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Short Technology Assessment Report commissioned by the NHS R&D HTA Programme on behalf of the HTA Programme's Therapeutic Procedures Panel

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FINAL PROTOCOL

Title of the project

Surgical procedures and non-surgical devices for the management of non-apnoeic snoring: a systematic review of clinical effects and associated treatment costs

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1. Plain English Summary

There are a number of different non-surgical devices and surgical procedures for the treatment of non-apnoeic, or primary snoring. The aim of all of these devices or procedures is to prevent generation of the 'snoring sound', though preventing the narrowing or collapse of the upper airways during sleep. This review will systematically assess the clinical effects of these surgical procedures and devices used in the treatment of snoring. It will also estimate the costs associated with each treatment, delivered in a range of health care settings.

2. Scope of the current assessment

The objectives of this short report are to:

i. Undertake a systematic review of the clinical effects of surgical interventions and non-surgical devices for the management of non-apnoeic snoring.

ii. Estimate the range of the costs associated with each intervention based on current UK information, in relevant primary and secondary care treatment settings.

iii. Identify and prioritise interventions for which future primary research in the management of the snoring patient would be of benefit.

3. Background to non-apnoeic snoring

Snoring is the hallmark symptom of a spectrum of sleep-related breathing disorders collectively termed sleep disordered breathing (SDB). The pathophysiologic cause of SDB is sleep induced airway obstruction. Minimal airway obstruction causes non-apnoeic, or simple snoring. At the other extreme, complete airway obstruction causes obstructive sleep apnoea syndrome (OSAS). Non-apnoeic snoring is differentiated from OSAS by the number of apnoeic and hypopnoeic events per hour of sleep, as measured by the Respiratory Disturbance Index (RDI) or apnoea-hypopnoea index (AHI). Non-apnoeic snoring is generally classified as less than 5 events per hour.

Snoring is very common in the general population, with around 35%-45% of men and 15%-28% of women reporting habitual snoring.[1, 2] Risk factors for the development and worsening of snoring include increasing age, male gender, obesity (in part used as a proxy marker for neck circumference), alcohol ingestion, sedative use, smoking, and nasal obstruction, as well as being more common in respiratory conditions such as asthma and chronic obstructive pulmonary disease (COPD).[3-14] Prevalence estimates of snoring have varied considerably from 16%-89% depending on the populations studied, the definitions of snoring used, investigations performed and the study design.[15] Obviously, a large proportion of these populations would not be sufficiently disturbed by snoring to seek medical advice and, indeed, it is not clear from the current research what proportion of people would seek treatments if they were both successful and easily available.

3.1 Clinical significance

It has been clearly shown that systemic blood pressure fluctuates transiently with snoring.[16] However, the search for a potential association between heavy habitual snoring and hypertension, cerebrovascular disease and coronary artery disease has yielded conflicting results.[17-19] None of the studies linking non-apnoeic snoring and cardiovascular disease have used objective,

polysomnographic (PSG) measures of snoring, and studies that have excluded patients with diagnosed OSAS have found no such association.[18, 20] There is also unresolved debate as to whether non-apnoeic snoring alone without OSAS can cause significant sleep fragmentation, leading to excessive daytime sleepiness. Excessive daytime sleepiness (EDS) in patients with OSAS is a well-established correlate of the syndrome. However, attempts to assess this in non-apnoeic snoring, have been confounded by studies of mixed patient populations [with OSAS, Upper Airways Resistance Syndrome (UARS) and non-apnoeic snoring patients]being assessed, sleep fragmentation due to bed partner's attempts to stop the snoring, as well as high prevalence rates of moderate to severe sleepiness reported in the general population.[2, 21]

The clinical significance of non-apnoeic snoring may be somewhat equivocal, but its psycho-social impact is easily recognised. Loud intrusive snoring affects bed partners, family, and even neighbours. Noise pollution and its resulting social disability, relationship disharmony and threatened marriage break up[22]is an important reason why an individual, often pressurised by their partner, will seek medical advice. In this respect, non-apnoeic snoring is an unusual 'medical condition' in that it is one not commonly complained about by the individual concerned, but by their bed partner. The frequency and sound intensity of snoring by an individual may therefore not be as important a factor in seeking medical advice, as the amount of social disturbance caused.

