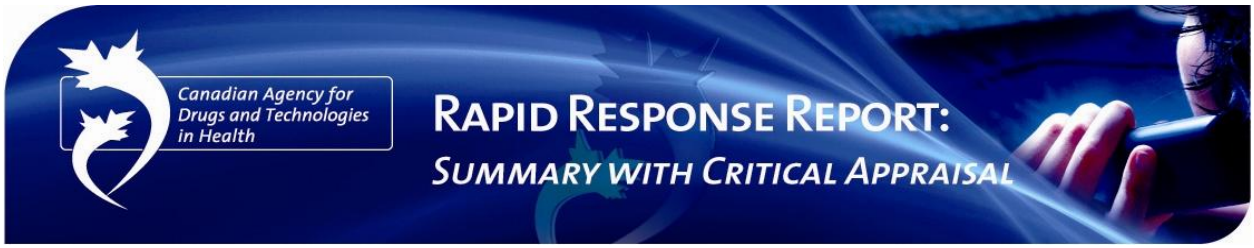

TITLE: Adaptive Servo Ventilation versus Continuous or Bi-Level Positive Airway Pressure: A Review of the Clinical Effectiveness, Cost-Effectiveness and Guidelines

DATE: 07 August 2012

CONTEXT AND POLICY ISSUES

Central sleep apnea syndromes (CSAS) are characterized by sleep disordered breathing (SDB) resulting in nocturnal awakenings and daytime sleepiness due to insufficient respiratory effort.[1] The prevalence of SDB in heart failure (HF) patients is as high as 47% to 76% in those with reduced left ventricular ejection fraction (LVEF).[2] Post-hypocapnia hyperventilation underlies central apnea associated with congestive heart failure (CHF), high altitude sickness, and primary central sleep apnea syndrome[1] CSAS due to obstructive sleep apnea (OSA) and Cheyne-Stokes respiration (CSR) commonly occur in CHF patients due to insufficient respiratory effort followed by hyperventilation.[1] The prevalence of CSR is 30% to 40% in patients with CHF.[1] Continuous positive airway pressure (CPAP) therapy reduces the apnea-hypopnea index (AHI), improving LVEF.[2] Complex sleep apnea (CompSA) or CPAP-emergent central apneas occur in patients with OSA when CPAP is started, constituting 6% to 20% of OSA patients.[3] While evidence suggests that CSAS and CSR may confer higher morbidity and mortality in CHF patients, some patients do not respond or tolerate conventional CPAP or bi-level positive airway pressure (BiPAP) therapy.[1]

Adaptive servo ventilation (ASV) devices generate PAP with variable pressure in response to a patient's expiration.[4] The expiratory positive airway pressure (EPAP) is titrated manually to eliminate SDB.[4] The pressure support varies, increasing with hypopnea and decreasing with hyperventilation.[3] The backup rate is set either by clinical judgment or automatically.[3] If spontaneous breathing does not occur by a set time, a mandated breath is delivered to prevent apnea.[3] In advanced ASV devices, SDB is corrected by EPAP automatically adjusted using algorithms.[3]

This review summarizes the clinical effectiveness, cost-effectiveness, guidelines and recommendations regarding ASV versus conventional CPAP or BiPAP for patients with sleep apnea or CHF.

RESEARCH QUESTIONS

1. What is the comparative clinical effectiveness of adaptive servo ventilation compared with continuous positive airway pressure, bi-level positive airway pressure or adaptive servo ventilation with a different machine for adults with sleep apnea or congestive heart failure?

2. What is the cost-effectiveness of adaptive servo ventilation compared with continuous positive airway pressure or bi-level positive airway pressure for adults with sleep apnea or congestive heart failure?

3. What are the evidence-based guidelines regarding the use of adaptive servo ventilation for the treatment of adults with sleep apnea or congestive heart failure?

KEY MESSAGE

The evidence suggests that ASV is effective in treating sleep apnea and CHF compared with CPAP or BiPAP. No evidence was found regarding the cost-effectiveness of ASV.

METHODS

Literature Search Strategy

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2012, Issue 7), ECRI (Health Devices Gold), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. No filters were applied to limit the retrieval by study type. The search was also limited to English language documents published between January 1, 2007 and July 4, 2012.

