Auto-titrating Nasal Continuous Positive Airway Pressure Systems in the Management of Obstructive Sleep Apnea

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Auto-titrating Nasal Continuous Positive Airway Pressure Systems in the Management of Obstructive Sleep Apnea

David Hailey MSc PhD Grad RIC¹
Philip Jacobs BCom DPhil CMA¹
Irvin Mayers MD FRCPC²
Shaila Mensinkai MA MLIS³

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¹ Department of Public Health Sciences, University of Alberta, Edmonton, Alberta, Canada
² Department of Medicine, University of Alberta, Edmonton, Alberta, Canada
³ Canadian Coordinating Office for Health Technology Assessment, Ottawa, Ontario, Canada
Reviewers

*These individuals kindly provided comments on this report.*

**External Reviewers**

Robert Dales, MD, Diplomat American Board of Sleep Medicine, MSc
Professor of Medicine
Head of Respirology
University of Ottawa
Ottawa, Ontario

Malcolm King, PhD FCCP
Professor, Department of Medicine,
Pulmonary Division
University of Alberta
Edmonton, Alberta

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Gina Bravo, PhD
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**Authorship**

All authors participated in planning the project, made comments on sections of the report drafted by other authors and assisted in preparing responses to reviewers’ comments.

David Hailey was the project lead and lead author for the report.

Philip Jacobs, the lead author for material on economic issues, provided input to all aspects of the project and contributed to drafting and review of the report.
Irvin Mayers, the clinical content expert, provided advice and guidance on literature and analysis, assisted with abstract selection and data extraction and helped to revise the draft report.

Shaila Mensinkai designed and performed the literature search, provided updates on the literature during the project, wrote material in the report related to literature searching and verified bibliographic references.

**Conflicts of Interest**

No conflicts were disclosed by any of the authors.
**Technology Name**
Auto-titrating nasal continuous positive airway pressure (APAP)

**Disease/Condition**
Obstructive sleep apnea syndrome (OSA) is a sleep and breathing disorder defined as a combination of complete cessations of airflow (apneas) and partial cessations of airflow (hypopneas) lasting at least 10 seconds and occurring at least five times per hour of sleep. OSA may be associated with excessive daytime sleepiness, cognitive and personality problems and high blood pressure.

**Technology Description**
Moderate to severe OSA is usually treated using a nasal continuous positive airway pressure (CPAP) device. Continuous pressure applied to the upper airways through a nasal mask keeps the airways open while the patient is asleep. Auto-titrating CPAP (APAP) devices have been developed in which the positive pressure level applied to the patient through the mask continuously changes during sleep.

**The Issue**
APAP devices address some of the disadvantages of CPAP devices, such as the resource-intensive nature of manual adjustment of pressure settings (titration) and the problems of compliance with CPAP treatment. APAP might permit unattended titration in sleep laboratories or at home.

**Assessment Objectives**
The objective of this report is to systematically review the evidence from comparative studies for the efficacy, effectiveness and costs of APAP devices in their use for:
- the diagnosis of OSA;
- titration to determine pressure values for treatment with CPAP; and
- the treatment of OSA, using variable-pressure mode.

**Methods**
Two reviewers independently extracted data from 39 relevant studies obtained from a comprehensive literature search. The study population was patients diagnosed with severe OSA who may require treatment using CPAP. Patients suffering from cardiac, pulmonary and other medical conditions were excluded from most of the studies.

Outcomes for the diagnosis of OSA and for titration included accuracy, costs and identification of adverse conditions; all in comparison with sleep laboratory studies using polysomnography (PSG).

For the therapeutic use of APAP, outcomes considered were compliance with treatment, effects on sleep patterns, other relevant physiological measures, quality of life and costs; all in comparison with treatment using conventional fixed CPAP.

**Conclusions**
- Observational studies show there is a potential use for APAP for the diagnosis of OSA. Further validation is needed from studies with stronger methodology.
- The use of APAP in auto-titration (i.e. unattended adjustment of pressure) has not been established.
- For the treatment of OSA, studies show that APAP uses a lower treatment pressure than CPAP. However, clinical outcomes with APAP are no better than those with CPAP. It is uncertain whether there is better compliance with the use of APAP.
- Preliminary estimates show that APAP might provide cost savings over CPAP under certain conditions, but further cost studies are required.

This summary is based on a comprehensive health technology assessment report available from CCOHTA’s website (www.ccohta.ca): Hailey D, Jacobs P, Mayers I, Mensinkai S. *Auto-titrating nasal continuous positive airway pressure systems in the management of obstructive sleep apnea.*

**Canadian Coordinating Office For Health Technology Assessment (CCOHTA)**
600-865 Carling Avenue, Ottawa, ON, Canada K1S 5S8 Tel: 613-226-2553 Fax: 613-226-5392 www.ccohta.ca

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EXECUTIVE SUMMARY

The Issue

Obstructive sleep apnea (OSA) syndrome is associated with repetitive narrowing or collapse of the pharynx during sleep, with pertinent symptomatology. It is defined by a combination of apneas (complete cessation of airflow) and hypopneas (partial cessation of airflow) lasting at least 10 seconds and occurring a minimum of five times per hour. OSA may be associated with daytime sleepiness, cognitive and personality problems and hypertension.

The initial treatment of choice for moderate to severe OSA is nasal continuous positive airway pressure (CPAP), where continuous pressure is applied to the upper airways. This is done most commonly through a nasal mask connected to an airflow generator while the patient is asleep and breathing spontaneously. The pressure prevents closure of the airways. Compliance with CPAP treatment can be a problem. Diagnosis of OSA and manual adjustment (titration) of CPAP settings for a patient are commonly undertaken in a sleep laboratory using polysomnography (PSG).

Auto-titrating CPAP (APAP) devices have been developed in which the positive pressure level applied to the patient through the mask continuously changes during sleep. Such devices, which use various methods, have the potential to address the resource-intensive nature of manual titration and the problems of compliance with CPAP treatment.

Objective

Our objective in this report is to review the evidence from comparative studies for the efficacy, effectiveness and costs of APAP devices in their use for:

- the diagnosis of OSA;
- titration to determine pressure values for treatment with CPAP; and
- the treatment of OSA, using variable-pressure mode.

Clinical Review

Methods: We searched several electronic databases from 1994 onwards using MeSH headings, subject headings, text words, key words, device names, product names and appropriate operators to capture relevant studies. We searched the reference lists in relevant articles to identify additional studies.

For the diagnosis of OSA using APAP, the outcomes considered were accuracy of diagnosis and costs and identification of adverse conditions, all in comparison with sleep laboratory studies using PSG. For titration using APAP to determine final pressure settings for CPAP, the outcomes of interest were estimates of accuracy for final settings and identification of adverse conditions and costs. For the therapeutic use of APAP in variable-pressure mode, the outcomes of interest were compliance with treatment, effects on sleep patterns, other relevant physiological measures, quality of life and costs.
Results: We found three observational studies on the use of APAP in the diagnosis of OSA. These suggest that APAP has some potential in this application but further validation is needed from studies with stronger methodology.

For comparisons of APAP titration with CPAP manual titration, we located six studies, three with randomized designs. In all but one, titration was attended (i.e. a technician was present). Overall, treatment pressures estimated by APAP and CPAP were comparable.

All but three of the studies that were located on the therapeutic use of APAP for OSA used randomized designs. In 14 studies that considered short-term treatment outcomes (one or two nights), outcomes were similar for APAP and CPAP. Some of these also considered titration. In 12 studies where treatment pressures were compared, pressures for APAP were lower than for CPAP in nine studies and there was no significant difference in two. The results from 12 studies of longer term APAP treatment indicate that lower treatment pressures are achieved with APAP. None of the studies found any significant difference in clinical outcome measures between APAP and CPAP treatment. In three of four studies where information on patient preferences was obtained, patients preferred APAP over CPAP.

We found one study that included comparative cost information. The costs of titration with APAP at home were lower than those for titration in a laboratory with the same device in constant-pressure mode, and using PSG. Estimates based on data from Alberta suggest that APAP might provide cost savings in certain scenarios. Further evidence is needed to establish such findings in different settings.

Several different types of APAP device, which differ in their method of operation, are commercially available. Results from the use of one type of machine are not necessarily generalizable to APAP with other equipment.

Conclusion

There is insufficient evidence from comparative studies to support the use of APAP in the diagnosis of OSA. There is evidence, mainly from small studies, of its efficacy in attended titration in sleep laboratories. Its use in unattended titration is not established. There is evidence that APAP is as effective as CPAP in the treatment of OSA.

Caution is still required in the use of APAP as further studies must establish its effectiveness and cost-effectiveness. Users of APAP should be aware of the performance of the device being used and the evidence of its efficacy. In most studies, patients suffering from cardiac, pulmonary and other medical conditions were excluded. There are potential safety issues for such individuals if APAP is used in settings without prompt access to technical support. Instituting APAP titration as a cost-savings measure remains unproven and without careful patient selection, may be hazardous.

On the basis of the literature available for this assessment, we conclude that APAP shows promise, but its place in health care is yet to be established.
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# ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
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<tbody>
<tr>
<td>AASM</td>
<td>American Academy of Sleep Medicine</td>
</tr>
<tr>
<td>AHI</td>
<td>apnea-hypopnea index</td>
</tr>
<tr>
<td>APAP</td>
<td>auto-titrating CPAP</td>
</tr>
<tr>
<td>BMI</td>
<td>body mass index</td>
</tr>
<tr>
<td>CHF</td>
<td>congestive heart failure</td>
</tr>
<tr>
<td>CPAP</td>
<td>continuous positive airway pressure</td>
</tr>
<tr>
<td>ESS</td>
<td>Epworth Sleepiness Scale</td>
</tr>
<tr>
<td>FEV</td>
<td>forced expiratory volume</td>
</tr>
<tr>
<td>FVC</td>
<td>forced vital capacity</td>
</tr>
<tr>
<td>MWT</td>
<td>maintenance of wakefulness test</td>
</tr>
<tr>
<td>NC</td>
<td>non-completers</td>
</tr>
<tr>
<td>NSD</td>
<td>no significant difference</td>
</tr>
<tr>
<td>NSS</td>
<td>not statistically significant</td>
</tr>
<tr>
<td>OSA</td>
<td>obstructive sleep apnea</td>
</tr>
<tr>
<td>( P_{\text{eff}} )</td>
<td>effective treatment pressure</td>
</tr>
<tr>
<td>( P_{95} )</td>
<td>95th percentile pressure</td>
</tr>
<tr>
<td>PSG</td>
<td>polysomnography</td>
</tr>
<tr>
<td>RCT</td>
<td>randomized controlled trial</td>
</tr>
<tr>
<td>RCT-C</td>
<td>randomized cross-over study</td>
</tr>
<tr>
<td>RDI</td>
<td>respiration disturbance index</td>
</tr>
<tr>
<td>REM</td>
<td>rapid eye movement</td>
</tr>
<tr>
<td>SF-36</td>
<td>short form 36</td>
</tr>
<tr>
<td>SS</td>
<td>statistically significant(ly)</td>
</tr>
<tr>
<td>y</td>
<td>year</td>
</tr>
</tbody>
</table>
GLOSSARY

Central apnea: Apnea where inspiratory muscle activity fails following an exhalation.