The complex social impact of snoring is difficult to quantify. It is usually addressed by means of a questionnaire directed at both the snorer and their bed partner. Most questionnaires have been designed to assess symptoms of OSAS, and are therefore not particularly useful for quantifying the severity of snoring. The actual problems of which snorers complain, generally centre around disturbing other's sleep, poor sleep quality, lethargy and sore throat.[23]

3.2 Aetiology

Snoring is due to the turbulent flow of air through the upper airways, and can arise from transient obstruction at several anatomical levels.[24-26] This multi-level obstruction occurs in different regions of the pharynx to varying proportions in different individuals. In some individuals it is predominantly palatal and nasopharyngeal, whereas in others it can be retroglossal or hypopharyngeal.

Upper airway narrowing with sleep onset is a normal physiological process,[27] but partial obstruction occurs due to a failure of the upper airway dilator muscles to stabilise the airway during sleep. Their innervation is complex and subject to reflex control. When a slight narrowing occurs, the speed of airflow through the narrowed segment increases, which in turn provokes increased inspiratory negative pressure, further exacerbating the collapse. Studies comparing snorers and non-snorers have confirmed that snorers generate more negative inspiratory pressures,[28]prolonged inspiration time,[28]and limitation of respiratory flow.[29] These changes lead to unstable, turbulent airflow within the upper airway and tissue vibration, causing the production of a snoring sound. It has been consistently observed that snoring is worse during slow wave sleep and during the early part of the night, whilst it is relatively rare during rapid eye movement (REM) sleep cycles.[30]

The trauma to the upper airway tissues during snoring can damage both muscle fibres and peripheral nerve fibres, and this further impairs the stabilising action of the muscles, increasing the tendency of the airway to obstruct. This is further compounded by oedema due to vibration injury from snoring.[31]

The pattern of dynamic pharyngeal narrowing varies among non-apnoeic snorers, and identification of the sites of obstruction has important implications in the consideration of treatment strategies, especially surgical interventions.

3.3 Management

3.3.1 Diagnosis

The aim of investigating patients presenting with signs consistent with non-apnoeic snoring, is generally to rule out more severe sleep disordered breathing (ie. OSAS or UARS) and other conditions. On initial assessment, care is taken to elicit evidence of any symptoms indicative of OSAS. Depending on the history and examination findings, one of several screening procedures may be invoked. For individuals with a low index of suspicion of OSAS, overnight pulse oximetry will suffice. However, if the index of suspicion is high then a formal polysomnography may be performed.

3.3.2 Assessment of the site of airway narrowing

Several techniques have been used to localise the anatomical level at which the snoring noise is being generated in any individual. Identification of the primary sound generator(s) may be used to decide the most appropriate treatment options and potentially provide some prediction of treatment outcome. The most commonly used techniques are:

- Fibreoptic nasal endoscopy with Muller's manoeuvre.
- Sedation (sleep) nasendoscopy.
- Upper airway pressure recordings during sleep
- Acoustic analysis
- Imaging

The Muller manoeuvre involves fibreoptic visualisation of the pharynx while forced inspiratory effort is performed against closed nasal and oral airways. Flexible nasendoscopy allows direct visualisation of the extent of airway collapse at the different levels during the manoeuvre. The extent of collapse at the velopharynx relative to collapse at the oropharyngeal level is used to predict surgical outcome.[32] There are a number of limitations to the test. The patient is awake and therefore the pharyngeal muscular tone is much higher than in sleep, inspiratory effort may vary from patient to patient, thereby varying the degree of collapse, and there is relatively large inter-observer variation in determining the level of collapse.

Sedation (sleep) nasendoscopy requires the sedation of the patient. Once snoring is achieved a fibreoptic nasendoscope is used to visualise the level of sound production and pharyngeal collapse. It would be expected that only patients in whom soft palate flutter predominates would benefit from a palatoplasty procedure. This technique is reasonably reliable at identifying the site of obstruction,[33] and the cross-sectional area of the pharynx can be estimated to within 10% by this method when linked to a computer.[34] The technique however, has two major limitations. Firstly, it is unlikely that sedation-induced sleep correlates well with natural sleep. Therefore any observed snoring source and/or reduction in pharyngeal diameter under sedation may not also occur during natural sleep. Secondly, there is no currently standardised protocol for sedation. This results in wide variation from individual to individual, between sequential studies on the same individual, and between centres. This is further compounded by evidence that most surgical failures for non-apnoeic snoring occur at the level of the palate.[35] Therefore the poor

predictive value of sleep nasendoscopy for the outcome of laser uvulopalatoplasty,[36]probably reflects a combination of limitations in both the test and the procedure.

