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Federaal Kenniscentrum voor de Gezondheidszorg
Centre Fédéral d'Expertise des Soins de Santé
Belgian Health Care Knowledge Centre

ORGANISATION OF DIAGNOSIS AND TREATMENT OF OBSTRUCTIVE SLEEP APNOEA SYNDROME: AN INTERNATIONAL COMPARISON

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HEALTH SERVICES RESEARCH

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- **The external experts were consulted about a (preliminary) version of the scientific report. Their comments were discussed during meetings. They did not co-author the scientific report and did not necessarily agree with its content.**
- **Subsequently, a (final) version was submitted to the validators. The validation of the report results from a consensus or a voting process between the validators. The validators did not co-author the scientific report and did not necessarily all three agree with its content.**
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LIST OF ABBREVIATIONS

ABBREVIATION	DEFINITION
AASM	American Academy of Sleep Medicine (https://aasm.org/)
AHI	Apnoea Hypopnoea Index (number/hour)
AMSTAR-2	A MeaSurement Tool to Assess systematic Reviews
APAP	Auto-adjusting Positive Airway Pressure
AUC	Area Under the Curve
BiPAP	Bi-level Positive Airway Pressure
BIM – RVV	Bénéficiaire de l'Intervention Majorée – Rechthebbende op verhoogde verzekeringstegemoetkoming
BASS	Belgian Association for Sleep research and Sleep Medicine
BMI	Body Mass Index (weight (kg) / height (cm)2)
CADTH	Canadian Agency for Drugs and Technologies in Heath
CAHI	Central Apnoea-Hypopnoea Index
CBA	Cost-benefit analyses
CCA	Cost-consequence analyses
CEA	Cost-effectiveness analyses
CMA	Cost-minimization analyses
CPAP	Continuous Positive Airway Pressure
CSA(S)	Central Sleep Apnoea (Syndrome) – (CSAS – SASC)
CUA	Cost-utility analyses
HAS	Haute Autorité de Santé (France)
HTA	Health Technology Assessment
ICER	Incremental cost-effectiveness ratio
ECG	Electrocardiogram

EEG	Electroencephalogram
ESS	Epworth Sleepiness Scale
EMG	Electromyogram
EOG	Electro-oculogram
ESRS	European Sleep Research Society (https://esrs.eu/)
FOSQ	Functional Outcomes of Sleep Questionnaire
GRADE	Grading of Recommendations Assessment, Development and Evaluation
GP	General practitioner
HPG	Home Polygraphy
HSAT	Home Sleep Apnoea Testing
INAMI – RIZIV	Institut national d'assurance maladie invalidité – Rijksinstituut voor ziekte- en invaliditeitsverzekering
KCE	Belgian Health Care Knowledge Centre
LR-	Negative Likelihood Ratio
LR+	Positive Likelihood Ratio
MAD	Mandibular advancement device
MRD	Mandibular Reposition Device (MRA – OAM)
MWT	Maintenance of Wakefulness Test
nCPAP	Nasal Continuous Positive Airway Pressure
NICE	National Institute for Health and Care Excellence
OAHI	Obstructive Apnoea-Hypopnoea Index
OAI	Obstructive Apnoea Index
ODI	Oxygen Desaturation Index
OSA(S)	Obstructive Sleep Apnoea (Syndrome) – (OSAS – SAOS)

OSAHS	Obstructive Sleep Apnoea-Hypopnea Syndrome
PAP	Positive Airway Pressure (includes CPAP, BiPAP, auto-CPAP, nCPAP, ASV)
PAT	Peripheral Arterial Tonometry
PG	Polygraphy
PM	Portable Monitor
PSG	Polysomnography
QALY	Quality-adjusted life year
QUADAS-2	Quality Assessment of Diagnostic Accuracy Studies-2
RDI	Respiratory Disturbance Index
REI	Respiratory Event Index (used for HSAT)
RERA	Respiratory Effort-Related Arousal
RP	Respiratory Polygraphy
SAQLI	Sleep Apnoea Quality of Life Index
SDB	Sleep-disordered breathing
SF-36	Short-form 36 Questionnaire
UAS	Upper Airway Stimulation
USPSTF	U.S. Preventive Services Task Force

SCIENTIFIC REPORT

1 INTRODUCTION

1.1 Rationale

Obstructive sleep apnoea syndrome (OSAS) is a chronic condition that results from repeated closure of the upper airway during sleep resulting in reduced airflow (hypopnea) or complete airflow cessation (apnoea) leading to oxygen desaturation and arousals from sleep.[1] Upper airway obstruction during sleep is often associated with anatomical abnormalities or obesity-related peripharyngeal fat that cause narrowing of respiratory passages, decreased pharyngeal muscle tone, and insufficient neuromuscular responses to airway obstruction. This common sleep disorder is associated with adverse health outcomes including excessive sleepiness, impaired quality of life (QoL), increased motor vehicle crashes (MVC), and cardiovascular events.[2]

Approximately 110 000 person-years are currently (year 2018) treated for OSAS in Belgium through an INAMI – RIZIV convention (138 000 different patients in year 2018 according to another source, see section 4.2.1). Both their diagnosis and disease management are hospital based. Diagnosis occurs in acknowledged sleep labs through anamnesis, physical examination and polysomnography (PSG) and sometimes additional other tests. Treatment, which is mainly done using Continuous Positive Airway Pressure (CPAP) during sleep, is also managed and followed-up by acknowledged sleep centres. The sleep centres receive a daily lump sum per patient for this long-term follow-up and for the provision of the device. This reimbursement of health care can occur only in the frame of a convention between sleep centres and the National Institute for Health Insurance (INAMI – RIZIV) (more details on that convention can be found in chapter 5).

Given the rapidly rising requests for OSAS diagnostic and treatment services, this traditional hospital-centred model is increasingly viewed as unnecessarily expensive and inefficient for the evaluation and treatment of patients at high risk of OSAS.[3]

Alternative organizational and budgeting schemes exist in other countries. For example, an international comparison published in 2011 reported that the diagnosis of OSAS is based only on polysomnography (PSG) in just five European countries (Austria, Belgium, Cyprus, Greece, and Lithuania), but it can be either PSG or polygraphy (PG) in other countries.[4] Other differences among countries concern the use of telemonitoring, procedures for PAP titration, reimbursement of the diagnostic procedures and follow-up, and in the qualification requirements of sleep physicians.[4]

Therefore, an international comparison of OSAS diagnosis, treatment, monitoring and budgeting may provide valuable insights for a possible reform of OSAS management in Belgium. In that context, INAMI – RIZIV has submitted to the Belgian Health Care Knowledge Centre (KCE) the three following research questions:

1. How is the management of OSAS organized in neighbouring countries, including the budgeting?
2. Which diagnosis techniques and treatments (in the first, second and third lines of care) should be reimbursed in priority?
3. How could the management of OSAS and reimbursement be better organized in Belgium?

Concomitantly, another stakeholder (Centre de Santé de l'Amblève, Aywaille) submitted a similar but more focused question on the feasibility of the ambulatory management of OSAS by the first line of care in Belgium. This health centre carries out a pilot-project on the diagnosis and treatment of OSAS in the first line of care (http://ned.mycarenet.be/chronic-care/3c4h) (see section 6.4.3 for more details).

1.2 Scope

The aim of this research was an in-depth comparison of how diagnosis and management of OSAS in adults is organized in a sample of European countries in order to draw lessons for a possible reform of the Belgian model. The main expected output of the research was thus a set of alternative organizational and budgeting scenarios of OSAS management. It was acknowledged from the start of the research that the relative efficiency of the scenarios could not be established, particularly in the absence of comparative trials.[3]

This research did also not aim at producing a comprehensive clinical guideline for the diagnosis and treatment of OSAS. First, such an aim was not in line with the initial research questions submitted to KCE by stakeholders. Second, a comprehensive clinical guideline is being prepared by the National Institute for Health and Care Excellence (NICE – UK) with an expected release in the second part of 2020 (https://www.nice.org.uk/guidance/gid-ng10098/documents/final-scope).

1.3 Methods

A mixed methods approach was applied to address this complex topic.

First, **an overview of the literature** on main issues relating to the diagnosis, treatment, and cost-effectiveness of OSAS was carried out. It was not aimed at performing an exhaustive and systematic review but at providing an evidence-based overview for a general medical readership. We searched Medline (PubMed) for recent (2015-2020) systematic reviews and meta-analyses of the epidemiology, diagnosis, and management of adult OSAS, and manually searched the references of selected articles. The search for the published economic literature was also performed pragmatically, looking for publications in Medline (OVID) and Google, and snowballing from the references in the most recent and relevant identified articles. The literature was searched up to 02/2020, using a combination of the following broad concepts: 1) economic evaluation (HTA / cost-effectiveness / cost-utility…), 2) sleep apnoea and 3) treatment or (home-based) diagnosis. For the cost-effectiveness of PAP/MAD treatment, our search mainly focused on reports from Health Technology Assessment (HTA) agencies for which the

individual websites of the national HTA agencies was searched. Studies with publication dates ≤ 2005, were discarded. Full economic evaluations were considered, i.e. studies comparing at least two alternative procedures in terms of both costs and health outcomes. As such, cost-minimization analyses (CMA), cost-utility analyses (CUA, with results expressed as incremental cost per quality-adjusted life year (QALY) gained), cost-effectiveness analyses (CEA, with results expressed as cost per life-year LY gained), cost-benefit analyses (CBA, with a monetary valuation of health outcomes), and cost-consequence analyses (CCA[a]) were all eligible. For the comparison between hospital-based or home-based strategies for OSAS diagnosis and PAP titration, being a fairly recent topic, the search was expanded to also consider partial economic evaluations. Cost-comparison studies, not considering health outcomes, were thus eligible.

Second, **an international comparison** of how the diagnosis, treatment, monitoring and budgeting of OSAS is organized in six countries (Belgium, England, Finland, France, Germany and the Netherlands) was carried out. This was achieved by means of a written questionnaire survey (for details see the box hereunder).

International comparison of OSAS management in Belgium, England, Finland, France, Germany, and the Netherlands

- A questionnaire was developed and pre-tested (face-validity). Parts of a previous questionnaire were included.[4] Sections included the diagnostic pathway, titration, treatment follow-up, and funding.
- Apart from Belgium, countries were selected if they presented an alternative organization of OSAS diagnosis and management as desc ribed by experts or in the literature (scientific or grey). Specific aspects of this selection process are presented in Appendix 1.
- Two experts per country, including Belgium, were identified through scrutinizing the international networks of Belgian experts, review of grey literature, and authorship of scientific publications, particularly experts who participated in previous international comparisons of OSAS.[4, 5]
- Questionnaires were written in English, but respondents could respond in their own language when it was possible for the authors to understand (EN, FR, NL). The questionnaire is available on demand. Responses were in free-text to allow for more nuances by the respondents. The questionnaires were completed based on expert opinion. However, the main respondents were invited to get the support of colleagues for completing some responses, if required. Moreover, the main respondents were invited to cite his/her sources of information as often as possible. Respondents received a relatively small financial compensation for their contribution.
- Questionnaires were analysed by KCE experts. Only for England just one respondent replied with valid answers. No coding and no formal analysis of content was used given the factual nature of the information and the restricted number of countries. The information provided by the experts of the six countries was completed by national clinical protocols, guidelines and regulatory documents on the organization and the funding of OSAS management (Appendix 1). Comparative descriptive tables were made. All respondents were re-contacted for clarifications, discussion of divergent answers between the two country experts, and provision of additional information.

[a] Cost-consequence analyses examine both costs and consequences, without the necessity of focusing on a single consequence and without combining disparate consequences into a single, commensurable measure.

Third, apart from the analysis in the international comparison, the description of the **current situation in Belgium** relied on:

- The analysis of the financing rules for the management of OSAS
- The analysis of INAMI – RIZIV data collected in the frame of the OSAS convention with sleep centres
- The analysis of the data from the Belgian Permanent Sample (EPS), which also allowed computing costs related to OSAS diagnosis and treatment (details can be found in section 4.1)
- The consultation of key stakeholders, including sleep specialists, general practitioners, private providers of material and/or services, representatives of patient organisations, and representatives of the sickness funds and INAMI – RIZIV.

Finally, based on the analysis of data listed above, we elaborated **scenarios** for a possible reform of the organization and budgeting of OSAS management in Belgium. Scenarios were also discussed with key stakeholders.

2 OVERVIEW OF EVIDENCE ON OSAS

2.1 Definition of OSAS

Obstructive Sleep Apnoea (OSA) is characterised by repeated episodes of complete (apnoea) or partial (hypopnoea) obstructions of the upper airway during sleep, resulting in episodic reduction (hypopnea) or cessation (apnoea) of airflow despite respiratory effort. Most people with OSA have a narrow upper airway, typically caused by fat deposition in the parapharyngeal fat pads and pharyngeal muscles or abnormalities in craniofacial structure.[6] Obstructive apnoeas and hypopnoeas result in large changes in intrathoracic pressure, intermittent hypoxemia, and arousal from sleep. OSA is traditionally quantified by the apnoea-hypopnoea index (AHI), respiratory disturbance index (RDI) or respiratory event index (REI) measured during sleep. These indicators have been defined by the American Academy of Sleep Medicine (AASM) (see Table 1).[7-9] The third edition of the International Classification of Sleep Disorders (ICSD-3) defines OSAS as a PSG-determined obstructive AHI ≥ 5 events/hour associated with the typical symptoms of OSAS (e.g., unrefreshing sleep, daytime sleepiness, fatigue or insomnia, awakening with a gasping or choking sensation, loud snoring, or witnessed apnoea's), or an obstructive AHI ≥ 15 events/h (even in the absence of symptoms).[8, 10] In addition to apnoeas and hypopnoeas that are included in the AHI, the RDI includes respiratory effort-related arousals (RERAs).

Table 1 – Definitions of OSAS-related terms and index by the AASM

Abbreviation	Indicator	Definition
-	Apnoea	The cessation of airflow (≥90% decrease in airflow compared to baseline using an oro-nasal thermal sensor (diagnostic study), PAP device flow (titration study), or an alternative apnoea sensor) lasting at least 10 seconds.[11] Apnoea's are classified as obstructive, mixed, or central based on the pattern of respiratory effort. An obstructive apnoea is associated with continued or increased inspiratory effort throughout the entire period of absent airflow. A central apnoea is associated with absent inspiratory effort throughout the entire period of absent airflow. Mixed apnoeas are associated with absent inspiratory effort in the initial portion of the event, followed by resumption of inspiratory effort in the second portion of the event.
-	Hypopnea	Hypopnoea in adults is scored when the peak signal excursions drop by ≥ 30% of pre-event baseline using nasal pressure (diagnostic study), PAP device flow (titration study), or an alternative sensor, for ≥ 10 seconds in association with either ≥ 3% arterial oxygen desaturation or an arousal (2012 AASM definition).[11]
AHI	Apnoea Hypopnoea Index	The total number of apnoeas plus the total number of hypopnoeas per hour of sleep
HSAT	Home Sleep Apnoea Testing	The use of unattended diagnostic studies to assess for OSA without the determination of sleep quality. Also referred to as out-of-centre sleep testing or portable monitoring.
OSA	Obstructive Sleep Apnoea	A sleep related breathing disorder that involves a decrease or complete halt in airflow despite an ongoing effort to breathe. OSA severity is defined as: -Mild for AHI or RDI ≥ 5 and < 15/h -Moderate for AHI or RDI ≥ 15 and ≤ 30/h -Severe for AHI or RDI > 30/h
OSAS	Obstructive sleep apnoea syndrome	OSA with an AHI ≥ 5 events/h AND evidence of daytime sleepiness, or an obstructive AHI ≥ 15 events/h (even in the absence of symptoms).[8, 10]
RDI	Respiratory Disturbance Index	The total number of apnoeas plus the total number of hypopnoeas plus the total number of respiratory effort-related arousals per hour of sleep
REI	Respiratory Event Index	Total number of respiratory events scored per hour of monitoring time. The REI is used for Home Sleep Apnoea Testing (HSAT), as the total sleep time is unknown in the absence of electroencephalogram.
RERA	Respiratory Effort-Related Arousal	A sequence of breaths characterized by increasing respiratory effort, inspiratory flattening in the nasal pressure or PAP device flow channel leading to an arousal from sleep. Respiratory effort-related arousals do not meet criteria for hypopnoea and have a minimum duration of at least 10 seconds in adults or the duration of at least two breaths in children.
SDB	Sleep-disordered breathing	A range of disorders, with most falling into the categories of OSA, central sleep apnoea (CSA) or sleep-related hypoventilation.

AASM: American Academy of Sleep Medicine.

It should be noted that there is variability in the definition of a hypopnoea event. The AASM Scoring Manual recommended definition requires that changes in flow (≥30% decrease in flow from baseline) be associated with a 3% oxygen desaturation or a cortical arousal (2012 guideline), but allows an alternative definition that requires association with a 4% oxygen desaturation without consideration of cortical arousals (2007 guideline).[10, 12] Depending on which definition is used, the AHI index may be considerably different in a given individual. For example, it was measured in two Spanish cohorts that the prevalence of an AHI ≥30 events/h increased by 14% with a criterion of a 3% oxygen desaturation, compared to 4% oxygen desaturation.[13] The discrepancy between these and other hypopnoea definitions used in research studies introduces complexity in the evaluation of evidence regarding the diagnosis of OSAS.[10] Moreover, a fixed AHI index as the sole diagnosis criterion for OSAS is problematic, as AHI rises continuously with age and is highest in the elderly.[14] More fundamentally, the definition of OSAS based only on the AHI index has been strongly challenged recently.[15] This approach is based on two shortcomings. First, it is assumed that when the AHI is increased, the presenting symptoms and signs are caused by OSA. This premise results in a substantial number of false positive cases, and consequently, in medical overconsumption. Second, it is assumed that AHI indicates clinical severity of OSA. None of these associations seem to be substantiated by sound scientific evidence.[15]

2.2 Epidemiology

2.2.1 Prevalence

Common risk factors for OSAS include obesity,[16] advanced age,[14] male gender,[14] post-menopausal status in women, race (more present in African individuals), and craniofacial dysmorphisms.[2] Obesity is a prominent risk factor for OSAS. OSAS is approximately twice as common in individuals who are overweight and four times as common in individuals with obesity compared with individuals without overweight or obesity.[6] Rates of OSAS have risen concomitantly to rise of obesity rates.[16] For example, in the United States the prevalence of OSAS increased by approximately 30% between 1990 and 2010, with absolute increases of 4.2% in women and 7.5% in men.[16] When these figures are extrapolated to Belgium, based on BMI distribution in the Belgian population (<70 years), 7.7% of adult men and 2.6% of adult women would suffer from OSAS (personal communication Dr. Verbraecken).

The prevalence of OSA varies significantly based on the population being studied (age, obesity prevalence) and how OSA is defined (e.g. testing methodology, scoring criteria used, and AHI threshold). A recent literature-based analysis reported prevalence figures from 16 countries (17 studies).[12] The prevalence of OSAS in men at an AHI cut-off of ≥ 15 events/h went from 3.9% in New Zealand[17] (in 2009; individuals aged 30-59 years; application of 2007 AASM definition of AHI) to 49.7% in men and 23.4% in women in Switzerland[18] (in 2015; individuals aged 40-85 years; application of 2012 AASM definition of AHI). The percentage of OSAS patients was even higher when the criterion of AHI≥ 5/h and symptoms was used.[19]This study is often cited as the demonstration of the very high OSAS prevalence in the general population (as it was based on a representative sample), implying that the problem is usually underestimated in other evaluations.[a] On the contrary,

[a] Of note, the study participants were relatively old, with 40% of male individuals being aged ≥ 60 years. The authors also discussed the impact of using the more liberal definition of hypopnoea from the 2012 AASM guideline instead of previous definitions, and measuring air flow reduction with nasal pressure sensors which can detect more subtle breathing variations than thermistors used in previous studies. The authors discussed the impact of using the more liberal definition of hypopnoea from the 2012 AASM guideline

these results indicate that the definitions provided by the AASM are too sensitive and may lead to frank over-diagnosis of OSAS. In fact, only a minority of participants in the Swiss population study presented symptoms.[18] In the multi-country study mentioned above, 15.7% of the Belgian population aged 30-69 years would have an AHI ≥ 15 event/hour, translating in 931 859 cases.[12] These figures seem clearly overestimated on clinical ground.

As such, lot of uncertainty remains around the actual disease prevalence of OSAS. Moreover, a substantial proportion of OSA cases detected by means of PSG are asymptomatic. For example, In the Swiss study cited above the proportion of symptomatic male participants with an ESS>10 or a Berlin score ≥ 2 was 14% and 31%, respectively.[18] There are thus various phenotypes of OSAS, which are not captured by the standard definition based on the isolated measurement of AHI or RDI.[20-22] Other indicators may be more appropriate. For example, it has been shown that longer obstructive sleep apnoea and hypopneas (but not AHI) is associated with higher odds of moderate-to-severe arterial hypertension.[23] Also, the hypoxic burden of sleep apnoea, rather than AHI, predicts cardiovascular mortality.[24] Obstructive sleep apnoea is a heterogeneous condition. In conclusion, there is a consensus around the rise of OSA prevalence as measured by the AHI index, mainly linked to the increase of obesity rate, but exact figures are difficult to assess and the clinical significance of an elevated AHI is unclear.[15] There are various OSA phenotypes, a minority of patients with an elevated AHI being symptomatic and little is known on their appropriate treatment.[15]

2.2.2 Association between AHI and clinical outcomes

2.2.2.1 Association with sleepiness

Although the arousals from sleep generally do not wake the patient, this sleep fragmentation is the primary cause of excessive sleepiness in individuals with OSAS.[6] Individuals with OSAS often feel unrested, fatigued, and sleepy during the daytime.[10] They may suffer from impairments in vigilance, concentration, cognitive function, social interactions and quality of life (QoL). These declines in daytime function can translate into higher rates of job-related and motor vehicle accidents. The latter has prompted specific legislative rules in some countries such as a ban on driving or handling large machines when OSAS is not under control.[25]

Sleepiness is not a requirement for diagnosis of OSA, as shown by the diagnostic criteria of the International Classification of Sleep Disorders, third edition (ICSD-3).[26] This definition which is not based on clinical symptoms poses problems in terms of clinical significance. Recent studies have shown that many of those diagnosed with OSA do not suffer from subjective sleepiness previously considered a cardinal symptom of OSA.[20, 27] Excessive sleepiness is reported by only 15% to 50% of people with OSA identified through general population screening.[6] There is a poor correlation between the level of sleep disordered breathing (SDB) based on AHI and symptom profile (particularly as measured by the Epworth Sleepiness Scale, ESS).[28-30] Moreover, standard polysomnographic baseline variables are poor predictors of the response to CPAP therapy.[31]

instead of previous definitions, and measuring air flow reduction with nasal pressure sensors which can detect more subtle breathing variations than thermistors used in previous studies.[18] Finally, 29% of participants declined to have PSG, which might have caused a significant selection bias.[18]

2.2.2.2 *Association with cardiovascular conditions*

The consequences of untreated OSAS are wide ranging and are believed to result from the fragmented sleep, intermittent hypoxia and hypercapnia, intrathoracic pressure swings, and increased sympathetic nervous activity that accompanies disordered breathing during sleep. Patients with untreated OSAS may be at increased risk of developing cardiovascular disease, including difficult to control blood pressure, coronary artery disease, congestive heart failure, arrhythmias and stroke.[10] OSAS is also associated with metabolic dysregulation, affecting glucose control and risk for diabetes. Persons with severe (AHI ≥30) or moderate to severe OSAS (AHI ≥15) die at about twice the rate of controls (HR=2.07; 95%CI, 1.48 to 2.91) when pooling data from multivariate analyses (6 studies with mean duration of follow-up ranging from 3.4 to 20 years).[8] Persons with severe or moderate to severe OSA have also increased cardiovascular mortality.

However, recent reports indicate that a significantly increased risk of co-morbidities is only evident in subjects with more severe SDB, calling into question the clinical significance of mild sleep apnoea as presently defined.[30] The association between OSAS and hypertension, cardiovascular diseases and mortality rate may vary with patient phenotype. For example, this association has been reported to be higher in younger subjects with OSA (men≤70 years),[32] and in those with excessive daytime sleepiness.[8] Obstructive sleep apnoea is a heterogeneous condition. Whether asymptomatic individuals bear the same morbidity burden as symptomatic ones and whether they should be treated in the same way is still unclear today.[33, 34] For example, there seems to be a relationship between OSA clinical phenotypes and CPAP treatment outcomes.[35]

There is also controversy in the literature regarding the extent to which OSAS independently contributes to various outcomes beyond the contributions of age (independently from BMI), BMI, and other potential confounders (e.g., physical activity, diet).[8, 9] Although the cohort studies controlled for many potential confounders, residual confounding due to health-related factors that are associated with OSA and that were generally not accounted for is possible.[8] Studies are also needed to evaluate whether improvement in AHI (for mild to severe OSA) leads to improvement in health outcomes. These represent critical gaps in the current evidence base.[9]

Although OSA is associated with adverse cardiovascular risk factors and increased risks of cardiovascular disease it remains unclear whether the most common therapy for OSA, positive airway pressure (PAP, see section 2.4.1) which provides symptomatic relief is also associated with cardiovascular outcomes and cardiac death.[36, 37] The largest of these studies included 10 RCTs and retrieved RCTs up to March 2017.[37] This study concluded that the use of PAP, compared with no treatment or sham, was not associated with reduced risks of cardiovascular outcomes or death for patients with sleep apnoea.[37] A very recent large RCT studied the effect of PAP treatment in non-sleepy acute coronary syndrome patients (EES score ≤ 10) with or without OSA (defined by AHI).[38] OSA patients were randomly assigned to CPAP or usual care and compared to a reference group of non-OSA patients. Among the non-sleepy patients, the presence of OSA was not associated with an increased prevalence of cardiovascular events and treatment with CPAP did not significantly reduce this prevalence.[38]

In conclusion, clinical outcomes traditionally associated with OSA are inconstantly observed, and when they are present the PAP treatment does not necessarily improves them.[15]

2.3 Diagnosis of OSAS

This section is mainly based on the systematic reviews by Kapur et al.,[10] Jonas et al.,[8, 9] and Abrahamyan et al. 2018,[39] the latter being only about portable monitors type IV. No systematic update of these reviews were carried out, as explained in section 1.2. These reviews form the basis of the AASM guidelines for OSAS diagnosis and screening in the USA and in many other countries.[8-10]

2.3.1 Screening for OSAS

Potential screening questionnaires and clinical prediction tools include the Epworth Sleepiness Score (ESS), STOP Questionnaire (Snoring, Tiredness, Observed Apnoea, High Blood Pressure), STOP-Bang Questionnaire (STOP Questionnaire plus BMI, Age, Neck Circumference, and Gender) developed for preoperative screening, Berlin Questionnaire developed for use in the primary care setting, Wisconsin Sleep Questionnaire, and the Multivariable Apnoea Prediction (MVAP) tool.[10] In the presence of symptoms (see below), these screening tools can be used to assess the pre-test probability of individuals who should undergo a diagnostic polysomnography (PSG) or a polygraphy (PG).[10] Although none of these instruments have been adequately validated in a primary care setting,[9] they are simple to administer and can be used in any setting. Reviewing these questionnaires in detail was beyond the scope of this report.

On the basis of a thorough systematic review, the US Preventive Services Task Force concluded that the evidence was insufficient to assess the balance of benefits and harms of screening for OSA in asymptomatic adults or adults with unrecognized symptoms.[8, 9] However, screening may be appropriate in individuals whose occupation involves driving or in patients with resistant hypertension.[6] Testing the presence of OSAS should be done, after a thorough sleep history, in adult patients presenting with signs and symptoms that indicate an increased risk of moderate to severe OSA. These are excessive daytime sleepiness combined with at least two of the following three criteria: habitual loud snoring, witnessed apnoea (or gasping or choking), or diagnosed hypertension.[10] Habitual snoring would be present in 50% to 60% and witnessed apnoeas during sleep in 10% to 15% of cases.[6] OSAS would be present in 73% to 82% of individuals with resistant hypertension, 76%to 85% of individuals with atrial fibrillation, 65% to 85% of individuals with type 2 diabetes, 71% of individuals with stroke, and 71% to 77% in patients undergoing bariatric surgery.[6] It is also important that other aspects of a sleep history be collected, as many patients suffer from more than one sleep disorder or present with atypical sleep apnoea symptoms. A thorough physical examination that includes the respiratory, cardiovascular, and neurologic systems, is also needed, to detect medical conditions associated with increased risk for OSAS, such as obesity, hypertension, stroke, and congestive heart failure.[6, 10]

2.3.2 Polysomnography-based diagnosis

The reference standard test used to diagnose OSAS is overnight polysomnography (PSG) conducted in a sleep laboratory, supervised by a qualified sleep technician and with an analysis under the responsibility of a sleep specialist physician.[10, 30, 40] The PSG reports on several physiologic parameters captured through seven or more recording channels (see Table 2). The main diagnostic parameter calculated based on PSG is the apnoea-hypopnoea index (AHI). As already mentioned, the diagnosis of OSAS is made if the AHI is ≥ 5 events/h for patients reporting symptoms (e.g., daytime sleepiness, snoring) or ≥15 events/h, regardless of symptoms.[10]

Although considered the gold standard for OSA diagnosis, PSG suffers from two unresolved and potentially important limitations:

1. The sensitivity of PSG to detect patients in need of treatment is likely to vary with OSAS phenotypes. A high AHI may not be related to significant clinical symptoms but other patients with a relatively low AHI may be very symptomatic (see section 2.2.2). Therefore, PSG may result in either over-diagnosing non-clinically significant sleep disorders or in under-diagnosing syndromes with serious morbidities. This is the reason why the assessment of OSAS severity should not be based on AHI alone, but take into account both the level of SDB and symptom profile, and possibly also related co-morbidities such as systemic hypertension, especially where associated with a nocturnal non-dipping blood pressure profile.[10, 30] Patients presenting

with relatively mild OSAS based on AHI but who are very symptomatic may be given a trial therapy with CPAP, typically for two months, and further management decisions are then guided by the clinical response to this trial. In this context, the CPAP trial forms part of the diagnostic process rather than an active management decision.[30] For example the Dutch updated guidelines[a] use this approach.

2. Night-to-night variability of SDB complicates the diagnosis, especially in the mild category.[30] The current guidelines presuppose that the number of obstructive events is consistent in consecutive nights. However, considerable variability on repeated measurements has been found. This is as true for lab-based PSG,[41-43] as for other types of monitors.[44-47b] In contrast, a meta-analysis of four studies comparing AHI data between 2 consecutive nights of PSG found no statistically or clinically significant differences.[10] Nonetheless, a subset of individuals had considerable night-to-night variability in their AHIs. Using an AHI cut-off of ≥ 5 to diagnose OSA, three of the studies identified that 9.9% to 25% of subjects had an AHI < 5 on the first PSG but an AHI ≥ 5 only on the second one. Likewise, using an AHI cut-off of ≥ 15 or 20 as a potential treatment threshold, two of the studies observed that 7.6% and 25% of subjects crossed this threshold only on the second study. OSA severity was also noted to vary in a subset of subjects with 26% to 35% changing the severity classification of their OSA (in either direction) on the two nights, though the majority were a shift of a single category (e.g., mild to moderate). The quality of evidence for night-to-night variability was high, but there was limited evidence from which to assess the efficacy of single-night PSG versus two-nights PSG.[10] Thus in that meta-analysis, a second night of PSG in symptomatic patients allows for the diagnosis of OSA in 8% to 25% of patients with initial false negative studies. When the initial PSG is negative and there is still clinical suspicion for OSA, the AASM suggests that a second PSG be considered for the diagnosis of OSAS (weak recommendation, very low evidence quality).[10] However, routinely repeating a PSG in patients with an initial negative PSG has potential downsides. There is a risk that repeat testing could lead to false positive cases being identified, and unnecessarily treated. In addition, the routine use of a two-night study protocol would cause inconvenience to the patient, increased utilization of resources and healthcare costs, and perhaps even delays in the care of other patients awaiting PSG.[10]

2.3.3 HSAT-based diagnosis

2.3.3.1 Evidence review

Home sleep apnoea testing (HSAT) is intended to offer a more patient-centred approach by permitting a simplified home sleep testing in a more familiar and comfortable setting, at lower front costs and shorter waiting times than PSG.[39, 48]

HSAT can be done with portable monitors (PM). The sleep monitors are classified as type I–IV where PSG is a type I device for in-laboratory PSG testing, and type II–IV are portable sleep monitors for PG.[c10] A type II portable monitor (PM) is a full unattended portable PSG (≥ 7 channels), i.e. the same monitoring sensors as full PSGs (Type I) but without video and audio surveillance are used (see Table 2). Type III monitors have four to seven channels but no EEG, and measure limited cardiopulmonary

[a] https://www.nvalt.nl/kwaliteit/richtlijnen/slaap/_/Slaap/Richtlijn%20OSA%20bij%20volwassenen%20%28geaccordeerd%20april%202018%29.pdf

[b] The study by Stoberl et al. is based on ambulatory studies and based on using nocturnal oximetry. The main outcome of interest was the coefficient of variation (CV) of the oxygen desaturation index (ODI; ≥4% dips per h) as a measure of variability of OSA severity during 2 weeks of CPAP-withdrawal.

[c] This classification of sleep study devices fails to consider new technologies, such as peripheral arterial tonometry (PAT), and thus an alternative classification scheme has been proposed: the SCOPER classification, which incorporates Sleep, Cardiovascular, Oximetry, Position, Effort and Respiratory parameters. The SCOPER system allows for the inclusion of technologies such as PAT, but it is not yet widely used by clinicians.[10]

parameters: two respiratory variables (e.g. effort to breathe, airflow), oxygen saturation, and a cardiac variable (e.g., heart rate or electrocardiogram). Type IV monitors have one to three channels measuring only 1 or 2 parameters, typically oxygen saturation and heart rate, or in some cases, just air flow.[10] A major limitation of type III and type IV PMs is their inability to distinguish between the sleep and the wake periods since they do not include an EEG. Consequently they report only REI.[10] Only type II monitors can record AHI and make the distinction between various sleep problems.

Table 2 – Classification of monitors used for diagnosis of obstructive sleep apnoea

Type of PM	Nb. channels	Typical parameters	Measures AHI	Used in Belgium
I (facility-based)	≥ 7 (12-16)	EEG, EOG, EMG, ECG/heart rate, airflow (nasal, oral, or both), respiratory effort (thoracic or abdominal movement), SaO2, body position, leg movement, snoring. In addition, audio and video monitoring and registration is used.	Yes	Yes
II (portable)	≥7	EEG, EOG, EMG, ECG or heart rate, airflow, respiratory effort (thoracic or abdominal movement), SaO2	Yes	Yes
III (portable)	≥4 (4-7)	Ventilation, airflow, or both; respiratory effort (thoracic or abdominal movement); ECG or heart rate; SaO2	No (REI)	Yes
IV (portable)	≥1 (1-3)	Usually SaO2; may include additional channels, provided the monitor does not qualify as type III, i.e. Jaws Activity (JAWAC), PAT	No (REI)	Yes

AHI, apnoea-hypopnea index; ECG, electrocardiogram; EEG, electroencephalogram; EMG, electromyogram; EOG, electro-oculogram; PAT: Peripheral Arterial Tone; PM: portable monitor; SaO2, arterial oxygen saturation.

The diagnostic performance of portable monitors against lab-based PSG were assessed in three systematic reviews: Kapur et al. 2017,[10] Jonas et al. 2017,[8] and Abrahamyan et al. 2018 (only portable monitors type IV).[39] Quality appraisal of these reviews was based on the AMSTAR-2 checklist (A MeaSurement Tool to Assess systematic Reviews).[49] Methods of the three reviews are presented in Table 3. Table 4 to Table 6 report the sensitivity and specificity of the various types of PMs in those three reviews.

Table 3 – Methods of the three systematic reviews on diagnosis performance of portable monitors

Authors	Publication years covered	Databases searched	Quality appraisal tool	Quality of evidence	Comments	AMSTAR-2
Kapur et al. 2017[10]	June 2016	Medline (PubMed) Embase	GRADE QUADAS-2	See Table 4 for quality per outcome	The much lower number of studies included in comparison with Jonas et al. 2017[8] is probably due to the exclusion of studies on PM used in-lab	Moderate
Jonas et al. 2017[8]	October 2015	Medline (PubMed) Cochrane Library Embase CT.gov and ICTRP	USPSTF	Fair to Good	Small total sample size (PM type II), missing data (PM types II and IV), and some lack of independent scoring of portable monitor and polysomnography results (types II and IV) Heterogeneity of scoring criteria or methods and portable monitor Heterogeneity of results across portable monitor settings (laboratory, home) and for more severe OSA (PM type III) Reporting bias not detected	High
Abrahamyan et al. 2018[29]	January 2010 to May 2016	Medline (Ovid) Cochrane Library	QUADAS-2	Risk of bias in more than 40% of the studies	Only studies on Portable Monitor type IV were reviewed Many of the studies presented methodological flaws: no random order of the tests, no blinded assessment of performances of the devices, substantial proportion of patients excluded for technical failure or other errors varying from 0 to 25%, and poor reporting quality	High

AMSTAR: A MeaSurement Tool to Assess systematic Reviews; CT.gov: Clinical Trials.gov; GRADE: Grading of Recommendations Assessment, Development and Evaluation; ICTRP: WHO International Clinical Trials Registry Platform; QUADAS-2: Quality Assessment of Diagnostic Accuracy Studies-2; USPSTF: U.S. Preventive Services Task Force.

The review by Kapur et al. 2017 excluded studies where HSAT was used in-lab,[10] the review by Abrahamyan et al. 2018 included only studies with type IV PM,[39] whereas the review by Jonas et al. 2017 was much more inclusive than the two previous ones.[8] Although methods and results differ to some extent between these three systematic reviews (see Table 3), all three reported wide variations of sensitivity and specificity from study to study. For example, in Kapur et al. the sensitivity and specificity of type III PMS for detecting AHI ≥15 was 62% to 94% and 25% to 97%, respectively.[10] The corresponding results were 49% to 92% and 79% to 97%, respectively, in the systematic review by Jonas et al. 2017.[8] Results were inconsistent and imprecise for type IV PMs.[8] However, the accuracy or the Area Under the Curve (AUC) was high with a lower bound of the range being above 80% for nearly all types of PM at the cut-offs of ≥5 AHI per hour or ≥15 AHI per hour.[1] Sensitivities decreased and specificities increased for detecting moderate or severe OSA (AHI≥15) or severe OSA (AHI ≥30). As for PSG, there was sparse data on reliability of PMs.[1]

Based on the review by Kapur et al. 2017,[10] the AASM **supports the use of PSG or HSAT with a technically adequate device in uncomplicated patients with moderate to high risk of OSAS** (strong recommendation, moderate evidence quality). The formulation of these recommendation statements was guided by evidence from the 26 validation studies that evaluated the diagnostic accuracy of HSAT against PSG (see Table 4). The authors also based their recommendation on the results of 7 RCTs that compared clinical outcomes from different management pathways[a], one of which was the application of a PSG confirmation for patients in whom HSAT did not establish an OSAS diagnosis. In those trials, the use of HSAT has not been demonstrated to provide inferior clinical benefit compared to PSG when used in the appropriate context in terms of subjective sleepiness, quality of life and CPAP adherence.

Specifications of the AASM recommendation are as follows:

- A technically adequate HSAT device[b] incorporates a minimum of the following sensors: nasal pressure, chest and abdominal respiratory inductance plethysmography, and oximetry; or peripheral arterial tonometry (PAT) with oximetry and actigraphy. Therefore, the AASM guideline supports HSAT only with type II or type III devices.
- A technically adequate diagnostic test includes a minimum of 4 hours of technically adequate oximetry and flow data, obtained during a recording attempt that encompasses the habitual sleep period[c].
- An increased risk of moderate to severe OSAS is indicated by the presence of excessive daytime sleepiness and at least two of the following three criteria: habitual loud snoring, witnessed apnoea or gasping or choking, or diagnosed hypertension[d].

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[a] The four RCTs that were most generalizable to clinical practice administered HSAT at academic or tertiary sleep centers with highly skilled sleep medicine providers and technical staff. HSAT recordings were reviewed by a sleep medicine specialist.

[b] Among the four RCTs that were most generalizable to clinical practice, three used conventional Type III devices (nasal pressure, thoracic and abdominal excursion using RIP technology, oxygen saturation, EKG, body position, and oral thermistor in some cases) and one used a 4-channel device based on PAT with three additional channels (heart rate, pulse oximetry, and actigraphy). Additional guidance on technical specifications regarding HSAT is provided in the AASM Manual for the Scoring of Sleep and Associated Events.

[c] Overall, the body of evidence investigating the minimum number of hours of adequate data on HSAT required to accurately diagnose OSA is very limited. There are no data to suggest that fewer than 4 hours of technically adequate recording compromises the accuracy of test results, and there is no direct evidence on the impact of a minimum number of recording hours of HSAT on clinical outcomes.

[d] These three signs are based on inclusion conditions for the four RCT most generalizable to clinical practice.

- An uncomplicated patient is defined by the absence of:
    1. Conditions that place the patient at increased risk of non-obstructive sleep-disordered breathing (e.g., central sleep apnoea, hypoventilation and sleep related hypoxemia). Examples of these conditions include significant cardiopulmonary disease, potential respiratory muscle weakness due to neuromuscular conditions, history of stroke and chronic opiate medication use[a].
    2. Concern for significant non-respiratory sleep disorder(s) that require evaluation (e.g., disorders of central hypersomnolence, parasomnias, sleep related movement disorders) or interfere with accuracy of HSAT (e.g. severe insomnia).
    3. Environmental or personal factors that preclude the adequate acquisition and interpretation of data from HSAT.

The AASM further recommends:

In patients with significant comorbidities (i.e. 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), **only PSG should be used** (strong recommendation, very low evidence quality).[10] This recommendation is based on the limited data available regarding the validity of HSAT in such patients (three validation studies). The overall quality of evidence was very low due to imprecision, indirectness, and risk of bias. The likelihood of non-obstructive sleep-disordered breathing should be considered by the clinician, when determining which types and severity of cardiorespiratory diseases may be inappropriate for HSAT.

The AASM recommends that **in patients with negative HSAT, performing a confirmatory PSG is recommended[b]** since REI tends to underestimate the true AHI (strong recommendation, low quality evidence).[10] This recommendation is based on two elements:

- The included RCTs on the clinical benefits of using HSAT vs. PSG used HSAT in the context of a management pathway that required PSG confirmation for patients in whom HSAT did not establish an OSA diagnosis. Therefore, there is no evidence available on the clinical adequacy of two consecutive HSAT.
- The authors of the review speculate that a negative HSAT will result in a higher likelihood that a second HSAT test will also be negative, inconclusive or technically inadequate.[10]

[a] The absence of such pathologies were the inclusion conditions for the four RCT most generalizable to clinical practice.

[b] The authors of the review recognize that there may be specific circumstances in which repeat HSAT is appropriate after an initial failed HSAT. These circumstances would include cases in which both of the following are present: the clinician determines that there is a high likelihood of successful recording on a second attempt, and the patient expresses a preference for this approach.

Table 4 – Accuracy of Portable Monitors against lab-based PSG (review by Kapur et al. 2017)

Type of PM	Number of studies/participants	AHI per hour	Prevalence* of OSAS	Sensitivity range	Specificity range	Accuracy range	FN per 1000	FP per 1000	Evidence quality
Type II	2/116	≥5	87%	0.88 to 0.97	0.50 to 0.56	84% to 91%	26 to 104	57 to 65	High
	2/116	≥15	64%	0.94 to 0.95	0.76 to 0.77	88% to 88%	32 to 38	83 to 86	High
Type III	7/1001	≥5	87%	0.90 to 1.00	0.30 to 0.67	84% to 91%	0 to 87	43 to 91	Moderate[a]
	6/457	≥15	64%	0.62 to 0.94	0.25 to 0.97	65% to 91%	38 to 243	11 to 270	Moderate[b]
Type IV 2-3 channels	3/292	≥5	87%	0.80 to 0.96	0.65 to 0.83	81% to 93%	35 to 174	22 to 45	Moderate[c]
	5/443	≥15	64%	0.66 to 0.88	0.62 to 1.00	72% to 87%	77 to 218	0 to 137	Moderate[d]
Type IV 1 channel	1/100	≥5	87%	0.96	0.82	94%	35	23	Moderate
	4/235	≥15	64%	0.55 to 0.91	0.70 to 0.82	60% to 88%	58 to 288	65 to 108	Moderate[e]

** Prevalence in the population under study as determined by PSG. AHI: Apnoea Hypopnoea Index; FN: False Negative; FP: False Positive; PM: Portable Monitor; PSG: Polysomnography. All results are from Kapur et al. 2017.[10]*

Table 5 – Accuracy of Portable Monitors against lab-based PSG (review by Jonas et al. 2017)

Type of PM	Number of studies/participants	AHI per hour	Prevalence* of OSAS	Sensitivity range	Specificity range	AUC	FN per 1000	FP per 1000	Evidence
Type II	3/160	≥5	?	0.88 to 0.96	0.50 to 0.84	0.86 to 0.90	?	?	?
	3/160	≥15	?	0.85 to 0.94	0.77 to 0.95	0.89 to 0.94	?	?	?
Type III	21/1691	≥5	?	0.87 to 0.96	0.60 to 0.76	0.89 to 0.96	?	?	?
	21/1691	≥15	?	0.49 to 0.92	0.79 to 0.97	0.85 to 0.97	?	?	?
Type IV	81/8231	≥5	?	0.65 to 1.00	0.35 to 1.00	NR	?	?	?
	81/8231	≥15	?	0.07 to 1.00	0.15 to 1.00	NR	?	?	?

