUP (2), RFTA (8), pillars (2)	AHI, daytime sleepiness, adverse events	Moderate evidence: LAUP without effect. Low evidence: MMA with pronounced effect, UPPP, RFTA, and pillars with moderate effect. Complication rates decline in more recent studies	1a
Camacho et al. [117]	2015	International	Systematic review (meta-analysis)	OSA	12 (number of studies)	MMA (9), tracheostomy (9)	AHI, lowest SpO_2 saturation	MMA: significant reduction in AHI by −72.69 (95% CI −84.08 to −61.31), significant increase in lowest SpO_2 saturation by 19.24 (95% CI 12.96–25.52) Tracheostomy: LSAT pre-intervention 55.17 ± 16.46%, post-intervention 79.38 ± 4.36% ($p = 0.011$), no data on AHI due to small case number	1a

Table 6 (Continued)

Author	Year	Country	Study type	Population	Patient number	Intervention	Endpoint	Effect	EL
Camacho et al. [70]	2016	International	Systematic review (meta-analysis)	OSA	17 (number of studies)	Tonsillectomy	AHI, ESS, SpO_2	Significant improvement AHI, ESS, SpO_2	1a
Choi et al. [105]	2013	International	Meta-analysis	OSA (snoring without OSA)	7 OSA (7 snoring) (number of studies)	Pillar-soft palate implant vs. placebo	AHI, ESS, (snoring), extrusion rate for all 14 studies	Pillar implants reduce AHI, ESS (in OSA), and snoring with moderate effect over a period of 3 to a maximum of 29 months. Extrusions are described in 9.3% of patients	1a
Constantino et al. [89]	2019	International	Review and meta-analysis	OSA	Qualitative analysis 12, quantitative analysis 9 (number of studies respectively)	Upper airway stimulation	AHI, ODI, ESS	AHI reduction 55.1%/56.2% (Inspire), 27%/53.5% (ImThera), and 54.4%/44.3% (Apnex) after 6/12 months, ODI reduction 43.7%/53.4% (Inspire), 27.2%/47.6% (ImThera), and 47.6%/24.9% (Apnex) after 6/12 months, significant ESS reduction in all groups	1a
Farrar et al. [106]	2008	International	Meta-analysis	OSA	16 (number of studies)	RFTA soft palate, tongue base, or both vs. placebo	AHI, ESS, adverse effects	Moderate reduction in AHI and ESS, lasting 24 months in case series. Controlled study with comparable effect on quality of life and daytime sleepiness to CPAP and better than placebo	1a
Fehrm et al. [73]	2017	Sweden	Randomized clinical trial	OSA	65	UPPP	Blood pressure	Significant improvement in systolic and diastolic blood pressure at 6 months and limited improvement at 24 months	1b
Franklin et al. [118]	2009	International	Meta-analysis	OSA and snoring	4 (number of studies)	LAUP (2), RFTA of the tongue base (1) or soft palate (1) vs. waiting or placebo	Daytime sleepiness, AHI, snoring, adverse effects (also uvulopalatoplasty and UPPP)	LAUP and RFTA of the tongue base has no effect on daytime sleepiness and AHI, RFTA of the soft palate reduces snoring. No randomized studies available for all other surgical techniques, hence not included in the analysis. In 31% and 27%, difficulty swallowing after uvulopalatopharyngo- and palatoplasty, respectively. Complication rates decline in more recent studies	1a
Handler et al. [112]	2014	International	Review	OSA	27 (number of studies)	Tongue suspension (6), all other studies with UPPP	AHI	Tongue suspension alone with response rate of 36.6%; in combination with UPPP, as good as genioglossus advancement and hyoid suspension (62.1% vs. 61.6%)	1a
Holmlund et al. [109]	2014	Sweden	Randomized clinical trial	OSA	35	Sham/RF soft palate	ESS, secondary AHI, subjective snoring	No effect	1b

Table 6 (Continued)

Author	Year	Country	Study type	Population	Patient number	Intervention	Endpoint	Effect	EL
Holty et al. [100]	2010	International	Meta-analysis	OSA	22 (number of studies)	MMA vs. CPAP and case series	AHI, long-term effects	MMA reliably reduces severity, comparable to ventilation therapy in cohort studies, increased maxillary advancement, and lower preoperative BMI with positive predictive value. Transient facial paresthesia in 100%, persisting in 14.2% at 12 months	1a
Joar et al. [74]	2018	Sweden	Randomized clinical trial	OSA	65	TE-UPPP	Karolinska Sleep Questionnaire, FOSQ	Karolinska Sleep Questionnaire: all subvalues significantly improved; FOSQ: all subvalues significantly improved except "Social outcome"	1b
Li et al. [65]	2011	International	Review	OSA	13 (number of studies)	Nasal surgery vs. placebo	AHI, ESS, snoring	No effect on AHI, ESS and snoring diminish	1a
Lin et al. [111]	2008	International	Review	OSA	49 (number of studies)	Multilevel surgery	AHI, O_2 saturation, proportion of REM, snoring (VAS), daytime sleepiness, quality of life	Significant improvement in AHI (AHI reduction > 50% to a value < 20) in 66.4% of all patients. Success rate higher for AHI > 40 (69.3%) than for AHI < 40 (56.5%). No worsening 3–8 years postoperatively. Significant improvement in all other parameters investigated	1a
Marklund et al. [119]	2012	International	Review	OSA	55 (number of studies)	MAD vs. placebo MAD vs. placebo MAD vs. CPAP MAD vs. surgery	AHI, RDI, PSG, daytime sleepiness, quality of life, cardiovascular parameters, long-term effects	MAD more effective than placebo Degree of protrusion correlates with efficacy CPAP is superior to MAD in AHI reduction. Daytime sleepiness, quality of life, cardiovascular parameters comparable Long-term effect weaker than initial improvement	1a
Maurer et al. [110]	2012	Germany	Randomized clinical trial	OSA	22	Pillars vs. placebo surgery	AHI, AI, HI, mean SaO_2, minimum SaO_2, ESS, snoring	HI, AHI, minimum SaO_2, and snoring significantly reduced in verum group, but no significant group difference	1b
Murphey et al. [120]	2015	International	Systematic review (meta-analysis)	OSA	18 (number of studies)	Glossectomy (midline glossectomy 13, submucosal minimally invasive lingual excision 4, lingual tonsillectomy 3)	AHI, LSAT, ESS, snoring (VAS), surgical success (Sher)	Significant reduction in AHI by –27.81 (95% CI –33.00 to –22.62), significant increase in LSAT by 7.68 (95% CI 5.34–10.02), significant reduction in ESS by –5.49 (95% CI –7,17 to –3.81), significant reduction in snoring (VAS) by –5.60 (95% CI –6.57 to –4.63), surgical success rate 59.56% (95% CI 52.99–65.96)	1a
Noller et al. [8]	2017	International	Systematic review (meta-analysis)	OSA	11 (number of studies)	Mandibular advancement surgery	AHI, minimum SpO_2 saturation	Significant reduction in AHI by –34.8 (95% CI –43.9 to –25.8), significant reduction in LSAT by 12.80 (95% CI 4.86–20.73)	1a
Pang et al. [83]	2016	International	Systematic review	OSA	5 (number of studies)	ESP vs. UPPP	AHI	AHI significantly lower after expansion sphincter pharyngoplasty than after UPPP (–7.32, 95% CI [–11.11, –3.52])	1a
Pang et al. [84]	2018	International	Systematic review	OSA	6 (number of studies)	Anterior palatoplasty	AHI, ESS, Snore Score	Significant reduction in AHI 16.3 to 7.1; significant improvement in Snore Score from 7.5 to 3.1; significant improvement in ESS from 11.3 to 7.3	1a

Table 6 (Continued)

Author	Year	Country	Study type	Population	Patient number	Intervention	Endpoint	Effect	EL
Pirklbauer et al. [101]	2011	International	Review	OSA	28 (number of studies)	MMA vs. CPAP and case series	AHI, long-term effects, daytime sleepiness	MMA comparable with ventilation therapy, positive effects on daytime sleepiness, quality of life, no negative effect on facial aesthetics	1a
Samutsakorn et al. [121]	2018	International	Systematic review	OSA	4 (number of studies)	Tongue base tonsillectomy with soft palate surgery	AHI, SpO_2 min, ESS	Significant improvement in: AHI (mean difference: 18.51, 95% CI [−31.72, −5.31]); SpO_2 min (mean difference: 5.26, 95% CI [0.10, 10.42]); ESS (mean difference: −5.44, 95% CI [−8.69, −2.18])	1a
Sommer et al. [67]	2016	Germany	Randomized clinical trial	OSA	Control: 19/OP: 23/+19 crossover	TE-UPPP	AHI	AHI: 35.7 ± 19.4 → 28.6 ± 19.3 (control)/33.7 ± 14.5 → 15.4 ± 14.1 (OP)	1b
Strollo et al. [90]	2014	International	Randomized treatment withdrawal	OSA	126 (46 in randomized arm)	Active vs. inactive stimulation	Primary: AHI, ODI Secondary: T90, ESS, FOSQ	All target parameters significantly improved, inactive stimulation without effect, 12-month follow-up	1b
Stuck et al. [68]	2018	International	Systematic review	OSA	48 (number of studies, of which 3 RCT)	TE-UPPP	ESS, AHI	AHI: mean difference: −18.59 (95% CI −34.14, −3.04) ESS: mean difference: −5.37 (95% CI −7.03, −3.72) In RCTs: AHI: 35.4 to 17.9 (−49.5%); mean difference: −20.41, 95% CI −32.78, −8.04 (−1.80, −1.15)	1a
Sundaram et al. [82]	2005	International	Review	OSA	7 (number of studies)	Surgery	AHI, snoring, fatigue	No effect, long-term data lacking	1a
Vicini et al. [102]	2010	Italy	Randomized clinical trial	OSA	50	MMA vs. APAP	AHI, ESS	AHI and ESS identical, satisfaction overall higher with MMA, 12-month follow-up	1b
Volner et al. [122]	2017	International	Systematic review (meta-analysis)	OSA	5 (number of studies)	Transpalatal advancement	AHI	Significant improvement: mean difference: −36.25 [−48.5, −24.1]	1a
Wu et al. [123]	2017	International	Meta-analysis	OSA	18 (number of studies)	Nasal surgery	AHI, ESS	Significant reduction in AHI by −4.15 (95% CI −6.48 to −1.82), significant reduction in ESS by −4.08 (95% CI −5.27 to −2.88)	1a
Zaghi et al. [103]	2016	International	Meta-analysis	OSA	45 (number of studies)	MMA	AHI	Significant reduction in AHI by −47.8 ± 4.7	1a

Inspire (Inspire Medical, Golden Valley, MN, USA), ImThera (ImThera/LivaNova, London, UK), Apnex (Apnex Medical, St. Paul, MN, USA)

AHI apnea–hypopnea index, ***APAP*** automatic CPAP, ***BMI*** body mass index, ***CI*** confidence interval, ***CPAP*** continuous positive airway pressure, ***EL*** evidence level, ***ESS*** Epworth Sleepiness Scale, ***FOSQ*** Functional Outcome of Sleep Questionnaire, ***LAUP*** laser-assisted uvulopalatoplasty, ***ODI*** oxygen desaturation index, ***OHS*** obesity hypoventilation syndrome, ***OSA*** obstructive sleep apnea, ***MMA*** maxillomandibular advancement, ***RFTA*** radiofrequency surgery, ***RCT*** randomized clinical trial, ***TE-UPPP*** Tonsillectomy with uvulopalatopharyngoplasty, ***MAD*** mandibular advancement splint, ***UPPP*** uvulopalatopharyngoplasty)

Table 7 Sleep-related hypoventilation syndrome/hypoxemia syndrome (according to ICSD-3)		
1	Sleep-related hypoventilation	
	1.1	Obesity hypoventilation syndrome
	1.2	Congenital central alveolar hypoventilation syndrome
	1.3	Late-onset central hypoventilation with hypothalamic dysfunction
	1.4	Idiopathic central alveolar hypoventilation
	1.5	Sleep-related hypoventilation due to a medication or substance
	1.6	Sleep-related hypoventilation due to a medical disorder – Parenchymal lung disease – Vascular lung disease – Lower airway obstruction – Neuromuscular or chest wall disorders
2	Sleep-related hypoxemia	

Multilevel surgery is currently widely promoted, but controlled studies are missing to demonstrate its success. All case reports of a series of patients show a relatively constant response rate of 50–70% (weighted mean 66.4%) [111]. Response rates do not differ when tongue suspension is used as the retrolingual procedure instead of the most often used procedure of genioglossus advancement with or without hyoid suspension [112]. Another study also showed no difference between lingual tonsillectomy (using CO_2 laser) and hyoid suspension in combination with radiofrequency therapy of the tongue base [113]. In a randomized trial by Babadamez et al. [114], the authors were unable to show a significant difference between three different techniques of tongue base resection combined with UPPP [114]. Also, the response rate may decline over a period of 5 years [115].

The low level of evidence for hyoid suspension, midline glossectomy (cryosurgery, laser, robot-assisted), and lingualplasty has been already reported in a previous version of this guideline. Nothing has changed during the newly investigated time period [85, 116]. There is insufficient evidence for the following treatment procedures: laser-assisted soft palate surgery, uvula capping, cautery-assisted palatal stiffening operation, injection snoreplasty, radiofrequency surgery of the tonsils, transpalatal advancement pharyngoplasty, and isolated genioglossal advancement.

An overview of studies on surgical treatment is presented in ◘ **Table 6**.

Recommendations. Reviewed and retained:

- Surgeries to improve nasal breathing should be considered in cases of obstructed nasal breathing and consequent CPAP intolerance (evidence level 4, grade B recommendation).
- If anatomical findings are appropriate, i.e., small mandible and narrow craniofacial structure, maxillary and/or mandibular advancement (bimaxillary advancement) should be considered, particularly if other treatments (CPAP, MAD) are not possible or not sufficiently tolerated (evidence level 1b, grade A recommendation).