Upper airway pressure recordings during sleep. It has been shown that monitoring by use of pressure transducers within the oesophagus during sleep produces similar results to a full PSG, at significantly less cost.[37] However, the invasive nature of the test may influence the duration of sleep and the lowest stage of sleep attained. Furthermore, only the lowest limit of the obstructed airway segment is determined, and the test may not adequately localise the level of tissue obstruction as opposed to the segment of airway collapse.

Acoustic analysis of the snoring sound has developed since the early 1990's. Acoustic techniques have been used in an effort to create theoretical mathematical models of snoring sound production, and from this derive the level at which the sound is produced. Acoustic analysis has indicated that frequencies around 20 hertz are associated with palatal fluttering, whereas obstruction at other sites gives a more diffuse frequency range. To date, acoustic analysis has been used to help diagnose OSAS,[38]as an objective outcome measurement of snoring surgery,[39-41] and in an attempt to differentiate the underlying mechanism of sound production.[42, 43] Although these techniques seem to hold some promise as a screening tool, they still require considerable further refinement.

Imaging techniques that have been used in attempts to identify structures involved in snoring sound generation include fluoroscopic techniques, computerised tomography (CT) scanning, magnetic resonance imaging (MRI), and cephalometric radiography (plain radiography of the airways). These techniques have had only limited success[44-46]and may do little to guide therapeutic intervention. Furthermore, practicality, cost and excess radiation exposure have proved major limitations. Currently therefore, cephalometic radiography is only indicated in patients with a retrolingual site of obstruction, with contributing skeletal abnormalities, in whom surgical procedures directed at this site are planned.

Overall, given the present level of uncertainty of the tests outlined above in the prediction of the level at which snoring sound is produced, there is likely to be large variation in current practice, as to which, if any, tests are performed. Coupled with patient preference and resource availability, definition of treatment alternatives may still be based on history and examination alone.

3.4 Interventions for non-apnoeic snoring

Surgery is not the only means by which a reduction of snoring can be achieved. Several non-surgical methods have been used. These include weight reduction,[47] the use of sleep positioning devices,[48] and a reduction of alcohol intake.[10] These are generally indicated either as a first line treatment option, or as an adjuvant intervention depending upon the patients lifestyle risks factors for snoring, and the pathophysiological mechanism of snoring sound production.

The different surgical and non-surgical alternative treatment options for non-apnoeic snoring can broadly be grouped into the following categories:

(a) Patient administered interventions, such as sleep position adjustment, non-prescription (over the counter) medication, nasal dilators, and lifestyle changes (such as weight loss, smoking cessation, and limitation of alcohol intake).

(b) Physician administered non-surgical devices, such as continuous positive airway pressure and oral appliances (mandibular repositioning appliances and tongue retaining devices).

(c) Surgical interventions, such as nasal surgery, palatal shortening surgery, and intra-palatal surgery.

The scope of the current research will focus upon the latter two categories, as the provision of these treatment options will impact directly on NHS resources. Whilst it is acknowledged that a number of individuals use NHS resources for interventions aimed to modify lifestyle factors, such as smoking cessation and weight loss, these resources are likely to be used primarily for other health indications, with snoring reduction/cessation being a secondary aim. Furthermore, the majority of patients and physicians will only consider the more intensive or invasive treatment options to be assessed in the current research, once non-invasive forms have proven ineffective or difficult to tolerate. Further information on the effects of non-prescription treatments for snoring or OSAS is available in a review by the American Academy of Sleep Medicine Clinical Practice Review Committee.[49]

A brief outline of the main non-surgical devices and surgical techniques available as treatment options for the management of non-apnoeic snoring is given below.

3.4.1 Non-surgical devices

3.4.1.2 Continuous positive airway pressure

The mainstay of non-surgical treatment for snoring is continuous positive airway pressure (CPAP). The positive airway pressure acts as a pneumatic stent to resist airway collapse. CPAP is administered through a nasal mask, nasal prongs, or a mask that covers both the nose and mouth. Although CPAP is highly effective, compliance rates tend to be low due its airway-drying effect, the discomfort of wearing the device, and to some extent the noise of the machine.