Cheyne-Stokes respiration: A form of periodic breathing in which an episode of apnea or hypopnea is followed by respirations of increasing depth and frequency. The cycle then repeats itself.

Efficacy: The performance of a technology under ideal conditions or conditions of best practice.

Effectiveness: The performance of a technology under “routine” conditions, for example, when it has become widely distributed in a health care system.

Mixed apnea: Apnea in which both central and obstructive apnea occur during the same episode.

Obstructive apnea: Apnea where inspiratory muscle activity is present without airflow.

Titration: Adjustment of CPAP settings during sleep to provide optimum values for a patient.
1 INTRODUCTION

1.1 Background

This assessment was undertaken to help decision makers who are involved in the management of persons with obstructive sleep apnea (OSA). In recent years, the numbers of persons in Canada diagnosed with OSA have increased, as have the numbers of sleep laboratories, particularly in Ontario. Our assessment considers auto-titrating nasal continuous positive airway pressure (APAP) systems, a technology that may modify the management of OSA and the use of sleep-laboratory services.

OSA is a syndrome that is associated with repetitive narrowing or collapse of the pharynx during sleep, and with pertinent symptomatology. It is defined by a combination of apneas (complete cessation of airflow) and hypopneas (partial cessation of airflow) lasting at least 10 seconds and occurring a minimum of 5 times per hour. The syndrome includes the laboratory feature of an apnea plus hypopnea index (AHI) greater than 5 events per hour in addition to the clinical symptom of excessive sleepiness. Sequelae include excessive daytime sleepiness, cognitive and personality problems, and hypertension. It has been estimated that 2 to 4 per cent of the adult population in the US suffers from OSA. Rates in Canada are likely similar.

A commonly used treatment for moderate to severe OSA is nasal continuous positive airway pressure (CPAP), which involves the application of continuous pressure to the upper airways while the patient is asleep and breathing spontaneously. This prevents closure of the airways and the resulting apnea. The most commonly used interface is a nasal mask connected to an airflow generator. Other interfaces include nasal pillows and full face masks. The American Academy of Sleep Medicine (AASM) notes that this treatment has been shown to reduce subjective and objective measures of daytime sleepiness in randomized placebo controlled trials. Other treatments for OSA include upper airway surgical procedures that range from uvulopalatopharyngoplasty (UPPP) and laser-assisted uvulopharyngoplasty (LAUP) to less common procedures such as hyoid resuspension and mandibular advancement. Non-surgical approaches include the use of dental appliances to widen the upper airway during sleep and weight-loss counselling.

Diagnosis of OSA and adjustment (titration) of CPAP settings to provide optimum values for a patient, involve observation with level 1 polysomnography (PSG). This approach uses continuous recording of several variables during sleep. These measurements are primarily aimed at determining sleep stages and monitoring respiratory function. With this diagnostic modality, the patient is required to stay overnight in a sleep laboratory under the observation of a qualified PSG technologist.

The goal of titration is to identify an effective pressure that will prevent apnea, hypopnea (episodes of breathing shallower and/or slower than normal), snoring and arousals due to respiratory effort in all body positions and sleep stages. Titration with PSG to obtain an appropriate treatment pressure is “attended,” i.e. a technician is present to adjust the pressure and to intervene if there are mask leaks or persistent hypoxemia after airway patency is restored.
Because of the costs and the potential sleep disruption due to laboratory testing, simplified, automated systems were developed. These could be potentially exported to the home and might eliminate the need for observation by a PSG technologist.

Auto-titrating CPAP (APAP) devices have been developed in which the positive pressure level applied to the patient through the mask changes during sleep, taking account of the disappearance and reappearance of apnea and hypopnea and other physiological events. Such devices can address some of the disadvantages of attended titration and of treatment with conventional CPAP including:

- the resource-intensive nature of manual titration (typically, a technician can monitor only two patients at a time)
- the inability with certain patients to obtain treatment pressure if a “split night” approach is used (diagnosis and then titration occurring in one night)
- the possibility of the fixed pressure value being higher than needed for the entire night, with a possible increase in mask leaks and pressure intolerance (the minimum necessary treatment pressure may change according to sleep stage and other conditions)
- the problems of compliance with CPAP treatment.

Our assessment considers the evidence related to the efficacy, effectiveness and costs of APAP for the management of OSA at home and in the laboratory.

### 1.2 Technology Overview

The availability of APAP devices could change the management of moderate to severe OSA. Use of this technology could alter the way in which sleep laboratories are operated and might lead to certain investigations being conducted outside a laboratory. APAP also offers a possible alternative treatment to conventional CPAP. APAP devices are more expensive than conventional CPAP systems, but overall costs could be lower if the use of APAP improves treatment compliance and health outcomes and if it could divert certain patients from sleep laboratories.

Issues of interest include the effectiveness and costs of APAP, and its appropriate place in relation to sleep laboratories and the use of conventional CPAP. There is particular interest in the provision of diagnostic services to persons with sleep disorders in their homes, without necessarily being referred to sleep laboratories or other specialized services.

Several APAP devices are available. They differ in regard to the variables that they monitor to determine changes in pressure of air delivered to the patient and in regard to the methods used to respond to physiological changes. Variables monitored, often in combination, may include airflow (apnea or hypopnea), snoring (airway vibration), flow versus time profile (evidence of flattening as a surrogate for airflow limitation) and impedance, using the forced oscillation technique.\(^3,4\)
The algorithms used in APAP to determine if and to what extent the pressure should be changed vary from product to product. As various APAP devices use different monitoring methods and algorithms that affect their performance, the results obtained using one machine may not be generalizable to all APAP devices.3

Most APAP devices start with a low baseline pressure and then increase this (titrate) as needed. If no physiological events are detected, the device will gradually decrease pressure, to allow the minimum effective pressure to be delivered. As a result, the mean pressure is often lower than the optimal fixed CPAP device pressure.

APAP devices allow information about changes in pressure over time to be transferred to a computer for analysis. Such data could be reviewed by a clinician and an appropriate fixed pressure determined. Common alternatives are to identify either the maximum pressure or the 95th percentile pressure (P_{95}), which is exceeded 5% of the time. Most devices can compute pressure statistics over several days. This is helpful if more than one night is needed to select an appropriate fixed pressure.

Mask or mouth leaks tend to raise the baseline flow delivered by APAP devices and diminish variations in flow during inspiration and expiration. The resulting airflow change may be interpreted as an episode of apnea or hypopnea and prompt an increase in pressure that may increase the leak.3 Many APAP devices have algorithms that limit pressure increases when leaks exceed given values or when increases in blower speed no longer result in increases in mask pressure. Other units have leak alarms to prompt the patient or technician to adjust the mask.

Berry et al.3 note that central apnea during the use of APAP is a difficult problem in certain patients. Central apneas of the Cheyne-Stokes type are common in patients with severe congestive heart failure (CHF) and may also occur in patients with neurological diseases. Central apneas may appear in patients with OSA and CHF during a CPAP titration or after arousals. A few devices incorporate approaches to identify central apnea or limit the pressure increases for apnea in the absence of associated snoring or airflow limitation, but the problem persists in certain patients.

Current APAP devices do not measure the variables needed to determine sleep stages. Without this information, it is impossible to determine the true AHI, which is expressed as events per hour of sleep. Thus, AHI values must be estimated.

### 1.3 Indications for the Technology

Because APAP systems function by recognizing obstructive respiratory events or surrogate measures, they have an inherent diagnostic capability.2 For person with OSA, APAP systems can also be used for CPAP titration and for long-term variable pressure treatment.

For APAP in its diagnostic role, issues to consider include how close is the correlation with results obtained using PSG, whether the performance of the APAP device changes with the severity of OSA and whether diagnostic use at home is appropriate.
APAP devices can be used to determine an optimal fixed titration pressure level for treatment with a conventional CPAP device. The titration could be done as an attended study (in which a technologist can intervene) or as an unattended study either in the sleep laboratory or at home.

Unattended CPAP titration in the sleep laboratory or at home is regarded as potentially the most useful application of APAP devices,\(^3\) as patients without reasonable access to a sleep laboratory could still be titrated and started on treatment. For effective unattended titration, the patient should be well educated about using the device, and be able to apply the mask properly and adjust it if leaks occur. Proper mask fitting is essential.

Other issues to consider in the use of APAP titration, particularly at home, are safety of the patient who did not undergo diagnostic PSG to exclude non-OSA breathing disorders, possible hazards through unrecognized arrhythmia during titration and accuracy of the final CPAP device pressure setting.

The ability of APAP to allow treatment with the lowest effective pressure has been suggested as a factor that could increase acceptance or adherence to treatment, reducing pressure intolerance and leaks. Berry et al.\(^3\) note, however, that many patients do not consider pressure intolerance to be a major discomfort with CPAP treatment. Other factors, such as mask discomfort, cumbersome apparatus and airway dryness may contribute to dissatisfaction.

In the following analysis, the use of APAP in the management of OSA at home is of interest, but studies on its use for titration in the laboratory are also considered.
2 OBJECTIVES

Our objective in this report is to review the evidence from comparative studies for the efficacy, effectiveness and costs of APAP devices in their use for:

1. diagnosis of OSA
2. titration to determine CPAP device pressure values
3. treatment of OSA, using variable pressure mode.