Modified:

- In the case of clinically suspected oropharyngeal obstruction due to tonsillar hyperplasia, tonsillectomy with UPPP should be considered, particularly if other treatments (CPAP, MAD) are not possible or not sufficiently tolerated (evidence level 1a, grade A recommendation).
- Procedures for neurostimulation of the hypoglossal nerve should be considered in patients with CPAP intolerance or ineffectiveness with an AHI 15–65/h and a BMI up to 35 kg/m^2 in the absence of anatomic abnormalities and moderate to severe OSA (evidence level 1b, grade B recommendation).

The recommendations on surgical treatment methods were accepted with strong consensus (recommendation on TE-UPPP with 11/12, and remaining recommendations with 13/13).

5 Sleep-related hypoventilation/ sleep-related hypoxemia

The ICSD-3 [124] differentiates between sleep-related hypoventilation and sleep-related hypoxemia. For sleep-related hypoventilation, a distinction is made between six entities, whereas no subdivision is proposed for hypoxemia (see ◘ **Table 7**). According to the ICSD-3, sleep-related hypoxemia is present when either PSG or nocturnal pulse oximetry records oxygen saturation of ≤ 88% for ≥ 5 min in the absence of sleep-related hypoventilation.

Sleep-related hypoxemia is usually caused by an internistic or neurological disease and cannot be explained by a sleep-related breathing disorder, which, however, may be concomitantly present.

Some patients with sleep-related hypoxemia also exhibit daytime hypoxemia. Due to the clinical significance obesity hypoventilation syndrome and sleep-related hypoventilation due to a medical disorder, this section deals exclusively with these entities.

5.1 Obesity hypoventilation syndrome (OHS)

The diagnostic criteria are as follows:

a. Hypercapnia (daytime $paCO_2 \geq$ 45 mm Hg)
b. BMI > 30 kg/m^2
c. Hypoventilation is not primarily defined by another disorder

Some definitions additionally stipulate the presence of an SRBD, most commonly OSA (90%).

The prevalence of OHS among patients with OSA ranges, depending on the study, from 4 to 50%; individuals with a BMI > 30 kg/m^2 can be expected to have OHS with a frequency of 10–50%.

5.1.1 Main findings

Since 90% of OHS patients have OSA, they often also complain of symptoms of OSA, such as nonrestorative sleep, daytime sleepiness, and impaired concentration. This can result in symptoms being attributed exclusively to OSA, and the diagnosis of OHS being overlooked. Compared to OSA or obese patients, OHS patients more frequently experience short-

ness of breath and are more likely to present with clinical symptoms of peripheral edema, pulmonary hypertension, and cor pulmonale. Compared to eucapnic patients with a BMI > 30 kg/m^2, hospitalization rates, morbidity, and mortality are higher in OHS patients. In addition to respiratory complications such as increased need for invasive ventilation in hospital, in particular cardiovascular sequelae, such as arterial hypertension, heart failure, cor pulmonale, and angina pectoris, contribute to the greater morbidity. As a result, quality of life in OHS patients is significantly limited.

5.1.2 Diagnosis

In the case of a BMI > 30 kg/m^2 and corresponding clinical suspicion, blood gas analysis is performed to detect daytime hypercapnia. However, hypoventilation already begins to manifest with nocturnal hypercapnia before the full picture is achieved, making nocturnal determination of pCO_2 (arterial, capillary, transcutaneous, end-tidal) necessary in the case of a BMI > 30 kg/m^2 [125–127]. PSG is required to confirm sleep-disordered breathing.

Recommendation. Reviewed and retained:

– In the case of clinical suspicion or predisposing underlying disease, the diagnosis of sleep-related hypoventilation should be made by means of nocturnal arterial or capillary blood gas analysis or nocturnal transcutaneous or end-tidal CO_2 measurement. For the diagnosis of OHS, daytime arterial blood gas analysis is required. To diagnose sleep-related hypoxemia, nocturnal oximetry should be performed in conjunction with CO_2 measurement at night (evidence level 1b, grade A recommendation).

Modified:

– In patients with a BMI of > 30 kg/m^2 and symptoms of an SRBD, determination of venous bicarbonate while the patient is awake as well as arterial or capillary pCO_2 or transcutaneous/end-tidal CO_2 should be performed to exclude concomitant hypoventilation during sleep (evidence level 1b, grade A recommendation).

The recommendations on the diagnosis of OHS were adopted with strong consensus (13/13).

5.1.3 Treatment

With regard to instrument-based treatment, a differentiation should be made between OHS patients with relevant OSA and OHS patients without upper airway obstruction. In stable OHS patients with severe OSA, both CPAP therapy and noninvasive ventilation (NIV) proved to be equally effective treatments in two recent randomized studies [128, 129]. In the study by Masa et al., both instrument-based therapies were superior to conservative therapy alone in terms of symptom improvement and PSG parameters [129]. Also, when considering long-term effects, CPAP and NIV were equally effective in OHS patients with severe OSA [130]. If a relevant rise in pCO_2 is seen during treatment initiation under CPAP titration, or a relevant persistent drop in oxygen saturation occurs (SaO_2 < 80% for ≥ 10 min), switching to NIV is required [131–133]; this is also the treatment of choice in OHS without concomitant relevant OSA [132–134]. If CPAP therapy has been started, clinical follow-up after 3 months is also judicious here. If a clinical improvement and normocapnia are seen, CPAP therapy is continued; otherwise, a switch to NIV is considered [132, 133].

Oxygen can reduce respiratory drive and increases transcutaneous CO_2, at least in acute situations. Evidence for the chronic setting is not available [135]. In contrast, NIV improves respiratory response, blood gases, the micro- and macrostructure of sleep, quality of life, hemodynamic parameters, and survival in OHS patients. Both fixed-pressure support NIV and volume-targeted NIV have been shown to be effective. Comparative studies show differing results. In addition, the expiratory pressure can also be automatically adjusted [136].

Weight reduction should be considered an important measure to address cause in OHS, although ventilatory therapy should not be delayed. If conservative approaches to weight reduction fail, bariatric surgery represents a possible treatment alternative. This has been shown to reduce body weight and improve lung function and blood gases.

Recommendations. Reviewed and retained:

– In the case of OHS, bariatric surgery should be considered once weight loss measures have been exhausted (evidence level 2c, grade B recommendation).

Modified:

– In patients with OHS and relevant OSA, CPAP therapy should be attempted (evidence level 1b, grade B recommendation).

New:

– In OHS patients with severe hypercapnia or without concomitant upper airway obstruction, NIV should primarily be initiated (evidence level 1b, grade B recommendation).

The recommendations on the treatment of OHS were adopted with strong consensus (9/9).

5.2 Sleep-related hypoventilation due to a medical disorder

Typical disorders in the following respective disease groups are given in italics in parentheses: obstructive airway diseases (e.g., *COPD*), restrictive lung disease (e.g., *interstitial lung disease*), obesity (*OHS*), and neuromuscular or chest wall diseases (*kyphoscoliosis, post-tuberculosis [TB] syndrome, post-polio syndrome, muscular dystrophy*) predispose affected individuals to the development of sleep-related hypoventilation.

5.2.1 Main findings

Patients' symptoms are uncharacteristic and often obscured by those of the underlying disease. Since the impaired ventilation predominates, patients typically complain of dyspnea on exertion, decreased exercise capacity, often leg edema, and, as a result of hypercapnia, headache. Sleep maintenance disorders and waking with shortness of breath are the most common sleep-related symptoms. Daytime sleepi-

ness can also be a prominent symptom. Systematic investigations on the leading and sleep-related symptoms are not available.

5.2.2 Onset, course, and complications

The underlying disease causes reduced capacity and/or increased load on the respiratory system, which can still be compensated for in the early stages of the disease. As the underlying disease progresses, hypoventilation and hypercapnic phases occur initially in REM sleep, leading to metabolic compensation in the form of bicarbonate retention; this subsequently also reduces the respiratory response to hypercapnia. In the further course, hypoventilation/hypocapnia in non-REM sleep develops, as does, ultimately, the full picture of awake hypercapnic respiratory failure.

5.2.3 Diagnosis

The diagnosis of manifest daytime alveolar hypoventilation is made, by definition, using arterial blood gas analysis. For the further diagnostic work-up while awake, lung function testing and measurement of respiratory muscle strength and load are helpful. ECG, laboratory work-up, and chest X-ray, as well as echocardiography where necessary, are performed depending on medical history and clinical findings. Irrespective of the underlying disease, daytime hypercapnia is regularly preceded by hypoventilation in REM sleep, and later also in non-REM sleep [137–139], which may worsen the prognosis of these patients [140, 141]. Observational studies suggest that nocturnal hypercapnia is an indicator for disease severity and long-term prognosis [142].

Since the uncharacteristic symptoms of alveolar hypoventilation are often wrongly attributed exclusively to the underlying disease, there is a risk of overlooking the early phase of chronic ventilatory failure with its episodes of hypoventilation only at night, thereby delaying appropriate treatment. Therefore, if patients are at risk of developing secondary alveolar hypoventilation, measurement of nocturnal breathing at regular intervals is indicated. The risk rises significantly from a vital capacity of < 50% predicted in restrictive disorders [139]. Pulse oximetry alone is not sufficient to detect sleep-related hypoventilation. Arterial $paCO_2$ measurements at night are not feasible. Therefore, transcutaneous or end-tidal pCO_2 measurement in combination with respiratory polygraphy is required to confirm sleep-related hypoventilation. Hypercapnia measured in transcutaneous capnometry directly demonstrates hypoventilation [143]. Continuous CO_2 measurement alone has the one disadvantage that it remains unclear whether the patient has reached REM sleep. Therefore, the procedure is good for the positive detection of hypoventilation, but not suited to its exclusion. Thus, in the case of nocturnal symptoms in the absence of confirmation of hypoventilation or long-term capnometry on respiratory polygraphy, PSG is indicated.

Recommendations. Reviewed and retained:

- Being the most sensitive method to detect sleep-related hypercapnia, transcutaneous capnometry is recommended. This can be performed in conjunction with respiratory polygraphy or polysomnography (evidence level 2, grade C recommendation).
- With regard to the initiation of ventilation therapy in patients with neuromuscular or chest wall disorders and a vital capacity of < 50%, hypoventilation in sleep should be excluded (evidence level 1b, grade A recommendation).
- Polysomnography is the diagnostic standard for the exclusion and differential diagnosis of SRBDs in the context of sleep-related hypoventilation or hypoxemia (evidence level 2, statement).

The recommendations on the diagnosis of hypoventilation syndrome were adopted with strong consensus (13/13).

5.2.4 Treatment

In the case of chronic underlying diseases, their treatment alone is generally not sufficient to eliminate hypoventilation. From a treatment perspective, therefore, NIV during sleep via a mask is performed with the aim of increasing alveolar ventilation and preventing hyperventilation. The main criteria for initiating long-term NIV therapy in sleep-related hypoventilation due to a medical condition include symptoms and sequelae of ventilatory failure, such as dyspnea and edema, as well as reduced quality of life in the form of nonrestorative sleep as a result of sleep maintenance disorders or hypersomnia. Furthermore, the guideline of the German Society of Pneumology and Respiratory Medicine [132, 133] on noninvasive and invasive ventilation in chronic respiratory failure formulates the following criteria:

- In the case of sleep-related hypoventilation due to lower airway obstruction:
  - a diurnal $paCO_2 \geq 50$ mm Hg or
  - a nocturnal $paCO_2 \geq 55$ mm Hg or
  - an increase in nocturnal $CO_2 \geq 10$ mm Hg, as measured transcutaneously, with a diurnal $paCO_2$ of between 45 and 50 mm Hg; in addition, long-term NIV should be initiated after an acute exacerbation requiring ventilation if daytime hypercapnia > 53 mm Hg persists 14 days after discontinuation of acute ventilation.
- In the case of sleep-related hypoventilation due to a chest wall disorder:
  - a diurnal $paCO_2 \geq 45$ mm Hg or
  - a nocturnal $paCO_2 \geq 50$ mm Hg or an increase in nocturnal $CO_2 \geq 10$ mm Hg, as measured transcutaneously
- In the case of sleep-related hypoventilation due to a neuromuscular disease:
  - a diurnal $paCO_2 \geq 45$ mm Hg or
  - a nocturnal $paCO_2 \geq 45$ mm Hg or
  - a nocturnal $CO_2 \geq 50$ mm Hg, as measured transcutaneously, or
  - a rapid decrease in forced vital capacity (FVC)

The aim of ventilation is normocapnia by eliminating hypoventilation under ventilation in sleep and reducing $paCO_2$ to daytime normocapnia. Ventilation can be initiated during the day and at night. Over the course of the initial set-up, the effectiveness of ventilation must be assessed by blood gas analysis both under spontaneous breathing and under ventilation, and supplemented with nocturnal measurements.