3.4.1.3 Mandibular repositioning appliances (MRAs)

Mandibular repositioning appliances consist of an upper and lower dental bite-plate connected by an angled strut. The device, which is inserted intraorally at night, anteriorly displaces the position of the mandible and/or tongue with the aim of enlarging the retroglossal space and thus reducing the degree of upper airway obstruction and pharyngeal collapse.[50] The maximal degree of mandible protrusion varies from device to device, but is usually around 75% of the maximum possible. The adverse effects of MRAs include excess salivation, xerostomia, tempro-mandibular joint pain, dental pain, myofacial pain and bite change. One or more of these effects will occur in around 50%-80% of patients.[51] The vast majority settle within four weeks, but overall compliance is around 50%-75%.[51, 52]

There are presently approximately 50 different MRAs available. The cheapest are the “boil-and-bite” type mouthpieces that are fitted by the user. These are made of thermolabile material that can be directly moulded to the patient’s teeth. This type of device is available for sale on the internet for less than £50 (e.g.http://www.britishsnoring.co.uk). Custom-made appliances are generally fitted by a dentist or dental technician. Construction of these devices usually requires dental impressions, manufacturing by a dental laboratory, and fitting by a dentist. Taking the

impression and fitting do not have a standard dental charge, and there is marked variation in the UK in these charges.

3.4.2.3 Tongue retaining devices (TRDs)

Tongue retaining devices affect geniglossus muscle activity, but effects on other upper airway muscles have not been evaluated.[53, 54] These devices hold the anterior part of the tongue forwards during sleep by means of a negative pressure in a soft bulb which is applied to the tongue.[55] Unlike the mandibular repositioning appliance, the tongue retainer can be used in edentulous patients.

3.4.2 Surgical procedures

The aim of palatal surgery is to limit the collapsibility of the oropharyngeal segment. This is usually done by reducing the amount of soft palate, the uvula and/or removing the tonsils, or by stiffening the existing palatal tissue structure.

3.4.2.1 Uvulopalatopharyngoplasty (UPPP or UP3)

UPPP is designed to reduce the excess tissue found in the palate, uvula, and posterior and lateral pharyngeal walls. When present, the tonsils are also included in the excision in order to optimise the opening of the airway at this level.[56] The amount of tissue excised varies, depending on individual palatal anatomy. The procedure is performed under general anaesthetic. A number of studies have indicated that UPPP is often complicated by severe post-operative pain.[57] Additionally, there may be some long-term complications with the procedure, such as nasopharyngeal regurgitation, persistent palatal dryness, long-term voice changes, and a partial loss of taste.[58] Estimates of the success of the procedure vary from 9% to 100%,[59, 60] but few studies have employed objective outcome measures. One small study in which patient's snoring levels were objectively assessed, indicated that snoring was reduced in between 75% and 100% of patients in the short-term.[61] The long-term efficacy would appear to fall to around 50%, but this has only been measured using subjectively assessed outcome measures.[62] This decline may represent long-term changes in the pharynx following surgery, or perhaps more likely, changes in self-reporting over time as the placebo effect diminishes. This would appear probable, as when measured objectively snoring volume does not appear to change significantly over time following UPPP.[61]

3.4.2.2 Palatoplasty procedures

In an attempt to overcome the somewhat radical nature of UPPP and its potential complications, a variety of techniques limited to the soft palate were developed. These are all based on the supposition that palatal flutter is one of the most important sound generator mechanisms in snore production. Therefore, reducing palatal flutter or vibration, should theoretically, reduce snoring. These palatoplasty procedures are based on one of two predominant themes – either reducing the length of the palate or stiffening the soft palate tissues.

3.4.2.3 Laser assisted uvulopalatoplasty (LAUP)

In the UK LAUP is generally performed under general anaesthetic as a day case procedure, and is argued to be a safer, more economical and more comfortable alternative to UPPP. The procedure involves laser excision of the uvula and a small portion of the soft palate. Unlike UPPP, LAUP

can be repeated in order to obtain the desired effect upon the airway. The number of procedures varies with some patient requiring up to four sessions. The aim of staging treatment is to excise the minimal amount of palatal tissue needed to reduce snoring effectively while reducing the risk of venopharyngeal insufficiency. Although LAUP is generally associated with fewer complications than UPPP, post-operative pain is reported to be similar for both procedures.[63, 64] This may negatively affect patient compliance, and is likely to be influential in patients abandoning treatment before the optimal amount of soft palate has been excised.[65]