For the diagnostic and titration applications, our primary interest is the comparison between the use of APAP and the use of PSG in a sleep laboratory. The use of APAP at home and in the laboratory is considered. In the therapeutic application, we focus on the comparison between the treatment of OSA using APAP in variable pressure mode and treatment using conventional fixed pressure CPAP.
3 METHODS

We searched MEDLINE®, EMBASE®, BIOSIS Previews®, PASCAL, INSPEC® and F-D-C Reports from 1994 using the OneSearch® feature on the DIALOG® on-line search system. The search was conducted using MeSH headings, subject headings, text words, keywords, device names, product names and appropriate operators to capture relevant studies. Due to the small set of results, a clinical filter was not used. The search addressed human studies, with no language restrictions. The Cochrane Library and CINAHLdirect® on-line service were searched separately. The search strategy is shown in Appendix A. Clinical trials registries, web sites of health organizations and relevant professional bodies were consulted to identify studies and ongoing reviews. Reference lists of relevant articles were searched to identify additional studies.

In addition, regular DIALOG® alerts were established using the same search strategy until April 2003 on MEDLINE®, EMBASE®, BIOSIS Previews®, PASCAL, INSPEC® and F-D-C Reports. Updates were performed on PubMed and the Cochrane Library, issue 1, 2003, in February 2003.

3.1 Selection Criteria

Inclusion criteria specified comparative studies with APAP for persons with OSA who may require treatment using CPAP.

3.1.1 Use of APAP for diagnosis of OSA

Outcomes considered were accuracy of diagnosis, costs and identification of adverse conditions, all in comparison with sleep laboratory studies using PSG.

3.1.2 Use of APAP for titration

The outcomes of interest using APAP to determine final CPAP settings for titration, were estimates of accuracy of final pressure settings, identification of adverse conditions and costs, in comparison with sleep laboratory studies. Measures of physiological parameters were also considered.

3.1.3 Use of APAP for treatment of OSA

For the therapeutic use of APAP in variable pressure mode, outcomes of interest were compliance with treatment, effects on sleep patterns, other relevant physiological measures, quality of life and costs, all in comparison with treatment using conventional fixed CPAP.
3.2 Data Extraction Strategy

Two reviewers (DH and PJ) conducted independent screening of all citation titles and abstracts retrieved, using the selection criteria listed in section 3.1. The reviewers read citation abstracts (or titles only, if the abstract was unavailable) to make inclusion decisions for subsequent full-text review. Differences were resolved by consensus. Selected articles were reviewed independently by the same two reviewers and accepted for assessment if they met the selection criteria. Duplicate publications of the same trial were excluded, and the most recent or most informative article selected. All selection decisions for abstracts and retrieved papers were discussed with the clinical author (IM). Data from selected studies were extracted independently by the two reviewers and the clinical author.

A series of non-quantitative reviews was undertaken in view of the heterogeneity of the studies and the small numbers of studies that applied to each type of APAP device.

3.3 Estimates of Cost

To illustrate the potential cost implications, estimates were made for the use of APAP and CPAP in different settings, based on data from sources in Edmonton, Alberta.

4 RESULTS

4.1 Quantity and Quality of Research Available

From the literature search and the review of citations, 238 potentially relevant abstracts were identified and 45 reports were selected for further review. Updating the literature search identified a further 74 citations, from which 61 reports were selected for review. From the 61 reports, 39 that described studies on APAP were selected for analysis. The document flow is shown in Figure 1.

Three of the selected studies, all prospective non-randomized comparisons, described the use of APAP in diagnosis. Six studies addressed APAP for titration: one was a randomized controlled trial (RCT), two used a randomized crossover design (RCT-C) and three were non-randomized prospective comparisons. A paper that included follow-up data to one of the RCT-C studies was also selected.

Fourteen studies (one RCT, 10 RCT-C and three non-randomized comparisons) considered short-term treatment outcomes (single-night comparisons). Ten studies (five RCTs and five RCT-Cs) addressed longer term treatment with APAP. One RCT of longer term treatment included a comparison of costs for the APAP and CPAP methods used. No other studies reported on the comparative costs of APAP and alternative approaches. Three studies that compared the performance of different APAP devices and two that considered non-comparative approaches to the appraisal of titration were included in the analysis to provide background.
312 citations identified from electronic search

251 citations excluded:
Non-comparative studies (215)
Narrative reviews (36)

61 potentially relevant reports retrieved for scrutiny (full text)

22 reports excluded:
Contained insufficient information (9)
No comparison with PSG and conventional CPAP (10)
Trial design inappropriate for review (2)
Inappropriate APAP technology (1)

39 relevant reports describing 38 unique studies:
Diagnosis (3)
Titration (8)
Short-term treatment (14)
Longer term treatment (10)
Device performance (3)
4.2 Patient Group

Most of the patients studied had been diagnosed with severe OSA. Criteria for inclusion commonly included minimum values for body mass index (BMI) in kg/m$^2$ and for the apnea-hypopnea index (AHI). The AHI is measured in number of episodes of apnea and hypopnea per hour. A few studies also included patients with other types of sleep-related breathing disorders. In many studies, patients with CHF or chronic lung disease were excluded. None of the studies included patients with a substantial amount of central apnea at baseline.\(^3\)

4.3 Comparators

4.3.1 Use of APAP for diagnosis

For studies of APAP in the diagnosis of OSA, the comparator was diagnosis with PSG and the outcome measure was the AHI.

4.3.2 Use of APAP for titration

In titration studies, the comparator was manual titration using conventional CPAP. The primary comparator was the value for the mask pressure selected for subsequent use of CPAP by the patient. Titration pressures in the literature and reported here are given in centimetres of water (cm H$_2$O) unless otherwise indicated. Most of the titration studies also compared AHI values. A number considered other types of measures, providing an indication of treatment outcomes.

4.3.3 Use of APAP for treatment

The comparator for treatment studies was the use of conventional CPAP. AHI was the most commonly used measure, with an AHI of less than 10 typically taken as an indication of satisfactory outcome. Other measures of performance included the Epworth Sleepiness Scale (ESS), the maintenance of wakefulness test (MWT), arousal index and values describing sleep architecture, including the proportion of rapid eye movement (REM) sleep. Several longer term studies considered compliance with treatment, in terms of hours of use per night and days of use during the study. In a few studies, information was obtained on patient satisfaction and preferences by using survey methods and one measured quality of well-being.

4.4 Assessment of Clinical Effectiveness

4.4.1 Use of APAP in diagnosis

We found three comparative studies that addressed the use of APAP in the diagnosis of OSA. All used versions of the AutoSet\textsuperscript{®} device (Appendix B, Table 2). Huang et al.\textsuperscript{5} found a sensitivity of 70% and a specificity of 100%, based on data from 11 patients, as part of a study that also considered therapeutic applications. In a larger series, Gugger\textsuperscript{6} reported a sensitivity of 97% and a specificity of 77% in the diagnosis of patients who had an AHI of more than 20 events per hour. A previous study by Gugger et al.,\textsuperscript{7} using an earlier version of the AutoSet\textsuperscript{®}
that only detected episodes of apnea, gave a sensitivity of 82% and a specificity of 90%, for diagnoses based on episodes of apnea (more than 20 per hour). None of these studies specifically considered interventions based on diagnostic findings. Limitations included small sample sizes and absence of information on patients who did not have OSA.

### 4.4.2 Use of APAP in titration

As noted in the review by Berry et al.,\(^3\) two approaches have been taken in studies on the use of APAP in titration. In the first, fixed CPAP treatment pressures selected by APAP are compared with those determined by conventional manual CPAP titration. This is consistent with the objectives of our assessment. Factors influencing such comparisons include the type of APAP device, the method used to select the effective treatment pressure (\(P_{eff}\)) from the APAP titration, and the manual titration algorithm.

The second, non-comparative, approach is to determine a treatment pressure with APAP, use this in fixed CPAP treatment, and then determine whether treatment is acceptable (\(AHI<10/h\)) and/or whether clinical outcomes are acceptable.

An important issue is whether the APAP titration procedure can be used in unattended mode without intervention from a technician. Avoidance of attended operations would reduce costs and increase the flexibility of the method.

#### a) Comparative studies

We located six studies that compared APAP titration with manual titration, focusing on treatment pressures\(^8\text{--}^{13}\) obtained on successive nights. Details appear in Appendix 2, Table 3.

In this group of investigations, no significant difference (NSD) between pressures derived from APAP and from manual titration was found in an RCT and an RCT-C. In three non-randomized comparisons, established pressures using APAP were SS (statistically significantly) lower than those from manual titration. In the remaining study, an RCT-C, mean pressure (\(P_{95}\)) for APAP was SS higher than that for manual titration. In the follow-up to this work,\(^{14}\) new criteria were used for manual titration and differences between APAP and manual titration were small. There was NSD in pressures when titration was repeated after three months of CPAP treatment. In a further follow-up titration at eight months, mean pressure with APAP was lower than that for manual titration, the difference just reaching statistical significance.

The follow-up of patients undertaken in the RCT\(^{11}\) provided information on their acceptance of treatment methods. At six weeks after titration, there was NSD between numbers in the two groups who were successfully established and wished to continue with CPAP treatment, though there was a trend in favour of APAP. There was NSD in ESS scores between the two groups, with means being lower for those who had received manual titration. According to the review by Berry et al.,\(^3\) the RCT used unattended APAP titration. The other studies were attended.

#### b) Non-comparative studies

Three studies that were selected for review included non-comparative approaches to evaluating APAP titration, with outcomes being assessed after establishment of a pressure value. In a small series reported by Berkani et al.,\(^{15}\) 10 patients had APAP treatment for two weeks after
unattended APAP titration in a hospital. At two weeks, 8 out of 10 had AHI<10 (7 ± 5) and arousal awakening index <10. Increasing APAP pressure by 2 cm in the two patients with poor results brought AHI to <10.

In a study reported by Sériès, a pressure estimated from a formula based on BMI, neck circumference and AHI was used in a home APAP titration to determine a value for $P_{\text{eff}}$, which was then used for six weeks treatment with CPAP. The ESS was reduced significantly from baseline. An earlier study by Sériès and Marc, details of which appear in Table 5 of Appendix 2, used a similar approach, based on an estimated reference pressure for APAP. Improvements in ESS after APAP treatment based on the estimated reference pressure were similar to those for treatment using CPAP or APAP with $P_{\text{eff}}$ values defined by manual titration.

