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Review Article

Early diagnosis of sleep related breathing disorders

Abstract

Obstructive sleep apnea (OSA) being the most frequent sleep related breathing disorder results in non-restorative sleep, an increased cardiovascular morbidity and mortality as well as an elevated number of accidents. In Germany at least two million people have to be expected. If obstructive sleep apnea is diagnosed early enough then sleep may regain its restorative function, daytime performance may be improved and accident risk as well as cardiovascular risk may be normalised. This review critically evaluates anamnestic parameters, questionnaires, clinical findings and unattended recordings during sleep regarding their diagnostic accurracy in recognising OSA.

There are numerous tools with insufficient results or too few data disqualifying them for screening for OSA. Promising preliminary results are published concerning neural network analysis of a high number of clinical parameters and non-linear analysis of oximetry itself or in combination with heart rate. Nasal pressure recordings can be used for risk estimation even without expertise in sleep medicine. More data is needed.

Unattended portable monitoring used by qualified physicians is the gold standard procedure when screening methods for OSA are compared. It has a very high sensitivity and specificity well documented by several meta-analyses.

Keywords: sleep related breathing disorders, obstructive sleep apnea, diagnostics, early diagnosis, screening, questionnaires, unattended portable monitoring

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1 Introduction

Medical doctors, patients and health care providers consider the prevention of diseases as an essential tool to improve the general health status of the population. Different kinds of prevention are distinguished. Primary prevention aims at avoiding the appearance of diseases. The most cited example of primary prevention is vaccination; the target group for vaccination are healthy people without having the disease. If the patient is already affected secondary prevention shall hinder the progression and chronification of the disease. For a few years the German health care systems offers coloscopy to every adult above the age of 45 years in order to recognise early forms of colonic cancer. Secondary prevention is performed in clearly defined risk groups. Tertiary prevention covers the avoidance of subsequent harm or recurrence of an already diagnosed illness; medical rehabilitation after the acute phase of a disease is the most common example [1].

Sleep related breathing disorders (SRBD) emerge during childhood as well as during adulthood. They bear negative consequences on physical, intellectual and mental recreation during sleep impairing daytime performance as a result. Furthermore, SRBD are proven to be relevant factors for the development and aggravation of systemic arterial hypertension and comorbidities. If SRBD last too long some of the symptoms and sequelae are irreversible. Therefore, early recognition of SRBD and thus early therapy is important to rapidly eliminate its symptoms and to avoid the occurrence of typical comorbidities. Hence, early diagnosis of SRBD is attributed to secondary prevention.

Obstructive sleep apnea (OSA) is the most common type of SRBD. It has a prevalence of 2% in women and 4% in men between 30 and 60 years [2]. So far nobody knows how to safely avoid the appearance of OSA in a healthy person; on the other hand it is well known that sleep may regain its restorative function, that daytime performance may improve, and that the risk for accidents and cardiovascular diseases may be reduced if OSA is treated successfully. Taking these two factors into account it is reasonable to choose methods of early diagnosis for OSA-prevention. This is the more important as at least 75% of adult OSA-patients are not yet diagnosed [3]. The essential diagnostic tools available are history, clinical examination, standardised questionnaires, unattended and attended recordings of sleep and breathing. Attended polysomnography is considered to be the gold standard when diagnosig OSA because that method can even detect minor and very discrete forms of SRBD. Anamnestic parameters, questionnaires, clinical paramters, and unattended recordings during sleep have the potential for screening for OSA. In this article their importance will be

Table 1: Classification of Sleep Related Breathing Disorders (according to ICSD 2 [4])

- Primary Central Sleep Apnoea
  - Central Sleep apnoea Due to Cheyne Stokes Breathing Pattern
  - Central Sleep apnoea Due to High-Altitude Periodic Breathing
  - Central Sleep apnoea Due to Medical Condition Not Cheyne Stokes
  - Central Sleep apnoea Due to Drug or Substance
  - Primary Sleep apnoea of Infancy
- Obstructive Sleep Apnoea Syndromes
  - Obstructive sleep apnoea, adult, paediatric
- Sleep Related Hypoventilation/Hypoxaemic syndromes
  - Sleep Related Non-obstructive Alveolar Hypoventilation, Idiopathic
  - Congenital Central Alveolar Hypoventilation Syndrome
  - Sleep Related Hypoventilation/Hypoxaemia Due to:
    - Lower Airways Obstruction
    - Neuromuscular and Chest Wall Disorders
    - Pulmonary Parenchymal or Vascular Pathology
- Sleep apnoea/Sleep Related Breathing Disorder, Unspecified

evaluated accounting for the available scientific evidence and practical considerations. Each tool used for screening of SRBD has to be validated against methods of a higher diagnostic level. In general this is polysomnography. Comparisons with portable monitoring are only included exceptionally. Attended recordings during natural sleep themselves like polysomnography are not suitable for screening at least due to high personal input during the night and increased cost.

2 Sleep related breathing disorders

2.1 Classification

In the second edition of the International Classification of Sleep Disorders (ICSD 2) [4] published in 2005 SRBD constitute one of the eight major categories of sleep disorders being divided further into five subgroups (Table 1). It is essential to know the subgroups and their different diagnoses because symptoms, comorbidities and prognosis differ relevantly.

Central sleep apnea syndromes are mainly triggered by hypocapnia with concomitant shift of the apnea threshold during sleep inducing hypopneas or apneas. The physiological reflex to impaired breathing consists of an increase of ventilatory drive and an arousal; in central sleep apnea this useful reflex mechanism reacts excessively destabilising ventilatory control and preprogramming the persistence of periodic breathing.

Hypoventilation- and hypoxaemia syndromes are characterised by insufficient ventilatory drive. Either central CO_2-receptors are damaged like e.g. in congenital central hypoventilation syndrome or ventilatory drive cannot be transformed to sufficient ventilation due to neuromuscular, pulmonary or chest wall disorders like e.g. in kyphoscoliosis.

The majority of patients with SRBD belongs to OSA. These patients show a sufficient ventilatory drive but due to morphologic changes of the upper airway and/or impaired coordination of ventilatory and pharyngeal muscles the airway partially or completely collapses during sleep. Snoring is most often the symptom which makes the patient visit a doctor. Different patterns of SRBD can be found in the same patient influencing both diagnosis and treatment.

This publication will focus on OSA in adults being the SRBD with the highest prevalence.

2.2 Symptoms of obstructive sleep apnoea

OSA is characterised by a recurrent partial or complete pharyngeal collapse causing breathing impairments such as apnoeas, hypopnoeas and respiratory effort related arousals. Impaired breathing is terminated by arousals lasting a few seconds which reopen the upper airway so that ventilation is normalised (Figure 1). The extent of oxygen desaturation does not only depend on the duration of each breathing disturbance but also on a preexisting damage of the cardiopulmonary system. Each arousal terminating the respiratory event activates the sympathicus [5], accelerates the heart rate (Figure 1) and increases the systemic arterial blood pressure [6], [7], [8]. Elevated systolic as well as diastolic arterial blood pressure has been shown in many OSA patients not only during the night but also during the day [9]. OSA is considered as an independant risk factor for arterial hypertension [10] including all cardiovascular sequelae [11]. A clearly elevated incidence of fatal and non-fatal heart attacks and strokes has been found in OSA patients [12]. The repetitive alternation of apnoea and arousal disrupt sleep in terms of sleep quality and quantity, respectively [13], [14]. Excessive daytime sleepiness and loss of concentration are further consequences of OSA. The typical symptoms are displayed in Table 2 [15]. Women with OSA suffer from problems falling asleep or maintaining sleep in more than 50% [16] increasing the risk of misjudgement.

