Module 1 Conceptual aspects of OSA: actual insights

1.1. Introduction

Obstructive sleep apnoea (OSA) is a functional disorder of the upper airway characterized by repetitive complete (apnoea) or partial (hypopnea) obstruction occurring during sleep. This disorder may cause sleep disturbance, insufficient restoration of alertness and vigilance during wakefulness (with daytime sleepiness and fatigue as a consequence), as well as impairment of cardiovascular and metabolic functions.

OSA is investigated by means of polysomnography (PSG) or polygraphy (PG) and is quantified as the number of apnoeas plus hypopnoeas per hour of sleep (apnoea-hypopnoea-index – AHI).

If presenting daytime and nighttime symptoms or cardiometabolic comorbidities are caused by OSA, the term OSA syndrome (OSAS) is used. If there is no causal relationship, then the term 'OSAS' is inappropriate. However, the terms 'OSA'and 'OSAS' are used interchangeably in the medical literature. To avoid any misinterpretation, the following definitions are proposed:

- OSA: is a condition characterized by an increased AHI, by convention ≥ 5/h
- Asymptomatic OSA: no symptoms are present despite an increased AHI
- Symptomatic / clinically relevant OSA: the presence of symptoms and/or comorbidities that may be ascribed to OSA
- Coincident OSA: the presence of symptoms and/or comorbidities that are not caused by OSA
- OSAS: obstructive sleep apnea syndrome, with symptoms and/or comorbidities caused by OSA and improving under treatment

In this guideline the use of 'OSA' as a general term is elected. Further in this document it will be discussed that the prevalence of OSA is very high, whereas most subjects in the general population are asymptomatic. The classical picture of the obese middle-aged male who snores and is excessively sleepy during the day is only part of a broad disease spectrum. OSA is a heterogeneous disorder with many different clinical phenotypic aspects (Ye, 2014). Because of this heterogeneity, neither OSA nor OSAS can be defined from one unifying pathological concept.

It is postulated that OSA is determined by four pathogenetic factors (Eckert, 2013; Zinchuk, 2016):

- An anatomic factor represented by the critical closing pressure (Pcrit) of the upper airway
- Loop gain, which reflects the propensity for unstable breathing
- Arousal threshold: the tendency to easily arouse from sleep
- Muscle responsiveness: the rate of activation of the upper airway muscles during obstructive episodes

The degree to which these factors are operational in the individual patient is highly variable. Therefore, a composite pathophysiologic phenotype may be defined based on the relative contribution of each of these factors.

Apnoeas and hypopnoeas are associated with various systemic effects, e.g. intrathoracic pressure swings, cortical arousals, hypoxemia en hypercapnia, blood pressure and cardiac rhythm oscillations. Neurologic, cardiovascular and metabolic effects of OSA are largely mediated by these effects (Xu, 2015). Hypoxemia may either be expressed as the oxygen desaturation index (ODI) or the sleep time during which the SpO_2 is lower than 90% (CT90). Both intermittent and chronic hypoxemia play a role in the clinical consequences of OSA and have more predictive value than AHI (Rosenzweig, 2015).

The extent to which these effects cause chronic end-organ strain or damage is also highly variable among individual patients. Moreover, the relationship between AHI/hypoxaemia and complaints is not clear. Some patients with high AHI / severe hypoxemia may be minimally symptomatic, whereas individuals with low AHI / subtle hypoxemia may have serious complaints. While by convention the AHI is considered to be a measure of OSA severity, there is no (or only a weak) correlation between the AHI and indices of systemic effects such as oxygen desaturation. Furthermore, end-organ impact such as hypertension is not well predicted by the AHI. Therefore, there is indirect evidence to accept that differences in individual susceptibility to systemic effects of OSA define its ultimate clinical picture. It is anticipated that the discovery of relevant biomarkers may elucidate the cellular mechanisms that underlie the differences in susceptibility / tolerance to pathogenic processes in OSA (De Luca Canto, 2015; Khalyfa, 2016).

