Australian Government

Department of Health and Ageing

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National Horizon Scanning Unit
Horizon scanning report

The Pillar procedure: For the treatment of obstructive sleep apnoea and snoring

September 2006

AHTA

Adelaide Health Technology Assessment

Online ISBN: 1 74186 126 8
Publications Approval Number: 3940

Electronic copies can be obtained from http://www.horizonscanning.gov.au

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The production of this *Horizon scanning report* was overseen by the Health Policy Advisory Committee on Technology (HealthPACT), a sub-committee of the Medical Services Advisory Committee (MSAC). HealthPACT comprises representatives from health departments in all states and territories, the Australia and New Zealand governments; MSAC and ASERNIP-S. The Australian Health Ministers' Advisory Council (AHMAC) supports HealthPACT through funding.

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Executive Summary

The Pillar® palatal implant system is designed to treat patients suffering from obstructive sleep apnoea or excessive snoring. The procedure involves the implantation of three small (18mm) polyethylene inserts, which are permanently implanted at the junction of the hard and soft palate. The procedure is easily performed in a clinic setting under local anaesthetic. This procedure could be easily performed in rural and remote settings, but does, however, require a trained ear, nose and throat surgeon to conduct the procedure which may limit the accessibility of this population. Time taken to perform the procedure is short and patients report only mild discomfort after the procedure and resume normal work and eating activities immediately after the procedure. In addition, no detrimental changes in speech or the ability to swallow were noted after implantation.

Obstructive sleep apnoea is the partial reduction (hypopnoea) or the complete cessation (apnoea) of airflow, which occurs during sleep as a result of pharyngeal narrowing or collapse. Obstructive sleep apnoea is associated with disrupted sleep, loud snoring and episodes of apnoeas, whilst both apnoea and hypopnoea are associated with hypoxaemia and arousal. In addition, obstructive sleep apnoea has been linked to an increased risk of cardiovascular disease, including hypertension, myocardial infarction, stroke and motor vehicle accidents.

Mild obstructive sleep apnoea has been estimated to affect approximately 20 per cent of the population, with prevalence two to three times higher in males than in females. More severe obstructive sleep apnoea has been estimated to affect between 2-4 per cent of men and 1-2 per cent of women in Western countries. Given the current population of 20.5 million, it is likely that OSA syndrome affects between 410,000 and 820,000 males, and between 205,000 and 410,000 females, in Australia.

Current treatment options for obstructive sleep apnoea include lifestyle modifications (eg weight loss), invasive surgical procedures or the "gold standard", continuous positive airways pressure. Continuous positive airways pressure involves the delivery of positive air at a predetermined pressure through either a nose or full-face mask, worn throughout the night. Continuous positive airways pressure only treats the symptoms of obstructive sleep apnoea and is *not curative,* therefore it must be worn indefinitely, which may lead to compliance issues.

The Pillar® palatal implant system appears to be safe with few adverse events associated with the procedure reported. The partial extrusion of the implants was the most common adverse event. This seems to cause little pain, physical damage or inconvenience to patients and was rectified by the removal of the implant with or without local anaesthetic. In the majority of cases the extruded implants were

replaced, however some patients experienced resolution of their symptoms without re-implantation.

The Pillar® palatal implant system leads to statistically significant improvements in symptoms when used for the treatment of patients who suffer from *either* obstructive sleep apnoea or excessive snoring. A statistically significant reduction in the number of objectively measured apnoea/hypopnoea episodes (AHI), and the subjectively measured outcomes of daytime sleepiness and snoring, was observed in patients with obstructive sleep apnoea. The reduction in AHI is of great importance in this patient group. Although the reduction in AHI was reported to be statistically *significant,* it should be noted that AHI levels at follow-up were *high* (range 9 to 28) with *large* standard deviations. This not only indicates a great deal of variation within the group but as *AHI levels of 5-10 are considered abnormal,* casts doubt on whether Pillar® implantation delivers a clinical benefit to patients. One study highlighted that the Pillar® procedure was more effective in patients who underwent adjunctive surgical procedures and for those with only *mild* not moderate obstructive sleep apnoea.

All snoring studies reported a statistically significant reduction in snoring levels. If a subjective improvement is defined as a 50 percent reduction in the level of snoring, most studies achieved a measure of clinical success. In addition, daytime sleepiness was significantly reduced in the snoring studies; however values for this parameter were low at baseline.

There are currently no cost-effectiveness data available on the use of the Pillar® palatal implant system for the treatment of patients with obstructive sleep apnoea. The Pillar® implants cost approximately $1,600. An additional cost for the surgeon to perform the procedure, which is not covered by the MBS, may increase the total cost of the procedure to approximately $2,000.

The consequences of sleep disorders may be costly in economic terms and lives lost, as a result of transport and workplace accidents, lost productivity and health costs from co-morbidities, including inappropriate use of sleep medications and an increased use of medical resources. Estimated costs to the Australian community for sleep disorders range from $3-7 billion per year.

Further investigation is required to establish which patients (mild or moderate obstructive sleep apnoea) would benefit the most from this procedure, and whether greater success would be achieved in conjunction with more invasive surgical procedures. In addition, long term follow-up of obstructive sleep apnoea patients may indicate whether or not the observed reductions in AHI delivered a clinical benefit to these patients.

HealthPACT Advisory

The pillar procedure is a minor surgical procedure for the treatment of obstructive sleep apnoea in adults and involves the insertion of three small implants into the soft palate resulting in scarring and therefore stiffening of the palate that results in reduced palatal movement. The procedure is relatively safe although extrusion of the implants can occur.

It appears to be effective in reducing both snoring and daytime sleepiness, although this is based on level IV evidence (predominantly case series). Of note though, is that although the procedure results in a statistically significant reduction in the rate of obstructive sleep apnoea episodes, as measured by the AHI (apnoea - hypoapnoea index), it does not reduce the rate of these episodes to a level which would be considered normal, ie an AHI of less than five .

At this stage further studies are required to determine its effectiveness in treating sleep apnoea compared to CPAP or other surgical interventions. As the treatment provides a permanent effect and avoids the use of CPAP there is likely to be a strong patient preference for the pillar procedure, as well as possible cost savings should it be found to be as effective as CPAP. At this stage the procedure cannot be recommended and should be reviewed in 12-months.

Introduction

The National Horizon Scanning Unit, Discipline of Public Health, University of Adelaide, on behalf of the Medical Services Advisory Committee (MSAC), has undertaken an Horizon Scanning Report to provide advice to the Health Policy Advisory Committee on Technology (Health PACT) on the state of play of the introduction and use of the Pillar® palatal implant system (Register ID number 224).

Restore Medical Inc provides the Pillar® palatal implant system for the treatment of patients with obstructive sleep apnoea. This technology would be offered through an otorhinolarynologist or specialist sleep disorder clinics and is currently in limited use in Australia and New Zealand.

This Horizon Scanning Report is intended for the use of health planners and policy makers. It provides an assessment of the current state of development of the Pillar® palatal implant system, its present use, the potential future application of the technology, and its likely impact on the Australian health care system.

This Horizon Scanning Report is a preliminary statement of the safety, effectiveness, cost-effectiveness and ethical considerations associated with the Pillar® palatal implant system for the treatment of obstructive sleep apnoea.

Background

Description of the technology

The procedure

It has been suggested that one of the major factors contributing to OSA and snoring is soft palate tissue. Although OSA is caused by the collapse of the airway, which can occur at various sites of the airway, snoring is caused by the vibration of the soft palate. The Pillar® palatal implant system has been designed to achieve palatal stiffening, reducing vibration by inducing fibrosis and submucosal scarring of the palate. Wind tunnel modelling established that once the palate was stiffened, then an increase in critical air speed would be required to initiate palate movement of vibration. Therefore with stiffening of the palate, movement of the palate is reduced, resulting in a reduction in snoring and the ability of the soft palate to obstruct the airway (Restore Medical Inc 2006).

The Pillar® palatal implant system involves the permanent placement of three small inserts (18mm in height) at the junction of the soft and hard palate (Figure 1). The inserts are made of woven polyethylene terephthalate (Figure 2), which has favourable characteristics for use as an implant in humans including

biostablility, promotion of tissue in-growth and a well characterised inflammatory response. The composition of the implants results in fibrous tissue formation after approximately four weeks but not the extrusion of the implant itself (Nordgard et al 2004; Restore Medical Inc 2006).

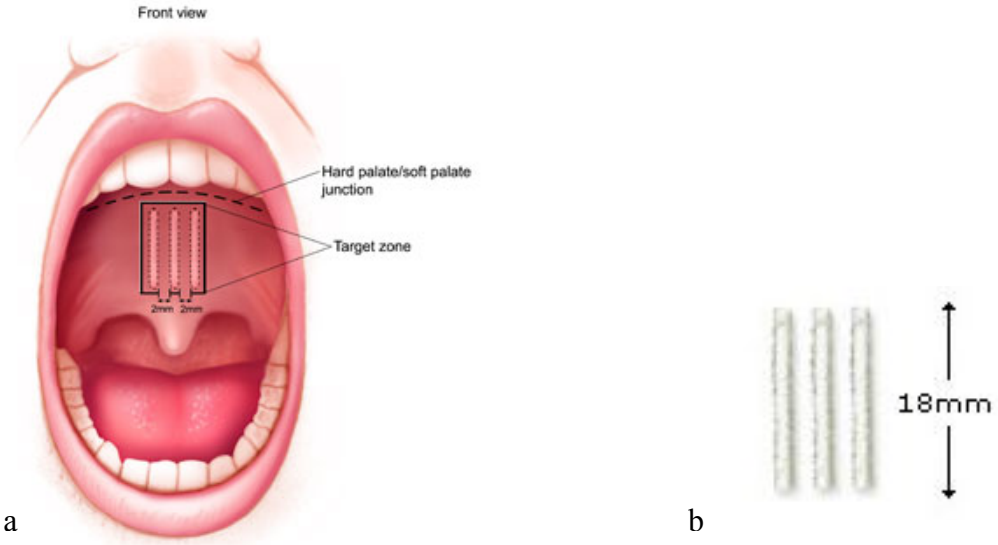

Figure 1 Implantation of the Pillar® system into the soft palate (a) and illustrating the size of the implants (b) (printed with permission Restore Medical).

Insertion of the Pillar® implants can be performed in the clinic under local anaesthesia (Xylocaine 20% spray) and does not require a hospital stay. The procedure is performed by an ear, nose and throat surgeon and takes approximately 15 minutes. The Pillar® implants are inserted into the palate via a sterile delivery tool (Figure 2). Each implant requires its own non-reusable delivery tool, which are disposed of in the same manner as medical sharps. Patients may resume normal diet and exercise on the same day, and should be prescribed antibiotics as a prophylaxis against infection and an anti-inflammatory medication if required (Nordgard et al 2004; Restore Medical Inc 2006).

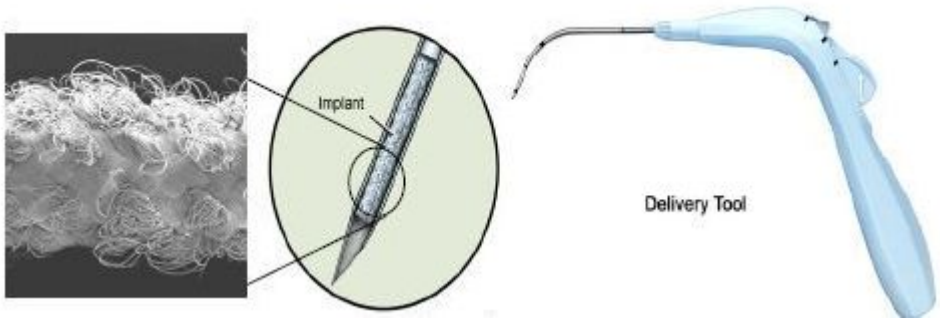

Figure 2 Schematic drawing of the Pillar® implant system (printed with permission Restore Medical).