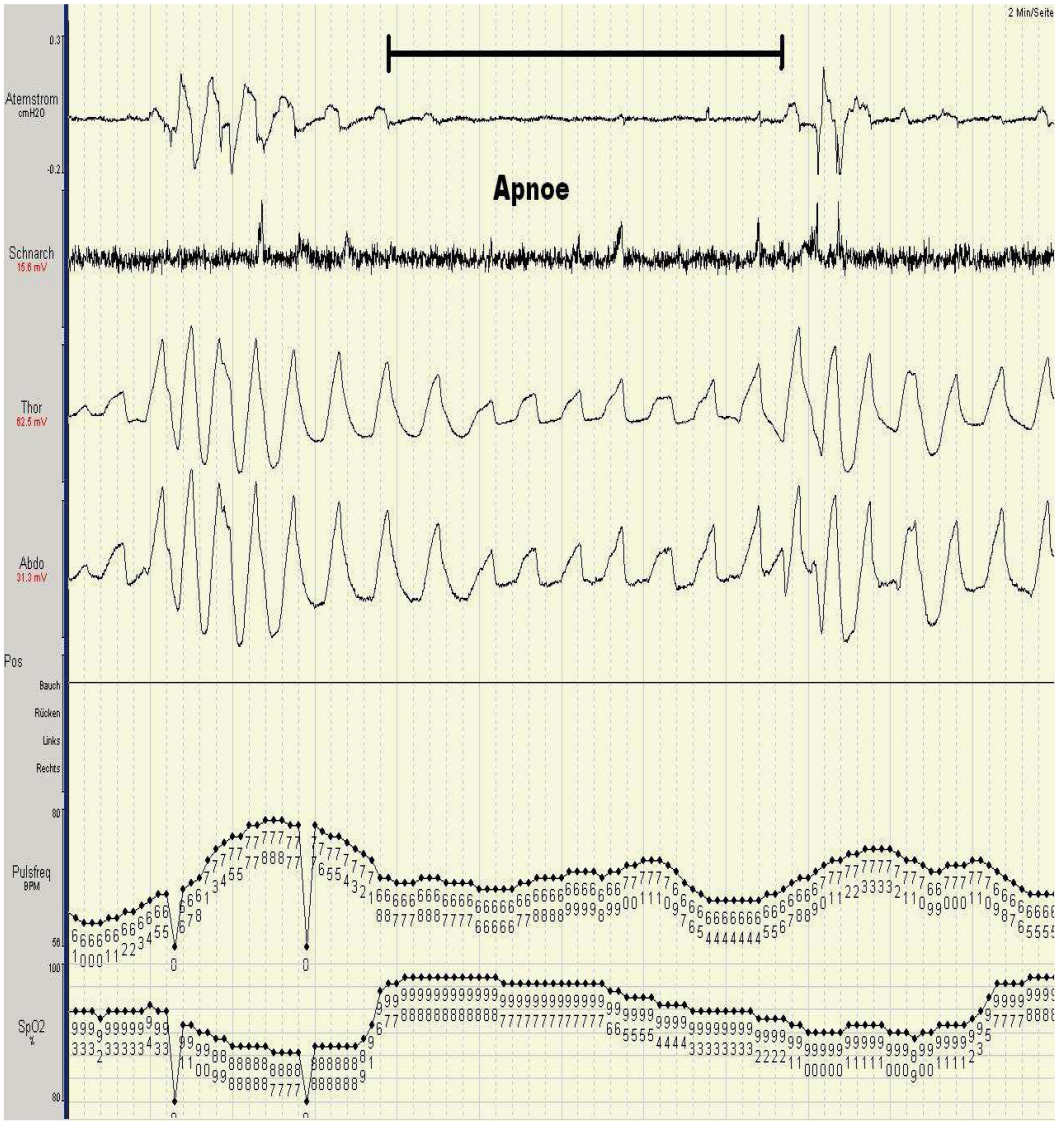

Figure 1: Two minutes of polygraphic recording showing an obstructive apnea. There is a rise of pulse rate during recuperation of breathing as autonomous sign of the central nervous system arousal. (Schnarch: snoring; Thor: thorax movement; Abd: abdominal movement; Pos: body position; Pulsfreq: pulse rate; SpO2: oxygen saturation)

Table 2: Symptoms of obstructive sleep apnoea (according to Guilleminault 1976 [15])

Cardinal symptoms
Loud, irregular snoring
Excessive daytime sleepiness
Abnormal fatigue and performance deficit
Common symptoms
Breathing pauses
Restless sleep
Morning dryness
Morning headache
Memory and concentration problems
Facultative symptoms
Nycturia
Excessive sweating
Awakening with dyspneoa
Sexual dysfunction
Depressive mood

In many cases simple snoring is the only symptom for years. As other features of OSA develop slowly and daytime symptoms are not specific many patients seek professional help rather late. As a result diagnosis is delayed and treatment often started when cardiovascular comorbidities have already appeared.

3 Possibilities of early diagnosis of obstructive sleep apnoea

3.1 Principle of stepwise diagnostic approach

In Germany the stepwise diagnostic approach for obstructive sleep apnoea has been first implemented in 1991 by the „Arbeitskreis Klinischer Schlafzentren“ [17]. It has been modified in 2004 [18] and it is still valid within the scope of the social security system (BUB-Richtline). There

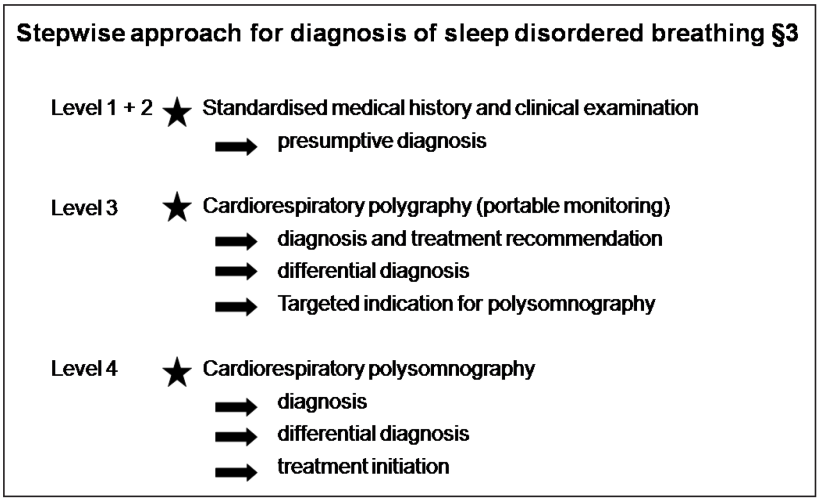

Figure 2: Stepwise approach according to the German BUB-guidelines [18]

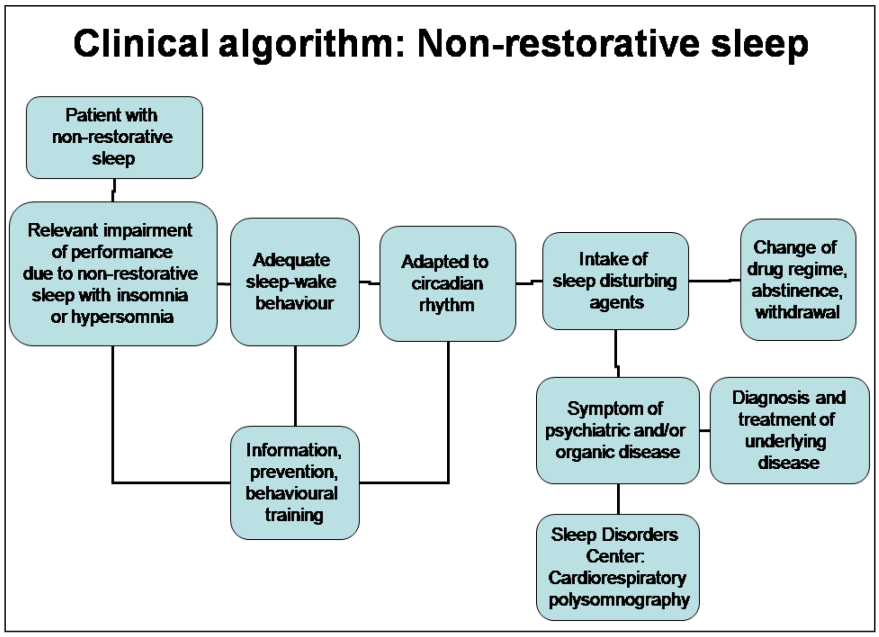

Figure 3: Diagnostic flow chart for the cardinal symptom "Non-restorative sleep" of the German Sleep Society (DGSM) [127]

is a mandatory sequence of taking history, questionnaires, clinical examination, portable monitoring and fully attended polysomnography (Figure 2) in order to make the diagnosis very cost effectively in patients who are suspected of OSA. In principle this stepwise approach contains the same diagnostic tools generally being used for screening investigations. If there is no persistent suspicion of OSA after the investigations of level 1 and 2 a portable monitoring (polygraphy, level 3) is not intended. If the portable monitoring shows normal resultsor the diagnosis of OSA can be clearly made then polysomnography should be dropped. The structure of this stepwise approach presupposes per se that sensitivity as well as specificity of the investigations level 1 to 3 are high. As an unclear result of one level automatically leads to the next level snorers receive a portable monitoring in all cases because snoring is one of the main symptoms of OSA.