** Prevalence in the population under study as determined by PSG. AHI: Apnoea Hypopnoea Index; AUC: Area Under the Curve; FN: False Negative; FP: False Positive; PM: Portable Monitor. PSG: Polysomnography. All results are from Jonas et al. 2017.[8]*

[a] Wide range of values for specificity

[b] Wide range of values for sensitivity and specificity

[c] Wide range of values for sensitivity

[d] Wide range of values for sensitivity and specificity

[e] Wide range of values for sensitivity

Table 6 – Accuracy of Portable Monitors type IV against lab-based PSG (review by Abrahamyan et al. 2018)

Type of PM	Number of studies/participants	AHI per hour	Prevalence* of OSAS	Sensitivity range	Specificity range	Accuracy range	FN per 1000	FP per 1000	Evidence
Type IV 1 channel	13/?	≥5	?	0.68 to 1.00	0.43 to 0.97	?	?	?	?
	13/?	≥15	?	0.65 to 1.00	0.58 to 0.98	?	?	?	?
Type IV 2 channels	2/?	≥5	?	0.77 to 0.93	0.83 to 0.92	?	?	?	?
	2/?	≥15	?	0.66 to 0.74	0.25 to 0.97	?	?	?	?
Type IV ≥3 channels	3/?	≥5	?	0.96 to 1.00	0.65 to 0.83	?	?	?	?
	3/?	≥15	?	0.66 to 0.88	0.62 to 1.00	?	?	?	?

** Prevalence in the population under study as determined by PSG. AHI: Apnoea Hypopnoea Index; FN: False Negative; FP: False Positive; PM: Portable Monitor; PSG: Polysomnography. All results are from Abrahamyan et al. 2018.[39]*

In Belgium, the type IV Brizzy (Nomics), which measures mandibular movements, seems to be used in many instances, at least for screening patients and selecting those who should undergo a hospital-based PSG for diagnosis confirmation (400 devices sold up to 2020 with 4400 sleep studies performed in the year 2019; personal communication Didier Leclercq). Therefore, we did a rapid review of the evidence on the performance of portable monitors relying on the measurement of mandibular movements. Methods, tables with quality appraisal and results can be found in Appendix 2. Accuracy of the devices reviewed seems high. But again, number of studies was low (one per device) and confirmatory studies are needed.

There are many other portable monitors used in Belgium, and the same kind of evidence review should be carried out when one specific model and brand is considered for medical use and accreditation by the health authorities. This is beyond the scope of the current project.

2.3.3.2 Discussion

Severity of OSA is mainly defined on the AHI score (see section 2.2.2). However, there has been recently a strong questioning of the significance of AHI as a marker of OSA and of clinical OSA severity.[15] In some instances, the definition or recording methods of the AHI have been adapted to meet specifications issued by stakeholder parties.[15] There are various phenotypes of OSA patients, some of them displaying very few or no symptoms. However, the AHI has no discriminatory power to differentiate clinical subtypes from one another.[22] Moreover, AHI values depends on the characteristics of the assessment procedures. Therefore, PSG may result in either over-diagnosing non-clinically significant sleep disorders or in under-diagnosing syndromes with serious morbidities.

If AHI may not be a real marker of clinical disease, this bears three major consequences. First, when OSA is defined as an AHI ≥ 15/h, the prevalence of OSA is amazingly high in the population as demonstrated by a survey in a representative sample of the general population in which 23.4% in women and 49.7% in men in Switzerland.[18] However, only a minority of participants in that survey presented symptoms. The percentage of OSAS patients was even higher when the criterion of AHI≥ 5/h and symptoms was used.[19] These

results indicate that the definitions provided by the AASM are too sensitive and may lead to frank overdiagnosis of OSAS.

Second, AHI is not an appropriate indicator for screening for OSA in asymptomatic patients. This is why the US Preventive Services Task Force recommends to not screen asymptomatic patients or adults with unrecognized symptoms.[8, 9 6] Testing the presence of OSAS should be done, after a thorough sleep history, in adult patients presenting with signs and symptoms that indicate an increased risk of moderate to severe OSA. These are excessive daytime sleepiness combined with at least two of the following three criteria: habitual loud snoring, witnessed apnoea (or gasping or choking), or diagnosed hypertension.[10] The assessment of OSAS severity should not be based on AHI alone, but take into account both the level of SDB and symptom profile, and possibly also related co-morbidities such as systemic hypertension, especially where associated with a nocturnal non-dipping blood pressure profile.[10, 30]

Third, it is not unexpected that clinical trials including subjects with an AHI ≥ 15/h as the major selection criterion demonstrated inconsistent outcome effects (see section 2.2.2 and section 2.4.1). On the contrary, patients presenting with relatively mild OSAS based on AHI but who are very symptomatic may be given a trial therapy with CPAP, typically for two months, and further management decisions are then guided by the clinical response to this trial. In this context, the CPAP trial forms part of the diagnostic process rather than an active management decision.[30] Treatment responsiveness should be the real target of OSA care. This purpose could be formulated as a requirement for continuing treatment and its reimbursement.[15]

In conclusion, more research to determine the diagnostic criteria for OSA is required to include factors that reflect different clinical and pathophysiological phenotypes and relevant comorbidities.[34]

HSAT with portable monitors is an attractive diagnosis strategy intended to offer a more patient-centred approach.[39, 48, 50] A major limitation of type III and type IV PMs is their inability to distinguish between the sleep and the wake periods since they do not include an EEG. Consequently they report only REI and they are unable to detect comorbid sleep disorders such as insomnia.[10] Standard PSG and PG yield different AHI values because not only the scoring of hypopnoeas is different, but also because the former has the total sleep time in the denominator, whereas the latter figures the total recording time).[51] Overall, patients investigated using PG are likely to have a 30% lower AHI on average, compared to patients investigated by PSG.[51]

Notwithstanding, based on the review by Kapur et al. 2017,[10] the AASM supports the use of HSAT with a technically adequate device in uncomplicated patients with moderate to high pre-test risk of OSAS (strong recommendation, moderate quality evidence) The range of sensitivity and specificity in type II and type III PMs overlap widely, and any type of portable monitors is recommended by the AASM for HSAT. However, type II monitors are the only ones able to measure AHI and offer the advantage to be a comprehensive study sleep, allowing not only OSA diagnosis but also several other sleep disorders diagnosis.

The AASM recommends performing a confirmatory PSG in patients with a negative HSAT (strong recommendation, low quality evidence). The limitations imbedded in these recommendations are mostly due to the absence of evidence and not to evidence of inappropriateness. The consequences of such an approach need consideration.

First, even in a population with high pre-test probability (i.e. 80 % of patients having an AHI≥15/h), the strategy of the AASM would result in a retest PSG in more than 20% of the patients even with an excellent test (95% sensitivity and 95% specificity). A multicentric study assessed the results of a strategy where patients with high clinical probability of OSAS were diagnosed by HSAT, and the remainder by lab-based PSG.[52] Patients with a high pretest probability of OSAS represented 55% of the study population (202/366). The authors reported that a confirmatory PSG was needed in 39% (78/202) of patients diagnosed primarily by HSAT. Of note, a HSAT with a positive results (AHI ≥ 10/h) was also assessed by a specialist in sleep medicine and the majority of the retest PSG was retest at that level. The costs of the HSAT was reduced by 20% in comparison with a strategy where PSG is applied in any patient. Interestingly, with a strategy where all patients were tested by HSAT (i.e. without considering pre-test probability), a retest PSG was needed in 57% of the cases,

but still the cost was 18% lower than a strategy with generalized diagnostic strategy.[52]

Studies showed that type II monitors can exhibit a better sensitivity range, i.e. resulting in less false negative results and therefore less subsequent retesting.[8-10] Such monitors can also be used in patients with comorbidities.[6, 50, 53] Moreover, a better understanding of factors associated with inadequate or failed HSAT could help to optimize efficiency of care with regard to choosing the most appropriate diagnostic method for a given patient and clinical situation.[10]

Second, the recommended strategy of not retesting the patients with a positive HSAT does not take into account the false positive HSAT and the subsequent inappropriate treatments (actually, the sensitivity is consistently higher than the specificity) and waste of resources. This said, if the HSAT is applied in a population with high pre-test risk of OSA, as recommended by the AASM, the positive predictive value will be high and the proportion of false positive reduced.

It has been argued that Type II monitors could prevent from repetitive testing of patients in borderline diagnosis situations (grey zone) as it allows the correct assessment of hypopnea and displays a relatively low failure rate.[50] Moreover, it was demonstrated that Type II recording's quality is similar if hook-up is performed at home or in the hospital, allowing simplification of the technique and avoiding sleep technician's displacements from the hospital to patient's home.[54] These advantages of Type II monitors indicate that such portable monitors could be a first choice to perform HSAT. However, it has also been suggested that Type II HSAT is an interesting option in patients with negative Type III sleep testing.[50]

Sequential HSAT might another approach to limit the need for confirmatory PSG.[47] For example, it can be computed that with a pre-test probability of OSAS at 47%, a positive likelihood ratio (LR+) at 8.46% and a negative likelihood ratio (LR-) at 0.11%, corresponding to a sensitivity and specificity of around 90% (see Appendix 2 for an example),[55] 5% of all tests would be false negative and 6% false positive. A positive test would result in a post-test probability of 88% (95% CI: 77%; 94%), and a negative test in a post-test probability of 9% (95% CI: 4%; 19%). A positive retest in those with a first positive test would result in a post-test probability of 98% (95% CI: 92%; 100%) (1% false positive). A negative re-test in those with a first negative test would result in a post-test probability of 1% (95% CI: 0%; 7%) (1% false negative). Such a pathway reduces greatly false positive tests with HSAT, reduces greatly the chance of denying treatment to patients with OSAS, and reduces the utilization of resources in comparison with a systematic PSG in all patients (current situation in Belgium) or a PSG in case of a negative HSAT (recommendation of the AASM). However, such a pathway needs to be tested in adequate studies. These simulations make sense only if the test re-test of the device is high (which is most of the time not reported) and study results are unbiased. More research is needed to assess the validity of such an approach. Of note, recording HSAT over two nights to increase diagnosis accuracy is already practiced in England (see section 3.1.2) Another approach in case of negative HSAT in individuals with high pre-test probability of OSAS would be to do a cPAP trial.[30] Our international comparison of OSAS diagnosis strategies reported that this is sometimes practised in Finland (see section 3.1.2).

HSAT is recommended in uncomplicated patients with moderate to high pre-test risk of OSAS.[10] However, high diagnostic accuracy has also been reported in patients with only moderate suspicion of OSA or with comorbid obstructive lung disease or heart failure.[6] More research evaluating HSAT devices in more diverse patient populations.

A number of limitations may impact the applicability of the evidence on portable monitors:

- Many different types of portable devices were tested. For example, Abrahamyan et al.[39] retrieved 24 studies published between 2010 and 2016 testing ten different types of Type IV PMs. The number of studies and the number of patients evaluated for one specific type of PM is therefore usually low, which render the evaluation of its performance difficult.

- The range of sensitivities and specificities is wide for Type III and Type IV PMs making general conclusions on performance difficult. Part of this inconsistency between studies might be due to the great number of different PMs tested. Another source of imprecision might be due to variations in study populations (countries, age, gender, BMI and comorbidity profile).
- The quality of evidence may be affected by methodological flaws. In the review by Abrahamyan et al.,[39] a risk of bias was detected in more than 40% of the studies (no random order of the tests, no blinded assessment of performances of the devices, substantial proportion of patients excluded for technical failure or other errors varying from 0 to 25%, and poor reporting quality).
- The majority of devices were tested in a hospital setting. Only 29% of studies testing type IV monitors were tested in the home setting.[39] Thus the applicability of those results to a home setting is very limited. However, the review by Kapur et al. 2017 was restricted to studies on home-based HSAT.[10]
- The reviews included studies up to year 2015 or 2016. Therefore evidence on more recent PMs with potentially better performance results was not included. We did an update for type IV PMs relying on the registration of mandibular movements. The same limitations were observed: very limited number of studies for a given PM, hospital setting, and no reliability results (see Appendix 2).

Although the recommendation of the AASM to use HSAT for OSAS diagnosis in uncomplicated patients should be encouraged, it is impossible to recommend the utilization of one specific PM, given these limitations.

Future research should also focus on evaluating HSAT devices in patients with different pre-test probabilities for OSAS. AASM recommends that prediction questionnaires should not be used in isolation for diagnostic purposes. But they do not question their role in screening. The first step of ruling out OSA requires a test with the highest possible sensitivity. For instance, the STOP-BANG has a sensitivity of 93% for AHI≥5, 95% for AHI≥15, and 94% for AHI≥30, as measured by PSG (meta-analysis of 9 studies).[10] Applying HSAT in such high risk population would increase greatly the positive predictive value. However, there is no consensus on the evaluation of the disease probability.[51]

2.4 Treatment of OSAS

2.4.1 Positive Airway Pressure

PAP is currently the primary therapy used to treat adult OSAS across the spectrum of disease severity.[2] This form of treatment applies a continuous positive pressure throughout the respiratory cycle to splint the airway open.

A good-quality systematic review (search strategy until October 2013, with last update in February 2018) was published recently and served as the basis for the elaboration of recommendations by the AASM.[2, 56] Another systematic review by Jonas et al. 2017 was identified (search strategy until October 2015, last surveillance in October 2016).[8, 9]

The main findings are qualitatively similar between the two reviews, i.e. the estimate of the effect size may vary somewhat but the direction and the overall strength of the various associations are consistent. Therefore, we summarized hereunder only the evidence reviewed by Patil et al. as this is the most recently updated one,[2, 56] and cross-checked it with findings by Jonas et al. 2017.[8, 9]

A total of eighty RCTs investigated the use of PAP to improve one or more of the following outcomes: OSA severity, sleepiness, quality of life (QoL), sleep quality, mood, neurocognitive function, motor vehicle crashes, blood pressure, left ventricle ejection fraction, fasting glucose, haemoglobin A1c, incident cardiovascular events, and incident mortality. Participants in the studies were from clinic-based populations and were predominantly male, obese, with moderate to severe OSA and self-reported sleepiness. Participants were randomized to a control intervention which could be sham CPAP, conservative measures or no intervention, sham surgery, placebo tablet, or nasal dilator strips.[2, 56] A statistical significance of a difference between intervention and control groups does not necessarily imply that the difference is clinically meaningful. Clinical significance thresholds were set

at: ≥15 AHI/h for OSAS severity; 2 points on the EES for self-reported sleepiness; 0.2 standardized mean difference (SMD) on the Maintenance of Wakefulness Test (MWT) or the Oxford Sleep Resistance Test (OSLER) sleep latency for objective wakefulness; 0.2 SMD on the Calgary Sleep Apnoea QoL Index (Sleep Apnoea Quality of Life Index – SAQLI) and the Functional Outcomes of Sleep Questionnaire (FOSQ), and 3 points on the SF-36, for quality of life; 1 mmHg for diastolic blood pressure and 2 mmHg for systolic blood pressure. When the difference is both statistically and clinically significant, we refer in the text to a clinically significant difference.

1. OSA severity

A meta-analysis of eleven RCTs demonstrated a clinically significant mean difference in OSAS severity of −23 events/h (95% CI: −29 to −18 events/h) with PAP compared to controls. An additional meta-analysis of these studies comparing OSA severity before and after PAP treatment demonstrated a clinically significant mean reduction in OSA severity of −29 events/h (95% CI: −37 to −20 events/h) or an AHI reduction of 86% with PAP. Overall, the analyses support the conclusion that CPAP is effective in reducing OSA severity as measured by the AHI or RDI, across the spectrum of OSAS severity. The quality of evidence for OSAS severity was high.[2, 56]

2. Sleepiness

A meta-analysis of 38 RCTs demonstrated a statistically significant reduction in self-reported sleepiness of −2.4 points in the ESS score (95% CI: −2.8 to −1.9 points) in participants on PAP compared to controls. A meta-analysis of seven RCTs using the Maintenance of Wakefulness Test (MWT) or Oxford Sleep Resistance Test (OSLER) sleep latency to assess objective wakefulness demonstrated a clinically significant SMD in objective sleepiness of 0.5 (95% CI: 0.2 to 0.8) with the use of PAP. In contrast, a meta-analysis of seven RCTs using the Multiple Sleep Latency Test (MSLT) to assess objective sleepiness demonstrated no clinically significant difference in sleep latency with the use of PAP. Overall, the authors concluded that the analyses support the conclusion that treatment of OSAS with PAP results in clinically (and statistically) significant improvements in self-reported sleepiness and the ability to maintain wakefulness. The overall quality of evidence for sleepiness was high.[2, 56]

3. Quality of life

A total of nineteen RCTs investigated the efficacy of PAP to improve Quality of Life (QoL) in adults with OSA. Meta-analyses of sleep-related QoL as assessed by the Calgary Sleep Apnoea QoLIndex (SAQLI) and the Functional Outcomes of Sleep Questionnaire (FOSQ), demonstrated a statistically significant improvement with SMD of 0.3 (95% CI: 0.1 to 0.5). However, meta-analyses of global QoL, as assessed by the SF- 36 component scores, demonstrated no clinically significant improvement (In Jonas et al. 2017, there was a SMD of 2.3 (95% CI: 0.2; 4.4) only on the SF-36 physical component score).[8] Overall, the analyses suggest that PAP is effective in improving sleep-related QoL, but not overall QoL in adults with OSA. The overall quality of evidence, based on the critical outcome of sleep-related QoL, was moderate due to imprecision.[2, 56]

4. Blood pressure

A total of 26 RCTs measured blood pressure (BP) before and after PAP therapy initiation. PAP therapy was associated with a statistically significant reduction in 24-hour systolic BP and diastolic BP of −1.5 mmHg (95% CI: −2.3 to −0.7 mmHg) and −1.6 mmHg (95% CI: −2.2 to −0.9 mmHg), respectively. There was also a clinically significant reduction in 24-hour mean BP of −2.6 mmHg (95% CI: −3.9 to −1.4 mmHg) with PAP therapy.[a] The quality of evidence for BP in all participant types with OSAS ranged from moderate to high, depending on the time and type of BP measured, and was downgraded due to imprecision.[2, 56]

[a] 24-hour (or 48-hour) ambulatory BP measurements is considered to be the most accurate method to diagnose hypertension and the best predictor of future cardiovascular risk.

5. Fasting glucose and haemoglobin A1c

A total eight RCTs assessed fasting glucose before and after 6 to 12 weeks of PAP therapy in primarily obese, male participants. The efficacy of PAP in reducing HbA1c in adults with OSA was evaluated using a meta-analysis of four RCTs. Overall, analyses did not support that PAP reduces fasting glucose or HbA1C in adults with OSA with or without type 2 diabetes mellitus. The quality of evidence for the efficacy of PAP to reduce fasting glucose and haemoglobin A1c was high in finding no clinically significant reduction.[2, 56]

6. Cardiovascular events

Six RCTs assessed the impact of PAP therapy on cardiovascular event rate, which were variably defined by composite outcomes followed for an average of 3 to 5 years. The meta-analysis did not demonstrate a clinically significant reduction in the rate of cardiovascular events occurring with the use of PAP. The quality of evidence for cardiovascular event rate ranged from low to moderate, based on the types of studies pooled for meta-analysis, and was downgraded due to study type and imprecision.[2, 56]

7. All-cause mortality

Four RCTs assessed the impact of PAP therapy on all-cause mortality. The meta-analysis did not demonstrate a clinically significant reduction in all-cause mortality with the use of PAP. The quality of evidence was downgraded due to imprecision.[2, 56]

8. Neurocognitive function

A total of nine RCTs investigated the efficacy of PAP for improvement in neurocognitive function. The meta-analyses demonstrated no clinically significant differences between PAP and control groups in any of the domains of neurocognitive function tested, which included executive function, processing speed, attention and vigilance, memory, and intelligence. The quality of evidence for neurocognitive function ranged from low to high and was downgraded due to imprecision in certain domains.[2, 56]

9. Mood

The efficacy of PAP in improving mood, specifically anxiety and depression, in adults with OSA was evaluated through a meta-analysis of five studies that reported on the Hospital Anxiety and Depression Scale (HADS anxiety and HADS depression). No clinically significant improvements in mood using PAP was demonstrated. However, the studies did not specifically enrol participants with anxiety or depression at baseline. The quality of evidence for depression and anxiety was high.[2, 56]

10. Motor vehicle crashes (MVC)

The efficacy for CPAP in reducing MVC in adults with OSA was evaluated using meta-analyses examining the relative risk reduction of obstacles hit during driving simulation in four RCTs. Meta-analyses of RCTs did not demonstrate a clinically significant reduction in obstacles hit or percent obstacles hit using a driving simulator. Ten non-randomized studies with pre- and post-CPAP assessment of MVC by self-report or objective reports were also retrieved. Their meta-analysis demonstrated a mean crash rate risk ratio of 0.3 (95% CI: 0.2 to 0.4). The quality of evidence from RCTs for the use of PAP to reduce MVC was downgraded due to imprecision and was moderate. The quality of evidence from observational studies for the use of PAP to reduce MVC was low and was downgraded due to study design.[2, 56]

11. Hospitalization

No RCTs were available.

12. Harms

Adverse events were reported in nine RCTs.[1, 8] Overall, 2% to 47% had specific adverse events while using PAP. Commonly reported harms were oral or nasal dryness, eye or skin irritation, rash, epistaxis, and pain. These side effects can result in sleep disruption and poor sleep quality thereby reducing patient adherence to PAP, and should be carefully monitored and managed by a clinician. No strong evidence was available.

In conclusion, benefit of PAP therapy has been demonstrated on sleepiness (high quality evidence), sleep related quality of life (high quality evidence),

blood pressure (moderate quality evidence). Effect on MVC could be demonstrated only in observational studies (low quality evidence). PAP has no effect on reducing fasting glucose or HbA1C in adults with OSA with or without type 2 diabetes mellitus (high quality evidence). Effect on cardiovascular events, mortality, neurocognitive functions and mood are not demonstrated. This has already demonstrated in other previous meta-analyses and in a more recent RCT (see section 2.2.2.2).[36-38]

2.4.2 *Home-based APAP versus in-laboratory PAP titration for initiation of PAP*

In auto-adjusting PAP (APAP) computer algorithms allow to dynamically increase the delivered pressure when obstructive breathing events are detected, and to periodically reduce it when no events are detected for some period of time. APAP in the ambulatory setting is increasingly being utilized as an alternative to traditional in-laboratory PAP titrations monitored by PG or PSG for the initiation of OSAS treatment.[2] The potential benefits of PAP initiation using home APAP over in-laboratory titration are a reduced time to initiation of therapy, particularly in areas with limited sleep-laboratory resources, reduced time away from home, lower overall cost, and greater access to care.

A recent good-quality systematic review (search strategy until October 2013, with last search update up to February 2018) served as the basis for AASM recommendations.[2, 56]

A total of ten RCTs were identified that compared initiation of PAP using home APAP titration versus in-laboratory PAP titration with PG or PSG in improving one or more of the following outcomes: AHI/RDI, adherence to PAP therapy, sleepiness, and QoL. Participants were predominantly middle-aged males with sleepiness and moderate to severe OSAS. Most studies reviewed excluded participants with the following comorbidities or conditions: congestive heart failure, chronic opiate use, significant lung disease such as chronic obstructive pulmonary disease, neuromuscular disease, history of uvulo-palatopharyngoplasty, sleep-related oxygen requirements, or expectation for nocturnal arterial oxyhemoglobin desaturation due to conditions other than OSA, including hypoventilation syndromes and central sleep apnoea syndromes. For the in-laboratory titration protocol, six studies used only full night in-laboratory titration and four studies used a combination of full night and split-night in-laboratory titration.

In these studies most participants using home APAP had mask fitting and education on PAP use at a sleep centre. Some studies also offered daytime nap acclimatization. Follow-up by trained staff early during the treatment period was common. All studies used the home APAP device in auto-adjustment mode for a brief period (2–7 nights) and then switched to a fixed pressure.[2, 56]

1. OSAS severity

Three RCTs reported on the AHI assessed after at least 6 weeks of treatment. Residual OSA severity was obtained in-laboratory (two studies) or from the PAP device itself (one study). Overall, the analysis demonstrated similar effects on OSA severity in adults with OSA when PAP is initiated via home APAP or in-laboratory PAP titration. The quality of evidence for OSA severity was high.[2, 56]

2. Adherence

The meta-analysis of ten RCTs demonstrated similar levels of PAP adherence (assessed after at least 1 month of treatment) in adults with OSA with PAP initiation by either home APAP or in-laboratory titration. The quality of evidence for adherence was high.[2, 56]

3. Sleepiness

A meta-analysis of nine RCTs reported on the ESS assessed after at least 1 month of treatment (range 1 month to 3 months). Overall, the analysis suggests that initiation of therapy using home APAP compared to an in-laboratory titration in adults with OSA results in similar effects on sleepiness. The quality of evidence for sleepiness was high.[2, 56]

4. Quality of life

A meta-analysis combining two RCTs measuring sleep-related QoL with FOSQ, two RCTs measuring sleep-related QoL with SAQLI, and one RCT measuring both FOSQ and SAQLI demonstrated no clinically significant difference in sleep-related QoL when comparing PAP initiation using home APAP versus an in-laboratory titration. Overall, the quality of evidence for QoL was considered moderate[a] by the authors.[2, 56]

5. Side effects

No studies were identified that reported on side effects of either strategy.

2.4.3 PAP versus other treatments for OSAS

Although PAP is currently the primary therapy used to treat adult OSA, a number of other therapeutic approaches exist, e.g. mandibular advancement devices (MADs), weight loss strategy, bariatric surgery, airway surgery, positional therapy, oropharyngeal exercises, nasal valves, or hypoglossal nerve stimulation devices. It was beyond the scope of this project to review all therapeutic options of OSAS. Hence, we reviewed here the evidence on the efficacy of mandibular advancement devices because they are usually the alternative treatment recommended for patients non-adherent or intolerant to PAP and they are reimbursed in the INAMI – RIZIV convention (see chapter 5).[57] We also reviewed evidence on the efficacy of lifestyle interventions as obesity is a prominent risk factor and advice on exercise and dietary control is/should be almost universally provided to all patients with OSAS.

2.4.3.1 Efficacy of Mandibular Advancement Devices (MAD)

These devices consist of plates made to fit the upper and lower teeth. Positions of these plates can be adjusted, allowing advancement of the mandible relative to the maxilla, resulting in increased upper airway volume and consequently, reduced airway collapsibility. Evidence on MADs was reviewed in a good-quality systematic review by Jonas et al. 2017.[8, 9] This review included ten RCTs assessing the effect of MADs on AHI, ESS, and blood pressure. Six RCTs compared MADs with sham devices that did not advance the mandible, one compared a MAD with a placebo tablet, two compared MADs with no treatment, and one compared MAD with conservative management of OSAS using a weight loss strategy. Most studies were conducted in Europe. Treatment durations ranged from 4 to 12 weeks for most studies, but one study lasted only 1 week and one lasted 24 weeks. Mean age of participants ranged from 45 to 59 years. The vast majority of participants in all trials were men. All studies included participants with mild to moderate OSAS, and six studies also included participants with severe OSAS. Mean baseline ESS scores ranged from 11 to 14, indicating excessive daytime sleepiness. One study included only participants with known hypertension.

1. OSAS severity

MADs improved AHI more than sham devices ((-12.6 AHI/h; 95% CI: -15.5 to -9.7); six RCTs; 307 participants) and more than other controls ((-8.2 AHI/h; 95% CI: -13.9 to -2.5); five RCTs; 358 participants)), although these improvements were below the threshold of clinical significance.[8, 9]

[a] The quality of evidence for the SF-36 physical and mental component summary scores was low due to very high imprecision. The quality of evidence for SF-36 vitality was high. The quality of evidence for combined FOSQ and SAQLI was moderate.

2. Sleepiness

Nine RCTs reported sufficient data for meta-analysis. MADs improved ESS more than both sham ((-1.5 point; 95% CI: -2.8 to -0.2); five RCTs; 267 participants) and other controls ((-1.7 points; 95% CI: -2.2 to -1.2); five RCTs; 358 participants), although these improvements were below the threshold of clinical significance.[8, 9]

3. Quality of life

Five included RCTs reported at least one quality-of-life measure. All five used the SF-36, two also used the SAQLI, and two also used the FOSQ. Because of inconsistency, imprecision, and heterogeneity of reporting, findings are insufficient to make conclusions about the potential benefits of MADs for improving quality of life.[8, 9]

4. Blood pressure

Five RCTs reported sufficient data for meta-analysis. Blood pressure outcomes were reported in a variety of ways (i.e., 24-hour, diurnal or nocturnal, systolic or diastolic). Only one of the trials reported any statistically significant differences between a MAD and sham for some of its blood pressure measures (diurnal systolic blood pressure, -3.0 mmHg [95% CI: -5.6 to -0.4]). The meta-analyses found no statistically significant differences between MADs and comparators for any of the measures.[8, 9]

5. Cardiovascular events, all-cause mortality, neurocognitive function, motor vehicle crashes

There were insufficient data for analysis.

6. Adverse events

Commonly reported harms of treatment with MADs include oral mucosal, dental, or jaw symptoms, such as mucosal or dental pain, discomfort or tenderness, mucosal erosions, and jaw or temporomandibular joint pain or discomfort. Less common harms include oral dryness and excess salivation. Limited study data suggest that 7% of patients discontinue treatment with MADs because of harms.[8, 9] The tolerability seems good with good adherence demonstrated up to two years.[58]

The comparative effect of MADs versus PAP was reviewed in a recent systematic review of twelve RCTs (either parallel or crossover) including a total of 743 participants.[59] In all included RCTs, all subjects underwent a baseline assessment including polysomnography first and then they were randomized to any of the possible options of treatment available (MAD, CPAP, or, if applicable, a third group—placebo treatment or other treatment) for a pre-determined amount of time (2 weeks up to 6 months). Various types of CPAP and MADs were used in the studies with different titration protocols. CPAP decreased AHI significantly more compared to MAD (SMD = -8.2; 95% CI: -13.1, -3.3) (moderate quality of evidence). However, no differences were observed in quality of life (SF-36 mental health or SF-36 physical functioning), cognitive and functional outcomes. Results were unclear for sleepiness.[59] Similar results were reported in a previous meta-analysis including eight RCTs, with a difference statistically significant between CPAP and MADs on AHI (-10.06; 95%: -14.21, -5.91) and oxygen desaturation index (ODI) (-7.82; 95%CI: -13.04 to -2.59).[60]

2.4.3.2 *festyle interventions*

Lifestyle interventions such as exercise training and dietary weight loss can also be effective means of treating OSAS. A recent good-quality[a] meta-analysis was carried out (search strategy up to May 2018).[61] The intervention was specified as either a diet (very low-calorie diets) or exercise/physical activity intervention, or a combination of the two. Three of the included RCTs utilized CPAP therapy in combination with lifestyle intervention, whereas the remaining studies excluded participants receiving current treatment for OSAS. The age of the participants in the studies ranged from 18 to 80 years, with mean baseline AHI ranging from 9.0 to 43.4 events/h (overall mean: 27.1 events/h) and mean baseline BMI ranging from 28.0 to 36.8 kg/m^2 (overall mean: 32.4 kg/m^2). The timeframe of the intervention varied from 1 month to 1 year. The primary outcome measure was the severity of OSAS as measured by the AHI. A secondary outcome of interest was body mass index (BMI).

The meta-analysis included ten RCTs with a total of 702 participants, grouped into three subgroups of diet (four RCTs, 217 participants), exercise (four RCTs, 117 participants) and combined intervention (two RCTs, 368 participants). The weighted mean difference in AHI (−8.09 events/h, 95% CI: −11.94 to −4.25) and BMI (−2.41 kg/m2, 95% CI: −4.09 to −0.73) were both statistically significant in favour of lifestyle interventions over control arms.[61]

Another recent systematic review also concluded that exercise training could reduce OSAS severity.[62] However, this result should be considered cautiously given the very low quality of some of the studies (n=8) included.

There is not a single trial comparing the relative efficacy of lifestyle interventions with CPAP and MADs. However, a network meta-analysis (eighty RCTs; search strategy up to September 2015) allowed investigating such comparisons.[60] It showed that CPAP decreased AHI the most (-25.27 events/hour; 95% CI: -22.03, -28.52) followed by exercise training (-17.23 events/hour; 95% CI: -25.82 to -8.64), MADs (-15.20 events/hour; 95% CI: -19.50 to -10.91), and dietary weight loss (-12.27events/hour; 95% CI: -18.79 to -5.75).[60] While the difference between exercise training and CPAP was not statistically significant (-8.04 events/hour; 95% CI: -17.00 to 0.92), those between CPAP and MADs and between CPAP and dietary weight loss were significant.[60] The differences in the AHI reduction between exercise training and MADs, between exercise training and dietary weight loss, and between MADs and weight loss were not statistically significant. The Epworth sleepiness scores (ESS) was significantly improved by exercise training (-3.08 points; 95% CI: -5.48, -0.68), albeit with a non-significant difference compared to MADs and CPAP.[60]

[a] Results of quality assessment based on the AMSTAR-2 checklist: CINAHL, Cochrane, Embase, OVID Medline and Scopus were searched up to May 2018; only English language; list of excluded studies provided; selection of paper on title and abstract done by Covidence software; double data extraction; triple assessment of risk of bias (with Cochrane risk of bias tool); correct meta-analysis; results accounting for study quality; conflict of interest not reported.

2.4.4 Telemonitoring of PAP

Telemonitoring includes the remote monitoring of PAP parameters such as PAP use, residual OSA severity, unintentional mask leaks, and PAP settings during treatment initiation and follow-up. We retrieved two systematic reviews from 2019 by Patil et al. and by Murphie et al.[2, 63]

The systematic review by Patil et al. 2019 included five RCTs (498 participants) evaluating the use of remote monitoring of PAP variables to trigger early interventions versus no such system as an adjunct to PAP therapy for the treatment of adults with OSA.[2] Outcomes assessed included adherence to PAP therapy, sleepiness, QoL and PAP-associated side effects. All studies evaluated outcomes at 2–3 months after PAP initiation. However, details about the triggers for intervention and the intensity of the intervention used when poor usage patterns were identified varied greatly across studies resulting in heterogeneity of results. Some studies only triggered interventions based on low usage while other studies also triggered interventions for significant mask leaks, high delivered pressures, and/or high residual AHI. The interventions also varied substantially, ranging from text messages to telephone calls, in-person visits with sleep staff, and even in-person visits with a sleep physician.[2] The meta-analysis demonstrated a clinically significant improvement in adherence (0.98 hours/night; 95% CI: 0.53; 1.42; high quality evidence), but not in sleepiness (assessed by ESS), with the use of telemonitoring. Other outcomes, such as QoL or PAP-associated side effect severity scores were studied in a minority of studies and did not statistically differ with or without telemonitoring.[2]

The systematic review by Murphie et al. 2019 (searched strategy up to November 2015) also included five RCTs, two of which were in common with Patil et al. 2019.[2, 63] It did not obtain clear results and concluded that more research is needed to establish whether real time telemonitoring is a clinical and cost effective for persons using CPAP therapy.[63]

Based on this evidence, the AASM suggests that clinicians use telemonitoring-guided interventions during the initial period of PAP therapy in adults with OSA (moderate quality evidence; conditional recommendation).[56]

Considerations on legal and ethical aspects of telemonitoring are presented in Appendix 3.

2.4.5 Management of OSA in primary care vs sleep unit setting

The systematic review by Kunisaki et al. 2016 (search strategy up to May 2016) included four randomized controlled trials (RCTs) and four observational studies which evaluated case-finding and care provided by non-sleep specialist practitioners (e.g. primary care physician, physician's assistant, nurse, technologist, or respiratory therapist) versus sleep specialist physicians (SSP).[3] The systematic review was rated moderate quality based on the AMSTAR 2 checklist.[a]

No studies assessed specifically the diagnosis of OSAS. As regards care provided, patient-centred outcomes were infrequently and inconsistently reported. When reported there was no significant difference in clinical outcomes between OSAS treated by primary care physician/nurses and SSPs (moderate strength[b] of evidence for quality of life). Intermediate outcomes were more commonly reported. Sleep symptom scores were similar between groups (moderate quality evidence). There was little evidence that treatment compliance differed between patients treated by

[a] The answer was a partial "yes" for the following domains: "explicit statement that the review methods were established prior"; "comprehensive literature search strategy". The answer was "no" for the following domains: "list of excluded studies and reason"; "sources of funding of the included cited"

[b] Strength of evidence was rated as high, moderate, low, or insufficient based on precision, consistency, directness, and risk of bias of the individual studies.

SSPs and those not, including the proportion of patients with 4 hours or more of CPAP use on 70% or more of nights (moderate quality evidence).[3] Very few studies reported other intermediate outcomes, e.g. residual AHI on CPAP.

Four more recent RCTs investigated the same questions.

- Tarraubella et al. 2018. organized a multicentre, open-label, two-arm, parallel group, non-inferiority randomised controlled trial including 302 subjects with suspected OSAS and/or resistant hypertension (149 in 11 primary care (PC) units, 153 in 1 sleep unit (SU) in Catalonia).[64] The patients allocated to the PC group were exclusively managed by the PC unit. The PC physicians decided on the type of sleep study (PG or PSG) and the decision whether to prescribe CPAP treatment. The realisation and scoring of sleep studies was performed by a certified sleep specialist from a private external company. After 6 months, the adjusted difference between groups for the mean change in the ESS score was −1.25 (one-sided 95% CI: −1.88; p=0.025), supporting the non-inferiority (margin set at ESS score -2.0) of PC management. [64] No difference in the Health Utilities Index was observed between groups.
- Sanchez-Quiroga et al. 2018[40] tested a similar approach as Tarraubella et al. 2018[64] with 307 patients with an intermediate to high OSA probability, but the PC arm involved a portable monitor with automatic scoring and semiautomatic therapeutic decision-making (versus PSG in the SU). Based on the Epworth Sleepiness Scale (main outcome), the PC protocol was non-inferior to the in-laboratory protocol.[40]
- In Sanchez-de-la-Torre et al. 2015[65] 101 patients who were diagnosed with OSAS in the SU and required CPAP treatment were randomly assigned to either PC (8) management or SU (1) management. One PC physician and one nurse from each of the eight PC units in the study participated in an education programme (6 h) that included the theoretical and practical aspects managing patients with sleep apnoea. At 6 months, the CPAP compliance was not statistically different between groups.[65]
- In Hui et al. 2017 172 individuals suspected of OSAS were randomized either to a home-based or a hospital-based approach.[66] Following detection of AHI ≥ 15/hr by Embletta sleep study at home or polysomnography at hospital, patients received CPAP for 3 months after an overnight APAP titration at home or in hospital respectively. At 3 months, there was no difference in Epworth sleepiness score (main outcome), but greater improvement in Sleep-Apnoea-Quality-of-Life-Index (SAQLI) (difference=0.3 (95% CI: 0.02, 0.6), p = 0.033).[66] Waiting time to start treatment was 145 days shorter in the home-based group.

In all studies, a lower cost has been reported.

2.4.6 Discussion

Benefit of PAP therapy has been demonstrated on sleepiness (high quality evidence), sleep related quality of life (high quality evidence), 24-hour mean blood pressure (moderate quality evidence). Effect on MVC could be demonstrated only in observational studies (low quality evidence). PAP has no effect on reducing fasting glucose or HbA1C in adults with OSA with or without type 2 diabetes mellitus (high quality evidence). Effect on global QoL as assessed by SF-36, cardiovascular events, mortality, neurocognitive functions and mood are not demonstrated. The ASSM recommends to treat OSAS patients presenting excessive sleepiness with PAP (high-quality evidence, strong recommendation).[2, 56]

Many questions remain unanswered, though. Robust estimates of effect of PAP on hypertension, CVD, neurocognitive outcomes, and metabolic disorders are not available. Part of these disappointing results may be due to the use of AHI as a selection criteria. There is an uncertain relation between a decreased AHI and improvement of symptoms. If insufficient symptomatic improvement is present despite an adequate decrease in AHI and good adherence to therapy, another diagnosis than OSAS must be envisaged. The syndrome severity should be primarily defined by the seriousness of symptom scores (plus response to therapy) and not by the AHI. Current evidence on the efficacy of PAP to treat OSAS is from RCTs presenting heterogeneous populations (e.g. all patients versus severe OSAS only), methods (e.g. comparator being sham CPAP, conservative

measures or no intervention), and outcomes measurement (e.g. various scales to measure quality of life). The clinical significance of a mean reduction of 2 points on the ESS (with potential subjective over-reporting) and 1 to 2 points (mmHg) for blood pressure measures is somewhat uncertain.[1, 9] Whether improvement in AHI (for mild to severe OSA) also leads to improvement in health outcomes is not well established. Moreover, the trial design was often inappropriate for measuring the outcomes, e.g. study duration was often too short to determine benefit for many health outcomes and small number of total events observed across studies resulted in low study power. Good-quality studies that evaluate the effect of PAP (or any other OSAS treatments) on hard health outcomes (e.g. all-cause and cardiovascular mortality, cardiovascular disease and cerebrovascular events, metabolic disorders, motor vehicle crashes, and cognitive impairment) that include various OSAS phenotypes (with or without sleepiness, with mild-moderate or moderate-severe OSAS, etc…) are needed.[34] To improve both medical outcomes and cost containment of healthcare, more attention should be focused on personalised medicine. The current one-size-fits-all approach to OSA based on AHI impairs adequate management of many patients who may be helped otherwise by targeted and multifaceted treatment.[15, 34]

There is no evidence of inferiority of APAP at home compared to in-laboratory PAP titration. This was also demonstrated in a previous systematic review.[3] On that basis the AASM recommends positive airway pressure therapy be initiated using either APAP at home or in-laboratory PAP titration in adults with OSA and no significant comorbidities (high quality evidence from ten RCTs; strong recommendation).[56] Studies are needed in patients with comorbid conditions commonly seen in sleep clinic populations (e.g. obstructive and restrictive lung disease, Congestive Heart Failure (CHF), pulmonary hypertension, neuromuscular disease, (potentially) co-existing central sleep apnoea, etc.) to determine the benefits, risks, and contraindications of APAP versus in-laboratory based PAP titration. Also, in the RCTs included in the review mask fittings and education on PAP use at a sleep centre and/or close follow-up by trained staff during the treatment period were provided to the home APAP group, i.e. a titration of PAP with no involvement of a sleep lab has not been tested.[56] The potential harms of initiating therapy with APAP at home after adequate patient education is provided are difficulties in identifying and immediately addressing problems related to mask fit or leaks.[56] That problems could be detected by adequate telemonitoring.

Telemonitoring for home-based APAP titration and to assess adherence and treatment efficacy in PAP-treated OSAS patients, in the view of prompting rapid corrective measures, is attractive.[67-69] It is widely used in many countries (see the international comparison in section 3.2.4). However, evidence on the benefits or harms of telemonitoring is scarce. Available RCTs have small sample size and interventions and outcomes are very heterogeneous.[2, 63] An effect was observed on adherence (about one more hour of utilization of the PAP per night), but other effects were poorly studied. Better adherence could be linked to an increased sense of accountability or to the prompt reaction of the responsible clinician. The AASM suggests that clinicians use telemonitoring-guided interventions during the initial period of PAP therapy in adults with OSA.[56] However, more research is needed on the impact of telemonitoring on health parameters, patient satisfaction and cost-effectiveness. Legal and ethical aspects of telemonitoring must also be considered (see Appendix 3).

Obviously, PAP is not the only treatment of OSAS. In the frame of this report, we reviewed evidence on MADs and lifestyle interventions. MADs reduce effectively OSAS severity and sleepiness,[8, 9] but less than CPAP.[59, 60] Whether better long-term adherence of OSAS treatment with MAD than with PAP could compensate this lower efficacy is unknown. MADs are effective treatment options, particularly for individuals with mild to moderate OSAS.[6] Exercise training and dietary weight loss are also effective in reducing AHI and improving subjective parameters.[60, 61] In particular, a network meta-analysis found a nonsignificant difference for AHI reduction between exercise training and CPAP and between exercise training and MAD.[60] There is a dose-dependent association of exercise with lower prevalence of OSAS.[6] The improvements in sleep apnoea severity and daytime sleepiness seem partly independent of changes in body weight, BMI, or total body fat, and could be mediated by reductions in fat deposition in the structures surrounding the airway including the tongue, leading to increased

pharyngeal lumen size.[60] Fat redistribution, reduced night-time fluid resorption from the legs, increased pharyngeal muscle strength, and improved sleep quality are other potential mechanisms.[6] The beneficial effects of exercise training suggest that this can be a particularly useful adjunctive treatment to CPAP or MAD. Although dietary weight loss ranked last in that meta-analysis, it was reported previously that a 10% weight gain was associated with a 32% increase in the apnoea severity and a 10% weight loss was associated with a 26% reduction in AHI.[70] Additional high-quality RCTs are needed to strengthen the evidence.

Finally, the inferiority of OSAS management by primary health care providers other than sleep medicine specialists could not be demonstrated in several studies.[3, 40, 64, 66] In two of the recent trials,[40, 66] the diagnosis was also made by the primary care team, whereas in the other two, the diagnosis was made by sleep medicine specialists. Comparative effectiveness trials are needed in order to determine whether such results can be achieved in routine practice, outside of controlled research settings. The available data suggest that with some appropriate training, professionals not specialised in sleep medicine can potentially provide equivalent outcomes, but the operationalization of such training is unclear. Therefore, future comparative effectiveness trials should describe their training programs.[3] Of note, management and follow-up of OSAS patients (mask-fitting, therapeutic education, data recording, maintenance of the device) is already often done by private service providers, i.e. not by sleep medicine specialists. This is also the case in Belgium. Costs of OSAS management by primary health care professionals were reported to be lower but a thorough cost-effectiveness analysis is warranted.

2.5 Cost-effectiveness of treatment with PAP or MAD

This chapter aims at providing a general overview of the cost-effectiveness of treating OSAS patients with PAP or MAD.