As a general rule, therapy is administered as NIV via a mask covering the nose or nose and mouth during the entire period

Table 8 Studies on NIV therapy in alveolar hypoventilation while awake or asleep in the setting of neuromuscular disorders (NMD); restrictive thoracic disorders and obesity hypoventilation syndrome (OHS)

Author	Year	Country	Study type	Population	Patient number	Intervention	Study endpoint	Effect on study endpoint	EL
Masa et al. [130]	2019	Spain	RCT	OHS with severe OSA	97 NIV vs. 107 CPAP	NIV vs. CPAP over 5.4 years	Hospital days/year Survival; cardiovascular events, among others	CPAP and NIV equivalent	1a
McArdle et al. [136]	2017	Australia	Randomized crossover trial	OHS; COPD; NMD	11 OHS; 9 COPD; 5 NMD	NIV with fixed EPAP vs. automatic EPAP each for 1 night	AHI	No significant difference	3
Howard et al. [128]	2017	Australia	RCT	OHS	27 NIV vs. 30 CPAP	NIV vs. CPAP for 3 months	Treatment failure (lack of fall or rise in $paCO_2$; use < 2 h/night); quality of life	No significant difference regarding treatment failure No significant difference in quality of life	1b
Masa et al. [134]	2016	Spain	RCT	OHS without severe OSA	40 NIV vs. 46 controls	NIV vs. lifestyle modification for 2 months	Primary: $paCO_2$ Secondary: symptoms; quality of life; ESS; PSG; 6-MWD among others	$paCO_2$ significantly lower under NIV ESS; PSG parameters and some quality of life parameters significantly better under NIV	1b
Gonzalez-Bermejo et al. [155]	2016	France	RCT	ALS	37 stimulation vs. 37 sham stimulation	Diaphragm stimulation vs. sham diaphragm stimulation	Primary: NIV-free survival	Study stopped early due to excess mortality in stimulation group	1b
Masa et al. [129]	2015	Spain	RCT	OHS	71 NIV 80 CPAP 70 lifestyle modification	NIV vs. CPAP vs. lifestyle modification for 2 months	Primary: $paCO_2$ Secondary: symptoms; ESS; quality of life; 6-MWD; PSG among others	$paCO_2$ significantly lower under NIV vs. lifestyle modification; no difference to CPAP. $paCO_2$ under CPAP only better than lifestyle modification after adjustment to compliance Symptoms and PSG better with NIV and CPAP; no difference between NIV and CPAP	1b
Ward et al. [141]	2005	Great Britain	RCT	Neuromuscular disorders; daytime normocapnia; hypoventilation in sleep	12 per group	NIV vs. standard therapy for 2 years	$tcpCO_2$ at night S_aO_2 at night Need for NIV in control group	$ptcpCO_2$ at night S_aO_2 at night Daytime respiratory failure requiring NIV in 11/12 of control patients	1b
Vianello et al. [150]	1994	Italy	CCS	Duchenne muscular dystrophy	2× 5	NIV vs. standard therapy for 2 years	Death	0/5 NIV patients died; 4/5 control patients died	3b
Simonds et al. [12]	1995	Great Britain	Case series	NMD; KS; PPS; COPD; bronchiectasis	180	NIV	NIV use (no use corresponded to death)	Better survival rates than before the NIV era; except in COPD and bronchiectasis	4

Table 8 (Continued)

Author	Year	Country	Study type	Population	Patient number	Intervention	Study endpoint	Effect on study endpoint	EL
Schönhofer et al. [152]	2001	Germany	CCS	Stable respiratory failure	Each 10 patients	NIV vs. standard therapy	Muscle function; BGA	Muscle function and BGA better with NIV	1b
Buyse et al. [144]	2003	Belgium	Case series	Stable respiratory failure in KS	18 vs. 15 patients	NIV vs. O_2	BGA; survival	Both better with NIV, although baseline values worse	4
Jäger et al. [146]	2008	Sweden	CCS	Stable respiratory failure in post-TB	85 NIV; 103 O_2	NIV or O_2	Survival	Better with NIV	2c
Gustafson et al. [145]	2006	Sweden	CCS	Stable respiratory failure in KS	100 NIV; 144 O_2	NIV or O_2	Survival	Better with NIV	2c
Budweiser et al. [142]	2007	Germany	Cohort; historical controls	Stable respiratory failure in OHS	126	NIV	BGA; PFT; survival compared to historical control group	All parameters better over the course of treatment. Survival better than in historic control group	4
Piper et al. [131]	2008	Australia	RCT	Stable respiratory failure in OHS	2× 18	BPAP vs. CPAP	Daytime $paCO_2$	Reduction with both treatment forms	1b
Bourke et al. [151]	2006	Great Britain	RCT	Orthopnea or hypercapnia in ALS	22 vs. 19	NIV vs. standard	QoL; survival	Both better in patients without bulbar symptoms	1b
Simonds et al. [149]	1998	Great Britain	Case series	DMD with respiratory failure	23	NIV	BGA; survival	1- and 5 -year survival rates of 85 and 73%, respectively; BGA better. In historical control, life expectancy < 1 year in respiratory failure	4
Annane et al. [156]	2014	France	Meta-analysis	NMD	8 RCTs	NIV vs. standard therapy	Survival; BGA; symptoms	All better with NIV	1a

ALS amyotrophic lateral sclerosis, *BGA* blood gas analysis, *BPAP* bilevel positive airway pressure, *COPD* chronic obstructive pulmonary disease, *CPAP* continuous positive airway pressure, *DMD* Duchenne muscular dystrophy, *EL* evidence level, *CCS* case–control study, *KS* kyphoscoliosis, *PFT* pulmonary function test, *QoL* quality of life, *NIV* noninvasive ventilation, *NMD* neuromuscular disorders, $paCO_2$ arterial partial pressure of carbon dioxide, paO_2 arterial oxygen partial pressure, *post-TB* post-TB syndrome, *PPS* post-polio syndrome, $tcpCO_2$ transcutaneously measured partial pressure of carbon dioxide, *RCT* randomized controlled study

Table 9 Studies on NIV therapy in alveolar hypoventilation while awake or asleep in the setting of COPD

Author	Year	Country	Study type	Population	Patient number (*n*)	Intervention	Study endpoint	Effect on study endpoint	EL
Murphy et al. [157]	2017	Great Britain	RCT	COPD patients with persistent hypercapnia 14 days after discontinuation of acute ventilation	59 O_2 therapy vs. 57 O_2 therapy + NIV	NIV + O_2 vs. O_2 alone for 12 months	Hospital readmission, death	Significant prolongation of time to inpatient readmission under NIV Fewer deaths in the NIV group	1b
Struik et al. [158]	2014	The Netherlands	RCT	COPD patients with persistent hypercapnia 48 h after discontinuation of acute ventilation	101 NIV vs. 100 standard therapy	NIV vs. standard therapy for 1 year	Primary: hospital readmission or death Secondary: $paCO_2$, pulmonary function, quality of life, among others	No difference regarding readmission or death $paCO_2$ Significantly lower under NIV, trend toward better quality of life under NIV No difference regarding exacerbation rate, pulmonary function, subjective dyspnea	1b
Meecham Jones et al. [159]	1995	Great Britain	RCT, crossover	Stable hypercapnic COPD	14	NIV vs. standard therapy each for 3 months	Daytime $paCO_2$ and paO_2, sleep, QoL	All target parameters significantly better with NIV	1b
Clini et al. [160]	2002	Italy	RCT	Stable hypercapnic COPD	43 vs. 47	NIV vs. standard therapy for 2 years	BGA, QoL, hospitalization, ICU days, survival	Fall in daytime $paCO_2$, improved QoL and dyspnea	1b
Budweiser et al. [142]	2007	Germany	Prospective observational study (POS)	Stable hypercapnic COPD	99 vs. 41	NIV vs. standard therapy for up to 4 years	Survival	Higher survival rate under NIV	2c
Strumpf et al. [161]	1991	USA	RCT, crossover	Stable hypercapnic COPD	7	NIV vs. standard therapy for 3 months	BGA, QoL, sleep	n. s.	1b
Gay et al. [162]	1996	USA	RCT	Stable hypercapnic COPD	7 vs. 6	NIV vs. placebo NIV for 3 months	BGA, PFT	n. s.	1b
Casanova et al. [163]	2000	Italy	RCT	Stable hypercapnic COPD	52	NIV vs. standard therapy for 1 year	Exacerbation rate, hospitalization, intubation, mortality, dyspnea, BGA	Dyspnea less pronounced with NIV	1b
Wijkstra et al. [164]	2003	Canada	Meta-analysis of 4 studies	Stable hypercapnic COPD	86	NIV vs. standard > 3 weeks	PFT, BGA, sleep	n. s.	1a
Garrod et al. [165]	2000	Great Britain	RCT	Stable hypercapnic COPD	23 vs. 22	NIV + training vs. training	6-Min walk test, symptoms, pO_2	All significantly better with NIV	1b

Table 9 (Continued)

Author	Year	Country	Study type	Population	Patient number (*n*)	Intervention	Study endpoint	Effect on study endpoint	EL
Tsolaki et al. [166]	2008	Greece	CCS	Stable hypercapnic COPD	27 vs. 22	NIV vs. standard (NIV decliners)	QoL, BGA, dyspnea	All significantly better with NIV	3b
Kolodziej et al. [167]	2007	Canada	Meta-analysis of 15 studies	Stable hypercapnic COPD	–	NIV vs. standard	Multiple	QoL better with NIV, BGA in uncontrolled studies better with NIV	1a

ALS amyotrophic lateral sclerosis, *BGA* blood gas analysis, *BPAP* bilevel positive airway pressure, *COPD* chronic obstructive pulmonary disease, *CPAP* continuous positive airway pressure, *DMD* Duchenne muscular dystrophy, *EL* evidence level, *CCS* case–control study, *ICU days* number of days on an intensive care unit, *KS* kyphoscoliosis, *PFT* pulmonary function test, *QoL* quality of life, *NIV* noninvasive ventilation, *NMD* neuromuscular disorders, $paCO_2$ arterial partial pressure of carbon dioxide, paO_2 arterial oxygen partial pressure, *post-TB* post-TB syndrome, $tcpCO_2$ transcutaneously measured partial pressure of carbon dioxide, *RCT* randomized controlled study

of sleep. Since REM sleep represents a particularly critical phase, the effectiveness of ventilation in sleep should be documented by means of transcutaneous CO_2 measurement ($tcpCO_2$) plus respiratory polygraphy. In the case of uncertainty regarding nocturnal hypoventilation during REM sleep, PSG is indicated.

NIV can be administered as assisted, assist-control, or as purely controlled ventilation. There are no data on the superiority of one or other of these modes. Patients with neuromuscular and thoracic cage disorders often tolerate the controlled mode subjectively very well, while COPD patients generally prefer the assisted mode. Achieving an optimal, individually tailored set-up is crucial to good acceptance and treatment success. Only a handful of methodologically high-quality controlled studies are available on the effects of NIV (see ◘ **Tables 8 and 9**). In slowly progressive muscle diseases, kyphoscoliosis, and previous history of tuberculosis, NIV achieves a dramatic clinical improvement both in the acute and in the long-term setting, meaning that controlled trials in these conditions are now questionable from an ethical perspective. Whereas in the past these patients died from respiratory failure, life expectancy with NIV can be virtually normal [144–150]. As a result, quality of life under NIV is also massively improved, the hospitalization rate drops, and symptoms are reduced [124, 151]. In some cases, physiological parameters such as blood gas and lung function may even normalize [131, 141, 152]. The abovementioned diseases carry an unrestricted indication for treatment. For rapidly progressive neuromuscular diseases such as amyotrophic lateral sclerosis (ALS) and Duchenne muscular dystrophy, there is one controlled study and several case series showing a significant survival benefit with NIV [149, 151, 153, 154]; however, progression of the underlying disease limits the beneficial effects of NIV. The indication for ventilation therapy needs to be made on a case-by-case basis in these patients. As part of this, the ethical discussion on patient acceptance of any invasive ventilation that may be required needs to be had as early as possible. Diaphragm stimulation to treat ventilatory failure in ALS should not be performed, since a randomized study showed increased mortality with this procedure [155].

COPD patients represent the largest group of patients that fulfill the indication criteria for NIV. Shorter-term controlled investigations demonstrated improved quality of life, a reduction in hospitalization rate, improved sleep quality, as well as improved physical training and blood gases [159, 163, 165–168]. Several controlled studies, albeit with significant shortcomings, found no reduction in mortality for the NIV-treated group of patients [160–162, 164]. A meta-analysis [158] demonstrated no differences in terms of BGA, pulmonary function, and quality of life for seven studies. An important point of criticism of these studies was the lack of substantial reduction in $paCO_2$ as a result of NIV therapy. In a randomized controlled study, in contrast, life expectancy in COPD patients significantly improved under NIV, while quality of life was reduced [169]. The German multicenter study in stable GOLD stage IV COPD patients with daytime hypercapnia confirmed these improved mortality figures as a result of NIV [170]. In that particular study, ventilation therapy led to a significant reduction in daytime $paCO_2$. On the basis of this evidence, an attempt at NIV therapy should be undertaken in COPD if the abovementioned indication criteria are met. Treatment effect and compliance should be assessed at around 3 months, and a decision should be made regarding treatment continuation.

Following acute COPD exacerbation requiring ventilation, continuous NIV should be initiated if hypercapnia ($paCO_2 > 53$ mm Hg) persists following discontinuation of acute ventilation [157, 158].

For further details on the treatment of chronic respiratory failure, the reader is referred to the German S2 guideline of the German Society for Pneumology and Respiratory Medicine "Treating chronic respiratory failure with invasive and non-invasive ventilation" [132, 133].

Recommendations. Reviewed and retained:

– If nocturnal hypoventilation persists under CPAP, noninvasive fixed pressure support ventilation (without or with target volume) should be initiated

(evidence level 1b, grade B recommendation).
- Oxygen therapy alone is not recommended in OHS (evidence level 2c, grade A recommendation).

Modified:
- Initiation of NIV is recommended in symptomatic patients with lower airway obstruction, neuromuscular disorders, or chest wall disorders with hypercapnia while awake ($paCO_2 \geq 50$ mm Hg in diseases with lower airway obstruction or ≥ 45 mm Hg in neuromuscular or chest wall disorders) or asleep ($paCO_2 \geq 55$ mm Hg in disorders with lower airway obstruction, ≥ 50 mm Hg in chest wall disorders, or ≥ 45 mm Hg in neuromuscular disorders, or a $tcpCO_2$ rise ≥ 10 mm Hg in lower airway obstruction and chest wall disorders, or $tcpCO_2 \geq 50$ mm Hg in neuromuscular disease) (evidence level 1b, grade A recommendation).

The recommendations on the treatment of hypoventilation syndrome were adopted with strong consensus (9/9).

6 Appendix

6.1 Guideline report

6.1.1 Scope and purpose

The present update relates to the S3 guideline "Non-restorative sleep/sleep disorders" and specifically to the chapter "Sleep-related breathing disorders" therein. The above guideline on SRBDs was published in 2015 in the journal *Somnologie* [171].

Since the last publication of the guideline, a number of relevant findings relating to some aspects of this guideline have been published, thereby necessitating a reassessment of individual guideline statements and recommendations; the present update has been prepared for these chapters. All other contents, chapters, and recommendations in the guideline for which no update has been submitted remain valid in their current form (see also Chap. "Concept of the update").

This guideline is aimed at medical and nonmedical professional groups (e.g., psychologists, natural scientists), nursing staff, self-help groups, and interested lay persons; it also serves as an information source for MTAs.