Intended purpose

The Pillar® palatal implant system is intended to treat *adult* patients suffering from obstructive sleep apnoea (OSA). OSA was first described in 1965 and results from the intermittent obstruction of the upper airway. This syndrome may also be referred to as obstructive sleep apnoea –hypopnoea (OSAH). OSA is the partial reduction (hypopnoea) or the complete cessation (apnoea) of airflow, which occurs during sleep as a result of pharyngeal narrowing or collapse. In adults, apnoea is defined as the cessation of airflow for >10 seconds and hypopnoea is defined as ≥50% decrease in airflow. The symptoms of OSA include disrupted sleep, loud snoring, excessive daytime sleepiness , reduced neurocognitive function episodes of apnoeas. Both apnoea and hypopnoea are associated with hypoxaemia and arousal; however these episodes are more severe in apnoeas. All of these symptoms may result in a decreased quality of life for the patient and their family members (Lim et al 2006; Sundaram et al 2005). In addition, OSA has been linked to an increased risk of cardiovascular disease, including hypertension, myocardial infarction, stroke and the incidence of motor vehicle accidents (Cistulli & Grunstein 2005, Findlay et al 2000). A number of risk factors for OSA exist including ageing, family history, and obesity in adults and adenoidal-tonsillar hypertrophy in children (Pack 2006 489).

To diagnose OSA, patients undergo overnight polysomnographic recordings, usually in a sleep disorder laboratory. Readings taken include electroencephalogram, electrooculogram, electromyogram, respiratory airflow, respiratory effort and arterial oxygen saturation measurements. The number of apnoeas or hypopneas per hour of sleep is reported as the apnoea-hypopnoea index (AHI) and an AHI of 5-10 is considered abnormal (Shochat & Pillar 2003). Specifically, according to the peak international sleep medicine body, OSA severity is measured by the AHI cut points of >5 (mild), >15 (moderate), and >30 (severe). An AHI of 5 or less is deemed within normal limits and confers a negative diagnosis (or effective treatment) (Chesson et al 1997).

Clinical need and burden of disease

In Western countries, mild OSA has been estimated to affect approximately 20 per cent of the population, with prevalence two to three times higher in males than in females (Strohl & Redline 1996; Young et al 2002). In addition to male sex, other established risk factors for the condition include advanced age, menopause and obesity (Young et al 2002). Given the ageing population in Australia and increases in the prevalence of obesity, it is possible that the prevalence of OSA will continue to rise in the near future.

OSA and the presence of daytime sleepiness, commonly referred to as OSA syndrome, has been estimated to affect between 2-4 per cent of men and 1-2 per cent of women in Western countries (Stradling & Davies 2004; Young et al 2002).

Given the current population of 20.5 million [1], it is likely that OSA syndrome affects between 410,000 and 820,000 males, and between 205,000 and 410,000 females, in Australia. Although the condition is widely recognised, the majority of affected individuals remain undiagnosed. In a community survey of 4,925 adults in the United States, it was found that as many as 82 and 92 per cent of the men and women, respectively, were likely to have undiagnosed OSA syndrome (Young et al 1997).

As previously mentioned, OSA has been associated with a variety of negative health-related outcomes. It has been reported that patients with obstructive sleep apnoea are at a higher risk of experiencing automobile crashes, and that these crashes tend to be of a more severe nature (Findley et al 2000). There is also evidence to suggest that OSA has a causal role in the development of hypertension and cardiovascular disease (Young et al 2002). When comparing patients with untreated OSA to patients who had been treated for OSA with tracheostomy, an age-adjusted odds ratio of mortality due to cardiovascular disease of 4.9 was reported (Partinen et al 1988).

At present, the diagnosis of OSA requires patients to stay overnight at a sleeping laboratory. In 2001, an informal listing by the patient support group *'Sleep Disorders Australia'* identified a total of 79 adult (non-paediatric) clinical sleep laboratories across the country. Of these laboratories, 56 were in the private sector, 19 were in the public sector, while the remaining 4 contained a mixture of public and private beds (Pack 2006). During 2005, a total of 65,295 polysomnograms were performed by the combined sectors (HCP 2006). This figure may under-represent the number of OSA patients as sleep laboratories operate as outpatient clinics, therefore sleep studies conducted in these settings will not be recorded in hospital separation data.

In addition to lifestyle modifications, the standard method of treatment for more severe cases of OSA is continuous positive airway pressure, or in some cases bilevel positive airway pressure. Both treatments require overnight testing on the patient to determine an appropriate level of pressure. In Australia in 2003/2004, 10787 hospital separations for continuous positive airway pressure and 3267 separations for bilevel positive airway pressure testing were reported (AIHW 2006).

Stage of development

The Pillar® palatal implant system is manufactured by Restore Medical Inc (United States) and is distributed in Australia and New Zealand by Technology for Life Pty Ltd. The Pillar® system has been registered by the Australian Therapeutic Goods Administration (ARTG number 118161) in June 2005.

[1] Estimates obtained from the Australian Bureau of Statistics population clock, accessed on the 6th June (http://www.abs.gov.au/ausstats/abs@.nsf/)

Since August 2005, approximately 230 patients have been implanted with the Pillar® system in Australia, with a smaller number of patients treated in New Zealand. Implantation of the Pillar® system is currently being carried out in approximately 34 private practices throughout Australia. The Pillar® palatal implant system does not currently have a Medicare Benefits Schedule (MBS) item number, however Technology for Life Pty Ltd have applied for registration by the Prostheses and Devices Committee. There is currently no private health insurance rebate available to patients implanted with the Pillar® system (personal communication Technology for Life Pty Ltd, June 2006).

Treatment Alternatives

Existing comparators

Treatment options for people suffering from OSA comprise behavioural modifications, continuous positive airways pressure, medication, or a range of upper airway surgical procedures.

Behavioural measures include:

- Weight loss. Moderate weight loss may markedly reduce the severity of apnoea. In the case of morbidly obese individuals (body mass index >35kg/m^2), bariatric surgery may be considered;
- Alteration of body position. The supine sleeping position is associated with an increased number of apnoea episodes. Patients can undergo therapy that trains them to avoid the supine position, by sewing an uncomfortable object into the back of their pyjamas eg a tennis ball; or
- Dietary. The reduction or complete abstinence of alcohol may reduce the number of apnoea episodes. Cigarette smoking has also been implicated as a risk factor for OSA (Shochat & Pillar 2003).

Drug treatments for OSA have, in the past, been relatively unsuccessful and are associated with serious side effects, tolerance and complications. The rationale behind drug therapy is to alter the ventilatory drive and sleep architecture in a positive manner to minimise sleep-disordered breathing. Common drugs used include progesterone (stimulates the central respiratory centres), methylxanthine drugs such as theophylline (relaxes bronchial smooth muscle) and antidepressants (decreases REM sleep and in so doing decreases the number of respiratory events, which tend to higher during REM sleep)(Cistulli & Grunstein 2005; Shochat & Pillar 2003).

Continuous positive airways pressure (CPAP) is the most widely used treatment option for OSA and is considered to be the “gold standard” treatment. CPAP involves the delivery of positive air at a predetermined pressure through either a nose or full-face mask. The device is worn throughout the night and the continuous air pressure acts as a pneumatic splint, keeping the airway open. Variations on CPAP have been developed including bi-level positive airways

pressure, which allows for the separate adjustment of inspiratory and expiratory pressure. The auto-CPAP automatically adjusts the pressure in response to changes in airflow resistance. CPAP treats the symptoms of OSA and is *not curative,* therefore it must be worn indefinitely, which may lead to compliance issues. CPAP is effective in reducing, or eliminating altogether, the number of oxygen desaturation and arousal events associated with apnoea. Adverse effects of CPAP include nasal congestion and dryness, which may be overcome with the addition of a humidifier (Cistulli & Grunstein 2005; Shochat & Pillar 2003).

Surgical procedures aim to relieve nasal obstruction by increasing the surface area of the airway or to bypass the pharyngeal airway. Interventions include:

- Tracheostomy, which bypasses the pharyngeal airway, creating an artificial airway in the trachea. This procedure is usually performed when all other options have failed as, although it has a 100% success rate, it is associated with severe adverse effects and discomfort.
- Tonsillectomy and adenoidectomy are acceptable treatments in children;
- Pharyngeal reconstruction (uvulopalatopharyngoplasty) was originally considered a treatment for snoring but is now commonly used for OSA. This procedure increases the area of the retro palatal airway and involves the removal of pharyngeal tissue, including part of the soft palate, uvula, tonsillar pillars and excess tonsil material. The success rate for this procedure is approximately 50%. Other procedures used for pharyngeal reconstruction are laser-assisted uvulopalatoplasty, uvulopalatal flap and radiofrequency ablation techniques.
- Genioglossus advancement and hyoid myotomy, which are indicated for obstructions in the hypopharyngeal area. These procedures are extensive, with long recovery periods as they involve creating a forward movement of the tongue, creating an enlargement of the hypopharynx. Success rates are approximately 60-70%.
- Maxillomandibular advancement is usually reserved for patients with *severe* OSA due to anatomical abnormalities, who have not benefited from other surgical procedures. This major surgical procedure involves the advancement of the maxillary and mandibular compex by bilateral osteotomies, enlarging both the retrolingual and retropalatal airways (Shochat & Pillar 2003; Sundaram et al 2005).

A recent Cochrane review concluded that the available evidence, from small studies, did not support the use of surgery to treat people with mild or moderate OSA (Sundaram et al 2005).

The Pillar®, in comparison to existing surgical techniques, is less invasive and does not require an in-hospital stay or extensive rehabilitation and would therefore be considered a more acceptable treatment option.

The majority of studies assessed in this Horizon Scanning report examined the use of the Pillar® implant system to treat habitual snoring. Results for the treatment of snoring and OSA are presented separately. *All* of the literature included in this assessment is case series evidence (level IV intervention evidence) and is therefore of poor quality for determining effectiveness. Two peer reviewed case series and two abstracts reported results on the use of the Pillar® implant system for the treatment of patients with OSA. In addition, eight peer reviewed case series were assessed in this report on the safety and effectiveness of the Pillar® implant system for the treatment of chronic primary snoring.

Of the 12 case series included for assessment in this report, ten were supported by research grants from Restore Medical Inc.

Safety

All Pillar® implantation procedures were performed in a clinic situation under local anaesthesia. No studies included in this assessment reported bleeding, haematomas or infection during the procedure or during the immediate post-implantation period.

The most common adverse event reported was the partial extrusion of the Pillar® implants (Table 1). In most cases, patients experienced the extrusion of one of the three implants; however in a small number of patients two of the three implants were extruded. Only one patient experienced extrusion of all three implants which were replaced without incident. Time to extrusion varied from Day 28 to Day 299. The study by Skjøstad et al (2006) compared the implantation of normal Pillar® implants to a more rigid version. The more rigid version resulted in extrusion at Day 1 for one patient. Partial extrusion in all studies occurred in 4.3 to 25 per cent of patients. This translated to 1.4 to 8.8 per cent of implants extruding. The majority of the extruded implants were removed with or without local anaesthetic and in the majority of cases replaced. Some patients did not opt for replacement of the extruded implants as their symptoms improved from baseline with the remaining implants in place.