Two comparative studies by Randerath et al. measured AHI values for two APAP modes, but did not compare these with values for manual titration. In both studies, AHI was at acceptable levels after both modes of APAP operation (Table 3).

### 4.4.3 Use of APAP in treatment

#### a) Short-term treatment studies

Short-term measures of outcome were included in 14 studies, with one night of APAP compared to one night of CPAP (Table 4, Appendix 2). A few also considered titration and in 12 studies, there was comparison of treatment pressures. Those for APAP were SS lower than those for CPAP in nine and there was NSD in two. The remaining study reported maximum rather than mean pressure for APAP, which was higher than that obtained with manual titration.

Indications of treatment outcomes were similar for the two approaches. All studies measured AHI. In 12, there was NSD in AHI values, with scores for APAP being lower in four of these. In the other two studies, values for APAP were SS higher than those for CPAP.

There was NSD in sleep architecture measures for eight of nine studies. In one study, there was SS higher stage 3 and 4 sleep for the group who received APAP. There was NSD in arousal index scores in 11 studies or for sleep time in three.

#### b) Longer term treatment studies

Ten longer term studies of APAP treatment (five RCTs and five RCT-Cs) were identified, in addition to the RCT of Stradling et al., referred to in section 4.4.2, with measurements over periods from 7 to 180 days. One RCT addressed the use of APAP in a subset of patients who had sleep stage and body position dependence related to respiratory performance. In this group (n=12), ESS was SS lower with APAP than with CPAP.

In the remaining nine studies, the clinical results tended to match the indications obtained from short-term investigations. Treatment pressures were lower for APAP than for CPAP (SS lower in 7/8 studies), but there was NSD for clinical measures including AHI scores (7/7), daytime sleepiness (6/6), arousals (3/3), % REM sleep (3/3) or oxygen saturation (1/1).
Eight reviewed publications gave information on the overall use of APAP as compared to CPAP. In four studies, there was NSD in the use made of the treatment methods. In three studies, APAP was used for more hours per night than CPAP (SS), though in two of the studies, there was NSD in the number of nights used. In one study, there was NSD in use per night, but APAP was used more nights per week for periods longer than four hours.

One study measured patient well-being, using the short form 36 (SF-36). Scores reported for the vitality and mental health measures were higher during the use of APAP than they were with CPAP. The clinical significance of the differences is unclear.

Four papers reported the results of surveys of patient preferences and opinion. Planès et al. reported satisfaction with both APAP and CPAP for a large majority of the patients involved. Massie et al. found that during APAP, patients reported more restful sleep, better quality sleep, less discomfort from pressure and less trouble getting to sleep. Randerath et al. reported that 75% of responders (there were five drop-outs) preferred APAP. In the study by d’Ortho et al., 15 (60%) responders preferred APAP, 8 preferred CPAP and 2 chose surgery. In the same study, there was NSD in the subjective assessment of symptoms experienced using the two treatment methods. In the follow up to titration reported by Stradling et al., there was NSD between those who had been manually titrated and the APAP titration group with regard to numbers successfully established on CPAP after six weeks. Thirteen from the manual titration group and one from the APAP group wished to discontinue with treatment at six weeks.

In the study by Planès et al., the time from diagnosis of OSA to initiation of treatment was longer in the CPAP group than in the APAP group (47.2 days versus 11.8 days). This difference was attributed to the waiting time for the PSG study needed to initiate CPAP treatment.

### 4.5 Comparisons of APAP Devices

Three recent papers consider the comparative performance of different types of APAP devices and raise issues regarding their clinical use. Two of these report the results of bench studies. Farré et al. tested five APAP devices using a generator to reproduce patterns of ventilation and snoring observed in patients with OSA. They found that the responses of the various devices to apneas, hypopneas, flow limitation and snoring differed considerably and suggest that the effectiveness of APAP assessed in clinical tests does not have validity that can be generalized. A few differences could be irrelevant, but others could affect clinical outcomes.

A study by Lofaso et al. used an artificial lung model to evaluate the snoring detection sensitivity of six APAP devices. The threshold value at which APAP detected snoring differed between the devices by up to three-fold. The least sensitive device and one of the most sensitive were compared in a small RCT using 12 patients with OSA who needed CPAP. Patients received APAP treatment during PSG. Snoring detection sensitivity was SS lower with the less sensitive device (50% versus 92%, p=0.03). These authors suggest that further studies are needed to evaluate and compare APAP devices.
Kessler et al.\textsuperscript{43} compared automated titration using the AutoSet\textsuperscript{®} and Somnosmart\textsuperscript{®} devices in an RCT-C design over two nights for 16 patients with OSA. The titrations were unattended. The $P_{95}$ value was significantly lower with the AutoSet\textsuperscript{®} than with the Somnosmart\textsuperscript{®} (7.0 cm versus 9.9 cm, $p=0.005$). Limits of agreement in a Bland and Altman analysis were $+9.3$ and $-3.2$ cm. They conclude that unattended in-hospital automated titration cannot reliably replace manual titration and is unable to determine an accurate pressure level for fixed CPAP therapy.

### 4.6 Assessment of Costs

#### 4.6.1 General considerations

Prices for APAP equipment are higher than those for CPAP devices. Recent prices quoted by suppliers for purchase via the Internet are about US$400 to US$600 for CPAP devices and US$900 to US$1,200 for APAP. Factors that could offset the higher cost of APAP devices are the reduced use of sleep laboratories including reduced use of technician time and a decrease in numbers of those waiting to be diagnosed and titrated in these laboratories. Comparison with split-night studies in a sleep laboratory might be less favourable for APAP. The potential for APAP use in the home is unestablished, however, so the economic picture is incomplete.

#### 4.6.2 Information from the literature

The only study located that included comparative cost information was the RCT conducted by Planès et al.\textsuperscript{32} In this study, APAP treatment was started at home for one group of patients. Data on pressure levels and hours of APAP use were transmitted daily to a sleep laboratory and the pressure range for treatment set after a week. In the other group of patients, manual titration was performed in a sleep laboratory using overnight PSG and the APAP device in constant pressure mode. For treatment, the APAP device was used in variable pressure mode for the group titrated at home, and in constant pressure mode for the group titrated in the laboratory. Follow up lasted two months.

Costs of therapy per patient in the APAP group was €1,264±352 (C$1=0.76 euros) compared with €1,720±455 for the CPAP group (laboratory titration with APAP device in constant pressure mode). Planès et al. conclude that the use of APAP initiated at home reduces the cost of treatment. A limitation in their analysis is that the same device was used for both groups of patients, whereas it would have been more realistic to compare the use of APAP with that of a less expensive conventional CPAP device for those whose treatment started with a laboratory titration. Also, limited details are provided about hospital care in the cost analysis, which is said to include the capital cost of the bed used. These authors make projections for APAP and CPAP in North America, suggesting a cost advantage for APAP. Several assumptions are made. Our analysis shows that these may be inapplicable in Canada.

#### 4.6.3 Estimates of APAP costs in Canada under different scenarios

To provide more information on the cost issues associated with APAP, a modelling analysis was undertaken with data on the use of APAP and CPAP that would apply to the management of OSA in Edmonton, Alberta.
Costs associated with the care of sleep apnea include those for the diagnosis of the condition, titration for persons who choose treatment with a positive airway pressure machine, and the purchase price of the machine, with mask and tubing. There are also the costs associated with the treatment of co-morbidities and with additional physician consultations.\textsuperscript{32,44} There is no evidence about differences in the “other care” category and maintenance costs are excluded. Thus, we focus on the operating costs of diagnosis, titration and treatment and the costs of the APAP and CPAP machines.

In this analysis, we take a five-year horizon, which is the approximate lifetime of a positive airway pressure machine. All diagnosis, treatment and equipment (CPAP and APAP) costs are assumed to occur in the first year. Also, the APAP and CPAP machines are assumed to have equal efficacy. This assumption is consistent with the results from our literature review.

We focus on five scenarios for our analysis. First, we examine the traditional mode of care, which is sleep laboratory diagnosis and titration and treatment using a CPAP machine. In the second scenario, we assume that diagnosis and titration occur in a sleep laboratory and that the patient buys an APAP machine. In scenario three, we assume laboratory diagnosis, titration with an APAP machine at home and purchase of a CPAP machine by the patient. In the fourth scenario, we assume that diagnosis and titration occur at home with APAP and that the patient buys a CPAP machine. In the fifth scenario, we focus on home diagnosis, home titration and treatment, all with an APAP machine. There are other possible scenarios, but the point of this analysis is to determine the net effect of APAP in diagnosis, titration and treatment.

The assumed cost categories of our analysis are shown in Table 1. The “base case” analysis, which is care in a traditional setting, results in a cost of $2,700. When home APAP is used for titration in place of sleep laboratory titration and the patient buys a CPAP machine, the cost is $2,150. The cost of laboratory diagnosis and treatment, with the purchase of an APAP machine, is $3,750. The lowest cost occurs with home diagnosis and titration and with the purchase of a CPAP machine. The cost in the final scenario, which is home-based with APAP, is $2,650.

These estimates indicate that in certain scenarios, APAP offers cost advantages in diagnosis and titration. The role of APAP in home diagnosis, however, is still controversial and there are few data on its use in titration outside the laboratory. As expected, treatment with APAP is more expensive than treatment with CPAP.
Table 1: Costs for alternative hypothetical approaches to management of sleep apnea

<table>
<thead>
<tr>
<th>Resource category</th>
<th>Laboratory diagnosis and titration, treatment with CPAP</th>
<th>Laboratory diagnosis and titration, treatment with APAP</th>
<th>Laboratory diagnosis, home titration with APAP, treatment with CPAP</th>
<th>Home diagnosis and titration with APAP, treatment with CPAP</th>
<th>Home diagnosis and titration with APAP, treatment with CPAP</th>
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<td>$750\textsuperscript{*}</td>
<td>$750\textsuperscript{*}</td>
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<td>750\textsuperscript{**}</td>
<td>$200\textsuperscript{**}</td>
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<td>$1,200\textsuperscript{†}</td>
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<tr>
<td>Other care</td>
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<td>Same</td>
<td>Same</td>
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<td>Same</td>
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<tr>
<td>Total (excluding other services)</td>
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<td>$3,750</td>
<td>$2,150</td>
<td>$1,600</td>
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</tr>
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</table>

\textsuperscript{*} Estimated direct price of night laboratory service, including physician fee, from Capital Health Authority, Edmonton.