6.1.2 Composition of the guideline group and interest group involvement

Steering committee.
- Dr. med. Alfred Wiater, Cologne
- Prof. Dr. med. Boris A. Stuck, Marburg

Authors.
- Prof. Dr. med. Boris A. Stuck, Marburg
- Prof. Dr. med. Michael Arzt, Regensburg
- Prof. Dr. med. Ingo Fietze, Berlin
- Prof. Dr. med. Wolfgang Galetke, Hagen
- Dr. med. Holger Hein, Hamburg
- Simon D. Herkenrath, Solingen
- Priv. Doz. Dr. med. Benedikt Hofauer, Freiburg
- Prof. Dr. med. Joachim T. Maurer, Mannheim
- Prof. Dr. rer. physiol. Thomas Penzel, Berlin
- Prof. Dr. med. Maritta Orth, Mannheim
- Prof. Dr. med. Geert Mayer, Schwalmstadt-Treysa
- Prof. Dr. med. Winfried Randerath, Solingen
- Prof. Dr. med. J. Ulrich Sommer, Wuppertal
- Prof. Dr. med. Armin Steffen, Lübeck
- Prof. Dr. med. Clemens Heiser, Munich

Scientific medical societies. To ensure the representativeness of the guideline group, the following societies, professional groups, and patient representatives were invited to collaborate:
- German Society for Sleep Research and Sleep Medicine (*Deutsche Gesellschaft für Schlafforschung und Schlafmedizin*), **DGSM**
- German College of General Practitioners and Family Physicians (*Deutsche Gesellschaft für Allgemeinmedizin und Familienmedizin*), **DEGAM**
- German Society of Internal Medicine (*Deutsche Gesellschaft für Innere Medizin*), **DGIM**
- German Association of General Practitioners (*Deutscher Hausärzteverband*)
- *Deutsche Gesellschaft für Geriatrie e. V.*, **DGG**
- German Society of Otorhinolaryngology, Head and Neck Surgery (*Deutsche Gesellschaft für Hals-Nasen-Ohren-Heilkunde, Kopf- und Hals-Chirurgie e. V.*), **DGHNO-KHC**
- German Society for Cardiology—Heart and Circulatory Research (*Deutsche Gesellschaft für Kardiologie, Herz- und Kreislaufforschung e. V.*), **DGK**
- German Society for Pediatric and Adolescent Medicine (*Deutsche Gesellschaft für Kinder- und Jugendmedizin e. V.*), **DGKJ**
- German Society for Oral and Maxillofacial Surgery (*Deutsche Gesellschaft für Mund-, Kiefer- und Gesichtschirurgie e. V.*), **DGMKG**
- German Society for Neurology (*Deutsche Gesellschaft für Neurologie e. V.*), **DGN**
- German Respiratory Society (*Deutsche Gesellschaft für Pneumologie und Beatmungsmedizin e. V.*), **DGP**
- German Association for Psychiatry, Psychotherapy and Psychosomatics (*Deutsche Gesellschaft für Psychiatrie und Psychotherapie, Psychosomatik und Nervenheilkunde e. V.*), **DGPPN**
- German Psychological Society (*Deutsche Gesellschaft für Psychologie*), **DGPS**
- German Society of Dental Sleep Medicine (*Deutsche Gesellschaft für Zahnärztliche Schlafmedizin*), **DGZS**
- German Office of the German Orthodontic Society (*Deutsche Geschäftsstelle der Deutschen Gesellschaft für Kieferorthopädie e. V.*), **DGKFO**
- German Society for General and Visceral Surgery (*Deutsche Gesellschaft für Allgemein- und Viszeralchirurgie e. V.*), **DGAV**
- German Society of Anaesthesiology and Intensive Care Medicine (*Deutsche Gesellschaft für Anästhesiologie und Intensivmedizin e. V.*), **DGAI**
- Professional Association of German Neurologists (*Berufsverband Deutscher Neurologen*), **BDN**
- Federal Association of Physicians for Chest, Sleep, and Mechanical Ventilation Medicine (*Bundesverband der Pneumologen, Schlaf- und Beatmungsmediziner*), **BdP**

- German Association of Psychologists (*Berufsverband Deutscher Psychologinnen und Psychologen e. V.*), **BDP**
- German Association of Cardiologists in Private Practice (*Bundesverband niedergelassener Kardiologen e. V.*), **BNK**
- Professional Association of German Psychiatrists (*Berufsverband Deutscher Psychiater*), **BVDP**
- German Professional Association of Otolaryngologists (*Deutscher Berufsverband der Hals-Nasen-Ohrenärzte e. V.*), **BVHNO**
- German Sleep Society (*Bundesverband Schlafapnoe und Schlafstörungen Deutschlands e. V.*), **BSD**
- *Bundesverband Gemeinnützige Selbsthilfe Schlafapnoe Deutschland e. V.* (German association of not-for-profit sleep apnea self-help) **GSD**
- German Restless Legs Association (*Deutsche Restless Legs Vereinigung e. V.*), **RLS e. V.**
- German Narcolepsy Association (*Deutsche Narkolepsie Gesellschaft e. V.*), **DNG**
- *Selbsthilfegruppe Schlafapnoe/ chronische Schlafstörungen Solingen e. V.* (Solingen self-help group for sleep apnea/chronic sleep disorders)

The following societies, professional groups, and patient representatives expressed their willingness to collaborate and named a representative for the nominal group process:

- German Society for Sleep Research and Sleep Medicine (*Deutsche Gesellschaft für Schlafforschung und Schlafmedizin*), **DGSM** (representatives: Prof. Stuck, Dr. Wiater)
- German College of General Practitioners and Family Physicians (*Deutsche Gesellschaft für Allgemeinmedizin und Familienmedizin*), **DEGAM** (representative: Frau Prof. Dr. Baum, proxy: Herr Dr. Stephan Hoffmann)
- German Association of General Practitioners (*Deutscher Hausärzteverband*; representative: Frau Prof. Dr. Baum, proxy: Herr Dr. Stephan Hoffmann)
- German Society of Otorhinolaryngology, Head and Neck Surgery (*Deutsche Gesellschaft für Hals-Nasen-Ohren-Heilkunde, Kopf- und Hals-Chirurgie e. V.*), **DGHNO-KHC** (representative: Prof. Dr. Clemens Heiser, proxy: Priv. Doz. Dr. Michael Herzog)
- German Society for Cardiology—Heart and Circulatory Research (*Deutsche Gesellschaft für Kardiologie, Herz- und Kreislaufforschung e. V.*), **DGK** (representative: Herr Prof. Dr. Arzt)
- German Society for Oral and Maxillofacial Surgery (*Deutsche Gesellschaft für Mund-, Kiefer- und Gesichtschirurgie e. V.*), **DGMKG** (representative: Herr Prof. Dr. Dr. Hans Pistner)
- German Society for Neurology (*Deutsche Gesellschaft für Neurologie e. V.*), **DGN** (representative: Prof. Dr. Geert Mayer)
- German Respiratory Society (*Deutsche Gesellschaft für Pneumologie und Beatmungsmedizin e. V.*), **DGP** (representative: Herr Dr. N. Büchner, proxy: H. Woehrle)
- German Association for Psychiatry, Psychotherapy and Psychosomatics (*Deutsche Gesellschaft für Psychiatrie und Psychotherapie, Psychosomatik und Nervenheilkunde e. V.*), **DGPPN** (representative: Dr. Lukas Frase)
- German Psychological Society (*Deutsche Gesellschaft für Psychologie*), **DGPS** (representative: Frau Prof. Dr. Angelika Schlarb)
- German Society of Dental Sleep Medicine (*Deutsche Gesellschaft für Zahnärztliche Schlafmedizin*), **DGZS** (representative: Herr Dr. Markus Heise)
- German Society for General and Visceral Surgery (*Deutsche Gesellschaft für Allgemein- und Viszeralchirurgie e. V.*), **DGAV** (representative: Herr Dr. Matthias Schlensak)
- German Society of Anaesthesiology and Intensive Care Medicine (*Deutsche Gesellschaft für Anästhesiologie und Intensivmedizin e. V.*), **DGAI** (representative: Herr Dr. Martin Rösslein)
- German Society of Internal Medicine (*Deutsche Gesellschaft für Innere Medizin*), **DGIM** (representative: Herr Prof. Dr. Hendrik Bonnemeier) *Bundesverband der Pneumologen, Schlaf- und Beatmungsmediziner*, **BdP** (representative: Herr Dr. Christian Franke)
- German Association of Psychologists (*Berufsverband Deutscher Psychologinnen und Psychologen e. V.*), **BDP** (representative: Frau Dr. Johanna Thünker, proxy: Herr Prof. Dr. Erich Kasten)
- German Professional Association of Otolaryngologists (*Deutscher Berufsverband der Hals-Nasen-Ohrenärzte e. V.*), **BVHNO** (representative: Dr. med. Andreas H. Schmidt)
- German Sleep Society (*Bundesverband Schlafapnoe und Schlafstörungen Deutschlands e. V.*), **BSD** (representative: Herr Werner Waldmann)
- *Bundesverband Gemeinnützige Selbsthilfe Schlafapnoe Deutschland e. V.* (German association of not-for-profit sleep apnea self-help) **GSD** (representative: Herr Ralf Kiehne)
- German Restless Legs Association (*Deutsche Restless Legs Vereinigung e. V.*), **RLS e. V.** (representative: Herr Dr. Joachim Paulus)
- German Narcolepsy Association (*Deutsche Narkolepsie Gesellschaft e. V.*), **DNG** (representative: Herr Tobias Schmid)
- *Selbsthilfegruppe Schlafapnoe/ chronische Schlafstörungen Solingen e. V.* (Solingen self-help group for sleep apnea/chronic sleep disorders; representative: Herr Hartmut Rentmeister)

The following societies, professional groups, and patient representatives expressed their willingness to collaborate, but failed to appoint a representative for the nominal group process despite multiple requests to do so:

- *Deutsche Gesellschaft für Geriatrie e. V.*, **DGG**
- Professional Association of German Neurologists (*Berufsverband Deutscher Neurologen*), **BDN**
- German Association of Cardiologists in Private Practice (*Bundesverband niedergelassener Kardiologen e. V.*), **BNK**
- Professional Association of German Psychiatrists (*Berufsverband Deutscher Psychiater*), **BVDP**

The German Society for Pediatric and Adolescent Medicine (*Deutsche Gesellschaft für Kinder- und Jugendmedizin e. V.*),

DGKJ, did not appoint a representative after being informed, upon inquiry, that the guideline refers to adults.

The German Office of the German Orthodontic Society (*Deutsche Gesellschaft für Kieferorthopädie e. V.*), **DGKFO**, (representative: Herr Prof. Bert Braumann) canceled its participation in the consensus conference after reviewing the handouts.

6.1.3 Methodological procedure

The update of the guideline was guided by the Association of the Scientific Medical Societies in Germany *(Arbeitsgemeinschaft der Wissenschaftlichen Medizinischen Fachgesellschaften e. V.*, **AWMF**) throughout the entire development process.

In a first step, the chapters that required updating were identified. Chapters requiring revision were defined as those in relation to which new scientific insights, among other reasons, could potentially result in a change to the recommendations contained therein. Accordingly, no update was undertaken when no new scientific insights were available or these did not conflict with the current recommendations. To this end, the guideline coordinator (B. A. Stuck) inserted all guideline recommendations, with references to the corresponding chapters, into a table and made these available to the members of the steering committee of the previous guideline, as well as to the authors responsible for the update, if available. These included the following persons: J. T. Maurer (Mannheim), I. Fietze (Berlin), G. Mayer (Schalmstadt-Treysa), W. Galetke (Hagen), W. Randerath (Solingen), B. A. Stuck (Marburg), J. U. Sommer (Wuppertal), T. Penzel (Berlin), B. Hofauer (Freiburg), C. Heiser (Munich), and A. Steffen (Lübeck). The abovementioned individuals assessed each chapter of the previous version of the guideline to determine whether an update was needed, as described above. A chapter was selected when more than 25% of the abovementioned persons deemed one or more of the recommendations in the chapter to require updating.

Each selected chapter was then assigned to a group of authors, who revised the chapter on the basis of the present text after selecting and evaluating the literature (see below). Already at this stage, attention was paid to achieving author groups with an interdisciplinary composition.

Independently of this, a text passage was identified that had led to misinterpretation in the clinical implementation of the previous guideline and had often been the subject of discussion, despite the fact that the passage was not a recommendation. The relevant passage has been modified in this update for greater precision.

Voting in the consensus conferences was carried out using the nominal group technique and was moderated by Priv. Doz. Dr. H. Sitter, Marburg. In advance of the conferences, all those involved in the consensus-development process received an invitation specifying objectives and the conference venue. Priv. Doz. Dr. H. Sitter's function ensured independent moderation. Handouts included the manuscript of the necessary updates as well as the recommendations. During the consensus conferences, the statements/recommendations were presented, and positions on these were recorded using a round-robin procedure and summarized by the moderator. A pre-vote and discussion on the individual comments took place, and a ranking list was created. It was ensured that the individual points raised could be discussed. A final vote on each recommendation or all alternatives was held.

The nominal group process (consensus conference) took place in Frankfurt on 23.01.2020. The following mandate holders or specialist medical societies participated:

Priv. Doz. Helmut Sitter (AWMF), Prof. Boris A. Stuck (DGSM), Dr. Alfred Wiater (DGSM), Dr. Stephan Hoffmann (DEGAM/*Deutscher Hausärzteverband*), Prof. Dr. Clemens Heiser (DGHNO-KHC), Priv. Doz. Dr. Michael Herzog (DGHNO-KHC), Prof. Dr. Arzt (DGK), Prof. Dr. Dr. Hans Pistner (DGMKG), Dr. N. Büchner (DGP), Holger Woehrle (DGP), Dr. Lukas Frase (DGPPN), Prof. Dr. Angelika Schlarb (DGPS), Dr. Matthias Schlensak (DGAV), Dr. Martin Rösslein (DGAI), Prof. Dr. Hendrik Bonnemeier (DGIM), Dr. Christian Franke (BdP), Dr. Johanna Thünker (BDP), Dr. med. Andreas H. Schmidt (BVHNO), Ralf Kiehne (GSD), Dr. Joachim Paulus (RLS e. V.), Herr Hartmut Rentmeister (GSD-SH), and, as representatives of the author group, Prof. Dr. Wolfgang Galetke, Simon Herkenrath, Priv. Doz. Dr. Benedikt Hofauer, Prof. Dr. Joachim Maurer, Prof. Dr. Maritta Orth, Prof. Dr. Thomas Penzel, Prof. Dr. Winfried Randerath, Prof. Dr. Ulrich Sommer, and Prof. Dr. Ingo Fietze.