3.4.2.4 Radiofrequency ablation (somnoplasty)

Radiofrequency ablation is designed to shrink redundant tissue of the soft palate and improve the texture of the remaining palate so that it becomes more dynamically stable.[66] Radiofrequency energy (at a variety of frequencies and energy levels) is released into the palate tissue submucosally using an electrode delivery device. This creates a lesion within the palate. The body will reabsorb this dead tissue, thus reducing the volume of the palate and shortening it. The area of the palate most commonly treated is the base of the uvular to the posterior nasal spine. The procedure may be performed on an outpatient basis, with use of a topical local anaesthetic. Like LAUP, the procedure can be repeated a number of times if the snoring symptoms persist. The most frequently reported complications with the procedure are mucosal erosion and ulceration.[67]

Radiofrequency ablation has also been used for the reduction of turbinates and base of the tongue ablation for the treatment of non-apnoeic snoring.[68, 69]

Palatal Stiffening Procedures

There are a number of different palatal stiffening techniques used in the treatment of snoring. These include the cautery-assisted palatal stiffening operation (CASPO), injection snoreplasty, diathermy assisted uvulopalatoplasty (DAUP), laser palatoplasty, and Pillar implants.

3.4.2.5 Cautery-assisted Palatal Stiffening Operation (CASPO)

Cautery-assisted palatal stiffening uses cautery to burn the soft palate causing fibrosis and consequent stiffening upon healing. The procedure is performed during a single out-patient visit, under local anaesthetic. As with radiofrequency ablation and LAUP, the procedure can be repeated until the desired effect on snoring is gained. The procedure is less invasive than either UPPP or LAUP and there are generally fewer post-operative complications observed.

3.4.2.6 Injection snoreplasty

Injection snoreplasty is performed on an outpatient basis, with use of a topical local anaesthetic. A sclerosing agent (such as 3% sodium tetradecyl sulphate, ethanol, and doxycycline or alcohol) is injected into the soft palate anterior to the uvula, which creates blistering, causing subsequent fibrosis and stiffening upon healing. Like CASPO, the procedure may need to be repeated until the optimal treatment benefit is attained.

3.4.2.7 Pillar Implants

The Pillar Implant system is theorised to stiffen and reduce the fluttering movement of the soft palate through the implantation of woven Dacron mesh inserts into pockets created in the soft

palate.[70] As with CASPO and injection snoreplasty, the subsequent stiffening of the palate that occurs is due to fibrosis of the palatal tissue upon healing. The technique is performed as a one stage procedure, which may be combined with other upper airway procedures for snoring.

3.4.2.8 Tongue-Based Suspension Procedure

The tongue based suspension procedure involves the insertion of a titanium screw into the genioturbucle of the posterior aspect of the mandible in the floor of the mouth. A loop of suture is then passed through the tongue base and attached to the mandible bone screw. The resulting suspension or hammock of the tongue base by the device, effects geniglossus muscle activity preventing posterior tongue displacement and occlusion with the posterior pharyngeal wall.[71]

3.4.2.9 Surgery to improve nasal patency

When routine tests show snoring may be related to nasal obstruction, then septoplasty, septorhinoplasty, turbinate reduction or sinus surgery may be indicated.[71] Previous studies estimate that 50% - 69% of non-apnoeic snorers with nasal symptoms have improved levels of snoring with nasal surgery alone.[72, 73]

Given the number of options available in both the surgical and non-surgical management of non-apnoeic snoring, an assessment of the clinical effects and the associated costs of the various strategies is required.

4. Methods for synthesis of evidence of clinical effects

4.1 Electronic database searches

A comprehensive search syntax using Medical Subject Headings (MeSH) and free text terms for non-apnoeic snoring combined with terms for the included interventions will be developed. This will build upon the search syntax devised and used for the scoping searches (Appendix 1).

This will be used to identify relevant studies indexed on the following databases:

- MEDLINE
- Cochrane Controlled Trials Register (CCTR)
- Embase
- CINHAL

Searches will be limited to studies published between 1980 and 06/2007. All retrieved bibliographic references will be duplicated and managed in Reference Manager software.

4.2 Inclusion and exclusion criteria

4.2.1 Participants

Adults (≥ 18 years of age) eligible for surgical and/or non-surgical management of primary snoring will be included. Patients must have undergone investigations to exclude possible obstructive sleep apnoea (OSAS) such as polysomnography, modified polysomnography or at a minimum overnight oximetry. Patients with a Apnoea-Hypopnoea Index (AHI) score <5 will be classified as non-apnoeic snorers.