\textsuperscript{**} Estimated price of home diagnosis, including physician fee, from Canadian Liquid Air.

\textsuperscript{†} Estimated price of CPAP machine in Edmonton, plus mask and tubing.

\textsuperscript{‡} Estimated price of APAP machine in Edmonton, plus mask and tubing.
5 DISCUSSION

5.1 Discussion of Specific to Each APAP Application

In this report, we consider the use of APAP for the management of OSA in three applications: diagnosis of OSA, titration to obtain pressure values for treatment with CPAP and treatment.

5.1.1 Use of APAP in diagnosis

There was little information from controlled studies. Results from the three observational studies that were identified suggest a potential use of APAP in diagnosis. Validation for this is needed using studies with stronger methodology and larger numbers of subjects. Attention must be given to validation in clinical settings as there is no evidence for the efficacy of APAP in this application outside a sleep laboratory. There are potential hazards through missed diagnoses and risks for patients with some co-morbidities. Examples include higher upper airway resistance syndrome, severe desaturation and potential cardiac events.

5.1.2 Use of APAP in titration

For use in titration, APAP showed promise to the extent that in several comparative studies, treatment pressures estimated through the use of this approach were either similar to those derived through manual titration, or lower, with no adverse physiological effects. Values for AHI were of NSD in those studies where this measure was reported. The authors of these studies conclude that APAP is a feasible alternative to manual titration. A few recent studies, such as those by Randerath et al.,\textsuperscript{8-10} have shown that its use can result in lower treatment pressures.

Sample sizes were small in most of these studies. The promising results in terms of values for pressure and AHI must be qualified by the exclusion of patients with serious medical conditions in several studies and the use of attended titration in most cases. Results from the comparative studies of different machines (mentioned in section 4.5) also suggest the need for caution in the use of APAP for this application.

In non-comparative studies (described in section 4.4.2), satisfactory clinical results (such as AHI values) were reported for patients who had received APAP or CPAP treatment after the use of APAP to set treatment pressures.

5.1.3 Use of APAP in treatment

Short-term treatment results were noted in 14 papers that described studies on the feasibility of APAP in comparison to CPAP treatment, for one night. Six APAP devices were used, one of them an experimental design. The outcomes measured varied between studies, but the overall pattern was of lower treatment pressures with APAP than CPAP and NSD in clinical outcome measures.
A randomized design was used in 11 studies. Most enrolled small numbers of patients and excluded those with serious medical conditions. Three studies reported patient opinions. In the first, there was NSD in subjective evaluation of sleep quality or symptoms or of tolerance for treatments. In the second, no patient expressed a preference for APAP. In the third, which had a low response rate for completion of a questionnaire, there was NSD in the assessment of side effects, but quality of sleep was rated higher for APAP treatment.

The longer term studies of APAP treatment consistently found that there were lower treatment pressures with APAP than with CPAP. This difference had little effect on outcomes. In four studies, there was an indication of greater use of APAP than CPAP. None of the studies, however, found any significant difference in clinical outcome measures (AHI, ESS, arousal index and sleep architecture).

Information obtained from patients in three studies indicated a preference for APAP over CPAP. Subjective measures of well-being and sleep quality favoured APAP in one study. In the study by Stradling et al., there was NSD in the numbers of patients successfully established on treatment after six weeks of either APAP or CPAP, though there was a trend in favour of APAP.

All longer term studies used randomized designs. The measures that were used varied, as indicated in section 4.4.3. The numbers of patients were small (25 or fewer) in five studies. In a larger trial, there was a high drop-out rate. Those studies reporting patient opinions and preferences gave few details of how these were obtained or of individual responses.

5.2 General Discussion

In this assessment, we intended to review the evidence of efficacy, effectiveness and costs of APAP for the management of OSA. Overall, the data indicate that while the technology shows promise, its effectiveness is still unestablished. Questions remain regarding APAP’s role in diagnosis and titration at home and for performing unattended titrations in sleep laboratories.

The studies included in this review address the efficacy of APAP in different applications, usually using patient populations that excluded persons with CHF or obstructive respiratory disorders. The studies also excluded patients with a substantial amount of central apnea or high upper airway resistance syndrome. Different devices were used in the studies. Findings from one type of device may not be generalizable to situations where other equipment is used. There is no evidence that one APAP technology is superior to another, though there are substantial differences in performance between machine designs. The overall patterns of results from studies using different types of machine were similar. None established any difference in clinical outcomes between APAP and CPAP.

As noted by Berry et al., most patients in the studies had already had a formal sleep study and some had a conventional CPAP titration or were being treated with CPAP, before they were first treated with APAP. The results in such patients may differ from those for naive, untreated patients. The performance of APAP under routine conditions, at home or in a general population of patients who have moderate to severe OSA is still unestablished.
APAP’s potential for diagnosis was shown in three non-randomized studies in which it was used for small groups of patients in laboratory settings. There was some promise, but also an indication that some patients could be misdiagnosed. There was no information on the use of APAP for diagnosis at home or appraisal of potential risks to patients through inaccurate findings. The patient population was largely derived from tertiary-care referral centres and may be dissimilar to the populations in community care.

Most of the comparative studies on titration undertaken in a laboratory were attended. Interventions were necessary for a few patients during attended APAP titration to stop mask leaks, adjust the mask or provide supplemental oxygen for nocturnal hypoxemia.

Information comparing APAP titration at home with manual titration in a laboratory is limited. Many of the studies located for this review were undertaken using protocols in which participating patients had some experience with using CPAP. Several studies used unattended APAP titration to determine a fixed CPAP and then treated patients with this pressure, obtaining acceptable values for AHI.

In the studies on treatment of OSA with APAP, it was shown that APAP allowed the use of lower treatment pressure than CPAP, but this was not necessarily associated with increased use of the device. No study found any difference in clinical outcomes between APAP and CPAP. SS differences, had they been found, would not necessarily have been of clinical significance.

There were indications, from poorly described surveys, of some patient preference for APAP.

Recommendations from the AASM suggest a cautious approach to the use of APAP at this stage. Patients with CHF or chronic lung disease and those expected to have nocturnal arterial oxyhemoglobin desaturation due to conditions other than OSA are not candidates for APAP titration or treatment. APAP devices are not recommended for split-night titration. The use of unattended APAP to either initially determine pressures for fixed CPAP or for self-adjusting APAP treatment in CPAP-naive patients is unestablished.

The AASM recommends that patients being treated with fixed CPAP on the basis of APAP titration or being treated with APAP must be followed up to determine treatment effectiveness and safety.
6 CONCLUSIONS

Caution is still required in the use of APAP as further studies must establish its effectiveness and cost-effectiveness. Users of APAP should be aware of the performance of the device being used and the evidence of its efficacy. In most studies, patients suffering from cardiac, pulmonary and other medical conditions were excluded. There are potential safety issues for such individuals if APAP is used in settings without prompt access to technical support. Instituting APAP titration as a cost-savings measure remains unproven and without careful patient selection, may be hazardous.

On the basis of the literature available for this assessment, we conclude that APAP shows promise, but that its place in health care is yet to be established.
7 REFERENCES


### Appendix 1: Databases Searched and Search Strategies

Guide to Search Syntax (DIALOG®, Cochrane Library)

- `?` Truncation symbol. Retrieves plural and variant endings of a term
- `!` Retrieves narrower terms under the subject heading
- `()` Words must be adjacent to each other
- `(1n)` Words within one word of each other in any order
- `ab` Search in article abstract.
- `de` Descriptor i.e., subject heading (a controlled, thesaurus term)
- `ME` Medical subject heading
- `ND` Device name
- `PN` Product name
- `ti` Search in titles
- `tw` Text word

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<td>7. #1 OR #6</td>
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<td><em>Performed 09 August 2002</em> <em>The Cochrane Database of Systematic Reviews = 1 reference; The Cochrane Controlled Trials Register=74 references; 1 abstract by INAHTA and other healthcare agencies</em></td>
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<td>The National Library of Medicine</td>
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<td>MeSH headings and keywords to mirror Dialog search. Appropriate syntax used for PubMed.</td>
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<td>Search of major sleep-related associations using Google™ search engine.</td>
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**Appendix 2: Summaries of Comparative Studies on APAP**

**Abbreviations**

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Full Form</th>
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<tbody>
<tr>
<td>AHI</td>
<td>apnea-hypopnea index</td>
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<td>APAP</td>
<td>autotitrating CPAP</td>
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<tr>
<td>BiPAP</td>
<td>Bilevel Positive Airway Pressure machine</td>
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<tr>
<td>BMI</td>
<td>body mass index</td>
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<tr>
<td>COPD</td>
<td>chronic obstructive pulmonary disease</td>
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<td>CPAP</td>
<td>continuous positive airway pressure</td>
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<tr>
<td>ESS</td>
<td>Epworth Sleep Score</td>
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<tr>
<td>FEV</td>
<td>forced expiry volume</td>
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<td>FVC</td>
<td>forced vital capacity</td>
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<tr>
<td>MWT</td>
<td>maintenance of wakefulness test</td>
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<tr>
<td>NC</td>
<td>non-completers</td>
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<tr>
<td>NSD</td>
<td>no significant difference</td>
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<tr>
<td>NS</td>
<td>not statistically significant</td>
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<tr>
<td>OSA</td>
<td>obstructive sleep apnea</td>
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<tr>
<td>P\text{eff}</td>
<td>effective treatment pressure</td>
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<tr>
<td>P_{95}</td>
<td>95th percentile pressure</td>
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<tr>
<td>PSG</td>
<td>polysomnography</td>
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<tr>
<td>RCT</td>
<td>randomized controlled trial</td>
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<tr>
<td>RCT-C</td>
<td>randomized cross-over study</td>
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<tr>
<td>RDI</td>
<td>respiratory distress index</td>
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<tr>
<td>REM</td>
<td>rapid eye movement</td>
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<tr>
<td>SaO\text{2}</td>
<td>oxygen saturation</td>
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<tr>
<td>SS</td>
<td>statistically significant(ly)</td>
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<td>First author, year</td>
<td>Setting</td>
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<tr>
<td>Huang X., 1998&lt;sup&gt;5&lt;/sup&gt;</td>
<td>PRC, hospital sleep disorders centre</td>
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<tr>
<td>Gugger M., 1997&lt;sup&gt;6&lt;/sup&gt;</td>
<td>Switzerland, sleep laboratory, university hospital</td>
</tr>
<tr>
<td>Gugger M., 1995&lt;sup&gt;7&lt;/sup&gt;</td>
<td>Switzerland, sleep laboratory</td>
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### Table 3: APAP – comparative titration studies