Most authors suggested that partial extrusion may occur due to the superficial implantation of the Pillar® implant, and is therefore an operator error and may reflect the level of training or expertise of the clinician involved. All studies concluded that implants should be placed deep within the palatal muscle to minimise the potential for extrusion. In addition, Ho et al (2006) suggested that the length of the soft palate may be a critical factor in the success of Pillar® implantation, noting that a patient with a short palate (24mm) experienced partial extrusion, which would emphasise the need for careful patient selection.

Table 1 Extrusion or re-implantation of Pillar® implant

Study	Level of Intervention Evidence	Study Design	Population	Outcomes
Obstructive sleep apnoea studies				
Friedman et al (2006)	IV	Retrospective case series	125 patients with mild to moderate OSA	Of a total of 372 implants placed, 10/372 (2.7%) were partially extruded. All were removed under local anaesthetic. New implants were inserted at a later date.
Nordgård et al (2006) Supported by a grant from Restore Medical Inc	IV	Case series	25 consecutive patients with mild to moderate OSA	3/25 (12.0%) experienced extrusion or required re-implantation of implants 1/25 (4.0%) perforation of posterior palatal surface *twice* before the third implant was correctly placed. Partial extrusion was experienced after 60 days and implant was removed. 1/25 (4.0%) had *3mm* of a partially extruded implant removed 1/25 (4.0%) had midline implant replaced during initial procedure
* Restore Medical Inc*	IV	Case series	46 patients with mild to moderate OSA	Partial extrusion rate = 1.4% 1/46 (2.2%) partial extrusion of implant after 60 days. Implant removed. 1/46 (2.2%) had *3mm* of a partially extruded implant removed after 90 days
* Walker et al Abstract Supported by a grant from Restore Medical Inc	IV	Case series	28 patients with mild to moderate OSA	Partial extrusion of implants occurred in a small number of patients (data not given). All partially extruded implants removed and replaced.
Snoring studies				
Ho et al (2006) Supported by a grant from Restore Medical Inc	IV	Case series	12 consecutive patients with disturbing snoring	Only 34/36 implants were deployed 2/12 (16.7%) patients experienced partial extrusion of 3/34 (8.8%) of implants at 3, 4 and 4.5 months after implantation
Kühnel et al (2005)	IV	Case series	106 patients suffering from habitual snoring	Total number of patients 99/106 (7/106 deviated from protocol) 19/297 (6.4%) implants partially extruded. Implants removed and replaced.

Maurer et al (2005)	IV	Case series	15 patients with chronic primary snoring	2/45 (4.4%) of implants partially extruded after 30 days in 2/15 (13%) of patients. One implant was removed without anaesthesia and one implant was removed under local anaesthesia.
Maurer et al (2005) Supported by a grant from Restore Medical Inc	IV	Case series	40 patients with chronic primary snoring	10/40 (25%) patients experienced partial extrusion of 13/120 (10.8%) implants. Extrusion occurred at a median of 53 days post-implantation (range 21-299 days) 2/40 (5%) experienced partial extrusion of more than one implant which were replaced. The remaining 8 patients did not have the extruded implants replaced.
Nordgård et al (2004) and Nordgård et al (2006) Supported by a grant from Restore Medical Inc	IV	Case series	35 patients with chronic primary snoring	One patient was excluded after a tonsillectomy during the Pillar® recovery period. A total of 6/34 (17.6%) patients experienced partial extrusion of 9/102 (8.8%) implants 2/102 (2.0%) implants did not deploy correctly during implantation 2/102 (2.0%) implants were partially extruded during implantation 4/34 (11.8%) patients had these implants replaced immediately 2/34 (5.9%) patients experienced partial extrusion at Day 28 and Day 60. Implants were *not* replaced.
Romanow and Catalano (2006) Supported by a grant from Restore Medical Inc	IV	Case series	25 consecutive patients with chronic primary snoring	2/75 (2.7%) partial extrusion rate for implants 1/25 (4.0%) patients experienced partial extrusion at 71 days
Skjøstad et al (2006) Supported by a grant from Restore Medical Inc	IV	Case series	20 consecutive patients with chronic primary snoring Patients received either regular Pillar® implants (n=10) or a stiffer version (n=10)	4/10 (40%) patients in the rigid implant group experienced partial extrusion (on Day 1, weeks 4, 7 and 15) 0/10 (0%) patients in normal implant group experienced partial extrusion

OSA = obstructive sleep apnoea, * Abstracts did not include the date of presentation

Visual analogue scales were used to measure the effect of the Pillar® procedure on levels of pain, dysphagia and speech. Higher scores indicate increased levels of pain, increased difficulty with swallowing and speech. Lower scores indicate a reduction in symptoms, for example, reduced pain. A visual analogue scale (VAS) tries to measure a characteristic or an attitude that ranges across a continuum of values which can not be easily measured ie pain. This assessment is highly subjective but is of value when looking at change within individuals, but of less value when comparing across a group of individuals at one time point (Gould et al 2001).

Ten of the 12 studies included for assessment reported on levels of pain before and after treatment, with the majority of studies using VAS to record any differences (Table 2). It appears that the Pillar® implantation procedure is not painful, requiring the use of a local anaesthetic for implantation, with mild analgesia (500mg paracetamol) prescribed as a precautionary measure in the days following the procedure. Baseline pain VAS scores were low in all cases and were elevated slightly in the 24-72 hours after implantation, before returning to baseline scores.

Table 2 Pain associated with Pillar® procedure

Study	Level of Intervention Evidence	Study Design	Population	Outcomes
Obstructive sleep apnoea studies				
Friedman et al (2006)	IV	Retrospective case series	125 patients with mild to moderate OSA	Only Group I (Pillar® alone, n=29) were assessed for pain using the VAS analogue scale All patients reported a pain level from 3-5 for the first 24 hours. 1/29 (3.4%) experienced pain for more than 3 days (score not stated)
Nordgård et al (2006) Supported by a grant from Restore Medical Inc	IV	Case series	25 consecutive patients with mild to moderate OSA	The VAS of pain from baseline to post-implantation remained unchanged (mean ± SD) Baseline 0.5 ± 1.1 Day 90 0.5 ± 1.1, *p*=0.869
*Restore Medical Inc	IV	Case series	46 patients with mild to moderate OSA	Pain assessed on VAS scale increased slightly at 24-72 hours before returning to baseline (mean ± SD) Baseline 0.7 ± 1.5 24-72 hours 2.2 ± 2.3

* Walker et al Abstract Supported by a grant from Restore Medical Inc	IV	Case series	28 patients with mild to moderate OSA	Pain assessed on VAS scale Scores increased at 24-72 hours returning to baseline at 30-day follow-up (raw data not given)
Snoring studies				
Maurer et al (2005)	IV	Case series	15 patients with chronic primary snoring	Pain assessed on VAS (mean ± SD) Day 2 1.9 ± 1.8 90 days 0.1 ± 0.2, p <0.01 All patients were prescribed 500mg paracetamol for Day 1. 3/15 (20%) patients required paracetamol for 2, 3 and 4 days respectively
Maurer et al (2005) Supported by a grant from Restore Medical Inc	IV	Case series	40 patients with chronic primary snoring	Pain assessed on VAS (mean ± SD) Baseline 4.9 ± 3.3 90 days 0.2 ± 0.6, p <0.05 All patients were prescribed 500mg paracetamol for 1-4 days
Nordgård et al (2004) and Nordgård et al (2006) Supported by a grant from Restore Medical Inc	IV	Case series	35 patients with chronic primary snoring	One patient was excluded after a tonsillectomy during the Pillar® recovery period Post-operative pain was reported to be mild by all patients. Mean time of post-operative analgesic consumption was 1.3 days (range 0-6 days). Mean total dose was 2.1 pills of 50mg diclofenac (range 0-15 pills) 8/34 (23.5%) required no analgesia. Pain assessed on VAS scale Scores increased at Day 2 and returned to slightly above baseline at 30-day follow-up (raw data not given)
Romanow and Catalano (2006) Supported by a grant from Restore Medical Inc	IV	Case series	25 consecutive patients with chronic primary snoring	Pain assessed on VAS (mean ± SD) Baseline (n=24) 0.7 ± 1.1 30 days (n=25) 0.5 ± 0.9, p=0.134 90 days (n=21) 0.5 ± 1.6, p=0.046

Skjøstad et al (2006) Supported by a grant from Restore Medical Inc	IV	Case series	20 consecutive patients with chronic primary snoring Patients received either regular Pillar® implants (n=10) or a stiffer version (n=10)	Post-operative pain was reported to be mild by all patients. Mean time of post-operative analgesic consumption was 0.95 days. 11/20 (55%) required no analgesia.

OSA = obstructive sleep apnoea, VAS = Visual analogue scale for throat and mouth pain (0= no pain, 10= excruciating pain), SD = standard deviation, * Abstracts did not include the date of presentation

Dysphagia or difficulty in swallowing was an outcome reported in eight of the 12 studies and was assessed using VAS scores (Table 3). An increase in VAS scores would indicate that patients had more difficulty swallowing after the Pillar® procedure than before implantation. As with the pain scores, baseline values for dysphagia were low, increasing slightly in the 24-72 hours after implantation before returning to baseline values. The Pillar® procedure had no effect on the patient's ability to swallow.

Table 3 Dysphagia associated with Pillar® implantation

Study	Level of Intervention Evidence	Study Design	Population	Outcomes
Obstructive sleep apnoea studies				
Friedman et al (2006)	IV	Retrospective case series	125 patients with mild to moderate OSA	Only Group I (Pillar® alone, n=29) were assessed using the VAS analogue scale 0/29 (0%) reported dysphagia
*Restore Medical Inc	IV	Case series	46 patients with mild to moderate OSA	Dysphagia assessed on VAS scale increased slightly at 24-72 hours returning to baseline (data not given) Baseline 0.4 ± 0.8 24-72 hours 1.9 ± 1.8
*Walker et al Abstract Supported by a grant from Restore Medical Inc	IV	Case series	28 patients with mild to moderate OSA	Dysphagia assessed on VAS scale Scores increased at 24-72 hours returning to baseline at 30-day follow-up (raw data not given)

Snoring studies				
Maurer et al (2005)	IV	Case series	15 patients with chronic primary snoring	Dysphagia assessed on VAS scale Scores returned to baseline levels at 90 days post-implantation (raw data not given)
Maurer et al (2005) Supported by a grant from Restore Medical Inc	IV	Case series	40 patients with chronic primary snoring	Dysphagia assessed on VAS scale Baseline 0.4 ± 0.6 90 days 0.1 ± 0.4, NS
Nordgård et al (2004) and Nordgård et al (2006) Supported by a grant from Restore Medical Inc	IV	Case series	35 patients with chronic primary snoring	One patient was excluded after a tonsillectomy during the Pillar® recovery period Dysphagia assessed on VAS scale Scores returned to baseline levels at 14 days post-implantation (raw data not given)
Romanow and Catalano (2006) Supported by a grant from Restore Medical Inc	IV	Case series	25 consecutive patients with chronic primary snoring	Dysphagia VAS scores Baseline (n=24) 0.7 ± 1.0 30 days (n=25) 0.6 ± 1.0, p=0.643 90 days (n=21) 0.3 ± 0.3, p=0.077

OSA = obstructive sleep apnoea, VAS = Visual analogue scale for difficulty swallowing (0= no difficulty, 10 = extreme difficulty), NS = not significant, * Abstracts did not include the date of presentation

The effect of the Pillar® procedure on speech was assessed using VAS scores and was an outcome reported in six of the 12 studies (Table 4). An increase in VAS score would indicate deterioration in speech or ability to speak. Similar to the pain and dysphagia scores, baseline values for difficulties with speech were low and remained either unchanged or slightly elevated after implantation before returning to baseline values. The Pillar® procedure had no effect on patient's speech.