We report here the results of three recent systematic reviews of the economic literature[71-73] and we complete this information with the results of the three primary studies performed by the UK (2008),[74] French (2014)[71] and Canadian (2017)[75] HTA agencies. The recent reviews by Toraldo et al.[76] and by Kim et al.[75] were not considered as they are no formal systematic reviews, but rather very short narrative reviews of low quality. Primary studies included in these systematic review can be found in Appendix 4.

Reviews of full economic evaluations

The 2019 systematic review by Wickwire et al.[73] searched the economic literature published up to 09/2018 and identified five[a] full economic evaluations of PAP treatment (including CPAP, APAP, Bi-level PAP) for OSAS patients. The review was limited to empirical full economic evaluations, i.e. economic evaluations build along a RCT, a case-control study or a prospective study. Model-based (e.g. Markov) full economic evaluations were excluded. The five economic evaluations were performed in the UK (2), France (1), Spain (1) and Canada (1). The follow-ups ranged from 6 weeks to 5 years and the studies were all performed from the health care payer perspective. PAP treatment of OSAS patients was reported to be cost-effective in all studies, with ICERs ranging from dominant (less costly and more clinically effective than its comparator) to $ 26 000 per QALY compared with no treatment or supportive care. Wickwire et al.[73] further highlighted that PAP treatment was most cost-effective among patients with severe OSAS and a high treatment adherence.

[a] The studies by Lojander et al.[77] and Quinell et al.[78] were also considered in Wickwire et al.[73] but discarded here as they evaluated the cost-effectiveness of lifetime counselling.

In 2015, McMillan et al.[72] published a review of the existing cost-effectiveness evidence on whether CPAP is a cost-effective treatment for OSAS patients. The literature was searched up to 04/2012 and 10 full economic evaluations were retained (4 from the USA, 3 from the UK, 1 form Canada, 1 from Spain and 1 from New Zealand). All studies were performed from the health care payer perspective (but one with a societal viewpoint) and most of them were Markov models. All studies compared CPAP with no treatment, and two also compared CPAP with MAD. McMillan et al.[72] report that, across all studies, the results of the cost-effectiveness analyses led the authors to conclude that CPAP was a cost-effective treatment for patients with OSAS whatever the comparator (i.e. no treatment or MAD). The ICERs ranged from dominant (less costly and more clinically effective than its comparator) to $ 15 000 per QALY, and were lower than the typical willingness to pay for an additional QALY used in each of the countries considered. In general, the cost-effectiveness results were robust to alternative assumptions on parameter inputs.

In 2014, the French Haute Autorité de Santé (HAS)[71] issued a systematic review of 7 full economic evaluations of OSAS treatments published up to 07/2013. The studies were performed in the USA (3), UK (2), Canada (1) and New Zealand (1). Most studies modelled adult populations with at least moderate OSAS (AHI ≥ 15). In one study patients with mild OSAS (AHI 5-14) were also modelled. All studies compared CPAP with no treatment, and two of them also compared CPAP with MAD. All but one studies adopted a health care payer perspective (societal perspective in 1 study) and the time horizons varied from 5 year (3 studies) to a lifetime (in one study the time horizon was limited to one year). In 6 studies, CPAP generated higher costs than its comparators (MAD or no intervention), but also greater health benefits in terms of QALYs gained. In those studies, the ICERs ranged from € 2477 to € 11 944 per QALY compared to no intervention, and from € 5010 to € 20 330 per QALY compared to MAD. In one study, treatment with CPAP was the dominant strategy as it generated fewer costs and more QALYs than its comparator.

Primary full economic evaluations performed by HTA agencies

In 2008, the UK National Institute for Health and Care Excellence (NICE)[74] assessed the cost-effectiveness of three interventions (CPAP, MAD and lifestyle change) over a lifetime horizon, and recommended the use of CPAP devices for adults with moderate or severe OSAS. NICE estimated the cost-effectiveness of treating OSAS adults with CPAP at around £ 4 000 per QALY in the base-case analysis and below £ 10 000 per QALY in most alternative scenarios, compared to dental devices and lifestyle change (health care payer perspective). This is well below the UK threshold of £ 20 000 – £ 30 000 per QALY. In patients with mild OSAS, the ICER was slightly higher at £ 20 500 per QALY. NICE concluded that CPAP is an effective and cost-effective treatment in adult populations with moderate to severe OSAS.

In 2014, the French HAS[71] assessed the cost-effectiveness of four interventions (CPAP, MAD, lifestyle change and no treatment) for patients with low and moderate OSAS (health care payer perspective) over a lifetime time horizon. Severe OSAS were not considered. CPAP treatment was the most cost-effective intervention for low to moderate OSAS patients with cardiovascular comorbidities, with an ICER of € 10 100 per QALY. In patients without cardiovascular comorbidities, MAD was the most cost-effective treatment with an incremental cost of € 33 000 per QALY.

In 2017, the Canadian Agency for Drugs and Technologies in Heath (CADTH)[75] explored the cost-effectiveness of five interventions for the treatment of OSAS patients: PAP, MAD, maxillomandibular advancement surgery, lifestyle modification (weight loss, change of sleep position) and no treatment. They adopted a lifetime horizon and health care payer perspective. Results were stratified per disease severity. In patients with mild OSAS (AHI 5-14), no treatment was the most cost-effective intervention. In patients with moderate (AHI = 15 to 29) and severe (AHI = 30-59) OSAS, PAP was the most cost-effective treatment with incremental costs of CAN$ 8000 and CAN$ 7420 per QALY, respectively. In patients with a very severe OSAS (AHI ≥ 60), maxillomandibular advancement surgery was the most cost-effective with an ICER of CAN$ 17 125 per QALY.

The upcoming update (foreseen for 2020) of the UK NICE guidance will not cover CEAs (https://www.nice.org.uk/guidance/gid-ng10098/documents/final-scope).

Conclusion

As demonstrated in the above studies, there seems to be little doubt about the cost-effectiveness of PAP therapy for OSAS patients, especially for those with moderate to severe disease (AHI ≥ 15). However, this conclusion relies on rather old primary studies as the last comprehensive and systematic review of the literature searched the literature only up to 07/2013. Many new economic evaluations of OSAS treatments have been published since then, that now compare all available treatment options together (not only pairwise comparisons), and a new systematic review is thus needed. However, this was outside the scope of this study.

2.6 Cost-effectiveness of home-based versus hospital-based strategies

This chapter aims at providing a general overview of the cost-effectiveness of a home-based versus hospital-based strategy for the diagnosis of OSAS patients and the titration of PAP.

Full-night attended PSG at the hospital/sleep centre is considered the gold standard for OSAS diagnosis and PAP titration. Home-based unattended diagnostic and titration sleep tests with PG are an alternative approach performed in several countries. Whether home sleep testing can be a cost-effectiveness alternative to hospital/sleep-centre testing was explored in several studies, whose main results are reported in Table 7 below.

Four studies were cost-utility analyses,[79-82] two were cost-minimization analyses[52, 83] and another 2 cost-consequence analyses.[84, 85] Three studies were cost comparisons.[86-88]

The studies were classified according the time horizon they considered. Eight studies adopted a short time-span of less than a year, some of them limiting their analysis to a few month and only considering the diagnosis and titration processes.[52, 79, 83-88] Three studies adopted much longer time-horizon (≥ 5 years), in which the consequences of doing hospital versus home-based PG diagnosis and titrations were assessed over the long-term management of OSAS.[80-82]

Table 7 – Economic evaluations of home versus hospital/sleep-centre diagnosis of OSAS patients

Author, year, country	Study type, time-horizon, costing perspective (costing year), population	Interventions compared, management phases considered	Devices used, unit costs	Test sensitivity and specificity	Efficacy / effectiveness	Results and sensitivity analysis
Short-term time horizon (less than a year)						
Bravata 2018 USA[87]	- Cost-comparison, simulation of scenarios - Time horizon: not reported (the scenarios stop after titration) - Direct medical and non-medical costs - Costing year: 2007 - Veterans with an 85% probabiltiy of OSAS (severity not defined)	Lab PSG - Full-night † - Split-night ‡ Home PG * Diagnosis and titration	- PSG: not reported - Home PG: type III device - Auto-CPAP: not reported Diagnostic PSG: $200 Split-night PSG: $305 Titration PSG: $305 Home PG: $234	Not reported Prob Lab PSG is positive = 0.85 Prob Home PG is positive = 0.70 Patients do lab PSG if home PG is negative.	Not applicable as limited to a cost-comparison	Cost per patient: Lab PSG: $1410 Home PG: $1220
Stewart 2017 Canada[88]	- Cost-comparison, retrospective analysis of data from 2006 to 2013 - Time horizon: not reported (the analysis stops after titration) - Direct medical costs - Costing year: 2014 - 10 000 patients (mean age 52 years, 65% male), 55% probability of OSAS (AHI ≥ 15), mean AHI = 28.5 (SD 29.8)	Lab PSG: - Full-night † - Split-night ‡ Home PG * Diagnosis and titration	- Lab PSG: Sandman version 9 (Mallinckrodt Inc., Canada). - Home PG: Embletta X10 (Embletta, USA) type III - Auto-CPAP: ResMed S8 or S9 (ResMed, USA) Diagnostic PSG: CAN$384 Titration PSG: CAN$523 Split-night PSG: CAN$660 Home PG: CAN$141 Auto-titration: CAN$197	Not reported Prob Lab PSG is positive = 0.83 Prob Home PG is positive = 0.78 Patients do lab PSG if home PG is negative.	Not applicable as limited to a cost-comparison	Costs per patient (SD): Lab PSG: CAN$746 (192) Home PG: CAN$419 (269) If the probability that Home PG is positive is below 20%, the costs of Lab PSG are below the costs of Home PG

Author, year, country	Study type, time-horizon, costing perspective (costing year), population	Interventions compared, management phases considered	Devices used, unit costs	Test sensitivity and specificity	Efficacy / effectiveness	Results and sensitivity analysis
Corral 2017 Spain[79]	- CUA, RCT-based with 6-month follow-up - Direct medical and non-medical costs - Costing year: 2015 - 430 patients (median age 50 years, 70.5% male) and 60-75% probability of OSAS (AHI ≥ 15)	Lab PSG Full-night† + auto-titration Home PG + auto-titration Diagnosis, titration and treatment	- Home PG: Embla-Embletta; Natus, Pleasanton, CA - Auto-CPAP: S8-Autoset; Resmed, Sydney, Australia Input costs: not reported	Not reported No referral to lab PSG if home PG is negative	Difference in QALY improvement is not significant. QALY improvement versus baseline: - PSG: 0.008 (0; 0.01) - Home PG: 0.004 (0; 0.1)	Cost per patient (95% CI): PSG: €736 (702; 771) Home PG: €320 (282; 358) QALY difference PSG vs Home PG: 0.004 (0; 0.01) ICER PSG vs Home PG: €103 000 per QALY gained
Kim 2015 USA[83]	- CMA, RCT-based: HomePAP with 3 months FU extrapolated to 1 year - Direct medical and non-medical costs - Costing year: 2011 - 373 patients (mean age 46 years, 60% male) with a high (not defined) probability of moderate to severe OSAS (AHI ≥ 15)	Lab PSG: - Full-night † - Split-night ‡ Home PG * Diagnosis, titration and treatment	- PSG: not reported - Home PG: type III portable limited-channel sleep device (EmblettaX-30, Embla Inc., CO, USA) - Auto-CPAP: REMStar Auto-M Series; Philips-Respironics, PA, USA) Diagnostic PSG: $782 Split-night PSG: $782 Titration PSG: $782 Home PG: $167 Auto-titration: $0	Not reported Patients do lab PSG if home PG is negative.	3 months improvement in clinical outcomes are equivalent (SF-36 Vitality score and FOSQ questionnaire)	Cost per patient (95% CI): Lab PSG: $1840 (1660-2015) Home PG: $1575 (1439-1716) Results are not robust (overlap between the 95% CI).
Masa 2013 Spain[52]	- CMA, RCT-based - Time horizon: not reported (analysis limited to diagnosis) - Direct medical and non-medical costs - Costing year: 2009	Lab PSG Full-night† Home PG * Diagnosis only	- PSG: not reported - Home PG: BreastSC20; Breast Medical AB; Sweden	PSG: not reported Home PG: - sensitivity 0.96 - specificity 0.57	Equal diagnostic efficacy (to achieve this the cost of confirmatory PSGs for invalid home PG results was added)	Cost per patient for diagnosis: Lab PSG: €574 Home PG: €476

Author, year, country	Study type, time-horizon, costing perspective (costing year), population	Interventions compared, management phases considered	Devices used, unit costs	Test sensitivity and specificity	Efficacy / effectiveness	Results and sensitivity analysis
	- 366 patients (mean age 48.6 years, 76% male) with a 90% probability of OSAS (AHI ≥ 5)		Input costs: not reported	Patient referral to lab PSG if home PG negative		
Andreu 2012 Spain[84]	- CCA, RCT-based with 6 months FU - Direct medical costs - Costing year: not reported - 65 patients (mean age 52 years, 83% male) with a high (not reported) probability of moderate to severe OSAS (AHI ≥ 15), mean AHI = 43 (SD 20)	Lab PSG Full-night† Home PG * Diagnosis and treatment (no titration as the right pressure is derived with a mathematical formula)	- PSG: Somnostar Alpha 41001; SensorMedics, CA, USA - Home test: Stardust Polygraph1; Phillips Respironics Inc., PA, USA PSG: €300 PG: €72 CPAP treatment: not reported	Not reported No patient referral to lab PSG if home PG negative	No differences in CPAP adherence, in ESS, in FOSQ, or in symptom scores after 6 months	Cost per patient (SD): Lab PSG: €849 (11) Home PG: €590 (43) No sensitivity analysis
Rosen 2012 USA[85]	- CCA, RCT-based: HomePAP with 3 months FU - Direct medical costs - Costing year: 2011 - 197 patients (mean age 48 years, 65% male) with confirmed OSAS (AHI ≥ 15)	Lab PSG: - Full-night † - Split-night ‡ Home PG * Diagnosis and titration	- PSG: not reported - Home PG: type III portable limited-channel sleep device (EmblettaX-30, Embla Inc., CO, USA) - Auto-CPAP: REMStar Auto-M Series; Philips-Respironics, PA, USA) Diagnostic PSG: $672 Split-night PSG: $725 Titration PSG: $725 Home PG: $177 Auto-titration: $58.6	Not reported Patients do lab PSG if home PG is negative.	No significant difference in improvement in ESS scores, FOSQ score, SAQLI score, or in SF-36 Vitality subscale	Cost per patient: Lab PSG: $1000 Home PG: $744 No sensitivity analysis

Author, year, country	Study type, time-horizon, costing perspective (costing year), population	Interventions compared, management phases considered	Devices used, unit costs	Test sensitivity and specificity	Efficacy / effectiveness	Results and sensitivity analysis
Ayas 2010 USA[86]	- Cost-comparison, decision tree - Time horizon: 1 month - Direct medical costs - Costing year: not reported - Symptomatic patients with suspected OSAS (not further defined)	Lab PSG Full-night† Home PG * Diagnosis, titration and treatment	- PSG: not reported - Home PG: type III device - Auto-CPAP: not reported PSG: $1018 Home PG: $125 CPAP treatment: $88 per month	Lab PSG: - sensitivity 1.00 - specificity 1.00 Home PG: - sensitivity 0.90 - specificity 0.90 Patients do lab PSG if home PG is negative.	Not applicable as limited to a cost-comparison	If pre-test probability of OSAS is > 0.47, Home PG costs less than Lab PSG Results are sensitive to the cost of home PG.
Long-term time horizon (more than 5 years)						

Moro 2016 USA[81]	- CUA, Markov model
	- Time horizon: (1 and) 10 years
	- Direct medical costs
	- Costing year: not reported
	- Adults with 0-100% probability of moderate to severe OSAS (AHI ≥ 15)
		Lab PSG:
		- Full-night †
		- Split-night ‡
		Home PG *
		Empiric treatment §
		No testing and no treatment
		
		Diagnosis, titration and treatment
			Not reported
			
			PSG: $800
			Home PG: $200
			Auto-titration: $200
			Untreated OSA (cOSA): $0 – 5000 (assumption)
			CPAP treatment: $1000 per year
				PSG:
				- sensitivity 0.93
				- specificity 0.97
				Home PG:
				- sensitivity 0.91
				- specificity 0.83
				
				Back-up lab PSG if home PG is negative
					Treatment efficacy assumed to be 100%.
					
					Utilities:
					- No OSA = 1
					- Untreated OSA = 0.8
					- Treated OSA = 1
						Time-horizon 1 year:
						- if probability OSAS < 20%, do home PG
						- if pretest probability OSAS > 20%, treat all patients empirically
						
						Time horizon 10 years (no back-up lab PSG):
						- if OSAS probability > 80%, treat all patients empirically;
						- if OSAS probability < 80%:
						  ○ Home PG if cost of untreated OSA < $2000 per year
						  ○ Lab PSG if cost of untreated OSA > $2000 per year

Author, year, country	Study type, time-horizon, costing perspective (costing year), population	Interventions compared, management phases considered	Devices used, unit costs	Test sensitivity and specificity	Efficacy / effectiveness	Results and sensitivity analysis
						Time horizon 10 years (with back-up lab PSG): - if OSAS probability > 30%, do home PG - if OSAS probability < 30%, Lab PSG is preferred: o No treatment if cost of untreated OSA < $1000 per year o Lab PSG if cost of untreated OSA > $1000 per year
Pietzsch 2011 USA[82]	- CUA, Markov model - Time horizon: life - Direct medical costs - Costing year: 2008 - 50-year-old males with a 50% probability of moderate to severe OSAS (AHI ≥ 15)	Lab PSG Full-night† Lab PSG Split-night‡ Home PG * Empiric treatment § No testing and no treatment Diagnosis, titration and treatment	Not reported Home PG: type III Diagnostic PSG: $811 Split-night PSG: $891 Titration PSG: $891 Home PG: $209 Auto-titration: $209 CPAP treatment per year: not reported	Full-night PSG: - sensitivity 0.97 - specificity 1.00 Split-night PSG: - sensitivity 0.89 - specificity 0.94 Home PG: - sensitivity 0.91 - specificity 0.83 88% of patients do lab PSG if home PG is negative.	Higher risks for untreated OSA patients. Hazard ratios for: - motor vehicle collision: 3.0 - hypertension: 1.8 - incident MI: 2.8 - incident stroke: 1.7 Utilities: - Well: 1 - Hypertension: 0.96 (0.95–1) - Post-MI: 0.86 (0.80–1) - Post-stroke: 0.81 (0.78–1) - OSAS untreated: 0.84 (0.80–0.93)	50% OSA probability: - Full-night PSG: $17 130 per QALY (versus no testing / no treatment) - All options dominated by full-night PSG 20% OSA probability: - Full-night PSG: $19 000 per QALY (versus no testing / no treatment) - All options dominated by full-night PSG 80% OSA probability: - Split-night PSG: $16 600 per QALY compared to no treatment

Author, year, country	Study type, time-horizon, costing perspective (costing year), population	Interventions compared, management phases considered	Devices used, unit costs	Test sensitivity and specificity	Efficacy / effectiveness	Results and sensitivity analysis
					- OSAS treated: 0.93 (0.84–0.98) - No OSAS treated: 0.98 (0.96–1)	- Full night PSG: $57 000 per QALY compared to split-night PSG
Deutch 2006 USA[80]	- CUA, Markov model - Time horizon: 5 years - Direct medical costs - Costing year: 2004 - 30-64-year-old symptomatic patients (85% male) with an 82% probability of OSAS (AHI ≥ 10)	Lab PSG Full-night† Lab PSG Split-night‡ Home PG * Diagnosis, titration and treatment	Not reported Diagnostic PSG: $788 Split-night PSG: $852 Titration PSG: $852 Home PG: $218 Auto-titration: $218 CPAP treatment per year: $1600 in year 1, $821 in year 2, $700 in years 3 to 5	Full-night PSG: - sensitivity 0.97 - specificity 1.00 Split-night PSG: - sensitivity 0.93 - specificity 0.90 Home PG: - sensitivity 0.95 - specificity 0.73 Patients (not all of them) do lab PSG if home PG is negative.	Utilities: - No OSAS: 0.435 (0.435-0.75) - OSAS treated: 0.55 (0.55-0.87) - OSAS untreated: 0.32 (0.32-0.63) - No OSAS treated: 0.32 (0.32-0.63) Higher death rate for untreated OSAS, odds ratio: 2.87 (1.17-7.51)	Full-night PSG costs more but is also more clinically effective than Home PG ICER Full-night PSG versus Home PG: $7380 per QALY gained At a $15 000 per QALY threshold, the probability that Full-night PSG is cost-effective is 95%; against 5% for Home PG.

*† Lab PSG Full-night: two overnight sleep-centre PSGs, one for the diagnosis followed with one for titration with CPAP. ‡ Lab PSG Split-night: one overnight sleep-centre PSG with diagnosis during the first part of the night, followed with CPAP titration during the remainder of the same night. * Home PG: diagnosis with a home-based portable device followed with home-based APAP autotitration. § Empiric treatment: treat all patients empirically without testing. CCA: cost-consequence analysis, CEA: cost-effectiveness analysis, CI: confidence interval, CMA: cost-minimization analysis, cOSA: cost of untreated OSA, CUA: cost-utility analysis, ESS: Epworth sleepiness scale, FOSQ: functional outcome sleep questionnaire, FU: follow-up, PG: polygraphy, PSG: polysomnography, SAQLI: Calgary sleep apnoea quality of life index, SD: standard deviation.*

Short time horizon

The eight studies with a short time horizon (less than a year) conclude that home diagnosis and titration of OSAS patients is as clinically effective as hospital/sleep lab diagnosis and titration of OSAS patients,[52, 79, 83-85] but also less expensive than hospital/sleep lab management of OSAS patients. Only one study was a cost-utility analysis,[79] in which the incremental cost-effectiveness ratio (ICER) of hospital/sleep lab PSG versus home-PG was over € 100 000 per quality-adjusted life-year (QALY), which is usually considered too expensive. In those studies, the pre-test probability of OSAS was fairly high and ranged 65-75%[79] to 100%.[85]

As the diagnostic accuracy of home PGs is inferior to lab PSG (i.e. home PG has lower sensitivity and specificity), assuming a high prevalence of OSAS in the population avoids most of the false-positive tests associated with home-testing. The results of these studies are thus not generalizable to patients with lower prevalence of OSAS. Ayas et al.[86] report indeed that if the pre-test probability of OSAS is below 47%, hospital/sleep lab PSG is less costly than home PG.

However, restricting the analysis to inappropriate short time horizons (e.g. the diagnosis only[52] or up to the titration in some studies,[85, 87, 88] fails to capture the full consequences of misdiagnosis. In the above studies, the long-term impact (health outcome and cost) on the false-negative patients when a high prevalence of OSAS is assumed was thus ignored.

Long time horizon

The three studies with a longer time horizon (at least 5 years) are more cautious as to the broader use of home testing. These studies were cost-utility analyses that modelled the 5-year,[80] 10-year[81] and lifetime[82] costs and health consequences of a home versus hospital/sleep-lab OSAS diagnosis.

In Deutch et al.,[80] with an 82% prevalence of OSAS, sleep lab PSG (full-night) was found to be more expensive but also more clinically effective (in terms of QALYs gained) than home-based PG, resulting in an acceptable ICER of US$ 7400 per QALY. Uncertainty was explored in probabilistic sensitivity analyses in which all parameters (e.g. OSAS pre-test probability, tests sensitivities and specificities…) were varied simultaneously. At a threshold of $ 15 000 per QALY, the probability that sleep-lab PSG was more cost-effective than home-based PG was 95%. Details of the univariate sensitivity analyses were not provided.

In Moro et al.,[81] besides in-laboratory PSG and home PG, a third option was considered which is to treat all patients empirically without performing any diagnosing test. As expected this option was the most cost-effective when assuming a very high prevalence of OSAS (> 80%) in the population tested. At a lower OSAS prevalence (< 80%), the in-laboratory PSG diagnosis was favoured when the cost of untreated OSAS was high (over US$ 2000 per untreated OSAS per year), in order to minimise the false negative diagnoses; while when the cost of untreated OSAS was low (below $ 2000), home PG was the preferred option. Interestingly, Moro et al.[81] explored the impact of the presence or absence of in-laboratory PSG backup for the negative home PG tests. When in-laboratory back-up is available, home PG was preferred across a large range of pre-test probabilities of OSAS (except when this probability was very low, i.e. between 10-20%, in which case in-laboratory PSG was preferred. This strategy was however associated with ICERs only slightly lower than $ 50 000 per QALY. Without laboratory PSG backup for the negative home PG results, the in-laboratory PSG diagnosis option was the most preferred at longer time horizons.

In Pietzsch et al.,[82] with a 50% pre-test probability of having OSAS, the preferred diagnosing strategy among all strategies modelled (Lab PSG, Home PG, no diagnosis and treatment, empiric treatment) was in-laboratory PSG with a cost of US$ 17 000 per QALY. This was justified by the superior diagnostic accuracy of this test, largely compensating its higher cost in the long term. Similar results were obtained with an OSAS prevalence of 20% and 80%.

Conclusion

When considering a short-term horizon (≤ 1 year), home PG was usually found to be more attractive (both in terms of costs and consequences) than laboratory PSG. With a short time horizon however, the long-term costs and health consequences of the home-PG missed diagnoses are ignored and the conclusions of such studies are questionable.

With a long-term horizon (at least 5 years), the full impact of the increased number of false-positive and false-negative home-PG tests compared with in-lab PSG is considered. Based on the results of three US studies, in-laboratory PSG diagnosis is then usually found to be the most cost-effective option, especially when the cost of untreated OSAS is high and when there is no in-laboratory PSG backup to the negative home-PG test results. When in-laboratory PSG backup is available, home PG becomes the preferred option unless the pre-test probability of OSAS is below 30%.

These conclusions assume however an accurate estimation of the sensitivity and the specificity of the PG portable devices, of the pre-test probability of OSAS, and of the cost of untreated OSAS. More specifically, an accurate estimate of the precision of the home-based tests is hampered by the numerous type of portable monitors available on the market. Note further that none of the studies reviewed here made a comparison with home-based PSG (Type II portable monitor).

3 INTERNATIONAL COMPARISON

Two experts per country were invited to fill in the questionnaires (see methods in section 1.3). Their names are referenced in the text, where appropriate. However, these experts did not take part in the drafting of this chapter and cannot be held responsible for its content.

3.1 Diagnosis of OSAS

3.1.1 Screening by questionnaires

The diagnosis of OSAS is based in all countries on the criteria recommended by the AASM (see section 2.1), i.e. a mild OSAS corresponds to 5-15 AHI per hour of sleep, a moderate OSAS to 15-30 AHI and a severe AHI to more than 30 AHI per hour of sleep. The Epworth Sleepiness Scale (ESS) is used in all selected countries to assess somnolence.[a] Although the STOP-Bang questionnaire was initially developed to screen patients for suspected OSA pre-operatively, it now also widely used for assessing OSA outside the pre-operative context,[b] except in England. The use of other questionnaires such as the Insomnia Severity Index (ISI) questionnaire is more variable.[c] Some countries have developed their own screening tool, such as the Basic Nordic Sleep Questionnaire[d] for every patient who is admitted to sleep recording in Finland (Dr. Brander).[90] Questionnaires to exclude other pathologies may be used, such as the IRLS[e] for assessing Restless Legs Syndrome in the Netherlands, or the BDI-II[f] (Becks Depression Inventory) in Germany (Dr. Schulz). In the Netherlands a specific Patient-Reported Apnoea Questionnaire (PRAQ) was developed to measure patient outcomes, but it is not commonly used (Dr. Sastry).[89]

a http://epworthsleepinessscale.com/about-the-ess/

b http://stopbang.ca/osa/screening.php

c https://mapi-trust.org/questionnaires/isi/

d https://link.springer.com/chapter/10.1007/978-1-4419-9893-4_6

e https://www.respiratorysleepqld.com.au/wp-content/uploads/DrAR-Restless-Legs-Rating-Scale-v1.pdf

f https://www.depression-test.net/beck-depression-inventory.html

3.1.2 Home-based diagnosis

In Belgium, the diagnosis must be based on the results of a hospital-based PSG. This is compulsory to get the treatment reimbursed by the Sickness Fund.[57] Therefore, there is in principle no home-based diagnosis of OSAS.[a] However, locally, the practice may vary somehow. For example, a pilot project in the Sleep Lab in the University Hospital of Liege relies on a home-based screening of OSAS with PG in almost every patients, i.e. in patients without comorbidities (such as heart failure, severe COPD, suspicion of obesity hypoventilation syndrome) or suspicion of others sleep disorders such as periodic limb movement disorders (Dr. Fanielle). Such screening allows to prioritize patients who need a PSG for diagnosis confirmation and to reduce the waiting time for such patients. Other health care providers (e.g. Centre de Santé de l'Amblève, in Aywaille) or private service providers (e.g. SleepClinic, see section 3.4) provide home-based diagnosis either with ambulatory PSG (portable monitor type II) or PG (type III or type IV) (see section 2.3.3). In this case, however, patients are not entitled to the reimbursement of diagnosis and subsequent treatment.

In Germany a diagnosis pathway similar to Liege University Hospital is reported and a PG is always done before undergoing a PSG. Although a home-based diagnosis by PG is recommended in patients with high pre-test probability (daytime sleepiness, breathing pauses and snoring) by the national clinical guideline on OSAS,[91] the field practice differs (Dr. Schulz).

Almost all patients with OSA who had PG[b] at home and are suspected to suffer from OSAS are admitted to a sleep lab where PSG is carried out to confirm the diagnosis (even in those with an AHI > 15/h at PG). One reason may be that most private practitioners don't wish to be responsible for missing or confirming a possibly life-changing diagnosis. Another reason may be that PAP initiation is almost exclusively performed under the supervision of a sleep lab (Dr. Schulz). As a result, OSAS diagnosis is almost exclusively done in hospital-based or private sleep labs over 1 night, although a PG is first performed in almost all patients. Only in rare cases, the diagnosis is exclusively based on PG at home (Dr. Schulz). Some physicians in private practice do not send their patients to the sleep lab, i.e. they diagnose OSAS by ambulatory PG and then hand out a PAP device to the patients to try it at their homes. A 4-6 channel PG is recommended and used in 80-90% of cases and a 1-3 channels PG (only measuring airflow and/or pulse oximetry) can be used (10%-20% of cases) under particular conditions (stable clinical condition and absence of significant accompanying cardiopulmonary or neurological diseases).[91]

In the remaining countries (Finland, France, the Netherlands and England), the diagnosis approach differs radically from what is reported in Belgium and Germany, as PSG is not compulsory and a home-based PG is used in a substantial proportion of patients as a stand-alone diagnosis test. This would go from 30-40% of diagnoses in England[c] (Dr. Steier) to 70-80% in France[d] (Dr. Pépin) and the Netherlands[e], and up to 90-99% in Finland[f], although

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a This approach is not allowed anymore in Belgium since 2006 (Dr. Verbraecken).

b In Germany, home-based PG can be done with Type III portable monitor, e.g. Somnotouch, Nox, Miniscreen, Embletta.

c In England, typically, most centres in England are organized in sleep laboratories that are associated with hospitals. Respiratory sleep labs may be associated with District General Hospital's, but polysomnography is typically available in tertiary referral centres (e.g. university). Home studies, particularly screening studies (pulse oximetry, watchPAT, Embletta or Apnoealink) may be used in the home setting and are frequently recorded over two nights. Pulse oximetry is accepted within the NHS as surrogate marker, largely due to capacity issues for PG/PSG (Dr. Steier).

d In France, mandibular movement signal is used in clinical research (Dr. Pépin).

e In the Netherlands, WatchPAT' is regularly used in three sleep centres but several centres are performing pilot evaluations. Also Embletta is used in some centres for this purpose. Many of the sleep examinations at home are carried out by service providers such as Vivisol, Medic Tefa or Vitalaire, including PG and PSG with complete analysis.

f In Finland, overnight pulse oximetry appears to be used in <5% of the cases (but mainly with transcutaneous capnography when nocturnal

those percentages can differ between sleep labs. Home-based diagnosis with PG is usually applied in patients at high pre-test probability of OSAS without symptoms of severe or unstable comorbidities suggesting another associated sleep disorder (e.g. periodic limb movement disorder, narcolepsy, parasomnias or seizures). Portable monitors of type 2, type 3 or type 4 (e.g. pulse oximetry in England) can be used, without a specific model or brand being recommended.

For the installation of the portable monitors two main strategies are used. In Finland and Germany, the functioning of the device is explained in a consultation at the hospital and the patient installs it himself at night at home. He returns the device the next morning to the hospital/sleep lab or private clinic. This is also the case in a pilot project at the University of Liège in Belgium. In Belgium, France and usually in the Netherlands,[a] the patient comes to the sleep lab for the PM to be installed and goes back home. Finally, in England the organization depends on the test used. For pulse oximetry patients may pick it up at the sleep lab or receive them by post. For Embletta and WatchPAT, most patients will be set up overnight at the sleep lab and return the equipment the day after. In all countries, a minority of patients are set up at home.[b] However, private providers may offer more often home-based PG or PSG (see section 3.4).

In all countries, a manual scoring of results is recommended, done either by a technician (supervised by a MD or not) or a MD specialized in sleep medicine (in a minority of cases). However, experts report a significant proportion of diagnoses being based first on an automated pre-analysis followed by a manual check, particularly when the results of the automated reading are not clear-cut (e.g. in Finland). In reality, according to experts, automated scoring is done in most of the countries, especially when the test is a PG and when the diagnosis is done by private providers (e.g. in France, Finland, Germany and England).

Recommendations vary on what should be done in case of a negative home-based PG (see Table 8). For example, in Finland it is recommended to repeat PG (for instance in case of technical problems) or have a CPAP trial (rarely done). Performing a PSG is also an option but this is done in a minority of cases. Interestingly, in England home-based PG are frequently recorded over two nights for better accuracy, i.e. results are considered valid (Dr. Steier). Where PSG is used for the diagnosis in first intention, the recommendation also vary between countries in case of a negative result (see Table 8).

hypoventilation/obesity hypoventilation syndrome is suspected). One centre performs 30% of PG with WatchPat (Dr. Brander). “In my hospital /sleep unit and in Helsinki primary care NOX T 3 is used. In private sector and in other parts of Finland also ApnoeaLink and Remote Analysis” (Dr. Brander).

[a] In some cases, ambulant PGs can also be done by the patient at home after looking at an instruction film and written instruction available in the recorder case (Dr. Asin).

[b] Less of 5% of patients with home-based studies in England (Dr. Steier).

Table 8 – Home-based diagnosis of OSAS in selected countries

Country	% Home-based diagnosis	Channels required	Action in case of a negative PG	Action in case of a negative PSG
Belgium	0%[a]	Nasal flow snoring, thoracic and abdominal effort, body position, oxygen saturation, heart rate	NA	Repeat PSG (but not reimbursed)
England	Any patients[b] 30-40% by PG	All types of PM can be used; pulse oximetry is predominantly used Home-based PG are frequently recorded over two nights for better accuracy	Consider PSG	Consider PSG, followed by a multiple sleep latency test to exclude other sleep pathologies. But frequently a negative PSG contains many learning points as to why the patient might be sleepy (and not have OSA),
Finland	In any patient 90-99% by PG[c]	Nasal flow, snoring, thoracic and abdominal effort, body position, oxygen saturation, pulse rate, heart rate, leg movements (recommended) Pulse-oximetry is used occasionally (<5%), often with capnography WatchPAT is used	Repeat PG Consider CPAP trial (rarely) Consider PSG (rarely)	Repeat PSG or have a CPAP trial[d]
France	In uncomplicated patients patients with high pretest probability 60 to 90% 60 to 80% by PG 10% by PSG	Nasal flow, thoracic and abdominal effort, body position, oxygen saturation, pulse rate, heart rate Type II or type III PM are used	Do PSG	Repeat PSG and seek for alternative diagnosis (neurological, infectious, depression, etc…)

[a] PSG is compulsory in all cases. However, home-based diagnosis with PG or PSG is applied by some health care providers or some private service providers.

[b] Particularly in the screening (pre-anaesthetics) of OSA and for patients with learning disability or mental health issues who may not attend the hospital setting easily or without carer (Dr. Steier).

[c] The primary care sector is responsible in most cases for the basic diagnostics.

[d] CPAP trial is not very often used but is less laborious than repeating PSG or polygraphy. If the APAP device increases pressure and patient is less sleepy, the trial is considered successful (Dr. Saaresranta).

Germany	In uncomplicated patients with high pretest probability 100% by PG PSG is compulsory in all cases[a]	Nasal flow, snoring, thoracic or abdominal effort, body position, oxygen saturation, pulse rate Type II and type III PM are used Type 3 Monitor (Flow, one effort, oxygen saturation, pulse rate, snoring, body position)	Repeat PG (Dr. Schulz) Do PSG (Dr. Fietze)	Repeat PSG
The Netherlands	In uncomplicated patients patients with high pretest probability 70% 39% by PG 31% by PSG	Nasal flow, thoracic and abdominal respiratory effort, oximetry) PAT with oximetry and actigraphy is also used (Dr. Sastry)	Do PSG[b]	Repeat PSG in case of a negative test and strong clinical suspicion of OSA

PAT: Peripheral Arterial Tone; PG: Polygraphy; PSG: Polysomnography; PM: Portable Monitor

3.2 Treatment of OSAS

3.2.1 Lifestyle recommendations

In Belgium, France, Finland and Germany only general advice on healthy lifestyle is usually given. In the Netherlands, a more pro-active strategy is applied. In that country, lifestyle changes including weight management are a recognized treatment for all severities of OSA and may be the only treatment in mild cases. Since 2019, patients with OSA and a BMI of at least 25 are entitled to a lifestyle coach, which is covered by their basic health insurance package.[c] However, not enough coaches are currently available and it mainly depends on the involved sleep specialist whether it is limited to general advice or whether coaching is offered (Dr. Sastry). In England as well, a multi-disciplinary team with dietician and metabolic services can be available in sleep labs, but not necessarily in non-tertiary services (Dr. Steier).

[a] Although the national clinical guidelines stipulates that PG can be performed in patients with high pre-test probability (daytime sleepiness and breathing pauses and snoring), and the diagnosis can be done on that basis. If PG reveals AHI<15/h, a PSG is recommended (Dr. Schulz). Though by law (BUB Guidelines) PSG should be mandatory, insurance companies accept the diagnosis by polygraphy (Dr. Fietze).

[b] There is no specific recommendation in the national guideline but the AASM recommendation is cited, i.e. performing a PSG in case HSAT is either negative, inconclusive or technically inadequate. It is ultimately left to the discretion of the sleep specialist how to proceed. As in the Dutch DBC system individual tests are not reimbursed, the number of PG/PSG performed to achieve a diagnosis in an individual patient is of no interest to the health insurances (Dr. Sastry).

[c] To follow training as a lifestyle coach in The Netherlands, a previous recognized training as e.g. dietician or physiotherapist is required.

3.2.2 PAP versus other treatment

In Belgium, PAP is currently the most applied OSAS treatment, whereas MAD use remains anecdotic although on the rise (see figures in section 4.2.1). This is not the case in every country. For example, in the Netherlands, among the 47 836 OSAS cases detected in year 2017, grossly 60% were treated with PAP, 30% with MADs and 10% with other treatments (mainly OSA-surgical interventions and Sleep Position Trainers). The 2009 Dutch national guideline for diagnosis and treatment of OSA (updated in 2017)[a] recommended MADs for mild to moderate OSA, i.e. the group of beneficiaries is greater than in Belgium where only patients with a ≥ 15 are eligible for treatment. Contrary to the approach in other countries, Dutch health-insurers support the prescription of MADs in patients with mild to moderate OSA and occasionally some health-insurers actually demand medical substantiation if CPAP instead of MADs are prescribed in such patients (Dr. Sastry & Dr. Asin)

In most countries, the vast majority of MADs are custom-made, going from 0% of ready-made devices in Belgium, Finland and the Netherlands, to 10% in France, and 5-10% (Dr. Schulz) to 20% (Dr. Fietze) in Germany. The remarkable exception is England where 90% of MADs are ready-made (Dr. Steier).

3.2.3 Titration of PAP

In Belgium, the vast majority of titrations is done in-hospital, with PSG in 95% of the cases and PG in 2.5%. Only 2.5% are home-based titration with PG.[b] Again, practices vary locally. In the University Hospital of Liège, 40% of titrations are home-based, either by APAP or CPAP with telemonitoring (Dr. Fanielle), whereas no home-based titration is performed at the University Hospital of Antwerp. APAP-only titration is not used as it is currently compulsory to perform a PSG or a PG to assess the adequacy of the treatment.[57]

In contrast, titration based on APAP is common up to 60-90% (see Table 8). In England, Finland, France and the Netherlands, home-based APAP-only is the dominant titration technique (90-95% of all patients in Finland, France and the Netherlands (Dr. Asin), and 80% in England). In Finland and England, some of these titrations by APAP-only are sometimes performed in hospital. The case of Germany is in-between. About 10-20% of titration are home-based, usually based on APAP followed by a PG, with big regional variations, APAP-only being used between 0% titration (Dr. Schulz) to 50% (Dr. Fietze).

Split-night protocols are rarely applied in any country. Some sleep labs do it in Germany in patients with an AHI > 15/h as judged by prior PG done at home (PG is performed in all patients prior to a PSG). The only notable exception is England where 60% of titration are done during split-nights in an attempt to reduce waiting lists (Dr. Steier).

3.2.4 Follow-up of treatment

In every country under scrutiny, the clinical follow-up is more intensive in the first months of the treatment (see Table 9). However, the long-term follow up of PAP treatment varies greatly by country. In Belgium, a patient must be seen every year by the sleep specialist, which is the condition for continuation of the payment of the daily lump sum by the National Health Insurance.[57] Such an annual follow-up is also applied in England, France, and Germany. In France, this annual follow-up can be passed over to the GP 16 months after the start of the treatment in uncomplicated patients. In Finland and the Netherlands, there is no fixed follow-up medical consultations scheduled after month 12 and no renewal of the prescription is required.

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a https://www.nvalt.nl/kwaliteit/richtlijnen/slaap/_/Slaap/Richtlijn%20OSA%20bij%20volwassenen%20%28geaccordeerd%20april%202018%29.pdf

b Communication from INAMI/RIZIV.

Table 9 – Clinical follow-up of OSAS patients in selected countries

Country	Timing of medical consultations	Action
Belgium	For PAP: at month 3, 12 and annually thereafter For MAD: at month 6, 12 and annually thereafter	The annual consultation is necessary for renewal of the prescription by the MD.
England	At month 3, annually thereafter	The annual consultation is necessary for renewal of the prescription by the MD.[a]
Finland	Usually 2 controls in the first year, either face-to-face or by telemonitoring[a] Routine check-up at year 5 or no medical follow-up after month 12	No renewal of prescription is required.
France	For PAP: at month 1, 4 and annually thereafter For MAD: at month 1, 4 and every 6 months thereafter for a dental follow-up	CPAP prescription is renewed by the sleep physician at months 4 and 12 and afterwards every 12 months based on patient acceptance, adherence and clinical improvement. On demand home-based oximetry maybe performed (by private providers) in case of residual events or suspicion of obesity hypoventilation syndrome (in estimated 5 to 10% of CPAP-treated patients once a year). CPAP prescription can be renewed by the GP after 16 months in case of treatment success with good adherence, no important side effect and clinical improvement. MAD prescription is renewed by the sleep physician every 2 years if clinical improvement and at least 50% reduction in AHI.[b]
Germany	At month 3[c] and annually thereafter	The annual consultation is necessary for renewal of the prescription by the MD.
The Netherlands	For PAP: telemonitoring at week 1, 3, 10 and after 1 year in over 53% of centres (estimate). No telemonitoring thereafter in uncomplicated OSAS but direct machine readings are used. For problematic patients telemonitoring is used for a longer period. For MAD: The national guideline requires a P(S)G re-evaluation of the MAD treatment in case the AHI was at least 15 at diagnosis. (In case of an AHI < 15 at diagnosis a P(S)G may be performed in case of persistence of symptoms with the MAD or in case of considerable weight gain)	No renewal of prescription is required for PAP. Service providers are required to do annual readings and report to the sleep clinic in case of problems. Patients are instructed to read out their device-AHI and to contact their sleep clinic when necessary (in one centre; Dr. Sastry). Prescription renewal may be required for MAD, usually after 5 years, depending on the health insurance. Moreover, in case of significant increase in weight or progression of complaints while using the MAD, a new sleep study may be required.

AHI: Apnoea Hypopnoea Index; MAD: Mandibular Advancement Device; PAT: Peripheral Arterial Tone; PG: Polygraphy; PSG: Polysomnography; PM: Portable Monitor

Telemonitoring to measure adherence to treatment, residual AHI, or mask leaks, is widely used in four of the analysed countries (100% of patients in England, France and Finland[d]; ≥53 % estimated in the Netherlands). Only in Belgium and Germany (5-10% of patients) is the telemonitoring rate much lower. In Belgium the practice appears highly variable among sleep labs.

[a] If a patient is not seen within a year there is no guarantee on the CPAP and the contract with the funding Clinical Commissioning Groups (NHS) ceases (Dr. Steier).

In UZA Hospital, telemonitoring is not used (Dr. Verbraecken), whereas it is used in 100% of patients in the pilot project at Liège University Hospital (Dr. Fanielle). There is no fee for telemonitoring within the National Health Insurance (INAMI-RIZIV). The technique was initiated for free by the companies, but they later started with a fee for service. According to some, the cost is too high compared to the benefits.