Non-restorative sleep is another cardinal symptom of OSA. For this cardinal symptom the German Sleep Society worked out a guideline according to an interdisciplinary consensus (Figure 3). This guideline does not include portable monitoring. Instead it directly recommends a fully attended polysomnography if bad sleep habits, organic and psychiatric reasons are excluded. The rationale for this recommendation is that there are many causes for non-restorative sleep and portable monitoring misses the correct diagnosis in most cases. In daily practice medical doctors will be forced to act according to that directive [18] if snoring is mentioned at all. As clinical symptoms of OSA strongly vary the directive (BUB-Richtlinie) is called in by health care providers for each patient receiving diagnosis in sleep medicine regardless which cardinal symptoms are presented.

3.2 History and questionnaires

3.2.1 History

History is the basis of all diagnostic medical procedures. History itself in its classical way requires a good knowledge of the symptoms of OSA, cannot be comprised as a distinct entity and therefore may only be used for OSA screening if history is taken in a standardised way. However, the accuracy obtained when choosing a few aspects of the medical history was not satisfying (Table 3).

3.2.2 Epworth Sleepiness Score (ESS)

The ESS is a tool to quantify subjective daytime sleepiness [19]. Patients are asked to score the likelihood of dozing off in eight different situations. The score for each item may range between zero (never dozing) and 3 (high chance of dozing). Scores above 10 are indicative for hypersomnia. There is a validated German version [20]. The ESS is regularly used in clinical diagnostics in sleep medicine. It quantifies an unspecific symptom which can be found not only in OSA but also in many other sleep disorders. Primarily it has not been developped with the purpose of diagnosing OSA. Correlation with the AHI is low. Sensitivity (42%) and specificity (68%) of an ESS cut-off value of 12 are given in one single publication [21]. These data support the statement that the ESS is not suitable for the early diagnosis of OSA [22]. However, it is useful to better assess sleepiness during the course of the disease e.g. before and after therapy.

3.2.3 Berlin questionnaire

3.2.3.1 Description

In 1996 the Berlin questionnaire has been adopted during a conference of sleep specialists and general practicioners in Berlin. It includes a limited set of questions concerning well known risk factors and symptoms of OSA (Figure 4). There are five questions about snoring (category 1), four about daytime sleepiness (category 2), one question about blood pressure and general questions about age, social background, gender, body height and weight as well as neck circumference. All symptom related questions focus on cardinal symptoms of OSA. Each answer is given a certain score. Category 1 and 2 are considered positive for OSA if the symptom score sums up to two or more which is equivalent to a frequency of three to four times per week. The third category is positive if either the BMI is above 30 kg/m² or an arterial hypertension is present. A high risk for having OSA is presumed if at least two categories are positive. All other constellations are considered as low risk patients [23].
As an Indian modification category three is already considered positive if the BMI is above 25 kg/m². In category 2 (concerning sleepiness) the item „driving a car“ is replaced by monotonous situations every Indian is acquainted with like waiting at a doctor's or watching TV [24].
Due to its simple structure the Berlin questionnaire is well suited fort he screening of large populations. It does neither take long to fill in the questionnaire nor is it difficult for personnel without extensive medical training to help patients as well as to analyse the questionnaire.

3.2.3.2 Results

The Berlin questionnaire has been validated in different patient groups using different recording devices during sleep as a control. The main results are displayed in Table 4. In the initial publication of Netzer et al. [23] the questionnaire was given to 1008 consecutive patients of several general practicioners regardless the reason of their visit. 744 patient filled in the questionnaire and were classified as high or low risk patients for having OSA according to the criteria given. In alphabetical order the first 75 patients of the high risk group and the first 65 patients of the low risk group were selected and screened with a portable four-channel monitoring device (oronasal airflow by thermistor, chest wall movements, oxygen saturation and pulse rate). Recordings with bad technical quality were discarded. Finally in that validation sample there were 69 patients with high risk and 31 patients with low risk. Given the results obtained the authors concluded that sensitivity, specificity and predictive values were sufficient in order to use the Berlin questionnaire as a tool for early diagnosis of OSA. However with four-channel monitoring one cannot score sleep stages neither respiratory arousals without airflow reduction of more than 50%. The Respiratory Disturbance Index (RDI) will be underestimated in four-channel monitoring. Respiratory arousals cause the same symptoms as common apnoeas and hypopnoeas. It has to be kept in mind that sensitivity, specificity as well as predictive values will probably change if the questionnaire is validated against polysomnography. The major limitations of the study are its skewness and the comparison to four-channel monitoring data.
Seven years later Sharma and co-workers validated the questionnaire in comparison to polysomnography [24]. 320 consecutive outpatients were selected who suffered neither from severe internal diseases nor from addiction. The modified Berlin questionnaire as described above was administered to a subgroup of 180 patients who had answered in the affirmative at least one of four preceding questions concerning snoring, morning tiredness, arterial hypertension or overweight. Out of 80 high risk patients 55 agreed to stay overnight for attended polysomnography. Out of the 100 low risk patients only 49 accepted polysomnography. Both groups were approximately equal in number. Although polysomnography was performed the diagnosis of OSA was made without accounting for respiratory arousals. The authors described better statistical results in their study than Netzer et al.
At the same time Weinreich and colleagues checked the diagnostic impact of the questionnaire in 153 patients who stayed in a rehabilitation centre due to chronic obstructive pulmonary disease. They compared the results

Table 3: Studies concerning history, clinical findings and prediction models

Author	Parameter	Number	Prev. OSA	Cut-off (PSG)	Sensi-tivity	Speci-ficity	pos. pred. value	neg. pred. value	Parameter
Gyulay 1993 [128]	history	98	43%	AHI>15	79%	51%	56%	76%	age, weight, hypertension, apnoeas while asleep
Herer 1999 [129]	history	102	39%	AHI>15	80%	45%	49%	78%	EDS, snoring, apnoeas while asleep, hypertension
Viner 1991 [34]	finding	410	46%	AHI>10	52%	70%	nd	nd	„Pharynx not normal“
Hoffstein 1993 [35]	finding	594	46%	RDI>10	51%	71%	60%	63%	history and pharyngeal finding pathologic
Crocker 1990 [59]	pr. model	105	34%	AHI>15	92%	51%	49%	92%	apnoeas while asleep, hypertension, BMI, age
Rowley 2000 [62]	acc. [59]	370	67%	AHI> 10	84%	39%	73%	55%	apnoeas while asleep, hypertension, BMI, age
Rowley 2000 [62]	acc. [34]	370	67%	AHI>10	96%	13%	69%	62%	age, weight, gender, snoring
Rowley 2000 [62]	acc. [60]	370	67%	AHI>10	76%	54%	77%	52%	apnoeas, hypertension, snoring, neck circumference
Rowley 2000 [62]	acc.[61]	370	67%	AHI>10	87%	35%	73%	57%	apnoeas, gasping air, snoring, BMI, age, gender
Gurubhagav. 2001 [63]	acc. [61]	359	69%	AHI>5	82%	70%	63%	86%	apnoeas, gasping air, snoring, BMI, age, gender
Roche 2002 [64]	pr. model	108	74%	AHI>15	61%	64%	37%	83%	history , T_{80} O_2, gender
Rodsutti 2004 [58]	pr. model	243	72%	AHI>5	100%	31%	79%	100%	age, weight, gender, snoring, apnoeas while asleep
Kirby 1999 [65]	NNW	150	65%	AHI>10	99%	80%	88%	98%	45 parameters

PSG = polysomnography, Prev. = prevalence, T_{80} O_2 = time in % with $Sa0_2$ below 80%, NNW = neuronal network, EDS = excessive daytime sleepiness, nd = no data
Parameter: parameters chosen for calculation of OSA probability
The screening method is the test statistically evaluated. All studies have been prospectively performed compared to PSG.
Publications with insufficient data were not included in this table.