Table 4 Effect of Pillar® procedure on speech

Study	Level of Intervention Evidence	Study Design	Population	Outcomes
Obstructive sleep apnoea studies				
*Walker et al Abstract Supported by a grant from Restore Medical Inc	IV	Case series	28 patients with mild to moderate OSA	Speech assessed on VAS scale Scores remained unchanged or below baseline throughout 30-day follow-up (raw data not given)
Snoring studies				
Maurer et al (2005)	IV	Case series	15 patients with chronic primary snoring	Speech assessed on VAS scale Scores returned to baseline levels at 14 days post-implantation (raw data not given)
Maurer et al (2005) Supported by a grant from Restore Medical Inc	IV	Case series	40 patients with chronic primary snoring	Speech assessed on Vas scale Baseline 0.7 ± 1.8 90 days 0.1 ± 0.2, $p < 0.05$
Nordgård et al (2004) and Nordgård et al (2006) Supported by a grant from Restore Medical Inc	IV	Case series	35 patients with chronic primary snoring	One patient was excluded after a tonsillectomy during the Pillar® recovery period Speech assessed on VAS scale Scores returned to below baseline levels at 30-day follow-up (raw data not given)
Romanow and Catalano (2006) Supported by a grant from Restore Medical Inc	IV	Case series	25 consecutive patients with chronic primary snoring	Speech assessed on Vas scale Baseline (n=24) 0.7 ± 1.5 30 days (n=25) 0.6 ± 1.1, $p=0.520$ 90 days (n=21) 0.5 ± 1.3, $p=0.027$

OSA = obstructive sleep apnoea, VAS = Visual analogue scale for disturbance of speech (0= no difficulty, 10 = extreme difficulty),
* Abstracts did not include the date of presentation

Few adverse events were reported by studies (Table 5). The most common adverse event, other than those mentioned above, was the sensation of having a foreign body in the throat, which was reported by one (2.9%) and four (4.1%) of patients in two studies. It was not stated whether this was resolved for these patients. The most serious adverse event was that of oedema of the uvula reported in one patient by Nordgård et al (2004). This was resolved by Day 5.

Table 5 Other adverse events

Study	Level of Intervention Evidence	Study Design	Population	Outcomes
Snoring studies				
Kühnel et al (2005)	IV	Case series	106 patients suffering from habitual snoring	Total number of patients 99/106 (7/106 deviated from protocol) 4/99 (4.1%) had sensation of foreign body
Nordgård et al (2004) and Nordgård et al (2006) Supported by a grant from Restore Medical Inc	IV	Case series	35 patients with chronic primary snoring	One patient was excluded after a tonsillectomy during the Pillar® recovery period 1/34 (2.9%) had minor oedema at base of uvula, resolved at Day 5 1/34 (2.9%) had sensation of foreign body at 90-day follow-up 2/34 (5.9%) had mild transient metallic taste

In summary, the Pillar® palatal implant system appears to be safe. The most common adverse event is the partial extrusion of the implants. This seems to cause little pain, physical damage or inconvenience to patients and can be easily rectified by the removal of the implant with or without local anaesthetic. In most cases the extruded implants were replaced, however some patients experienced resolution of their symptoms without re-implantation. Patients did not appear to find the implantation procedure painful, suffering only mild discomfort for a short period after the procedure was performed. No detrimental changes in speech or the ability to swallow were noted after implantation.

Effectiveness

The objective outcome measure in the majority of studies included for assessment was the apnoea/hypopnoea index (AHI), the sum of total apnoeas and hypopnoeas per hour (Table 6). The AHI is calculated during polysomnography, a comprehensive sleep study conducted overnight.

Three of the four OSA studies reported AHI values which were significantly reduced at time of follow-up when compared to baseline values. However, it should be noted that AHI values at follow-up are still considered to be high (ranging from 9 to 28) bearing in mind that an *AHI of 5-10 is considered abnormal*. It is unclear from these studies how great a reduction in AHI would be of clinical benefit to patients. An increasing number of contemporary findings demonstrate the importance of reducing the AHI, in many cases to near or below five events per hour of sleep (thereby controlling OSA) in order to improve numerous physiological, health outcomes and quality of life measures. This has been demonstrated in cardiovascular disease, heart failure, endocrinology and health related quality of life. Importantly, all indicate the importance of 'highly effective treatment' with a substantial decrease in the AHI over 'sub-therapeutic treatment' (smaller reductions in AHI) as a necessity to confer improved health outcomes. The classification of objective success, commonly adopted by surgeons in assessing surgery outcomes, and defined as either a reduction in AHI by 50% or an AHI < 20 is highly criticised in respiratory medicine circles as being insufficient and not related to *clinically significant reductions*. It does not meet the standards set down by the American Academy of Sleep Medicine in that an AHI of 20 still represents moderate OSA (Elshaug et al in press).

Interestingly, the study conducted by Friedman et al (2006) reported a significant reduction in AHI when the patient group was considered as a whole ($p<0.0001$), however for those patients treated with the Pillar® procedure alone, and *not* in conjunction with other surgical procedures, there was no significant reduction in the AHI ($p=0.269$). This may be a reflection of small patient numbers included in each group. Patients with *mild OSA* in the group that had the Pillar® procedure combined with adjunctive nasal procedures demonstrated a statistically significant reduction in their AHI ($p=0.017$) compared to non-significant reduction for those patients with *moderate OSA* ($p=0.297$). However this patient group was small and baseline AHI values were high. Other treatment groups included in this analysis were not stratified into mild and moderate OSA patients; therefore it is difficult to conclude whether the Pillar® procedure is would be more effective in patients with the milder or moderate forms of OSA.

Only four of the eight snoring studies reported polysomnographic data. Of these, two reported an increase in the AHI. The baseline AHI levels of patients included in these studies were lower in comparison to those of patients with OSA. Although these changes from baseline were statistically non-significant, the reported AHI value at 90-day follow-up in one snoring study was 8.3 (± 11.5)

which would then be classified as abnormally high and indicative of obstructive sleep apnoea. The two remaining snoring studies reported no clinically meaningful changes in polysomnographic measures.

Table 6 Objective outcome measures: Polysomnographic parameters

Study	Level of Intervention Evidence	Study Design	Population	Outcomes
Obstructive sleep apnoea studies				
Friedman et al (2006)	IV	Retrospective case series	125 patients with mild to moderate OSA Group I received Pillar® implant alone (n=29) Group II received Pillar® implant and adjunctive nasal procedures (n=37) Group III received Pillar® implant in conjunction with multiple adjunctive nasal and oropharyngeal procedures (n=55) Group IV received Pillar® implant as a salvage procedure after failed UPP (n=4)	AHI (mean ± SD) Objective success defined by authors as a reduction of AHI by >50% and an AHI <20 All patients, n=125 Baseline 22.3 ±16.7 3-6 months 16.3 ± 15.6 % change -25.0 ± 42.4 *p* <0.0001 Success rate 43/125 (34.4%) Pillar alone (Group I), n=29 Baseline 12.7 ±8.2 3-6 months 11.5 ± 12.9 % change -20.2 ± 32.8 *p* = 0.269 Success rate 7/29 (24.1%) Pillar + nasal, mild OSA (Group II) n=22 Baseline 12.9 ±4.3 3-6 months 9.3 ± 5.8 % change -21.3 ± 51.3 *p* = 0.017 Success rate 8/22 (36.4%) Pillar + nasal, moderate OSA (Group II) n=15 Baseline 30.3 ±11.6 3-6 months 26.2 ± 19.8 % change -17.1 ± 48.2 *p* = 0.297 Success rate 7/15 (46.7%) Pillar + multiple (Group III), n=55 Baseline 28.4 ±20.3 3-6 months 18.1 ± 16.7 % change -32.5 ± 41.5 *p* <0.0001 Success rate 21/55 (38.2%) Pillar + UPP (Group IV), n=4 Baseline 29.4 ±9.3 3-6 months 28.2 ± 12.1 % change -3.9 ± 41.6 *p* = 0.833 Success rate 0/4 (0.0%)

				Comparison of present study participants to historical control group who underwent nasal procedures alone Nasal + moderate OSA Baseline 19.3 ± 2.6 3-6 months 28.9 ± 14.0 % change 51.9 ± 76.3 $p = 0.025$ Success rate 2/14 (14.3%)
Nordgård et al (2006) Supported by a grant from Restore Medical Inc	IV	Case series	25 consecutive patients with mild to moderate OSA	AHI (mean ± SD) Baseline 16.2 ± 4.6 Day 90 12.1 ± 9.1 $p < 0.05$ AHI ≤ 10 12/25 (48.0%)
[a] Restore Medical Inc	IV	Case series	46 patients with mild to moderate OSA	[b] AHI (mean ± SD) *for all patients* Baseline 16.7 ± 4.7 Day 90 12.9 ± 13.0 $p < 0.03$
[a] Walker et al Abstract Research supported by a grant from Restore Medical Inc	IV	Case series	28 patients with mild to moderate OSA	Changes in observed apnoeas by bed partner Baseline 71% Day 30 20%
Snoring studies				
Ho et al (2006) Supported by a grant from Restore Medical Inc	IV	Case series	12 consecutive patients with disturbing snoring	Data not presented for those patients with extruded implants (n=2) and one patient lost to follow-up AHI (mean ± SD) n=9 Baseline 4.8 ± 5.7 Day 90 8.3 ± 11.5 NS
Maurer et al (2005)	IV	Case series	15 patients with chronic primary snoring	Baseline / Day 90 AI 1.0 ± 1.0 / 1.3 ± 1.6 HI 2.9 ± 2.0 / 3.6 ± 3.9 RDI 3.9 ± 2.1 / 4.9 ± 4.9 ODI 4.2 ± 3.2 / 6.4 ± 5.7, $p<0.05$ O_2 mean (%) 94.9 ± 1.4 / 94.6 ± 1.8 O_2 min (%) 89.3 ± 4.5 / 86.0 ± 6.1, $p<0.05$ SE (%) 88.2 ± 6.7 / 84.6 ± 8.1

Maurer et al (2005) Supported by a grant from Restore Medical Inc	IV	Case series	40 patients with chronic primary snoring		Baseline	Day 90	
				AI	0.7 ± 0.8	1.1 ± 1.4	NS
				HI	3.0 ± 2.2	4.5 ± 4.7	p<0.05
				RDI	3.7 ± 2.3	5.5 ± 5.4	p<0.05
				ODI	3.4 ± 2.9	5.3 ± 5.1	NS
				O_2 mean (%)	94.6 ± 1.8	94.3 ± 1.7	NS
				O_2 min (%)	89.8 ± 4.1	87.1 ± 5.8	p<0.05
				SE (%)	88.2 ± 8.1	83.7 ± 12.1	NS
Nordgård et al (2006) Supported by a grant from Restore Medical Inc	IV	Case series	35 patients with chronic primary snoring Same study group as Nordgård et al (2004) but longer follow-up	AHI (mean ± SD)			
				Baseline	Day 360		
				2.2 ± 2.3	3.3 ± 3.8	NS	

AHI = apnoea./ hypopnoea index (number per hour), OSA = obstructive sleep apnoea, UPP = uvulopalato-pharyngoplasty, SD = standard deviation, NS = not significant, AI = apnoea index (number per hour), HI = hypopnoea index (number per hour), RDI = respiratory disturbance index (number per hour), ODI = oxygen desaturation index (number per hour), O_2 mean = mean oxygen saturation, O_2 min = minimal oxygen saturation, SE = sleep efficiency, [a] Abstracts did not include the date of presentation, [b] Authors presented separate data for those patients with a decreased AHI, an improvement in snoring and no improvement at all. Results were recalculated by evaluators using paired t-test

The level of daytime somnolence is determined using the Epworth Sleepiness Scale (ESS) (Table 7). The ESS consists of a questionnaire, completed by patients, consisting of eight questions, concerned with their likelihood of falling asleep or dozing during particular activities (sitting and reading, stopped for a few minutes in traffic whilst driving etc). Each activity is scored from 0 to 3; 0 = would *never* doze or sleep, 1 = *slight* chance of dozing or sleeping, 2 = *moderate* chance of dozing or sleeping, 3 = *high* chance of dozing or sleeping. Scores for all answers are added up. A score of 10 or more, out of a possible 24, is considered sleepy and patients should assess whether they are obtaining adequate sleep and may need to consult a sleep disorder specialist. A score of 18 or more is considered very sleepy (Sleep Disorders Center 2004).