<table>
<thead>
<tr>
<th>First author, year</th>
<th>Setting</th>
<th>Intention of study</th>
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<th>Device</th>
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<th>Period</th>
<th>Compliance</th>
<th>Outcomes</th>
<th>Conclusions (comments)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Randerath W.J., 2000&lt;sup&gt;8&lt;/sup&gt;</td>
<td>Germany, hospital sleep laboratory</td>
<td>To determine whether treatment with APAP device is possible for patients with OSA and to find best range of pressure values</td>
<td>Patients referred with OSA, 9 of 10 were males BMI=32.0 AHI=18.2</td>
<td>Somnosmart</td>
<td>Non-randomized comparison, all patients had manual titration on night 1, APAP on nights 2 and 3 (Comparison of APAP modes was an RCT-C, details not considered here) n=10</td>
<td>3 x 1 night</td>
<td>Manual $P_{eff}=8.0$; in comparison, mean pressures for two APAP modes were 5.6 ($p&lt;0.01$) and 7.3 ($p&lt;0.05$)</td>
<td>Significantly lower pressure required with APAP compared with manual titration</td>
<td></td>
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<tr>
<td>Randerath W.J., 1999&lt;sup&gt;9&lt;/sup&gt;</td>
<td>Germany, hospital sleep laboratory</td>
<td>To compare APAP pressure values with those of manual titration and determine whether presetting an upper pressure limit for APAP gave an advantage over free-range APAP</td>
<td>Hypersomnia and AHI&gt;10 AHI=31.6 BMI=32.4 ESS=12.1 11/11 male</td>
<td>Somnosmart</td>
<td>Non-randomized comparison, all patients had manual titration on night 1, APAP on nights 2 and 3 (Comparison of APAP modes was an RCT-C, details not considered here) n=11</td>
<td>3 x 1 night</td>
<td>Manual $P_{eff}=9.3$; in comparison, mean pressures for two APAP modes were 5.4 ($p&lt;0.01$) and 5.1 ($p&lt;0.01$)</td>
<td>Significantly lower pressure with APAP compared with manual titration</td>
<td></td>
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<tr>
<td>Randerath W.J., 1999&lt;sup&gt;10&lt;/sup&gt;</td>
<td>Germany, university sleep laboratory</td>
<td>To investigate PSG parameters and profile of treatment pressure in APAP machine</td>
<td>21/22 male, mean AHI=25.2</td>
<td>Somnosmart</td>
<td>Prospective comparison, manual CPAP followed by APAP for each subject n=22</td>
<td>2 x1 nights</td>
<td>Mean pressure 5.4 mbar APAP, 8.6 CPAP (SS)</td>
<td>Mean treatment pressures can be reduced by use of APAP (All other comparisons are between APAP and diagnostic PSG values)</td>
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Table 3: APAP – comparative titration studies (cont’d)

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<tr>
<th>First author, year</th>
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<th>Conclusions (comments)</th>
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<tr>
<td>Stradling J.R., 1997&lt;sup&gt;11&lt;/sup&gt;</td>
<td>UK, hospital, two sleep laboratories</td>
<td>Comparison of titration with APAP and manual</td>
<td>All with disabling symptoms of OSA (usually on basis of high ESS) Male to female ratio unreported</td>
<td>Horizon Unattended</td>
<td>RCT N=112, 61 in manual titration arm, 52 in APAP NSD between groups before titration</td>
<td>Overnight with 6 weeks follow-up</td>
<td>(122 randomized, 9 cancelled) 1 NC (APAP)</td>
<td>P&lt;sub&gt;eff&lt;/sub&gt; 8.7 manual, 8.2 APAP (NS) 64% manual and 73% APAP patients successfully established on CPAP at 6 weeks (NS); ESS = 7.3 and 8.9 (NS) 23% and 25% undecided (NS), with ESS =12.7 and 15.8 (NS) 13 (6%) from manual group and 1 from APAP “failed” at 6 weeks (wished not to continue) (SS)</td>
<td>Substitution of APAP for manual titration does not reduce number accepting treatment at 6 weeks and may slightly improve this.</td>
</tr>
<tr>
<td>Lloberes P., 1997&lt;sup&gt;12&lt;/sup&gt;</td>
<td>Spain, sleep laboratory</td>
<td>Comparison of PSG and APAP titration</td>
<td>Documented OAS, not previously treated with CPAP BMI=31.7 kg/m&lt;sup&gt;2&lt;/sup&gt; AHI=53.3 ± 19.0 Male to female ratio unreported</td>
<td>AutoSet (Partially attended, could adjust mask)</td>
<td>RCT-C, n=20 Comparison: PSG and manual titration Also n=9 for sleep characteristics, compared with CPAP results from 20 in titration study</td>
<td>1 day</td>
<td>All complied</td>
<td>Mean pressure 10.3 versus 10.1 cm H&lt;sub&gt;2&lt;/sub&gt;O, NSD NSD in sleep characteristics between APAP (n=9) group and CPAP (n=20) group</td>
<td>Gives similar P&lt;sub&gt;eff&lt;/sub&gt; to manual titration”… adequate CPAP titration can be achieved with APAP.” (No details on method of randomization and comparison of sleep characteristics between two groups of doubtful validity)</td>
</tr>
<tr>
<td>First author, year</td>
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<tr>
<td>Teschler H., 1996</td>
<td>Germany, hospital department</td>
<td>To test if APAP device produced adequate improvement in sleep and breathing.</td>
<td>Confirmed OSA, all male BMI=33.8±1.3 Excluded stroke, cardiac failure, daytime respiratory failure, nocturnal myoclonus</td>
<td>AutoSet Attended</td>
<td>(a) diagnostic, PSG (b) manual titration (c) APAP (d) CPAP using value from RCT-C for stage (c) n=21</td>
<td>4 x 1 nights</td>
<td>1 excluded, unable to obtain adequate seal with mask</td>
<td>Mean pressure 9.9 cm APAP versus 8.6 cm manual (p&lt;0.001) RDI lower with APAP than manual (2.8 versus 10.1 p&lt;0.01).</td>
<td>Conclude that AutoSet is suitable for automated titration (Considering only RCT-C component, in the manual titration, no attempt to eliminate snoring or flow limitation)</td>
</tr>
<tr>
<td>Teschler H., 1997</td>
<td>Germany, hospital department</td>
<td>To follow up titration measurements from 1996 study with new criteria – to determine whether APAP produces similar pressure to manual titration that aims to eliminate snoring</td>
<td>subjects from 1996 study n=16</td>
<td>AutoSet</td>
<td>RCT-C Goal of manual titration now to eliminate snoring, apneas and hypopneas</td>
<td>2 x 1 nights, with titration comparison repeated after 3 mo and 8 mo of home use.</td>
<td>No drop-outs</td>
<td>At 3 mo $P_{eff} = 11.0$ for CPAP, $P_{st} = 10.6$ for APAP 8 mo figures 10.4 and 9.7 (p = 0.03)</td>
<td>“As expected, $P_{eff}$ for manual titration higher with new criteria. Little variation of APAP pressure with time” AASM review indicates random order for titrations not clearly stated</td>
</tr>
<tr>
<td>First author, year</td>
<td>Setting</td>
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<tr>
<td>Ficker J.H., 2003¹⁸</td>
<td>Germany, university sleep laboratory</td>
<td>To compare APAP and CPAP during initiation of treatment</td>
<td>n = 100 patients ESS &gt;8 AHI &gt; 10 Excluded those with prior CPAP, central apnea, severe nasal obstruction, obstructive pulmonary disease, congestive heart failure.</td>
<td>Somnosmart</td>
<td>PSG followed by RCT</td>
<td>2 x 1 night</td>
<td>Of 100 patients recruited, 5 did not tolerate treatment (2 APAP and 3 CPAP)</td>
<td>Treatment pressure=6.0 for APAP, 9.0 for CPAP (p&lt;0.001) NSD in AHI (APAP 4.7, CPAP 3.7); ESS (7.0 versus 7.6), arousal index, apnea index, oxygen desaturation index</td>
<td>In short term, equally good therapeutic results and compliance can be obtained with this APAP device as with conventional CPAP</td>
</tr>
<tr>
<td>Randerath W.J., 2001¹⁹</td>
<td>Germany, university sleep laboratory</td>
<td>To test whether APAP with a reduced pressure range was as effective as CPAP</td>
<td>Untreated OSA, AHI&gt;10 BMI=32.5 Excluded COPD, beta blockers, neurological, psychiatric disorders 33/37 males</td>
<td>APAP FOT Somnosmart</td>
<td>APAP with upper pressure limit lowered to 13.3 hPa versus CPAP n=37</td>
<td>2 x 1 night</td>
<td>Mean pressure = 5.7 hPa APAP versus 8.3 CPAP (p&lt;0.01) NSD in AHI score reduction (5.0 versus 4.6), arousals or % REM between two modes</td>
<td>APAP FOT device with reduced upper pressure as effective as CPAP for OSA and mean pressure substantially reduced</td>
<td></td>
</tr>
<tr>
<td>Randerath W.J., 2001²⁰</td>
<td>Germany, university sleep laboratory</td>
<td>Comparison of treatment of APAP with CPAP</td>
<td>Untreated OSA, AHI&gt;10 BMI=31.4, AHI=32.2 Excluded COPD, certain medications, neurological and psychiatric disorders 20/25 males</td>
<td>Somnosmart</td>
<td>RCT-C n=25 Questionnaire for patient assessment</td>
<td>2 x 1 night</td>
<td>16/25 completed questionnaire</td>
<td>Mean pressure 5.5 for APAP, 8.3 for CPAP (p&lt;0.001) NSD in AHI score reduction (5.5 APAP, 6.6 CPAP) NSD in arousals between two modes. Total sleep time reduced from baseline for both, did not reach SS.</td>
<td>APAP at least as effective as CPAP (High drop-out for patient responses)</td>
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Table 4: APAP – short term treatment studies (cont’d)