BERLIN QUESTIONNAIRE

Height (m) _____ Weight (kg)_____ Age_____ Male / Female

Please choose the correct response to each question.

CATEGORY 1

1. Do you snore?
a. Yes
b. No
c. Don't know

If you snore:

2. Your snoring is:
a. Slightly louder than breathing
b. As loud as talking
c. Louder than talking
d. Very loud – can be heard in adjacent rooms

3. How often do you snore
a. Nearly every day
b. 3-4 times a week
c. 1-2 times a week
d. 1-2 times a month
e. Never or nearly never

4. Has your snoring ever bothered other people?
a. Yes
b. No
c. Don't Know

5. Has anyone noticed that you quit breathing during your sleep?
a. Nearly every day
b. 3-4 times a week
c. 1-2 times a week
d. 1-2 times a month
e. Never or nearly never

CATEGORY 2

6. How often do you feel tired or fatigued after your sleep?
a. Nearly every day
b. 3-4 times a week
c. 1-2 times a week
d. 1-2 times a month
e. Never or nearly never

7. During your waking time, do you feel tired, fatigued or not up to par?
a. Nearly every day
b. 3-4 times a week
c. 1-2 times a week
d. 1-2 times a month
e. Never or nearly never

8. Have you ever nodded off or fallen asleep while driving a vehicle?
a. Yes
b. No

If yes:

9. How often does this occur?
a. Nearly every day
b. 3-4 times a week
c. 1-2 times a week
d. 1-2 times a month
e. Never or nearly never

CATEGORY 3

10. Do you have high blood pressure?
Yes
No
Don't know

Figure 4: Berlin questionnaire [23]

Table 4: Studies concerning the Berlin questionnaire

Patients	Author	Study	Comparison to Number	Cut-off	Sensi-tivity	Speci-ficity	pos. pred. value	neg. pred. value	Comment (see legend)
random sample	Netzer 1999 [23]	prospective 4-channel PG	100	AHI>5	89%	71%	86%	77%	1008/744/100 (69/31)
preselection	Sharma 2006 [24]	prospective PSG	104	AHI>5	86%	95%	96%	82%	320/180/104 (55/49)
COPD	Weinreich 2006 [25]	prospective airflow	153	AHI>10	63%	54%	38%	74%	153/153/151 (77/76)
Neurol. Sleeplab	Ahmadi 2008 [26]	retrospective PSG	130	AHI>5	68%	49%	50%	49%	130/130/130 (76/54)

PG= Polygraphy, PSG = Polysomnography
Comment: examined patients / utilisable examinations / examinations used for validation (test positive / test negative)
Neurol. Sleeplab = Neurologic sleep laboratory
The screening method is the test statistically evaluated.

to AHI whereas flow was measured by nasal pressure being linearised to pneumotachography. Sensitivity, specificity and predictive values of the Berlin questionnaire were considerably worse than in the publications mentioned previously. The authors attributed the difference to the overall worse health status of the patients causing increased daytime sleepiness even without OSA being present. As a result answers of category 2 do not differ between patients with or without OSA [25].
Ahmadi and co-workers came to the same conclusion when retrospectively analysing the data of 130 patients of a sleep disorders centre focussing on neurologic-psychiatric disorders. They could indeed improve sensitivity and specificity by dropping the questions of category 2 (sleepiness) but could not obtain satisfying results even then [26].
The Berlin questionnaire has been further used to estimate the OSA risk of certain patient groups. Based on a patient sample of 6223 patients from general practicioners Netzer calculated a high OSA risk in 36% of the US-American and 26% of the European patients [27]. The annual telephone poll "Sleep in America" included the Berlin questionnaire fort he first time in 2005 providing data of 1506 persons standing for a representative population sample. 31% of the men and 21% of the women fulfilled the criteria for having a high risk for OSA [28]. Moreno found a high risk in 26% of 10101 brasilian truck drivers [29]. When looking at 886 american soldiers of the Veteran Administration with a mean age of 62 years Mustafa and colleagues even found a high risk in 47% [30]. 245 veterans of the army of Puerto Rico had a high risk in 34% of the cases [31]. Chung et al. found the same in 24% of their patients prior to an elective general, ophthalmologic, urologic, neurosurgical, orthopedic or plastic operation [32]. However, comparing the OSA risk of asthmatics (39,5% high risk) and general internal medicine patients (27,2% high risk) as Auckley et al. did [33] has to be regarded with caution according to the results of Weinreich et al. [25].
In any case the data show that a positive anamnestic and clinical risk profile for OSA is much more prevalent than previous studies suggested [2].

3.2.3.3 Summary

The Berlin questionnaire is an easy to fill in and to evaluate questionnaire existing in many languages. It has been validated in patients without the suspicion of OSA collected at general practicioners as well as in groups of outpatient clinics with different sleep related cardinal symptoms. Studies validating the questionnaire in large general populations are lacking. However, they are necessary to clarify its impact on cross-sectional surveys.
The existing data may be summarised:

a) The Berlin questionnaire seems to be suitable for clinical routine and surveys because it is easy to use without sleep medical expertise.
b) Sensitivity, specificity and predictive values of the questionnaire seem to be helpful for screening patients at general practicioners.
c) Patient groups suffering from daytime sleepiness for other reasons do not benefit from the questionnare.
d) The number of patients at high risk for OSA might be higher than supposed due to data based on polysomnography studies.
e) The questionnaire is not accurate enough for the early diagnosis of OSA among the general population.

3.3 Clinical findings

3.3.1 Clinical examination

3.3.1.1 Description and results

Clinical examination as well as history taking are basic medical activities. Clinical examination can differ according to the medical specialty. Eventually, one doctor may need further help from colleagues to obtain the necessary clinical findings. OSA patients are characterised by pharyngeal obstructions during sleep suggesting that apart from general findings such as Body Mass Index (BMI) or neck circumference otolaryngological findings are of particular importance when screening for OSA.
There are only a few prospective studies comparing clinical findings with OSA diagnosis made by PSG (Table 3). In the beginning subjective impression of the clinician who performed the clinical examination was used to predict OSA [34], [35]. The results were disappointing. Sensitivity in particular was very low so that clinical impression cannot be recommended for the early diagnosis of OSA. Documentation of clinical findings was not standardised either jeopardising intra-as well interrater reliability. Dreher et al. tried to improve reproducibility by inventing clearly described clinical findings. However, they did not find significantly different findings (neither nose, tonsils, palate nor tongue base) when applying their approach to 52 patients with an AHI>10 and 49 with an AHI<10 [36]. A Canadian group developed a decision tree using the distance between skin surface above the hyoid and cricomental line, overbite and position of palatopharyngeal arch in order to predict OSA. They could indeed unfailingly predict the existence or absence of OSA in their validation sample of 50 patients if a certain constellations was given. Unfortunately two thirds of their patients did not have this constellation and fell into a diagnostic grey where diagnosis could not be made. As a result this model cannot be used for early recognition of OSA either [37]. Another finding – the Mallampati index – did not relevantly differ between patients with or without OSA in another study from San Francisco [38]. The same is true for a cut-off BMI <28 kg/m² which could detect an AHI<20/h only with a sensitivity of 39% [21].

3.3.1.2 Summary

a) Clinical examination of the upper airway requires experience and training in order to come to a correct assessment.
b) Statistical measures are too bad to recommend clinical examination for early diagnosis of OSA.