All of the four OSA studies included in this assessment demonstrated a reduction, and therefore an improvement, in ESS scores when compared to baseline (p<0.001). The study by Friedman et al (2006) reported that 64 per cent of the whole patient group had a reduction in their ESS scores. When considered in separate patient groups, a greater proportion of patients who had the Pillar® procedure in combination with adjunctive nasal procedures had a reduction in ESS scores (70.3%). The three other OSA studies reported a statistically significant reduction in ESS scores (p<0.001). However it should be noted that the longest follow-up period in these studies was 3-months.

Seven of the eight snoring studies reported ESS scores. The majority of these studies had low baseline ESS scores, indicating that day time sleepiness was not a problem for most patients enrolled in these studies. Despite this, most studies reported a statistically significant reduction in ESS scores indicating reduced self-reported daytime sleepiness. In particular the studies by Maurer et al (2005) and

Nordgård et al (2006) reported a significant reduction in ESS persisting at 12-months follow-up.

Table 7 Subjective outcome measures: Changes in daytime somnolence

Study	Level of Intervention Evidence	Study Design	Population	Outcomes
Obstructive sleep apnoea studies				
Friedman et al (2006)	IV	Retrospective case series	125 patients with mild to moderate OSA Group I received Pillar® implant alone (n=29) Group II received Pillar® implant and adjunctive nasal procedures (n=37) Group III received Pillar® implant in conjunction with multiple adjunctive nasal and oropharyngeal procedures (n=55) Group IV received Pillar® implant as a salvage procedure after failed UPP (n=4)	Subjective improvement in ESS defined as *any* improvement in ESS (0-24) All patients 80/125 (64.0%) Pillar alone 15/29 (51.7%) Pillar + nasal 26/37 (70.3%) Pillar + multiple 37/55 (67.3%) Pillar + UPP 2/4 (50%)
Nordgård et al (2006) Supported by a grant from Restore Medical Inc	IV	Case series	25 consecutive patients with mild to moderate OSA	ESS (0-24) (mean ± SD) Baseline 9.7 ± 3.6 Day 90 5.5 ± 3.5 $p < 0.001$
[a] Restore Medical Inc	IV	Case series	46 patients with mild to moderate OSA	[b] ESS (mean ± SD) *for all patients* Baseline 9.04 ± 4.4 Day 30 5.5 ± 3.6 $p < 0.0001$

[a] Walker et al Abstract Supported by a grant from Restore Medical Inc	IV	Case series	28 patients with mild to moderate OSA	ESS (0-24) (mean ± SD) Baseline 11.3 ± 4.5 Day 30 7.6 ± 3.6 $p < 0.001$
Snoring studies				
Ho et al (2006) Supported by a grant from Restore Medical Inc	IV	Case series	12 consecutive patients with disturbing snoring	Data not presented for those patients with extruded implants (n=2) and one patient lost to follow-up ESS (0-24) (mean ± SD) n=9 Baseline 8.9 ± 5.6 Day 90 5.7 ± 5.6 $p < 0.007$
Kühnel et al (2005)	IV	Case series	106 patients suffering from habitual snoring	Total number of patients 99/106 (7/106 deviated from protocol) Significant reduction in ESS at 12 month follow-up, p< 0.0001
Maurer et al (2005)	IV	Case series	15 patients with chronic primary snoring	ESS (0-24) (mean ± SD) Baseline 5.3 ± 3.2 Day 90 3.4 ± 2.9 $p = 0.002$ Fatigue VAS score (mean ± SD) Baseline 2.1 ± 2.3 Day 90 0.7 ± 0.8 $p = 0.01$
Maurer et al (2005) Supported by a grant from Restore Medical Inc	IV	Case series	40 patients with chronic primary snoring	ESS (0-24) (mean ± SD) Day 0 6.1 ± 3.2 Day 90 4.3 ± 3.3 $p < 0.05$ Day 360 4.9 ± 3.1 $p <0.05$
Nordgård et al (2004) Supported by a grant from Restore Medical Inc	IV	Case series	35 patients with chronic primary snoring	ESS (0-24) (mean) Baseline 9.3 Day 90 4.6 $p < 0.001$ No SD provided
Nordgård et al (2006) Supported by a grant from Restore Medical Inc	IV	Case series	35 patients with chronic primary snoring Same study group as Nordgård et al (2004) but longer follow-up	ESS (0-24) (mean ± SD) Baseline 9.3 ± 4.1 Day 360 5.6 ± 3.8 $p < 0.001$

Romanow and Catalano (2006) Supported by a grant from Restore Medical Inc	IV	Case series	25 consecutive patients with chronic primary snoring	ESS (0-24) (mean ± SD)		
				Day 0 (n=24)	8.3 ± 3.7	
				Day 30 (n= 23)	7.4 ± 3.7	*p* = 0.024
				Day 90 (n=21)	7.3 ±4.5	NS
				VAS (0-10) (mean ± SD)		
				Day 0 (n=24)	3.7 ± 2.8	
				Day 30 (n= 25)	2.3 ± 2.2	*p* = 0.006
				Day 90 (n=21)	2.3 ± 2.1	*p* = 0.016

OSA = obstructive sleep apnoea, ESS = Epworth sleepiness scale UPP = uvulopalato-pharyngoplasty, SD = standard deviation, [a] Abstracts did not include the date of presentation, [b] Authors presented separate data for those patients with a decreased AHI, an improvement in snoring and no improvement at all. Results were recalculated by evaluators using paired t-test, NS = not significant

Snore levels were measured pre- and post-Pillar® implantation by the bed partner scoring the loudness of snoring using the subjective visual analogue scale (VAS) from 0 to 10, where 0= no snoring, and 10 = an intensity that forces partner to leave bedroom (Nordgård et al 2006) (Table 8).

The four OSA studies reported a reduction in snoring levels as reported by their bed partners. The study by Friedman et al (2006) reported a 50 per cent reduction in snoring levels in 79 to 100 per cent of all patients enrolled. The remaining three studies reported a statistically significant reduction from quite high baseline values to midrange VAS scores at follow-up ($p<0.001$).

A statistically significant reduction in VAS scores was reported by all eight snoring studies, at follow-up times ranging from 30 to 360 days. If a subjective improvement in snoring is defined as a 50 per cent reduction in the level of snoring, then most studies achieved this clinical endpoint. The study by Skjøstad et al (2006) compared implantation with normal Pillar® implants to a more rigid version. Patients implanted with the rigid version did not achieve a significant reduction in snoring levels, whereas those in the normal Pillar® group did ($p<0.01$). The study by Maurer et al (2005) objectively assessed other snoring parameters (loudness, vibration frequency etc) by a recorder attached to a nasal cannula. The only parameters to be significantly reduced from baseline were the reported number of snores per hour ($p<0.007$) and the percentage of respiratory events with an increased resistance to airflow ($p=0.008$).

Table 8 Subjective outcome measures: Changes in snoring

Study	Level of Intervention Evidence	Study Design	Population	Outcomes
Obstructive sleep apnoea studies				
Friedman et al (2006)	IV	Retrospective case series	125 patients with mild to moderate OSA Group I received Pillar® implant alone (n=29) Group II received Pillar® implant and adjunctive nasal procedures (n=37) Group III received Pillar® implant in conjunction with multiple adjunctive nasal and oropharyngeal procedures (n=55) Group IV received Pillar® implant as a salvage procedure after failed UPP (n=4)	Subjective improvement in snoring defined as a 50% reduction of snoring, n (%) All patients 110/125 (88.0%) Pillar alone 23/29 (79.3) Pillar + nasal 32/37 (86.5) Pillar + multiple 51/55 (92.7) Pillar + UPP 4/4 (100%)
Nordgård et al (2006) Supported by a grant from Restore Medical Inc	IV	Case series	25 consecutive patients with mild to moderate OSA	VAS (0-10) (mean ± SD) Baseline 8.4 ± 1.2 Day 90 4.3 ± 2.6 $p < 0.001$
[a] Restore Medical Inc	IV	Case series	46 patients with mild to moderate OSA	[b] VAS (mean ± SD) *for all patients* Baseline 8.4 ± 1.4 Day 90 4.6 ± 2.5 $p < 0.0001$

[a] Walker et al Abstract Supported by a grant from Restore Medical Inc	IV	Case series	28 patients with mild to moderate OSA	Change in VAS (mean ± SD) 30 days follow-up Baseline 8.4 ± 1.5 Day 30 5.2 ± 2.7 $p = 0.001$ 82% of bed partners noted an improvement in patient's snoring at 30 days
Snoring studies				
Ho et al (2006) Supported by a grant from Restore Medical Inc	IV	Case series	12 consecutive patients with disturbing snoring	Data not presented for those patients with extruded implants (n=2) and one patient lost to follow-up VAS (0-100) (mean ± SD) n=9 Baseline 79 ± 17.2 Day 90 48 ± 20.4 $p < 0.008$
Kühnel et al (2005)	IV	Case series	106 patients suffering from habitual snoring	Total number of patients 99/106 (7/106 deviated from protocol) Significant reduction in VAS at 6 month follow-up, p value not stated
Maurer et al (2005)	IV	Case series	15 patients with chronic primary snoring	Snoring assessed by bed partner VAS scores Baseline 7.3 ± 1.6 Day 90 2.5 ± 2.1 $p < 0.001$ Snoring assessed by recorder attached to oro-nasal cannula Baseline / Day 90 SI 8.9 ± 5.6 / 5.7 ± 5.6 $p < 0.007$ Res (%) 29 ± 13 / 21 ± 13 $p = 0.008$ Db 16 ± 8 / 12 ± 7 NS Max Db 17 ± 8 / 15 ± 6 NS Vib 96 ± 106 / 126 ± 76 NS
Maurer et al (2005) Supported by a grant from Restore Medical Inc	IV	Case series	40 patients with chronic primary snoring	VAS (0-10) *n= 32* Day 0 7.1 ± 2.0 Day 90 4.2 ± 2.7 $p < 0.05$ Day 360 4.8 ± 2.7 $p < 0.05$
Nordgård et al (2004) Supported by a grant from Restore Medical Inc	IV	Case series	35 patients with chronic primary snoring	VAS (0-10) (mean) Baseline 7.3 Day 90 3.6 $p < 0.001$ No SD provided