Selection Criteria and Methods

One reviewer screened citations to identify health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies, economic evaluations and guidelines on ASV for sleep apnea or CHF. Potentially relevant articles were ordered based on titles and abstracts, where available. One reviewer considered full-text articles for inclusion according to the selection criteria listed in Table 1.

Table 1. Selection Criteria

Population	Adults with central sleep apnea (CSA) or complex sleep apnea (CompSA), or with congestive heart failure (CHF)
Intervention	Adaptive servo ventilation (ASV) (e.g. Respironics AutoSV, ResMed ASV)
Comparator	Continuous positive airway pressure (CPAP), bi-level positive airway pressure (BiPAP), adaptive servo ventilation (ASV) (one machine versus another)
Outcomes	Improvement in apnea-hypopnea index (AHI), Epworth sleepiness scale, hospitalizations or survival
Study Designs	Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials (RCT), non-randomized studies, economic evaluations and guidelines

Exclusion Criteria

Articles were excluded if they did not satisfy the selection criteria, if they had incomplete methods, were included in a selected systematic review, were narrative reviews or case reports.

Critical Appraisal of Individual Studies

A critical appraisal of the included studies was performed based on study design. Systematic reviews were assessed using the Assessment of Multiple Systematic Reviews (AMSTAR) criteria.[5] Randomized and non-randomized studies were assessed for quality using the Down's and Black instrument.[6] Instead of calculating numeric scores, the strengths and limitations of the studies were described. Clinical practice guidelines were assessed using the Appraisal of Guidelines for Research and Evaluation (AGREE) criteria.[7]

SUMMARY OF EVIDENCE

Quantity of Research Available

The literature search yielded 366 citations. Upon screening titles and abstracts, nine potentially relevant articles were retrieved for full-text review. No additional potentially relevant reports were identified from grey literature or hand searching. Of the nine potentially relevant reports, three were contained in the selected systematic review, and two contained irrelevant populations. Four publications were included in this review. The process of study selection is outlined in the PRISMA flowchart (Appendix 1).

A summary of the study characteristics, critical appraisal and study findings for systematic reviews, RCTs and non-randomized studies can be found in Appendices 2, 3 and 4, respectively. Also, grading of recommendations and levels of evidence, guidelines and recommendations on ASV, and critical appraisal of guidelines are summarized in Appendices 5, 6, and 7 respectively.

Clinical Effectiveness and Recommendations on ASV for Sleep Apnea and CHF

Summary of Study Characteristics

The clinical effectiveness and evidence-based recommendations regarding ASV for sleep apnea and CHF were reported in one systematic review,[2] a RCT,[3] a non-randomized study[4] and a guideline.[1] The systematic review assessed the effectiveness of ASV for the treatment of SDB in HF patients.[2] A RCT compared the effectiveness of BiPAP autoSV Advanced with the conventional BiPAP autoSV for the treatment of CSA.[3] A non-randomized retrospective analysis compared the effectiveness and compliance of VPAP-AdaptSV® and BiPAP-AutoSV® for the treatment of CompSA.[4] An American Academy of Sleep Medicine (AASM) guideline reported evidence-based recommendations regarding ASV for the treatment of CHF-related CSAS.[1] All reports in this review were published in the United States between 2011[1,3,4] and 2012.[2]

1. Clinical Effectiveness on ASV for Sleep Apnea and CHF

Systematic Review

A systematic review and meta-analysis identified 14 studies that compared ASV with control conditions in 538 HF patients.[1] Control groups involved no treatment, poor compliance with ASV, sub-therapeutic ASV, CPAP, BiPAP, and nasal oxygen. Overall, 88% of patients were male, ranging in age from 39 to 75 years.[2] Changes in AHI for ASV and control groups were meta-analysed from seven parallel studies.[2] Changes in LVEF, quality of life (QoL), walking test and oxygen consumption were also measured.[2]

RCTs and non-randomized studies

A prospective, multicentre RCT compared the effectiveness of advanced SV (Advanced BiPAP autoSV) with conventional SV(BiPAP autoSV) for treating CSA.[3] Thirty-seven consecutive patients were randomly assigned to two full-night polysomnographies (PSGs) while treated with the previously marketed autoSV or the new autoSV Advanced device.[3] The studies were blinded and centrally scored to report AHI and central apnea index (CAI).[3]