3.3.2 Additional investigations during wakefulness

3.3.2.1 Lung function testing

Flow-volume-loops have been investigated because overweight sleep apnoea patients often display oscillations during the inspiratory part of the loop [39]. There are four publications published about twenty years ago comprising 594 patients [40], [41], [42], [43]. The sensitivity reached 12% to 67% and specificity ranged between 29% and 86%. Other parameters of lung function were not superior [44], [45]. As a result common lung function parameters are not suitable for early diagnosis of OSA. Therefore, Zerah-Lancer and co-workers generated a prediction formula for OSA using additional lung function parameters (specific respiratory conductance) and arterial oxygen saturation [46]. The validation sample included 101 overweight snorers with more than 15 apnoeas or hypopnoeas per hour in half of them. Sensitivity as well as positive predictive value were both 100%, specificity was 84% and negative predictive value 86% [47]. So far this promising method has neither been validated in patients with other pulmonary diseases nor by other scientific teams.

3.3.2.2 Imaging techniques

Craniofacial anomalies are common in OSA patients. Various imaging techniques have been investigated in order to predict OSA such as lateral cephalometry [48], [49], [50], [51], [52], [53], [54], CT scan [49], [52] and MRI [55]. All studies focussed on correlations between morphologic parameters to AHI or other sleep data. Predictive values for OSA (AHI>10) have been looked at only by Julia-Serda [54]. They developed an equation using several cephalometric parameters, ESS, gender, neck circumference and nocturnal desaturations. Even though they included oxygen desaturations during sleep sensitivity of the equation was 94% and specificity only 83% in a sample of 92 controls and 115 OSA-patients. This is not superior to Pulse oximetryalone. Taking into account the weak data basis, the necessary radiation dose (X-ray and CT-scan) or he high cost (MRI) imaging techniques cannot be recommended as screening tool for OSA.

3.3.2.3 Other techniques

The assessment of nasal pressure for five minutes during the day as well as its non-linear and non-stationary signal extraction needs further evaluation despite good preliminary statistical results [56]. The same is true for a CPAP-trial without any pretherapeutical registration of breathing during sleep. In that study OSA was presumed if the patient used CPAP at least two hours per night and wished to continue therapy [57].

3.3.2.4 Summary

a) Simple lung function parameters are not suitable for early diagnosis of OSA. Eventually, more sophisticated parameters can predict OSA with satisfying accuracy.
b) Imaging techniques have no importance for OSA screening.
c) Other examinations during the day need further investigation to be evaluated sufficiently.

3.3.3 Prediction models

3.3.3.1 Description and results

As neither anamnestic data nor clinical findings alone obtained sufficient diagnostic accuracy investigators looked at combinations of several parameters. Typically they combined information about snoring, witnessed apnoeas and the existence of arterial hypertension with clinical findings such as gender, age, BMI and neck circumference. Rodsutti et al. [58] developed a model assigning numbers to anamnestic data and clinical findings in order to calculate a risk value for the existence of OSA. They validated their formula in a second sample of 243 patients obtaining impressive 100% for sensitivity and negative predictive value recommending the model for level 1 and level 2 of the German stepwise diagnostic approach (BUB). On the opposite, specificity and positive predictive value were too low to use that simple model for screening surveys. Rowley validated four existing prediction models based on linear regression [59], [34], [60], [61] in a sample of 370 patients suspected having OSA who were admitted to a sleep laboratory. While sensitivities are acceptable specifities cannot convince [62]. Other prediction models using only a few parameters [63] or adding oximetry during sleep [64] did not yield better results (Table 3).
Neural network prediction formulas offer new chances as Kirby described. At first the neural network learned patterns of OSA in a sample of 255 patients with and without OSA (AHI>10). 45 items from nine categories were included (demography, nocturnal symptoms, observation by bed partner, daytime symptoms, medical history, medication, social status, anthropometry, clinical findings). Another sample of 150 patients of a sleep laboratory was used to validate the prediction model showing an impressive sensitivity and negative predictive value as well as a good specificity and positive predictive value [65]. El-Solh [66] supplied his neural network with 12 parameters only and was less successful. Comparing these results leads to the assumption that the far better

diagnostic accuracy of Kirby's model is mainly due to the higher number of parameters involved .
Pillar could show that the prediction model he developed based upon the data from a typical sleep laboratory sample cannot simply be transferred to the general population. When applying his model to a population sample sensitivity was as low as 32% [67]. It has not been investigated yet whether such a relevant loss of sensitivity constitutes a problem for neural network models, too.

3.3.3.2 Summary

a) Prediction models based on linear regression and using a combination of anamnestic data and clinical findings are characterised by high sensitivity but insufficient specificity.
b) There are promising models based on artificial neural networks which are supplied by many easily obtainable parameters from different categories.
c) Data from the general population are lacking.

3.4 Unattended recording during sleep

Unattended recording of certain physiological signals during sleep enables the assessment of breathing disorders or their consequences. If simple and robust devices are used for this purpose OSA can be directly diagnosed early and cost effectively. So far single-channel devices (pulse oximetry or airflow), two-channel devices (pulse oximetry and airflow, pulse oximetry and heart rate) and multi-channel devices (polygraphy with 4- to 7-channels) have been investigated.

3.4.1 Pulse oximetry

3.4.1.1 Description of procedure

Arterial oxygen saturation can be continuously monitored non-invasively by using pulse oximetry at the ear lobule or finger tip. Pulse oximetry is used in many medical disciplines as a standard measurement for patients under intensive care. For sleep medicine purposes data have to be stored in order to be evaluated at any time after the recording is finished.
Apnoeas as well as hypopnoeas are typically accompanied by desaturations. Depending on the device and the definition used drops of oxygen saturation of 2%, 3%, 4% or 5% compared to the 15 minute average are considered relevant. In some other studies resaturations were counted alone or in combination with desaturations and, finally, oxygen variability regardless of clear cut-off values for desaturations. Relevant events can be expressed as oxygen desaturation or oxygen variation index.

3.4.1.2 Results

Due to sufficient data available only prospective studies have been included into this analysis comparing pulse oximetry with PSG. For that reason some publications had to be discarded even though they might have had promising evaluation algorithms [68].
The majority of the studies compared desaturations indices obtained by Pulse oximetry alone to AHI by polysomnography. Svanborg only included the apnoea index during PSG; neglecting hypopnoeas reduces the power of the impressive predictive values [69]. The German Health Technology Assessment Report 2002 included eight studies into their meta-analysis of pulse oximetry (Table 5). Sensitivity ranged from 63% to 70% and specificity reached 77% [70].
Levy [71] and Magalang [72] used an oxygen variability index to detect OSA. The statistical results obtained were not better than relying on desaturations only. The Spanish group of Zamarron tried to extract additional and different information of the oximetry signal by implementing nonlinear methods. They used the following methods which will not be described in detail: (1) approximate entropy – quantification of regularity of time series [73], [74], [75], [76], [77], (2) central tendency measure [77], [78], [79]. There are validation studies for both methods (Table 5), whereas there are only pilot studies for some other methods (Radial Basis Function Classifiers [80], Lempel-Ziv complexity [78]). Furthermore, Zamarron used the oximetry signal to extract pulse frequency and to analyse it by means of spectral analysis as well as approximate entropy [75], [81]. Sensitivity (71%), specificity (79%) and predictive values were worse than analysing pulse oximetry alone with the same method [74]. It has to be mentioned that an identical patient sample was used to test several algorithms causing the limitation of multiple testing. Further validations are necessary in larger populations to assess the clinical impactof these promising methods.
Patients with chronic heart failure very often suffer from obstructive as well as central sleep apnea accompanied by desaturations in almost every case. Therefore, solitary pulse oximetry seems to be a very promising tool for these patients. When investigating 50 patients with chronic heart failure (12 OSA, 24 central sleep apnoea, 14 without sleep disordered breathing) pulse oximetry at home obtained a sensitivity of 85% and a specificity of 93% compared to PSG [82]. Such results are rarely found in other publications looking at mixed patient samples. However, these results have not been confirmed yet.
Early diagnosis of common diseases does not only have a medical but also an health-economical impact. In a retrospective analysis of 100 patients Epstein et al. [83] calculated that approximately 43 US-$ could be saved per patient by using pulse oximetry before PSG. This was only true if there were no further diagnostic steps after normal pulse oximetry. Because of the either low sensitivity (74%) or specificity (55%) the authors concluded that the overall economical benefit for the health care system was too low to compensate the loss of diagnostic accuracy. As a result they did not recommend the use of pulse oximetry before PSG.