As yet, there is insufficient evidence to show that treatment of OSA with continuous positive airway pressure (CPAP) is effective at reducing the incidence of cardiovascular complications (Abuzaid, 2017; McNicholas 2018; Yu, 2017). Insufficient CPAP compliance has been inferred as a plausible cause. However, selection bias may be another explanation. In most clinical trials recruitment of patients is based on AHI cut-offs, which may not reflect the true severity of the disease. Selection of patients in whom OSA has a demonstrable impact on the cardiovascular end-organs might yield different outcomes.

1.2. Complaints and comorbidities of OSA

There is extensive literature on symptoms, signs and comorbidities of OSA, the review of which is outside the scope of this module. We refer to the chapter of Obstructive sleep apnea, adult in the ICSD-3 (AASM, 2014) for more details. Table 1 summarizes the most important features of OSA.

Table 1 Symptoms and morbidities of OSA according to the ICSD-3 (AASM, 2014)

Complaints and signs during the daytime
• excessive daytime sleepiness
• fatigue
• nonrestorative sleep
Complaints and signs at night
• insomnia
• awakening with breath holding, gasping, or choking
• observed snoring or breathing interruptions
Comorbidities
• hypertension
• a mood disorder
• cognitive disfunction
• coronary artery disease
• congestive heart failure
• atrial fibrillation
• stroke
• type 2-diabetes mellitus

The list of associated symptoms and disorders is not limited. The function of virtually each organ can be affected by the systemic effects of OSA. While a relation between OSA and certain organ disorders may be presumed, causality is often hard to prove.

Excessive daytime sleepiness is the most reported and most closely studied complaint of OSA. The history taken from the patient and family members is the most relevant source of information. Based on the history, the evolution over time, severity, circumstances and psychosocial impact of this symptom can be assessed. Complaints of excessive sleepiness may substantially improve with CPAP or other therapy (Patel, 2003, Marshall, 2006). Motor vehicle accidents related to drowsy driving have also been shown to decrease with CPAP therapy (Tregear, 2010).

While excessive daytime sleepiness may be evaluated by employing questionnaires such as the Epworth Sleepiness Scale (ESS) (Johns, 1991), the computed outcomes of these tools are not reliable for severity scoring in individual patients (Kingshott, 1995; Turnbull, 2017; Kapur, 2017). Detailed history taking is mandatory for judging the severity of somnolence, and should comprise a thorough review of the circumstances during which sleepiness appears (AASM, 1990). These are:

- sleepiness occurring during activities that require little attention, e.g. watching television, reading or traveling as a passenger;
- sleepiness occurring during situations that require some attention and that involve some social motivation to stay awake, e.g. attending activities such as concerts, meetings, or presentations;
- sleepiness occurring during activities that require more active attention, e.g. eating, during conversation, walking, or driving, thus causing marked impairment in social or occupational function.

Questionnaires such as STOP-BANG (Chung, 2009; Farney, 2011), NoSAS (Marti-Soler, 2016) and a survey in combination with recording of nasal flow (Eijsvogel, 2016) are useful for screening and assessment of treatment effects in cohorts, but lack validity to correctly identify individuals with a high pre-test probability of having symptomatic OSA (Ramachandran, 2009). While careful history taking is the best method for this purpose, a detailed description of this technique is outside the scope of the current module. We refer to the ESRS textbook of sleep medicine for more detailed information (Grote and Puertas, 2014).

Related comorbidities should be evaluated by means of anamnesis, physical examination and additional investigations with special attention for the respiratory, cardiovascular and neurologic tracts (Kapur, 2017). Inspection of the mouth and throat, including the state of dentition, is particularly important.

There is no evidence to support the application of clinical tests such as the multiple sleep latency test (MSLT) or maintenance of wakefulness test (MWT) for the objective appraisal of excessive sleepiness in OSA. The correlation between ESS and MSLT appears to be weak and statistically nonsignificant (Benbadis, 1999).