A non-randomized study compared compliance with VPAP-AdaptSV® and BiPAP-AutoSV® for the treatment of CompSAS.[4] Seventy-six consecutive patients were retrospectively analyzed after undergoing VPAP-AdaptSV® or BiPAP-AutoSV® in a non-randomized parallel design study.[4] Effectiveness and compliance were assessed at four and six weeks of use.[4]

Summary of Critical Appraisal

Systematic Review

The systematic review and meta-analysis performed a comprehensive literature search based on pre-defined criteria.[2] While study selection was performed independently by two reviewers using explicitly defined criteria, it is unclear whether data extraction also was performed in duplicate.[2] Detailed study characteristics were provided for the included studies and publication bias was assessed.[2] A conflict of interest statement was provided and the review was independent of industry funding.[2]

RCTs and non-randomized studies

The RCT explicitly described the research question, eligibility criteria, intervention, comparator, outcomes, and finding.[3] While consecutive patients were randomized to BiPAP autoSV Advanced or conventional BiPAP autoSV, the method of randomization was not reported.[3] Participants were blinded to treatment and the studies were scored blindly at a central location in order to reduce the risk for information bias.[3] The study was industry sponsored.[3]

The non-randomized study explicitly described the research question, eligibility criteria, outcomes and findings; however, differences between VPAP-AdaptSV® and BiPAP-AutoSV® devices were not described.[4] There is potential for information bias as the study was not randomized, and patients and assessors were not blinded to treatment. The choice of device was at the discretion of the managing physician or based on availability of device.[4] The findings are representative of the entire population from which they were recruited and drop outs were treated as non-compliers.[4]

Summary of Findings

Systematic Review

In the systematic review, a meta-analysis of seven studies showed that ASV improved AHI (weighted mean difference [WMD]: -14.64 events per hour, 95% confidence interval [CI] -21.03, -8.25, p=0.0001) and LVEF (LEVF: 0.40, 95% CI, 0.08, 0.71; p=0.1) in HF patients.[2] ASV significantly improved six minute walk test compared with control groups based on a meta-analysis of two parallel studies involving 145 patients (WMD: 32.82, 95% CI 4.21, 61.42, p=0.02).[2] No significant differences in QoL or maximal oxygen consumption were found between ASV and control conditions.[2]

RCTs and non-randomized studies

The RCT showed that BiPAP autoSV Advanced was more effective than conventional BiPAP autoSV for the treatment of SDB in CSA patients.[3] AHI during BiPAP autoSV Advanced was significantly lower than AHI during BiPAP autoSV and CPAP nights across four nights of study (6±6 versus 10±10, p<0.001).[3] The central apnea index decreased significantly during BiPAP autoSV Advanced compared to BiPAP autoSV (0.6±1 versus 3±4, p<0.001)[3] The reduction in AHI was associated with improved oxygen saturation.[3]

The non-randomized retrospective analysis suggested that VPAP-Adapt® and BiPAP-AutoSV® are comparable in controlling CompSAS.[4] BiPAP-AutoSV® recipients had significantly higher AHI index than VPAP-AdaptSV® recipients (49 per hour [28-60] versus 35 per hour [19.5-49.5], p<0.0001).[4] Compliance was comparable between groups. At four to six week follow-up, 56 patients (74%) were using their device.[4] Mean nightly use was five hours for the VPAP-AdaptSV® group and six hours for BiPAP-AutoSV® group (p=0.081).[4] Improvements in Epworth Sleepiness Scale (ESS) scores were higher in the BiPAP-AutoSV® group than in the VPAP-AdaptSV® group (4 [1-9] versus 2.5 [0-5], p=0.02).[4]

2. Cost-Effectiveness of ASV for Sleep Apnea and CHF

No economic evaluations were found regarding ASV for sleep apnea and CHF.