Following the review of the nominal group process, questions that had not been definitively dealt with were put to a final consensus in a nonanonymized Delphi process. The authors as well as participants in the nominal group process were invited to take part in the Delphi process. This process was opened on 21.02.2020 and closed on 15.03.2020. Responses were collected by B. A. Stuck and A. Wiater and put to a vote on 16.03.2020. All representatives appointed by the medical societies and organizations involved were invited to vote. The voting procedure was completed on 31.03.2020. The following mandate holders or specialist medical societies participated in the voting procedure: Prof. Stuck/Dr. Alfred Wiater (DGSM), Prof. Dr. Clemens Heiser/Priv. Doz. Dr. Michael Herzog (DGHNO-KHC), Prof. Dr. Arzt (DGK), Prof. Dr. Dr. Hans Pistner (DGMKG), Dr. Lukas Frase (DGPPN), Prof. Dr. Angelika Schlarb (DGPS), Dr. Christian Franke (BdP), Dr. Johanna Thünker (BDP), and Dr. med. Andreas H. Schmidt (BVHNO). Based on the results of the vote, appropriate changes were made to the text; one round was sufficient to reach a consensus.

Since this is an S3 guideline, the consensus process included the following elements:

Logical appraisal (clinical algorithm), formal consensus development, evidence-basing, and decision analysis. In the case of an S3 guideline, a solution is found using conditional logic (if... then... logic) in several steps based on a clearly defined question. Clinical studies and meta-analyses are included for evidence-basing. Using the graph algorithms, the procedure should be presented in a clear, simple, and concise manner.

6.1.4 Writing the guideline/ consensus process

A preliminary draft of the update was written under the guidance of the person responsible for the guideline, Boris A. Stuck, and by the authors of the individual chapters.

6.1.5 Systematic literature search

The literature search was conducted for all studies published in the PubMed database from April 2014 onwards (the period of the literature search for the original guideline ended in 04/2014). The following were defined as inclusion criteria:

Publications in German or English, prospective or retrospective clinical trials, randomized controlled trials, controlled clinical trials, systematic reviews, meta-analyses, guidelines of the AWMF as well as of the European and North American medical societies (Practice Guidelines, Guidelines) in German or English. The following were defined as exclusion criteria: original articles published in a language other than English or German, experimental animal studies, letters to the editor, case reports, expert opinions, reviews that provided only a general overview of the topic rather than a systematic summary of the literature. The search was restricted to adults (19+).

To this end, the following search strategy was used: "sleep apnea" OR "snoring" with the following limits: publication date 01042014-30042019, humans, clinical trial, meta-analysis, practice guideline, guideline, randomized controlled trial, review, controlled clinical trial, guideline, English, German, adult: 19+years.

6.1.6 Appraisal

The literature was appraised by two independent reviewers according to the Oxford Centre for Evidence-based Medicine Levels of Evidence (2009). In addition to the selection of literature and classification of the level of evidence, a critical appraisal of the literature/studies was also carried out by the authors.

6.1.7 Clinical algorithms

In all, two clinical algorithms were updated (see Sect. 6.2 "Algorithms"):

- Diagnostic approach in obstructive sleep apnea
- Treatment approach in obstructive sleep apnea

6.1.8 External review and adoption

Following completion of the consensus process, DEGAM called for more extensive changes and additions to the content, which could not be made in the context of the current process. As a result, DEGAM stated that it could not endorse the guideline.

Once the consensus process had been completed, the DGAI concluded that anesthesia issues had largely been left unconsidered in the update and, for this reason, also did not approve the guideline.

The chairpersons of the remaining medical societies deliberated on and approved the guideline in June 2020.

6.1.9 Editorial independence

Financing of the guideline. The guideline was developed and the consensus conferences held exclusively with funds from the German Society for Sleep Research and Sleep Medicine (DGSM).

Disclosing and managing conflicts of interest. In order to avoid bias in the guideline process due to conflicts of interest, a number of preventive mechanisms were put in place: (1) systematic recording and appraisal of conflicts of interest of all persons involved in the guideline process, as well as resulting measures; (2) the interdisciplinary composition of the guideline group; and (3) the publication of a consultation version in order to allow those not directly involved in the guideline process the opportunity to comment.

All authors and participants in the nominal group process disclosed potential conflicts of interest using the form made available by the AWMF for this purpose. The two members of the steering committee reviewed participants' conflicts of interest, and graded these as low, moderate, or high in line with AWMF recommendations. Equivocal cases were discussed within the whole guideline group. The guideline group reviewed the self-assessment of the conflicts of interests of the two steering committee representatives.

In the case of minor conflicts of interest, simple disclosure was sufficient; in the case of moderate conflicts of interest on a range of topics, the person in question was excluded from the respective voting process; and in the case of major conflicts of interest, the person in question was additionally excluded from the discussion process. Direct connections to industry or other interest groups associated with relevant direct or indirect financial contributions (e.g., to conduct clinical trials or cover travel expenses/speakers' fees) relating to questions dealt with in the guideline were deemed to be moderate conflicts of interest.

The individual conflict of interest declarations are held by the guideline coordinator (Stuck), and a summary is available to the public on the homepage of the AWMF.

6.1.10 Dissemination and implementation

The guideline is disseminated via the specialist journal *Somnologie* and can be viewed online on the homepage of the AWMF (http://www.awmf.org).

6.1.11 Period of validity and update procedure

The updated chapters, or this update, remain valid for 3 years from the time of publication. A revision of the entire guideline on SRBD is scheduled for the end of that 3-year period at the latest.

6.2 Algorithms

(■ Figs. 1 and 2)

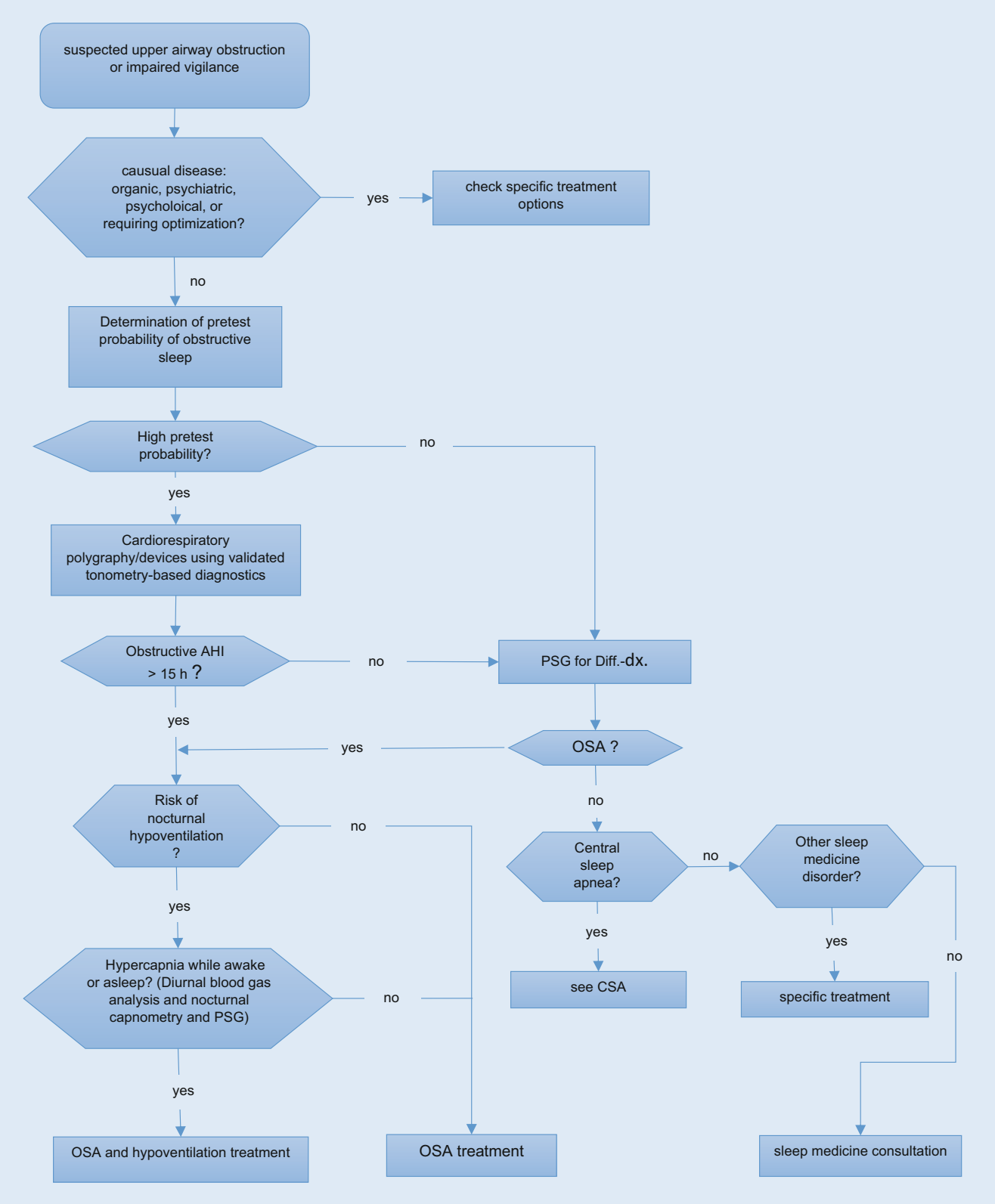

Fig. 1 ▲ Diagnostic algorithm for suspected obstructive sleep apnea. *AHI* apnea–hypopnea index, *OSA* obstructive sleep apnea, *CSA* central sleep apnea, *PSG* polysomnography

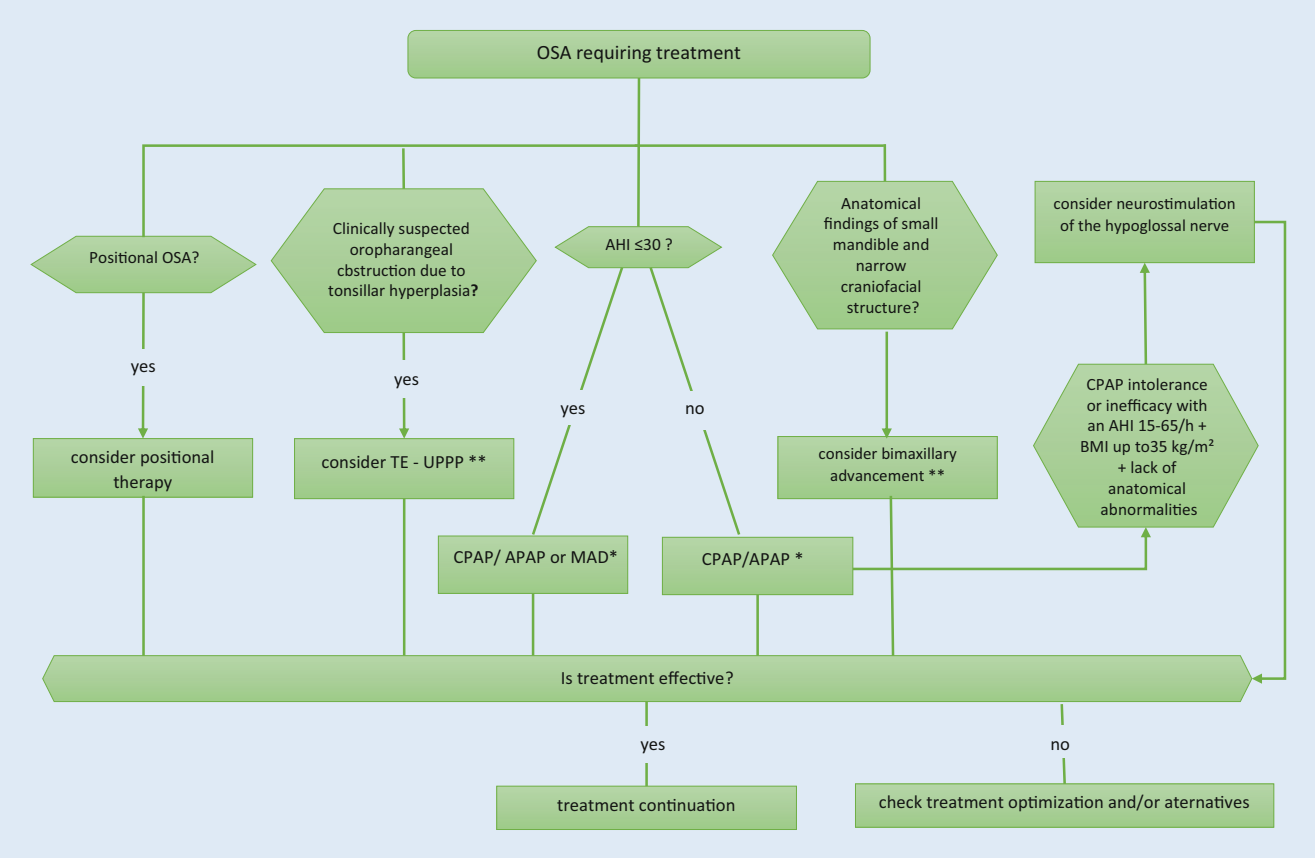

Fig. 2 ▲ Treatment algorithm for obstructive sleep apnea. *In the case of CPAP intolerance and impaired nasal breathing, consider surgery to improve nasal breathing. **Particularly if alternative therapy (CPAP, MAD) is not possible or not sufficiently tolerated. *AHI* apnea–hypopnea index, *OSA* obstructive sleep apnea, *CPAP* continuous positive airway pressure, *APAP* automatic CPAP, *TE-UPPP* tonsillectomy and uvulopalatopharyngoplasty, *BMI* body mass index, *MAD* mandibular advancement device

Corresponding address

Prof. Dr. med. Boris A. Stuck
Department of Otorhinolaryngology, Head and Neck Surgery, University Hospital Marburg, Philipps-Universität Marburg
Baldingerstraße, 35043 Marburg, Germany
Boris.Stuck@uk-gm.de

Acknowledgements. The publisher would like to thank Christine Rye (Windsor, GB), who translated the article from German into English.

Funding. Open Access funding enabled and organized by Projekt DEAL.