Adherence to treatment is a crucial parameter to follow up. Definition of an acceptable adherence level, and measures taken in case of insufficient adherence are displayed in Table 10. Whereas a withdrawal of the treatment in case of low adherence is considered in every country, Belgium and France seem to be the only two countries where a strict rule applies. In Belgium (UZA[e]) and in England, a patient accompaniment to improve adherence has been developed.

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[a] Timing and practice vary from centre to centre. In some centres patients have treatment adequacy control every year or every second year at the hospital-based or primary care based sleep apnoea nurse. In Turku University Hospital there is 1-year control visit in 1/3 of patients, others are only checked with the wireless telemonitoring and with phone calls if needed. The routine check-up is at five years after treatment start (Dr. Saaresranta). In Helsinki University Hospital, there are controls 1-2 times during the first year (first after 2-4 weeks and, if no problems, after 3-12 months). After that there are no further routine checks ups (Dr. Brander).

[b] For MAD a systematic PSG or PG is recommended to evaluate treatment efficacy after the titration period.

[c] At month 6 according to Dr. Fietze.

[d] In Finland, it is used 2-3 times during the first year of treatment and thereafter only when the patient contacts the sleep unit (if he or she has problems with the device or the treatment) (Dr. Brander), and practice differs from centre to centre.

[e] “We contact the patients who had difficulties during the titration night in the hospital. We also have a contact phone for patients who have difficulties when using CPAP at home. For MAD there is a longer titration period, where they have different contacts with the care team.” (Dr. Verbraecken) In UZA, the adherence on CPAP would be 71% after 1 year, 60% on the long run.

Table 10 – Adherence to PAP treatment

Country	Adherence criterion	Measurements	Measures taken if low adherence
Belgium	≥4 hours per night on average[a]	Reading of CPAP data annually[b]. For MAD, objective assessment of adherence with a chip is not mandatory.	Prescription renewal only for next 3 months. If adherence remains poor during that period, the daily lump sum paid to the hospital is withdrawn for 1 year. The treatment can start again on the basis of a request by the prescribing physician. A new PSG is necessary if the initial PSG is older than 2 years.
England	≥4 hours per night during at least 70% of the nights	By telemonitoring or during the annual follow-up	No "official" cut-off of adherence under which the reimbursement is stopped.[c]
Finland	≥4 hours per night on average during the last year	Routinely by telemonitoring[d]. Timing varies among sleep centres.	Treatment is stopped and the patient has to return the device.
France	≥4 hours per night[e]	Every 28 days by telemonitoring	The level of reimbursement of the home care provider is lowered during several months. If there is no improvement after 6 months, the treatment is stopped.
Germany	≥5 hours[f] per night, 5 nights per week	Annually by reading CPAP data. Not all health care insurance companies monitor the regular use of the device	No official requirements and no regular controls[g]
The Netherlands	≥4 hours per night, 5 nights per week	Telemonitoring is mainly used during the trial period but some clinics and providers perform a read-out of the device. Providers are required to do annual readings (and report back to the sleep clinic in case of problems (see above). If service	Coverage of re-imbursement by the health insurance may be discontinued in case of insufficient CPAP usage.

a Assessed at month 3 and at month 12, annually thereafter.

b Except for the 2 first measurements done at month 3 and month 12.

c "Patients will be given plenty of time and chances to discuss this and improve adherence. They are also referred to special CPAP failure clinics to discuss alternatives to CPAP. To enhance treatment adherence, teaching sessions are provided, either group or individual. Interpreters can be booked. Positive and negative healthcare framing messages have been trialled and are used to encourage adherence, reminders are sent and remote monitoring allows interaction and direct patient feedback" (Dr. Steier).

d In Helsinki University Hospital, adherence if measured during sleep unit outpatients visits if there are any, and routinely at least twice during the first year by telemonitoring (after 2-4 weeks and 3-12 months of treatment). There are no regular checks up of adherence after the 1st year. In Turku University Hospital all patients are telemonitored for 5 years.

e At least 112 hour of utilization over 28 days. However to account for temporary difficulties with the CPAP, a minimum of 56 hours is accepted as the lower bound.

f 4h per night according to Dr. Fietze.

g "Even if a patient is not able to use the device for the whole night he may nevertheless have some benefit from treatment. In these circumstances, the doctor is asked to forward a statement detailing why the target of running hours was not reached. Thus, therapy may be continued despite of less than optimal adherence. Moreover, not all health care insurance companies monitor the regular use of the PAP device. In these cases, it may well be that the device rests unused at the patient's home" (Dr. Schulz).

	providers do a device reading it is either by telemonitoring or machine read-out

CPAP: Continuous Positive Airway Pressure; PAP: Positive Airway Pressure; PSG: Polysomnography.

3.3 Funding

In all countries surveyed, the health care resources consumed for the diagnosis of OSAS patients are covered according to the general payment mechanisms defined by the respective National (or regional) health care systems (e.g. retrospective fee-for-service, prospective diagnosis related group (DRG), prospective capitation, mixed systems…). Depending on the health care systems, the payments obtained are defined nationally and are equal among all health care providers (e.g. Belgium, France), or they are defined at the local/regional level or through negotiations and may vary between providers (e.g. the Netherlands, Finland and Germany). OSAS patients are mostly covered by public health care insurance, sometimes complemented with a top-up voluntary private insurance. In few countries, patients may choose to opt-out of the public health care insurance (i.e. for 11% of patients in Germany). They are then totally covered by the private insurance sector. Except in England, all patients incur out-of-pocket expenses (mainly co-payments) for an OSAS diagnosis (limited to a defined yearly amount in the Netherlands).

In Belgium, only one PSG per year in covered by the health insurance, and PGs are not reimbursed as such. By contrast, in England, Finland, France, Germany, and the Netherlands there is no restriction as to the number of PG/PSG diagnoses performed and covered[a].

Of all the countries explored, Belgium is the only one working with a convention for the reimbursement of a treatment with PAP/MAD. The reimbursement of the costs for the titration and treatment of OSAS patients usually follows the same procedure as for the diagnosis of OSAS patients (i.e. following the general payment mechanisms in each country, see above), with some exceptions. In France and in Belgium, specific rules were developed to cover the costs incurred for the treatment (and also the titration in Belgium) of OSAS patients with PAP (and also with MAD in Belgium). These rules are described in the "OSAS Convention"[57] in Belgium and in the "Arrêté du 13 Décembre 2017" in France[b]. In both countries virtually all costs incurred for a treatment with PAP and its follow-up (also for MAD in Belgium) are covered through daily (Belgium) or weekly (France) lump-sums payed by the health insurance. Daily out-of-pocket payments are also defined for the patients in Belgium, while there is no such out-of-pocket expense for patients in France. The amounts reimbursed for a PAP treatment in France vary according to the patient's adherence to the treatment. For MAD, the dental care preparation and the device are fully reimbursed in France (one MAD reimbursed every 3 years). In Germany, annual fees are payed to the private home-care providers by the health insurance to cover the PAP device (and accessories) and its maintenance (e.g. € 230 for a CPAP). MAD devices are usually not reimbursed, though discussions to do so are ongoing. In the Netherlands, daily fees to home care providers are also paid by the health insurers to cover the PAP device and accessories, and its maintenance. For MAD, the dental care preparation and the device are fully reimbursed (one MAD reimbursed every 3-5 years).

With the exception of France and England, all patients incur out-of-pocket expenses (mainly co-payments) for an OSAS treatment.

[a] In the Netherlands, a lump sum is negotiated for a certain number of services per patient. Repeat PSGs are thus covered to some extent, but in any case a repeat PSG is a financial loss for the sleep clinic.

[b] https://www.legifrance.gouv.fr/affichTexte.do?cidTexte=JORFTEXT000036209897&categorieLien=id

Table 11 – Main public funding mechanisms for PAP / MAD treatment of OSAS patients in selected countries

	Reimbursement of:			PSG / PG reimbursement	Private home-care providers
	Diagnosis	Titration	Treatment & follow-up		
Belgium	Follows the general national public payment mechanisms - Fee-for-service - Prospective payment for inpatient stay Patient co-payment	Within the "OSAS convention" between the public health insurance and the recognised sleep centres Daily lump-sum (flat) reimbursements for PAP/MAD Patients co-payment		Only one PSG reimbursed per year PG not reimbursed outside the convention	Paid by the sleep centres (terms defined in contracts) for PAP treatment and follow-up
France	Follows the general national public payment mechanisms - Fee-for-service - Prospective DGR for inpatient stay Includes patient co-payment		Weekly lump-sum reimbursements for PAP (varies with adherence to treatment and telemonitoring) Reimbursement for MAD (every 3 year) No patient co-payment	No restriction to the number of PG/PSG	National payment mechanisms (diagnosis & titration) and lump-sum payments (treatment & follow-up) by the public health insurance
Finland	Follows the public payment mechanisms defined at the local/regional level (> 300 municipalities) - Mixed system of retrospective fee-for-service, prospective budget, and prospective DRGs Patient co-payment Reimbursement for MAD			No restriction to the number of PG/PSG	Direct payment by the municipalities, according to the public payment mechanisms (diagnosis, titration & treatment)
Germany	Follows the public payment mechanisms defined at the local/regional level (16 Länder) - Fee-for-service and capitation - Prospective DRG and contracts for inpatient stays and hospital care Patient co-payment No reimbursement for MAD (under discussion)			No restriction to the number of PG/PSG	Annual fee paid directly by the health insurers for treatment & follow-up
The Netherlands	Follows the public payment mechanisms defined at the regional level - Fee-for-service and capitation, bundled payment for integrated care and pay-for-performance - Adapted DRG system and negotiations for hospital costs Patient co-payment Reimbursement for MAD (every 3-5 years)			No restriction to the number of PG/PSG (within the negotiated lump sum)	Daily fee paid directly by the health insurers for treatment and follow-up

England	Follows the general national public payment mechanisms - Capitation, pay-for-performance - Prospective DRG No patient co-payment Provision of MAD, free of charge, in some areas of England.	No restriction to the number of PG/PSG -

DRG: diagnosis related group; PG: Polygraphy; PSG: Polysomnography; MAD: Mandibular Advancement Device

3.3.1 Belgium

The Belgian Health Care System[a]

In Belgium, health insurance is compulsory and nearly the total population (99%) is covered. The compulsory health insurance is managed by the National Institute for Health and Disability Insurance (INAMI – RIZIV) and is implemented through five private, not-for-profit national associations of sickness funds and additionally one fund for railway personnel and one public sickness fund. In addition to this compulsory insurance, Belgians may purchase supplementary voluntary healthcare insurance which is either provided by the sickness funds or by private profit-making insurers, and that covers any cost-sharing left after the reimbursement of compulsory health insurance or additional services (e.g. single room hospitalisation, dental care).

Public sources (including compulsory health insurance coverage) made up 77% of all health expenditures in 2017. Direct out-of-pocket payments accounted for 18% of overall health spending. The share of private voluntary health insurance is relatively limited and represents the remaining 5% of all expenditures in 2017, mostly for inpatient expenditures.

The majority of physicians are self-employed and are mainly paid through a fee-for-services system. Patients can access specialist care without a referral although with referral the out-of-pocket amount is reduced.

For hospitals, funding is essentially based on a prospective budget system linked with the patient-related activity. The "justified activity" of each hospital is defined according to the number and type of admissions for a reference year. Each person admitted is granted a length of stay justified according to his/her pathology.

The (ambulatory and inpatient) medical services that are covered by the compulsory health insurance are described in a nationally established list called "nomenclature" and are reimbursed according to a fee-for-service system.

In Belgium, the health care services consumed to diagnose OSAS patients are covered by fee-for-service (for the consultations and medical services) or through a prospective budget system linked with the patient-related activity (for inpatient services). Only one PSG is reimbursed per year, and PG is not listed on the fee schedule meaning that it is not reimbursed by the health insurance. For the hospital or sleep lab PSG, the reported cost estimate is € 800-900 (including one overnight stay[b]), of which € 30-40 is paid by the patient.

[a] Sources: HIT Belgium 2010 (and website updates) and Country health profile Belgium 2019. http://www.euro.who.int/en/about-us/partners/observatory/publications/health-system-reviews-hits/full-list-of-country-hits/belgium-hit-2010 http://www.euro.who.int/__data/assets/pdf_file/0006/419451/Country-Health-Profile-2019-Belgium.pdf?ua=1

[b] In this section, the costs reported for the hospital/sleep lab also include the cost of an overnight stay.

With the exception of the hospital stays and the physician follow-up consultations, all health procedures (including the home- or hospital-based PSG/PG titration) consumed for the treatment of OSAS patients with PAP or MAD are covered through daily lump-sums according to the "OSAS convention" which is an agreement between the Belgian compulsory health insurance (INAMI – RIZIV) and the sleep centres. The daily lump-sum paid by the Health Insurance (INAMI – RIZIV) to the health care providers are:

- CPAP Start package (first 6 months): € 2.57 per day
- CPAP Basic package (after the first 6 months): € 1.54 per day
- MAD Start package (first 6 months): € 5.14 per day
- MAD Basic package (after the first 6 months): € 0.43

For PAP, the co-payment for a regular patient is € 0.25 per day of treatment (no time limit). For MAD treatment, since 01/02/2020, the co-payment for a regular patient is € 0.5 per day during the first 6 months of treatment (for initial and renewal treatment).[a]

PAP reimbursement is first granted for a period of 3 months. Subsequent reimbursements are then granted per 12-month periods provided adequate therapeutic compliance (i.e. at least 4 hours use per night) is confirmed during the annual medical consultations through a read-out of the device. Non-adherent patients are offered a new 3-month trial during which PAP treatment is still reimbursed. If this trial fails, reimbursement is stopped for 1 year.

MAD reimbursement is first granted for a period of 6 months. If treatment efficacy is demonstrated at 6 months (PG/PSG), subsequent reimbursements are then granted per 12-month periods if the physician confirms treatment compliance (i.e. at least 4 hours per night). Non-adherent patients are offered a new 3-month trial with MAD reimbursement. If this trial fails, reimbursement is stopped for 1 year.

Telemonitoring is not part of the OSAS convention.

In 2018, the total INAMI – RIZIV budget allocated to the treatment of OSAS patients (diagnosis excluded) was € 64.8 million, of which € 63.5 for PAP treatment and € 1.3 for MAD treatment. The patient co-payment was slightly less than € 8 million (patient contribution for MAD was € 0 until 31/01/2020).

3.3.2 France

The French Health Care System[b]

Health expenditure in France is mostly publicly funded (78% in 2017), but private complementary voluntary health insurance (VHI) also plays an important role (13% of all health spending). The remaining 9 % is paid directly out of pocket by patients. VHI in France is not used to jump public sector queues or to obtain access to elite providers. Its primary role is complementary coverage for patient co-insurance amounts and other user charges.

The payment mechanism for ambulatory health care professionals and services is based on fee-for-service. This is complemented with a pay-for-performance system for doctors since mid-2000.

Since 2004/2005, hospital acute care and hospitalization at home, providing care equivalent to hospital care but in the patient's own home, are paid per DRG under the medical activity-based payment system (tarification à l'activité; T2A).

[a] http://www.ejustice.just.fgov.be/cgi_loi/change_lg.pl?language=fr&la=F&table_name=loi&cn=2019110311

[b] Sources: Country Health Profile France 2019 and Health in Transition France 2015. http://www.euro.who.int/__data/assets/pdf_file/0007/419803/Country-Health-Profile-2019-France.pdf?ua=1 and http://www.euro.who.int/__data/assets/pdf_file/0011/297938/France-HiT.pdf?ua=1

In France, the health care services consumed to diagnose OSAS patients and for their device titration is fully covered by fee for service[a] (ambulatory PG/PSG, doctors' consultations…) or per DRG (hospital/sleep lab). Home care providers are also covered on a fee-for-service basis (with concurrent intervention of private insurances). The following costs are reported by the French experts:

- Home PG diagnosis: € 180-200 (Dr. Gagnadoux)
- Home PSG: € 240-260 (Dr. Gagnadoux)
- Hospital/sleep lab PSG (including overnight stay): € 500-600 (Dr. Pépin & Dr. Gagnadoux)
- Home titration (APAP only): € 145-250 (Dr. Pépin)
- Hospital/sleep lab titration PSG (including overnight stay): € 500-700 (Dr. Pépin)

On 13/12/2017, new rules for the reimbursement of CPAP treatment were issued. CPAP is now covered by the French Health Care Insurance through weekly lump-sums whose amount is conditional on the effective use of the device by the patient.[b] [c] PAP devices are loaned to patients and installed in their homes by private home-care providers. The lump-sums are directly paid by the French Social Health Insurance to the private home-care provider. There is no patient out-of-pocket payment. The basic lump-sum is € 17.5 per week during the first 13 weeks of PAP treatment. After this initial period, the lump-sum varies according the patient's adherence to the treatment and whether the patient agrees to be telemonitored or to have his/her adherence data recorded:

- If the patient agrees to be telemonitored or have his/her adherence data recorded, the lump-sum is € 17 per week if adherence is > 112 hours during 28 days; €14.5 if adherence is between 56-112 hours; and € 5 if adherence is <56 hours.
- If the patient refuses to be telemonitored or have his/her data recorded, the lump-sum received by the home-care provider is € 9.8 for every week.

The payment to the provider is thus reduced when a patient does not fully adhere to its treatment. As there is no patient co-payment, this acts as a strong incentive for the provider to monitor the patient adherence and try to solve the problems.

For MAD, dental care preparation is fully reimbursed and one MAD (~ € 300) is reimbursed every 3 years.

The global annual budget spent by the public health care insurance for PAP therapy was € 637 539 748 in 2017 and € 646 743 713 in 2018 (Dr. Gagnadoux).

[a] Dr. Pépin commented: "We would expect new payment models covering all the clinical pathway rather than a repetition of fees for service".

[b] LegiFrance. Arrêté du 13 Décembre 2017: https://www.legifrance.gouv.fr/eli/arrete/2017/12/13/SSAS1735167A/jo/texte

[c] https://blog.reseau-morphee.fr/2017/07/20/modifications-conditions-de-prescription-machines-a-ppc/

3.3.3 Finland

The Finnish Health Care System[a]

The Finnish health system is governed at national and local levels. At the national level, the Ministry of Social Affairs and Health is responsible for health reforms and policies. Local authorities (over 300 municipalities) play a key role in purchasing and providing health services. They fund and organise (often jointly) the provision of primary care, and form 20 hospital districts to fund and provide hospital care. All residents of Finland, as long as they are registered as living in one of the municipalities, have access to publicly funded health services. However, while all residents are covered by municipal health care, availability of services, particularly in terms of primary care, varies across municipalities.

Three-quarters of health spending is financed through public sources, the remaining 25% paid by private sources. Most of this private expenditure comes from out-of-pocket payments (about 20% in 2017), the remaining comes from private insurance (about 5%).

In primary health care, municipalities prospectively fund the budget of the health centres they maintain. For GP consultations in the health centres, patients can choose to pay per visit (the majority of patients) or by annual charge. Fees for care provided at home depend on whether the service is occasional (paid per visit) or long-term (paid monthly).

Most hospital districts use DRGs for municipal invoicing at least for a part of funding. In addition, bed day charges or treatment package pricing are used for assigning the costs to municipalities. Daily inpatient hospital fees are also charged to the patient (co-payments covering examinations, treatment, medicines and meals).

When municipalities and hospital districts buy services from private providers, contracts and payment mechanisms vary considerably. These contracts are arranged by open competition (tenders).

In Finland, the ambulatory health care services delivered by the public sector (>95% of cases, with or without subcontract with private provider) for the diagnosis of OSAS patients and their treatment with PAP or MAD are covered by a mixed system of prospectively budget and retrospective fees for service (e.g. most GP consultations). Patient co-payment is approximately 5-7%. The health care services provided in public hospitals or sleep lab are mostly covered using a prospective DRG payment system, and also per diem. Patient co-payments represent 4-10%.

There are no restrictions in the number of (home or hospital-based) PG/PSG performed and reimbursed per year.

To be entitled to a reimbursement, the treatment prescription must be based on a pulmonologist's decision (AHI>15 or AHI<15 with symptoms, usually excessive daytime sleepiness).

Though they vary across municipalities, the following cost estimates were reported by the experts consulted:

- Home-based OSAS diagnosis: € 300 (Dr. Saaresranta) to € 500 (Dr. Brander)
- Hospital-based OSAS diagnosis: € 530 (Dr. Saaresranta) to € 900 for a PG, € 1200 for a PSG (Dr. Brander)
- Home-based titration: € 450 (Dr. Saaresranta) to € 900 (Dr. Brander[b])
- Hospital-based titration: € 1100 (Dr. Saaresranta) to € 1500 (Dr. Brander)

[a] Sources: Country Health Profile 2019 and HIT 2019 http://www.euro.who.int/__data/assets/pdf_file/0004/419458/Country-Health-Profile-2019-Finland.pdf?ua=1 https://apps.who.int/iris/bitstream/handle/10665/327538/18176127-eng.pdf?sequence=1&isAllowed=y

[b] The cost estimated by Dr. Brander also covers treatment initiation and monitoring fee.

According to the experts consulted, the budget spent in Finland for the management of OSAS patients is estimated at about € 27 million for PAP and € 2 million for MAD in 2019 (for a population or ca 5.5 million). This estimate is based on expert opinion, and no official source is mentioned.

3.3.4 Germany

The German Health Care System[a]

The German health system is split into public social health insurance (SHI) and private health insurance (PHI[b]), with a number of criteria determining who is insured in which. Employees are usually insured in the SHI, but people whose income is above a fixed threshold or who belong specific professional groups, e.g. self-employed or civil servants, can opt to enrol in PHI for full insurance. The SHI system currently consists in 109 sickness funds covering 87% of the population. About 11 % of the population is covered under one of the 41 private health insurance companies. Other specific groups (e.g. soldiers, police) are covered under special governmental schemes. Patient out-of-pocket expenses are on average 12.5%.

Responsibilities for health system governance are complex and divided among three levels: the federal level, the states (16 Länder) and the statutory organizations of payers (associations of the sickness funds and the Federal Association of Sickness Funds) and providers (SHI physicians and dentists).

Reimbursement mechanisms for ambulatory services are different between the public and private sectors. SHI physicians in ambulatory care (GPs and specialists) are generally reimbursed on a fee-for-service basis combined with a budget for cost control (i.e. contact capitation). Payments to SHI physicians are thus limited to covering a predefined maximum number of patients per practice and reimbursement points per patient, setting thresholds on the number of patients and of treatments per patient for which a physician can be reimbursed. SHI physicians in ambulatory care bill their regional associations and the regional associations receive the money from the sickness funds in the form of negotiated annual capitations (morbidity-based). For the treatment of private patients, GPs and specialists get a fee-for-service. Private tariffs are usually higher than the tariffs in the SHI.

Since 2003, all acute inpatient cases are reimbursed with DRG-based payments revised annually. This system applies to all hospitals, irrespective of ownership status (i.e. private versus public hospitals). Additionally, contracting parties (the German Hospital Federation and the associations of the statutory sickness funds and private health insurers) are authorized to negotiate for reimbursements that are not covered by DRGs by means of supplementary fees (case-based or per diem remuneration) for certain complex or cost-intensive services, and/or for very expensive drugs.

According to the German experts interviewed, roughly 80% of OSAS patients are managed in the public sector, the remaining 20% in the private sector. The management of OSAS (diagnosis and treatment) in the public sector is covered by a mixed fee-for-service/capitation (ambulatory care) or DRG (hospital care) system. The SHI reimbursements for the management of OSAS are however not harmonized and vary between the various regions of the country.

[a] Sources:
http://www.euro.who.int/__data/assets/pdf_file/0005/419459/Country-Health-Profile-2019-Germany.pdf?ua=1
https://international.commonwealthfund.org/countries/germany/
Stephani V, Quentin W, Van den Heede K, Van de Voorde C, Geissler A. Payment methods for hospital stays with a large variability in the care process. Health Services Research (HSR) Brussels: Belgian Health Care Knowledge Centre (KCE). 2018. KCE Reports 302.

[b] Private health insurance has two facets in Germany: (1) to fully cover a portion of the population (substitutive PHI) and (2) to offer supplementary and complementary insurance for SHI-covered people.

The following costs were reported for the management of OSAS:

- Home-based PG: € 100-200 (Dr. Schultz)
- Hospital-based PSG (including overnight stay): € 500-800 (Dr. Fietze); € 800-900 (Dr. Schultz)

Health care insurance companies pay annual fees to home care providers covering the costs of the PAP device itself as well as those for masks, filters etc.[a] The annual fee is approximately € 230 per year for a CPAP device, while the yearly costs for BiPAP, BiPAP-ST and ASV are € 400 / € 700 / € 1300 respectively (Dr. Schultz).

The first control after initiation of PAP therapy usually occurs after 3 months. Though regular yearly controls are recommended afterwards, not all hospitals/sleep centres do so and it may thus well be that some patients are not controlled at all or only after longer time intervals. Experts report either no regular follow-up controls (Dr. Fietze) or annual follow-up visits (Dr. Schultz).

Treatment adherence is usually documented by reading out the PAP memory card, and the doctor has to sign a form which is forwarded to the health insurance company. In case of low adherence or if the patient does not show up at a follow-up visit, reimbursement may be stopped and the device returned. However, not all health care insurance companies monitor the regular use of the PAP device. In these cases, the device may stay unused at the patient's home. No telemedicine approach in sleep medicine is covered by the German insurance so far.

In most cases, MAD devices are not reimbursed by the German public health insurance. The patient must pay for the device itself unless he/she has a private health insurance, which usually covers up to 100% of the costs. MAD's costs are in the range of € 500-1500. There are currently discussions among the German regulatory agencies (G-BA, Gemeinsamer Bundesausschuss) for MAD to be reimbursed within the public health insurance, if there is a clear indication for a MAD (i.e. if there is PAP-resistant OSAS and not only simple snoring).

The budget spent in Germany for the management of OSAS patients was not reported by the consulted experts.

3.3.5 The Netherlands

The Dutch Health Care System[b]

Dutch citizens are obliged to purchase statutory health insurance from private insurers for a standard basic benefits package and health insurers have to accept anyone who applies for an insurance policy. At the end of 2014, less than 0.2% of the population was uninsured. The standard basic package is defined by the government, based on the advices from the National Health care Institute (Zorginstituut Nederland), and roughly includes GP-care, maternity care, hospital care, home nursing care, pharmaceutical care and mental healthcare. Since 2016, every insured adult must pay an annual deductible (i.e. a franchise) of € 385 for health care costs.[c] The deductible is levied on all future healthcare expenditures that year, except for GP care, maternity care, home nursing care and care for children <18 years. Practically, the first € 385 (still in 2020) of healthcare expenditure from the basic package must be paid out-of-pocket before the insurance takes over. Apart from the overall deductible, patients are required to share some of the costs of selected services, such as medical transportation or medical devices. Out-of-pocket expenses represented 11.1% of health care spending in 2017.

[a] Most home care providers only offer a limited number of PAP devices and masks free of extra-charges. If a patient wants another PAP model or a specific mask, he has to pay for it on his own.

[b] https://international.commonwealthfund.org/countries/netherlands/
https://www.oecd-ilibrary.org/docserver/9ac45ee0-en.pdf?expires=1580135304&id=id&accname=guest&checksum=C41CBB4C5AD145381555E5BAB1E02F91
http://www.euro.who.int/__data/assets/pdf_file/0016/314404/HIT_Netherlands.pdf?ua=1

[c] Only if health-care costs are generated. If not, only monthly fees are paid.

In addition to statutory insurance, most of the population (84%) purchases complementary voluntary health insurance covering dental care, alternative medicine, physiotherapy, eyeglasses and lenses, contraceptives, and the full cost of co-payments for drugs. People with voluntary coverage do not receive faster access to any type of care, nor do they have increased choice of specialists or hospitals.

GPs are paid by a combination of mixed fee-for-service/capitation (75% of the spending), bundled payments for integrated care (15% of the spending), and pay-for-performance (focused on issues such as accessibility and referral patterns, 10% of the spending). Ambulatory care centre specialists are paid fee-for-service, and the fee schedule is negotiated with insurers.

Hospital reimbursement for medical treatments are determined through negotiations between each insurer and each hospital. Hospitals are paid through an adapted type of diagnosis-related group (DRG) system: Diagnosis Treatment Combinations ("Diagnose-Behandel-Combinatie", DBC). The rates for approximately 70 percent of hospital services are freely negotiable; the remaining 30 percent are set nationally. The DBC system covers both outpatient and inpatient as well as specialist costs, strengthening the integration of specialist care within the hospital organization.

As of 2015, home care is a shared responsibility of the national government, municipalities (day care, household services), and insurers (nursing care at home). Municipalities are funded through a global grant provided by the national government. They have a large margin of freedom in how they organize services. Long-term care is mostly provided by private organizations, including home care providers.

For the patient, the costs of diagnosis and treatment of OSAS are completely covered by the basic package of health insurance, with the exception of an annual mandatory deductible (i.e. a franchise, only paid when health-care cost are generated) per patient (€ 385) and a monthly health insurance fee. Reimbursement of consultations is mostly provided on a fee-for-service basis (mixed fee-for-service and capitation system for GPs). Reimbursement of all procedures incurred for OSAS is provided within the DBC system (i.e. the Dutch diagnosis-treatment-combination). The reimbursement obtained for a particular DBC may vary considerably between sleep clinics (health care provider) depending on the negotiations of the sleep clinics with individual health insurers. Usually an annual lump-sum is agreed upon, depending on the level of expertise of the clinic, the complexity of patients and of the diagnoses, as well as the diagnostic methods involved, treatments offered and the quality of the treatment. These negotiated tariffs are confidential.

Reimbursement by the health insurers is also provided separately to the private home-care providers to provide the patient with the medical devices (e.g. CPAP equipment) and related services. The reimbursement is about € 1-2 per day (Dr. Sastry).

CPAP treatment is usually initiated for a 3-month period. When the health care provider confirms that the trial period was successful, provisional CPAP prescription is made final. [a] After the trial period, it is the duty of the service providers to monitor adherence at least annually (by direct device readings or telemonitoring) and to report insufficient usage of the device to the health insurance. The health insurance may then decide to discontinue reimbursement and terminate treatment. In practice, the health insurance usually also informs the sleep clinic involved to provide them an opportunity to take up the problem with the patient to prevent withdrawal of treatment.

[a] Market competition between service providers has led to a situation since a few years where the health care providers do not pay anything to the service providers, even if the patient is completely attended to by the service providers during the trial period (which occurs in many Dutch clinics). Only once the trial period is completed successfully and the provisional prescription is made definite, do the service providers receive re-imbursement (from the health insurances). An unsuccessful CPAP trial is thus always a financial loss for the service providers (Dr. Sastry).

Reimbursement is also provided for MAD, totalling about € 931 for dentist consultations, X-rays and taking an imprint. Patients are eligible for a new MAD after 3 to 5 years.

The global annual budget spent on OSAS patients in the Netherlands was not reported by the experts consulted.

3.3.6 England

The UK Health Care System[a]

The United Kingdom's health care system is largely funded by taxes and is mostly free at point of access. In some cases patients do have to make co-payments (for goods and services covered by the NHS but requiring cost sharing, e.g. dental care) and direct payments (for services not covered by the NHS, e.g. basic ophthalmic services, or for private treatment outside the NHS). Residents of England may use the services of the public National Health Service (NHS), and they are also free to purchase private health insurance. In 2017, private medical insurance made up 3.1% of total health expenditure.

In England in the public sector, primary care is mainly financed through a capitation[b] system (where lump-sum payments are made to care providers based on the number of patients in their target population). In England, GP services also include a pay-for-performance component. For secondary/tertiary care,[c] annual global contracts[d] are the main payment system for hospitals in Scotland, Wales and Northern Ireland. In England, since 2004, a DRG system (called Healthcare Resource Groups) is used to determine the pricing for inpatient health care services and is based on "National Tariff" that reflects the full cost of provision and includes all the operating expenses.

In England, the National Health Service (NHS) is basically a public health care system that pays for the entire management of OSAS diagnosis and treatment. There is barely no patient co-payment for OSAS patients (Dr. Steier). Private healthcare insurers often do not provide specific sleep associated investigations (e.g. PSG) or equipment, in which case patients are often referred by their GP's to the NHS (despite of being privately insured). MADs can be entirely paid by the NHS if the patients is referred by a GP or specialist. However, in many areas of England they are not; patients are then encouraged to purchase them privately.

The following costs are reported by Dr Steier:

- Home-based OSAS diagnosis: not available
- Hospital-based OSAS diagnosis: not available
- Home-based titration: £ 200-300 (depending on comorbidities)
- Hospital-based titration: £ 1200 with PSG

The global annual budget spent on OSAS patients in England was not reported by the expert consulted.

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a Source : UK HIT 2015 and UK Country Health Profile 2019: http://www.euro.who.int/__data/assets/pdf_file/0006/302001/UK-HiT.pdf?ua=1 and https://ec.europa.eu/health/sites/health/files/state/docs/2019_chp_uk_english.pdf

b Capitated payment, or capitation, means paying a provider or group of providers to cover the majority (or all) of the care provided to a specified population across different care settings. The regular payments are calculated as a lump sum per patient.

c Stephani V, Quentin W, Van den Heede K, Van de Voorde C, Geissler A. Payment methods for hospital stays with a large variability in the care process. Health Services Research (HSR) Brussels: Belgian Health Care Knowledge Centre (KCE). 2018. KCE Reports 302. D/2018/10.273/36

d A block contract is a payment made to a provider to deliver a specific service. For example, a hospital could be given a block contract to undertake acute care in a particular geographical area. Block contracts are paid in advance of the service being undertaken and the value of the contract is independent of the actual number of patients treated or the amount of activity undertaken.

3.4 Involvement of service providers

In every country surveyed, except in England,[a] for-profit private companies provide home services related to the diagnosis and/or treatment (mainly PAP renting or leasing, and device maintenance). We refer hereunder to service providers.

In **Belgium**, there are many service providers. Their activities and costing were appraised during a specific survey (see Appendix 5 for methods and specific results). Service providers are either subcontracted by sleep labs within the INAMI – RIZIV convention or outside this convention in a minority of cases. In the latter case, services are not reimbursed by the public health insurance and charged to the patient, since the reimbursement convention for a patient can only be signed between the National Health Insurance (RIZIV – INAMI) and the hospital/sleep lab. In Belgium, the diagnostic PSG by a sleep lab is compulsory. However, some service providers provide HSAT outside the convention, mainly with type II but also with other types of portable monitors. According to our survey, titration is seldom performed by service providers. For treatment of OSAS, PAP devices are either owned by the sleep lab or rent to a service provider. In the latter case, the contract can include maintenance of all parts, the yearly reading of PAP data (effective pressure, residual events, leaks, and adherence), including the assessment of adherence, the transmission of such data to the prescribing physician, as well as the preparation of the yearly documents necessary for the renewal of the reimbursement by the National Health Insurance (INAMI – RIZIV). For example, in 2019 only one such company (Vivisol) ensured the rent with full service of nearly 14 000 PAP devices, i.e. more than 10% of the overall number of patients that year, and overall in Belgium around 30% of PAP devices would be rent by service providers (personal communication Jean-Paul Maeyaert, Vivisol). A minority (<2%) of contracts are directly with patients who do not fulfill reimbursement conditions. Some service providers are specialized in telemonitoring solutions. A company (personal communication Jean-louis Pirlot, ResMed) manages the telemonitoring of 20 000 PAP devices. Finally, some service providers ensure the manufacturing of MAD devices. Services are paid by the subcontracting hospitals[b]. The prescribing physician has the final responsibility of all aspects.[57] There is currently no specific legal framework for activities run by service providers.

In **France**, the place of such private companies (Prestataires de Santé à Domicile; https://www.fedepsad.fr/psad.php) is even more prominent, as they also perform the vast majority of titrations at home (without concurrent PG or PSGs). There are many home care companies that are involved in CPAP delivery and technical support. Home care providers own the CPAP. In contrast with Belgium, private providers are directly paid (fees for service) by the national health insurances (70%) and complementary private insurances (30%) as part of a package including CPAP delivery and technical support (Dr. Pepin).

In **the Netherlands**, the role played by private service providers is the most developed. First several home service providers[c] offer the service of diagnosis at home (home P(S)G with or without analysis of the raw data (Dr. Sastry). Second GPs, i.e. no sleep specialists as in the other countries, can also refer their patients directly to the Dutch Sleep Institute (Nederlands Slaap Instituut, NSI[d]) that is not hospital-based and offers country-wide sleep services. The NSI sets up patients for P(S)G in their homes (and offers consultations in offices). On their website they claim to perform more than 2 500 sleep tests per year (https://www.nederlandsslaapinstituut.nl/over-ons/) (Dr. Sastry). Third, as explained in section 3.2.4, after one year of treatment, the CPAP provider takes over in case of uncomplicated treatment (most often the provider has an outpatient clinic in the cooperating hospital), i.e. a medical doctor is no more involved on a regular basis in the patient follow-

[a] In the NHS, the equipment remains property of the issuing Trust – this is true for the diagnostic as well as for the therapeutic devices (Dr. Steier).

[b] A minority (<2%) of contracts are directly with patients who do not fulfil reimbursement conditions.

[c] For example: Vivisol, Medic Tefa, Vitalaire, see above in section 3.1.2 on Home-based diagnosis.

[d] https://www.nederlandsslaapinstituut.nl/

up. The health insurers pay the service providers a negotiated sum for the provision of CPAP equipment and related services.

In **Finland** also, private providers can be subcontracted by the public sector (not in all districts; Dr. Brander) to perform home-based diagnosis test, or they can work independently. If subcontracted by the public sector, the hospital or primary health care centre pays the costs directly (Dr. Saaresranta).

A third configuration of such public-private partnership is observed in some states of **Germany** where the PAP device is owned by the health care insurance companies and the home care providers are paid for utilization and maintenance (Dr. Schulz). In other regions, PAP devices are property of the hospital or leased. The supply of the devices through the provider happens after the titration in the sleep lab (Dr. Fietze). The home care providers are private companies run by state-certified technical engineers. Some companies also have medical doctors in their teams.

3.5 Accreditation of specialists in sleep medicine and of sleep labs

In the majority of the countries surveyed, the title of sleep specialist is not officially recognized (see Table 12). **Germany** is a remarkable exception. In that country, there is a standardized training and examination to become a sleep medicine specialist or a somnologist. To become a sleep medicine specialist one has to work for at least 18 months and on a full-time basis in a sleep lab and pass an exam. A further prerequisite for qualification is to have a specialization in pulmonary medicine, ENT medicine or general internal medicine (Allgemeinmedizin). A title of 'somnologist' is also available for psychologists and medical-technical employees, nurses and technical staff. Courses and trainings are organised by the DGSM (Deutsche Gesellschaft für Schlafforschung und Schlafmedizin[a] / German Sleep Society). There is a lack of recognised sleep medicine specialists in Germany due to a lack of interest, leading to long waiting lists. For the reimbursement of PSG a physician, has to be an accredited sleep specialist. However, for reimbursement of PG on an ambulatory basis physicians have to participate in a short course called *the GBA-Course* (GBA, Gemeinsamen Bundesausschusses). This 'GBA-Kurs' usually runs over two weekends. In this course, the principles and practice of PG are taught.

The DGSM also controls the quality of diagnosis and therapy of sleep labs which in turn get an official accreditation for successfully participating in this process. Accreditation has to be renewed every two years. However, not all sleep labs participate in the accreditation process of the DGSM as this is on a voluntary basis and not mandatory to receive reimbursements (Dr. Schulz). In practice quality of care seems uneven between centres (more automatic reading without manual control, etc. in some centres).

In **Belgium,** in contrast to Germany no such national examination exists and there is no specific specialty in sleep medicine or *'somnology'*. In theory, every physician with one of the agreed specialities (pulmonary medicine, neurology, psychiatry) could call himself a sleep specialist. Some universities do have a short module on sleep medicine in their basic MD training package. The professional organisation of physicians that practice sleep medicine in Belgium, BASS (Belgian Association of Sleep research and Sleep medicine[b]) demands this recognition as a specialty since many years but their efforts have so far not succeeded. The current convention between INAMI – RIZIV and the sleep centres only describes the additional training requirements for diagnosing physicians, specialist ENT physicians and MAD device specialists in the first annex of the convention. The criteria refer to a minimum number of hours per week spent on sleep medicine, a minimum number of patients treated, and having followed (by 1/1/2020) one out of a list of training courses (see Appendix 6 for more details). In addition the convention states that the physician should be a specialist in sleep medicine (somnologist), once this title would have been created (something that did not happen so far). Current courses are organized by the BASS, by hospitals, and by universities. There is no harmonisation of these courses. Practical training is organized informally and without much quality control (Dr. Verbraecken). To be an acknowledged sleep centre, additional conditions must be fulfilled. They do not concern the quality of care.

a https://www.dgsm.de

b https://belsleep.org/bass.aspx

Also in **the Netherlands**, no formal qualification as specialist in sleep medicine exists. Although there is no defined formal training, the diagnosing physician is in most cases a specialist in pulmonary medicine who is trained during his mandatory professional education in respiratory medicine. Some ENT specialists are also working in this field. Even when the title sleep specialist is not a protected specialization, a number of physicians passed the ESRS examination (see below in this section). Moreover, the Dutch professional organisations are attempting to develop a sub specialization of pulmonologist in sleep medicine. In the Netherlands there are many professional organisations for sleep medicine. Among those, the Dutch association of pulmonologists NVALT (Nederlandse Vereniging van Artsen voor Longziekten en Tuberculose[a,b]) has developed criteria for basic and advanced training in sleep medicine for specialists in pulmonary medicine and those in training as well as a self-evaluation questionnaire for respiratory sleep centres. This organisation was also the main author of the guidelines on the management of OSA in adults (updated in 2017)[c]. Another society, the Dutch Society for Sleep-Wake Research NSWO (Nederlandse vereniging voor Slaap-Waak Onderzoek[d]) is the Dutch member of the European Sleep Research Society (ESRS). Though intended to represent scientific and clinical sleep medicine, the NSWO seems more research oriented. To fill this gap, the Dutch Sleep Medicine Association SVNL (Slaapgeneeskunde Vereniging Nederland) was formed in 2015. It developed out of the foundation Federation of general Sleep Clinics FSC (stichting Federatie algemene SlaapCentra). So far, 17 sleep clinics have been accredited by either the SVNL or previously the FSC[e]. A national sleep congress is now held every two years by these two associations (NSWO and SVNL) and they may perhaps develop to be seen as the representatives of sleep medicine in The Netherlands (Dr. Sastry).

The system of reimbursement of sleep clinics based on the quality and expertise they provide is an advantage. Also, sleep medical treatment is more evidence-based (national guidelines) and uniform due to the independent investigations by the Dutch health authority ZIN (Dr. Sastry). Additionally there is also a strong patient association for sleep apnoea (Apneuvereniging) that regularly performs its own annual surveys and publishes reports on the situation of sleep medicine in the Netherlands. Finally, Zorginstituut Nederland ZIN is, since 2016, evaluating the whole chain of health care for sleep apnoea. This includes the diagnostic process, treatment and follow-up.

In **France**, there is a specialized university degree in sleep medicine (Transversal FST: Formations Spécialisées Transversales[f]) including 2 years of training. This sleep FST is open to residents in pulmonary medicine, cardiology, ENT, psychiatry, stomatology, paediatrics and neurology. However, no formal medical specialisation in sleep medicine exists. Actually a very limited training is required allowing to GPs and different medical specialties to run sleep studies (Dr. Pépin). A specific qualification is now required to prescribe CPAP but not to make a diagnosis of OSAS (Dr. Gagnadoux). In addition, there are also regional and national schemes with 3-4 weeks of theoretical training and 3-4 week of practical training in a sleep laboratory with final exams, and more limited trainings (DPC: Développement professionnel continu) corresponding to several congress venues and management of clinical cases (trainings validated by the

a https://www.nvalt.nl/

b The NSI is not a governmental organization but a private organization offering out-of-hospital sleep services. They are not a service provider in the context of offering CPAP equipment. They offer sleep consultations, ambulatory diagnostic P(S)Gs and CPAP titrations and have, to this end, doctors as well as nurses in their service. GPs can refer patients to them as well as to any sleep clinic. Home care service providers also offer P(S)Gs (as well as supervision of CPAP out patient CPAP titrations), not independently, but as a service to e.g. pulmonary departments (Dr. Sastry).

c https://www.nvalt.nl/kwaliteit/richtlijnen/slaap/_/Slaap/Richtlijn%20OSA%20bij%20volwassenen%20%28geaccordeerd%20april%202018%29.pdf

d https://www.nswo.nl

e (http://www.slaapgeneeskundevereniging.nl/accreditatie/aangesloten-centra/)

f https://www.ssipi-mg.com/les-fst-et-les-options/

national societies). New training courses and dedicated research programs funded by national agencies are being set-up.

Also in **the UK** there is no formal speciality in sleep medicine. Patients will be diagnosed while being under the care of a consultant. For OSAS, this consultant needs to have trained formally in pulmonary medicine. As part of the pulmonary medicine training, after medical school there is the core medical training (foundation years, typically 3 years) followed by the specialist training with rotations through sleep and ventilation centres (at least 6 years). There are different interviews and qualifications on the way e.g. the MRCP assessments (Membership of the Royal Colleges of Physicians[a]) with different parts and practical tests), as well as an exit exam for the specialty before becoming a consultant. In the UK, the consultants involved in running sleep laboratories are pulmonary medicine physicians, neurologists and psychiatrists. Non-medical professionals from allied healthcare professions may qualify as clinical nurse specialist or consultant physiologists.