Studies that include patients with significant co-morbidities, such as chronic obstructive pulmonary disease (COPD), neuro-muscular disorders, asthma, or heart failure will be excluded. Additionally, studies including groups of patients with a diagnosis of OSAS or UARS (AHI≥5) and patients with a diagnosis of non-apnoeic snoring will only be included where outcomes are reported separately for each patient group.

4.2.2 Interventions

Studies that assess one or more of the following interventions will be included:

- Continuous Positive Airway Pressure (either nasal or full face mask)

Oral appliances
- Mandibular repositioning appliances (MRAs)
- Tongue retaining devices (TRDs)

Surgery to improve nasal patency
- Septoplasty
- Turbinate reduction
- Sinus surgery

(or any combination of the above three)

Defined snoring surgical techniques
- Uvulopalatopharyngoplasty (UPPP) either with or without tonsillectomy
- Laser-assisted uvulopalatoplasty (LAUP)
- Diathermy assisted uvulopalatoplasty (DAUP)
- Uvulectomy alone (using either laser assisted or diathermy assisted techniques)
- Palatal stiffening techniques (including but not limited to injection snoreplasty, cautery-assisted palatal stiffening, and Pillar implants)
- Radiofrequency ablation (RFA) of the soft palate (somnoplasty)
- Tongue-base Suspension Procedures

All comparisons for the identified interventions will be versus each other, placebo or no intervention as applicable.

Studies that assess adenoidectomy or tonsillectomy used either alone or in combination with each other will be excluded. Additionally, studies that assess life-style modification interventions, such as weight loss, sleep positioning devices, smoking or alcohol reduction programmes for the management of non-apnoeic snoring, will only be included if directly compared to one of the surgical or non-surgical interventions outlined above. Studies of non-prescription treatments, such as lubricant nasal and oral sprays, internal and external nasal dilators, herbal remedies, ear plugs, dietary supplements and magnetic therapy, will also be excluded.

4.2.3. Outcomes

Both objective and subjective outcome measures of snoring and daytime sleepiness will be included.

Objective measures
- Snoring recording and/or acoustic analysis of snoring sound

- Polysomnography or modified polysomnography

Subjective measures
- Epworth Sleepiness Scale Score (ESS)/symptoms of daytime sleepiness
- Patient and partner questionnaires and/or linear analogue scales related to snoring severity
- Patient and partner health-related quality of life (using a scale or linear analogue scale)
- Sleep quality of bed partner

Adverse events
- Short and long term side effects/complications of treatment. Where possible these will be dichotomised and considered separately.

- Need for further repeat procedures (other than those specified in the treatment protocol)

4.2.4 Study designs

Controlled studies of any duration of follow-up will be included. These will include:
- Randomised and quasi-randomised controlled trials (RCTs)
- Cross-over trials
- Controlled clinical trials (CCTs)

Pre-post studies which report outcome measures which are measured objectively (i.e) PSG, acoustic analysis of snoring sound or snoring recordings will also be included.

Pre-post studies which report only outcomes that are measured subjectively, retrospective case series and prospective and retrospective surveys will be excluded.

4.2.3.5 Publication language and status

Due to the time frame of the assessment, only studies published in English as a full journal article will be included. The details of all foreign language papers which appear, on the basis of title and abstract alone, to meet the above pre-specified inclusion criteria will be tabulated and reported in an appendix.

4.3 Conduct of the review

The review will be undertaken following the guidance on the conduct of systematic reviews published by the Centre for Reviews and Dissemination.[74]

Two reviewers will be involved in all key stages of the review process. Any discrepancies throughout the review will be resolved through examination of the relevant papers, and involvement of a third reviewer if necessary.

4.3.1 Selection of primary studies

The abstracts and titles of references retrieved by the electronic searches will be screened for relevance. Full paper copies of potentially relevant studies will be obtained. The retrieved articles will be assessed for inclusion by one reviewer and independently checked by a second, using the pre-specified inclusion/exclusion criteria. All duplicate papers will be double checked and excluded.

4.3.2 Data extraction and quality assessment strategy

Data will be extracted from the included studies using a standardised data extraction form. Where multiple publications of the same study exist, data will be extracted from all publications together, with priority given to data reported on an intention-to-treat basis. All data will be managed in Microsoft Access. The quality of the individual studies will be assessed according to standard methodological criteria listed in CRD Report 4 (Appendix 2).[74]

4.3.3 Methods of data synthesis

Studies will be grouped by the intervention (and comparator where applicable), study design and outcome measures. Demographic data for each study and relevant results will be presented in tables.