Nordgård et al (2006) Supported by a grant from Restore Medical Inc	IV	Case series	35 patients with chronic primary snoring Same study group as Nordgård et al (2004) but longer follow-up	VAS (0-10) (mean) Baseline 7.3 ± 2.1 Day 360 4.8 ± 3.1 $p < 0.001$
Romanow and Catalano (2006) Supported by a grant from Restore Medical Inc	IV	Case series	25 consecutive patients with chronic primary snoring	VAS (0-10) (mean ± SD) Day 0 (n=25) 8.5 ± 1.4 Day 30 (n= 25) 5.0 ± 2.1 $p < 0.001$ Day 90 (n=21) 4.4 ± 2.5 $p < 0.001$
Skjøstad et al (2006) Supported by a grant from Restore Medical Inc	IV	Case series	20 consecutive patients with chronic primary snoring Patients received either regular Pillar® implants (n=10) or a more rigid version (n=10)	VAS (0-10) (mean) Implant Baseline Day 180 Normal 7.7 4.7 $p < 0.01$ Rigid 8.1 6.1 NS No SD provided

OSA = obstructive sleep apnoea, UPP = uvulopalato-pharyngoplasty, SD = standard deviation, [a] Abstracts did not include the date of presentation, [b] Authors presented separate data for those patients with a decreased AHI, an improvement in snoring and no improvement at all. Results were recalculated by evaluators using paired t-test, SI = snoring index (number of snores per hour), Res (%) = resistance occurrence index, percentage of all respiratory events whose spectral profile suggests increased resistance to airflow, Db = palatal snoring loudness decibels, Vib = primary vibration frequency of all snoring events, Max Db = maximum relative loudness (decibels) of loudest 10% of all snoring events

Only two studies reported the time taken to perform implantation using the Pillar® system (Table 9). These two studies confirmed that the procedure is quick to perform with an average time of 7 to 8 minutes. This time included time to perform re-implantation if required, and "learning curve" time for the surgeon, that is initial procedures took longer to perform than those performed later in the studies.

Table 9 Time to perform implantation of Pillar® devices

Study	Level of Intervention Evidence	Study Design	Population	Outcomes
Snoring studies				
Nordgård et al (2004) and Nordgård et al (2006) Supported by a grant from Restore Medical Inc	IV	Case series	35 patients with chronic primary snoring	Average operation time 8 minutes (range 3-16 minutes), decreasing with experience and including extra time for re-implantation
Skjøstad et al (2006) Supported by a grant from Restore Medical Inc	IV	Case series	20 consecutive patients with chronic primary snoring Patients received either regular Pillar® implants (n=10) or a more rigid version (n=10)	Average operating time 7.4 minutes

In summary, case series evidence, most of which used subjective outcomes, suggests that the Pillar® palatal implant system reduces the symptoms of *both* obstructive sleep apnoea and excessive snoring. Patients with OSA demonstrated a statistically significant reduction in the number of objectively measured apnoea/hypopnoea episodes, and the subjective measures of daytime sleepiness and snoring. In this patient group, the reduction in AHI is of greatest importance and although this reduction *was significant* it should be noted that AHI levels reported at follow-up remained *high.* It is unclear whether the observed reductions in AHI are sufficient to deliver a clinical benefit to these patients. In addition, follow-up AHI levels had large standard deviations, indicating a great deal of variation within the group. One study highlighted that the Pillar® procedure was more effective in patients who underwent adjunctive surgical procedures and for those with *mild not moderate* obstructive sleep apnoea. Further investigation is required to establish which patients would benefit the most from this procedure.

All snoring studies reported a statistically significant reduction in subjective snoring levels. In addition, self-reported daytime sleepiness was significantly reduced in chronic snorers; however values for this parameter were low at baseline.

Cost Analysis

There are currently no cost-effectiveness data available on the use of the Pillar® palatal implant system for the treatment of patients with obstructive sleep apnoea. The Pillar® implants are inserted into the palate via a non-reusable sterile delivery tool and each implant requires its own delivery tool. The cost of three implants is approximately $1,600. There is an additional cost for the surgeon to perform the procedure, which is not covered by the MBS and may increase the total cost of the procedure to approximately $2,000. The cost of the initial consultation and assessment may be covered by the MBS. In addition, after the Pillar® procedure is performed, a nasendoscopy is required, which is covered by the MBS (item number 53054, fee $106.25) (personal communication Technology for Life Pty Ltd, June 2006).

Patients considering the Pillar® implant system may be required to undergo a polysomnograph study, which is a prerequisite fro all other forms of OSA treatment (CPAP and surgery). In addition, it may be recommended that patients implanted with the Pillar® system undergo a follow-up sleep study to assess the effectiveness of the procedure. The current fee on the MBS schedule for the overnight investigation of sleep apnoea using a polysomnogram in adults aged 18 years and over is $508.90 (MBS Item Numbers 12203, 12207).

The proposal for a national sleep agenda produced by the Australasian Sleep Association states that the consequences of sleep disorders are costly in economic terms and lives lost. These costs may be as a result of transport and workplace accidents, lost productivity and health costs from co-morbidities, including inappropriate use of sleep medications and an increased use of medical resources. Obstructive sleep apnoea has been associated with hypertension, myocardial infarction, stroke, heart and respiratory failure. Approximately five per cent of visits to general practitioners have been attributed to underlying sleep disorders, despite patients initially presenting with symptoms of depression and anxiety (ASA 2003).

In 2004, it was estimated that the total health costs of sleep disorders to the Australian community, including the costs of other health problems caused by sleep apnoea, was approximately $628 million. The indirect financial costs of sleep disorders resulting from work-related injuries, motor vehicle accidents and lost productivity was estimated to total a further $5.6 billion in the same time period. Finally, an estimated $4.1 billion was attributed to the loss of healthy life caused by sleep apnoea. The resulting total cost of sleep disorders to the Australian community in 2004 was therefore in the vicinity of $10.3 billion (Access Economics 2004).

Informed Consent

Clinicians have an ethical obligation to inform patients of the effectiveness of treatment with the Pillar® implant system, and to tailor that information to the patients' circumstances. The Pillar® implant system appears to be effective in treating the symptoms of snoring. At this stage, the evidence indicates that the reduction in symptoms of obstructive sleep apnoea associated with treatment with the Pillar® implant system is of statistical, rather than clinical, significance. It would be important to emphasise with patients that there is a difference here between a statistical reduction in symptoms of OSA and a clinical important outcome.

There are slightly different consent issues for patients seeking the Pillar® implant system for the treatment of snoring symptoms. Snoring, without sleep disordered breathing, is not harmful in itself and may be regarded as a social, rather than medical, problem. However, snoring has been indicated as a major cause of marital disharmony and it is likely that the bed partner would be the driving force behind seeking treatment and requesting the Pillar® procedure (Ho et al 2004). This may present a moral dilemma for the treating clinician as he or she would be treating one individual to satisfy the needs of another. At the very least, clinicians should be obliged to discuss the procedure with both the patient *and* with bed partners.

Access Issues

Implantation of the Pillar® devices can be performed easily in a clinic setting, requiring only local anaesthetic spray, and may therefore be considered an ideal procedure to perform in a rural or remote setting. The procedure does, however, require a trained ear nose and throat surgeon, which may be the limiting factor in performing this operation in areas outside regional centres.

From a patients' perspective, one of the important sequelae of treatment with the Pillar® implant system is partial extrusion of the implant. Patients need to be fully informed of the relatively high risk of the implants partially extruding. The surgeon and patient will need to work together to establish a way to address this problem, should it arise. In particular, rural and remote patients should bear in mind that they may need to wait a considerable time for a suitable practitioner to be available to remove the extruded implant they may need to make contingency arrangements to go to larger regional centres for the removal.

Social impact

Excessive snoring may be caused by an increase in body mass index and/or excessive alcohol intake, both of which are modifiable risk factors (Parker et al 2005). It is possible that offering patients access to treatment with the Pillar® implant system will discourage them from, or allow them to avoid, addressing

these modifiable risk factors. These risk factors contribute to significant morbidity and mortality in Australia, therefore any treatment which may decrease the likelihood of lifestyle change should be scrutinised carefully.

Training and Accreditation

Training

Restore Medical Inc and Technology for Life Pty Ltd conduct a training programme with *all* ear, nose and throat surgeons who intend to use the Pillar® palatal implant system. New trainers observe the procedure being conducted by an experienced practitioner, then perform the procedure in at *least* three patients whilst being observed by the trainer. There are currently 40 ear, nose and throat surgeons undergoing training (personal communication Technology for Life Pty Ltd, June 2006).

To access Medicare funding a sleep medicine practitioner must be a Fellow of the Royal Australasian College of Physicians, necessitating post-medical degree training for 7 or more years, including a period of 1 to 3 years in full-time sleep medicine training. The Royal Australasian College of Physicians (RACP) recognises Sleep Medicine as a subspeciality of internal medicine and offers postgraduate training (Flemons et al 2004). In addition, the RACP produced a document describing the criteria for accreditation of advanced training sites in adult sleep medicine (RACP 2002). Although OSA needs to be diagnosed by a qualified sleep medicine practitioner, this qualification is not necessary for a clinician to use the Pillar® system to treat patients diagnosed with OSA.

Clinical Guidelines

There are currently no guidelines for the treatment of obstructive sleep apnoea In Australia or New Zealand. The Australasian Sleep Association and the Thoracic Society of Australia and New Zealand have produced guidelines for sleep studies in adults (Hensley et al 2005).

Limitations of the Assessment

Methodological issues and the relevance or currency of information provided over time are paramount in any assessment carried out in the early life of a technology.

Horizon Scanning forms an integral component of Health Technology Assessment. However, it is a specialised and quite distinct activity conducted for an entirely different purpose. The rapid evolution of technological advances can in some cases overtake the speed at which trials or other reviews are conducted. In many cases, by the time a study or review has been completed, the technology may have evolved to a higher level leaving the technology under investigation obsolete and replaced.

An Horizon Scanning Report maintains a predictive or speculative focus, often based on low level evidence, and is aimed at informing policy and decision makers. It is not a definitive assessment of the safety, effectiveness, ethical considerations and cost effectiveness of a technology.

In the context of a rapidly evolving technology, an Horizon Scanning Report is a 'state of play' assessment that presents a trade-off between the value of early, uncertain information, versus the value of certain, but late information that may be of limited relevance to policy and decision makers.

This report provides an assessment of the current state of development of the Pillar® palatal implant system, its present and potential use in the Australian public health system, and future implications for the use of this technology.

Search Strategy used for the Report

The medical literature (Table 11) was searched utilising the search terms outlined in Table 10 to identify relevant studies and reviews, until June 2006. In addition, major international health assessment databases were searched.