3. Guidelines and Recommendations on ASV for Sleep Apnea and CHF

Summary of Study Characteristics

The AASM recently developed evidence-based recommendations regarding ASV for the treatment of CHF-related CSAS.[1] The purpose of the practice parameter was to review the available evidence for the management of CSAS in adults and determine the most effective treatment option.[1] Many of the recommendations are based on studies that used AHI and LVEF as outcome measures.[1] A total of 77 articles were reviewed, graded and extracted.[1] The practice parameters were developed by the Standards of Practice Committee of the AASM and approved by the Board of Directors.[1]

Summary of Critical Appraisal

The AASM clearly described the objective, clinical questions and target populations for the guideline.[1] The guideline was based on a comprehensive literature search but was limited to

English language articles.[1] The criteria whereby studies were included and assessed for quality were reported but details of expected health benefits were not.[1] Recommendations were evidence-based and externally reviewed.[1] While no barriers to implementation or criteria for audit were provided, the guidelines will be reviewed, updated and revised as new information becomes available.[1] The guideline was independent of industry funding.[1]

Summary of Findings

The AASM guideline recommends that ASV be targeted to normalize AHI for treating CHF-related CSAS.[1] While the overall quality of evidence for ASV is moderate and there is no long term data, there are sufficient data to demonstrate improvement in AHI and LVEF.[1] One study suggested overall better compliance with ASV compared with CPAP.[1] The generalizability of these findings is limited in that most studies were industry sponsored and different manufacturers used different algorithms to detect respiratory events and determine characteristics of pressure delivery.[1] There is uncertainty regarding what the optimal settings should be based on an overall limited experience with using these devices.[1] While ASV costs more and is not as widely available as CPAP, the data for ASV are comparable if not better than data supporting CPAP use.[1] A summary of the clinical evidence and evidence-based recommendations regarding ASV versus conventional CPAP or BiPAP for sleep apnea and CHF is found in Table 2.

Table 2. Summary of the Clinical Effectiveness, Cost-Effectiveness, Guidelines and Recommendations on ASV for Adults with Sleep Apnea or CHF

Intervention	Evidence	Results
Clinical Effectiveness of ASV for Adults with Sleep Apnea or CHF		
ASV	1 systematic review[2]	• ASV significantly reduced AHI and improved cardiac function in patients with CHF and SDB compared to no treatment, sub-therapeutic ASV, CPA, BiPAP or oxygen.[2]
BiPAP autoSV Advanced	1 RCT[3]	• BiPAP autoSV Advanced was more effective than conventional BiPAP autoSV in treating SDB in patients with CSA.[3]
VPAP-AdaptSV®	1 non-randomized study[4]	• BiPAP-AutoSV® and VPAP-AdaptSV® were comparable in controlling CSA and compliance is high.[4] • BiPAP-AutoSV® recipients has significantly higher AHI and improved ESS scores compared to VPAP-AdaptSV® recipients.[4] • At four to six weeks, 74% of patients were using their device; mean nightly use of 6 hours and 5 hours in BiPAP-AutoSV® and VPAP-AdaptSV® users, respectively.[4]
Guidelines and Recommendations on ASV for Adults with Sleep Apnea or CHF		
ASV	AASM[1]	• ASV to normalize AHI is indicated for treating CHF-related CSAS.[1] • Generalizability of these findings are limited in that most studies were use different algorithms to detect respiratory events and deliver air pressure so there is uncertainty about optimum settings.[1] • While ASV costs more and is not as common as CPAP, data for ASV are consistent and comparable if not better than that supporting CPAP use.[1]

AASM: American Academy of Sleep Medicine; AHI: apnea-hypopnea index; ASV: adaptive servo ventilation; BiPAP: bi-level positive airway pressure; CHF: congestive heart failure; CPAP: continuous positive airway pressure; CSA: central sleep apnea; SDB: sleep disordered breathing

Limitations

The evidence included in this review has inherent limitations that restrict its usefulness in drawing conclusions about the clinical and cost-effectiveness and recommendations on ASV versus conventional CPAP or BiPAP for sleep apnea and CHF. Most studies reviewed in this report or included in the systematic review were industry funded. The RCT and non-randomized study may suffer from information bias as the RCT did not report the method of randomization[3] and devices were prescribed at the discretion of the managing physician or based on availability in the non-randomized study.[4] No evidence was found regarding the cost-effectiveness of ASV for the treatment of sleep apnea and CHF. While one guideline reported evidence-based recommendations on the use of ASV for CHF-related CSAS, its generalizability is limited in that there is uncertainty about the optimal settings for device use.[1]