Again, in **Finland** no formal specialty in sleep medicine exists and sleep medicine is mainly practiced by medical specialists such as specialists in pulmonary medicine, ENT specialists, clinical neurophysiologists and neurologists. There are national recommendations but, in practice, every licensed physician can diagnose and treat OSAS. However, PG are mostly scored by clinical neurophysiologists and pulmonologists. In the public sector, only pulmonologists, ENT specialists, orthodontists, some paediatricians start CPAP or MAD treatment but in the private sector more is allowed. Medical specialists can have the 2-year training called 'special competence in sleep medicine (sleep specialist)'. One participants of the survey told us that Finland has less than 30 doctors with an official degree of special competence in sleep medicine. Through national coordination and education, physicians are encouraged to achieve special competence in sleep medicine (comparable to a subspecialty) or acquire the European somnologist title from the ESRS[b] (see below).

a https://www.mrcpuk.org/

b www.esrs.eu

Table 12 – Overview of local training facilities for sleep specialists in selected countries

Country	Recognised specialty	Training required	Medical specialties concerned
Belgium	No	No Courses are organized by the BASS, by hospitals, and by universities. Practical training is organized informally and without quality control (Dr. Verbraecken)	Specialists in pulmonary medicine, neurology, psychiatry, internal medicine, paediatrics ENT and maxillofacial surgeons for surgical treatment of OSAS and mandibular advancement therapy
England	No	Training in respiratory medicine.[a] However, also neurologists and psychiatrists are involved.	Consultants involved in running sleep laboratories are Respiratory Physicians, Neurologists and Psychiatrists. Non-medical professionals from allied healthcare professions may qualify as clinical nurse specialist or Consultant Physiologists.
Finland	No	None officially	Medical specialists only such as pulmonologists; ENT specialists, clinical neurophysiologists, neurologists can become sleep specialists.
France	No	Partly A qualification is required to prescribe CPAP but not to make a diagnosis of OSAS. A very limited training is required allowing GPs and different medical specialties to run sleep studies. Various courses are available.[b]	Specialists in pulmonary medicine, ENT, neurology, cardiology, psychiatry, stomatology, paediatrics. GPs can also run sleep studies.
Germany	Yes	A special course called GBA-Course must be followed in order to be allowed to perform PG on an ambulatory basis (and to get reimbursed for it).	Any medical doctor can become a sleep specialist Mainly pulmonologists, cardiologists, psychiatrists, neurologists, ENT doctors, paediatricians and dentists

[a] A core medical training (foundation years, typically 3 years) followed by the specialist training with rotations through sleep and ventilation (at least 6 years). There are different interviews and qualifications on the way (e.g. the MRCP with different parts and practical tests), as well as an exit exam for the specialty before becoming a Consultant (Dr. Steier).

[b] There are regional and national diplomas with 3-4 weeks of theoretical training and 3-4 week of practical training in the sleep laboratory with final exams. We also have more limited training (DPC) corresponding to several congress venues and management of clinical cases (Training validated by the national societies). Recently, we started a FST (Formation Spécialisée Transversale) program corresponding to a one year training (Dr. Gagnadoux says 2 years) dedicated to sleep at the end of the cursus of several medical specialties (pneumologist, ENT, Neurology, cardiology, psychiatry, stomatology, pediatrician). According to Dr. Pépin, the number of individuals integrating the course will be very limited at the national level (10 to 20 at maximum).

		To become a sleep specialist one has to work for at least 18 months and on a full-time basis in a sleep lab and pass an exam. Only sleep specialists can have PSG reimbursed.	The title of somnologist (awarded by the DGSM, German Sleep Society[a]) is also accessible for psychologists and medical-technical employers and nurses and technical staff.
The Netherlands	No	Specific courses exist. The Dutch association of pulmonologists NVALT (Nederlandse Vereniging van Artsen voor Longziekten en Tuberculose) has developed criteria for basic and advanced training in sleep medicine for pulmonolgists and pulmonologists-in-training as well as a self-evaluation questionnaire for respiratory sleep centres.	Mainly pulmonologists but other disciplines can be involved in the diagnosis and treatment of sleep disorders.

BASS: Belgian Association for Sleep research and Sleep Medicine; CPAP: Continuous Positive Airway Pressure; OSAS: Obstructive Sleep Apnoea Syndrome

In addition to these national initiatives there is also the **European Sleep Research Society (ESRS) examination**. The ESRS[b] is the umbrella organisation of several European Sleep Research Societies.[92, 93] It is an international scientific non-profit organization and promotes all aspects of sleep research and sleep medicine. These include the publication of the Journal of Sleep Research (JSR),[c] the organization of scientific meetings, and the promotion of training and education (among them e-lessons, ESRS Sleep Medicine Lessons), the dissemination of information, and the establishment of fellowships and awards.

The ESRS also organises a central European examination for sleep medicine both for physicians and for sleep technologists.[d] These examinations take place alongside the ESRS annual conference and the next round will be conducted in Seville, Spain on September 22, 2020. The examination consists of both a written test, consisting of 50 multiple-choice questions mainly based on de ESRS textbook[e] and the AASM scoring manual,[f] but also of a test of practical skills, involving sleep staging, event scoring and interpreting excerpts from PSG recordings and also a full MSLT recording. It is required from participants that they can document at least 5 years of experience and having followed relevant and accredited (by ESRS) courses and meetings. They should be nominated for eligibility for the exam by the clinical director of their sleep centre or a member in good standing with the ESRS who can vouch for their experience. As the examination is in English candidates must have a good command of English.

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a Fulfil a service catalogue, mandatory courses, which are offered by the DGSM, followed by a practical and theoretical exam.

b www.esrs.eu

c https://onlinelibrary.wiley.com/toc/13652869/2020/29/2 (issue 2020 Volume 29 Issue 2)

d https://www.esrs-examination.eu/

e https://esrs.eu/product/sleep-medicine-textbook-ecrn/

f https://aasm.org/clinical-resources/scoring-manual/

4 ANALYSIS OF THE EPS DATABASE

Global national numbers are good for estimating the global number of patients, therapies, costs etc. but they fail to give additional information on the patient level, e.g. age, gender, history of use, adherence, etc. To achieve this we additionally turned to the EPS, the Belgian national sample to extract additional information.

4.1 Method

In Belgium, registered inhabitants, in principle, have a compulsory health insurance provided through one of the seven national sickness funds and funded by social security contributions withhold on wages and other earnings. For all sickness funds, healthcare reimbursement data of their members are gathered into databases at the "InterMutualistisch Agentschap – Agence InterMutualiste" (IMA – AIM), according to a legal framework, meaning that no informed consent is required. From this population a sample was selected (random selection stratified for age and gender). Sample proportion was 1/40 among subjects younger than 65 and 1/20 among subjects aged 65 years and older. This sample contains approximately 300 000 individuals that are followed since 2002. The sample is updated yearly to compensate for mortality and aging and new members are added according to the same sample size rules. The resulting database is referred to as "Échantillon permanent – Permanente steekproef" (EPS). For all the individuals in the sample demographic and socio-economic information is collected in addition to detailed information on health care expenditures which allows detailed analysis and a longitudinal follow-up of patients, unlike INAMI-RIZIV data.

KCE has a legal right to use those anonymised data for specific study purposes with an a priori internal control by our data managers and a posteriori control by the technical cell governing the EPS.

EPS data were obtained for the years 2011-2018, this last year being the most recent dataset available at the time of analysis.

For the analysis of the EPS database, the following definitions are used:

- A **case** is defined as an adult patient (≥ 18 years old) with a pseudo-nomenclature code for the OSAS convention. Pseudo codes for OSAS conventions (CPAP vs. MAD; lump sum for starting treatment vs. continuous treatment) are presented in Appendix 7.
- A **new case** is defined as a case with no OSAS convention in the 366 days preceding the start date of the convention.
- A **dropout** is defined as a case with no OSAS convention in the year following the index year[a, b]. Such cases must be censored on the last day of the index year. A patient without OSAS convention pseudocode (see Appendix 7) for more than 366 days is considered as a dropout.

The nomenclature codes for the identification of a PSG are listed in Appendix 7.

4.2 Analysis

4.2.1 Number of patients

Table 13 shows the number of patients in the OSAS convention in a given year. A patient is considered included in the OSAS convention for a given year if a convention pseudocode (see Appendix 7) has been billed at any time during the year. The estimate of total number of patients in 2018 is greater than the figures communicated by INAMI-RIZIV (see chapter 5). This could be due to a difference of the calculation method, i.e. INAMI-RIZIV reports person-years, or to an overestimate of the number of patients with an OSAS convention in the EPS. This has been confirmed by estimating the number of pseudocodes for the OSAS convention (see Table 49 in Appendix 7) from the EPS and comparing the figures to documents N from INAMI-RIZIV. Figure 1 shows the distribution by age.

[a] Be aware that a case can switch from PAP to MAD (2 different nomenclature code), i.e. this is not a dropout.

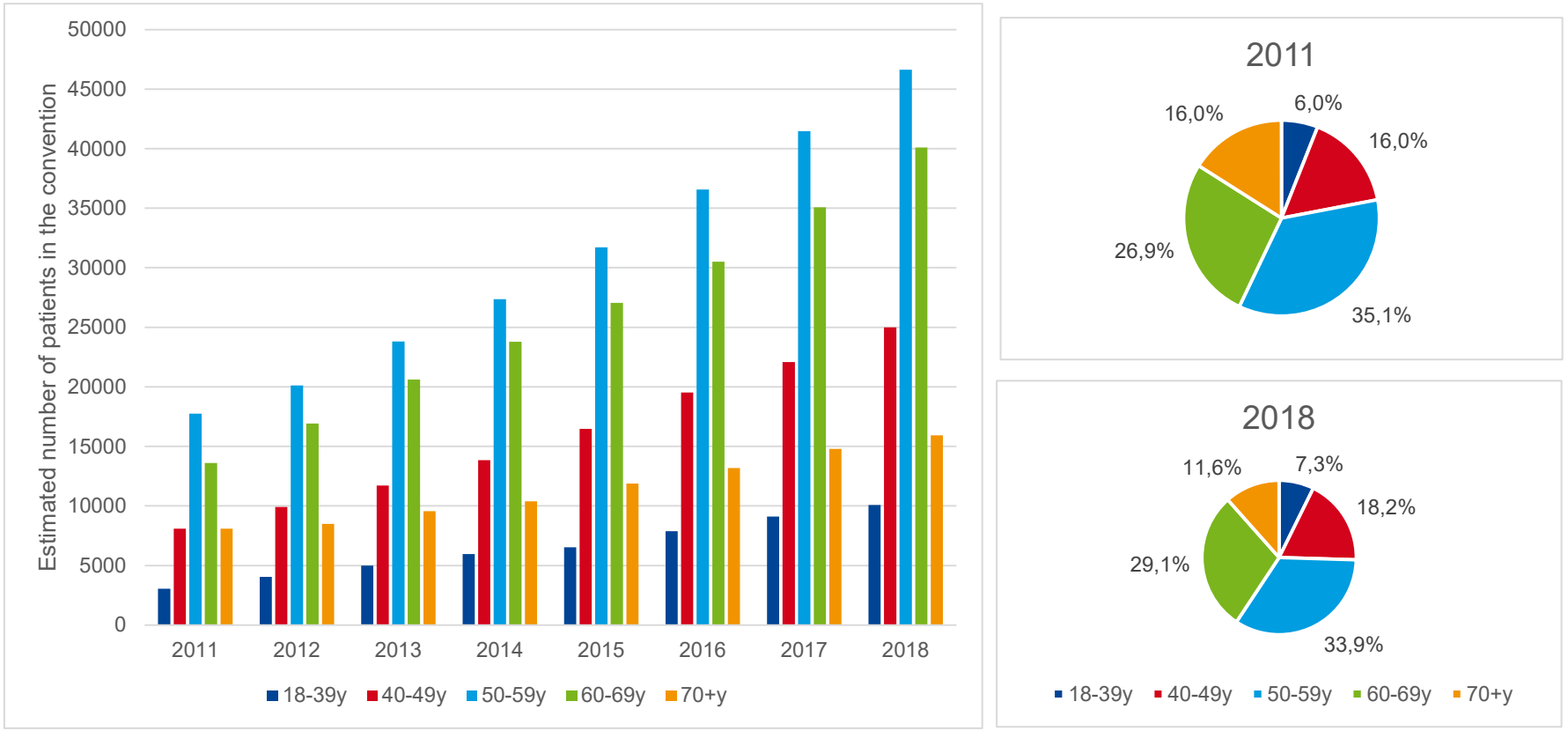
[b] Obviously for cases still alive in the year following the index year.

Table 13 – Estimated number of patients [95% CI] in course of the convention

Year	Number of patients with a convention	Male	Female	PAP	MAD
2011	50580 [48084, 53076]	40660 [38404, 42916] (80.39%)	9920 [8852, 10988] (19.61%)	50580 [48084, 53076] (100%)	0 (0%)
2012	59500 [56806, 62194]	47640 [45216, 50064] (80.07%)	11860 [10685, 13035] (19.93%)	59500 [56806, 62194] (100%)	0 (0%)
2013	70700 [67788, 73612]	55960 [53356, 58564] (79.15%)	14740 [13437, 16043] (20.85%)	70700 [67788, 73612] (100%)	0 (0%)
2014	81320 [78221, 84419]	63560 [60807, 66313] (78.16%)	17760 [16338, 19182] (21.84%)	81320 [78221, 84419] (100%)	0 (0%)
2015	93660 [90369, 96951]	72580 [69669, 75491] (77.49%)	21080 [19546, 22614] (22.51%)	93660 [90369, 96951] (100%)	0 (0%)
2016	107640 [104148, 111132]	83140 [80054, 86226] (77.24%)	24500 [22866, 26134] (22.76%)	107640 [104148, 111132] (100%)	0 (0%)
2017	122560 [118883, 126237]	94220 [90974, 97466] (76.88%)	28340 [26613, 30067] (23.12%)	122120 [118449, 125791] (99.64%)	440 [187, 693] (0.36%)
2018	137740 [133895, 141585]	104500 [101121, 107879] (75.87%)	33240 [31406, 35074] (24.13%)	136400 [132571, 140229] (99.03%)	1340 [895, 1785] (0.97%)

PAP: Positive airway pressure; MAD: Mandibular advancement device; figures between square brackets represent the 95% confidence interval.

Figure 1 – Age distribution of patients (CPAP and MAD) with a convention per year



Note: the period covered is 2011-2018, for Belgium (estimated).

New cases, by definition, don't have an OSAS convention pseudocode for one year before entering the convention. They will thus enter the convention at the earliest on 1 January 2012, since the first year of available data (2011) is used to make sure no convention pseudocodes. The incidence of new cases is show in Table 14 by year. MAD treatment was not available for patients in the OSAS convention before 2017. The annual growth rate of new cases is of 9.64%; this growth has been illustrated in Figure 2. More men than women enter the convention, but the difference is dwindling: women account for 24.2% in 2012 and 29.8% in 2018 (Figure 3).

Table 14 – Incidence of (new) cases [95% CI] by year (2012-2018, estimated)

	Number of new cases with a convention		Male		Female		PAP		MAD	
year	EPS	Belgium (estimated)	EPS	Belgium (estimated)	EPS	Belgium (estimated)	EPS	Belgium (estimated)	EPS	Belgium (estimated)
2012	418	13140 [11872, 14408]	314	9960 [8850, 11070]	104	3180 [2568, 3792]	418	13140 [11872, 14408]	0	-
2013	503	15560 [14200, 16920]	375	11780 [10591, 12969]	128	3780 [3120, 4440]	503	15560 [14200, 16920]	0	-
2014	519	16080 [14698, 17462]	371	11500 [10326, 12674]	148	4580 [3852, 5308]	519	16080 [14698, 17462]	0	-
2015	569	17500 [16067, 18933]	399	12400 [11186, 13614]	170	5100 [4339, 5861]	569	17500 [16067, 18933]	0	-
2016	626	19500 [17985, 21015]	466	14740 [13417, 16063]	160	4760 [4022, 5498]	626	19500 [17985, 21015]	0	-
2017	676	20600 [19065, 22135]	484	15040 [13717, 16363]	192	5560 [4783, 6337]	664	20160 [18642, 21678]	12	440 [189, 691]
2018	734	22820 [21205, 24435]	507	16020 [14650, 17390]	227	6800 [5944, 7656]	709	21880 [20298, 23462]	25	940 [566, 1314]
Total	4045	125200	2916	91440	1129	33760	4008	123820	37	1380 [930, 1830]

Figure 2 – Number of new cases per year (2012-2018, estimated)

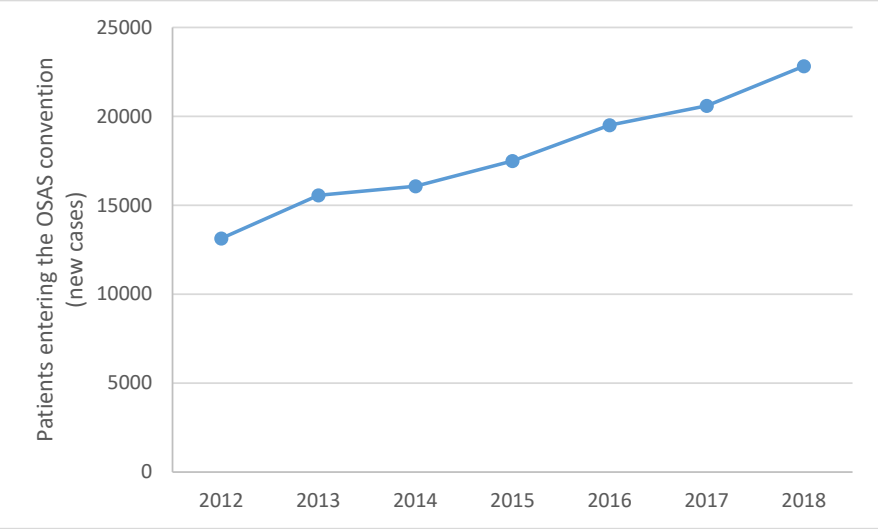
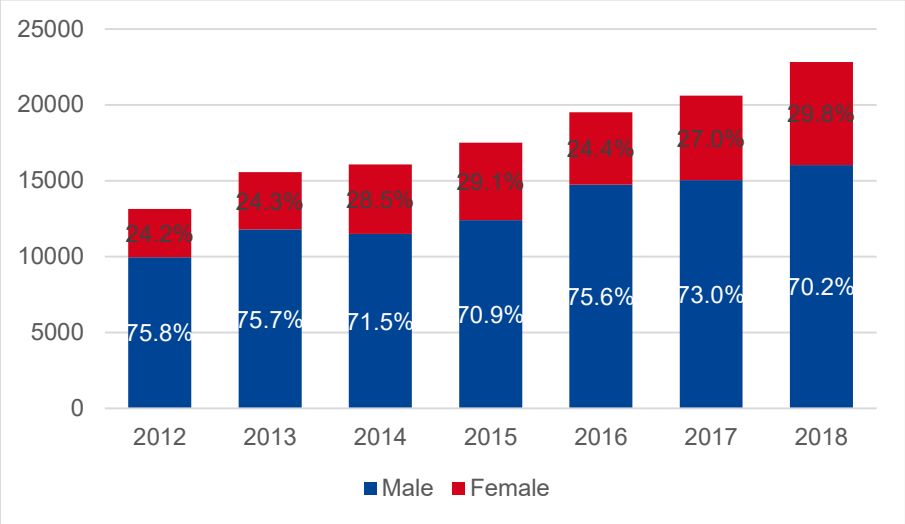


Figure 3 – Gender distribution for new cases (2012-2018, estimated)



4.2.2 Diagnostic procedure

4.2.2.1 Diagnostic PSG

To enter the OSAS convention, the patient has to undergo a prior diagnostic PSG which is valid for 2 years.

Table 15 – New patients with a PSG up to 2 years before entering the convention

	All patients				PAP				MAD			
PSG up to 2 years before entering the convention?	Yes		No		Yes		No		Yes		No	
	Belgian population (est.)	%	Belgian population (est.)	%	Belgian population (est.)	%	Belgian population (est.)	%	Belgian population (est.)	%	Belgian population (est.)	%
2013	14100 [12821, 15379]	90.62	1460 [1119, 1801]	9.38	14100 [12821, 15379]	90.62	1460 [1119, 1801]	9.38	-		-	
2014	14340 [13043, 15637]	89.18	1740 [1356, 2124]	10.82	14340 [13043, 15637]	89.18	1740 [1356, 2124]	10.82	-		-	
2015	16280 [14923, 17637]	93.03	1220 [900, 1540]	6.97	16280 [14923, 17637]	93.03	1220 [900, 1540]	6.97	-		-	
2016	17880 [16459, 19301]	91.69	1620 [1250, 1990]	8.31	17880 [16459, 19301]	91.69	1620 [1250, 1990]	8.31	-		-	
2017	18620 [17186, 20054]	90.39	1980 [1573, 2387]	9.61	18180 [16763, 19597]	90.18	1980 [1573, 2387]	9.82	440 [295, 585]	100.00	0	0.00
2018	20500 [19000, 22000]	89.83	2320 [1896, 2744]	10.17	19640 [18171, 21109]	89.76	2240 [1825, 2655]	10.24	860 [757, 963]	91.49	80 [0, 183]	8.51
Total	101720	90.77	10340	9.23	100420	90.73	0	9.27	1300	94.20	80	5.80

Note: figures cover the 2013-2018 period (estimate); figures between square brackets represent the 95% confidence interval.

The delay between the diagnostic PSG and the start of the convention is 117 days ([114, 120], CI 95%) on average (median=101 days, [98, 103] CI 95 %). This was assessed in new patients entering the convention between 2013 and 2018 for patiens with PAP, and between 2017 and 2018 for patients with MAD. The performance of a PSG was searched up to 2 years before entering the convention; as this is the maximum delay between the diagnostic PSG and the start of the convention.

No PSG was retrieved in 9.27% of patients with PAP, and in 5.80% of patients with MAD (Table 15 and Table 16). This is a puzzling finding as, in principle, a PSG is compulsory to enter the convention. A vast majority (88.58%) of patients have one diagnostic PSG billed, and a very tiny fraction of the patients (2,23%) has more than one PSG billed (Table 16). Most diagnostic PSG are done in inpatient setting (Table 17).

Table 16 – Diagnostic PSG (up to 2 years before entering the OSAS convention) per patient

Number of PSG up to 2 years before	All patients entering a convention (new cases)	Patients with CPAP (new cases)	Patients with MAD (new cases)
0	10 340 [9672, 11 008] (9.23%)	10 260 [9597, 10 923] (9.27%)	80 [0, 183] (5.80%)
1	99 260 [98 390, 100 130] (88.58%)	97 960 [97 094, 98 826] (88.51%)	1300 [1197, 1403] (86.75%)
2	2420 [1850, 2990] (2.16%)	2420 [1850, 2990] (2.19%)	-
3	40 [0, 95] (0.04%)	40 [0, 95] (0.04%)	-
Total	112 060	110 680	1380

Note: figures cover the 2013-2018 period (estimate); figures between square brackets represent the 95% confidence interval.

Table 17 – Diagnostic PSG: characteristics

Variable	Yes		No	
	Belgian population (est.)	%	Belgian population (est.)	%
Ambulatory PSG	1340 [935, 1745]	1.32 [0.92, 1.72]	100380 [99975, 100785]	98.68 [98.29, 99.08]
PSG during hospitalisation	99820 [99332, 100308]	98.13 [97.65, 98.61]	1900 [1412, 2388]	1.87 [1.39, 2.35]

Note: new cases only (2013-2018)

4.2.2.2 Hospitalisation for diagnostic PSG

Hospital stays for diagnostic PSG are in general one-night stays. This is the case for most of them (92.11%), while 5.04% of the stays are longer; 2.85% of the stays have the admission and discharge occurring on the same day: these are technical one-day (outpatient) stays, but they are labelled as inpatient stays (Table 18).The mean and median costs for these stays can be found in Table 19. These costs include all expenses during the stay. One can notice that stays with no night are more expensive than stays with 1 night. This could be explained by the fact that most of the expenses in these stay are due to lump sums billed either per stay or per day, and their amount varies per hospital.

Table 18 – Number of nights for hospital stays with diagnostic PSG

Number nights	Number of patients (Belgium, estimated) [CI 95%]	Proportion (%)[CI 95%]
0	2840 [2230, 3450]	2.85% [2.23, 3.46]
1	91 940 [90 979, 92 901]	92.11% [91.14, 93.07]
2	2520 [1944, 3096]	2.52% [1.95, 3.10]
3 or more	2520 [1996, 3044]	2.52% [2.00, 3.05]
Total	99 820	100%

Note: new cases only (2013-2018)

Table 19 – Total costs for hospital stays (EUR) with diagnostic PSG

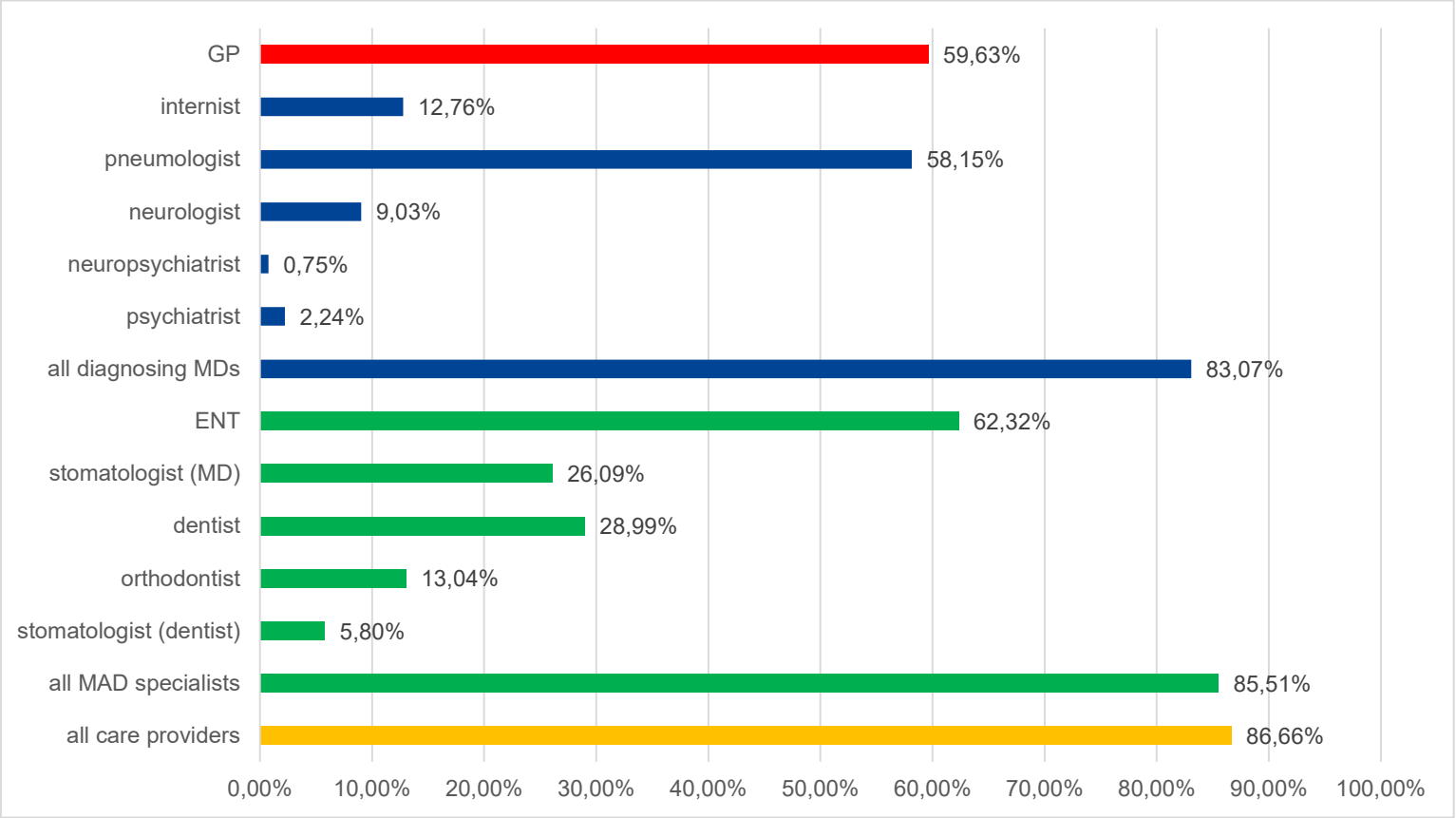
Number of nights (diagnostic PSG hospital stay)	RIZIV-INAMI		Patient costs: total		Patient costs: copayments		Patient costs: supplements	
	Mean [CI 95%] (EUR)	Median [CI 95%] (EUR)	Mean [CI 95%] (EUR)	Median [CI 95%] (EUR)	Mean [CI 95%] (EUR)	Median [CI 95%] (EUR)	Mean [CI 95%] (EUR)	Median [CI 95%] (EUR)
0	1185.92 [1126.55, 1245.29]	1035.55 [944.08, 1127.02]	113.85 [72.63, 155.06]	77.58 [77.27, 77.89]	64.44 [60.11, 68.77]	77.58 [77.27, 77.89]	49.41 [8.62, 90.19]	0 [-2.12, 2.12]
1	1047.26 [1040.27, 1054.25]	1006.85 [1000.29, 1013.41]	82.05 [77.74, 86.36]	77.89 [77.74, 78.04]	65.45 [64.41, 66.49]	77.58 [77.43, 77.74]	16.59 [12.44, 20.75]	-0.07
2	1858.16 [1772.56, 1943.76]	1648.18 [1576.85, 1719.50]	110.52 [90.85, 130.19]	102.03 [97.61, 106.45]	94.77 [87.87, 101.67]	98.59 [97.59, 99.60]	15.75 [0.19, 31.32]	1.55 [-0.63, 3.73]
3 or more	12728.00 [10176.02, 15279.38]	6257.61 [5190.99, 7324.23]	871.85 [687.91, 1055.79]	318.94 [244.23, 393.65]	475.57 [362.67, 588.48]	238.95 [203.46, 274.44]	396.28 [222.98, 569.58]	40.82 [25.47, 56.17]
1 or less	1051.41 [1044.17, 1058.66]	1008.26 [1001.21, 1015.31]	83.00 [78.55, 87.44]	77.89 [77.74, 78.04]	65.42 [64.40, 66.44]	77.58 [77.43, 77.74]	17.58 [13.29, 21.87]	-0.07
2 or less	1072.31 [1063.05, 1081.56]	1011.50 [1005.91, 1017.08]	83.71 [79.37, 88.08]	77.89 [77.74, 78.04]	66.18 [65.13, 67.23]	77.58 [77.43, 77.74]	17.53 [13.33, 21.73]	-0.07
All stays	1366.55 [1259.02, 1474.08]	1015.06 [1010.15, 1019.96]	103.61 [94.03, 113.18]	77.89 [77.74, 78.04]	76.52 [72.08, 80.96]	77.58 [77.43, 77.74]	27.09 [19.70, 34.48]	-0.06

Note: new cases only (2013-2018)

4.2.2.3 Medical consultations of practitioners before entering the convention

Pulmonologists are the most frequently medical specialists consulted before entering the convention. For MAD patients, an ENT specialist was consulted in 62 % of the cases. On average, a patient entering the convention had 3.47 medical consultations (95% CI: 3.38%, 3.55%). Details are provided in Table 20 (consultations per care provider) and Figure 4 (proportion of patient with at least one consultation for each type of care provider).

Figure 4 – Patients consultations up to 3 months before entering the convention



Note: calculations for MAD specialists (in green) include only MAD patients; period: 2012-2018.

Table 20 – Medical consultations up to 3 months before entering the convention

MD	Mean consultations: PAP	Median consultations: PAP	Mean consultations: MAD	Median consultations: MAD	Mean consultations: Total	Median consultations: Total
GP	1.35 [1.30, 1.40]	0.37 [0.34, 0.40]	1.39 [0.92, 1.87]	0.58 [0.29, 0.88]	1.35 [1.30, 1.40]	0.38 [0.35, 0.41]
Diagnosing physicians						
Internist	0.18 [0.16, 0.20]	0 [-0.06, 0.06]	0.06 [-0.02, 0.14]	0	0.18 [0.16, 0.20]	0 [-0.06, 0.06]
Pneumologist	0.91 [0.87, 0.94]	0.24 [0.22, 0.27]	0.56 [0.32, 0.81]	0.17 [-0.33, 0.33]	0.90 [0.87, 0.93]	0.24 [0.22, 0.26]
Neurologist	0.12 [0.10, 0.13]	0 [-0.07, 0.07]	0.14 [0.00, 0.29]	0 [-0.84, 0.84]	0.12 [0.10, 0.13]	0 [-0.07, 0.07]
Neuropsychiatrist	0.01 [0.01, 0.01]	0.14 [-0.28, 0.28]	0 [0.00, 0.00]	0 [0.00, 0.00]	0.01 [0.01, 0.01]	0 [-0.28, 0.28]
Psychiatrist	0.03 [0.03, 0.04]	0.08 [-0.17, 0.17]	0 [0.00, 0.00]	0 [0.00, 0.00]	0.03 [0.02, 0.04]	0 [-0.17, 0.17]
All diagnosing MDs	1.25 [1.21, 1.29]	0.56 [0.54, 0.58]	0.77 [0.46, 1.08]	0 [-0.38, 0.38]	1.24 [1.20, 1.28]	0.56 [0.54, 0.58]
MAD specialists						
ENT	0.18 [0.17, 0.20]	0 [-0.06, 0.06]	1.01 [0.69, 1.34]	0.39 [0.14, 0.64]	0.19 [0.18, 0.21]	0 [-0.06, 0.06]
General dentist	0.07 [0.06, 0.08]	0 [-0.09, 0.09]	0.81 [0.35, 1.27]	0 [-1.09, 1.09]	0.08 [0.06, 0.09]	0 [-0.09, 0.09]
Orthodontist	0.01 [0.00, 0.01]	0 [-1.32, 1.32]	0.26 [0.03, 0.50]	0 [-1.39, 1.39]	0.01 [0.01, 0.02]	0 [-1.08, 1.08]
Stomatologist (MD)	0.02 [0.01, 0.02]	0 [-0.19, 0.19]	0.46 [0.15, 0.78]	0 [-0.51, 0.51]	0.02 [0.02, 0.03]	0 [-0.18, 0.18]
Stomatologist (dentist)	0 [0.00, 0.01]	0 [-0.57, 0.57]	0.12 [-0.03, 0.27]	0	0.01 [0.00, 0.01]	0 [-0.60, 0.60]
All MAD specialists	0.29 [0.26, 0.31]	0 [-0.05, 0.05]	2.67 [1.96, 3.37]	1.71 [0.91, 2.51]	0.31 [0.29, 0.34]	0.03 [-0.05; 0.05]
Other	0.56 [0.52, 0.59]	0 [-0.62, 0.62]	0.65 [0.25, 1.05]	0 [-0.62, 0.62]	0.56 [0.52, 0.59]	0 [-0.04, -0.04]
All consultations	3.44 [3.36, 3.53]	2.44 [2.34, 2.54]	5.48 [4.49, 6.47]	4.17 [2.24, 6.09]	3.47 [3.38, 3.55]	2.45 [2.36, 2.55]

Note: period: 2012-2018; figures between square brackets represent the 95% confidence interval.

4.2.3 During the convention

4.2.3.1 Number of years in the convention

A patient is considered as a dropout case if no convention pseudocode is recorded for more than a year. The proportion of patients still in the convention after a number of years, has been calculated and results are shown in Table 21. A patient is considered for a given year only if the timeframe allows it (e.g. the proportion of new cases staying in the convention for one year could be evaluated in new cases of years 2012-2017; the proportion of new cases staying in the convention for two years could be evaluated in new cases of years 2012-2016; etc.) and if he did not die.

Table 21 – Adherence of patients to the convention (1-5 years, new cases)

Number of years in the convention	Patients still in the convention		Dropout patients		Total	
	% [CI 95%]	n [CI 95%]	% [CI 95%]	n [CI 95%]	%	n
1	85.26 [83.84, 86.67]	70320 [69153, 71487]	14.74 [13.33, 16.16]	12160 [10993, 13327]	100	83180
2	76.51 [74.57, 78.45]	47420 [46219, 48621]	23.49 [21.55, 25.43]	16040 [14805, 17275]	100	63480
3	72.61 [70.18, 75.04]	32080 [31006, 33154]	27.39 [24.96, 29.82]	12100 [11026, 13174]	100	45700
4	69.92 [66.82, 73.02]	19990 [19017, 20783]	30.08 [26.98, 33.18]	8560 [7677, 9443]	100	29940
5	69.38 [65.02, 73.74]	9200 [8622, 9778]	30.62 [26.26, 34.98]	4060 [3482, 4638]	100	14300

We defined episodes as a patient entering the convention and stopping over a full calendar year (at least 366 consecutive days without pseudocodes for the OSAS convention). Afterwards, he/she is considered a dropout. He/she can then enter the convention again to start another episode. Between 2011 and 2018, 94.48% [93.84, 95.12] of the patients had only one episode (they did not stop for one year or more then start over again), 5.04% [4.43, 5.65] had two episodes, and 0.48% [0.28, 0.68] had three episodes.

Prevalent diabetes was defined as patients that were delivered antidiabetic medication (variable PSEUDOPATH_0601 from the EPS: ≥90 DDD over the last available year of medication with ATC3=A10A or A10B, blood glucose lowering drugs, insulin or other).

Diabetes was present in 21.93% of the patients in the convention. Since some treatments do not involve medication and there is a proportion of patients not aware of their condition, the proportion of diabetic patients is probably underestimated.

4.2.4 Titration procedure

When a treatment with CPAP is prescribed, reimbursement within the OSAS convention is granted provided that treatment efficacy is proven. A potential PG or PSG is included in the convention, so it is not billed separately and therefore not recorded in the EPS. No hospital stay with a PG/PSG titration could thus be identified. Therefore, we could not analyse this titration procedure in the EPS database.

4.2.5 Follow-up period

4.2.5.1 Follow-up PSG (stratified per CPAP and MAD patients)

The absolute number and proportion of new cases receiving a follow-up PSG (at least 3 months after entering for the PAP patients, and at least 6 months for the MAD patients) per year is shown in Table 22.

Table 22 – Number of follow-up PSGs after 0-6 years of treatment

Years of treatment	0	1	2	3	4	5	6
2012	220 (1.67%)	360 (2.74%)	400 (3.04%)	520 (3.96%)	500 (3.81%)	400 (3.04%)	180 (1.37%)
2013	200 (1.29%)	580 (3.73%)	560 (3.6%)	440 (2.83%)	420 (2.7%)	200 (1.29%)	0 (0%)
2014	260 (1.62%)	700 (4.35%)	500 (3.11%)	600 (3.73%)	180 (1.12%)	0 (0%)	0 (0%)
2015	360 (2.06%)	760 (4.34%)	640 (3.66%)	200 (1.14%)	0 (0%)	0 (0%)	0 (0%)
2016	160 (0.82%)	620 (3.18%)	320 (1.64%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
2017	220 (1.07%)	160 (0.78%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
2018	120 (0.53%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)

Note: new cases (2012-2018); the % between brackets indicates the proportion of patients having a follow-up PSG in relation to the number of patients having entered the convention on a given year.

The length of stay of hospital stays where a follow-up PSG has been billed is shown in Table 23.

Table 23 – Follow-up PSG: hospital stays characteristics

Number of nights	N patients hospitalised (new cases, 2012-2018)	Proportion (new cases)	N patients hospitalised (all cases, 2011-2018)	Proportion (all cases)
0	240 [72, 407]	2.48 [0.75, 4.21]	540 [276, 803]	2.57 [1.32, 3.83]
1	8740 [8407, 9073]	90.29 [86.85, 93.73]	19220 [18763, 19677]	91.61 [89.43, 93.79]
2	460 [201, 718]	4.75 [2.08, 7.42]	820 [490, 1149]	3.91 [2.34, 5.48]
≥ 3	240 [92, 387]	2.48 [0.96, 4]	400 [200, 599]	1.91 [0.95, 2.86]

Hospital stay costs for stays with a follow-up PSG (no costs have been excluded in the calculation) can be separated in the following categories [95% CI]:

For the INAMI – RIZIV:

- All cases: € 1357.48 [1217.61, 1497.34] (median=€ 1047.91 [1032.30, 1063.51])
- New cases: € 1502.48 [1241.34, 1763.62] (median=€ 1049.63 [1024.15, 1075.11])

For the patient:

- All cases:
  - Patient costs: € 86.78 [77.06, 96.50] EUR (median=€ 77.99 [77.84, 78.14]) , which can be divided into:
  - Copayments: € 66.50 [62.37, 70.62] (median=€ 77.58 [77.45, 77.71])
  - Supplements: € 20.28 [11.65, 28.92] (median=€ 0.00 [-0.38, 0.38])
- New cases:
  - Patient costs: € 94.81 [77.07, 112.56] (median=€ 78.20 [77.97, 78.43]) , which can be divided into:
  - Copayments: € 66.86 [61.66, 72.05] (median=€ 77.89 [77.75, 78.03])
  - Supplements: € 27.95 [11.48, 44.43] (median=€ 0.00 [-0.42, 0.42])

5 FINANCING RULES FOR THE MANAGEMENT OF OSAS PATIENTS

In this chapter we describe how the management of OSAS patients is currently financed in Belgium. Treatments under consideration are limited to PAP and MAD. Two sources of financing are available:

1. The **OSAS convention**, which is an agreement between the Belgian compulsory healthcare insurance (INAMI – RIZIV) and the hospitals / sleep centres that defines the activities of the centres and their financing. The latest OSAS convention started on 01/01/2018. Reimbursements in this convention are provided as lump-sums per day of follow-up.
2. The **Belgian fee schedule**,[a] called “nomenclature – nomenclatuur”, that provides a list of medical and paramedical services (partially or fully) covered by the Belgian compulsory healthcare insurance (INAMI – RIZIV). Reimbursements in the Belgian fee schedule are provided per act, on a fee-for-service basis.

5.1 Diagnosis

The costs incurred to diagnose OSAS patients are not covered by the OSAS convention. Diagnostic costs are reimbursed per act, according to the Belgian fee schedule.

The first step towards a diagnosis of OSAS is usually a patient consultation with a general practitioner (GP) and an anamnesis. If the GP suspects an OSAS problem, the patient is referred to a specialist (the “diagnosing physician”) linked to a sleep centre to be tested with a polysomnography

[a] Medical and paramedical services covered by compulsory healthcare insurance are listed in a fee schedule, called “nomenclature – nomenclatuur”, which lists almost 9000 unique covered services. The list of reimbursable codes contains for each item the professional qualification needed to be eligible for reimbursement, a code-number, a description of the item, a key letter according to the medical or paramedical specialty, a coefficient and application rules. The coefficient gives for each procedure the relative value compared to other procedures with the same key letter. Multiplying the coefficient by the value of the key letter determines the amount of payment to the provider concerned (i.e. the fee).

(PSG). In Belgium, PSG is compulsory for the diagnosis of OSAS. Polygraphy (PG) is not covered by the Belgian fee schedule and not allowed for the diagnosis of OSAS. The **consultations with the GP and the diagnosing physician** are reimbursed on a fee-for-service basis, the last one depending on the type of physician consulted: an internist, a pneumonologist, a neurologist, a neuro-psychiatrist, or a psychiatrist. The total fee ("honoraire-honorarium") per consultation, together with the INAMI – RIZIV reimbursement and the patient co-payment are reported in Table 24.

In this table, *INAMI – RIZIV reimbursement* refers to the amount that the compulsory healthcare insurance reimburses to the patient or the amount that the healthcare insurance pays directly to the healthcare provider (in the case of use of the third-party payer system). INAMI – RIZIV reimbursements are reported for "regularly-insured" patients, i.e. patients that are not entitled to increased reimbursement ("Bénéficiaire de l'Intervention Majorée – Rechthebbende op verhoogde verzekeringstegemoetkoming", BIM – RVV). The *patient co-payment* is the difference between the official total fee and the amount that is reimbursed by the compulsory healthcare insurance. Supplements that are sometimes paid by the patient, i.e. the difference between the price freely set by providers and the official total fee, are not accounted for in this table.

Table 24 – Cost of a consultation to the medical doctors potentially involved in the diagnosis of OSAS patients

Consultation to a/an …		Code-number	Total fee (in 2019)	INAMI – RIZIV reimbursement ‡	Patient co-payment *
General practitioner	Non accredited	101032	€ 21.79	€ 15.79	€ 6.00
	Accredited †	101076	€ 26.27	€ 20.27	€ 6.00
OSAS diagnosing physicians:					
- **Internist**	Accredited †	102550	€ 46.50	€ 34.50	€ 12.00
- **Pulmonologist**	Accredited †	102631	€ 41.29	€ 29.29	€ 12.00
- **Neurologist**	Accredited †	102675	€ 59.96	€ 47.96	€ 12.00
- **Neuropsychiatrist**	Accredited †	102712	€ 49.46	€ 37.46	€ 12.00
- **Psychiatrist**	Accredited †	102690	€ 49.46	€ 37.46	€ 12.00

*† Physicians who participate to continuing medical education and reach a minimum threshold of medical activity per year can obtain an accreditation. This allows them to add a well-defined increment to the fee for a consultation. Accreditation of the diagnosing physician is required in the OSAS convention. ‡ Amount that the compulsory healthcare insurance reimburses to the patient. * The difference between the official total fee and the amount that is reimbursed by the compulsory healthcare insurance. GP: general practitioner, OSAS: obstructive sleep apnoea syndrome.*

In Belgium, the diagnosis of an OSAS patient must be based on the results of a hospital-based PSG. This is compulsory to get the treatment reimbursed by the INAMI – RIZIV within the OSAS convention (the diagnosis PSG remains valid during two years).[57] Therefore the average cost a **hospital stay for a diagnostic PSG** must be added. This was obtained from the analysis of the 2011-2017 data from the Belgian "Echantillon Permanent – Permanente Steekproef" (EPS), in which the patients who had a hospital-based diagnostic PSG up to 2 years prior to the start of their OSAS convention were analysed (n=1271, see section 4.2.2.2). The average cost of a hospital stay for the diagnosis of an OSAS patient with PSG was valued at € 1498.5 (95% CI: 1328; 1668) for the INAMI – RIZIV, and € 84 (95% CI: 76; 92) as co-payment for the patient. The rooms in which the patients spend a night for the PSG are individual rooms, but they cannot be labelled as "single rooms", implying that supplement can normally not be charged to patients.