Table 5: Studies concerning oximetry

Author	Study	Number	Prev. OSAS	Cut-off (PSG)	Sensi-tivity	Speci-ficity	pos. pred. value	neg. pred. value	Criteria (Oximetry)
Svanborg 1990 [69]	simultan	77	71%	AI>5	100%	32%	83%	100%	Desat 4%; ODI>2
Douglas 1992 [130]	simultan	200	46%	AHI>15	67%	92%	87%	77%	Desat 4%; ODI >5
Series 1993 [131]	before PSG	240	46%	AHI>10	98%	48%	61%	97%	Desat 4%; ODI >10
Gyulay 1993 [128]	before PSG	98	44%	AHI>15	65%	75%	67%	73%	Desat 2%; ODI >15
Duchna 1995 [132]	simultan	207	67%	AHI>5	97%	23%	72%	80%	Desat 4%; ODI >5
Levy 1996 [71]	simultan	301	64%	RDI>15	90%	75%	87%	81%	Variation index > 0,8
Rodriguez G 1996 [133]	before PSG	96	70%	AHI>10	91%	69%	87%	77%	Desat 4%; no other information
Chiner 1999 [134]	simultan	275	79%	AHI>15	82%	76%	93%	54%	Desat 4%; ODI >5
Vazquez 2000 [135]	simultan	241	49%	AHI>15	96%	88%	nd	nd	Desat >4% ; ODI >15
Zamarron 1999 [136]	simultan	233	53%	AHI>10	78%	85%	89%	78%	Fast Fourier analysis
Zamarron 2003 [102]	simultan	300	56%	AHI>10	90%	82%	86%	87%	Fast Fourier analysis
Magalang 2003 [72]	simultan	224	44%	AHI>15	91%	59%	nd	nd	Variation index >0,63
Del Campo 2006 [74]	simultan	187	59%	AHI>15	88%	83%	88%	83%	Approx. entropy>0,679
Alvarez 2007 [79]	simultan	187	59%	AHI>15	90%	83%	89%	85%	Central Tendency Measure

PG= Polygraphy, PSG = Polysomnography, Prev. = Prevalence, simultan = simultaneous, nd = no data
Criteria (Oximetry): Desat = Desaturation, ODI = Oxygen Desaturation Index, Approx. = Approximate
The screening method is the test statistically evaluated. All studies were performed prospectively compared to PSG.

3.4.1.3 Summary

a) Pulse oximetry is a simple and reliable tool and under this aspect has the potency for screening for OSA.
b) Without additional algorithms sensitivity and specificity are too low to show a relevant advantage compared to questionnaires.
c) Non-linear algorithms might improve the diagnostic accuracy of pulse oximetry
d) So far, only patients suspected of having OSA were investigated. Data from the general population are lacking..

3.4.2 Airflow measurement

Thermistors and nasal prongs for pressure recordings are the systems used for airflow measurement. The raw data recorded can be visually displayed and validated depending on the available software of the system. Thermistors produce a slow signal per se nasal pressure is a rapid signal. This difference influences the development of algorithms for automated analysis.

3.4.2.1 SleepStrip®

3.4.2.1.1 Description of the system

The SleepStrip® (Figure 5) has been brought to market at the end of the last millenium. It consists of a plastic strip taped to the upper lip bearing two nasal and one oral thermistor. The wings contain battery, processor and a binary result display not only showing the AHI but also the minimal recording time of five hours and the technical validity of the result. Visual editing of the raw data is impossible. The SleepStrip® is a single use device because the result is permanently displayed and cannot be erased for further use. Written instructions for use shall enable the patient to perform the entire measurement on his own requiring only a single visit at the doctor's office.

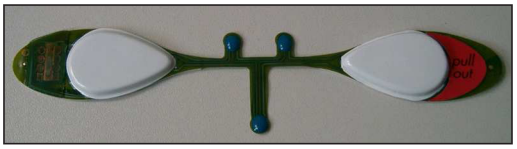

Figure 5: SleepStrip®, airflow is measured with a thermistor

3.4.2.1.2 Results

The system has been validated in three studies including patients suspected of having OSA (Table 6). The first publication [84] compared the AHI of the SleepStrip® with the AHI of the PSG simultaneously during one night in the sleep laboratory. 402 patients from Israel, Belgium and Germany were included. 88 recordings had to be discarded due to short recording time and 31 recordings due to technical failure. 288 (72%) recordings remained for data analysis. There was a positive correlation between PSG and SleepStrip® of r=0,73. The SleepStrip® overestimated AHI by 6 respiratory events in average. Satisfying sensitivity (80%) and specificity (86%) were only obtained for an AHI above 40; indeed, lower cut-off values for the AHI reduced significantly specificity.

Table 6: Studies concerning airflow measurements

Patients	Author	Study time point	Comp.	Number	Cut-off	Sensi-tivity	Speci-ficity	pos. pred. value	neg. pred. value	Comment (see legend)
Sleep Strip										
Sleep lab	Shochat 2002 [84]	simultan	PSG	288	AHI>0	86%	57%	nd	nd	402/288/288 (nd/nd)
Sleep lab	Pang 2006 [85]	after	PSG	32	AHI>5	55%	70%	80%	41%	39/32/32 (17/15)
Sleep lab	Hollingworth 2003 [86]	before	PSG/PG	130	AHI>0	55%	67%	75%	44%	48/17/17 (8/9)
Nasal pressure recording										
Sleep lab	Wang 2003 [93]	simultan	PSG	50	AHI>10	100%	88%	nd	nd	50/50/50 (nd/nd)
Sleep lab	de Almeida 2006 [95]	simultan	PSG	30	AHI>10	86%	88%	nd	nd	30/30/30 (nd/nd)
NIDDM	Erman 2007 [94]	simultan	PSG	59	AHI>15	91%	95%	91%	95%	68/59/59 (nd/nd)
Schlaflabor	Nakano 2007 [96]	simultan	PSG	117	AHI>10	97%	82%	nd	nd	120/117/117 (nd/nd)

PG= Polygraphy, PSG = Polysomnography, Comp. = comparison to, simultan = simultaneous, nd = no data, Approx. = Approximate
Comment: examined patients / utilisable examinations / examinations used for validation (test positive / test negative)
The screening method is the test statistically evaluated. All studies were performed prospectively.

Pang and co-workers compared the AHI as measured at home by the SleepStrip® with the AHi as measured by PSG in the sleep laboratory in 39 patients. 32 recordings could be used [85]. They found a low sensitivity and an acceptable specificity accompanied by an underestimation of the AHI for the SleepStrip®. AHI values above 40 could be excluded with reasonable specificity (95%) but sensitivity was very low (33%).

Early diagnosis is best possible in general population if no specific medical expertise is needed to perform the screening investigation. Having this idea in mind Hollingworth and colleagues [86] sent the SleepStrip® to patients who were asked to perform the recording on their own according to the instructions for use as given by the manufacturer. Then this recording was compared to the polygraphic or polysomnographic recording scheduled shortly afterwards. 30 of 48 patients sent back the SleepStrip® revealing 17 valid measurements (57%). In average the SleepStrip® underestimated OSA severity (mean AHI 9,4 versus 20,9). For the entire group sensitivity (32%) and specificity (36%) are low. They do not improve relevantly even if invalid recordings are excluded.

3.4.2.1.3 Summary

The SleepStrip® records breathing as a single-use device via a thermistor. Visual editing of raw data is impossible. The instructions for use seem to be simple and easy to understand. Under this prerequisite it may be considered as a good tool for OSA screening. There is a limited number of publications comprising only patients waiting for polygraphy or PSG.

a) It does not seem reasonable to have the patient perform his own recording because there are too many invalid measurements.

b) The results of the SleepStrip® are contradictory in comparison to PSG.

c) Sensitivity, Specificity, positive and negative predictive value of the SleepStrip® are unsatisfactory, so that it cannot be recommended for OSA screening.