Where appropriate, meta-analysis will be used to estimate a pooled summary measure of effect for relevant outcomes based on an intention-to-treat analysis. Where meta-analysis is conducted it will be carried out using fixed and random effects models, using STATA software. Heterogeneity will be explored through consideration of the interventions, study populations and study quality. Statistical heterogeneity will be assessed using the Chi-squared test for homogeneity and the I^2 statistic.

If studies are sufficiently heterogeneous to preclude estimating a pooled summary effect measure, results will be combined using a narrative synthesis.[75] Differences between the studies will be explored narratively by examining differences in the interventions, settings, participants baseline characteristics and study quality.

4.3 Costs of the interventions

A range of sources will be searched to identify the current UK costs associated with each of the interventions included in the review of clinical effects. These sources will include, but not be limited to, standard electronic bibliographic databases (such as Econ Lit and NHS EED), manufacturer's web-sites, the National Schedule of Reference Costs database, and Practitioners and Experts in the field.

Where applicable, a range of the cost estimates for each intervention associated with different care pathways will be estimated; for example treatment in a primary as opposed to a secondary care setting for the fitting of a mandibular repositioning device, will be given. Wherever possible, cost estimates will show a breakdown of the underlying resource use, such as hours of Ear, Nose and Throat (ENT) surgeon, or dentist/dental technician time, device cost and consumables. All costs and the applicable ranges will be tabulated and presented alongside the results of the review of clinical effects.

4.4 Identification of interventions for which primary research would be of benefit

Interventions for which future primary research would be of benefit will be identified and prioritised. This will be undertaken by considering the magnitude of any clinical effects, the size and the quality of the currently available evidence base, and the likelihood that a given treatment is, or will become widely used in the UK and/or the NHS.

5. Expertise in the Technology Assessment Group

5.1 Peninsula Technology Assessment Group

The Peninsula Technology Assessment Group is part of the Institute of Health and Social Care Research at the Peninsula Medical School. PenTAG was established in 2000 and carries out independent Health Technology Assessments for the UK HTA Programme and other local and national decision-makers. The group is multi-disciplinary and draws on individuals' backgrounds in public health, health services research, computing and decision analysis, systematic reviewing, statistics and health economics. The Peninsula Medical School is a school within the Universities of Plymouth and Exeter.

5.2 Team members' contributions

The PenTAG team members who will undertake the project have previously produced reports for NICE, the Health Technology Assessment Programme and the Department of Health. These projects have included Technology Assessment Reports, National Guidelines, and short reports. The members of the project team and their role in the project are listed below:

Ms Caroline Main Research Fellow; Peninsula Technology Assessment Group	Responsible for project coordination, drafting the protocol, study selection, data extraction and quality assessment, data synthesis, and drafting the final report
Ms Zulian Liu Research Assistant; Peninsula Technology Assessment Group	Responsible for data extraction and quality assessment, contributing to the results section and commenting on the draft report.
Ms Karen Welch Information Scientist; Wessex Institute for Health Research & Development; University of Southampton	Responsible for devising the search strategy, conducting the literature searches, drafting the search methodology section, and commenting on the final report
Dr Rob Anderson Senior Lecturer in Health Economics; Peninsula Technology Assessment Group	Responsible for identifying intervention costs, supervising drafting the cost results section and commenting on the final report.
Mr Graeme Weiner Consultant Ear, Nose and Throat Surgeon; Royal Devonshire and Exeter Hospital; Exeter	Responsible for providing clinical input at all project stages, commenting on the draft protocol and draft report
Dr Simon-Quentin Jones Honorary Clinical Lecturer; Cardiff University Dental Hospital; Cardiff	Responsible for providing clinical input at all project stages, commenting on the draft protocol and draft report
Professor Ken Stein Professor of Public Health; Peninsula Technology Assessment Group	Responsible for project direction, providing input and comments at all stages, and has overall responsibility for the report

6. Competing interests of authors

All authors declare that they have no competing interests.

7. Project timetable/milestones

The Health Technology Assessment Programme (HTA) have indicated that this project is allocated the equivalent of 0.66 TAR Units. The agreed project timetable and miles stones are:
Project progress report - Friday 16th November 2007.
Final report to HTA - Monday 17th December 2007.