The fee for a diagnostic PSG, which is already included in the average hospital cost derived above, is € 246.35 (code-number 477374-477385 in the Belgian fee schedule, "Polysomnographie après l'âge d'un an / Polysomnografie na de leeftijd van één jaar"). Only 1 PSG per year is reimbursed by the INAMI – RIZIV. In order to qualify for a treatment within the OSAS convention, the diagnostic PSG must be performed in the hospital/sleep centre. The PSG can thus not be outsourced to a medico-technical service provider. When performed in an inpatient setting (including one-day hospitalisations) (code-number 477385), the INAMI – RIZIV reimbursement is € 246.35 and there is thus no patient co-payment to the PSG itself.[a]

There is a **second consultation with the diagnosing physician** to share and discuss the results of the PSG with the patient (see Table 24). Supplements may be charged to patients consulting specialists not adhering to the official negotiated fees ("non-conventionné – niet-geconventioneerd"), but those were not estimated here.

When a patient is diagnosed with OSAS, i.e. diagnostic PSG with an AHI ≥ 15/hour, the diagnosing physician prescribes the best treatment option, which in the majority of cases is currently PAP or in some cases MAD.

Summary of the costs of the OSAS diagnostic

A summary of the average cost incurred by the INAMI – RIZIV and by the patient for the diagnosis of OSAS is provided in Table 25.

In 2016, the proportion of accredited GPs (in full-time equivalent) was 91% (Personal communication Pascal Meeus, 22/08/2019, for the HiT Belgium 2020). Accounting for this proportion and considering the costs reported in Table 24, the average fee for a GP consultation is valued at € 25.87, of which € 6 is the patient co-payment. For the average cost of a consultation with the diagnosing physician, in the absence information from the field, we assumed that each of the five relevant specialists have an equal probability of being consulted. This assumption only has a minor impact on the estimated average cost as the fees for a consultation to those specialists are relatively similar. Further, though the analysis of the 2011-2018 EPS data reveals that a small proportion of diagnostic PSG were coded as being performed ambulatory (1.15% of the patients within the OSAS convention who had one diagnostic PSG, see section 4.2.2.1), this is not allowed so far and we thus assumed in our model that all diagnostic PSGs are hospital-based.

[a] When an ambulatory PSG is performed (code-number 477374), the INAMI – RIZIV reimbursement is € 237.67 and the co-payment for a regularly insured patient is € 8.68.

Table 25 – Average costs for the diagnosis of an OSAS patient

	Frequency	INAMI – RIZIV reimbursement	Patient co-payment	Total fee (in 2019)
GP consultation	1	€ 19.87	€ 6.00	€ 25.87
First diagnosing physician consultation	1	€ 37.33	€ 12.00	€ 49.33
Hospital stay for diagnostic PSG (including the cost of the PSG)	1	€ 1498.52	€ 84.08	€ 1582.60
Second diagnosing physician consultation	1	€ 37.33	€ 12.00	€ 49.33
TOTAL		**€ 1593.05**	**€ 114.08**	**€ 1707.13**

GP: general practitioner, PSG: polysomnography.

Cost of a hospital stay for PSG diagnosis in Belgium

From the analysis of the 2011-2018 EPS data, the average cost of a hospital stay for the diagnosis of an OSAS patient with PSG was valued at € 1498.5 (95% CI: 1328; 1668) for the INAMI – RIZIV (including the cost of the PSG), and € 84 (95% CI: 76; 92) as co-payment for the patient. Two studies were identified in the literature, which also attempted to derive this cost for Belgium. Their estimates were much lower than ours.

In 2011, Bruyneel et al.[53] (Hôpital Saint Pierre, Brussels, Belgium) prospectively assessed the sleep efficiency, sleep duration and the costs of attended hospital-PSG in patients with a high clinical suspicion of OSAS. The cost of the PSG (€ 218) was obtained from the INAMI – RIZIV 2008 fee schedule ("nomenclature-nomenclatuur"). To this cost, the cost of one overnight stay in a university hospital (€ 839) was added, totalling € 1057 for a hospital-based PSG.

In 2000, Escourrou et al.[94] performed a survey (i.e. questionnaire) among 55 sleep centres across Europe, of which 8 were Belgian, to assess the costs of sleep studies performed in hospital. The type of sleep study performed (e.g. PSG or PG) was not specified. The average cost of the sleep study was valued at € 390 in Belgium.

None of those studies provided an accurate description of the methods they used.

5.2 Titration and treatment

Most of the costs incurred for the treatment of OSAS patients with PAP or MAD are covered by the OSAS convention, with the exception of the follow-up consultations and the potential hospital stays.

5.2.1 PAP

5.2.1.1 Costs covered by the 2018 OSAS convention

When a treatment with CPAP is prescribed, reimbursement within the OSAS convention is granted provided prior agreement by the medical advisor ("médecin conseil – adviserend arts") of the patient's sickness fund, and a proof of treatment efficacy. The proof of treatment efficacy is demonstrated by comparing the results of the diagnostic PSG with the results of the titration PSG or polygraphy (PG). The reimbursement for a CPAP treatment within the OSAS convention can only start when the patient is provided with a PAP device.

In the 2018 OSAS convention, two types of reimbursement packages are defined for the titration and treatment with PAP.

1. A **"start package"** in which PAP treatment is financed through a daily lump-sum received by the sleep centres that are part of the convention during the first 6 months of treatment. Since 01/01/2018 the daily lump-sum is € 2.82 per day (pseudo-code-number 779936, created on 01/01/2018), or € 514.65 during the first 6 months (182.5 days). The lump-sum covers all health services listed in the "basic package" (cfr. infra), together with the PAP titration that can be done:
   - in a sleep centre with PSG; or
   - at home with APAP, followed by PG (performed at home or in the sleep centre) or PSG (performed in the sleep centre).

   Of the total fee (€ 514.65), € 188.55 covers the PSG or the PG (home or hospital-based) titration. The rest (€ 326.10) covers the activities of the "basic package" (cfr. infra). Split-night titration (i.e. when diagnosis and titration are performed during the same night) is not allowed and not reimbursed in Belgium.
2. A **"basic package"** in which PAP treatment is financed through a daily lump-sum received by the sleep centres that are part of the convention after the first 6 months of treatment. Since 01/01/2018, this daily lump-sum is € 1.79 per patient per day (pseudo-code-number 779951, created on 01/01/2018) or € 653.35 per patient per year. Less than half of this fee (€ 307[a]) covers the PAP device and accessories (masks, humidifiers, tubes, filters); the rest (€ 346.35) covers the treatment coordination and organisation (with the exclusion of the medical procedures listed in the Belgian fee schedule "nomenclature – nomenclatuur", that are reimbursed per act), the support and surveillance by non-medical staff, the technical maintenance and repair of the material, the administration costs, the general hospital costs and the transport of staff members to the patient's home.

The OSAS convention allows the hospitals / sleep labs to subcontract some of these activities to a private provider of medical-technical services:

- The provision of the PAP devices and the accessories.
- The maintenance, repair and potential replacement of the devices.
- The training of the patient and his/her family.
- Picking up the devices (and accessories) when the titration or the treatment is over.
- The follow-up of the patient treatment adherence through reading and transfer of the PAP records to the hospital / sleep centre.
- In collaboration with the hospital / sleep centre, the monitoring of the patient motivation to enhance treatment adherence.
- The reading of the APAP records and the transfer of the print to the hospital / sleep centre.
- The execution of the titration PG and the transfer of the raw data to the hospital / sleep centre.

For these last two points, i.e. the reading and transfer of the APAP and PG records, the service provider is not allowed to interpret or analyse the data, and this remains the responsibility of the diagnosing physician. The diagnosing physician is also accountable for the accuracy of the PG itself. In general, outsourcing is only partial as the hospital / sleep centre is accountable for the correct execution of the convention for all parties. According to various informal sources, this outsourcing currently occurs in around 15%-20% of patients with OSAS.

[a] In the convention, the average commercial cost of the PAP device was estimated at € 512, and is amortized over 5 years. Possible discounts negotiated by the sleep centres with the device providers are not taken into account.

The devices are the property of the hospital / sleep centre, unless these services are outsourced in which case the devices belong to the service provider.

In the 2018 OSAS convention, it was assumed that PSG for titration would occur in 61% of new cases and home based APAP followed by PG (home- or hospital-based) in 39% of new cases. Since 1/1/2018, the sleep centres that are part of the convention have to report the method used for the titration of new CPAP patients. Accurate and exhaustive data from all sleep centres are not available yet, but in practice it appears that in 2018 about 95% of the new CPAP-patients had a titration done by PSG at the sleep centre. PG was performed in only 5% of the new patients, half at home and half at the sleep centre (personal communication INAMI – RIZIV, 2019). PG use is thus much lower than estimated in the 2018 OSAS convention. For the home-based PG, the "PAP start package" lump-sum of the OSAS convention covers the costs of the PG itself and the travel costs of a collaborator to the patient's home (Article 6, §7).

The daily lump-sums are charged to the healthcare insurance (INAMI – RIZIV) for the largest part, the rest being the patient co-payment. For a regularly insured patient treated at home, the co-payment is € 0.25 per day of treatment with PAP, equivalent to € 91.25 per year (pseudo-code-number 765951). There is no co-payment for patients entitled to increased reimbursement (BIM – RVV). Of the lump-sum, INAMI – RIZIV reimburses € 1.54 (€ 1.79 - € 0.25) for the basic package and € 2.57 (€ 2.82 - € 0.25) for the start package (2018 OSAS convention).[a]

Table 26 – Lump-sums for PAP treatment defined in the 2018 OSAS convention (per patient)

OSAS convention for PAP treatment		Per day				Per year		
		Lump-sum (total)	INAMI – RIZIV reimbursement	Patient co-payment	Duration in days	Lump-sum (total)	INAMI – RIZIV reimbursement	Patient co-payment
First year of treatment	Start package	€ 2.82	€ 2.57	€ 0.25	182.5	€ 514.650	€ 469.025	€ 45.625
	Basic package	€ 1.79	€ 1.54	€ 0.25	182.5	€ 326.675	€ 281.050	€ 45.625
	Total first year	-	-	-	365	€ 841.325	€ 750.075	€ 91.250
All subsequent years, per year	Basic package	€ 1.79	€ 1.54	€ 0.25	365	€ 653.350	€ 562.100	€ 91.250

PAP: positive airway pressure, OSAS: obstructive sleep apnoea syndrome.

[a] Source (accessed in September 2019): https://www.inami.fgov.be/fr/themes/cout-remboursement/maladies/respiratoires/Pages/syndrome-apnees-intervention-traitement-domicile.aspx#.XYOQjSgUmUk

Treatment reimbursement can start only when treatment efficacy is demonstrated by the diagnosing physician (by comparing the results of the diagnostic PSG with those of the titration PSG or PG, see above). The agreement for reimbursement is first given for 3 months after the start of the treatment and then every 12 months provided that the patient uses the PAP at least 4 hours per night on average. Thus, a print of the PAP internal memory must be provided with the request for extension. In non-adherent patients, there is a new trial for 3 months. If this trial fails, reimbursement is stopped for 1 year. No new PSG or PG is required once the agreement is granted. In case of stop-restart treatment, a new PSG is needed if the first one is older than 2 years.

5.2.1.2 Costs not included in the 2018 OSAS convention

1. The cost of **the hospital stay (excluding the PSG whose cost is covered by the convention)** must be added for 97.5% of the new PAP patients whose titration with PSG or PG is performed at the sleep centre. In the remaining patients (2.5%), titration is done at home with APAP and home-based PG. Patient supplements cannot be charged by the sleep centres once patients are enrolled in the OSAS convention (Article 17, §4).
2. The **consultation with the diagnosing physician** to share and discuss the results of the titration and demonstrate treatment efficacy.
3. After the first 3 months of treatment, the costs of annual (i.e. at months 15, 27, 39… after the start of the treatment) **consultations with the diagnosing physician** for the renewal of the reimbursement agreement must be accounted for. The costs of consultations with any other physicians is also outside the convention.
4. Once the initial reimbursement agreement is granted, no new PSG (or PG) is required for the annual reimbursement renewals (at months 15, 27, 39, etc after the start of the treatment), but this is at the discretion of the diagnosing physician. In patients in whom a new PSG is performed at the sleep centre, the costs of the PSG and of the hospital stay (1 night) must be added (only one PSG is reimbursed per year per patient in Belgium; PG is not reimbursed).

The fees for consultations by type of physician consulted are provided in Table 24.

5.2.1.3 Summary of the costs for a treatment with PAP

A summary of the costs incurred by the INAMI – RIZIV and by the OSAS patients for a treatment with PAP is provided in Table 27.

The average fee for a consultation with the diagnosing physician (i.e. an internist, a pneumologist, a neurologist, a neuropsychiatrist or a psychiatrist) was obtained by assuming that each of the five recognised specialisms have an equal probability of being consulted. This assumption only has a minor impact on the estimated average cost as the fees for a consultation to those specialists are relatively similar. The cost of a hospital stay for a titration PSG was assumed to be equal to that of a diagnostic PSG for an OSAS patient, after deduction of the cost of the PSG, i.e. € 1252.17 (€ 1498.52 - € 246.35) for the INAMI – RIZIV, and € 84 (95% CI: 76; 92) as co-payment for the patient (see above). We further assumed that there was no extra cost (outside the convention) in the 2.5% of patients whose titration is performed at home with an APAP followed by a home-PG.

We also assumed that for the annual extension for reimbursement, a new hospital-based PSG would be performed in about 10% of patients per year (see chapter on data analysis). In those 10% of patients, the costs of a hospital stay for a PSG was therefore added, i.e. € 1498.5 (95% CI: 1328; 1668) for the INAMI – RIZIV, and € 84 (95% CI: 76; 92) as co-payment for the patient.

Table 27 – Summary of the costs to treat an OSAS patient with CPAP

Average cost per patient	INAMI – RIZIV reimbursement	Patient co-payment	Total fee (in 2019)
First year of treatment			
CPAP start package in OSAS convention, 0-6 months	€ 469.03	€ 45.63	€ 514.65
CPAP basic package in OSAS convention, 6-12 months	€ 281.05	€ 45.63	€ 326.68
Hospital stay (excluding titration) for titration at the sleep centre in 97.5% of patients	€ 1252.17	€ 84	€ 1336.25
Extra cost for home titration followed by home PG in 2.5% of patients	€ 0.00	€ 0.00	€ 0.00
Diagnosing physician consultation: discussion of titration results and of treatment efficacy	€ 37.33	€ 12.00	€ 49.33
Diagnosing physician consultation @ 3 months after the start of the treatment	€ 37.33	€ 12.00	€ 49.33
TOTAL	**€ 1 295.30**	**€ 115.25**	**€ 1 410.55**
Each subsequent year of treatment			
CPAP basic package in OSAS convention, per year	€ 562.10	€ 91.25	€ 653.35
Diagnosing physician consultation: once every year	€ 37.33	€ 12.00	€ 49.33
Hospital stay for PSG in 10% of patients per year (including the cost of the PSG)	€ 149.85	€ 8.41	€ 158.26
TOTAL	**€ 749.29**	**€ 111.66**	**€ 860.94**

CPAP: continuous positive airway pressure, OSAS: obstructive sleep apnoea syndrome, PSG: polysomnography.

5.2.2 MAD

The option to treat OSAS patients with MAD within the OSAS convention started in 01/01/2017. Before this date, only PAP treatment was covered by the convention.

When a treatment with MAD is prescribed, a **consultation with the ear, nose and throat (ENT) specialist** linked with the sleep centre is required to confirm the relevance of a treatment with MAD for the patient. A further confirmation of the technical feasibility of the treatment (no dental or orthodontic contraindication) must also be delivered by a **MAD specialist**, which is either a general dentist, an orthodontist, a stomatologist or a maxillofacial surgeon linked with the sleep centre. Both consultations to the ENT or MAD specialists are outside the convention and are reimbursed on a fee-for-service basis, see Table 28 below.

Table 28 – Costs of a consultation to an ENT or a MAD specialist for OSAS patients being prescribed MAD

Consultation to a/an …		Code-number	Total fee (in 2019)	INAMI – RIZIV reimbursement ‡	Patient co-payment *
Ear, nose and throat specialist	Accredited †	101290	€ 29.04	€ 17.04	€ 12.00
MAD specialist:					
- **General dentist**	Accredited †	301011-301022	€ 22.50	€ 17.00	€ 5.50
- **Orthodontist**	Accredited †	301092-301103	€ 26.50	€ 21.00	€ 5.50
- **Stomatologist**	Accredited †	102535	€ 26.27	€ 14.27	€ 12.00
- **Maxillofacial surgeon**	Accredited †	101275	€ 24.13	€ 12.13	€ 12.00

*† Physicians who undergo continuing medical education and reach a minimum threshold of medical activity per year can obtain an accreditation. This allows them to add a well-defined increment to the fee for a consultation. Accreditation of the ENT and MAD specialists is required in the OSAS convention. ‡ Amount that the compulsory healthcare insurance reimburses to the patient. * The difference between the official total fee and the amount that is reimbursed by the compulsory healthcare insurance. ENT: ear, nose and throat. MAD: mandibular advancement device. OSAS: obstructive sleep apnoea syndrome.*

5.2.2.1 Costs covered by the 2018 OSAS convention

The reimbursement of MAD within the OSAS convention is granted provided approval of the treatment by the ENT and MAD specialists (through a written certificate), and by the medical advisor ("médecin conseil / adviserend arts") of the patient's sickness fund. The request for the reimbursement of MAD within the OSAS convention can be introduced only when the patient has received his/her MAD device from the MAD specialist.

In the 2018 OSAS convention, two types of reimbursement packages are defined for a treatment with MAD:

1. A "**start package**" in which MAD is financed through a daily lump-sum received by the sleep centres that are part of the convention during the first 6 months of MAD use. Since 01/01/2017, this daily lump-sum is € 5.64 per day (pseudo-code-numbers 779870 for first MAD use and 779892 for potential renewal after minimum 5 years) or € 1029.52 during the first 6 months (182.5 days).

   The majority of this fee (€ 882.16) covers the manufacturing of the MAD, the delivery to the patient and his/her education, the MAD titration to gradually increase the position of the lower jaw, and the concertation between the MAD specialist and the prescribing physician/ENT specialist. The rest of the fee (€ 147.36) covers the costs of a PG (performed at home or at the sleep-centre) or a hospital-based PSG as a proof of treatment efficacy (breathing improvement) within 5 months of treatment, the concertation between the patient and the MAD specialist, and the administration costs of the sleep centre.

2. A **"basic package"** in which MAD is financed through a daily lump-sum received by the sleep centres that are part of the convention after the first 6 months of treatment. Since 01/01/2017, this daily lump-sum is € 0.43 per day (pseudo-code-number 779914). The basic package for MAD is applicable for 4.5 years so the amount reimbursed over that period is € 705.61. The majority of this fee (€ 586.13) is meant for the MAD-specialist for the repair of the device, as well as for the delivery of

a micro-thermometric sensor[a] (on average one per patient every 5-year, see Annexe 9) to evaluate and encourage patient's treatment adherence. The rest of the fee (€ 119.48) covers the administration costs of the sleep centre.

The MAD is owned by the beneficiary. Until 31/01/2020, there was no co-payment for patients treated at home with MAD. Since 01/02/2020, patients have to pay € 0.5 per day during the first 6 months of MAD treatment (for an initial or a renewal device), which represents € 91.25 for the first year of treatment. Since 01/02/2020, of the lump-sums mentioned in the convention, INAMI – RIZIV reimburses thus € 5.14 (€ 5.64 - € 0.50) for the start package and € 0.43 (the full amount) for the basic package[b].

Since 1/1/2018, the sleep centres that are part of the convention have to report the method used to demonstrate the efficacy of MAD within 5 months of treatment. Accurate and exhaustive data from all sleep centres are not available yet, but in practice it appears that in 2018, about 40% of the new MAD-patients had a PSG at the sleep centre as a proof of treatment efficacy. PG was performed in 60% of new MAD patients, half at home (30% of patients) and half at the sleep centre (30% of patients) (personal communication INAMI – RIZIV, 2019).

Table 29 – Lump-sums for MAD treatment defined in the 2018 OSAS convention (per patient)

OSAS convention for MAD treatment		Per day				Per package duration		
		Lump-sum (total)	INAMI – RIZIV reimbursement	Patient co-payment	Duration in days	Lump-sum (total)	INAMI – RIZIV reimbursement	Patient co-payment
First 6 months of treatment	Start package	€ 5.64	€ 5.14	€ 0.5*	182.5 (0.5 year)	€ 1029.52	€ 938.27	€ 91.25
Subsequent 4.5 years of treatment	Basic package	€ 0.43	€ 0.43	€ 0	1643.5 (4.5 years)	€ 705.61	€ 705.61	€ 0

*MAD: mandibular advancement device, OSAS: obstructive sleep apnoea syndrome. * Since 02/2020.*

MAD reimbursement within the OSAS convention is first granted for 6 months after the start of the treatment (when the patient received his/her MAD). Within 5 months of treatment, treatment efficacy has to be demonstrated by the diagnosing physician with a PG (home-based or at the sleep centre) or a PSG (cfr. "start package" supra).

Each subsequent reimbursement agreement is granted for a 12-month period upon written confirmation from the MAD specialist of the patient compliance to the treatment (i.e. at least 4 hours of MAD; this indicator can be measured when MAD is equipped with a thermosensor though objective assessment with a chip is not mandatory) and in the absence of contraindication to the treatment.

In non-adherent patients, there is a new try limited to 3 months during which MAD treatment is still reimbursed. If this trial fails, reimbursement for MAD is stopped for 1 year.

[a] In annexe 5 of the OSAS convention, it is assumed that this is done in 20% of the MAD patients during one year, per year.

[b] Source (accessed January 2020): http://www.ejustice.just.fgov.be/cgi_loi/change_lg.pl?language=fr&la=F&table_name=loi&cn=2019110311

During the first 6 months of MAD treatment, all medical services performed in relation to MAD (including its manufacturing) are supposed to be covered by the "start package" of the OSAS convention, and the hospitals / sleep centres are not allowed to charge medical services through the Belgian fee schedule (Article 17, §4). This is the case, for example, for the consultation with the diagnosing physician to share and discuss the results of the proof of efficacy PSG / PG.

5.2.2.2 Costs not included in the 2018 OSAS convention

1. The cost of **a hospital stay** must be added for 70% of new MAD patients whose proof of treatment efficacy is demonstrated with a PSG / PG performed at the sleep centre. Patient supplements during the hospital stay cannot be charged by the sleep centres once patients are enrolled in the OSAS convention. In the remaining patients (30%), the proof of treatment efficacy is obtained with a home-PG.
2. Second, after the first 6 months of successful MAD treatment, the costs of regular **consultations with the MAD specialist** (at least once a year for the renewal of the reimbursement agreement) must be accounted for to confirm the patient's treatment adequacy and adherence. The same applies for consultations with any other health care provider.

5.2.2.3 Summary of the costs for a treatment with MAD

A summary of the costs incurred by the INAMI – RIZIV and by the OSAS patient for a treatment with MAD is provided in Table 30.

At the start of the treatment, all patients (100%) are assumed to incur at least 2 consultations, one to the ENT specialist to confirm treatment relevance, and one to the MAD specialist (i.e. a general dentist, an orthodontist, a stomatologist or a maxillofacial surgeon) to obtain a confirmation of no contra-indication to the treatment.

To obtain the average fee for a consultation with the MAD specialist (for treatment initiation and the subsequent yearly follow-up consultations), we assumed that each of the 4 recognised specialties has an equal probability of being consulted. This assumption only has a minor impact on the estimated average costs as the fees for a consultation to the MAD specialists are relatively similar (i.e. range € 22.50 to € 26.27 per consultation).

The cost of a hospital stay for the PSG/PG performed at the sleep centre as a proof of MAD treatment efficacy (70% of new MAD patients) was assumed to be equal to that of a diagnostic PSG for an OSAS patient, after deduction of the cost of the PSG, i.e. € 1252.17 (€ 1498.52 - € 246.35) for the INAMI – RIZIV, and € 84 (95% CI: 76; 92) as co-payment for the patient (see above). We assumed no extra costs (outside the convention) in the 30% of MAD patients whose proof of treatment efficacy within the first 5 months of treatment initiation is obtained with home-PG.

Table 30 – Summary of the costs to treat an OSAS patient with MAD

Average cost per patient	INAMI – RIZIV reimbursement	Patient co-payment	Total fee (in 2019)
First year of treatment (in case of MAD treatment for the first time or as renewal)			
One consultation to the ENT specialist in 100% of patients	€ 17.04	€ 12.00	€ 29.04
One consultation to the MAD specialist in 100% of patients	€ 16.10	€ 8.75	€ 24.85
MAD start package in OSAS convention, 0-6 months	€ 1029.52	€ 0.00	€ 1029.52
MAD basic package in OSAS convention, 6-12 months	€ 78.40	€ 0.00	€ 78.40
One-night stay for proof of treatment efficacy at the sleep centre in 70% of patients (at 5 months)	€ 876.52	€ 58.80	€ 935.32
Extra cost for proof of efficacy treatment at home in 30% of patients (at 5 months)	€ 0.00	€ 0.00	€ 0.00
TOTAL	**€ 2017.58**	**€ 79.55**	**€ 2097.13**
Each subsequent year of treatment (up to 4 years)			
MAD basic package in OSAS convention, per year	€ 156.80	€ 0.00	€ 156.80
MAD specialist consultation to check patient compliance, per year	€ 16.10	€ 8.75	€ 24.85
TOTAL	**€ 172.90**	**€ 8.75**	**€ 181.65**

ENT: ear, nose and throat, MAD: mandibular advancement device, OSAS: obstructive sleep apnoea syndrome.

5.3 Budget allocated to the OSAS convention

The total budget (INAMI – RIZIV and patient shares) allocated to the sleep centres that are part of the OSAS convention is a closed envelope amounting to € 72.7 million in 2018. The convention describes the rules to avoid exceeding the budget. For a treatment with CPAP, this is defined as a maximum number of invoiceable services, i.e. the number of patients treated by CPAP cannot increase more than 15% per year, with the year 2014 as a basis (67 202 patients). Therefore, since 2014, when the increase is larger than 15%, CPAP daily lump-sums charged by the sleep centres are automatically revised downwards, to keep the INAMI – RIZIV reimbursements stable (the patient co-payment of € 0.25 per day remains unchanged). There is no such rule for patients treated with MAD in the 2018 OSAS convention.

The estimated number of patients treated with CPAP or MAD within the OSAS convention and the yearly budgets spent by the INAMI – RIZIV and the patients are reported in Table 31 below (personal communication INAMI – RIZIV, 2019). Since 2005, the total budget has kept increasing (except in 2006 and 2015) to reach € 72.7 million in 2018; of which € 64.7 million paid by the INAMI – RIZIV and € 8 million paid out-of-pocket by the patient. In parallel, the number of patients treated within the OSAS convention has steadily increased from 15 950 in 2005 to 106 258 in 2018. Following this rise in the number of beneficiaries, the patient co-payments increased from € 5 million in 2014 to € 8 million in 2018 (+58% of patients compared to 2014).

Table 31 – Estimated number of patients and budget of the OSAS convention over time

	Estimated number of patients			INAMI – RIZIV expense in EURO			Patient co-payment in EURO			Total budget in EURO (INAMI – RIZIV and patient)		
	CPAP	MAD*	Total	CPAP	MAD*	Total	CPAP	MAD*	Total	CPAP	MAD*	Total
2005	15 950	0	15 950	na	-	na	na	-	na	20 663 867	-	20 663 867
2006	18 268	0	18 268	na	-	na	na	-	na	18 542 993	-	18 542 993
2007	22 639	0	22 639	na	-	na	na	-	na	22 644 704	-	22 644 704
2008	25 418	0	25 418	na	-	na	na	-	na	23 696 056	-	23 696 056
2009	31 212	0	31 212	na	-	na	na	-	na	28 827 093	-	28 827 093
2010	36 876	0	36 876	na	-	na	na	-	na	34 138 009	-	34 138 009
2011	43 195	0	43 195	na	-	na	na	-	na	40 522 861	-	40 522 861
2012	50 296	0	50 296	na	-	na	na	-	na	47 786 227	-	47 786 227
2013	58 699	0	58 699	na	-	na	na	-	na	56 306 754	-	56 306 754
2014	67 202	0	67 202	56 071 821	-	56 071 821	5 083 686	-	5 083 686	61 155 507	-	61 155 507
2015	78 473	0	78 473	50 654 116	-	50 654 116	5 925 940	-	5 925 940	56 580 056	-	56 580 056
2016	83 153	0	82 926	53 495 381	-	53 495 381	6 286 005	-	6 286 005	59 781 386	-	59 781 386
2017	102 076	93	102 169	60 092 230	182 896	60 275 126	7 707 500	0	7 707 500	67 799 730	182 896	67 982 626
2018	105 213	1045	106 258	63 487 778	1 296 026	64 783 804	7 948 706	0	7 948 706	71 436 484	1 296 026	72 732 510

*The number of patients was obtained by dividing the number of daily lump-sums recorded in a year by the number of days in that year (= person-year). * The opportunity to offer OSAS patients a treatment with MAD started on 01/01/2017. NA: information not available.*

An overview of the evolution of the lump-sums over time (since 2000) is provided in Table 32 below. The lump-sums include the INAMI – RIZIV expenses and the patient co-payment for CPAP (until 01/02/2020 there was no patient co-payment for a treatment with MAD). Before 01/09/2014, the lump-sums were (at least partly) indexed, either annually (before 2008) or in case the pivot index was exceeded (2008-2014). Since 01/09/2014, the lump-sums are no longer indexed. On 01/01/2006 and on 01/01/2008, CPAP lump-sums were decreased, essentially to reflect the worldwide prices reduction of the material for CPAP treatment. Applying the rule about the number of CPAP patients defined in the OSAS convention since 2014, the CPAP lump-sums were further decreased on 01/09/2014, 01/11/2016 and 01/01/2017 to keep the budget under control in spite of an increasing number of beneficiaries. With the new convention starting on 1/1/2018, the lump-sum (basic package) for CPAP is slightly lower than before (€ 1.79 per day), but this is compensated by the creation of a new lump-sum (start package) with a much higher fee that can charged during the first 6 months of a CPAP treatment (€ 2.82). The lump-sums of the new start and basic packages were computed to be budget neutral.

Table 32 – Evolution of the lump-sums defined in the OSAS convention

Lump-sum per patient per day (in Euro)*	Treatment with CPAP †		Treatment with MAD ‡		Reason for lump-sum modification
	Start package	Basic package	Start package	Basic package	
01/01/2000	-	3.25	-	-	Full annual indexation
01/01/2001	-	3.32	-	-	Full annual indexation
01/01/2002	-	3.42	-	-	Full annual indexation
01/01/2003	-	3.45	-	-	Full annual indexation
01/01/2004	-	3.51	-	-	Full annual indexation
01/01/2005	-	3.58	-	-	Full annual indexation
01/11/2005		2.66			Decrease of the lump-sum (for the centres that agreed on it)
01/01/2006	-	2.73	-	-	Decrease of the lump-sum for all centres (compared to situation before 1/11/2005)
01/01/2007	-	2.74	-	-	Partial annual indexation
01/01/2008	-	2.49	-	-	Decrease of the lump-sum to compensate the increase in the number of centres that are part of the convention
01/05/2008		2.51			Partial indexation when the pivot index is exceeded
01/09/2008		2.53			
01/09/2010	-	2.56	-	-	Partial indexation when the pivot index is exceeded
01/05/2011	-	2.58	-	-	Partial indexation when the pivot index is exceeded
01/02/2012	-	2.60	-	-	Partial indexation when the pivot index is exceeded
01/12/2012		2.63			
01/09/2014	-	1.97	-	-	Decrease of the lump-sum
01/11/2016	-	1.41	-	-	Temporary (2-month) decrease of the lumps-sum from € 1.97 to € 1.14 per day (up to 31/12/2016)
01/01/2017	-	1.89	5.64	0.43	Decrease of the lump-sum for CPAP (compared to situation before 1/11/2016)
01/01/2018	2.82	1.79	5.64	0.43	New OSAS convention with, for CPAP, a neutral switch from a system with a single lump-sum (basic package) to a system with 2 lump-sums (start and basic packages)

** The lump-sums for CPAP patients comprise the INAMI – RIZIV reimbursement and the patient co-payment (€ 0.25 per day, unchanged over years). For a treatment with MAD, the patient co-payment is € 0 so far. † Before 01/01/2018 CPAP treatment was reimbursed through a unique lump-sum "Basic package". ‡ The opportunity to offer OSAS patients a treatment with MAD started on 01/01/2017.*

6 SCENARIOS

The elaboration of these scenarios led to the formulation of recommendations geared towards Belgian decision-makers. These recommendations are only presented in the synthesis of the report written in the national languages.

6.1 Home Sleep Apnoea Testing (HSAT)

Home Sleep Apnoea Testing (HSAT) should be used in uncomplicated patients with moderate to high risk of OSAS

6.1.1 Rationale

- Home sleep apnoea testing (HSAT) either with ambulatory PSG (portable monitor Type II) or PG (Type III or Type IV) is intended to offer a more patient-centred approach by permitting a simplified home sleep testing in a more familiar and comfortable setting, at lower front costs and shorter waiting times than hospital-based PSG.[39, 48, 50]
- In Belgium, a diagnosis of OSAS must be based on the results of a hospital-based PSG to enter the INAMI – RIZIV convention and get the treatment reimbursed (see section 3.3.1). HSAT is currently not reimbursed.[57] Compulsory hospital-based PSG may result in long waiting lists in specific areas.

6.1.2 Supportive evidence

- The AASM makes the strong evidence-based recommendation that HSAT with a technically adequate device can be used in uncomplicated[a] patients with moderate to high risk of OSAS[b] (see section 2.4.1).[10, 95]
- HSAT in patients with high pre-test probability is currently applied in a substantial proportion of patients in England (30%-40%), France (60%-90%, mainly by PG), Finland (>90% by PG), the Netherlands (>70%, half by PG), and in Germany[c] (see section 3.1.2). In those countries, Type III and Type IV portable monitors are commonly used.
- HSAT is already practised in Belgium by some health care providers (e.g. University Hospital of Liege;[d] Centre de Santé de l'Amblève, in Aywaille) or by service providers[e] (e.g. SleepClinic), but it is not reimbursed (see section 3.1.2).These elements may be seen as a proof of concept (feasibility), although no formal evaluation has been carried out.

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a Uncomplicated patients are patients without; significant cardiorespiratory disease; potential respiratory muscle weakness due to neuromuscular condition; awake hypoventilation or suspicion of sleep related hypoventilation, central sleep apnoea, and sleep related hypoxemia; chronic opioid medication use; history of stroke or severe insomnia.

b An increased risk of moderate to severe OSAS is indicated by the presence of excessive daytime sleepiness and at least two of the following three criteria: habitual loud snoring, witnessed apnoea or gasping or choking, or diagnosed hypertension.

c In Germany, the national clinical guideline stipulates that OSAS diagnosis can be based on HSAT only. In practice, HSAT is nearly always done but practically every patient is referred to a sleep lab for a confirmatory PSG (see section 3.1.2).

d Although HSAT is practised in almost every patients, it is always followed by the compulsory lab-based PSG. In this case, HSAT can be seen as screening to prioritise patients who need a PSG for diagnosis confirmation and to reduce the waiting time for such patients.

e Service providers are for-profit private companies that provide home services related to the diagnosis and/or treatment (mainly PAP renting or leasing, and device maintenance).

- HSAT is considered cost-effective if negative results are confirmed by a lab-based PSG.

6.1.3 Points of attention

- HSAT was not evaluated in patients with significant comorbidities or other suspected sleep disorders (see section 2.3.3). Therefore, HSAT cannot be recommended for these patients until new evidence is generated. However, high diagnostic accuracy has also been reported in patients with only moderate suspicion of OSA or with comorbid obstructive lung disease or heart failure.[6, 50] Moreover, the proportion of diagnosis based on HSAT is high in other countries.
- HSAT will generate false positive results leading to over-treatment. However, if HSAT is applied in patients with high pre-test probability, the post-test probability will even be higher than before the test so false positive results become a minor issue.
- HSAT will generate false negative results leading to under-diagnosis and missed opportunities of treatment. If not addressed, this problem may jeopardize the long-term cost-effectiveness of HSAT (see section 2.6). The AASM recommends that a confirmatory lab-based PSG should be done in case of a negative HSAT in patients with moderate to high pre-test probability of OSAS (see section 2.3.3).[10] Other approaches, e.g. HSAT recorded over two nights for increasing accuracy (as in England) or a CPAP trial (sometimes in Finland), are applied in some countries. But more research is needed on the validity of such approaches.
- The reported range of sensitivity and specificity of portable monitors is wide (even for Type II portable monitors), and the number of studies assessing one specific brand/model is low. Therefore, it is difficult to recommend one specific model of portable monitor. Type II monitors are the only ones able to measure AHI and offer the advantage to be a comprehensive sleep study sleep.[50, 53]
- The budget impact analysis indicates that in the base-case, if 60% of diagnoses was based on HSAT instead of hospital-based PSG, the budget for the INAMI – RIZIV could be reduced by € 9.98 million per year (€ 6.76 million in the worst-case with a.o. 40% of diagnoses based on HSAT and € 15 million in the best-case with a.o. 80% of diagnoses based on HSAT), based on 2018 patient data. This extra budget could be used to face the increasing demand for the diagnosis and treatment of new OSAS patients (see section 7.1).

6.2 Home-based titration (HBT) of PAP

Home-based titration (HBT) of PAP should be a first choice in uncomplicated patients and APAP-only is used

6.2.1 Rationale

- Home-based titration (HBT) of PAP is intended to offer a more patient-centred approach in a more familiar and comfortable setting, at lower costs (no hospital stay) and shorter waiting times than a lab-based titration.[2] Home-based titration can be done with APAP (or fixCPAP[a]), followed or not by a control PSG or PG.
- In Belgium, the vast majority of PAP titrations are done at hospital, mainly during a PSG (95% of all titrations in 2018, personal communication INAMI – RIZIV). Titration based on APAP-only, i.e. not followed by a PSG or a PG, is not reimbursed separately by INAMI – RIZIV.

[a] Based on a calculated reference pressure

6.2.2 Supportive evidence

- There is no evidence of inferiority of home-based titration by APAP compared to in-laboratory titration.[56] On that basis the AASM strongly recommends positive airway pressure therapy be initiated using either APAP at home or in-laboratory PAP titration in adults with OSA and no significant comorbidities.[56]
- The current INAMI – RIZIV convention already stipulates that HBT by APAP followed by home-based PG is an option[a]. The convention also stipulates that the realisation of HBT, but not the reading, can be subcontracted by the sleep-lab to a service provider.
- HBT with a home-based PG is already practised in 30% of patients with a MAD in 2018 (personal communication INAMI – RIZIV, 2019). HBT with an APAP or a CPAP with telemonitoring is already practised in a substantial proportion of patients by some sleep labs (e.g. University Hospital of Liège).
- HBT based on APAP-only (i.e. not followed by a PSG or PG) is already performed in the vast majority of the cases (>90%) in England, France, Finland and the Netherlands. In Germany, HBT is also practised but with wide regional variability. In those countries, telemonitoring is widely used to detect residual respiratory events or mask leaks (see section 3.2.4). HBT based on APAP-only is already practised in Belgium by some service providers outside the INAMI – RIZIV convention (see section 3.2.3).

6.2.3 Points of attention

- HBT was not evaluated in patients with significant comorbidities (see section 2.4.2). With current evidence, HBT cannot be recommended for these patients.. However, titration with APAP-only is already performed in the vast majority of the cases in the studied countries.
- In the studies included in the meta-analysis cited above,[56] most participants using home APAP had mask fitting and education on PAP use at a sleep centre, i.e. the intervention was not fully home-based. However, this is not evidence that such tasks cannot be performed outside the sleep lab (see section 6.2.2)
- In case of MAD treatment, the titration requires necessarily a PG (or a PSG).
- The budget impact analysis indicates that in the base-case, if 50% of all titrations were performed at home with APAP and if half (50%) of those APAP-titrations were controlled by a home-PSG/PG (the other half being done with APAP-alone), the budget for the INAMI – RIZIV could be reduced by € 8.3 million per year (based on the 2018 number of patient). In the best-case scenario (assuming that 85% of all titrations are done with APAP-alone), the INAMI – RIZIV budget could be reduced by € 20.7 million, and by € 3.2 million in the worst case scenario simulating that only 20% of all titrations are done at home with APAP followed by a control home-PSG/PG (see section 7.2). This extra budget could be used to face the increasing demand for the diagnosis and treatment of new OSAS patients.

[a] Only in patients with a AHI≥30/h

6.3 Quality is promoted at all levels of care

6.3.1 Rationale

- In Belgium, as in the majority of the countries analysed in our international comparison, the title of sleep medicine specialist is not officially recognised.
- Having followed a training course is one of the conditions to be an acknowledged physician within the convention. There is no official definition of the content of those courses. There is no examination for most of them. Practical training is organized informally and without formal quality control (see section 3.5).
- The new law on the quality of health care (22/04/2019; applicable from 01/07/2021) stipulates that health care professionals only deliver care in domains where they have compentency and experience.[a] Health care professionals update a portfolio containing the data necessary to demonstrate their competency and required experience.
- Sub-optimal awareness of OSAS by first line health care professionals was reported by various stakeholders in Belgium, and in other countries.

6.3.2 Supportive evidence

- In Germany, there is a standardised training and examination to become an accredited sleep medicine specialist (see section 3.5 for the requirements). A title of 'somnologist' is also available for psychologists and medical-technical employees, nurses and technical staff. Courses and trainings are organised by the German Sleep Society (DGSM). For the reimbursement of a PSG a physician, in theory, has to be an accredited sleep specialist. However, for reimbursement of PG on an ambulatory basis physicians have to participate in a short course (GBA-Course) which usually runs over two weekends. In France also a subtitle in sleep medicine has been created recently.
- The ESRS (European Sleep Research Society) organises a central European examination for sleep medicine both for physicians and for sleep technologists. The examination consists of both a written test and a test of practical skills. It is required from participants that they can document at least 5 years of experience and having followed relevant and accredited (by ESRS) courses and meetings.

6.3.3 Points of attention

- In Belgium, the reimbursement of treatment is currently only possible if the diagnosing physician is an internist, a pulmonologist, a neurologist, a neuro-psychiatrist, a psychiatrist or a pediatrician (see section 3.5).
- Diagnosing physicians, specialist ENT physicians and MAD device specialists must fulfil criteria relating to a minimum number of hours per week spend on sleep medicine, a minimum number of patients treated, and having followed (by 1/1/2020) one out of a list of training courses. These requirements should be integrated in the portfolio every health professionals has to keep updated to demonstrate his competency and required experience according to the new law on health care quality.
- Currently the legal status and accreditation process of service providers is not defined. This should be defined by the authorities, and include training requirements.
- Trainings organised by professional associations and universities will empower GPs to manage OSAS patients.

[a] Law on the quality of health care: http://www.ejustice.just.fgov.be/cgi_loi/change_lg.pl?language=fr&la=F&cn=2019042220&table_name=loi

6.4 An integrated care pathway is defined and effective

An integrated care pathway involving sleep medicine specialists, general practitioners, other professionals of the first line of care and service providers is defined and effective

6.4.1 Rationale

- In Belgium, the follow-up (including maintenance of PAP and yearly renewal of the prescription) of OSAS patients can be reimbursed only within the INAMI – RIZIV convention, i.e. within the framework of an acknowledged sleep lab under the responsibility of a diagnosing physician specialised in sleep medicine.[57]
- Such a hospital-centred approach limits the involvement of the first line of care in the management of this chronic pathology. Moreover, the role of service providers is unclear. The articulation between the actors is ill-defined.
- There is little emphasis on the importance and efficacy of lifestyle interventions, whereas overweight and obesity are the most prominent modifiable risk factors.[60, 61]

6.4.2 Supportive evidence

- In the vast majority of studies on HSAT the diagnosis and titration were performed by sleep medicine specialists. There is thus little evidence available on the adequacy of OSAS diagnosis made by other health care providers such as general practitioners (see section 2.3.3 and section 2.4.2).[10, 56, 95]
- In contrast, the inferiority of OSAS management by primary health care providers other than sleep medicine specialists could not be demonstrated in several studies (see section 2.4.5).[3, 40, 64, 66] Service providers are already involved in the follow-up of OSAS patients, including in Belgium.
- In other countries, treatment follow-up of OSAS is organized differently. In France the long-term follow-up of OSAS patients can be done by the GP. In Finland and the Netherlands there is no formal medical follow-up by a sleep medicine specialist after the first year of treatment, and no yearly renewal of the prescription is required in those countries (see section 3.2.4).
- Dietary weight loss and exercise training (independently of weight loss) are also effective in reducing AHI and sleepiness.[60, 61] This translates into a more integrated approach in some countries. For example, in the Netherlands, patients with OSAS and a BMI of at least 25 are entitled to a lifestyle coach, which is covered by their basic health insurance package (see section 3.2.1).