Declarations

Conflict of interests Information on author conflicts of interest can be found in the electronic supplementary material (https://doi.org/10.1007/s11818-022-00349-5).

For this article no studies with human participants or animals were performed by any of the authors. All studies performed were in accordance with the ethical standards indicated in each case.

References

1. Steffy DD, Tang CS (2018) Radiographic evaluation of sleep-disordered breathing. Radiol Clin North Am 56(1):177–185
2. Whyte A, Gibson D (2018) Imaging of adult obstructive sleep apnoea. Eur J Radiol 102:176–187
3. De Vito A, Carrasco Llatas M, Ravesloot MJ, Kotecha B, De Vries N, Hamans E, Maurer J, Bosi M, Blumen M, Heiser C, Herzog M, Montevecchi F, Corso RM, Braghiroli A, Gobbi R, Vroegop A, Vonk PE, Hohenhorst W, Piccin O, Sorrenti G, Vanderveken OM, Vicini C (2018) European position paper on drug-induced sleep endoscopy: 2017 update. Clin Otolaryngol 43(6):1541–1552
4. Lechner M, Wilkins D, Kotecha B (2018) A review on drug-induced sedation endoscopy—Technique, grading systems and controversies. Sleep Med Rev 41:141–148
5. Rechtschaffen A, Kales A (1968) A manual of standardized terminology, techniques, and scoring system for sleep stages of human subjects. US Department of Health, Education, and Welfare Public Health Service—National Institute of Health, Washington DC
6. Silber MH, Ancoli-Israel S, Bonnet MH et al (2007) The visual scoring of sleep in adults. J Clin Sleep Med 3(2):121–131
7. Danker-Hopfe H, Anderer P, Zeitlhofer J et al (2009) Interrater reliability for sleep scoring according to the Rechtschaffen & Kales and the new AASM standard. J Sleep Res 18(1):74–84
8. Bonnet MH, Doghramji K, Roehrs T et al (2007) The scoring of arousal in sleep: reliability, validity, and alternatives. J Clin Sleep Med 3:133–145

9. Caples SM, Rosen CL, Shen WK et al (2007) The scoring of cardiac events during sleep. J Clin Sleep Med 3(2):147–154
10. Walters AS, Lavigne G, Hening W et al (2007) The scoring of movements in sleep. J Clin Sleep Med 3(2):155–167
11. Penzel T, Hein H, Rasche K et al (2000) Leitfaden für die Akkreditierung von schlafmedizinischen Zentren der Deutschen Gesellschaft für Schlafforschung und Schlafmedizin (DGSM). Somnologie 4:181–187
12. Redline S, Budhiraja R, Kapur V et al (2007) The scoring of respiratory events in sleep: reliability and validity. J Clin Sleep Med 3:169–200
13. Iber C, Ancoli-Israel S, Chesson A et al (2007) The AASM manual for the scoring of sleep and associated events: rules, terminology and technical specifications, 1 edn. American Academy of Sleep Medicine, Westchester
14. American Academy of Sleep Medicine, Berry RB, Budhiraja R, Gottlieb DJ et al (2012) Rules for scoring respiratory events in sleep: update of the 2007 AASM manual for the scoring of sleep and associated events. Deliberations of the sleep apnea definitions task force of the American Academy of Sleep Medicine. J Clin Sleep Med 8(5):597–619
15. American Academy of Sleep Medicine, Berry RB, Brooks R, Gamaldo CE et al (2016) The AASM manual for the scoring of sleep and asociated events: rules, terminology and technical specifications, version 2.3. American Academy of Sleep Medicine, Darien, pp 1–88
16. Berry RB, Brooks R, Gamaldo CE et al (2014) The AASM manual for the scoring of sleep and asociated events: rules, terminology and technical specifications, version 2.1. American Academy of Sleep Medicine, Darien, pp 1–62
17. Berry RB, Brooks R, Gamaldo CE et al (2015) The AASM manual for the scoring of sleep and asociated events: rules, terminology and technical specifications, version 2.2. American Academy of Sleep Medicine, Darien, pp 1–72
18. Collop NA, Anderson WM, Boehlecke B et al (2007) Clinical guidelines for the use of unattended portable monitors in the diagnosis of obstructive sleep apnea in adult patients. J Clin Sleep Med 3:737–747
19. Collop NA, Tracy SL, Kapur V et al (2011) Obstructive sleep apnea devices for out-of-center (OOC) testing: technology evaluation. J Clin Sleep Med 7:531–548
20. Danker-Hopfe H, Kunz D, Gruber G et al (2004) Interrater reliability between scorers from eight European sleep laboratories in subjects with different sleep disorders. J Sleep Res 13:63–69
21. Mokhlesi B, Cifu AS (2017) Diagnostic testing for obstructive sleep apnea in adults. JAMA 318:2035–3036
22. Shokoueinejad M, Fernandez C, Carroll E, Wang F, Levin J, Rusk S et al (2017) Sleep apnea: a review of diagnostic sensors, algorithms, and therapies. Physiol Meas 38:R204–R252
23. Penzel T, Hirshkowitz M, Harsh J et al (2007) Digital analysis and technical specifications. J Clin Sleep Med 3:109–120
24. American Thoracic Society (2004) Executive Summary on the systematic review and practice parameters for portable monitoring in the investigation of suspected sleep apnea in adults. Am J Respir Crit Care Med 169:1160–1163
25. Chesson AL, Berry RB, Pack A (2003) Practice parameters for the use of portable monitoring devices in the investigation of suspected obstructive sleep apnea in adults. Sleep 26:907–913
26. Flemmons WW, Littner MR, Rowley JA et al (2003) Home diagnosis of sleep apnea: a systematic review of the literature. An evidence review cosponsored by the American Academy of Sleep Medicine, the American Thorcic Society. Chest 124:1543–1579
27. Ross SD, Sheinhait IA, Harrison KJ et al (2000) Systematic review and meta-analysis of the literature regarding the diagnosis of sleep apnea. Sleep 23(4):519–532
28. Yalamanchali S, Farajian V, Hamilton C et al (2013) Diagnosis of obstructive sleep apnea by peripheral arterial tonometry: meta-analysis. JAMA Otolaryngol Head Neck Surg 139:1343–1350
29. Bibbins-Domingo K, US Preventive Services Task force (2017) Screening for Obstructive sleep apnea in adults. US Preventive Services Task Force Recommendation Statement. JAMA 317:407–414
30. Jonas DE, Amick HR, Feltner C, Weber RP, Arvanitis M, Stine A, Lux L, Harris RP (2017) Screening for Obstructive sleep apnea in adults. Evidence report and systematic review for the US Preventive Services Task Force. JAMA 317:415–433
31. Rosen IM, Kirsch DB, Chervin RD, Carden KA, Ramar K, Aurora N, Kristo DA, Malhotra RK, Martin JL, Olson EJ, Rosen CL, Rowley JA (2017) Clinical use of a home sleep apnea test: an American Academy of sleep medicine position statement. J Clin Sleep Med 13:1205–1207
32. Uddin MB, Chow CM, Su SW (2018) Classification methods to detect sleep apnea in adults based on respiratory and oximetry signals: a systematic review. Physiol Meas 39(3):03TR01
33. Deutsche Gesellschaft für Pneumologie und Beatmungsmedizin (DGP), Deutsche Gesellschaft für Schlafforschung und Schlafmedizin (DGSM), Verband Pneumologischer Kliniken (VPK), Bundesverband der Pneumologen (BdP) (2014) Positionspapier zur Diagnostik und Therapie schlafbezogener Atmungsstörungen bei Erwachsenen. Somnologie 18:53–57
34. Randerath WJ, Hein H, Arzt M et al (2014) Konsensuspapier zur Diagnostik und Therapie schlafbezogener Atmungsstörungen bei Erwachsenen. Pneumologie 68:106–123
35. Penzel T, Schöbel C, Fietze I (2015) Revise respiratory event criteria or revise severity thresholds for sleep apnea definition? J Clin Sleep Med 11(12):1357–1359
36. Yadollahi A, Giannouli E, Moussavi Z (2010) Sleep apnea monitoring and diagnosis based on pulse oximetry and tracheal sound analysis. Med Biol Eng Comput 48:1087–1097
37. Sabil A, Glos M, Günther A, Schöbel C, Veauthier C, Fietze I, Penzel T (2019) Comparison of apnea detection using oronasal thermal airflow sensor, nasal pressure transducer, respiratory inductance plethysmography and tracheal sound sensor. J Clin Sleep Med 15(2):285–292
38. Kagawa M, Tojima H, Matsui T (2016) Non-contact diagnostic system for sleep apnea-hypopnea syndrome based on amplitude and phase analysis of thoracic and abdominal Doppler radars. Med Biol Eng Comput 54(5):789–798
39. Crinion SJ, Tiron R, Lyon G, Zaffaroni A, Kilroy H, Doheny E, O'Hare E, Boyle P, Russell A, Traynor M, Kent BD, Ryan S, McNicholas WT (2019) Ambulatory detection of sleep apnea using a non-contact biomotion sensor. J Sleep Res 30:e12889
40. Paalasmaa J, Toivonen H, Partinen M (2015) Adaptive heartbeat modeling for beat-to-beat heart rate measurement in ballistocardiograms. IEEE J Biomed Health Inform 19(6):1945–1952
41. Mendonça F, Mostafa SS, Ravelo-García AG, Morgado-Dias F, Penzel T (2018) Devices for home detection of obstructive sleep apnea: a review. Sleep Med Rev 41:149–160
42. Blackwell T, Yaffe K, Laffan A, Redline S, Ancoli-Israel S, Ensrud KE et al (2015) Associations between sleep-disordered breathing, nocturnal hypoxemia, and subsequent cognitive decline in older community-dwelling men: the Osteoporotic Fractures in Men Sleep Study. J Am Geriatr Soc 63(3):453–461
43. Yaffe K, Laffan AM, Harrison SL, Redline S, Spira AP, Ensrud KE et al (2011) Sleep-disordered breathing, hypoxia, and risk of mild cognitive impairment and dementia in older women. JAMA 306(6):613–619
44. Ding X, Kryscio RJ, Turner J, Jicha GA, Cooper G, Caban-Holt A et al (2016) Self-reported sleep apnea and dementia risk: findings from the prevention of Alzheimer's disease with vitamin E and selenium trial. J Am Geriatr Soc 64(12):2472–2478
45. Spira AP, Stone KL, Rebok GW, Punjabi NM, Redline S, Ancoli-Israel S et al (2014) Sleep-disordered breathing and functional decline in older women. J Am Geriatr Soc 62(11):2040–2046
46. Ancoli-Israel S, Palmer BW, Cooke JR, Corey-Bloom J, Fiorentino L, Natarajan L et al (2008) Cognitive effects of treating obstructive sleep apnea in Alzheimer's disease: a randomized controlled study. J Am Geriatr Soc 56(11):2076–2081
47. Chong MS, Ayalon L, Marler M, Loredo JS, Corey-Bloom J, Palmer BW et al (2006) Continuous positive airway pressure reduces subjective daytime sleepiness in patients with mild to moderate Alzheimer's disease with sleep disordered breathing. J Am Geriatr Soc 54(5):777–781
48. Cooke JR, Ayalon L, Palmer BW, Loredo JS, Corey-Bloom J, Natarajan L et al (2009) Sustained use of CPAP slows deterioration of cognition, sleep, and mood in patients with Alzheimer's disease and obstructive sleep apnea: a preliminary study. J Clin Sleep Med 5(4):305–309
49. Cooke JR, Ancoli-Israel S, Liu L, Loredo JS, Natarajan L, Palmer BS et al (2009) Continuous positive airway pressure deepens sleep in patients with Alzheimer's disease and obstructive sleep apnea. Sleep Med 10(10):1101–1106
50. Moraes W, Poyares D, Sukys-Claudino L, Guilleminault C, Tufik S (2008) Donepezil improves obstructive sleep apnea in Alzheimer disease: a double-blind, placebo-controlled study. Chest 133(3):677–683
51. Berry RB, Uhles ML, Abaluck BK, Winslow DH, Schweitzer PK, Gaskins RA Jr. et al (2019) Nightbalance sleep position treatment device versus auto-adjusting positive airway pressure for treatment of positional obstructive sleep apnea. J Clin Sleep Med 15(7):947–956
52. Srijithesh PR, Aghoram R, Goel A, Dhanya J (2019) Positional therapy for obstructive sleep apnoea. Cochrane Database Syst Rev 5:CD10990
53. Benoist L, de Ruiter M, de Lange J, de Vries N (2017) A randomized, controlled trial of positional therapy versus oral appliance therapy for position-dependent sleep apnea. Sleep Med 34:109–117
54. Dieltjens M, Vroegop AV, Verbruggen AE, Wouters K, Willemen M, De Backer WA, Verbraecken JA, Van de Heyning PH, Braem MJ, de Vries N, Vanderveken OM (2015) A promising concept of combination therapy for positional obstructive sleep apnea. Sleep Breath 19(2):637–644
55. Eijsvogel MM, Ubbink R, Dekker J, Oppersma E, de Jongh FH, van der Palen J, Brusse-Keizer MG (2015) Sleep position trainer versus tennis ball technique