Excessive sleepiness in OSA patients may be part of a more global state of cognitive dysfunction. A meta-analysis of studies on subjectively perceived neurocognitive impairment demonstrated decrements in concentration and in some executive functions (Vaessen, 2015). On the other hand, objective neuropsychologic tests have only shown limited defects, that are mainly accounted for by a decrease in attention (Kylstra, 2013).

Of course, OSA is only one of the many possible causes of excessive sleepiness. The differential diagnosis of hypersomnolence is described in the last section of this module.

1.3. What is the definition of OSA?

Many sleep centers in different countries adhere to the International Classification of Sleep Disorders (ICSD) published by the American Academy of Sleep Medicine (AASM). The most recent version is the third edition, published in 2014 (ICSD-3). In this publication, OSA is defined as follows (summarized version of the original text):

- AHI ≥5/h combined with daytime symptoms (e.g. excessive daytime sleepiness, fatigue) and/or nighttime symptoms (e.g. insomnia, snoring, gasping) and/or cardiovascular, metabolic or psychiatric comorbidities
- AHI ≥15/h regardless of presence or absence of any symptoms or comorbidities

In contrast with ICSD-2 (AASM, 2005), other disorders that might explain the symptoms or comorbidities must not be excluded.

The definition of OSA by the AASM is flawed by conceptual errors. Several concerns can be raised:

- Semantic confusion between OSA and OSAS is maintained. AHI, being the result of a clinical test, is confused with a disease state, especially in the second sentence where it is claimed that AHI ≥15/h *per se* confirms the diagnosis of OSA.
- The presumption that incremental AHI cut-offs are associated with increasing disease severity is spurious (Kingshott, 1998; Tkacova, 2014; Guan, 2016; Tunbull, 2017).
- Most symptoms of OSA are nonspecific and may as well be caused by other illnesses. Therefore, the association with OSA may be due to coincidence. In that instance, symptoms will not improve under CPAP or other treatment.
- It has not been shown that treatment of asymptomatic OSA patients improves clinical outcomes (Turnbull, 2017).
- The Dutch Central Bureau for Driver's Licenses stipulates that medical assessment of OSA is only required if patients are symptomatic (the mere fact of an increased AHI is not sufficient to deny the driver's license).
- Official intstitutions do not recommended to screen for OSA in individuals who have no symptoms (Bibbins-Domingo, 2017).
- An AHI < 5/h does not exclude treatable obstructive sleep-disordered breathing. Symptomatic OSA in the presence of an AHI< 5/h has been observed in particular subgroups, e.g. women and children. Moreover, the AHI shows night-to-night variability and may rise above the 5/h threshold in a repeated sleep study (Kapur, 2017)

In summary, an increased AHI does not define clinically relevant OSA and higher AHI values do not reflect increasing disease severity in terms of symptom scores or seriousness of comorbidities. In the individual patient, OSA should be assessed not only by AHI, but also by indices of hypoxemia and relevant clinical features.

Recommendations:

- The cut-off for the diagnosis of clinically relevant OSA is maintained at an AHI score ≥ 5 in the presence of suggestive symptoms and comorbidities.
- A therapeutic trial is advised to evaluate symptomatic relief, thus confirming the causal role of OSA.
- Treatment in patients who experience symptomatic relief should be continued.
- If symptoms are not relieved, the diagnosis of clinically relevant OSA should be questioned.

1.4. How is the severity of OSA defined?

The severity classification of OSA proposed by the AASM spans three levels. The cut-offs 5-14, 15-29 and ≥30/h designate mild, moderate and severe OSA, respectively. They were originally based on recommendations for syndrome definition and measurement techniques in clinical research published by the AASM (AASM task force, 1999). However, these so-called 'Chicago criteria' have never been assessed prospectively in terms of clinically relevant outcomes. Subsequent guidelines (Epstein, 2009) and classifications (ICSD-2 and ICSD-3) produced by the AASM refer to the Chicago criteria but fail to add new evidence corroborating the validity of the scale. Therefore, the AASM severity classification of OSA is not validated for clinical use.