6.4.3 Points of attention

- In Belgium, service providers can deliver services only under the responsibility of the diagnosing physician as there is currently no legal framework defining their liability. Titration and maintenance of the PAP device is concerned, but also therapeutic education of the patient, transmission of data and even filling in the prescription renewal (see section 3.4). This happens in a substantial proportion of case (estimated to be around 15%-20%).
- The pilot project carried out in the Centre de Santé de l'Amblève, in Aywaille, which is part of the Chronic Care and Cure for Health-3C4H initiative (http://ned.mycarenet.be/chronic-care/3c4h) is a good example of such integrated care trajectory. Patients suspected of OSAS by the GP are proposed a home-based testing. The test relies on a Type IV portable monitor and is organized by a service provider. If the test indicates a moderate/severe OSAS, a CPAP trial is proposed to the patient. If clinical parameters improve, the patient can buy a CPAP which cost is partially covered by the Health Insurance in the frame of the pilot project. Treatment is telemonitored and followed up by a specialized physiotherapist, under the responsibility of the GP. In case of problem, the patient is referred to the specialist in sleep medicine. The evaluation of this pilot project will be made in 2021.

- Comparative effectiveness trials are needed to confirm that the management of OSAS patients by primary health care providers can generate good results in the routine practice, and what specific training is needed to achieve this.
- A HSAT or a HBT can only be prescribed by a sleep medicine specialist. Long-term patient follow-up is only reimbursed if the treating physician is a sleep medicine specialist. No involvement of interested GPs is planned.
- The current convention does not describe the role of each health professional involved with enough precision. The articulation with the first line of care is virtually absent. Effective lifestyle interventions are overlooked.

6.5 Funding mechanisms are adapted

Funding mechanisms enhancing the integrated care pathway are elaborated

6.5.1 Rationale

- Implementing the integrated care pathway presented in 6.4 requires adaptation of the financing rules.
- After the titration period is over, the lump sum received by the hospitals amounts to € 653.35 per patient per year, with medical consultations and potentially a yearly PSG reimbursed outside the convention. Patient co-payment is approximately € 90 per year. For MAD patients the lump-sum (€ 0.43 per day) paid to the hospital is € 156.8 per patient per year (see chapter 5). There is not patient co-payment for a treatment with MAD after the titration period.
- HSAT and HBT with APAP-only cannot be reimbursed.
- Financing of all health care relating to OSAS is channelled through acknowledged sleep labs, even for services achieved by subcontracted service providers.
- Even in case of no utilization of the PAP device, the lump sum is paid until the PAP data is downloaded and read during the annual visit to the sleep specialist.

6.5.2 Supportive evidence

- Of the countries explored, only Belgium works with a specific convention signed between the public healthcare insurance and recognised sleep centres for the reimbursement of PAP/MAD treatment of OSAS patients.
- Alternative financing schemes for the treatment (including titration) of OSAS exist in neighbouring countries:
  - In France, OSAS diagnosis and PAP titration are reimbursed per act (fee-for-service or DRG) while PAP treatment is exclusively provided by service providers and is reimbursed under the form of a lump-sum directly paid by the Social Health Insurance to the service providers. The fee may decrease if the patient's adherence to its treatment is suboptimal (see section 3.3).
  - In The Netherlands and in Germany, fees are also directly paid by the public health insurance to the service providers for the renting and the maintenance of the PAP device and its accessories (see section 3.3).
- The budget-impact analysis indicates that in the base-case, i.e. if the follow-up of PAP patients is performed by private service providers outside the OSAS convention at a cost of € 1 per day, the INAMI – RIZIV budget for the OSAS convention could be reduced by 35% per year (based on 2018 patient data). In the best-case, i.e. if the follow-up cost by the private provider is € 0.8 per day, the INAMI – RIZIV budget could be reduced by 48%, and by 22% in the worst case if the follow-up cost by the private provider is € 1.2 per day (see section 7.3).

6.5.3 Points of attention

- The total budget allocated to the sleep centres that are part of the OSAS convention is a closed envelope amounting to € 72.7 million in 2018. The convention describes the rules to avoid exceeding the budget, i.e. if the number of patients treated by CPAP increases more than 15% per year, the CPAP daily lump-sums are automatically revised downwards.
- The reimbursement of only one PSG per year might be a difficulty for some complicated cases. Costs for additional tests necessary to diagnose sleep problems other than OSAS are not covered. In some countries, such as in England, Germany, The Netherlands and Finland there is no restriction as to the number of PG/PSG diagnostic procedures performed and reimbursed.
- The current convention allows financing a multidisciplinary approach.

6.6 Telemonitoring is used in a substantial proportion of patients

6.6.1 Rationale

- Remote monitoring may improve adherence to treatment and allows detection and early correction of PAP-related problems such as residual respiratory events, Central Emergent Syndrome, or mask leaks.[2]
- In Belgium, remote monitoring is not commonly used. A low utilisation rate of PAP is usually detected during the annual consultation of the prescribing physician. Even if the PAP is not used by a patient, the daily lump sum is paid for that patient during a full year.

6.6.2 Supportive evidence

- The AASM suggests that clinicians use telemonitoring-guided interventions during the initial period of PAP therapy in adults with OSA.[56]
- In Belgium, telemonitoring of PAP is already used by some sleep labs and some service providers. About 30 000 PAP devices are connected (personal communication, J-L Pirlot).
- In European countries, telemonitoring is widely used to detect residual AHI or mask leaks, and to measure adherence to treatment (100% of patients in England, France and Finland[a]; ≥80 % in the Netherlands) (see section 3.2.4).
- In France, when telemonitoring reveals a low adherence, reimbursement of the service provider is cut down.

6.6.3 Points of attention

- The cost of telemonitoring is not accounted in the current calculation of the lump sum within the INAMI – RIZIV convention. Current estimation of telemonitoring cost would be about € 1.20 per patient per week, based on the cost reported for France and foreseen in Belgium.
- If non-adherent Belgian patients (utilisation rate of PAP is lower than 4 hours per night on average), there is a new trial for 3 months. If this trial fails, reimbursement is stopped for 1 year (see section).
- Ethical and privacy issues need to be evaluated.
- The cost-effectiveness of telemonitoring should be explored
- Telemonitoring of patients with MAD is not possible.

[a] In Finland, it is used 2-3 times during the first year of treatment and thereafter only when the patient contacts the sleep unit (if he or she has problems with the device or the treatment) (Dr. Brander), and practice differs from centre to centre.

7 BUDGET IMPACT OF THE OSAS ORGANISATIONAL SCENARIOS

In this section we simulate the impact on the INAMI – RIZIV budget of some of the organisational scenarios proposed for the treatment of OSAS patients. The budget impact on the patient is not explored as patient co-payments are assumed to remain unchanged. For all scenarios, we provide the results for a base-case situation, using the most probable values for the input parameters. We further explore the impact of varying those input parameters, and provide the results for a best and worst case situation.

7.1 Home sleep apnoea testing

What is the impact on the INAMI – RIZIV budget if a proportion of diagnosis is based on home sleep apnoea testing (HSAT) with portable monitors (Type II-IV) instead of hospital-based PSG?

In the current situation (2018 OSAS convention), 100% of the new OSAS patients who enter the convention are diagnosed with a hospital-based PSG, as this is a requirement.

For the simulation, it is assumed that each year 60% (range 40% to 80%) of the new patients are diagnosed at home with one HSAT. The range corresponds to the proportions of diagnoses performed with HSAT reported in our international comparison (see section 3.1.2). The remaining 40% (range 20% to 60%) are assumed to be patients with significant comorbidities who would have one hospital-based PSG. Only one PSG per complicated patient was modelled as, according to the results of the EPS data analysis, only a minority of patients (2.16%) have a second diagnostic PSG (see section 4.2.2.1). Further we assumed that patients with a negative HSAT result would require a confirmatory hospital-based PSG. The calculation of the proportion of such patients accounted for the proportion of patients tested by HSAT, the pre-test probability of OSAS (80%), and the sensitivity and specificity of HSAT (70% each, range 50% to 80%). The simulation was based on the number of new patients enrolled in the OSAS convention for the year 2018 (22 820 new patients in 2018, 21 880 with PAP, 940 with MAD) (EPS data, 2011-2018, see Chapter 4).

In the last OSAS convention (2018), the fee by the INAMI – RIZIV for a PG (Type III-IV portable monitor) at home or at the hospital was set at € 106.98 (see appendix 8 of the convention, note however that PG are no longer reimbursed since 2006). When outsourced to a private provider, the full-service cost for a home-PG was valued at € 250 by one company (Vivisol), while the cost for a home-PSG (Type II portable monitor) ranged between € 100 (Sleepclinic / Sleep-mobile, Som-Ambul) to € 350 (Vivisol), those costs being currently fully borne by the patient (see Appendix Appendix 5). We made the assumption that the cost of a HSAT would be € 200 (range € 100 to € 350) at the INAMI – RIZIV charge.

The cost of a hospital stay for a diagnostic PSG was valued at € 1498.5 (95% CI: 1328; 1668) for the INAMI – RIZIV (EPS data, 2011-2018, see Chapter 4).

Table 33 – Input values for the parameters of the HSAT scenario

Parameter	Base-case	Best-case*	Worst-case	Source
Number of new patients in the OSAS convention, per year	22 820 (21 880 PAP, 940 MAD)	-	-	EPS data, 2018
OSAS pre-test probability	80%	-	-	Literature review
Home-based HSAT sensitivity	70%	80%	50%	Literature review
Home-based HSAT specificity	70%	80%	50%	Literature review
Proportion of patients with a HSAT	60%	80%	40%	Assumption based on international comparison
Proportion of patients with a hospital-based PSG diagnosis	40%	20%	60%	Assumption based on international comparison
INAMI – RIZIV cost of a hospital stay for a diagnostic PSG (including the cost of the PSG)	€ 1498.5	€ 1668	€ 1328	EPS data, 2011-2018
INAMI – RIZIV cost for a HSAT (full service)	€ 200	€ 100	€ 350	Private providers and INAMI – RIZIV fees

** Input parameters under the best-case scenario all favour home-based PG diagnosis. EPS: Echantillon Permanent – Permanente Steekproef. HSAT: home sleep apnoea testing with Type II-IV portable monitor.*

Table 34 – Results for the HSAT diagnosis scenario

	% patients with HSAT	OSAS pre-test probability	HSAT sensitivity	HSAT specificity	New cases per year	Cost PG (€)	Cost PSG (€)	False negative PG	True negative PG	% HSAT patients with negative result (PSG retest)	Total % patients with PSG*	Costs per patient (€)	Total cost (€)	Cost difference with the current situation (€)
Current situation	0	0.8	0.7	0.7	22 820	200	1498.5	0.24	0.14	0	1	1498.5	34 195 770	-
Scenario with HSAT														
Base-case	0.6	0.8	0.7	0.7	22 820	200	1498.5	0.24	0.14	0.23	0.628	1061	24 213 344	-9 982 426
Best-case	0.8	0.8	0.8	0.8	22 820	100	1668	0.16	0.16	0.26	0.456	841	19 182 675	-15 013 095
Worst- case	0.4	0.8	0.5	0.5	22 820	350	1328	0.4	0.1	0.20	0.8	1202	27 438 768	-6 757 002

** Includes the proportion of patients with an initial hospital-based PSG diagnosis, and the proportion of HSAT patients with a negative results requiring a confirmatory hospital-based PSG. Note: Negative results indicate a cost reduction.*

In the base-case, if 60% of diagnoses was based on HSAT with Type II-IV portable monitors instead of hospital-based PSG, the health care budget for the INAMI – RIZIV could be reduced by € 9.9 million per year (based on 2018 patient data). This extra budget could be used to face the increasing demand for the diagnosis and treatment of new OSAS patients. Under the best-case scenario (with a.o. 80% of diagnoses based on HSAT), the INAMI – RIZIV budget could be reduced by € 15 million, and by € 6.7 million under the worst case scenario (with a.o. 40% of diagnoses based on HSAT). Note that the economic impact is on the whole INAMI – RIZIV health care budget, as the diagnosis of OSAS patients is not part of the OSAS convention.

7.2 Home-based titration with APAP

What is the impact on the INAMI – RIZIV budget if most of PAP titration is done with APAP?

In the current situation (2018 OSAS convention), about 95% of the new PAP-patients had a titration done by PSG at the sleep centre. APAP titration followed by PG was performed in only 5% of the new patients, half at home and half at the sleep centre (personal communication INAMI – RIZIV, 2019).

For the simulation, it is assumed that each year, 50% (range 20% to 85%) of the new PAP patients have a home-based titration with APAP, as this is already performed in the vast majority of the cases (80-90%) in England, France, Finland and the Netherlands. APAP can either be performed alone, or be followed by a control home-based PSG/PG. In the simulation, the proportion of patients with a control home-based PSG/PG was varied from 0% (APAP-alone, best-case) to 100% (APAP+home-PSG/PG for all, worst-case), with 50% for the base-case. The results for 10% stepwise increments from 0 to 100% are also presented. We further assumed that 20% (range 10% to 30%) of the PAP patients whose titration occurred at home with APAP would require a hospital-based PSG titration due to APAP technical failure or suboptimal treatment. The remaining 50% (range 15% to 80%) of new PAP patients will be titrated with PSG at the sleep centre. For the year 2018, the number of new PAP patients in which a titration was performed was 21 880 (EPS data, 2011-2018, see Chapter 4).

The current amount budgeted by the INAMI – RIZIV for the PAP titration of a patient within OSAS convention is € 188.55 (see OSAS convention, Annexe 8 about details on the CPAP start package). The average cost of a hospital stay for a PAP titration (excluding the cost of the PSG) was valued at € 1252.17 (95% CI: € 1421.65, € 1081.65) for the INAMI – RIZIV (EPS data, 2011-2018, see Chapter 4). The cost of a hospital-based PSG is € 246.35 (fee schedule code-number 477385).

When outsourced to a private provider, the cost of a full-service for a home-based titration with APAP-only was valued at € 160 by one company (Vivisol), this cost being currently borne by the patient (see Appendix 5). For the simulation, we made the assumption that the cost of a home-based titration with APAP would be reimbursed by the INAMI – RIZIV, at a cost of € 160 (range € 80 to € 240). Likewise, the cost of a full-service by a private provider for a home-PSG/PG was reported to range between € 100 (Sleepclinic / Sleep-mobile, Som-Ambul) to € 350 (Vivisol, see Appendix Appendix 5). We made the assumption that the cost of a home-PSG/PG would be € 200 (range € 100 to € 350) at the INAMI – RIZIV charge.

Table 35 – Input values for the parameters of the home-based APAP titration scenario

Parameter	Base-case	Best-case*	Worst-case	Source
Number of new PAP patients in the OSAS convention	21 880 PAP	-	-	EPS data, 2018
Proportion of PAP patients with a home-based titration with APAP	50%	85%	20%	Assumption and literature review
- **Proportion of APAP-titrated in which a home-based control PG/PSG is performed**	50%	0% (APAP-alone)	100% (APAP+home-PG/PSG for all)	Assumption
- **Proportion of APAP-titrated patients requiring a hospital-based PSG titration**	20%	10%	30%	Assumption
Proportion of PAP patients with a hospital-based PSG titration	50%	15%	80%	Assumption and literature review
INAMI – RIZIV cost of a hospital stay for PAP titration (excluding the cost of the PSG/PG)	€ 1252.17	€ 1421.65	€ 1081.65	EPS data, 2011-2018
INAMI – RIZIV cost for a titration PSG/PG within the CPAP start package of the convention	€ 188.55	-	-	OSAS Convention, annex 8
INAMI – RIZIV cost for a hospital-based PSG	€ 246.35	-	-	INAMI – RIZIV fee schedule
Potential INAMI – RIZIV cost of a home-based titration with APAP alone (full service)	€ 160	€ 80	€ 240	Private providers and assumption
INAMI – RIZIV cost of a home-based PG/PSG (full service)	€ 200	€ 100	€ 350	Private providers and assumption

** Input parameters under the best-case scenario all favour home-based PG diagnosis.*

Table 36 – Results for the home-based titration with APAP scenario

	% patients with APAP titration	% of APAP followed by home PG/PSG	% patients requiring confirmatory hospital-based PSG titration	Total % of patients with hospital-based PSG titration	Unit cost hospital stay (€)	Unit cost titration PSG/PG in convention (€)	Unit cost home-based APAP (€)	Unit cost home-based PG/PSG (€)	Total cost of home-based titrations (€)	Total cost of hospital-based titrations	Total costs	Cost difference with the current situation
Current situation	2.5%	100%	0%	97.5%	1252.17	188.55*	160	-	103 137	30 734 880	30 838 017	-
Scenario with APAP titration												
Base-case	50%	50%	20%	60.0%	1252.17	246.35	160	200	2 844 400	19 672 571	22 516 971	-8 321 046
Best-case	85%	0%	10%	23.5%	1421.65	246.35	80	100	1 487 840	8 576 522	10 064 362	-20 773 654
Worst-case	20%	100%	30%	86.0%	1081.65	246.35	240	350	2 581 840	24 988 710	27 570 550	-3 267 466
One-way sensitivity analysis on the base-case results. The % of APAP-titrated patients with a control home-based PSG/PG is varied from 0% to 100%												
0% (APAP-only)	50%	0%	20%	60%	1252.17	246.35	160	200	1 750 400	19 672 571	21 422 971	-9 415 046
10%	50%	10%	20%	60%	1252.17	246.35	160	200	1 969 200	19 672 571	21 641 771	-9 196 246

20%	50%	20%	20%	60%	1252.17	246.35	160	200	2 188 000	19 672 571	21 860 571	-8 977 446
30%	50%	30%	20%	60%	1252.17	246.35	160	200	2 406 800	19 672 571	22 079 371	-8 758 646
40%	50%	40%	20%	60%	1252.17	246.35	160	200	2 625 600	19 672 571	22 298 171	-8 539 846
50% (Base-case)	50%	50%	20%	60%	1252.17	246.35	160	200	2 844 400	19 672 571	22 516 971	-8 321 046
60%	50%	60%	20%	60%	1252.17	246.35	160	200	3 063 200	19 672 571	22 735 771	-8 102 246
70%	50%	70%	20%	60%	1252.17	246.35	160	200	3 282 000	19 672 571	22 954 571	-7 883 446
80%	50%	80%	20%	60%	1252.17	246.35	160	200	3 500 800	19 672 571	23 173 371	-7 664 646
90%	50%	90%	20%	60%	1252.17	246.35	160	200	3 719 600	19 672 571	23 392 171	-7 445 846
100%	50%	100%	20%	60%	1252.17	246.35	160	200	3 938 400	19 672 571	23 610 971	-7 227 046

*All simulations are based on an estimated 21 880 new PAP cases per year. * Cost reimbursed by the INAMI – RIZIV for a titration with PSG (hospital-based) or control PG (hospital or home-based) in the 2018 OSAS convention.*

In the base-case, i.e. if 50% of all titrations were performed at home with APAP and if half of those APAP-titrations were controlled with a home-PSG/PG, the budget for the INAMI – RIZIV could be reduced by € 8.3 million per year (based on 2018 patient data). This extra budget could be used to face the increasing demand for the diagnosis of new OSAS patients. In the best-case scenario (i.e. if 85% of all titrations were done with APAP-alone), the INAMI – RIZIV budget could be reduced by € 20.7 million, and by € 3.2 million in the worst case scenario if only 20% of all titrations were performed with at home with APAP followed by a control home-PSG/PG.

7.3 PAP follow-up performed by private service providers outside the OSAS Convention

What is the impact on the INAMI – RIZIV budget if the follow-up of PAP patients (i.e. the maintenance of the device and accessories, and the yearly renewal of the prescription) was exclusively performed by accredited private providers and if this service was reimbursed outside the INAMI – RIZIV OSAS convention?

In the current situation (2018 OSAS convention), the follow-up of PAP patients is reimbursed within the INAMI – RIZIV OSAS convention. The daily lump-sum (CPAP basic package) is € 1.54 per day (INAMI – RIZIV share only) or € 562.1 per year (see chapter 5).

When outsourced to a private provider, the cost of the full-service for PAP management was valued at € 1 (€ 0.8 to € 1.2) per day or € 365 (range € 292 to € 438) per year, based on a communication with Vivisol. This service consists in PAP renting, installation of the device at home, maintenance and replacement of supplies (masks, etc), telemonitoring, data recording / analysis and transmission to the physician and preparation of the annual prescription renewal via a web portal. For the simulation, we assumed that all PAP patients would now be managed by private service providers for their follow-up.

The number of PAP patients followed during a year was estimated to be 105 200, based on the 2018 accounting data for the OSAS convention provided by the INAMI – RIZIV (see Chapter 5).

Table 37 – Input values for the parameters of the private provider PAP follow-up scenario

Parameter	Base-case	Best-case*	Worst-case	Source
Average number of PAP patients followed within the OSAS convention	105 200	-	-	INAMI – RIZIV data, 2018
INAMI – RIZIV lump-sum reimbursed for PAP patient follow-up within the OSAS convention (per year)	€ 562.1	-	-	OSAS convention 2018
INAMI – RIZIV cost for PAP patient follow-up by private providers outside the OSAS convention (per year)	€ 365	€ 292	€ 438	Assumption based on private provider fee

** Input parameters under the best-case scenario all favour home-based PG diagnosis.*

Table 38 – Results for the private provider PAP follow-up scenario

	Number of PAP patients followed in a year	Cost FU convention, per patient per year	Cost FU private provider, per patient per year	Costs avoided with FU by private provider, per patient per year	Total cost FU	Cost difference with the current situation	% difference with the current situation
Current situation	105200	562.1	-	-	59 132 920	-	-
Scenario with private provider PAP follow-up							
Base-case	105200	562.1	365	197.1	38 398 000	-20 734 920	-35%
Best-case	105200	562.1	292	270.1	30 718 400	-28 414 520	-48%
Worst-case	105200	562.1	438	124.1	46 077 600	-13 055 320	-22%

In the base-case, i.e. if the follow-up of PAP patients is performed by private service providers outside the OSAS convention at a cost of € 1 per day, the INAMI – RIZIV budget for the OSAS convention could be reduced by 35% per year (based on 2018 patient data). In the best-case, i.e. if the follow-up cost by the private provider is € 0.8 per day, the INAMI – RIZIV budget could be reduced by 48%, and by 22% in the worst case if the follow-up cost by the private provider is € 1.2 per day.

REFERENCES

1. Jonas DE, Amick HR, Feltner C, Weber RP, Arvanitis M, Stine A, et al. In: Screening for Obstructive Sleep Apnea in Adults: An Evidence Review for the U.S. Preventive Services Task Force. Rockville (MD); 2017. Available from: https://www.ncbi.nlm.nih.gov/pubmed/28211654
2. Patil SP, Ayappa IA, Caples SM, Kimoff RJ, Patel SR, Harrod CG. Treatment of Adult Obstructive Sleep Apnea With Positive Airway Pressure: An American Academy of Sleep Medicine Systematic Review, Meta-Analysis, and GRADE Assessment. J Clin Sleep Med. 2019;15(2):301-34.
3. Kunisaki KM, Khalil W, Koffel E, Pfannes L, Koeller E, MacDonald R, et al. In: The Comparative Effectiveness, Harms, and Cost of Care Models for the Evaluation and Treatment of Obstructive Sleep Apnea (OSA): A Systematic Review. Washington (DC); 2016. Available from: https://www.ncbi.nlm.nih.gov/pubmed/28715166
4. Fietze I, Penzel T, Alonderis A, Barbe F, Bonsignore MR, Calverly P, et al. Management of obstructive sleep apnea in Europe. Sleep Med. 2011;12(2):190-7.
5. Hedner J, Grote L, Bonsignore M, McNicholas W, Lavie P, Parati G, et al. The European Sleep Apnoea Database (ESADA): report from 22 European sleep laboratories. Eur Respir J. 2011;38(3):635-42.
6. Gottlieb DJ, Punjabi NM. Diagnosis and Management of Obstructive Sleep Apnea: A Review. JAMA. 2020;323(14):1389-400.
7. Berry RB, Brooks R, Gamaldo C, Harding SM, Lloyd RM, Quan SF, et al. AASM Scoring Manual Updates for 2017 (Version 2.4). J Clin Sleep Med. 2017;13(5):665-6.
8. Jonas DE, Amick HR, Feltner C, Weber RP, Arvanitis M, Stine A, et al. Screening for Obstructive Sleep Apnea in Adults: Evidence Report and Systematic Review for the US Preventive Services Task Force. JAMA. 2017;317(4):415-33.
9. Bibbins-Domingo K, Grossman DC, Curry SJ, Davidson KW, Epling JW, Jr., et al. Screening for Obstructive Sleep Apnea in Adults: US

Preventive Services Task Force Recommendation Statement. JAMA. 2017;317(4):407-14.

10. Kapur VK, Auckley DH, Chowdhuri S, Kuhlmann DC, Mehra R, Ramar K, et al. Clinical Practice Guideline for Diagnostic Testing for Adult Obstructive Sleep Apnea: An American Academy of Sleep Medicine Clinical Practice Guideline. J Clin Sleep Med. 2017;13(3):479-504.
11. Berry RB, Budhiraja R, Gottlieb DJ, Gozal D, Iber C, Kapur VK, et al. Rules for scoring respiratory events in sleep: update of the 2007 AASM Manual for the Scoring of Sleep and Associated Events. Deliberations of the Sleep Apnea Definitions Task Force of the American Academy of Sleep Medicine. J Clin Sleep Med. 2012;8(5):597-619.
12. Benjafield AV, Ayas NT, Eastwood PR, Heinzer R, Ip MSM, Morrell MJ, et al. Estimation of the global prevalence and burden of obstructive sleep apnoea: a literature-based analysis. Lancet Respir Med. 2019;7(8):687-98.
13. Campos-Rodriguez F, Martinez-Garcia MA, Reyes-Nunez N, Selma-Ferrer MJ, Punjabi NM, Farre R. Impact of different hypopnea definitions on obstructive sleep apnea severity and cardiovascular mortality risk in women and elderly individuals. Sleep Med. 2016;27-28:54-8.
14. Gabbay IE, Lavie P. Age- and gender-related characteristics of obstructive sleep apnea. Sleep Breath. 2012;16(2):453-60.
15. Pevernagie DA, Gnidovec-Strazisar B, Grote L, Heinzer R, McNicholas WT, Penzel T, et al. On the rise and fall of the apnea-hypopnea index: A historical review and critical appraisal. J Sleep Res. 2020:e13066.
16. Peppard PE, Young T, Barnet JH, Palta M, Hagen EW, Hla KM. Increased prevalence of sleep-disordered breathing in adults. Am J Epidemiol. 2013;177(9):1006-14.
17. Mihaere KM, Harris R, Gander PH, Reid PM, Purdie G, Robson B, et al. Obstructive sleep apnea in New Zealand adults: prevalence and risk factors among Maori and non-Maori. Sleep. 2009;32(7):949-56.
18. Heinzer R, Vat S, Marques-Vidal P, Marti-Soler H, Andries D, Tobback N, et al. Prevalence of sleep-disordered breathing in the general population: the HypnoLaus study. Lancet Respir Med. 2015;3(4):310-8.
19. Heinzer R, Marti-Soler H, Haba-Rubio J. Prevalence of sleep apnoea syndrome in the middle to old age general population. Lancet Respir Med. 2016;4(2):e5-6.
20. Ye L, Pien GW, Ratcliffe SJ, Bjornsdottir E, Arnardottir ES, Pack AI, et al. The different clinical faces of obstructive sleep apnoea: a cluster analysis. Eur Respir J. 2014;44(6):1600-7.
21. Osman AM, Carter SG, Carberry JC, Eckert DJ. Obstructive sleep apnea: current perspectives. Nat Sci Sleep. 2018;10:21-34.
22. Keenan BT, Kim J, Singh B, Bittencourt L, Chen NH, Cistulli PA, et al. Recognizable clinical subtypes of obstructive sleep apnea across international sleep centers: a cluster analysis. Sleep. 2018;41(3).
23. Wu H, Zhan X, Zhao M, Wei Y. Mean apnea-hypopnea duration (but not apnea-hypopnea index) is associated with worse hypertension in patients with obstructive sleep apnea. Medicine (Baltimore). 2016;95(48):e5493.
24. Azarbarzin A, Sands SA, Stone KL, Taranto-Montemurro L, Messineo L, Terrill PI, et al. The hypoxic burden of sleep apnoea predicts cardiovascular disease-related mortality: the Osteoporotic Fractures in Men Study and the Sleep Heart Health Study. Eur Heart J. 2019;40(14):1149-57.
25. Bonsignore MR, Randerath W, Riha R, Smyth D, Gratziou C, Goncalves M, et al. New rules on driver licensing for patients with obstructive sleep apnoea: EU Directive 2014/85/EU. Eur Respir J. 2016;47(1):39-41.

26. Sateia MJ. International classification of sleep disorders-third edition: highlights and modifications. Chest. 2014;146(5):1387-94.

27. Kingshott RN, Engleman HM, Deary IJ, Douglas NJ. Does arousal frequency predict daytime function? Eur Respir J. 1998;12(6):1264-70.

28. Kim H, Dinges DF, Young T. Sleep-disordered breathing and psychomotor vigilance in a community-based sample. Sleep. 2007;30(10):1309-16.

29. Tam S, Woodson BT, Rotenberg B. Outcome measurements in obstructive sleep apnea: beyond the apnea-hypopnea index. Laryngoscope. 2014;124(1):337-43.

30. McNicholas WT. Diagnostic criteria for obstructive sleep apnea: time for reappraisal. J Thorac Dis. 2018;10(1):531-3.

31. Kingshott RN, Vennelle M, Hoy CJ, Engleman HM, Deary IJ, Douglas NJ. Predictors of improvements in daytime function outcomes with CPAP therapy. Am J Respir Crit Care Med. 2000;161(3 Pt 1):866-71.

32. Lavie P, Lavie L, Herer P. All-cause mortality in males with sleep apnoea syndrome: declining mortality rates with age. Eur Respir J. 2005;25(3):514-20.

33. Pien GW, Ye L, Keenan BT, Maislin G, Bjornsdottir E, Arnardottir ES, et al. Changing Faces of Obstructive Sleep Apnea: Treatment Effects by Cluster Designation in the Icelandic Sleep Apnea Cohort. Sleep. 2018;41(3).

34. Randerath W, Bassetti CL, Bonsignore MR, Farre R, Ferini-Strambi L, Grote L, et al. Challenges and perspectives in obstructive sleep apnoea: Report by an ad hoc working group of the Sleep Disordered Breathing Group of the European Respiratory Society and the European Sleep Research Society. Eur Respir J. 2018;52(3).

35. Gagnadoux F, Le Vaillant M, Paris A, Pigeanne T, Leclair-Visonneau L, Bizieux-Thaminy A, et al. Relationship Between OSA Clinical Phenotypes and CPAP Treatment Outcomes. Chest. 2016;149(1):288-90.

36. Abuzaid AS, Al Ashry HS, Elbadawi A, Ld H, Saad M, Elgendy IY, et al. Meta-Analysis of Cardiovascular Outcomes With Continuous Positive Airway Pressure Therapy in Patients With Obstructive Sleep Apnea. Am J Cardiol. 2017;120(4):693-9.

37. Yu J, Zhou Z, McEvoy RD, Anderson CS, Rodgers A, Perkovic V, et al. Association of Positive Airway Pressure With Cardiovascular Events and Death in Adults With Sleep Apnea: A Systematic Review and Meta-analysis. JAMA. 2017;318(2):156-66.

38. Sanchez-de-la-Torre M, Sanchez-de-la-Torre A, Bertran S, Abad J, Duran-Cantolla J, Cabriada V, et al. Effect of obstructive sleep apnoea and its treatment with continuous positive airway pressure on the prevalence of cardiovascular events in patients with acute coronary syndrome (ISAACC study): a randomised controlled trial. Lancet Respir Med. 2020;8(4):359-67.

39. Abrahamyan L, Sahakyan Y, Chung S, Pechlivanoglou P, Bielecki J, Carcone SM, et al. Diagnostic accuracy of level IV portable sleep monitors versus polysomnography for obstructive sleep apnea: a systematic review and meta-analysis. Sleep Breath. 2018;22(3):593-611.

40. Sanchez-Quiroga MA, Corral J, Gomez-de-Terreros FJ, Carmona-Bernal C, Asensio-Cruz MI, Cabello M, et al. Primary Care Physicians Can Comprehensively Manage Sleep Apnea Patients: A Non-inferiority Randomized Controlled Trial. Am J Respir Crit Care Med. 2018.

41. Newell J, Mairesse O, Verbanck P, Neu D. Is a one-night stay in the lab really enough to conclude? First-night effect and night-to-night variability in polysomnographic recordings among different clinical population samples. Psychiatry Res. 2012;200(2-3):795-801.

42. Ahmadi N, Shapiro GK, Chung SA, Shapiro CM. Clinical diagnosis of sleep apnea based on single night of polysomnography vs. two nights of polysomnography. Sleep Breath. 2009;13(3):221-6.

43. Levendowski DJ, Zack N, Rao S, Wong K, Gendreau M, Kranzler J, et al. Assessment of the test-retest reliability of laboratory polysomnography. Sleep Breath. 2009;13(2):163-7.

44. Sforza E, Roche F, Chapelle C, Pichot V. Internight Variability of Apnea-Hypopnea Index in Obstructive Sleep Apnea Using Ambulatory Polysomnography. Front Physiol. 2019;10:849.

45. Stoberl AS, Schwarz EI, Haile SR, Turnbull CD, Rossi VA, Stradling JR, et al. Night-to-night variability of obstructive sleep apnea. J Sleep Res. 2017;26(6):782-8.

46. Punjabi NM, Patil S, Crainiceanu C, Aurora RN. Variability and Misclassification of Sleep Apnea Severity Based on Multi-Night Testing. Chest. 2020.

47. Dzierzewski JM. Night-to-Night Fluctuations in Sleep Apnea Severity: Diagnostic and Treatment Implications. J Clin Sleep Med. 2020.

48. Corral-Penafiel J, Pepin JL, Barbe F. Ambulatory monitoring in the diagnosis and management of obstructive sleep apnoea syndrome. Eur Respir Rev. 2013;22(129):312-24.

49. Shea BJ, Reeves BC, Wells G, Thuku M, Hamel C, Moran J, et al. AMSTAR 2: a critical appraisal tool for systematic reviews that include randomised or non-randomised studies of healthcare interventions, or both. BMJ. 2017;358:j4008.

50. Bruyneel M, Ninane V. Unattended home-based polysomnography for sleep disordered breathing: current concepts and perspectives. Sleep Med Rev. 2014;18(4):341-7.

51. Escourrou P, Grote L, Penzel T, McNicholas WT, Verbraecken J, Tkacova R, et al. The diagnostic method has a strong influence on classification of obstructive sleep apnea. J Sleep Res. 2015;24(6):730-8.

52. Masa JF, Corral J, Sanchez de Cos J, Duran-Cantolla J, Cabello M, Hernandez-Blasco L, et al. Effectiveness of three sleep apnea management alternatives. Sleep. 2013;36(12):1799-807.

53. Bruyneel M, Sanida C, Art G, Libert W, Cuvelier L, Paesmans M, et al. Sleep efficiency during sleep studies: results of a prospective study comparing home-based and in-hospital polysomnography. J Sleep Res. 2011;20(1 Pt 2):201-6.

54. Bruyneel M, Libert W, Ameye L, Ninane V. Comparison between home and hospital set-up for unattended home-based polysomnography: a prospective randomized study. Sleep Med. 2015;16(11):1434-8.

55. Martinot JB, Borel JC, Cuthbert V, Guenard HJ, Denison S, Silkoff PE, et al. Mandibular position and movements: Suitability for diagnosis of sleep apnoea. Respirology. 2017;22(3):567-74.

56. Patil SP, Ayappa IA, Caples SM, Kimoff RJ, Patel SR, Harrod CG. Treatment of Adult Obstructive Sleep Apnea with Positive Airway Pressure: An American Academy of Sleep Medicine Clinical Practice Guideline. J Clin Sleep Med. 2019;15(2):335-43.

57. Institut national d'assurance maladie-invalidité – Rijksinstituut voor ziekte- en invaliditeitsverzekering (INAMI – RIZIV). Convention relative au diagnostic et au traitement du syndrome des apnées du sommeil - Overeenkomst aangaande de diagnose en de behandeling van het slaapapneusyndroom; Brussels 2018.

58. Attali V, Vecchierini MF, Collet JM, d'Ortho MP, Goutorbe F, Kerbrat JB, et al. Efficacy and tolerability of a custom-made Narval mandibular repositioning device for the treatment of obstructive sleep apnea: ORCADES study 2-year follow-up data. Sleep Med. 2019;63:64-74.

59. Schwartz M, Acosta L, Hung YL, Padilla M, Enciso R. Effects of CPAP and mandibular advancement device treatment in obstructive

sleep apnea patients: a systematic review and meta-analysis. Sleep Breath. 2018;22(3):555-68.

60. Iftikhar IH, Bittencourt L, Youngstedt SD, Ayas N, Cistulli P, Schwab R, et al. Comparative efficacy of CPAP, MADs, exercise-training, and dietary weight loss for sleep apnea: a network meta-analysis. Sleep Med. 2017;30:7-14.

61. Edwards BA, Bristow C, O'Driscoll DM, Wong AM, Ghazi L, Davidson ZE, et al. Assessing the impact of diet, exercise and the combination of the two as a treatment for OSA: A systematic review and meta-analysis. Respirology. 2019;24(8):740-51.

62. Lins-Filho OL, Pedrosa RP, Gomes JML, Dantas Moraes SL, Vasconcelos BCE, Lemos CAA, et al. Effect of exercise training on subjective parameters in patients with obstructive sleep apnea: a systematic review and meta-analysis. Sleep Med. 2020;69:1-7.

63. Murphie P, Little S, McKinstry B, Pinnock H. Remote consulting with telemonitoring of continuous positive airway pressure usage data for the routine review of people with obstructive sleep apnoea hypopnoea syndrome: A systematic review. J Telemed Telecare. 2019;25(1):17-25.

64. Tarraubella N, Sanchez-de-la-Torre M, Nadal N, De Batlle J, Benitez I, Cortijo A, et al. Management of obstructive sleep apnoea in a primary care vs sleep unit setting: a randomised controlled trial. Thorax. 2018;73(12):1152-60.

65. Sanchez-de-la-Torre M, Nadal N, Cortijo A, Masa JF, Duran-Cantolla J, Valls J, et al. Role of primary care in the follow-up of patients with obstructive sleep apnoea undergoing CPAP treatment: a randomised controlled trial. Thorax. 2015;70(4):346-52.

66. Hui DS, Ng SS, Tam WWS. Home-based Approach Noninferior to Hospital-based Approach in Managing Patients with Suspected Obstructive Sleep Apnea Syndrome. Am J Respir Crit Care Med. 2018;197(9):1233-4.

67. Bruyneel M. Telemedicine in the diagnosis and treatment of sleep apnoea. Eur Respir Rev. 2019;28(151).

68. Bruyneel M. Technical Developments and Clinical Use of Telemedicine in Sleep Medicine. J Clin Med. 2016;5(12).

69. Leger D, Elbaz M, Piednoir B, Carron A, Texereau J. Evaluation of the add-on NOWAPI(R) medical device for remote monitoring of compliance to Continuous Positive Airway Pressure and treatment efficacy in obstructive sleep apnea. Biomed Eng Online. 2016;15:26.

70. Peppard PE, Young T, Palta M, Dempsey J, Skatrud J. Longitudinal study of moderate weight change and sleep-disordered breathing. JAMA. 2000;284(23):3015-21.

71. Évaluation clinique et économique des dispositifs médicaux et prestations associées pour prise en charge du syndrome d'apnées hypopnées obstructives du sommeil (SAHOS). Volet 2 : Évaluation économique et analyse des bases de données

72. McMillan A, Bratton DJ, Faria R, Laskawiec-Szkonter M, Griffin S, Davies RJ, et al. A multicentre randomised controlled trial and economic evaluation of continuous positive airway pressure for the treatment of obstructive sleep apnoea syndrome in older people: PREDICT. Health Technol Assess. 2015;19(40):1-188.

73. Wickwire EM, Albrecht JS, Towe MM, Abariga SA, Diaz-Abad M, Shipper AG, et al. The Impact of Treatments for OSA on Monetized Health Economic Outcomes: A Systematic Review. Chest. 2019;155(5):947-61.

74. McDaid C, Griffin S, Weatherly H, Duree K, van der Burgt M, van Hout S, et al. Continuous positive airway pressure devices for the treatment of obstructive sleep apnoea-hypopnoea syndrome: a systematic review and economic analysis. Health Technol Assess. 2009;13(4):iii-iv, xi-xiv, 1-119, 43-274.

75. Kim J, Tran K, Seal K, Fernanda A, Glenda R, Messier R, et al. Interventions for the Treatment of Obstructive Sleep Apnea in

Adults: A Health Technology Assessment. Reports COU, editor. Ottawa (ON): Canadian Agency for Drugs and Technologies in Health (CADTH); 2017.

76. Toraldo DM, Passali D, Sanna A, De Nuccio F, Conte L, De Benedetto M. Cost-effectiveness strategies in OSAS management: a short review. Acta Otorhinolaryngol Ital. 2017;37(6):447-53.

77. Lojander J, Rasanen P, Sintonen H, Roine RP, Group HUSQS. Effect of nasal continuous positive airway pressure therapy on health-related quality of life in sleep apnoea patients treated in the routine clinical setting of a university hospital. J Int Med Res. 2008;36(4):760-70.

78. Quinnell TG, Bennett M, Jordan J, Clutterbuck-James AL, Davies MG, Smith IE, et al. A crossover randomised controlled trial of oral mandibular advancement devices for obstructive sleep apnoea-hypopnoea (TOMADO). Thorax. 2014;69(10):938-45.

79. Corral J, Sanchez-Quiroga MA, Carmona-Bernal C, Sanchez-Armengol A, de la Torre AS, Duran-Cantolla J, et al. Conventional Polysomnography Is Not Necessary for the Management of Most Patients with Suspected Obstructive Sleep Apnea. Noninferiority, Randomized Controlled Trial. Am J Respir Crit Care Med. 2017;196(9):1181-90.

80. Deutsch PA, Simmons MS, Wallace JM. Cost-effectiveness of split-night polysomnography and home studies in the evaluation of obstructive sleep apnea syndrome. J Clin Sleep Med. 2006;2(2):145-53.

81. Moro M, Westover MB, Kelly J, Bianchi MT. Decision Modeling in Sleep Apnea: The Critical Roles of Pretest Probability, Cost of Untreated Obstructive Sleep Apnea, and Time Horizon. J Clin Sleep Med. 2016;12(3):409-18.

82. Pietzsch JB, Garner A, Cipriano LE, Linehan JH. An integrated health-economic analysis of diagnostic and therapeutic strategies in the treatment of moderate-to-severe obstructive sleep apnea. Sleep. 2011;34(6):695-709.

83. Kim RD, Kapur VK, Redline-Bruch J, Rueschman M, Auckley DH, Benca RM, et al. An Economic Evaluation of Home Versus Laboratory-Based Diagnosis of Obstructive Sleep Apnea. Sleep. 2015;38(7):1027-37.

84. Andreu AL, Chiner E, Sancho-Chust JN, Pastor E, Llombart M, Gomez-Merino E, et al. Effect of an ambulatory diagnostic and treatment programme in patients with sleep apnoea. Eur Respir J. 2012;39(2):305-12.

85. Rosen CL, Auckley D, Benca R, Foldvary-Schaefer N, Iber C, Kapur V, et al. A multisite randomized trial of portable sleep studies and positive airway pressure autotitration versus laboratory-based polysomnography for the diagnosis and treatment of obstructive sleep apnea: the HomePAP study. Sleep. 2012;35(6):757-67.

86. Ayas NT, Fox J, Epstein L, Ryan CF, Fleetham JA. Initial use of portable monitoring versus polysomnography to confirm obstructive sleep apnea in symptomatic patients: an economic decision model. Sleep Med. 2010;11(3):320-4.

87. Bravata DM, Lightner N, Yaggi HK, Miech EJ. Economic Assessment of 4 Approaches to the Diagnosis and Initial Treatment of Sleep Apnea. Respir Care. 2018;63(1):50-61.

88. Stewart SA, Penz E, Fenton M, Skomro R. Investigating Cost Implications of Incorporating Level III At-Home Testing into a Polysomnography Based Sleep Medicine Program Using Administrative Data. Can Respir J. 2017;2017:8939461.

89. Abma IL, Rovers M, M IJ, Hol B, Westert GP, van der Wees PJ. The development of a patient-reported outcome measure for patients with obstructive sleep apnea: the Patient-Reported Apnea Questionnaire (PRAQ). J Patient Rep Outcomes. 2017;1(1):14.

90. Partinen M, Gislason T. Basic Nordic Sleep Questionnaire (BNSQ): a quantitated measure of subjective sleep complaints. J Sleep Res. 1995;4(S1):150-5.

91. Mayer G, Arzt M, Braumann B, Ficker JH, Fietze I, Frohnhofen H, et al. German S3 Guideline Nonrestorative Sleep/Sleep Disorders, chapter "Sleep-Related Breathing Disorders in Adults," short version: German Sleep Society (Deutsche Gesellschaft fur Schlafforschung und Schlafmedizin, DGSM). Somnologie (Berl). 2017;21(4):290-301.

92. Fischer J, Dogas Z, Bassetti CL, Berg S, Grote L, Jennum P, et al. Standard procedures for adults in accredited sleep medicine centres in Europe. J Sleep Res. 2012;21(4):357-68.

93. Pevernagie D, Stanley N, Berg S, Krieger J, Amici R, Bassetti C, et al. European guidelines for the certification of professionals in sleep medicine: report of the task force of the European Sleep Research Society. J Sleep Res. 2009;18(1):136-41.

94. Escourrou P, Luriau S, Rehel M, Nedelcoux H, Lanoe JL. Needs and costs of sleep monitoring. Stud Health Technol Inform. 2000;78:69-85.

95. Rosen IM, Kirsch DB, Carden KA, Malhotra RK, Ramar K, Aurora RN, et al. Clinical Use of a Home Sleep Apnea Test: An Updated American Academy of Sleep Medicine Position Statement. J Clin Sleep Med. 2018;14(12):2075-7.