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

One systematic review,[2] a RCT,[3] a non-randomized study[4] and one guideline[1] suggest that ASV is effective in treating sleep apnea and CHF compared with CPAP or BiPAP. In CHF patients with SDB, ASV significantly reduces AHI and improves cardiac function compared with no treatment, sub-therapeutic ASV, CPAP, BiPAP or oxygen based on a meta-analysis of seven studies.[2] BiPAP autoSV Advanced was more effective than conventional BiPAP autoSV for reducing AHI and treating SDB in CSA patients according to an RCT.[3] A non-randomized retrospective analysis suggests both VPAP-Adapt® and BiPAP-AutoSV® offer high compliance and are effectiveness in controlling CompSAS.[4] No evidence was found regarding the cost-effectiveness of ASV versus conventional CPAP or BiPAP for sleep apnea and CHF. Guidelines by the AASM recommend that ASV be targeted to normalize AHI for treating CHF-related CSAS. The generalizability of these findings is limited as most studies were industry sponsored and there is uncertainty regarding the optimal settings for use.[1] While ASV costs more and is not as widely available as CPAP, the data for ASV are comparable to that supporting CPAP use.[1]

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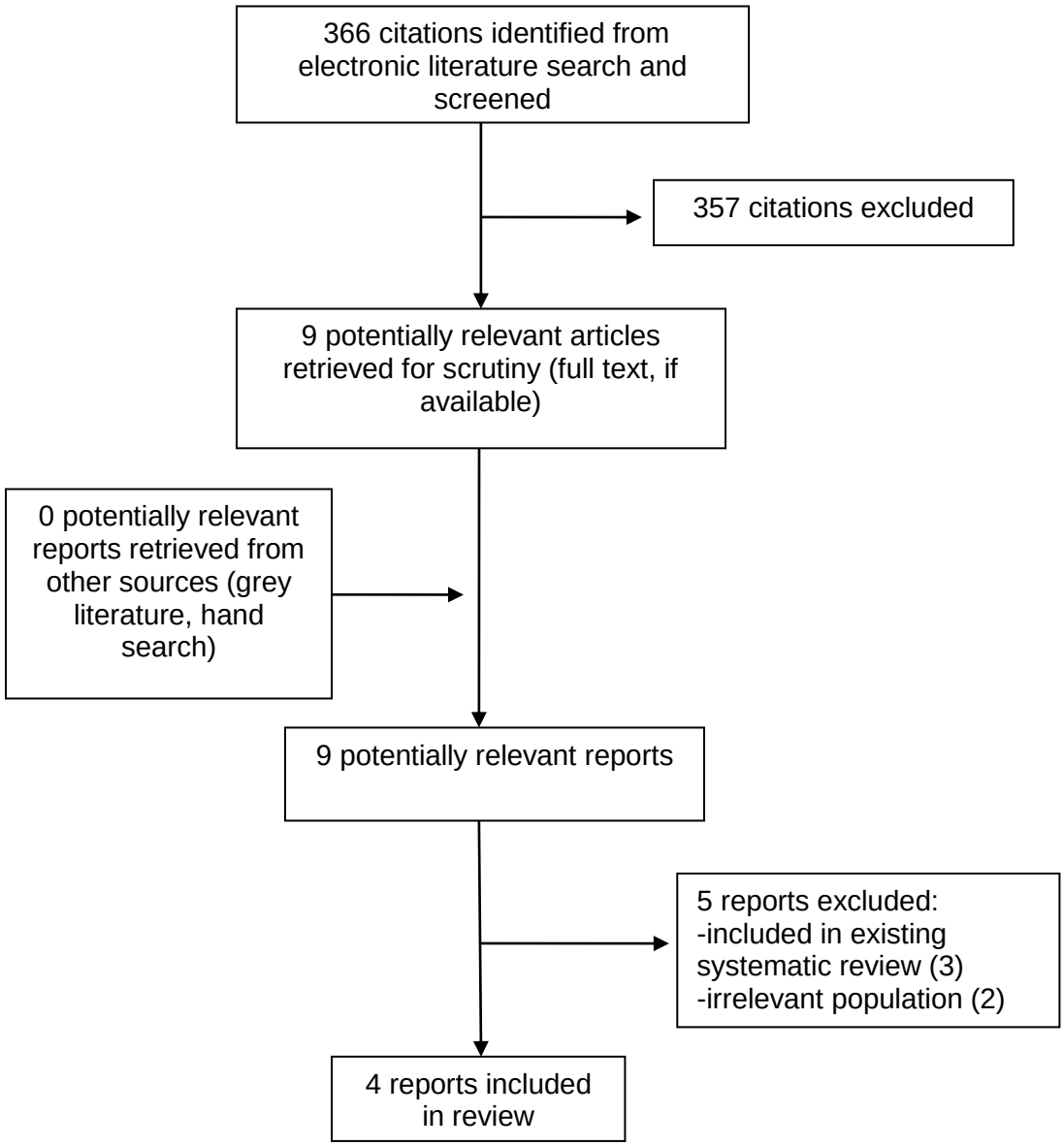
APPENDIX 1: Selection of Included Studies