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<tr>
<th>First author, year</th>
<th>Setting</th>
<th>Intention of study</th>
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<th>Device</th>
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<th>Period</th>
<th>Compliance</th>
<th>Outcomes</th>
<th>Conclusions (comments)</th>
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<tbody>
<tr>
<td>Ficker J.H., 2000[1]</td>
<td>Germany, hospital sleep laboratory</td>
<td>To establish therapeutic efficacy of APAP device</td>
<td>Mild to severe OSA Minimum AHI≥10, Minimum ESS≥10, BMI≥30 Excluded central apnea, contra-indications for CPAP, severe COPD, other conditions 18/18 male</td>
<td>Somnosmart</td>
<td>RCT-C after diagnostic PSG Double-blind Patient evaluation through 5-point questionnaire n=18</td>
<td>2 x 1 night</td>
<td>Not reported</td>
<td>Change in % REM reached statistical significance for APAP, not for CPAP NSD between two modes NSD in assessment of side effects, quality of sleep rated higher for APAP, p&lt;0.05</td>
<td>Therapeutic effect of APAP comparable to CPAP. Mean treatment pressure lower in most patients (Only single night comparison - authors note possibility that patients might have been aware when APAP was used)</td>
</tr>
<tr>
<td>Miyazaki S., 1999[2]</td>
<td>Japan, otolaryngology department, medical school</td>
<td>To evaluate efficacy of APAP</td>
<td>Mean AHI=68.3 Mean minimum SaO₂=73.8 BMI=28.6 10/11 male</td>
<td>Virtuoso</td>
<td>Attended Prospective, comparative, APAP and CPAP alternated each hour</td>
<td>1 day? (2 patients had both night and day PSG)</td>
<td>Not reported</td>
<td>Mean AHI with APAP=3.4, CPAP=4.2 (NS) NSD in ESS, arousal index, sleep architecture Mean pressure (kPa) APAP 0.84, CPAP 0.93 (p=0.038) Largest difference in pressure in lateral sleeping position NSD in subjective evaluation of two machines or in preferences. Most assessed quality of sleep as good, pressure acceptable, arousal uncommon</td>
<td>Efficacy of APAP less than CPAP but can detect optimum CPAP level (Maximum, rather than mean treatment pressures reported -)</td>
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### Table 4: APAP – short term treatment studies (cont’d)

<table>
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<tr>
<th>First author, year</th>
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<th>Compliance</th>
<th>Outcomes</th>
<th>Conclusions</th>
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<tbody>
<tr>
<td>Garcia Arroyo I., 1999(^{23})</td>
<td>Spain, hospital sleep laboratory</td>
<td>To compare manual and auto titration approaches in patients diagnosed with OSA</td>
<td>OSAS diagnosed by PSG, 18/19 male, Minimum AHI&gt;10/h, BMI=39, FEV/FVC=70, (PO_2)&gt;60mm Hg</td>
<td>Innovative (Attended?)</td>
<td>Observational, consecutive, all received both APAP with PSG and CPAP with PSG (n=19)</td>
<td>1 day</td>
<td>1 NC</td>
<td>Mean pressure 7.38 versus 7.09 cm, (NS) AHI 4.8 versus 5.6 (NS) NSD in arousals, sleep efficiency, daytime drowsiness. Minimum (O_2) saturation during REM sleep SS better with CPAP (p&lt;0.03)</td>
<td>Authors conclude APAP is as effective as titrated CPAP for treating patients with OSA (Report establishes only NSD in pressure values plus short-term outcomes)</td>
</tr>
<tr>
<td>Behbehani K., 1998(^{24})</td>
<td>USA, sleep laboratory</td>
<td>To compare performance of APAP and CPAP</td>
<td>Already on CPAP for 8 weeks, AHI 57.3±30.8 Those with “severe medical conditions” excluded 26/31 male</td>
<td>Experimental device based on BiPAP</td>
<td>RCT-C</td>
<td>1 night on each treatment</td>
<td>NSD in AHI scores (APAP 5.4 versus CPAP 4.2), sleep architecture, arousal Mean APAP pressure=8.4, CPAP=11.5 (SS)</td>
<td>APAP is as effective as CPAP for AHI and sleep architecture Mean APAP applied pressure lower than CPAP</td>
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<tr>
<td>First author, year</td>
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<tr>
<td>Plywaczewski R., 2000&lt;sup&gt;25&lt;/sup&gt;</td>
<td>Poland, sleep clinic</td>
<td>Comparison of APAP and CPAP titration</td>
<td>Obese patients with severe OSA, n=50 BMI=35±6 AHI=63±22 Male to female ratio not reported</td>
<td>Virtuoso Unclear if attended</td>
<td>Prospective, comparative for all patients (a) manual titration with CPAP (b) APAP plus PSG monitoring n=50</td>
<td>2 nights</td>
<td>Established pressure 8.2 for APAP, 9.2 for CPAP (p&lt;0.05) AHI: 7.7 for APAP, 5.6 for CPAP (NS; each p&lt;0.001 versus diagnostic PSG) REM % 4.5 APAP, 3.8 CPAP, NS, each p&lt;0.001 versus diagnostic PSG Arousals/h 12.8 APAP, 9.6 CPAP, NS.</td>
<td>APAP seems to be a reliable alternative to manual titration for patients with OSA, may help to cut waiting lists.</td>
<td></td>
</tr>
<tr>
<td>Ficker J.H., 1998&lt;sup&gt;26&lt;/sup&gt;</td>
<td>Germany, sleep laboratory</td>
<td>To evaluate therapeutic efficacy and treatment pressure of APAP machine versus CPAP</td>
<td>Untreated mild to severe OSA, AHI=53.7 Excluded cardiac disease, COPD, previous surgery 11/16 male</td>
<td>REM+auto</td>
<td>Manual titration, PSG followed by RCT-C Questionnaire for patient assessment n=16</td>
<td>2 x 1 day</td>
<td>Mean AHI=4.2 (APAP) versus 3.6 with CPAP (NS) NSD in sleep architecture, arousal index ESS=5.3 versus 6.5 (NS) Mean pressure=8.1 for APAP, 7.6 for CPAP (SS)</td>
<td>APAP as effective as CPAP, but reductions in treatment pressures with APAP were not achieved Unable to find decisive advantage of APAP over CPAP</td>
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</table>
Table 4: APAP – short term treatment studies (cont’d)

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<tr>
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<tbody>
<tr>
<td>Ficker J.H., 1997</td>
<td>Germany, sleep laboratory</td>
<td>Comparison of efficacy and acceptance of APAP versus CPAP</td>
<td>OSA Minimum AHI=10 BMI=30 21/25 male</td>
<td>Horizon</td>
<td>RCT-C Questionnaire for patient reports</td>
<td>2 x 1 day</td>
<td></td>
<td>AHI=4.4 for APAP, 2.8 for CPAP (p=0.044)  No patient preferred APAP  Mean pressure=7.2 for APAP versus 7.1 for CPAP (NS)</td>
<td>Neither pressure reduction nor improvement in compliance obtained were with APAP  APAP effectiveness less than that of CPAP</td>
</tr>
<tr>
<td>Hoster M., 1997</td>
<td>Germany, sleep clinic</td>
<td>To compare APAP with CPAP</td>
<td>Moderate to severe OAS BMI=30±5.8 AHI=73.4±32.4 SaO₂=77±8</td>
<td>AutoSet</td>
<td>RCT-C</td>
<td>2 x 1 night</td>
<td>Mean pressure for CPAP=10.0, for APAP mode=21.3% (readings)&gt;10  AHI=30.1 for APAP, 7.9 for CPAP (SS)  Snoring episodes 18.7 for APAP, 7.9 for CPAP (p=0.05)  NSD in sleeping time, sleep architecture, arousals</td>
<td>In patients who accept high pressure, CPAP remains method of choice</td>
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<tr>
<td>Hoster M., 1996</td>
<td>Germany, sleep clinic</td>
<td>To compare APAP with CPAP</td>
<td>OAS BMI=33, AHI=49, minimum SaO₂=75 12/12 males</td>
<td>Auto Adjust</td>
<td>RCT-C</td>
<td>2 x 1 night</td>
<td>Mean pressure 7.9 for APAP, 10.7 for CPAP (SS)  AHI=3.3 for APAP, 4.0 for CPAP (NS)  NSD in total sleep time, sleep architecture</td>
<td>APAP offers an alternative to BiPAP in case of pressure intolerance</td>
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<td>First author, year</td>
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<tr>
<td>Scharf M.B., 1996&lt;sup&gt;30&lt;/sup&gt;</td>
<td>USA, Sleep Disorders Centre</td>
<td>To compare APAP and CPAP efficacy</td>
<td>Minimum AHI=15 AHI=57.3 2 weeks of CPAP before RCT-C n=12</td>
<td>Horizon Autoadjust</td>
<td>RCT-C Single-blind n=12</td>
<td>2 x 1 nights</td>
<td>All patients complied but authors note pressure control problems arose for 7 subjects during APAP, requiring manual resetting in 5 cases.</td>
<td>AHI and SaO&lt;sub&gt;2&lt;/sub&gt; values for APAP and CPAP NSD from each other (4.4 versus 3.8; 82.6/84.2) % time in stage 3/4 sleep SS higher with APAP (32.6 versus 22.7 minimum)</td>
<td>APAP effectively controls OSA</td>
</tr>
<tr>
<td>Sharma S., 1996&lt;sup&gt;31&lt;/sup&gt;</td>
<td>Canada, sleep disorders centre</td>
<td>Evaluation of efficacy and safety of APAP</td>
<td>Moderately severe OSA, AHI &gt; 15 19/20 males Excluded if history of hospitalization with pulmonary, cardiac, neuromuscular or musculoskeletal disease within past 6 mo</td>
<td>Respironics prototype Attended</td>
<td>RCT-C Questionnaire for patient opinion n=20</td>
<td>2 x 1 nights</td>
<td>11/18 patients preferred APAP (NS)</td>
<td>NSD between modes for sleep architecture or sleep quality (included AHI=6.3 for APAP, 3.8 for CPAP) Pressure=10.1 for APAP, 12.3 for CPAP (p&lt;0.05) 11/18 patients preferred APAP (NS)</td>
<td>Effectiveness of APAP was comparable to that of CPAP, with lower pressure (No questionnaire details)</td>
</tr>
<tr>
<td>First author, year</td>
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<tr>
<td>Planès C., 2003</td>
<td>France, four sleep laboratories</td>
<td>To compare efficacy and cost of CPAP initiated in the laboratory with APAP initiated at home</td>
<td>n=35 (27 males) with severe OSA, AHI&gt;30, obstructive events&gt;80% total events, and clinical indications for CPAP according to American Thoracic Society recommendations</td>
<td>REM + auto (used in constant pressure mode for CPAP group)</td>
<td>RCT n=17 manual titration during PSG in sleep laboratory</td>
<td>60 days plus CPAP status at &gt;1 y</td>
<td>5 drop outs (3 CPAP, 2 APAP) 1 patient switched from APAP to CPAP At &gt;1 y 2 drop-outs from CPAP (both had frankly abnormal AHI at study completion); 1 from APAP interrupted treatment because of relief of symptoms</td>
<td>NSD in: - AHI (APAP 7.6 versus CPAP 10.4), - ESS (15.5 to 7.5 versus 14.7 to 7.6) - Sleep structure All but 2 in CPAP and 1 in APAP group were satisfied or very satisfied with treatment Time from therapy initiation from diagnosis 11.8 days for APAP, 47.2 days for CPAP, p&lt;0.01 Total cost: APAP € 1,263 versus CPAP € 1,720, p &lt;0.0</td>
<td>Treatment of OSA with APAP initiated at home is effective and reliable and reduces time from diagnosis to therapy and cost of treatment (comparison excludes cost of APAP device used in both groups; hospital costs include capital costs of bed used)</td>
</tr>
<tr>
<td>Massie C.A., 2003</td>
<td>USA, five sleep laboratories</td>
<td>To test hypothesis that CPAP use and outcomes can be improved by an APAP device in patients with OSA who require higher CPAP (10 cm</td>
<td>OSA</td>
<td>AutoSet</td>
<td>RCT-C 6 weeks each on CPAP and APAP n=46</td>
<td>84 days</td>
<td>2 drop-outs</td>
<td>Average nightly use greater in APAP mode (306 versus 271 min p=0.005); NSD in % of nights used (92 versus 88)</td>
<td>Patients who require higher fixed CPAP, use APAP more and report greater benefit from this therapy (Significance of differences in SF-36 scores unclear)</td>
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Table 5: APAP – longer term treatment studies (cont’d)