The first Manual for the Scoring of Sleep and Associated Events was published by the AASM in 2007 (Iber, 2007). In this manual, two options for hypopnoea scoring were proposed, a 'recommended' version and an 'optional' version. In the revised version of the Manual (Berry, 2012), yet another definition of hypopnoea was formulated. AHI scoring based on the 2012 Manual yields two- to threefold higher values than the AHI assessed in accordance with the 'recommended' option in the 2007 Manual (Ruehland, 2009; Peppard, 2013; Duce, 2015). Despite this huge increase in sensitivity, the AASM did not decide on a concomitant recalibration of the AHI-based severity scoring of OSA.

Several studies highlight discrepancies in AHI scoring due to differences in methodology, interrater variability and different levels of expertise. These methodologic issues have a substantial effect on AHI-based rating of disease severity (Danker-Hopfe, 2004; Magalang, 2013; Malhotra, 2013). Moreover, the AHI is known to fluctuate over time, and night-to-night variability may be quite extensive (Kapur, 2017).

Polysomnography (PSG) and limited-channel polygraphy (PG) are both used for the assessment of AHI, whereas the latter invariably yields lower AHI-results (Escourrou, 2015). It is mandatory, however, not to mix up these two methods and to unequivocally discern (AHI_{PSG}) from AHI assessed by PG (AHI_{PG}).

With these limitations in mind it is obvious that AHI should be forsaken as the one and only predictor of OSA severity. Other indices such as hypoxemia need to be taken into account. A significant dose-response relationship between $ODI_{4\%}$ – but not AHI – and the prevalence of hypertension has been demonstrated in OSA patients (Tkacova, 2014). The odds ratio for prevalent hypertension was highest in the fourth quartile, defined by an $ODI_{4\%}$ cut-off level ≥31,7/h. Hence, it can be postulated that relevant hypoxemia may be a sign of more severe OSA. Although a severity grading system based on ODI or CT90 is lacking, the task force of the present OSA guideline has proposed to consider a high desaturation index (i.e. $ODI_{4\%}$ ≥30/h) to be clinically relevant and to warrant treatment of these patients even in the absence of symptoms or comorbidities.

Despite intrinsic limitations as a predictor, AHI may be used as an outcome variable for assessing the physiologic effects of OSA treatment. While the therapeutic aim is to reduce the AHI below a level < 5/h, higher residual values may be tolerated. For the evaluation of effects of ENT surgery less stringent criteria are applied, i.e. a reduction of the AHI of at least 50% to an absolute value < 20/h (Elshaug, 2007; Sher, 1996). Causal implication of OSA in the clinical picture is proven if both AHI and symptoms are controlled by treatment.

The assessment of AHI is important in OSA patients who are eligible for treatment with a mandibular advancement appliance (MRA) or surgery. Outcomes of these treatment options are worse when AHI values are too high. On the other hand, evidence is lacking for restricting any of these therapeutic options based on minimal AHI criteria (i.e. AHI exceeding a certain threshold).

Symptoms and comorbidities define the clinical picture of OSA. These clinical parameters should be the primary basis for the evaluation of OSA severity. If symptom scores are high and decrease with treatment, OSA should be considered 'severe' regardless of the AHI. If symptomatic relief is unsatisfactory, then other causes should be implied.

It is as yet uncertain whether clinically relevant OSA may be present in subjects who are minimally symptomatic. CPAP trials designed to assess the incidence of hypertension and cardiovascular complications in these patient groups have been inconclusive (Barbe, 2012). Therefore, the prognostic relevance of an increased AHI or ODI in minimally symptomatic patients remains to be proven.

It is concluded that the appraisal of OSA severity based on AHI cut-off values is not founded on scientific grounds. A new classification must be developed including indices of hypoxemia, symptom scores and presence or absence of comorbidities. There is preliminary evidence to accept that relevant hypoxemia carries a risk for hypertension and cardiovascular complications in OSA patients. However, clinically useful criteria for classification of hypoxemia need to be validated.