Table 10 Search terms utilised

Search terms
MeSH
sleep apnea, obstructive; snoring; palate, soft; polyethylene terephthalates; prostheses and implants; prosthesis implantation
Text words
soft palate; snoring; sleep apn?ea; obstructive sleep apn?ea; pillar procedure; pillar implant*; pillar; palatal implant*
Limits
English, human

Table 11 Literature sources utilised in assessment

Source	Location
Electronic databases	
AustHealth	University library
Australian Medical Index	University library
Australian Public Affairs Information Service (APAIS) - Health	University library
Cinahl	University library
Cochrane Library – including, Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, the Cochrane Central Register of Controlled Trials (CENTRAL), the Health Technology Assessment Database, the NHS Economic Evaluation Database	University library
Current Contents	University library
Embase	Personal subscription
Pre-Medline and Medline	University library
ProceedingsFirst	University library
PsycInfo	University library
Web of Science – Science Citation Index Expanded	University library
Internet	
Current Controlled Trials metaRegister	http://controlled-trials.com/
Health Technology Assessment international	http://www.htai.org
International Network for Agencies for Health Technology Assessment	http://www.inahta.org/
Medicines and Healthcare products Regulatory Agency (UK).	http://www.medical-devices.gov.uk/
National Library of Medicine Health Services/Technology Assessment Text	http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=hstat
National Library of Medicine Locator Plus database	http://locatorplus.gov
New York Academy of Medicine Grey Literature Report	http://www.nyam.org/library/grey.shtml
Trip database	http://www.tripdatabase.com
U.K. National Research Register	http://www.update-software.com/National/
US Food and Drug Administration, Center for Devices and Radiological Health.	http://www.fda.gov/cdrh/databases.html
Websites of Specialty Organisations	Dependent on technology topic area

Availability and Level of Evidence

Two peer reviewed case series and two abstracts (case series) reported results on the use of the Pillar® implant system for the treatment of patients with obstructive sleep apnoea (level IV intervention evidence). Of these four studies, three were supported by research grants from Restore Medical Inc. In addition, eight peer reviewed case series were assessed in this report on the safety and effectiveness of the Pillar® implant system for the treatment of chronic primary snoring (level IV intervention evidence). Of these eight studies, six were supported by research grants from Restore Medical Inc. See Appendix B for profiles of these studies.

Sources of Further Information

Two trials are currently being conducted in the United States to assess the use of palatal implants in the treatment of patients with sleep apnoea. The Mayo Clinic in Minnesota began recruiting in December 2005 for enrolment in a randomised controlled trial, comparing the effectiveness of treatment with soft palatal implants, placebo or positive airway pressure in patients with mild to moderate sleep apnoea and snoring. This trial expects to enrol 84 patients. The University of Cincinnati began enrolment in October 2005 for a randomised controlled trial comparing the effectiveness of the Pillar palatal implant system compared to placebo or sham controlled, in patients with obstructive sleep apnoea. This trial expects to enrol 100 patients (CCT 2006).

Conclusions

The Pillar® palatal implant system is designed to treat patients suffering from obstructive sleep apnoea or excessive snoring. The procedure involves the implantation of three small (18mm) polyethylene inserts, which are permanently implanted at the junction of the hard and soft palate. The procedure is easily performed in a clinic setting under local anaesthetic.

This procedure could be easily performed in rural and remote settings, but does, however, require a trained ear, nose and throat surgeon to conduct the procedure which may limit the accessibility of this population. Time taken to perform the procedure is short with studies reporting a mean time of 7 to 8 minutes, with a range of 3 to 16 minutes. Patients report only mild discomfort after the procedure and resume normal work and eating activities immediately after the procedure. In addition, no detrimental changes in speech or the ability to swallow were noted after implantation.

Current treatment options for obstructive sleep apnoea include lifestyle modifications (eg weight loss), invasive surgical procedures or the "gold standard", continuous positive airways pressure. Continuous positive airways pressure involves the delivery of positive air at a predetermined pressure through either a nose or full-face mask, worn throughout the night. Continuous positive airways pressure only treats the symptoms of obstructive sleep apnoea and is *not curative,* therefore it must be worn indefinitely, which may lead to compliance issues. Thus surgical alternatives, including the Pillar procedure may be seen as providing a cure for the condition.

Studies included for assessment in this report where of low quality (intervention evidence level IV). Outcomes measures reported in studies included an objective measure of the number of apnoea/hypopnoea episodes (AHI) and subjective measures such as self assessed daytime sleepiness (ESS scores) and degree of snoring (VAS scores). Given the prevalence of both obstructive sleep apnoea and chronic snoring it would be feasible to conduct randomised controlled trials, with larger numbers of patients enrolled to make adequate comparisons and with objective assessments of clinically meaningful outcomes.

There appears to be few safety issues associated with the Pillar® palatal implant system in the published case series evidence with follow-up times ranging from one to six months for the obstructive sleep apnoea studies and three to twelve months for the snoring studies. The partial extrusion of the implants was the most common adverse event and occurred in 4.3 to 25 per cent of patients. In the majority of cases, only one of the three inserts were extruded, which translated to an extrusion rate of 1.4 to 8.8 per cent of inserts. Partial extrusion appeared to cause little pain, physical damage or inconvenience to patients and was rectified by the removal of the implant with or without local anaesthetic. In the majority of

cases the extruded implants were replaced, however some patients experienced resolution of their symptoms without re-implantation.

The Pillar® palatal implant system leads to statistically significant improvements in symptoms when used for the treatment of patients who suffer from *either* obstructive sleep apnoea or excessive snoring. Statistically significant reductions in the objectively measured AHI ($p<0.05$), subjectively measured ESS scores ($p<0.001$) and VAS snoring scores ($p<0.001$) were observed in patients with obstructive sleep apnoea. Although the reduction in AHI was reported to be statistically *significant,* it should be noted that all studies reported *large* standard deviations for AHI at follow-up, indicating a great deal of variation within the group. More importantly, AHI levels at follow-up were *high* in the sleep apnoea studies (range 9 to 28), when an AHI of 5-10 is considered abnormal. There was no discussion about the degree of improvement that is required in AHI to achieve clinical benefit. One study highlighted that the Pillar® procedure was more effective in patients who underwent adjunctive surgical procedures and for those with only *mild not moderate* obstructive sleep apnoea.

All snoring studies reported a statistically significant reduction in snoring levels ($p<0.05$). In addition, daytime sleepiness was significantly reduced in patients with chronic snoring ($p<0.05$); however values for this outcome were low at baseline.

There are currently no cost-effectiveness data available on the use of the Pillar® palatal implant system for the treatment of patients with obstructive sleep apnoea. The consequences of sleep disorders may be costly in economic terms and lives lost, as a result of transport and workplace accidents, lost productivity and health costs from co-morbidities, including inappropriate use of sleep medications and an increased use of medical resources. Estimated costs to the Australian community for sleep disorders range from $3-7 billion per year.

Further investigation is required to establish which patients (mild or moderate obstructive sleep apnoea) would benefit the most from this procedure, and whether greater success would be achieved in conjunction with more invasive surgical procedures. In addition, long term follow-up of obstructive sleep apnoea patients may indicate whether or not the observed reductions in AHI delivered a clinical benefit to these patients.

Appendix A: Levels of Evidence

Designation of levels of evidence according to type of research question

Level	Intervention [§]	Diagnosis [**]	Prognosis	Aetiology [†††]	Screening
I [*]	A systematic review of level II studies	A systematic review of level II studies	A systematic review of level II studies	A systematic review of level II studies	A systematic review of level II studies
II	A randomised controlled trial	A study of test accuracy with: an independent, blinded comparison with a valid reference standard, [§§] among consecutive patients with a defined clinical presentation [††]	A prospective cohort study [***]	A prospective cohort study	A randomised controlled trial
III-1	A pseudorandomised controlled trial (i.e. alternate allocation or some other method)	A study of test accuracy with: an independent, blinded comparison with a valid reference standard, [§§] among non-consecutive patients with a defined clinical presentation[††]	All or none [§§§]	All or none [§§§]	A pseudorandomised controlled trial (i.e. alternate allocation or some other method)
III-2	A comparative study with concurrent controls: Non-randomised, experimental trial [†] Cohort study Case-control study Interrupted time series with a control group	A comparison with reference standard that does not meet the criteria required for Level II and III-1 evidence	Analysis of prognostic factors amongst untreated control patients in a randomised controlled trial	A retrospective cohort study	A comparative study with concurrent controls: Non-randomised, experimental trial Cohort study Case-control study
III-3	A comparative study without concurrent controls: Historical control study Two or more single arm study [‡] Interrupted time series without a parallel control group	Diagnostic case-control study [††]	A retrospective cohort study	A case-control study	A comparative study without concurrent controls: Historical control study Two or more single arm study
IV	Case series with either post-test or pre-test/post-test outcomes	Study of diagnostic yield (no reference standard) [‡‡]	Case series, or cohort study of patients at different stages of disease	A cross-sectional study	Case series

Tablenotes

* A systematic review will only be assigned a level of evidence as high as the studies it contains, excepting where those studies are of level II evidence.

§ Definitions of these study designs are provided on pages 7-8 *How to use the evidence: assessment and application of scientific evidence* (NHMRC 2000b*)*.

† This also includes controlled before-and-after (pre-test/post-test) studies, as well as indirect comparisons (ie. utilise A vs B and B vs C, to determine A vs C).

‡ Comparing single arm studies ie. case series from two studies.

** The dimensions of evidence apply only to studies of diagnostic accuracy. To assess the effectiveness of a diagnostic test there also needs to be a consideration of the impact of the test on patient management and health outcomes. See *MSAC (2004) Guidelines for the assessment of diagnostic technologies*. Available at: www.msac.gov.au .

§§ The validity of the reference standard should be determined in the context of the disease under review. Criteria for determining the validity of the reference standard should be pre-specified. This can include the choice of the reference standard(s) and its timing in relation to the index test. The validity of the reference standard can be determined through quality appraisal of the study. See Whiting P, Rutjes AWS, Reitsma JB, Bossuyt PMM, Kleijnen J. The development of QADAS: a tool for the quality assessment of studies of diagnostic accuracy included in systematic reviews. *BMC Medical Research Methodology*, 2003, 3: 25.

†† Well-designed population based case-control studies (eg population based screening studies where test accuracy is assessed on all cases, with a random sample of controls) do capture a population with a representative spectrum of disease and thus fulfil the requirements for a valid assembly of patients. These types of studies should be considered as Level II evidence. However, in some cases the population assembled is not representative of the use of the test in practice. In diagnostic case-control studies a selected sample of patients already known to have the disease are compared with a separate group of normal/healthy people known to be free of the disease. In this situation patients with borderline or mild expressions of the disease, and conditions mimicking the disease are excluded, which can lead to exaggeration of both sensitivity and specificity. This is called spectrum bias because the spectrum of study participants will not be representative of patients seen in practice.

‡‡ Studies of diagnostic yield provide the yield of diseased patients, as determined by an index test, without confirmation of accuracy by a reference standard. These may be the only alternative when there is no reliable reference standard.

*** At study inception the cohort is either non-diseased or all at the same stage of the disease.

§§§ All or none of the people with the risk factor(s) experience the outcome. For example, no smallpox develops in the absence of the specific virus; and clear proof of the causal link has come from the disappearance of small pox after large-scale vaccination.

††† If it is possible and/or ethical to determine a causal relationship using experimental evidence, then the 'Intervention' hierarchy of evidence should be utilised. If it is only possible and/or ethical to determine a causal relationship using observational evidence (ie. cannot allocate groups to a potential harmful exposure, such as nuclear radiation), then the 'Aetiology' hierarchy of evidence should be utilised.