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| Randerath W.J., 2001 | Germany, university sleep laboratory | Investigate effectiveness of APAP, treatment pressure profiles, patient acceptance and side effects | Untreated OSA Minimum AHII ≥10, AHII=35.1±26/h 45/52 males | Somnosmart | (a) Manual titration then APAP, CPAP successive nights  
(b) RCT-C of APAP versus CPAP  
6 weeks on each treatment, followed by PSG | 84 days | 5 did not complete | AHI SS lower than baseline for APAP and CPAP (week 1=5.3 and 4.6; week 6=5.0 and 4.3; NSD between two treatments) | Mean pressure lower with APAP (5.7 versus 7.8 cm, APAP based on measurement of impedance enables effective treatment of OSA over 6 weeks at home  
(Fixed sequence for initial CPAP and APAP use; little detail on patient questioning) |
Table 5: APAP – longer term treatment studies (cont’d)

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<tr>
<td>Sériès F., 2001</td>
<td>Canada, hospital sleep clinic</td>
<td>To assess influence of sleep stage and body position on dependence of sleep apnea on treatment efficacy and compliance for APAP and CPAP</td>
<td>Newly treated OSA patients</td>
<td>Morphée Plus/Cloudnine</td>
<td>RCT, APAP versus CPAP, 24 patients in each arm</td>
<td>21 days</td>
<td>n=52</td>
<td>p&lt;0.001.  No difference in overall use, both 315.4 min/night and 98.4% of days. Decrease in arousals and increase in REM sleep for both methods. SS from baseline, NS between APAP and CPAP. 75% patients preferred APAP.</td>
<td>Patients with dependent breathing abnormalities treated with CPAP had more daytime sleepiness compared with APAP group (ESS score, p=0.08,) lower ability to stay awake, p=0.02. Patients with body position and/or sleep stage dependency of nocturnal breathing disturbances may benefit more from APAP than CPAP, at least in the early stages of their treatment. (8 of 48 patients were new, others had been in previous trials).</td>
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<tr>
<td>d’Ortho M.P., 2000&lt;sup&gt;36&lt;/sup&gt;</td>
<td>France, sleep laboratory, home treatment</td>
<td>To compare efficacy, patient tolerance, compliance, preference between APAP and CPAP</td>
<td>Untreated OSA, Excluded persons with restless legs, cardiac failure, cerebrovascular disease, lung disease</td>
<td>REM+auto</td>
<td>RCT-C, APAP versus CPAP</td>
<td>2 x 30 days</td>
<td>APAP= 4.1 h/night, CPAP= 4.7 (NS)</td>
<td>NSD in AHI, arousal index, slow wave sleep duration, report of daytime sleepiness Mean pressure lower with APAP than CPAP (8.7 versus 9.7, p=0.05) Tolerance and compliance similar NSD between modes in subjective assessment of symptoms or for tolerance of treatments When asked to choose at end of study, 15 chose APAP, 8 CPAP, 2 surgery</td>
<td>APAP is as effective as CPAP in resolving sleep-related breathing disorders Same compliance for APAP and CPAP, patients more likely to prefer APAP (Compliance in terms of number of nights used not given - basis for choice of modes at end of study unclear)</td>
</tr>
<tr>
<td>Hudgel D.W., 2000&lt;sup&gt;17&lt;/sup&gt;</td>
<td>USA, university hospital sleep laboratory and home treatment</td>
<td>Comparison of tolerance, compliance and symptomatic improvement</td>
<td>Untreated OSA, 7 upper airway resistance syndrome BMI=42.2 Excluded COPD, CHF, upper airway surgery, sedative or antidepressant therapy</td>
<td>Virtuoso Smart-CPAP</td>
<td>RCT-C APAP versus CPAP (Data for 18 males, 15 females who complied)</td>
<td>2 x 84 days</td>
<td>21 did not complete 24-week protocol and data incomplete for another 6 APAP pressure= 6.4 cm, CPAP=10.6 (p&lt;0.0001) NSD in ESS score reduction, both SS less than baseline Daily use=6.0 h for APAP versus 5.5 h for CPAP (p&lt;0.04), NSD in number of days (84% APAP, 82% CPAP)</td>
<td>Mean pressure less for APAP and daily use higher than for CPAP No difference in ESS (High proportion of non-completers)</td>
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### Table 5: APAP – longer term treatment studies (cont’d)

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<tr>
<td>Teschler H., 2000ª</td>
<td>Germany, university hospital sleep laboratory</td>
<td>To test if AHI reduction and pressure reduction using APAP were maintained at home</td>
<td>Untreated moderate to severe OSA AHI=52.9±8.1 Excluded asthma, COPD, CHF, allergic rhinitis 10/10 male</td>
<td>AutoSet</td>
<td>RCT-C, double blind</td>
<td>2 x 60 days</td>
<td>APAP=6.3 h/night, CPAP=6.1 (NS) Days used – APA=98.3% of days studied, CPAP=96.2% (NS)</td>
<td>In home use, NSD in AHI (APAP 4.0, CPAP 3.7) Median pressure delivery with APAP 77% of manual titration value</td>
<td>AHI and compliance with home APAP comparable to CPAP, with 23% reduction in median pressure required</td>
</tr>
<tr>
<td>Konermann M., 1998ª</td>
<td>Germany, clinical sleep laboratory</td>
<td>To compare performance of APAP and CPAP</td>
<td>Severe OSA Min AHI=20, (actual=38.3 and 35.5 for two groups) BMI=32 44/50 male</td>
<td>Horizon</td>
<td>RCT, Single blind, n=25 in each arm</td>
<td>3 to 6 mo follow-up 90 to 180 days</td>
<td>N=2 in CPAP arm withdrew Hours per night APAP=5.9, CPAP 5.6 (NS) Nights/week used&gt;4 h: APAP=6.5, CPAP=5.7 (p&lt;0.01)</td>
<td>NSD in AHI (2.4 versus 3.6), sleep efficiency or REM Mean pressure=6.5 for APAP versus 8.1 for CPAP (p&lt;0.01)</td>
<td>APAP is as effective as CPAP, compliance with treatment is better. (No details of individual or mean follow-up times. No information on approach used to estimate compliance)</td>
</tr>
<tr>
<td>Sériès F., 1997ª</td>
<td>Canada, hospital sleep clinic</td>
<td>To determine efficacy of APAP used with estimated pressure reference value (derived from formula based on BMI, neck circumference and AHI)</td>
<td>Previously untreated OSA BMI=36 Excluded life-threatening forms of OSA, non obstructive sleep-related breathing disorders n=36, 12 in each arm</td>
<td>Morphée Plus</td>
<td>RCT, single-blind APAP measured pressure versus APAP estimated pressure versus CPAP</td>
<td>21 days</td>
<td>Compliance estimated as effective treatment for &gt;4 h per night for at least 5 nights/week NSD between groups, though APAP groups had longer treatment</td>
<td>Similar changes in AHI, ESS, MWT for all groups</td>
<td>APAP is as effective as CPAP APAP using estimated pressure value is effective (Compliance NSD between groups, though trend in this small study favours APAP)</td>
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Table 5: APAP – longer term treatment studies (cont’d)

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<tr>
<td>Meurice J.C., 1996</td>
<td>Canada, hospital sleep clinic</td>
<td>To assess efficacy of APAP in comparison with CPAP</td>
<td>Untreated OSA, BMI=34.2, AHI=43.6, 16/16 male</td>
<td>Morphée Plus</td>
<td>RCT</td>
<td>21 days</td>
<td>Hours of home use SS higher for APAP group (6.5 h versus 5.1 h)</td>
<td>NSD between groups in ESS, AHI (1.7 versus 2.6)</td>
<td>APAP is as effective as CPAP and is used more (Numbers in each RCT arm unspecified)</td>
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