Recommendations:

- Do not assess severity of OSA exclusively on the basis of AHI cut-off values.
- Take several factors into account, including AHI, ODI and associated symptoms and comorbidities, in order to establish the severity of OSA.

1.5. What is the prevalence of OSA?

In essence, the prevalence of symptomatic OSA in the general population is unknown. To compare demographic studies on OSA is difficult because various definitions of OSA have been used. Similarly, disparate methods for scoring of AHI and stratification of disease severity have been applied. Causal relationships between an increased AHI and symptoms or comorbidities have not been investigated until present. Interventional trials are needed to demonstrate causality, and this type of research proves difficult in the epidemiological context. Hence, associations between increased AHI and symptoms or comorbidities in the general population may be coincidental.

The epidemiologic survey by Young et al. demonstrated a prevalence of OSA (defined by an AHI ≥5) in 24% of males and 9% of females in the general population (Young, 1993). A minority of these subjects (approximately 16% of the men and 22% of the women) reported sleepiness. While the causal relationship between these two characteristics was not investigated, it was hypothesized that symptomatic OSA was present in 4% of males and in 2% of females. Association by coincidence was not considered in this study.

In a recent Swiss survey including 40 to 85 year-old subjects of the general population, OSA (defined by an AHI ≥15) was identified in 49,7% of males and 23,4% of females (HypnoLaus study; Heinzer, 2015). Only a minority (approximately 13% in both gender groups) reported sleepiness. As in the previous survey, causality was not questioned. Scoring of the AHI was based on the 2012 AASM criteria, which yield a much higher case finding rate than previous scoring methods.

The prevalence of OSA is influenced by demographic factors such as age and gender. OSA is less frequently found in premenopausal women (Wimms, 2016). At older age, the prevalence of an increased AHI is higher in both gender groups (Ralls, 2012).

In conclusion, it can be contended that the prevalence of symptomatic OSA in the general population is unknown. The prevalence of OSA based on the current (sensitive) scoring method is extraordinarily

high. As the pre-test probability of case finding is high, uncertainty exists in individual patients whether and to what extent OSA plays a causal role in the clinical picture.

Recommendations:

- No recommendations are stated in this chapter.

1.6. Clinical testing for the diagnosis of OSA

Clinical tests for OSA aim at monitoring respiratory events during nocturnal sleep. Therefore, assessment of both aspects, events and sleep, seems important.

By convention, PSG is designated as the reference method for monitoring sleep and various events that occur during this state. PSG is a comprehensive method based on simultaneous recording of diverse biological signals, including brain activity (EEG), eye movements (EOG), muscle activity (EMG), respiration (flow derived from nasal pressure, temperature of inhaled and exhaled air and respiratory plethysmography), oxygen saturation (SpO_2; pulse oximetry), body posture, cardiac rhythm (ECG) and finger plethysmography (pulse oximetry). Other signals may be added to this montage, e.g. esophageal manometry, capnography, etc. Synchronous audiovisual recording may be applied for the investigation of motor and behavioural disorders of sleep.

Using PSG, the occurrence of respiratory events can be precisely related to sleep, sleep stages and other factors such as body position. Physiologic effects of respiratory events on continuity of sleep, blood gas exchange and cardiac frequency, among others, can be demonstrated and quantified with this technique. An important reason to opt for (video-)PSG is its suitability for diagnosing other sleep disorders that can occur separately from or in combination with OSA. PSG may be applied either in the sleep laboratory or in the home environment.

A description of adequate implementation and interpretation of PSG is outside the scope of this module. We refer to the AASM manual for the scoring of sleep and associated events (Berry, 2016). This manual is embraced as an international standard for the practice of PSG.

Tests that use only part of the conventional PSG montage are referred to as ‘polygraphy’ (PG). Most often, neurophysiological signals are omitted. An intrinsic limitation of this method is the fact that sleep, sleep stages and arousals cannot be detected. The equipment is portable and can be easily used in the home environment. Therefore, PG is also referred to as portable monitoring (PM) or home sleep apnea testing (HSAT) or out-of-center-sleep-testing (OCST).