APPENDIX 2: Summary of Study Characteristics

First Author, Publication Year Country	Study Design	Patient Characteristics	Intervention	Comparator	Clinical Outcomes Measured
Clinical Effectiveness of ASV for Adults with Sleep Apnea or CHF					
Systematic Reviews and Meta-analyses					
Sharma[2] 2012 United States	Systematic review 14 included studies: 4 no treatment, 3 poor compliance ASV, 1 sub-therapeutic ASV, 3 CPAP, 1 BiPAP, 2 oxygen (ranging 1-12 months duration)	Adults with CHF (N=538, 88% M, ranging 39-75 years)	ASV	Control: no treatment, sub-therapeutic ASV, CPAP, BiPAP, oxygen	Changes in AHI, LVEF, QoL, 6 minute walk, maximal oxygen consumption
Randomized Controlled Trials (RCTs)					
Javaheri[3] 2011 United States	Prospective, MC, RCT	Adults with CSA with AHI ≥15/h: 16 HT, 6 AF, 6 CAD, 2 CHF, 2 PM, 6 DM (n=37, 86% M, mean age: 63±11 years)	Advanced servo ventilator (BiPAP autoSV Advanced)	Conventional servo ventilator (BiPAP autoSV)	AHI, CAI
Non-Randomized Studies					
Kuzniar[4] 2011 United States	Non-randomized parallel design, retrospective cohort study	Adults with CSA (N=76, 35 VPAP-AdaptSV®, 41 BiPAP-AutoSV®, 80% M, ranging 53-78 years)	VPAP-AdaptSV® (ResMed Corp, San Diego, CA)	BiPAP-AutoSV® (Respironics, Murraysville, PA)	AHI, compliance, ESS score

AF: atrial fibrillation; AHI: apnea-hypopnea index; ASV: adaptive servo ventilation; BiPAP: bi-level positive airway pressure; CAD: coronary artery disease; CHF: congestive heart failure; CPAP: continuous positive airway pressure; CSA: central sleep apnea; DM: diabetes mellitus; ESS: Epworth Sleepiness Scale score; HT: hypertension; LVEF: left ventricular ejection fraction; M: male; MC: multicentre; QoL: quality of life; VPAP: variable positive airway pressure

APPENDIX 3: Summary of Critical Appraisal

First Author, Publication Year	Strengths	Limitations
Clinical Effectiveness of ASV for Adults with Sleep Apnea or CHF		
Systematic Reviews and Meta-Analyses		
Sharma[2] 2012 United States	• Comprehensive literature search based on pre-defined criteria • Study type inclusion criteria were explicitly defined • Study selection was performed by two independent reviewers • Article selection process included a literature exclusion flow chart • Detailed study characteristics were provided for included studies • Publication bias was assessed • Conflict of interest statement • Funding independent of industry	• Unclear if data extraction was performed in duplicate
Randomized Controlled Trials (RCTs)		
Javaheri[3] 2011 United States	• Explicitly described research question, eligibility criteria, intervention, outcomes and findings • Patients were randomized to two consecutive attended titration PSGs with either BiPAP autoSV Advanced or conventional BiPAP autoSV • Participants were blinded to treatment • Studies were scored blindly at a central location	• The method of randomization in not reported. • Industry funded
Non-Randomized Studies		
Kuzniar[4] 2011 United States	• Explicitly described research question, eligibility criteria, outcomes and findings • Findings are representative of the entire population from which they were recruited • Patients unavailable for follow-up were treated as non-compliers	• Differences between VPAP-AdaptSV® and BiPAP-AutoSV® were not described • Non-randomized, non-blind, comparison of two SV units • Choice of device used was at the discretion of the managing physician • If no device was specified, choice was made by technician based on availability of device • Unclear whether industry sponsored