Note 1: Assessment of comparative harms/safety should occur according to the hierarchy presented for each of the research questions, with the proviso that this assessment occurs within the context of the topic being assessed. Some harms are rare and cannot feasibly be captured within randomised controlled trials; physical harms and psychological harms may need to be addressed by different study designs; harms from diagnostic testing include the likelihood of false positive and false negative results; harms from screening include the likelihood of false alarm and false reassurance results.

Note 2: When a level of evidence is attributed in the text of a document, it should also be framed according to its corresponding research question eg. level II intervention evidence; level IV diagnostic evidence; level III-2 prognostic evidence etc.

Hierarchies adapted and modified from: NHMRC 1999; (Lijmer et al 1999; Phillips et al 2001; Bandolier editorial 1999)

Appendix B: Profiles of studies

Profiles of studies assessing the Pillar® implant system for the treatment of obstructive sleep apnoea

Study	Location	Study design	Study population	Study details	Outcomes assessed	Length of follow-up
Friedman, M. Vidyasagar, R. Bliznikas, D. Joseph, N.J. (2006)	Chicago, United States	Retrospective case series Intervention evidence level IV	125 patients with mild to moderate OSA	Group I received Pillar® implant alone (n=29) Group II received Pillar® implant and adjunctive nasal procedures (n=37) Group III received Pillar® implant in conjunction with multiple adjunctive nasal and oropharyngeal procedures (n=55) Group IV received Pillar® implant as a salvage procedure after failed uvulopalatopharyngoplasty (n=4)	Snore levels, change in AHI as determined by poly-somnography	3 - 6 month follow-up
Nordgård, S. Stene, B.K. Skjøstad, K.W. (2006) Research supported by a grant from Restore Medical Inc	Trondheim, Norway	Case series Intervention evidence level IV	25 consecutive patients with mild to moderate OSA	Inclusion criteria: >18 years age AHI = 10-30 BMI $\leq$30 kg/m^2 Soft palate length >25mm Tonsil size <50% of airway No significant nasal stenosis Bed partner present	Change in AHI as determined by poly-somnography Changes in ESS assessing daytime sleepiness and VAS for snoring intensity	90 days follow-up

Walker, R.P. * Levine, H.L. Abstract Research supported by a grant from Restore Medical Inc	Chicago, United States	Case series Intervention evidence level IV	28 patients with mild to moderate OSA	Inclusion criteria: >18 years age AHI = 10-30 BMI ≤30 kg/m^2 Soft palate length >25mm Tonsil size <50% of airway No significant nasal stenosis No previous pharyngeal surgery	Changes in ESS assessing daytime sleepiness and VAS for snoring intensity Partner observed apnoeas	30 days follow-up
Restore Medical Inc *	Multi-centre European	Case series Intervention evidence level IV	46 patients with mild to moderate OSA	Inclusion criteria: >18 years age AHI = 10-30 BMI ≤30 kg/m^2 Soft palate length >25mm Tonsil size <50% of airway No significant nasal stenosis Bed partner present	Change in AHI as determined by poly-somnography Changes in the ESS assessing daytime sleepiness and VAS for snoring intensity	90 days follow-up

OSA = obstructive sleep apnoea, AHI = apnoea-hypopnoea index, BMI body mass index, ESS = Epworth sleepiness score, VAS = Visual analogue score (0= no snoring, 10 = an intensity that forces partner to leave bedroom)

* The two abstracts did not include the date of presentation

Profiles of studies assessing the Pillar® implant system for the treatment of snoring

Study	Location	Study design	Study population	Study details	Outcomes assessed	Length of follow-up
Ho, W-K. Wei, W. Chung, K-F. (2006) Research supported by a grant from Restore Medical Inc	Hong Kong	Case series Intervention evidence level IV	12 consecutive patients with disturbing snoring	Inclusion criteria: AHI <15 BMI ≤ 30 kg/m^2	Change in AHI as determined by poly-somnography Changes in ESS assessing daytime sleepiness and VAS for snoring intensity	3 month follow-up
Kühnel, T.S. Hein, G. Hohenhorst, W. (2005)	Regensburg, Mannheim and Essen, Germany	Case series Intervention evidence level IV	106 patients suffering from habitual snoring	Inclusion criteria: Bed partner present Soft palate length >25mm No significant nasal stenosis BMI ≤ 30 kg/m^2	Changes in ESS assessing daytime sleepiness and VAS for snoring intensity	180 days

Maurer, J.T. Verse, T. Stuck. B.A. Hörmann, K. Hein, G. (2005)	Mannheim, Germany	Case series Intervention evidence level IV	15 patients with chronic primary snoring	Exclusion criteria: patients with OSA Inclusion criteria: Palatal flutter AHI <15 BMI ≤ 30 kg/m^2 Soft palate length >25mm	Changes in ESS assessing daytime sleepiness and VAS for snoring intensity Partner observed snoring Poly-somnographic parameters	90 days
Maurer, J.T. Hein, G. Verse, T. Hörmann, K. Stuck. B.A. (2005) Research supported by a grant from Restore Medical Inc	Mannheim, Germany	Case series Intervention evidence level IV	40 patients with chronic primary snoring	Exclusion criteria: patients with OSA Inclusion criteria: Palatal flutter AHI <15 BMI ≤ 30 kg/m^2 Soft palate length >25mm	Changes in ESS assessing daytime sleepiness and VAS for snoring intensity	12 months
Nordgård, S. Wormdal, K. Bugten, V. Stene, B.K. Skjøstad, K.W. (2004) Research supported by a grant from Restore Medical Inc	Trondheim, Norway	Case series Intervention evidence level IV	35 patients with chronic primary snoring	Inclusion criteria: >18 years age AHI = <10 BMI ≤30 kg/m^2 Soft palate length >25mm Tonsil size <50% of airway No significant nasal stenosis Bed partner present	Changes in ESS assessing daytime sleepiness and VAS for snoring intensity	90 days

Nordgård, S. Stene, B.K. Skjøstad, K.W. Bugten, V. Wormdal, K. Hansen, N.V. Nilsen, A.H. Midtlyng, T.H. (2006) Same study as above but long-term results reported Research supported by a grant from Restore Medical Inc	Trondheim, Norway	Case series Intervention evidence level IV	35 patients with chronic primary snoring	Inclusion criteria: >18 years age AHI = <10 BMI ≤30 kg/m^2 Soft palate length >25mm Tonsil size <50% of airway No significant nasal stenosis Bed partner present	Changes in ESS assessing daytime sleepiness and VAS for snoring intensity	12 months
Romanow, J.H. Catalano, P.J. (2006) Research supported by a grant from Restore Medical Inc	Mass-achusetts, United States	Case series Intervention evidence level IV	25 consecutive patients with chronic primary snoring	Exclusion criteria: patients with OSA Inclusion criteria: >18 years age Palatal flutter AHI ≤ 5 BMI ≤ 30 kg/m^2 Soft palate length >25mm No previous pharyngeal surgery Bed partner present	Changes in ESS assessing daytime sleepiness and VAS for snoring intensity	90 days
Skjøstad, K.W. Stene, B.K. Nordgård, S. (2006) Research supported by a grant from Restore Medical Inc	Trondheim, Norway	Case series Intervention evidence level IV	20 consecutive patients with chronic primary snoring	Patients received either regular Pillar® implants (n=10) or a stiffer version (n=10) Exclusion criteria: patients with OSA Inclusion criteria: >18 years age Palatal flutter AHI <15 BMI ≤ 30 kg/m^2 Soft palate length >25mm No previous pharyngeal surgery Bed partner present	Changes in VAS for snoring intensity	180 days

AHI = apnoea-hypopnoea index, BMI body mass index, ESS = Epworth sleepiness score, VAS = Visual analogue score (0= no snoring, 10 = an intensity that forces partner to leave bedroom), OSA = obstructive sleep apnoea

Appendix C: HTA Internet Sites

AUSTRALIA

- Centre for Clinical Effectiveness, Monash University
  http://www.med.monash.edu.au/healthservices/cce/evidence/

- Health Economics Unit, Monash University
  http://chpe.buseco.monash.edu.au

AUSTRIA

- Institute of Technology Assessment / HTA unit
  http://www.oeaw.ac.at/ita/welcome.htm

CANADA

- Agence d'Evaluation des Technologies et des Modes d'Intervention en Santé (AETMIS) http://www.aetmis.gouv.qc.ca/en/

- Alberta Heritage Foundation for Medical Research (AHFMR)
  http://www.ahfmr.ab.ca/publications.html

- Canadian Coordinating Office for Health Technology Assessment (CCHOTA) http://www.cadth.ca/index.php/en/

- Canadian Health Economics Research Association (CHERA/ACRES) – Cabot database http://www.mycabot.ca

- Centre for Health Economics and Policy Analysis (CHEPA), McMaster University http://www.chepa.org

- Centre for Health Services and Policy Research (CHSPR), University of British Columbia http://www.chspr.ubc.ca

- Health Utilities Index (HUI) http://www.fhs.mcmaster.ca/hug/index.htm

- Institute for Clinical and Evaluative Studies (ICES) http://www.ices.on.ca

DENMARK

- Danish Institute for Health Technology Assessment (DIHTA)
  http://www.dihta.dk/publikationer/index_uk.asp

- Danish Institute for Health Services Research (DSI)
  http://www.dsi.dk/engelsk.html

FINLAND

- FINOHTA http://www.stakes.fi/finohta/e/

FRANCE

- L'Agence Nationale d'Accréditation et d'Evaluation en Santé (ANAES) http://www.anaes.fr/

GERMANY

- German Institute for Medical Documentation and Information (DIMDI) / HTA http://www.dimdi.de/dynamic/en/

THE NETHERLANDS

- Health Council of the Netherlands Gezondheidsraad http://www.gr.nl/adviezen.php

NEW ZEALAND

- New Zealand Health Technology Assessment (NZHTA) http://nzhta.chmeds.ac.nz/

NORWAY

- Norwegian Centre for Health Technology Assessment (SMM) http://www.kunnskapssenteret.no/

SPAIN

- Agencia de Evaluación de Tecnologias Sanitarias, Instituto de Salud "Carlos III"I/Health Technology Assessment Agency (AETS) http://www.isciii.es/aets/

- Catalan Agency for Health Technology Assessment (CAHTA) http://www.aatrm.net/html/en/dir394/index.html

SWEDEN

- Swedish Council on Technology Assessment in Health Care (SBU) http://www.sbu.se/www/index.asp

- Center for Medical Health Technology Assessment http://www.cmt.liu.se/

SWITZERLAND

- Swiss Network on Health Technology Assessment (SNHTA)
  http://www.snhta.ch/

UNITED KINGDOM

- NHS Quality Improvement Scotland
  http://www.nhshealthquality.org/nhsqis/qis_display_home.jsp?pContentID=43&p_applic=CCC&pElementID=140&pMenuID=140&p_service=Content.show&

- National Health Service Health Technology Assessment (UK) / National Coordinating Centre for Health Technology Assessment (NCCHTA)
  http://www.hta.nhsweb.nhs.uk/

- University of York NHS Centre for Reviews and Dissemination (NHS CRD)
  http://www.york.ac.uk/inst/crd/

- National Institute for Clinical Excellence (NICE)
  http://www.nice.org.uk/

UNITED STATES

- Agency for Healthcare Research and Quality (AHRQ)
  http://www.ahrq.gov/clinic/techix.htm

- Harvard School of Public Health – Cost-Utility Analysis Registry
  http://www.tufts-nemc.org/cearegistry/index.html

- U.S. Blue Cross/ Blue Shield Association Technology Evaluation Center (TEC) http://www.bcbs.com/tec/index.html

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