The AASM has introduced a system for the classification of techniques and devices pertaining to PSG and PG. A guideline was first published in 1994, and updated in 2003 (Chesson, 2003). While PSG is classified as type 1 or 2 monitoring when it is performed in the sleep laboratory or at home, respectively, PG relates to types 3 and 4 sleep recording. Type 2, portable PSG, is rarely applied for clinical use in the USA. Type 3 is the most widely used technique for ambulatory diagnosis of OSA. Because type 4 comprises only one or two channels, it is deemed insufficient for reliable diagnosis of sleep-disordered breathing. Table1 presents an overview of these four recording techniques.

Table 1. Sleep recording techniques and montages according to the AASM

Type of recording	Montage
Type 1: conventional PSG, carried out in the sleep laboratory	A minimum of 7 channels, including EEG, EOG, chin EMG, ECG, airflow, respiratory movement, SpO_2
Type 2: portable PSG, applied out-of-center	Same configuration
Type 3: limited-channel polygraphy suitable for home sleep apnea testing	A minimum of 4 channels, including ventilation or airflow, ECG or cardiac frequency, SpO_2
Type 4: minimal set of channels	1 or 2 channels, typically including SpO_2 and airflow

While at first it was recommended to apply PM only in an invigilated environment, this restriction was abandoned in an updated edition of the guideline (Collop, 2007). Later on, Collop et al. proposed a new classification system for PM base on different physiologic parameters (Collop, 2011). However, this proposal was not adopted in common clinical practice. In a subsequent update of the practice guideline, the conventional allocation of sleep recording into four categories was maintained (Kapur, 2017). HSAT based on peripheral arterial tonometry (PAT) in combination with oximetry and actigraphy was added as it was considered equivalent to type 3 sleep recording, even though this method lacks registration of respiratory signals. This recent practice guideline also provides recommendations for clinical practice, using the GRADE method for medical evidence (Table 2).

According to the AASM, unsupervised ambulatory application of type 3 portable montoring or PAT may be utilized for the diagnosis of OSA (compared with PSG as a reference method) when the following requirements are met:

- extensive history taking by a certified sleep specialist;
- in case of high pre-test probability of OSA (based on clinical judgment);
- not in the presence of medical comorbidity or associated sleep disorders.

Table 2. Recommendations published by the AASM regarding diagnostic testing of OSA (including GRADE scores)

1. We recommend that clinical tools, questionnaires and prediction algorithms not be used to diagnose OSA in adults, in the absence of polysomnography or home sleep apnea testing. (STRONG)
2. We recommend that polysomnography, or home sleep apnea testing with a technically adequate device, be used for the diagnosis of OSA in uncomplicated adult patients presenting with signs and symptoms that indicate an increased risk of moderate to severe OSA. (STRONG)
3. We recommend that if a single home sleep apnea test is negative, inconclusive, or technically inadequate, polysomnography be performed for the diagnosis of OSA. (STRONG)
4. We recommend that polysomnography, rather than home sleep apnea testing, be used for the diagnosis of OSA in patients with significant cardiorespiratory disease, potential respiratory muscle weakness due to neuromuscular condition, awake hypoventilation or suspicion of sleep related hypoventilation, chronic opioid medication use, history of stroke or severe insomnia. (STRONG)
5. We suggest that, if clinically appropriate, a split-night diagnostic protocol, rather than a full-night diagnostic protocol for polysomnography be used for the diagnosis of OSA. (WEAK)
6. We suggest that when the initial polysomnogram is negative and clinical suspicion for OSA remains, a second polysomnogram be considered for the diagnosis of OSA. (WEAK)

The studies commissioned by the AASM do not expand on the significance of AHI_{PG} as compared with AHI_{PSG}. The relationship between these parameters is variable by nature because the denominator of AHI_{PG} is total recording time, whereas for AHI_{PSG} this is total sleep time. This discrepancy results in an important outcome bias (Escourrou, 2015). The discordance becomes particularly relevant in the case of co-occurrence between insomnia and OSA, which is a very frequent condition in daily practice (Lack, 2016). The insomnia goes unnoticed with the use of PG, while AHI_{PG} may be substantially underscored in comparison with AHI_{PSG}, thus reducing the severity rating of OSA.