in positional obstructive sleep apnea syndrome. J Clin Sleep Med 11(2):139–147
56. Beyers J, Vanderveken OM, Kastoer C, Boudewyns A, De Volder I, Van Gastel A et al (2019) Treatment of sleep-disordered breathing with positional therapy: long-term results. Sleep Breath 23(4):1141–1149
57. Jackson M, Collins A, Berlowitz D, Howard M, O'Donoghue F, Barnes M (2015) Efficacy of sleep position modification to treat positional obstructive sleep apnea. Sleep Med 16(4):545–552
58. Ha SC, Hirai HW, Tsoi KK (2014) Comparison of positional therapy versus continuous positive airway pressure in patients with positional obstructive sleep apnea: a meta-analysis of randomized trials. Sleep Med Rev 18(1):19–24
59. Laub RR, Tønnesen P, Jennum PJ (2017) A Sleep Position Trainer for positional sleep apnea: a randomized, controlled trial. J Sleep Res 26(5):641–650
60. de Ruiter MHT, Benoist LBL, de Vries N, de Lange J (2018) Durability of treatment effects of the Sleep Position Trainer versus oral appliance therapy in positional OSA: 12-month follow-up of a randomized controlled trial. Sleep Breath 22(2):441–450
61. Skinner MA, Kingshott RN, Filsell S, Taylor DR (2008) Efficacy of the 'tennis ball technique' versus nCPAP in the management of position-dependent obstructive sleep apnoea syndrome. Respirology 13(5):708–715
62. Caples SM, Rowley JA, Prinsell JR (2010) Surgical modifications of the upper airway for obstructive sleep apnea in adults: a systematic review and meta-analysis. Sleep 33(10):1396–1407
63. Camacho M, Certal V, Brietzke SE, Holty JE, Guilleminault C, Capasso R (2014) Tracheostomy as treatment for adult obstructive sleep apnea: a systematic review and meta-analysis. Laryngoscope 124(3):803–811
64. Certal V, Nishino N, Camacho M et al (2013) Reviewing the systematic reviews in OSA surgery. Otolaryngol Head Neck Surg 149(6):817–829
65. Li HY, Wang PC, Chen YP et al (2011) Critical appraisal and meta-analysis of nasal surgery for obstructive sleep apnea. Am J Rhinol 25:45–49
66. Browaldh N, Nerfeldt P, Lysdahl M et al (2013) SKUP3 randomised controlled trial: polysomnographic results after uvulopalatopharyngoplasty in selected patients with obstructive sleep apnoea. Thorax 68:846–853
67. Sommer JU, Heiser C, Gahleitner C, Herr RM, Hörmann K, Maurer JT, Stuck BA (2016) Tonsillectomy with uvulopalatopharyngoplasty in obstructive sleep apnea. Dtsch Arztebl Int 113(1-02):1–8
68. Stuck BA, Ravesloot MJL, Eschenhagen T, de Vet HCW, Sommer JU (2018) Uvulopalatopharyngoplasty with or without tonsillectomy in the treatment of adult obstructive sleep apnea—a systematic review. Sleep Med 50:152–165
69. Li HY, Wang PC, Lee LA et al (2006) Prediction of uvulopalatopharyngoplasty outcome: anatomy-based staging system versus severity-based staging system. Sleep 29:1537–1541
70. Camacho M, Li D, Kawai M, Zaghi S, Teixeira J, Senchak AJ, Brietzke SE, Frasier S, Certal V (2016) Tonsillectomy for adult obstructive sleep apnea: a systematic review and meta-analysis. Laryngoscope 126(9):2176–2186
71. Sahlman J, Seppä J, Peltonen M et al (2009) Surgical intervention represents a feasible option for patients with mild obstructive sleep apnoea. Acta Otolaryngol 129(11):1266–1273
72. Browaldh N, Bring J, Friberg D (2016) SKUP(3) RCT; continuous study: Changes in sleepiness and quality of life after modified UPPP. Laryngoscope 126(6):1484–1491
73. Fehrm J, Friberg D, Bring J, Browaldh N (2017) Blood pressure after modified uvulopalatopharyngoplasty: results from the SKUP3 randomized controlled trial. Sleep Med 34:156–161
74. Joar S, Friberg D, Bring J, Lowden A, Nagai R, Browaldh N (2018) Sleep quality after modified uvulopalatopharyngoplasty: results from the SKUP3 randomized controlled trial. Sleep 41(1):1
75. Lee MY, Lin CC, Lee KS et al (2009) Effect of uvulopalatopharyngoplasty on endothelial function in obstructive sleep apnea. Otolaryngol Head Neck Surg 140(3):369–374
76. Lin CC, Wang YP, Lee KS et al (2014) Effect of uvulopalatopharyngoplasty on leptin and endothelial function in sleep apnea. Ann Otol Rhinol Laryngol 123(1):40–46
77. Constantinidis J, Ereliadis S, Angouridakis N et al (2008) Cytokine changes after surgical treatment of obstructive sleep apnoea syndrome. Eur Arch Otorhinolaryngol 265(10):1275–1279
78. Marti S, Sampol G, Muñoz X et al (2002) Mortality in severe sleep apnoea/hypopnoea syndrome patients: impact of treatment. Eur Respir J 20(6):1511–1518
79. Browaldh N, Friberg D, Svanborg E et al (2011) 15-year efficacy of uvulopalatopharyngoplasty based on objective andsubjective data. Acta Otolaryngol 131:1303–1310
80. Walker-Engström ML, Tegelberg A, Wilhelmsson B et al (2002) 4-year follow-up of treatment with dental appliance or uvulopalatopharyngoplasty in patients with obstructive sleep apnea: a randomized study. Chest 121(3):739–746
81. Browaldh N, Bring J, Friberg D (2018) SKUP3: 6 and 24 months follow-up of changes in respiration and sleepiness after modified UPPP. Laryngoscope 128(5):1238–1244
82. Sundaram S, Bridgeman S, Lim J (2005) Surgery for obstructive sleep apnoea. Cochrane Database Syst Rev 19(4):CD1001
83. Pang KP, Pang EB, Win MT, Pang KA, Woodson BT (2016) Expansion sphincter pharyngoplasty for the treatment of OSA: a systemic review and meta-analysis. Eur Arch Otorhinolaryngol 273(9):2329–2333
84. Pang KP, Pang EB, Pang KA, Rotenberg B (2018) Anterior palatoplasty in the treatment of obstructive sleep apnoea—a systemic review. Acta Otorhinolaryngol Ital 38(1):1–6
85. Won CH, Li KK, Guilleminault C (2008) Surgical treatment of obstructive sleep apnea: upper airway and maxillomandibular surgery. Proc Am Thorac Soc 5(2):193–199
86. Göktas Ö, Solmaz M, Göktas G et al (2014) Long-term results in obstructive sleep apnea syndrome (OSAS) after laser-assisted uvulopalatoplasty (LAUP). Plos One 9(6):e100211
87. Heiser C, Edenharter G, Bas M, Wirth M, Hofauer B (2017) Palatoglossus coupling in selective upper airway stimulation. Laryngoscope 127(10):E378–E383
88. Heiser C, Hofauer B (2019) Addressing the tone and synchrony issue during sleep: pacing the hypoglossal nerve. Sleep Med Clin 14(1):91–97
89. Constantino A, Rinaldi V, Moffa A, Luccarelli V, Bressi F, Cassano M, Casale M, Baptista P (2020) Hypoglossal nerve stimulation long-term clinical outcomes: a systematic review and meta-analysis. Sleep Breath. https://doi.org/10.1007/s11325-019-01923-2
90. Strollo PJ Jr, Soose RJ, Maurer JT, de Vries N, Cornelius J, Froymovich O, Hanson RD, Padhya TA, Steward DL, Gillespie MB, Woodson BT, Van de Heyning PH, Goetting MG, Vanderveken OM, Feldman N, Knaack L, Strohl KP, STAR Trial Group (2014) Upper-airway stimulation for obstructive sleep apnea. N Engl J Med 370(2):139–149
91. Strollo PJ Jr, Gillespie MB, Soose RJ, Maurer JT, de Vries N, Cornelius J, Hanson RD, Padhya TA, Steward DL, Woodson BT, Verbraecken J, Vanderveken OM, Goetting MG, Feldman N, Chabolle F, Badr MS, Randerath W, Strohl KP, Stimulation Therapy for Apnea Reduction (STAR) Trial Group (2015) Upper airway stimulation for obstructive sleep apnea: durability of the treatment effect at 18 months. Sleep 38(10):1593–1598
92. Woodson BT, Gillespie MB, Soose RJ, Maurer JT, de Vries N, Steward DL, Baskin JZ, Padhya TA, Lin HS, Mickelson S, Badr SM, Strohl KP, Strollo PJ Jr, STAR Trial Investigators (2014) Randomized controlled withdrawal study of upper airway stimulation on OSA: short- and long-term effect. Otolaryngol Head Neck Surg 151(5):880–887
93. Woodson BT, Soose RJ, Gillespie MB, Strohl KP, Maurer JT, de Vries N, Steward DL, Baskin JZ, Badr MS, Lin HS, Padhya TA, Mickelson S, Anderson WM, Vanderveken OM, Strollo PJ Jr, STAR Trial Investigators (2016) Three-year outcomes of cranial nerve stimulation for obstructive sleep apnea: the STAR trial. Otolaryngol Head Neck Surg 154(1):181–188
94. Woodson BT, Strohl KP, Soose RJ, Gillespie MB, Maurer JT, de Vries N, Padhya TA, Badr MS, Lin HS, Vanderveken OM, Mickelson S, Strollo PJ Jr (2018) Upper airway stimulation for obstructive sleep apnea: 5-year outcomes. Otolaryngol Head Neck Surg 159(1):194–202
95. Heiser C, Maurer JT, Hofauer B, Sommer JU, Seitz A, Steffen A (2017) Outcomes of upper airway stimulation for obstructive sleep apnea in a multicenter German postmarket study. Otolaryngol Head Neck Surg 156(2):378–384
96. Vanderveken OM, Maurer JT, Hohenhorst W, Hamans E, Lin HS, Vroegop AV, Anders C, de Vries N, Van de Heyning PH (2013) Evaluation of drug-induced sleep endoscopy as a patient selection tool for implanted upper airway stimulation for obstructive sleep apnea. J Clin Sleep Med 9(5):433–438
97. Steffen A, Sommer JU, Hofauer B, Maurer JT, Hasselbacher K, Heiser C (2018) Outcome after one year of upper airway stimulation for obstructive sleep apnea in a multicenter German post-market study. Laryngoscope 128(2):509–515
98. Steffen A, Sommer UJ, Maurer JT, Abrams N, Hofauer B, Heiser C (2019) Long-term follow-up of the German post-market study for upper airway stimulation for obstructive sleep apnea. Sleep Breath 24(3):979–984
99. Friedman M, Jacobowitz O, Hwang MS, Bergler W, Fietze I, Rombaux P, Mwenge GB, Yalamanchali S, Campana J, Maurer JT (2016) Targeted hypoglossal nerve stimulation for the treatment of obstructive sleep apnea: six-month results. Laryngoscope 126:2618–2623
100. Holty JE, Guilleminault C (2010) Maxillomandibular advancement for the treatment of obstructive sleep apnea: a systematic review and meta-analysis. Sleep Med Rev 14(5):287–297
101. Pirklbauer K, Russmueller G, Stiebellehner L et al (2011) Maxillomandibular advancement for treatment of obstructive sleep apnea syndrome: a systematic review. J Oral Maxillofac Surg 69(6):e165–e176