BiPAP: bi-level positive airway pressure; PSG: polysomnography; SV: servo ventilation; VPAP: variable positive airway pressure

APPENDIX 4: Summary of Findings

First Author, Publication Year	Main Study Findings	Authors' Conclusions
Clinical Effectiveness of ASV for Adults with Sleep Apnea or CHF		
Systematic Reviews and Meta-Analyses		
Sharma[2] 2012	• Fourteen studies were identified.[2] • ASV significantly reduced AHI compared with control conditions according to seven parallel studies (n=352) (WMD: -14.64 events/h, 95% CI -21.03, -8.25, p=0.0001)[2] • ASV significantly improved cardiac function compared with control conditions according to 10 parallel studies (n=385) (WMD: 0.40, 95% CI 0.08, 0.71; p=0.01).[2] • ASV significantly improved 6 minute walk test compared with control according to two parallel studies (n=145) (WMD: 32.82, 95% CI 4.21, 61.42; p=0.02).[2] • No significant difference in the change in SF-36 Energy-Vitality scores was found between ASV and control conditions (WMD: 10.5 NS favouring ASV, 95% CI -2.37, 23.36; p=0.11).[2] • No significant difference in the change in maximal oxygen consumption was found between ASV and control conditions (WMD: 10.14, NS favouring ASV, 95% CI -0.09 20.38; p=0.051).[2] • No evidence of publication bias was found	• "In patients with CHF and SDB, ASV is more efficacious than control conditions in reducing the AHI and improving cardiac function and exercise capacity." (pg 3)[2] • "These data provide a compelling rationale for large-scale RCTs to assess the clinical impact of ASV on hard outcomes in these patients."(pg 3)[2]
Randomized Controlled Trials (RCTs)		
Javaheri[3] 2011	• AHI during BiPAP autoSV Advanced was significantly lower than SHI during BiPAP autoSV and CPAP nights across four nights of study (6±6 versus 10±10, p<0.001).[3] • CAI decreased significantly during BiPAP autoSV Advanced compared with BiPAP autoSV (0.6±1 versus 3±4, p<0.001).[3] • The reduction in AHI was associated with improved oxygen saturation.[3]	• "BiPAP autoSV Advanced was more effective than conventional BiPAP autoSV in the treatment of sleep disordered breathing in patients with CSA." (pg 1693)[3] • "In this short-term, randomized, crossover, single-night, efficacy study involving patients with CSA, BiPAP autoSV Advanced resulted in more effective treatment of both central and obstructive events." (pg 1698)[3] • "We speculate both the automated back-up rate and the automated EPAP determination features conferred such superiority

First Author, Publication Year	Main Study Findings	Authors' Conclusions
		to conventional servo ventilation." (pg 1698)[3] • "Long-term cardiovascular or mortality event driven studies are needed to determine the impact of such new technology on QoL, morbidity and mortality." (pg 1698)[3]
Non-Randomized Studies		
Kuzniar[4] 2011	• BiPAP-AutoSV® recipients had a significantly higher AHI index during their CPAP titration study than VPAP-AdaptSV® recipients [49/h (28-60) versus 35/h (19.5-49.5), p<0.0001].[4] • At 4-6 week follow-up, 56 patients (74%) were using their device.[4] • Mean nightly use was 5.0 h (2.8-6.4) for VPAP-AdaptSV® group and 6.0 h (3.5-7.2) for BiPAP-AutoSV® group (p=0.081).[4] • Improvements in ESS scores were higher in the BiPAP-Auto SV® group than in the VPAP-AdaptSV® group [4 (1-9) versus 2.5 (0-5), p=0.02].[4]	• "Our retrospective data indicate that the two SV devices are comparable means of controlling CSA and compliance is high." (pg 538)[4] • "While ongoing research will better define the phenotypes of patients now grouped as "CSA" and delineate the role of SV in treating CompSAS, our data indicate that both devices are effective acute and medium term treatment options."(pg 540)[4]