It is irrelevant to investigate if (and to what extent) PG can match with PSG. It seems more appropriate to address the question in which conditions PG may be effective at identifying clinically relevant OSA. The answer will be helpful in therapeutic decision making. Yet, this issue has not been well investigated. From clinical practice it is known that a combination of symptoms and signs, together with high AHI / ODI values increases the likelihood of successful OSA treatment (Masa, 2013). In case of treatment failure, however, the diagnosis of OSA should be reconsidered and full PSG should still be performed.

High accessibility and low costs are advantages of PG, at least when the technique is performed appropriately. The intrinsic limitations of PG together with the ongoing technological (r)evolution are factors that support the further development of PSG. There is a challenge to reduce its complexity and obtrusiveness. If this objective can be reached, the ambulatory use of PSG will probably become a widely accepted standard (Pevernagie, 2015).

Finally, it should be reminded that the efficient application of PG and PSG as diagnostic tools implies proficiency of the practitioner. Adequate knowledge and skills in the domain of sleep medicine are prerequisites for good clinical practice. These qualifications are key in the assessment of pre-test probabilities as well as post-test findings and therapeutic results.

Recommendations:

- The most recent AASM manual for the scoring of sleep and associated events should be used for appropriate application of equipment and for the practice of scoring.
- In patients with a high pre-test probability for clinically relevant OSA, a PG can be performed instead of a PSG.
- The primary use of PSG is preferred in patients with sleep symptoms and with a low pre-test probability for clinically relevant OSA, or the presence of medical comorbidities or associated (other) sleep disorders, or equivocal results of PG testing.
- Results of PSG and PG should be evaluated in the clinical context by a qualified practitioner.

1.7. Differential diagnosis of OSA

The dysfunctional complaints pertaining to sleep and daytime functioning are non-specific for OSA and may also occur in various other diseases. Because of this non-specificity, a causal relationship between OSA and particular complaints can only be established with certainty if symptoms improve under treatment of OSA (*diagnosis ex iuvantibus*).
Therefore, other sleep disorders must be taken into account, on the one hand for differential diagnostic reasons and on the other hand for their potential role as co-occurrent confounders. The opposite reasoning also holds true: if other sleep disorders do not respond well to treatment, a causal role for OSA must be considered.

OSA frequently co-occurs with other sleep disorders such as restless legs syndrome, narcolepsy and chronic insomnia disorder. The latter disorder is particularly important because it is estimated that

30 to 40% of OSA patients also suffer from sleeplessness and vice versa (Lack, 2016). Insomnia can be a symptom of OSA that responds to OSA treatment, but it can also be unrelated and its association with OSA may be coincidental (Pevernagie, 2012). Such complex sleep disorders necessitate an integrative approach by an experienced multidisciplinary team.

A frequent but much overlooked cause of excessive daytime sleepiness is chronic sleep deprivation (aka behaviourly induced insufficent sleep syndrome). To establish this diagnosis it is mandatory to take a proper history and to make use of sleep diaries and actigraphy (Kretzschmar, 2016). Research has pointed out that the nighttime sleep should be at least 7 hours on average in adults to maintain good health (Watson, 2015).

The clinical evaluation of OSA consists of an extensive sleep history and the detection of possible respiratory, neurologic and cardiovascular comorbidities (Kapur, 2017).
The diagnostic approach of comorbid sleep disorders is described above in the section on clinical tests for OSA. Since PG is exclusively apt for the diagnosis of clinically relevant OSA, the application of PSG is required when other sleep disorders are suspected that may or may not be present in combination with OSA.

Recommendations:

- Recommend adaptation of lifestyle when chronic sleep deprivation is suspected (i.e. a nocturnal sleep period < 7h)
- When scheduling diagnostic investigation of OSA, also aim at detecting other associated or co-occurring sleep disorders

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