102. Vicini C, Dallan I, Campanini A et al (2010) Surgery vs ventilation in adult severe obstructive sleep apnea syndrome. Am J Otolaryngol 31(1):14–20
103. Zaghi S, Holty JE, Certal V, Abdullatif J, Guilleminault C, Powell NB, Riley RW, Camacho M (2016) Maxillomandibular advancement for treatment of obstructive sleep apnea: a meta-analysis. JAMA Otolaryngol Head Neck Surg 142(1):58–66
104. Amali A, Motiee-Langroudi M, Saedi B, Rahavi-Ezabadi S, Karimian A, Amirzargar B (2017) A comparison of uvulopalatopharyngoplasty and modified radiofrequency tissue ablation in mild to moderate obstructive sleep apnea: a randomized clinical trial. J Clin Sleep Med 13(9):1089–1096
105. Choi JH, Kim SN, Choo JH et al (2013) Efficacy of the pillar implant in the treatment of snoring and mild-to-moderate obstructive sleep apnea: a meta-analysis. Laryngoscope 123:269–276
106. Farrar J, Ryan J, Oliver E et al (2008) Radiofrequency ablation for the treatment of obstructive sleep apnea: a meta-analysis. Laryngoscope 118:1878–1883
107. Bäck LJ, Liukko T, Rantanen I, Peltola JS et al (2009) Radiofrequency surgery of the soft palate in the treatment of mild obstructive sleep apnea is not effective as a single-stage procedure: a randomized single-blinded placebo-controlled trial. Laryngoscope 119:1621–1627
108. Woodson BT, Steward DL, Weaver EM et al (2003) A randomized trial of temperature-controlled radiofrequency, continuous positive airway pressure, and placebo for obstructive sleep apnea syndrome. Otolaryngol Head Neck Surg 128(6):848–861
109. Holmlund T, Levring-Jäghagen E, Franklin KA, Lindkvist M, Berggren D (2014) Effects of Radiofrequency versus sham surgery of the soft palate on daytime sleepiness. Laryngoscope 124(10):2422–2426
110. Maurer JT, Sommer JU, Hein G et al (2012) Palatal implants in the treatment of obstructive sleep apnea: a randomised, placebo-controlled single-centre trial. Eur Arch Otorhinolaryngol 269:1851–1856
111. Lin HC, Friedman M, Chang HW et al (2008) The efficacy of multilevel surgery of the upper airway in adults with obstructive sleep apnea/hypopnea syndrome. Laryngoscope 118:902–908
112. Handler E, Hamans E, Goldberg AN et al (2014) Tongue suspension: an evidence-based review and comparison to hypopharyngeal surgery for OSA. Laryngoscope 124:329–336
113. Verse T, Wenzel S, Brus J, Verse T (2015) Multilevel surgery for obstructive sleep apnea. Lingual tonsillectomy vs. hyoid suspension in combination with radiofrequency of the tongue base. Sleep Breath 19(4):1361–1366
114. Babademez MA, Yorubulut M, Yurekli MF et al (2011) Comparison of minimally invasive techniques in tongue base surgery in patients with obstructive sleep apnea. Otolaryngol Head Neck Surg 145(5):858–864
115. Hou J, Yan J, Wang B et al (2012) Treatment of obstructive sleep apnea-hypopnea syndrome with combined uvulopalatopharyngoplasty and midline glossectomy: outcomes from a 5-year study. Respir Care 57(12):2104–2110
116. Friedman M, Hamilton C, Samuelson CG et al (2012) Transoral robotic glossectomy for the treatment of obstructive sleep apnea-hypopnea syndrome. Otolaryngol Head Neck Surg 146(5):854–862
117. Camacho M, Teixeira J, Abdullatif J, Acevedo JL, Certal V, Capasso R, Powell NB (2015) Maxillomandibular advancement and tracheostomy for morbidly obese obstructive sleep apnea: a systematic review and meta-analysis. Otolaryngol Head Neck Surg 152(4):619–630
118. Franklin KA, Anttila H, Axelsson S, Gislason T, Maasilta P, Myhre KI, Rehnqvist N (2009) Effects and side-effects of surgery for snoring and obstructive sleep apnea--a systematic review. Sleep 32(1):27–36
119. Marklund M, Verbraecken J, Randerath W (2012) Non-CPAP therapies in obstructive sleep apnoea: mandibular advancement device therapy. Eur Respir J 39(5):1241–1247
120. Murphey AW, Kandl JA, Nguyen SA, Weber AC, Gillespie MB (2015) The Effect of Glossectomy for Obstructive Sleep Apnea: A Systematic Review and Meta-analysis. Otolaryngol Head Neck Surg 153(3):334–342
121. Samutsakorn P, Hirunwiwatkul P, Chaitusaney B, Charakorn N (2018) Lingual tonsillectomy with palatal surgery for the treatment of obstructive sleep apnea in adults: a systematic review and meta-analysis. Eur Arch Otorhinolaryngol 275(4):1005–1013
122. Volner K, Dunn B, Chang ET, Song SA, Liu SY, Brietzke SE, O'Connor P, Camacho M (2017) Transpalatal advancement pharyngoplasty for obstructive sleep apnea: a systematic review and meta-analysis. Eur Arch Otorhinolaryngol 274(3):1197–1203
123. Wu J, Zhao G, Li Y, Zang H, Wang T, Wang D, Han D (2017) Apnea-hypopnea index decreased significantly after nasal surgery for obstructive sleep apnea: A meta-analysis. Medicine (Baltimore) 96(5):e6008
124. American Academy of Sleep Medicine (2005) International classification of sleep disorders, (ICSD-3): diagnostic and coding manual, 2 edn. American Academy of Sleep Medicine, Westchester
125. Banhiran W, Junlapan A, Assanasen P, Chongkolwatana C (2014) Physical predictors for moderate to severe obstructive sleep apnea in snoring patients. Sleep Breath 18:151–158
126. Barbé F, Durán-Cantolla J, Capote F et al (2010) Long-term effect of continuous positive airway pressure in hypertensive patients with sleep apnea. Am J Respir Crit Care Med 181(7):718–726
127. Barbé F, Durán-Cantolla J, Sánchez-de-la-Torre M et al (2012) Effect of continuous positive airway pressure on the incidence of hypertension and cardiovascular eventsin nonsleepy patients with obstructive sleep apnea: a randomized trial. JAMA 307(20):2161–2168
128. Howard ME, Piper AJ, Stevens B, Holland AE, Yee BJ, Dabscheck E, Mortimer D, Burge AT, Flunt D, Buchan C, Rautela L, Sheers N, Hillman D, Berlowitz DJ (2017) A randomised controlled trial of CPAP versus non-invasive ventilation for initial of obesity hypoventilation syndrome. Thorax 72(5):437–444
129. Masa JF, Corral J, Alonso ML, Ordax E, Troncoso MF, Gonzalez M, Lopez-Martínez S, Marin JM, Marti S, Díaz-Cambriles T, Chiner E, Aizpuru F, Egea C, Spanish Sleep Network (2015) Efficacy of different treatment alternatives for obesity hypoventilation syndrome. Pickwick Study. Am J Respir Crit Care Med 192(1):86–95
130. Masa JF, Mokhlesi B, Benítez I, Gomez de Terreros FJ, Sánchez-Quiroga MÁ, Romero A, Caballero-Eraso C, Terán-Santos J, Alonso-Álvarez ML, Troncoso MF, González M, López-Martín S, Marin JM, Martí S, Díaz-Cambriles T, Chiner E, Egea C, Barca J, Vázquez-Polo FJ, Negrín MA, Martel-Escobar M, Barbe F, Corral J, Spanish Sleep Network (2019) Long-term clinical effectiveness of continuous positive airway pressure therapy versus non-invasive ventilation therapy in patients with obesity hypoventilation syndrome: a multicentre, open-label, randomised controlled trial. Lancet 393(10182):1721–1732
131. Piper AJ, Wang D, Yee BJ, Barnes DJ et al (2008) Randomised trial of CPAP vs. Bilevel support in the treatment of obesity hypoventilation syndrome without severe nocturnal desaturation. Thorax 63(5):395–401
132. Windisch W, Geiseler J, Simon K, Walterspacher S, Dreher M (2018) German national guideline for treating chronic respiratory failure with invasive and non-invasive ventilation: revised edition 2017—part 1. Respiration 96(1):66–97 (on behalf of the Guideline Commission)
133. Windisch W, Geiseler J, Simon K, Walterspacher S, Dreher M (2018) German national guideline for treating chronic respiratory failure with invasive and non-invasive ventilation—revised edition 2017: part 2. Respiration 96(2):171–203 (on behalf of the Guideline Commission)
134. Masa JF, Corral J, Caballero C, Barrot E, Terán-Santos J, Alonso-Álvarez ML, Gomez-Garcia T, González M, López-Martín S, De Lucas P, Marin JM, Marti S, Díaz-Cambriles T, Chiner E, Egea C, Miranda E, Mokhlesi B, Spanish Sleep Network, García-Ledesma E, Sánchez-Quiroga MÁ, Ordax E, González-Mangado N, Troncoso MF, Martinez-Martinez MÁ, Cantalejo O, Ojeda E, Carrizo SJ, Gallego B, Pallero M, Ramón MA, Díaz-de-Atauri J, Muñoz-Méndez J, Senent C, Sancho-Chust JN, Ribas-Solís FJ, Romero A, Benítez JM, Sanchez-Gómez J, Golpe R, Santiago-Recuerda A, Gomez S, Bengoa M (2016) Non-invasive ventilation in obesity hypoventilation syndrome without severe obstructive sleep apnoea. Thorax 71(10):899–906
135. Masa JF, Corral J, Romero A, Caballero C, Terán-Santos J, Alonso-Álvarez ML, Gomez-Garcia T, González M, López-Martínez S, De Lucas P, Marin JM, Marti S, Díaz-Cambriles T, Chiner E, Merchan M, Egea C, Obeso A, Mokhlesi B, Spanish Sleep Network (2016) The effect of supplemental oxygen in obesity hypoventilation syndrome. J Clin Sleep Med 12(10):1379–1388
136. McArdle N, Rea C, King S, Maddison K, Ramanan D, Ketheeswaran S, Erikli L, Baker V, Armitstead J, Richards G, Singh B, Hillman D, Eastwood P (2017) Treating chronic hypoventilation with automatic adjustable versus fixed EPAP intelligent volume-assured positive airway pressure support (iVAPS): a randomized controlled trial. Sleep 40(10):zsx136
137. Becker HF, Piper AJ, Flynn WE et al (1999) Breathing during sleep in patients with nocturnal desaturation. Am J Respir Crit Care Med 159(1):112–118
138. Fauroux B, Lofaso F (2005) Domiciliary non-invasive ventilation in children. Rev Mal Respir 22(2Pt 1):289–303
139. Ragette R, Mellies U, Schwake C et al (2002) Patterns and predictors of sleep disordered breathing in primary myopathies. Thorax 57(8):724–728
140. Fletcher EC, Donner CF, Midgren B et al (1992) Survival in COPD patients with a daytime PaO2 greater than 60 mm Hg with and without oxyhemoglobin desaruration. Chest 101(3):649–655
141. Ward S, Chatwin M, Heather S et al (2005) Randomised controlled trial of non-invasive ventilation (NIV) for nocturnal hypoventilation in neuromuscular and chest wall disease patients with daytime normocapnia. Thorax 60(12):1019–1024
142. Budweiser S, Riedel SG, Jorres RA et al (2007) Mortality and prognostic factors in patients with

obesity-hypoventilation syndrome undergoing noninvasive ventilation. J Intern Med 261:375–383
143. Storre JH, Steurer B, Kabitz H et al (2007) Transkutaneous pCO2 monitoring during inititiation of noninvasive ventilation. Chest 132:1810–1816
144. Buyse B, Meersseman W, Demendts M (2003) Treatment of chronic respiratory failure in kyphoscoliosis: oxygen or ventilation? Eur Respir J 22(3):525–528
145. Gustafson T, Franklin KA, Midgren B (2006) Survival of patients with kyphoscoliosis receiving mechanical ventilation or oxygen at home. Chest 130(6):1828–1833
146. Jäger L, Franklin KA, Midgren B (2008) Increased survivial with mechanical ventilation in posttuberculosis patients with combination of respiratory failure and chest wall deformity. Chest 133(1):156–160
147. Lyall RA, Donaldson N, Fleming T et al (2001) A prospective study of quality of Life in ALS patients treated with noninvasive ventilation. Neurology 57(1):153–156
148. Raphael JC, Chevret S, Chastang C et al (1994) Randomised trial of preventive nasal ventilation in Duchenne muscular dystrophy. Lancet 343:1600–1604
149. Simonds AK, Muntoni F, Heather S et al (1998) Impact of nasal ventilation on survival in hypercapnic Duchenne muscular dystrophy. Thorax 53(11):949–952
150. Vianello A, Bevilacqua M, Salvador V et al (1994) Long-term nasal intermittent positive pressure ventilation in advanced Duchenne's muscular dystrophy. Chest 105(2):445–448
151. Bourke SC, Tomlinson M, Williams TL et al (2006) Effects of non-invasive ventilation on survival and quality of life in patients with amyotrophic lateral sclerosis: a randomised controlled trial. Lancet Neurol 5(2):140–147
152. Schönhofer B, Barchfeld T, Wenzel M et al (2001) Long term effects of non-invasive mechanical ventilation on pulmonary haemodynamics in patients with chronic respiratory failure. Thorax 56(7):524–528
153. Dreyer P, Lorenzen CK, Schou L (2014) Survival in ALS with home mechanical ventilation non-invasively and invasively: a 15-year cohort study in west Denmark. Amyotroph Lateral Scler Frontotemporal Degener 15(1/2):62–67
154. Sanjuán-López P, Valiño-López P, Ricoy-Gabaldón J et al (2014) Amyotrophic lateral sclerosis: impact of pulmonary follow-up and mechanical ventilation on survival. A study of 114 cases. Arch Bronconeumol 50(12):509–513
155. Gonzalez-Bermejo J, Morélot-Panzini C, Tanguy ML, Meininger V, Pradat PF, Lenglet T, Bruneteau G, Forestier NL, Couratier P, Guy N, Desnuelle C, Prigent H, Perrin C, Attali V, Fargeot C, Nierat MC, Royer C, Ménégaux F, Salachas F, Similowski T (2016) Early diaphragm pacing in patients with amyotrophic lateral sclerosis (RespiStimALS): a randomised controlled triple-blind trial. Lancet Neurol 15(12):1217–1227
156. Annane D, Orlikowski D, Chevret S (2014) Nocturnal mechanical ventilation for chronic alveolar hypoventilation in patients with neuromuscular and chest wall disorders. Cochrane Database Syst Rev 13(12):CD1941
157. Murphy PB, Rehal S, Arbane G et al (2017) Effect of home noninvasive ventilation with oxygen therapy vs oxygen therapy alone on hospital readmission or death after an acute COPD exacerbation. JAMA 371:2177–2186
158. Struik FM, Sprooten RTM, Kerstjens HAM et al (2014) Nocturnal non-invasive ventilation in COPD patients with prolonged hypercapnia after ventilator support for acute respiratory failure: a randomized, controlled, parallel-group study. Thorax 69:826–834
159. Meecham Jones DJ, Paul EA, Jones PW et al (1995) Nasal pressure support ventilation plus oxygen compared with oxygen therapy alone in hypercapnic COPD. Am J Respir Crit Care Med 152(2):538–544
160. Clini E, Sturani C, Rossi A et al (2002) The Italien multicentre study on noninvasive ventilation in chronic obstructive pulmonary disease patients. Eur Respir J 20(3):529–538
161. Strumpf DA, Millman RP, Carlisle CC et al (1991) Nocturnal positive-pressure ventilation via nasal mask in patients with severe chronic obstructive pulmonary disease. Am Rev Respir Dis 144(6):1234–1239
162. Gay PC, Hubmayr RD, Stroetz RW (1996) Efficacy of nocturnal nasal ventilation in stable, severe chronic obstructive pulmonary disease during a 3-month controlled trial. Mayo Clin Proc 71(6):533–542
163. Casanova C, Celli BR, Tost L et al (2000) Long-term controlled trial of nocturnal nasal positive pressure ventilation in patients with severe COPD. Chest 118(6):1582–1590
164. Wijkstra PJ, Avendaño MA, Goldstein RS (2003) Inpatient chronic assisted ventilatory care: a 15-year experience. Chest 124(3):850–856
165. Garrod R, Mikelsons C, Paul EA (2000) Randomized controlles trial of domiciliary noninvasive positive pressure ventilation and physical training in severe chronic obstructive pulmonary disease. Am J Respir Crit Care Med 162(4Pt 1):1335–1341
166. Tsolaki V, Pastaka C, Karetsi E et al (2008) One-year non-invasive ventilation in chronic hypercapnic COPD: effect on quality of life. Respir Med 102(6):904–911
167. Kolodziej MA, Jensen L, Rowe B et al (2007) Systematic review of noninvasive positive pressure ventilation in severe stable COPD. Eur Respir J 30(2):293–306
168. Budweiser S, Heidtkamp F, Jörres RA (2008) Predictive significance of the six-minute walk distance for long-term survival in chronic hypercapnic respiratory failure. Respiration 75(4):418–426
169. McEvoy RD, Pierce RJ, Hillman D et al (2009) Australian trial of non-invasive ventilation in Chronic Airflow Limitation (AVCAL) Study Group. Thorax 64(7):561–566
170. Köhnlein T, Windisch W, Köhler D et al (2014) Non-invasive positive pressure ventilation for the treatment of severe stable chronic obstructive pulmonary disease: a prospective, multicenter, randomized, controlled clinical trial. Lancet Respir Med 2(9):698–705
171. Mayer G, Arzt M, Braumann B, Ficker JH, Fietze I, Galetke W, Maurer JT, Orth M, Penzel T, Pistner HP, Randerath W, Rösslein M, Stuck BA (2017) S3-Leitlinie Nicht erholsamer Schlaf/Schlafstörungen, Kapitel „Schlafbezogene Atmungsstörungen bei Erwachsenen". Somnologie 20(Suppl s2):S97–S180