AHI: apnea hypopnea index; ASV: adaptive servo ventilation; BiPAP: bi-level positive airway pressure; CAI: central apnea index; CHF: congestive heart failure; CI: confidence interval; CompSAS: complex sleep apnea syndrome; CSA: central sleep apnea; EPAP: expiratory positive airway pressure; h: hour; QoL: quality of life; RCT: randomized controlled trial; SDB: sleep disordered breathing; SV: servo ventilation; WMD: weighted mean difference; VPAP: variable positive airway pressure

APPENDIX 5: Grading of Recommendations and Levels of Evidence

<table>
<tr><th>Guideline Society or Institute, Publication Year, Country</th><th>Recommendation</th><th colspan="4">Overall Quality of Evidence</th></tr>
<tr><td rowspan="3">AASM[1]
2012
United States</td><td rowspan="2">“Final Standards of Practice Recommendations</td><td colspan="4">GRADE Approach to Rating Quality of Evidence</td></tr>
<tr><td>High[a]
⊕⊕⊕⊕+</td><td>Moderate[b]
⊕⊕⊕O+</td><td>Low[c]
⊕⊕OO+</td><td>Very Low[d]
⊕OOO+</td></tr>
<tr><td colspan="2">RCTs
Lower if risk of bias or inconsistency
Higher if large effect or dose response</td><td colspan="2">Observational studies
Lower if indirectness, imprecision/publication bias
Higher if residual confounding would reduce a demonstrated effect or suggest spurious effect if no effect was observed</td></tr>
<tr><td>Benefits clearly outweigh harm/burden
Benefits closely balanced with harm/burden
OR
Uncertainty in the estimates of benefit/harm/burden
Harm/burden clearly outweighs benefits” (pg 21)[1]</td><td>Standard

Guideline

Standard</td><td>Standard

Guideline

Standard</td><td>Guideline

Option

Standard</td><td>Option

Option

Standard</td></tr>
</table>

AASM: American Academy of Sleep Medicine; GRADE: Grading of Recommendations Assessment, Development and Evaluation; RCTs: randomized controlled trials
High[a]: Highly confident true effect lies close to the estimate of effect
Moderate[b]: Moderately confident true effect is likely close to estimate of effect but possibility it is different
Low[c]: Limited confidence in effect estimate, true effect may be substantially different from estimate of effect
Very Low[d]: Little confidence in effect estimate, true effect likely substantially different from estimate of effect

APPENDIX 6: Summary of Critical Appraisal of Guidelines Using AGREE

Guideline Society or Institute, Publication Year	Strengths	Limitations
AASM[1] 2012	• Objective, clinical questions and target populations are described • Relevant professional groups • Literature search was comprehensive for 1966 to June 2010, limited to English language • Inclusion/exclusion criteria were defined • Appraisal using GRADE • Recommendations are evidence based • Externally reviewed • Plan to update guidelines was described • Project was funded independently from industry	• Details of expected health benefits • Guideline was not pilot tested among target users • No implementation tools • No discussion of organizational barriers or audit criteria

AASM: American Academy of Sleep Medicine: GRADE: Grading of Recommendations Assessment, Development and Evaluation

APPENDIX 7: Guidelines and Recommendations

Guideline Society or Institute, Publication Year	Recommendations
AASM[1] 2012	1. "ASV targeted to normalize the AHI is indicated for the treatment of CSAS related to CHF [Standard]." (pg 27)[1] • "The overall quality of evidence for ASV is moderate. • While there is no survival or long-term data available for ASV at this time, there is a sufficient amount of data consistently demonstrating improvement in both the AHI and LVEF. • There was a study suggesting overall better compliance with ASV compared with CPAP. • Most of the available studies are industry sponsored, and different manufacturers utilize different algorithms to detect respiratory events and determine characteristics of pressure delivery. Therefore, generalizability is not possible or appropriate. • There is uncertainty as to what are the optimum settings, reflecting an overall lack of experience with using these devices. • The cost of these devices is several-fold greater than the cost of CPAP, and availability is not universal. Nonetheless, the data for ASV is consistent and is at least comparable if not better than the data supporting CPAP use." (pg 27)[1]

AASM: American Academy of Sleep Medicine; ASV: Adaptive servo ventilation; CHF: congestive heart failure; CPAP: continuous positive airway pressure; CSAS: central sleep apnea syndrome