3.4.2.2 Nasal pressure recordings

3.4.2.2.1 Description of method

Nasal pressure recordings via nasal prongs assesses pressure changes at both nostrils as it is used for oxygen application. There is a pressure drop during inspiration and a pressure rise during expiration at the nostrils. The tube of the nasal prongs is connected to a pressure sensor in the recorder. Nasal prongs are easy to put by the patient himself [87].

Airflow as measured by nasal pressure has shown a very good correlation to the signal of a pneumotachograph [88], [89]. This is also true for the analysis of single breaths [90]. Furthermore, flow limitations can be detected [91], [92]. Therefore, nasal pressure recordings seem to be ideally suited to accurately assess the number of impaired breaths in a simple and cost effective way.

3.4.2.2.2 Results

In Germany the system ApneaLink® (formerly known as "microMESAM®") is on the market. The pressure signal

is filtered further in order to extract snoring signals. Raw data can be displayed and checked for sufficient recording quality but there is no possibility of manual scoring. Hence, the user has to rely on and trust in the values given by automated scoring. There are two validation studies in comparison to PSG. The first one addresses a typical sample of sleep laboratory patients [93] and the second one looks at patients with non-insuline dependent Diabetes mellitus [94]. Sensitivity and specificity were excellent for both investigations choosing a cut-off value for the AHI of 10 or 15 events per hour, respectively (Table 6). Mild OSA with a cut-off AHI>5 was more often diagnosed falsely positive reducing specificity to 46% [93] and 50% [94], respectively. This reduction of specificity is at least partially due to methodological and statistical reason linked to the lowering of the cut-off AHI. The tendency to overscore impaired breathing when relying on automated scoring of nasal pressure only was found by de Almeida [95] as well when he published his experience with the "Sleep Check" system. Nakano [96] developed his own algorithm based on thermistor signals taken from 299 polysomnographies and compared it to nasal pressure recordings. Setting a cut-off of 10 respiratory events per hour he found a sensitivity of 92% and a specificity of 90% for the thermistor; nasal pressure recordings produced lower results (Table 6). This might be due to the different signal type of thermistor and pressure sensor. There were almost no invalid recordings in the studies mentioned above.

3.4.2.2.3 Summary

Nasal pressure recording flow signals can be linearised to pneumotachography for the flow range needed during sleep. Nasal pressure recordings are easy to perform. There are devices commercially available.

a) Invalid recordings are rare and signal quality can be checked.
b) Manual scoring of airflow is impossible as far as commercially available systems are concerned.
c) Sensitivity and specificity are high.
d) There is a tendency to overscore respiratory events which may increase the number of false positive findings for low cut-off values.
e) So far, investigations have been done in patient samples with suspected OSA. Data from the general population are necessary.

3.4.3 Recording of two parameters

3.4.3.1 Airflow and oximetry

For simultaneous recording of airflow and oxygen saturation two sensors are mandatory. An increased sensitivity and specificity is expected because apnoeas and hypopnoeas can be scored with almost the same definitions used for fully attended PSG [97]. Arousals cannot be recognized so that the scoring of respiratory effort related arousals is impossible. On the other hand there is a chance of developing new algorithms for early diagnosis of OSA by combining two signals.
Ayappa [98] merely used oxygen saturation to better detect hypopnoeas. However, he did not find an increased accuracy as compared to studies using nasal pressure recording alone. Combining thermistor and oximetry could not increase statistical results either [99]. Especially specificity was bad (Table 7). In both studies simultaneous as well as outpatient recordings were performed. There is a conspicuous discrepancy between the different recording settings. Baltzan who in addition scored the flow signal visually described a drop of sensitivity from 97% to 88% and a rise of specificity from 32% to 62% [99]. Ayappa found an increase of sensitivity to 96% as well as specificity to 93% [98]. Maybe these differences can be explained by the night to night variability of AHI [100], [101].

3.4.3.2 Pulse rate and oximetry

Researchers expected an increase of diagnostic accuracy when combining pulse rate and oxygen saturation because in OSA patients changes of oxygen saturation are linked to pulsre rate variations related to the autonomic arousal terminating the respiratory event. Both signals can be extracted from pulse oximetry [102], [81], [103]. It seems that diagnostic accuracy can be improved (Table 7). Again techniques of artificial intelligence have been implemented: Cross-approximate entropy quantifies reciprocal regularities of two time series (pulse rate and oximetry in this case) [104]. Until today no particular method has prevailed.
In Germany the iDoc-System "Schlafapnoe" is available recording pulse frequency and arterial oxygen saturation with a small finger pulse oximeter attached to the wrist. Even an unexperienced doctor can perform the recording. The data obtained will be sent to experienced sleep physicians who will edit them. It is not known to the author whether the algorithm of raw data analysis has been validated; there are no publications until now. The system is simple and offers a good patient comfort suggesting that it will be a good tool for the early diagnosis of OSA if sensitivity and specificity are satisfying.

3.4.3.3 Summary

a) Pulse oximetry can be used to extract and evaluate oxygen saturation as well as pulse rate. For airflow measurement a second sensor is required which has to be regarded as a disadvantage.
b) Combining airflow and oximetry has no relevant additional benefit compared to solitary airflow measurement by nasal pressure.
c) Non-linear algorithms have to be optimised in order to become beneficial for two-channel recordings as a tool for early diagnosis of OSA.

Table 7: Studies concerning two channel systems

Author	Study time point	Number OSA (PSG)	Prev.	Cut-off	Sensi-tivity	Speci-ficity	pos. pred. value	neg. pred. value	Criteria (both signals)
Baltzan 2000 [99]	simultan	86	41%	AHI>15	97%	32%	nd	nd	4% desaturation; 50% flow reduction; RDI>2
Ayappa 2004 [98]	pre/post	56	77%	RDI>18	88%	92%	97%	71%	apnoea-hypopnoea defined according [AASM 1999]; RDI>18
Zamarron 2003 [102]	simultan	300	56%	AHI>10	94%	82%	87%	92%	Fast-Fourrier-Analysis (SaO2, heart rate)
Alvarez 2006 [104]	simultan	74	60%	AHI>15	96%	73%	nd	nd	Cross approx. entropy (SaO2, heart rate)

PSG = Polysomnography, Prev. = prevalence, simultan = simultaneous, nd = no data
Criteria: necessary criteria in order to count respiratory events
The screening method is the test statistically evaluated. All studies were performed prospectively in comparison to PSG.

3.4.4 Portable monitoring (polygraphy)

3.4.4.1 Description of method

Cardiorespiratory polygraphy with at least 4 but typically 7 channels has become a standard diagnostic procedure for many years if OSA is suspected (Figure 6). The signals recorded are as follows: airflow, oxygen saturation, heart or pulse frequency, effort (in general using chest wall and abdominal belts), body position, snoring. With these devices not only the occurence of respiratory events can be assessed but also central and obstructive events can be distinguished.

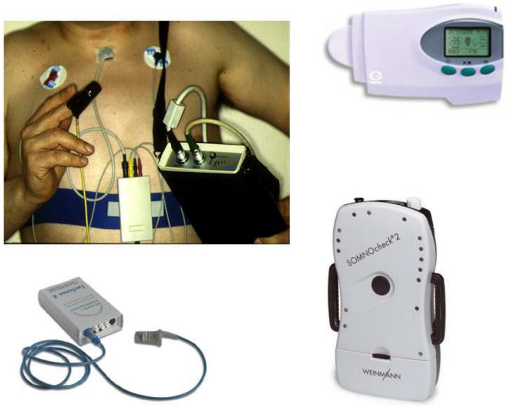

Figure 6: Different 4- to 7-channel devices for the diagnosis of OSA

There are many systems available today. They are mainly based on comparable recording signals and evaluation criteria. Regularly new devices with irrelevant changes are introduced into the market. Putting the device, reading out recorded data, analysis of the curves including elimination of artifacts as well as interpreting the entire recording requires an extended knowledge in sleep medicine. This is a limitation for the use of polygraphy in order to screen for OSA in the general population.