96. Martinot JB, Le-Dong NN, Cuthbert V, Denison S, Borel JC, Gozal D, et al. Respiratory Mandibular Movement Signals Reliably Identify Obstructive Hypopnea Events During Sleep. Front Neurol. 2019;10:828.

97. Rotty MC, Mallet JP, Borel JC, Suehs CM, Bourdin A, Molinari N, et al. The feasibility of a mandibular movement test as a screening tool for polysomnography candidates. Eur Respir J. 2017;50(5).

98. Cheliout-Heraut F, Senny F, Djouadi F, Ouayoun M, Bour F. Obstructive sleep apnoea syndrome: comparison between polysomnography and portable sleep monitoring based on jaw recordings. Neurophysiol Clin. 2011;41(4):191-8.

99. Pepin JL, Letesson C, Le-Dong NN, Dedave A, Denison S, Cuthbert V, et al. Assessment of Mandibular Movement Monitoring With Machine Learning Analysis for the Diagnosis of Obstructive Sleep Apnea. JAMA Netw Open. 2020;3(1):e1919657.

100. Maury G, Cambron L, Jamart J, Marchand E, Senny F, Poirrier R. Added value of a mandible movement automated analysis in the screening of obstructive sleep apnea. J Sleep Res. 2013;22(1):96-103.

101. Whiting PF, Rutjes AW, Westwood ME, Mallett S, Deeks JJ, Reitsma JB, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Ann Intern Med. 2011;155(8):529-36.

102. Vinck I, Stroobandt S, Gerkens S, De Laet C. Remote monitoring for patients with implanted defibrillator. Technology evaluation and broader regulatory framework. Belgian Health Care Knowledge Centre (KCE), Report 136C; Brussels 2010. D/2010/10.273/55.

103. Wet van 8 december 1992 tot bescherming van de persoonlijke levenssfeer ten opzichte van de verwerking van persoonsgegevens, Belgisch Staatsblad 18 maart 1993

104. Koninklijk Besluit van 13 februari 2001 ter uitvoering van de wet van 8 december 1992 tot bescherming van de persoonlijke levenssfeer ten opzichte van de verwerking van persoonsgegevens, Belgisch Staatsblad 13 maart 2001

APPENDICES

APPENDIX 1. METHODS OF THE INTERNATIONAL COMPARISON

Table 39 – Selection of foreign countries for the international comparison

Country	Characteristics of OSAS diagnosis and treatment
France	-60% of diagnosis are home-based with PG - Many office based physicians for diagnosis -Home titration with APAP -Telemonitoring: adherence to treatment is measured every month, with consequences on the level of reimbursement
Finland	-80% of diagnosis are home-based with PG -Home titration with APAP -Tenders for CPAP treatment
Germany	-37% of cases treated with positional therapy or surgery -Tenders for CPAP treatment -Telemonitoring
The Netherlands	-54% of diagnosis are home-based with PG -18% of diagnosis are based on ambulatory PSG -5% of diagnosis are hospital-based PG -Home titration with APAP -36% of treatment are MAD
England	- Sleep services can be provided by physicians or others who are non-specialized in the area of sleep specifically -Devices with 1–3 channels, of which evidence of efficacy is soundly based, are widely employed

Table 40 – National Protocols and other relevant documents in countries of the international comparison

Country	National protocols	References
Belgium	Slaapapneusyndroom: tegemoetkoming in de kosten van een thuisbehandeling met een nCPAP-toestel, met een auto-CPAP-toestel of met een mandibulair repositieapparaat Syndrome des apnées du sommeil : intervention dans le coût d'un traitement à domicile au moyen d'un appareil nCPAP, d'un appareil auto-CPAP ou d'une orthèse d'avancée mandibulaire	https://www.riziv.fgov.be/nl/themas/kost-terugbetaling/ziekten/ademhalingsziekten/Paginas/slaapapneesyndroom-tegemoetkoming-thuisbehandeling.aspx
Finland	Sleep apnoea: Finnish National guidelines for prevention and treatment 2002-2012 Sleep apnoea syndrome, 2017	https://www.sciencedirect.com/science/article/pii/S0954611102914496
	Sleep apnoea syndrome, Current Care Guidelines	https://www.kaypahoito.fi/hoi50088
France	Recommandations pour la pratique clinique du syndrome d'apnées hypopnées obstructives du sommeil de l'adulte, 2010	http://www.sfrms-sommeil.org/wp-content/uploads/2012/10/HS3_reco_sas2010-1.pdf
Germany	German S3 Guideline Nonrestorative Sleep/Sleep Disorders, 2017[a]	https://link.springer.com/content/pdf/10.1007/s11818-017-0136-2.pdf
The Netherlands	Richtlijn Diagnostiek en behandeling van obstructief slaapapneu (OSA) bij volwassenen, 2017	https://www.nvalt.nl/kwaliteit/richtlijnen/slaap/_/Slaap/Richtlijn%20OSA%20bij%20volwassenen%20%28geaccordeerd%20april%202018%29.pdf
UK	Continuous positive airway pressure for the treatment of obstructive sleep apnoea/hypopnoea syndrome, 2008[b]	https://www.nice.org.uk/guidance/ta139/resources/continuous-positive-airway-pressure-for-the-treatment-of-obstructive-sleep-apnoeahypopnoea-syndrome-pdf-82598202209221

[a] Short version of the chapter "Sleep-Related Breathing Disorders in Adults"

[b] A new NICE guideline is expected in November 2020 (https://www.nice.org.uk/guidance/gid-ng10098/documents/final-scope.

APPENDIX 2. EVIDENCE REVIEW ON TYPE IV MONITORS RECORDING MANDIBLE MOVEMENT

A search for studies was carried out in Pubmed on 24/02/2020 with the following search strategy: (brizzy OR somnolter OR JAWAC OR "jaw movement" OR "Jaw Activity" OR "mandibular movement" OR “mandible movement”) and (apnoea OR apnea). Inclusion criteria: diagnosis studies comparing PM measuring mandibular movements and PSG in adults; Exclusion criteria: studies in children; screening for obstructive problems during surgery.

The search retrieved 25 studies, of which 19 were excluded on title/abstract. Three studies were excluded on full text. The study by Martinot et al. 2019[96] was excluded because it focused on the use of mandible movements (measured by Brizzy) as surrogate markers of oesophageal pressure. The study by Rotty et al. 2017 was excluded because it was a research letter with no measurement of PSG.[97] The study by Cheliout-Heraut was excluded because it was not possible to differentiate results for the various categories of OSAS severity.[98] Three studies were included: Pépin 2020[99], Martinot 2017[55], and Maury 2013.[100] Quality appraisal of the studies (risk of bias, RoB) was based on the Quality Assessment of Diagnostic Accuracy Studies QUADAS-2 checklist (see Table 41).[101] Overall, the quality of these studies was high, except the study by Martinot et al. 2017 which presented a high risk of selection bias.[55] Two of these studies tested devices produced by the same company (Nomics, Liège, Belgium). One assessed Brizzy,[55] while the other assessed JawSens.[100]. The third study assessed Sunrise (from Sunrise, Namur, Belgium).[99] Although the type IV portable monitors tested tended to systematically underestimate the frequency of RDI as measured by PSG, such difference was quite small at the usual cut-offs of RDI ≥5/h and RDI ≥15/h. When the cut-offs of RDI as measured by the PM were adjusted to account for the under-estimation of RDI vs. AHI, the performance of the device was quite high.

At the cut-off of RDI ≥15/h, which is the cut-off to decide on treatment in Belgium, the Positive Likelihood Ratio ranged from 5.6 to 16.5 and the Negative Likelihood Ratio from 0.07 to 0.26 (see Table 42). As regards more particularly the Brizzy, the only study reported high diagnostic performance (see Table 42).[55]

Table 41 – Quality appraisal of studies reporting on the use of mandible movement analysis to screen for OSAS

Study	Patient selection RoB	Patient selection Applicability	Index test RoB	Index test Applicability	Reference standard RoB	Reference standard Applicability	Flow & timing RoB	Flow & timing Applicability
Pépin 2020[99]	Low[a]	Low	Low	Low[b]	Low[c]	Low	Low	Low[d]
Martinot 2017[55]	Unclear/High[e]	Unclear/High	Low	Low[f]	Low[g]	Low	Low[h]	Low
Maury 2013 [100]	Low[i]	Low	Low	High[j]	Low	Low	Low[k]	Low

RoB: Risk of Bias

a Possible exclusion criteria not reported

b Not at home

c The inter observer agreement for PSG double-scoring was 92% (95%CI: 89%; 94%)

d Index test (Sunrise) and standard test (PSG) were done at the same time in hospital

e The 13 volunteers who had no specific sleep complaints were recruited by word of mouth. They are significantly younger and slimmer than the other participants. This represents a selection bias and limits the applicability of findings to the general population of individuals suspected of OSAS.

f Not at home

g Index test (Brizzy) and standard test (PSG) were done at the same time at hospital

h 8% of records unavailable due to technical failure; however, it is not reported that technical failure concerned patients with a specific clinical profile

i The only exclusion criterion was ongoing continuous positive airway pressure treatment

j The main outcome was respiratory disturbance index (RDI) based on nasal airflow, pulse oximetry and mandible movement automated analysis, divided by the time between lights out and lights on. Therefore, no data on MMAA in isolation was available, and the reference time is not sleep time.

k 59/629 patients were excluded from the analysis: 22 because of technical failure; 37 patients with a history of OSA diagnosed by PSG

Table 42 – Performance of type IV Portable Monitors recording mandible movements against PSG results

Study	Technology	Methods	RDI cut-offs Events per hour	Sensitivity (95% CI)	Specificity (95% CI)	LR+ (95% CI)	LR- (95% CI)	AUC (95% CI)
Pépin 2020[99]	Sunrise (Sunrise)[a]	• 376 consecutive adults with suspected OSA enrolled in 1 centre (i.e. not home-based) • Simultaneous MM recording and PSG • Blinded reading of results • Pre-test prob. AHI > 5/h=82.5% • Pre-test prob. AHI > 15/h=55.7% • Optimal diagnostic cut-off Sr-RDI ≥7.63 events/h (for PSG-RDI≥5) and ≥12.65 events/h (for PSG-RDI≥15).	RDI ≥5	0.91 (0.89-0.92)	0.94 (0.91-0.97)	14.86 (9.86; 30.12)	0.10 (0.08-0.12)	0.95 (0.92; 0.96)
			RDI≥15	0.92 (0.90; 0.94)	0.84 (0.81; 0.87)	5.63 (4.92; 7.27)	0.10 (0.07; 0.12)	0.93 (0.90; 0.93)
Martinot 2017[55]	Brizzy (Nomics)[b]	• 100 consecutive subjects, 18 years and older with symptoms suggestive of sleep-disordered breathing (SDB) undergoing a single PSG in one centre (i.e. not home-based). Data available for 92 subjects • Simultaneous MM recording and PSG • Blinded reading of results • Pre-test prob. AHI > 5/h =81.5% (95% CI: 73.9; 88.0%)	RDI ≥5	93.2 (86.77; 97.04)	100.0 (51.0; 100.0)	3.73 (2.7; 20.4)	0.07 (0.03; 0.15)	0.96 (0.89; 0.99)
			RDI ≥15	89.0 (79.83; 94.31)	100.0 (83.18; 100.0)	8.46 (2.3; 31.5)	0.11 (0.06; 0.21)	0.97 (0.91; 0.99)

[a] Sunrise combines mandibular movement (MM) recordings with an automated analysis that is supported by machine learning. The Sunrise system is composed of coin-sized hardware attached by the sleep technician to the chin of the patient in the mentolabial sulcus. Its embedded inertial measurement unit enables MM sensing and communicates with a smartphone application for external control. To identify wake, the algorithm tested whether MM signals were fast, irregular, and non-predictable. For the identification of arousal movements, the algorithm detected brisk MM of large amplitude, indicating abrupt closure of the mouth characteristical of arousals. Respiratory effort was identified through oscillating MM at the breathing frequency. The Sunrise algorithm identifies respiratory disturbances as a period of respiratory effort ended by an arousal or an awakening. RDI consists of the total number of respiratory disturbances accompanied by respiratory effort divided by the total sleep time.[99]

[b] A mid-sagittal MM magnetic sensor (Brizzy, Nomics, Liege, Belgium) measured the distance in mm between two parallel, coupled, resonant circuits placed on the forehead and on the chin (Fig. 1). The transmitter generates a pulsed magnetic wave of low energy at 10 Hz. The change in the magnetic field is inversely related to the cube of the distance (d) between the chin and forehead probes. The probes were connected to an electronic module, and the distance was computed with a resolution of 0.1 mm before transmission to the PSG through a wired connection. The more negative the signal, the lower the mandibular position and the greater the mouth opening. The respiratory events identified by MM analysis alone cannot differentiate between apnoea, hypopnoea or RERAs as the flow is not measured.

		• Pre-test prob. AHI > 15/h=46.7% (95% CI: 38.0; 55.4%) for an AHI > 15/h TST • Optimal diagnostic cut-off Sr-RDI ≥5.9 events/h (for PSG-RDI≥5) and ≥13.5 events/h (for PSF-RDI≥15).						
Maury 2013 [100]	JawSens (Nomics)[a]	• 629 consecutive subjects referred for diagnostic PSG in one centre (i.e. not home-based). 570 were considered for the analysis, of whom 344 (60%) suffered from OSAS • Simultaneous MM recording and PSG • Blinded reading of results • Pre-test prob. AHI > 15/h=54% • Outcome: respiratory disturbance index (RDI) based on NAF, SpO2 and MMAA divided by the time between lights out and lights on	RDI ≥5	93 (90.57; 95.38)	72 (62.44; 79.99)	3.32 (2.47; 4.54)	0.1 (0.07; 0.14)	NR
			RDI ≥15	75 (70.02; 79.97)	95 (92.16; 97.62)	16.49 (9.45; 28.77)	0.26 (0.21; 0.32)	NR

AHI: Apnoea Hypopnoea Index MM: Mandibular Movement; MMAA: mandible movement automated analysis; NAF: Nasal Air Flow; PSG: Polysomnography; SpO2: pulse oximetry; Sr: Sunrise; LR+: Positive Likelihood Ratio, LR-: Negative Likelihood Ratio, AUC: Area under the curve.

[a] For technical details, see footnote on Brizzy

APPENDIX 3. LEGAL AND ETHICAL ASPECTS OF TELEMONITORING

Appendix 3.1. General principles

In 2010, a KCE report analysed the legal and ethical aspects surrounding telemonitoring for implanted defibrillators but the general principles are still applicable today.[102] Remote monitoring for patients with implanted defibrillator. Technology evaluation and broader regulatory framework. Health Technology Assessment (HTA) and Health Services Research (HSR). Brussels: Belgian Health Care Knowledge Centre (KCE). 2010. KCE Reports 136C. D/2010/10.273/55 (https://www.kce.fgov.be/en/remote-monitoring-for-patients-with-implanted-defibrillators-technology-evaluation-and-broader). This analysis, including the effect of new legislations such as GDPR, will be updated in a forthcoming KCE report on telemonitoring due to appear in 2021.

A wide range of legal issues such as the duty of professional secrecy and (data) security aspects, professional and product liability, patients' rights, etc… are conditioning the implementation and successful functioning of a remote monitoring system for any medical device.

There currently exists no regulatory framework specifically dealing with the issue of remote monitoring specifically. In principle, the EU only plays a subsidiary role in the field of health care. As such, the EU does not draw up harmonising regulations, but only fulfils an additional, regulatory role. It is the Member States that are involved in the management of health services and medical care, as well as in the allocation of the resources allocated to them.

Both the EU and the local Belgian legal framework applicable to remote monitoring in general were investigated.

Appendix 3.2. Relevant EU legislation

Although EU legislation does not address specifically eHealth systems and services, several Directives and Regulations have a direct impact on telemonitoring applications.

- processing of personal (health) data is mainly governed by the Regulation 2016/679 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation).[a]
- in the domain of liability, regulations are available in a fragmented way: objective liability of the producer of a defective product, liability of the data controller, liability of information system provider, etc… There is, however, no harmonised liability regime for professional liability for damage caused by healthcare services;
- dispositions with regard to transparency and identification of suppliers, service providers and other consumers' (patients) protection rules for e-services are provided in several Directives.
- Telemonitoring involves the use of medical devices often in combination with medical software. Moreover, the use of mobile communications and equipment for providing care or storing health results have become common practice (smartphones, tablets, apps). Medical software and mobile communication and equipment can under certain conditions also be considered as medical device. Medical devices need to comply the Regulation 2017/745 on medical devices, amending Directive 2001/83/EC, Regulation (EC) No 178/2002 and Regulation (EC) No 1223/2009 and repealing Council Directives 90/385/EEC and 93/42/EEC.[b]

a https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32016R0679

b https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32017R0745

Appendix 3.3. Duties, rights and responsibilities of the data controller, the data processor and the data subject

A number of duties, rights and responsibilities linked to the different roles (data controller, data processor, data subject) of intermediaries in the remote monitoring application are defined in EU data protection legislation and implemented in Belgian legislation (Law of 30 July 2018 regarding the protection of natural persons regarding the processing of personal data, hereinafter called as the Data Protection Law, DPL). The data controller holds most of the responsibilities. A contract between the parties involved, clarifying and defining their respective roles and responsibilities, is thus of an utmost importance. The data controller must inform the persons working under his/her authority on the relevant legal duties included in the DPL.. The data controller also holds a register with the categories of processing activities under his/her responsibility at disposition of the Belgian Data Protection Authority. Furthermore, a data protection officer, has to be appointed by the controller. The role of this person is amongst others to supervise the respect of the DPL when personal data are processed.

Persons accessing the personal health data need to be bound by a duty of professional secrecy or an equivalent contractual obligation. Both the data controller and the data processor have the obligation to take appropriate technical and organisational data protection measures against accidental or unlawful destruction, accidental loss, modification or unauthorised access or any other non-authorised processing.

As for all health data, health data collected within the telemonitoring application can be shared between the treating physician, his/her (para)medical team and the referring physician if the addressee is also bound by the duty of professional secrecy, if the sharing of the confidential information is necessary to ensure continuity and quality of care and if the patient has given his explicit or tacit consent, or if the disclosure is at least in his/her best interest. The necessity of the intervention of ICT staff and other experts in the treatment of personal data of the patient requires considering them as “collaborators” of the health care professionals bound by the same confidentiality rules.

Appendix 3.4. Patient rights and duties

The Belgian Patient’s Rights Law (issued on 22 August 2002) defines several patients’ rights that have a direct impact on the telemonitoring application.[103, 104]

This included:[102]

- informed consent;
- right to data access;
- right to freely choose a healthcare professional;
- patient collaboration.

Appendix 3.5. Liability issues

The following liability issues should be considered

- Is telemonitoring considered as the standard of care yet?
- contractual clauses and emergency systems;
- the role of Industry Employed Allied Professionals (such as directly employed or contracted manufacturer representatives, field clinical engineers, and industry employed technical specialists);
- centralisation of liability;
- product liability.

For new technology such as telemonitoring, the question always rises whether the technique was the most suitable treatment for the patient. Taking into account the standard of care, it is then examined whether a prudent and careful care provider of the same discipline would also have called upon telemedicine in similar circumstances. Few specific rules on medical liability have yet been issued at European level. The diversity of legislation on this subject in the Member States is an obstacle to the application of telemonitoring in the Member States. However, the Patients' Rights Directive (Directive 2011/24/EU of the European Parliament and of

the Council of 9 March 2011 on the application of patients' rights in cross-border healthcare[a]) requires the Member State of treatment to ensure that systems of professional liability insurance or a guarantee or similar arrangement appropriate to the nature and extent of the risk of the treatment are in place.

When physicians rely on telemonitoring, they cannot always be on standby for the patients they are monitoring. Consequently, a good stand-by arrangement will have to ensure that the information received via the medical device and/or the data centre can be timely processed. A waiting schedule between different physicians from other hospitals can be an option, especially in view of the increasing shortage of care providers and physicians in certain regions.

If personnel of the manufacturer/distributor of medical devices is involved in the telemonitoring, such as for technical support for the use of a device, it is important that this personnel is subject to an obligation of confidentiality. In addition, the personnel must be authorised to legally carry out the respective actions. Furthermore, liability for wrongful acting can also arise for personnel if harm was caused to the patient by this wrongful act. Harm to the patient can also be caused by a defective product (for instance the medical device), for which the producer of the product will be liable irrespectively of whether there is negligence or fault on their part.

[a] https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32011L0024

APPENDIX 4. COST-EFFECTIVENESS OF OSAS TREATMENTS

Table 43 – Studies covered by the reviews of the literature on the cost-effectiveness of OSAS treatments

Author and publication year of the review	Wickwire et al., 2019	McMillan et al., 2015	HAS report, 2014	Kim et al., 2017 (CADTH)
Literature search period	Up to 09/2018	Up to 04/2012	Up to 07/2013	Up to 2016
Number of studies reviewed	5	10	7	13
Català R, Villoro R, Merino M, et al. Cost-effectiveness of continuous positive airway pressure treatment in moderate-severe obstructive sleep apnea syndrome. Arch Bronconeumol. 2016;52(9):461-469.	x			
Poullié AI, Cognet M, Gauthier A, et al. Cost-effectiveness of treatments for mild-to-moderate obstructive sleep apnea in France. IJTAHC. 2016 Jan;32(1-2):37-45				x
Trakada G, Economou NT, Nena E, et al. A health-economic analysis of diagnosis and treatment of obstructive sleep apnea with continuous positive airway pressure in relation to cardiovascular disease. The Greek experience. Sleep Breath. 2015;19(2):467-72.				x
Tan KB, Toh ST, Guilleminault C, et al. A cost-effectiveness analysis of surgery for middle-aged men with severe obstructive sleep apnea intolerant of CPAP. J Clin Sleep Med 2015;11(5):525–535.				x
Pietzsch JB, Liu S, Garner AM, Kezirian EJ, Strollo PJ. Long-Term Cost-Effectiveness of Upper Airway Stimulation for the Treatment of Obstructive Sleep Apnea: A Model-Based Projection Based on the STAR Trial. Sleep. 2015;38(5):735–744.				x
McMillan A, Bratton DJ, Faria R, et al. A multicentre randomised controlled trial and economic evaluation of continuous positive airway pressure for the treatment of obstructive sleep apnoea syndrome in older people: PREDICT. Health Technol Assess 2015;19(40).	x			x
Sharples L, Glover M, Clutterbuck-James A, et al. Clinical effectiveness and cost-effectiveness results from the randomised controlled Trial of Oral Mandibular Advancement Devices for Obstructive sleep apnoea–hypopnoea (TOMADO) and long-term economic analysis of oral devices and continuous positive airway pressure. Health Technol Assess 2014;18(67).				x
Guest JF, Panca M, Sladkevicius E, et al. Clinical Outcomes and Cost-effectiveness of Continuous Positive Airway Pressure to Manage Obstructive Sleep Apnea in Patients With Type 2 Diabetes in the U.K. Diabetes Care 2014 May; 37(5): 1263-1271.				x
Pietzsch JB, Garner A, Cipriano LE, et al. An integrated health-economic analysis of diagnostic and therapeutic strategies in the treatment of moderate-to-severe obstructive sleep apnea. Sleep 2011;34(6):695-709.		x	x	
Gander P, Scott G, Mihaere K, Scott H. Societal costs of obstructive sleep apnoea syndrome. The New Zealand medical journal 2010;123(1321):13-23.		x	x	

Sadatsafavi M, Marra CA, Ayas NT, Stradling J, Fleetham J. Cost-effectiveness of oral appliances in the treatment of obstructive sleep apnoea-hypopnoea. Sleep Breath 2009;13(3):241-52.		x	x	x
Weatherly HLA, Griffin SC, Mc Daid C, et al. An economic analysis of continuous positive airway pressure for the treatment of obstructive sleep apnea-hypopnea syndrome. Int J Technol Assess Health Care 2009;25:26-34.				x
McDaid C, Griffin S, Weatherly H, et al. Continuous positive airway pressure devices for the treatment of obstructive sleep apnoea-hypopnoea syndrome: a systematic review and economic analysis. Health Technol Assess 2009;13(4): iii–iv, xi–xiv, 1–119, 143–274		x	x	
Tan MC, Ayas NT, Mulgrew A, et al. Cost-effectiveness of continuous positive airway pressure therapy in patients with obstructive sleep apnea-hypopnea in British Columbia. Can Respir J 2008;15(3):159-65.		x	x	x
Guest JF, Helter MT, Morga A, Stradling JR. Cost-effectiveness of using continuous positive airway pressure in the treatment of severe obstructive sleep apnoea/hypopnoea syndrome in the UK. Thorax 2008;63(10):860-5.	x	x	x	x
Ayas NT, Fitzgerald JM, Fleetham JA, et al. Cost-effectiveness of continuous positive airway pressure therapy for moderate to severe obstructive sleep apnea/hypopnea. Arch Intern Med 2006;166(9):977-84.		x	x	x
Pelletier-Fleury N, Meslier N, Gagnadoux F, et al. Economic arguments for the immediate management of moderate-to-severe obstructive sleep apnoea syndrome. Eur Respir J. 2004;23(1):53-60.	x			
Mar J, Rueda J, Durán-Cantolla J, Schechter C, Chilcott J. The cost-effectiveness of nCPAP treatment in patients with moderate-to-severe obstructive sleep apnoea. Eur Respir J 2003;21:515–22.		x		x
Chilcott J, Clayton E, Chada N, et al. Nasal Continuous Positive Airways Pressure in the Management of Sleep Apnoea. Leicester: Trent Institute for Health Services Research; 2000.		x		
Tousignant P, Cosio MG, Levy RD, Groome PA. Quality adjusted life years added by treatment of obstructive sleep apnea. Sleep 1994;17;52–60.	x	x		

HAS: French Haute Autorité de Santé, CADTH: Canadian Agency for Drugs and Technologies in Health.

APPENDIX 5. BELGIAN LANDSCAPE OF SERVICE PROVIDERS

Appendix 5.1. Background

In Belgium, the sleep centres are allowed to subcontract the titration and treatment to service providers.[57] Further, although the OSAS diagnosis is usually performed within the sleep centres (a condition to enter the OSAS convention), some service providers already offer this service at home.

This overview of the Belgian landscape of service providers is based on the answers from a questionnaire developed in house and addressed at home-care companies active in the field of OSAS in Belgium. Companies were identified through a list of contacts provided by BeMedTech (Medical Technologies Belgium) and through discussions with Belgian sleep centres. The questionnaire asked the companies to describe a.o. the nature of the services they provided for the diagnosis, titration and management of OSAS patients; the volume of their activities and the costs of the services provided. The websites of the service providers were consulted. The providers were not further contacted for the remaining questions. In the tables below, a question mark "?" indicates that the information was not found in the questionnaire, nor on the website.

The companies consulted are active in the following fields of activities (see Table 44):

- OSAS diagnosis:
  - Home sleep apnoea testing (HSAT) services for OSAS diagnosis (Sleepclinic / Sleep-mobile, Som-Ambul, Domo Sleep Well, Vivisol)
  - The production (Ectosense, Nomics, Resmed) or distribution (Vivisol) of HSAT portable monitors (PM)
- PAP / MAD titration and treatment:
  - PAP home-based titration (Vivisol)
  - PAP-related home services such as device installation, renting, and maintenance (Vivisol, Rmed, Linde, VitalAir)
  - The production (Resmed) or distribution (Vivisol, Oxysphair, Rmed, Linde) of PAP devices and accessories
  - The production of MAD devices (Sleepclinic / Sleep-mobile, Vivisol, Resmed, Rmed)
- Only one company, Vivisol, is active in all fields of activities mentioned above.

Table 44 – Core business of a selection of service providers active in the field of OSA in Belgium

	Sleepclinic Sleep-mobile	Som-Ambul	Domo Sleep Well	Vivisol	Oxysphair	Ectosense	Nomics	Resmed	Rmed	VitalAire	Linde
HSAT-based diagnosis with portable monitor (PM)											
- **Service provided with PSG**	x	x	x	x	?	-	-	-	-	-	-
- **Service provided with PG**	-	-	x	x	?	-	-	-	-	-	-
- **Type II PM sale (PSG)**	-	-	-	x‡	x‡	-	-	-	-	-	-
- **Type III-IV PM sale (PG)**	-	-	-	x‡	?	x†	x†	x†	-	-	-
Treatment with PAP/MAD											
- **PAP titration home service**	-	-	-	x	-	-	-	-	-	?	-
- **PAP-related home service***	-	-	-	x	?	-	-	-	x	x	x
- **PAP and accessories sale**	-	-	-	x‡	x‡	-	-	x†	x‡	-	x‡
- **MAD sale**	x	-	-	x†	-	-	-	x†	x	-	-

** CPAP installation, and/or leasing/rent, and/or maintenance… † Device producer. ‡ Device distributor/vendor. HSAT: Home Sleep Apnoea Testing, PM: portable monitor.*

Appendix 5.2. Home sleep apnoea testing

Sleepclinic / Sleep-mobile, Som-Ambul and Domo Sleep Well use the type II (PSG) portable monitor Dream from Medatec for home-based diagnosis. Domo Sleep Well also uses type III-IV portable monitors (Brizzy by Nomics and Dreamscan from Medatec). At Vivisol, both type II (PSG) and type III-IV (PG) monitors are used, and they report using “their own system”.

For the year 2019, Sleepclinic / Sleepmobile reports the greatest number of home-based PSGs performed (600 tests), against 282 for Som-Ambul and 10 for Vivisol. The cost for a home-based PSG varies form € 100 - € 120 (Sleepclinic / Sleep-mobile, Som-Ambul) to € 350 to the patient (Vivisol). Further, the INAMI – RIZIV may be charged with the cost of an ambulatory PSG (€ 237.67, code 477374). A home-based PG is reported to cost € 250 by Vivisol. The cost of a home-base PG was reported to be € 250 by one company (Vivisol).

Depending on the companies, the PSG monitor is installed to the patient home by a technician or a nurse, and is either collected the day after by a technician at the patient home or is returned by the patient. For a home-based PG, the patient is asked to install the equipment himself.

As a comparison, at the Centre de Santé de l’Amblève (CSA), the cost of a home-based diagnostic (with type IV Brizzy PG from Nomics) is € 40, to be paid by the patient. The device is installed at home by a nurse and there is no extra cost for the nurse time to set-up the devices at the patient home.

Table 45 – Type, volume and unit cost of HSAT-based diagnosis service provided by a selection of service providers active in Belgium

Service provided	Sleepclinic Sleepmobile	Som-Ambul	Domo sleep well	Vivisol	Oxysphair	Ectosense	Nomics	Resmed
HSAT-based diagnosis with type II PM (PSG)								
- **Number performed in 2019**	600	282	?	10***	?#	No	No	No
- **Portable monitor used**	Dream (Medatec)	Dream (Medatec)	Dream F (Medatec)	"our own system"	?	No	No	No
- **Cost to the patient**	€120	€100	?	€350	?	No	No	No
- **Cost to the INAMI–RIZIV***	?	€237.67	?	?	?	No	No	No
HSAT-based diagnosis with type III-IV PM (PG)								
- **Number performed in 2019**	No	No	Yes	10***	?#	No	No	No
- **Portable monitor used, type of device**	No	No	Brizzy, Nomics (Type IV) DreamScan, Medatec (Type III)	"our own system"	?	No	No	No
- **Cost to the patient****	No	No	?	€250	?	No	No	No
Producer / distributor of PM for HSAT-based diagnosis								
- **Name , type and unit cost of PM sold**	No	No	No	Multibrands	Embletta® MPR Sleep System (Type II)	Nightowl	Somnolter (Type III): € 5500† Brizzy (Type IV): €419 Brizzy plus	ApneaLink™ Air (Type III)
- **Data transmission**	No	No	No	Vivisoft	No	?	Brizzy Web Portal	AirView™

** The code number of an ambulatory PSG is 477374, a PSG is reimbursed once a year by the INAMI – RIZIV. ** The polygraphy is not reimbursed by the INAMI – RIZIV. † Excluding value added tax. *** PSG/PG home sleep testing services at Vivisol are asked both by private doctors and hospitals. # Oxysphair reports that they offer medico-technical services for OSAS patients, but no further information is provided. HSAT: Home Sleep Apnoea Testing, PG: polygraphy, PM: portable monitor, PSG: polysomnography.*

Appendix 5.3. Home-based services for PAP / MAD treatment

Vivisol and Som-Ambul both offer home-based titration services with APAP. The cost is € 160 per patient at Vivisol.

Vivsol is the sole company in Belgium offering a full service for PAP treatment and follow-up, including the renting of the device, its installation at the patient home, patient information, maintenance, telemonitoring, data transmission via a secured web portal (Vivisoft), preparation of the annual prescription renewal and disinfection and reset of the device after stop therapy. The partnership is in 98% of the cases between the individual sleep centres and Vivisol. It is usually based on a public tender and in almost all contracts the term is 1-4 years. This service costs € 1 per day.

Some companies propose specific services for PAP treatment and follow-up which mainly consists in home installation of a PAP device and mask fitting. This service is provided by Rmed and Linde and costs around € 70.

Several companies also offer their services for MAD preparation and sale. At Vivisol, a MAD device cost € 650 and is 3D-printed after intra-oral scanning. Sleepclinic/Sleepmobile sells MAD devices, at a cost of € 450 entirely borne by the patient. Resmed sells the custom-made Narval CC MAD device. Rmed sells ready-made MAD devices (€ 64.60 to € 139 depending on the device).

Most of those companies are also distributors (Vivisol, Oxysphair, Rmed, Linde) or producers (Resmed) of PAP devices and accessories. Details on the selling costs were obtained from the websites.

Table 46 – Type, volume and unit cost of PAP/MAD-related services provided by service providers (numbers for year 2019)

Services provided	Sleepclinic Sleepmobile	Vivisol	Oxysphair	Resmed	Rmed	VitalAire	Linde	Som-Ambul
Home-based PAP titration								
- **Number performed in 2019**	No	14	?	No	No	No	No	144
- **With CPAP or APAP?** - **With PSG / PG or APA only?**	No	CPAP + PG or APAP alone	?	No	No	No	No	APAP**
- **Cost for the patient**	No	APAP: €160	?	No	No	No	No	Not reported
Full service for PAP treatment*								
- **Number performed in 2019**	No	3471 home installations 14 000§ ongoing contracts	No	No	No	No	No	No
- **Service towards hospitals / private doctor / patient**	No	Hospitals (98%) Patients (2%)	No	No	No	No	No	No
- **Cost**	No	€1 per day	No	No	No	No	No	No
Specific service for PAP								
Installation of CPAP at home	Yes (8†)	Full service	?#	No	Yes	?§	Yes	No
- **Cost for the patient**	?	Full service	?		€70‡	?	€72.60	No

Renting CPAP	No	Full service	?	No	No	?	No	No
- Cost for the patient	No	Full service	?	No	No	?	No	No
Maintenance of CPAP and replacement of supplies (masks, humidifiers, etc.)	No	Full service	?	No	Yes (on demand)	?	No	No
Data recording and analysis	No	Full service	?	No	No	?	No	No
Data transmission to the prescribing/treating physician	No	Full service	?	No	No	Yes	No	No
Preparation of the annual prescription renewal	No	Full service	?	No	No	Yes	No	No
Other								
Provision of MAD	80	75	No	Yes	Yes	No	No	No
- Cost for the patient	€450	€650	No	Narval CC	Somnofit: €64.6 Somnofit-S: €139	No	No	No
Data exchange software	No	Vivisoft	No	AirView™	No	VitalAireWeb	No	No

** At Vivsol The full service consist in PAP renting, installation of the device at home, maintenance and replacement of supplies (masks, etc), data recording / analysis and transmission to the physician, preparation of the annual prescription renewal via web portal ViviSoft. ** Data transmitted via Airview. § Via web portal ViviSoft. † Installation of PAP at home only if the patient has difficulties to go to the provider, no further information provided. ‡ One-time package for home installation of a CPAP device and a CPAP mask. # Oxysphair reports that they offer medico-technical services for OSAS patients, but no further information is provided. MAD: Mandibular Advancement Device. § VitalAire reports that it is specialised in the follow-up of patients at home, but precise information on the services offered was not found on their website.*

Table 47 – PAP devices and accessories sold by private providers

Devices sold	Sleepclinic Sleepmobile	Vivisol	Oxysphair	Resmed	RMed	VitalAire	Linde	Som-Ambul
PAP devices	No	Costs on website	Costs on website	Yes	Costs on website	No	Costs on website	No
- APAP		Yes	Yes	AirSense™ 10 AutoSet™	Yes		Yes	
- CPAP		Yes	Yes	AirSense™ 10 Elite	Yes		Yes	
- Bilevel		Yes	Yes	AirCurve™ 10	Yes		Yes	
- Humidifier		Yes	Yes	Yes	Yes		Yes	
- Mask		Yes	Yes	Yes	Yes		Yes	
- Tube		Yes	Yes	Yes	Yes		Yes	
- Filter		Yes	Yes	Yes	Yes		Yes	

APPENDIX 6. TRAININGS IN SLEEP MEDICINE IN BELGIUM

In Belgium there is no specific specialty in 'sleep medicine' or 'somnology' and, in theory, every physician with the right speciality could call himself a sleep specialist. Some universities have indeed a short module on sleep medicine in their basic MD training package.

The professional organisation of physicians who practice sleep medicine in Belgium, BASS (Belgian Association of Sleep research and Sleep medicine[a]) demands this recognition as a specialty since many years but their efforts have so far not succeeded. The current convention between INAMI – RIZIV and the sleep centres only vaguely describes the additional training requirements for diagnosing physicians, specialist ENT physicians and MAD device specialists in the first annex of the convention. The criteria refer to a minimum number of hours per week spend on sleep medicine, a minimum number of patients treated for it, and having followed (by 1/1/2020) one out of a listed training courses (see Table 48), but very few requirements for practical experience. In addition the convention states that the physician should be a somnologist, once this title would have been created (which is not the case until now). Current courses are organized by the BASS, by hospitals, and by universities. Practical training is organized informally and without much quality control.

[a] https://belsleep.org/bass.aspx

Table 48 – Accepted trainings in the current Belgian convention

Course Title	Language	Duration	Organisation	Evaluation
Slaapcursus der Lage Landen deel 1 en deel 2	Dutch	30 hours over 2 years	Universiteit Antwerpen, Universitair Ziekenhuis Antwerpen, and the 'Nederlandse Vereniging Artsen Longziekten en Tuberculose' (NVALT)[a].	None
International Sleep Medicine Course (ISMC)	English	22 hours	Belgian Association for Sleep research and Sleep medicine (BASS)[b], NSWO[c] (Nederlandse vereniging Slaap Waak Onderzoek), BSS (British Sleep Society)[d]	None, but considered as preparation for European examination (ESRS)
Certificat interuniversitaire en Médecine du Sommeil	French	48 hours over two years	ULB+UCL+Ulg (interuniversitary training recognised by the three univerisities and by ARES" (Académie de la Recherche et de l'Enseignement de Fédération Wallonie-Bruxelles: http://www.ares-ac.be/fr/)	Written examination and compulsory practical training (200 hours over two years in recognised sleep-lab
European Sleep Research Society (ESRS): Examination in Sleep Medicine (certificate)	English		www.esrs.eu https://www.esrs-examination.eu/	Examination once yearly during annual ESRS conference. Both theoretical and practical examination. Candidates should have proven 5 year experience and be nominated.
Diplôme Inter-Universitaire (DIU) « Le Sommeil et sa pathologie », georganiseerd door « la Société Française de Recherche et Médecine du Sommeil » (SFRMS) en « la Société de Pneumologie de Langue Française (SPLF) ».	French		http://www.sfrms-sommeil.org/formation/diu/	unclear

An updated calendar on current courses and events for Belgium can be found on https://belsleep.org/education.aspx, hosted by BASS. However, as long as no separate specialty in sleep medicine exist in Belgium, the highest standard, nowadays, appears to be the ESRS examination.

[a] https://www.nvalt.nl/

[b] https://belsleep.org/bass.aspx

[c] https://www.nswo.nl/

[d] https://www.sleepsociety.org.uk/

APPENDIX 7. CODES USED IN THE DATA ANALYSIS

Table 49 – Pseudo-nomenclature codes for the OSAS convention

Pseudo code	Start date	End date	Description FR	Description NL	Usage
CPAP patients					
779936	01/01/2018	-	Forfait de départ nCPAP	nCPAP-startforfait	During the first 6 months of the OSAS convention
779951	01/01/2018	-	Forfait de base nCPAP	nCPAP-basisforfait	After the first 6 months of the OSAS convention
779096	01/01/1995	01/01/2018	Pression positive continue par voie nasale pendant la nuit	Continue positieve druk langs de neus 's nachts	From the first day of the OSAS convention on
779100	1/01/2008	01/01/2018			
MAD patients					
779870	01/01/2017	-	Forfait de départ OAM pour un nouveau patient OAM	MRA-startforfait voor een nieuwe MRA-patiënt	During the first 6 months of the OSAS convention
779881	01/01/2017	01/01/2018			
779892	01/01/2017	-	Forfait de départ OAM dans le cas du renouvellement de l'OAM	MRA-startforfait in geval van vernieuwing van het MRA	During the first 6 months of the OSAS convention
779903	01/01/2017	01/01/2018			
779914	01/01/2017	-	Forfait de base OAM	MRA-basisforfait	For 4.5 years after the first 6 months of the OSAS convention
779925	01/01/2017	01/01/2018			

CPAP: continuous positive airway pressure, MAD: mandibular advancement device.

Table 50 – Nomenclature codes for polysomnography (PSG)

Code	Start date	End date	Description FR	Description NL
477374-477385	01/04/1985	-	As from 01/11/2012: Polysomnographie de six heures au moins avec rapport et extraits des tracés. Enregistrement continu et simultané d'au moins 3 dérivations EEG, 2 dérivations EOG, 1 dérivation EMG et 3 paramètres respiratoires. As from 01/05/2016: Polysomnographie après l'âge d'un an.	As from 01/11/2012: Polysomnografie met een minimumduur van zes uur met verslag en uittreksels uit de tracés. Continu en gelijktijdig registreren van ten minste 3 EEG-derivaties, 2 EOG-derivaties, 1 EMG-derivatie en 3 ademhalingsparameters. As from 01/05/2016: Polysomnografie na de leeftijd van één jaar.
474552-474563	1/04/1985	1/05/2016	Examen polysomnographique d'une durée minimum de six heures avec protocole et extraits des tracés: Enregistrement	Polysomnografisch onderzoek met een minimumduur van zes uur met protocol en uittreksels uit de tracés: Continu en gelijktijdig registreren

			continu et simultané comprenant au moins l'E.E.G., l'E.O.G., l'E.C.G., l'oxymétrie continue et 2 paramètres respiratoires.	dat ten minste het E.E.G., het E.O.G., het E.C.G., de continue oxymetrie en twee ademhalingsparameters omvat.
474574-474585	1/04/1985	1/01/1995	Examen polysomnographique d'une durée minimum de six heures avec protocole et extraits des tracés : Enregistrement continu et simultané de minimum 8 dérivations dont au moins l'E.E.G., l'E.O.G., l'E.C.G., l'oxymétrie continue et deux paramètres respiratoires.	Polysomnografisch onderzoek met een minimumduur van zes uur met protocol en uittreksels uit de tracés: Continu en gelijktijdig registreren van minimum 8 derivaties, waaronder ten minste het E.E.G., het E.O.G., het E.C.G., de continue oxymetrie en twee ademhalingsparameters
477396-477400	1/04/1985	1/01/1995	Examen polysomnographique d'une durée minimum de six heures avec protocole et extraits des tracés : Enregistrement continu et simultané de minimum 8 dérivations dont au moins l'E.E.G., l'E.O.G., l'E.M.G., l'E.C.G., l'oxymétrie continue et deux paramètres respiratoires.	Polysomnografisch onderzoek met een minimumduur van zes uur met protocol en uittreksel uit de tracés: Continu en gelijktijdig registreren van minimum 8 derivaties, waaronder ten minste het E.E.G., het E.O.G., het E.M.G., het E.C.G., de continue oxymetrie en twee ademhalingsparameters

N.B.: these codes cannot be billed more than once a year for a given patient.

APPENDIX 8. FINANCING RULES

Table 51 – Costs of a consultation to a GP and to an OSAS diagnosing physician

Consultation to a/an …		Code-number	Total fee (in 2019)	INAMI – RIZIV reimbursement ‡	Patient co-payment *
General practitioner	Non accredited	101032	€ 21.79	€ 15.79	€ 6.00
	Accredited †	101076	€ 26.27	€ 20.27	€ 6.00
Internist	Non accredited	102034	€ 39.39	€ 26.39	€ 12.00
	Accredited †	102550	€ 46.50	€ 34.50	€ 12.00
Pulmonologist	Non accredited	102130	€ 34.38	€ 22.38	€ 12.00
	Accredited †	102631	€ 41.29	€ 29.29	€ 12.00
Neurologist	Non accredited	102174	€ 54.57	€ 42.57	€ 12.00
	Accredited †	102675	€ 59.96	€ 47.96	€ 12.00
Neuropsychiatrist	Non accredited	102211	€ 44.90	€ 32.90	€ 12.00
	Accredited †	102712	€ 49.46	€ 37.46	€ 12.00
Psychiatrist	Non accredited	102196	€ 44.90	€ 32.90	€ 12.00
	Accredited †	102690	€ 49.46	€ 37.46	€ 12.00

*† Physicians who undergo continuing education and reach a minimum threshold of activity per year can obtain an accreditation. This allows them to add a well-defined increment to the fee for a consultation. Accreditation of the diagnosing physician is a requirement In the OSAS convention, ‡ Amount that the compulsory healthcare insurance reimburses to the patient. * The difference between the official total fee and the amount that is reimbursed by the compulsory healthcare insurance. GP: general practitioner, OSAS: obstructive sleep apnoea syndrome.*