3.4.4.2 Results of portable monitoring

There are meta-analyses of good quality studies concerning the accuracy of polygraphy compared to PSG in the diagnostic process of OSA [70], [105], [106]. Therefore, tables listing the studies of these meta-analyses will not be included in this article. Perleth who incorporated the meta-analysis of Ross [105] found a sensitivity of 93% and a specificity of 86% setting a cut-off AHI>5 in 565 patients. In 612 other patients he calculated a sensitivity of 93% and a specificity of 71% setting a cut-off AHI>10 and finally in 321 further patients with a cut-off AHI>15 values were 92% and 81% respectively. There was a high prevalence of OSA in all studies (66%) so that the results may not be transferred to the general population [70]. Only one validation study looked at the general population of Barcelona in Spain. OSA prevalence among 116 persons was 24% (AHI>10) measured by conventional PSG. Simultaneous recording with a five-channel device result-

ed in a sensitivity of 89% and a specificity of 92% (cut-off AHI>5). Positive predictive value was 78% and negative predictive value 96%. Only 3 of 116 patients were false negative [107]. As a result portable monitoring with polygraphy systems seem to work with good sensitivity and specificity in the general population as well.
Flemons performed an evidence based literature research and came to the conclusion that attended polygraphy is able to diagnose and exclude OSA with sufficient accuracy. If they are used in an unattended setting – this means that the patient is putting and starting the entire system including all sensors completely on his own – the available data are considered not valid enough to give such a recommendation [106]. A more recent study with currently available devices confirmed the reduced quality during an unattended polygraphy (for cut-off AHI>15: sensitivity 94%, specificity 25%) [108]. It has not been investigated yet whether this problem is resolved when the recording device including all sensors are already put in the doctor's or sleep laboratory's office.
Less practical problems without a loss of diagnostic accuracy shall be achieved by extracting more and more biological signals from fewer sensors, with one single sensor at best. Under this condition the „Apnea Risk Evaluation System" (ARES) seems suitable for the early diagnosis of OSA. It consists of a single sensor (and the recorder) integrated into a frontlet. The system is able to assess almost all curves needed for a complete polygraphy. Sensitivity and specificity as well as positive and negative predictive value were slightly worse during the ambulatory recording than during the simultaneous PSG (97%, 86%, 94%, 94% versus 92%, 86%, 92%, 86%) [109]. Further validation is needed.
The improved accuracy of modern devices is further supported by a review of the Swiss sleep research society [110] who found sensitivities and specificities of more than 90% [111], [112], [113], [114], [115] with the exception of a study with heart failure patients [116].

3.4.4.3 Peripheral arterial tonometry (PAT)

Arousals of any origin activate the sympathetic system leading to a peripheral vasoconstriction. The latter can be measured by peripheral arterial tonometry (PAT) with a single use finger probe. Arousal detection by PAT correlated significantly with PSG arousal [117], [118], [119]. There is an extended version on the market (Watch-PAT®) comprising actigraphy as hint for sleep periods, heart rate and pulse oximetry. The sensors are placed around two fingers of one hand, data processor and recorder are fixed to the ipsilateral wrist in a cuff. Thus the patient remains completely mobile [120]. Evaluation and scoring of the Watch-PAT® signal is done automatically while the alhgorithm cannot be influenced or changed by the user. The system has been validated in OSA patients simultaneously to PSG as well as sequentially performing Watch-PAT® as an outpatient procedure [120], [121], [122], [123]. In addition, there was a study performed with a group of patients suffering from hypertension and diabetes [124]. Sensitivities for a Cut-off AHI>15 with simultaneous PSG range between 91% and 93% specificities between 73% and 86%. Used as a portable monitoring at home the statistical measures in the study of Pittman hit 96% and 100% [123], [124], [125].
The good results of Watch-PAT® have to be regarded with caution as many sleep disorders cause arousals. This may lead to a misinterpretation. Validation studies in larger population based samples are necessary.

3.4.4.4 Summary

a) Modern polygraphy systems as used for level 3 of the BUB-guidelines have excellent sensitivities and specificities.
b) Editing and evaluation of the data requires profound knowledge in sleep medicine.
c) They are suitable for early diagnosis of OSA if used by qualified doctors.
d) Larger population samples have to be investigated.
e) Until now it is not advisable to use polygraphy for OSA screening of the general population by untrained personnel because high expenditure of the examination is then linked to reduced accuracy.
f) PAT is able to detect arousals. An integration into polygraphy will probably improve diagnostic accuracy further.

4 Conclusion

Obstructive sleep apnoea (OSA) is one of the major reasons for non-restorative sleep and a confirmed risk factor for cardiovascular diseases as well as increased accident rate. At least 2% of adult women and 4% of men suffer from OSA [2]. Taking into account a population of 82 million people in Germany there are 68 million people older than 18 years and 50 million people between 21 and 65 years (data from German Federal Statistical Office). One has to expect at least 2 million OSA patients in Germany. Early diagnosis and as a result early therapy of the disease is not only of great importance for individual but also for sociomedical reasons. Calculations made by Fischer and Raschke have shown that in OSA patients there are 25 sick days more during the first years after medical rehabilitation compared to the year before if sleep disordered breathing had not been treated. If the patients were treated successfully they had 38 sick days less compared to the year before rehabilitation. They extrapolated the additional benefit of OSA treatment for additional diagnostic and therapeutical procedures in a cost benefit analysis which resulted in approximately 58 million Euro savings for all patients in rehabilitation centres during their first year after dismissal [126]. For these reasons simple, cost-effective and reliable tools with good diagnostic accuracy for the early diagnosis of OSA are needed. They should be simple enough to be used by physicians without any experience in sleep medicine. Due to night-to-night variability of the AHI

sensitivities and specificities of nearly 100% are impossible if different nights are compared. Anamnestic parameters or clinical findings alone have insufficient accuracy so that they are not suitable for early diagnosis. Additional investigations during wakefulness like lung function or imaging techniques are not better.

Questionnaires and prediction models combining anamnestic parameters with simple clinical findings like body weight and height are cheapest and can be used even without medical expertise. The available data suggest that a good diagnostic accuracy can only be achieved if many parameters are combined. The best results are attained with artificial neural networks which put themselves forward for OSA screening.

If vital signs like oxygen saturation, pulse rate or airflow are recorded as single parameters during sleep then non-linear methods of data analysis seem to be superior to linear methods. There are accuracies reported suggesting their suitability for early diagnosis of OSA. Combinations have limited capabilities to increase diagnostic accuracy further.

Undoubtedly, polygraphy with at least 4 or better 7 channels has the best diagnostic accuracy for diagnosing OSA with portable systems. However, performing and editing polygraphic recordings require a reasonable knowledge in sleep medicine. If performed under the umbrella of the social security system of Germany it is restricted to certified doctors. The limited availability and the expertise needed are clear disadvantages for its use as a screening tool. Almost every method evaluated in this publication have been validated in patients addressed to sleep centres because OSA was suspected. There are only the Berlin questionnaire and nasal pressure recordings via nasal cannula which have been tested in the general population. For all other methods those studies remain to be done. Very often there is only one pilot study leaving an uncertainty about the reproducibility of the results by other scientific groups.

Taking into consideration simplicity, necessary expertise, cost and accuracy of the various methods for the early recognition of OSA the following conclusions may be drawn:

a) History or clinical findings alone, prediction models with few parameters, solitary oximetry or heart rate analysis using linear standard analysis as well as the SleepStrip® cannot be recommended.

b) Further validation studies in the general population are needed regarding artificial neural networks with many parameters involved and regarding non-linear analysis of oximetry alone or in combination with heart rate. These methods have the potential to be used for early diagnosis of OSA.

c) Nasal pressure recordings with automated analysis of airflow signals seems to be appropriate even for physicians without knowledge in sleep medicine. These results have to be supported by further studies.

d) Portable monitoring with polygraphy by certified physicians is the gold standard for early recognition of OSA so far. It is the only method where evidence based and relevant meta-analyses exist due to the number and quality of publications available. As long as easier methods with a comparable accuracy do not exist it does not make sense to replace it.

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