8. References

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Appendix 1: Draft search syntax for the scoping searches

("Snoring/diagnosis"[MeSH] OR "Snoring/drug therapy"[MeSH] OR "Snoring/economics"[MeSH] OR "Snoring/epidemiology"[MeSH] OR "Snoring/prevention and control"[MeSH] OR "Snoring/psychology"[MeSH] OR "Snoring/rehabilitation"[MeSH] OR "Snoring/surgery"[MeSH] OR "Snoring/therapy"[MeSH])

No study design filters or language restrictions applied.

1268 hits identified; 497 marked as potentially relevant and downloaded.

Appendix 2: DATA EXTRACTION FORM AND QUALITY ASSESSMENT CRITERIA

Data extraction tables

<table>
<tr><td>Author:
Year:
Study ID:</td><td>Title:

Country:
Setting:
Study design:</td></tr>
<tr><td>Intervention</td><td>Intervention:
Comparator:
Concurrent treatment:
Prior treatment(s):</td></tr>
<tr><td>Participants</td><td>Total N:
Tests to exclude OSAS {Formal PSG; modified PSG; overnight oximetry; acoustic analysis; other (state)}
Inclusion criteria:
Exclusion criteria:
Sub-groups: {N-A snoring; OSAS; UARS}

Baseline characteristics
<table>
<tr><td></td><td>Intervention 1</td><td>Intervention 2</td><td>Intervention 3</td></tr>
<tr><td>N</td><td></td><td></td><td></td></tr>
<tr><td>Age {mean; range}</td><td></td><td></td><td></td></tr>
<tr><td>Male {n;%}</td><td></td><td></td><td></td></tr>
<tr><td>Female {n;%}</td><td></td><td></td><td></td></tr>
<tr><td>BMI {mean; range}</td><td></td><td></td><td></td></tr>
<tr><td>RDI score {mean; range}</td><td></td><td></td><td></td></tr>
<tr><td>ESS score {mean; range}</td><td></td><td></td><td></td></tr>
</table></td></tr>
<tr><td>Outcomes</td><td>Primary outcome measure:
Method of measurement:
Secondary outcome measure(s):
Method of measurement:
Total length of follow-up:
Follow-up assessment times:
Rate of attrition at each follow-up time:</td></tr>
<tr><td>Results</td><td>Outcome 1: method of measurement {e.g mean change from baseline; % change from baseline}

<table>
<tr><td></td><td>Intervention 1</td><td>Intervention 2</td><td>Intervention 3</td><td>Differences between groups</td></tr>
<tr><td>N</td><td></td><td></td><td></td><td></td></tr>
<tr><td>Effect size (95% CI: SD; p-value)</td><td></td><td></td><td></td><td></td></tr>
</table></td></tr>
</table>

<table>
<tr><td></td><td>
Outcome 2: method of measurement {e.g mean change from baseline; % change from baseline}
<table>
<tr><td></td><td>Intervention 1</td><td>Intervention 2</td><td>Intervention 3</td><td>Differences between groups</td></tr>
<tr><td>N</td><td></td><td></td><td></td><td></td></tr>
<tr><td>Effect size (95% CI: SD; p-value)</td><td></td><td></td><td></td><td></td></tr>
</table>
Outcome 3: method of measurement {e.g mean change from baseline; % change from baseline}
<table>
<tr><td></td><td>Intervention 1</td><td>Intervention 2</td><td>Intervention 3</td><td>Differences between groups</td></tr>
<tr><td>N</td><td></td><td></td><td></td><td></td></tr>
<tr><td>Effect size (95% CI: SD; p-value)</td><td></td><td></td><td></td><td></td></tr>
</table>
Adverse events:
</td></tr>
<tr><td>Authors conclusions</td><td></td></tr>
<tr><td>Reviewers Comments</td><td></td></tr>
</table>

Methodological assessment criteria

1. Study design	{RCT; X-over trial: CCT; pre-post study}
2. Were the study eligibility criteria specified?	{yes; no; partial}
3. Was a power calculation performed?	{yes; no}
4. Is the sample size adequate?	{yes; no; unclear}
5. Is the number randomized stated?	{yes; no; not applicable}
6. Is the study properly randomized?	{yes; no; not applicable; unclear}
7. Is allocation of treatment concealed?	{yes; no; not applicable; unclear}
8. Are adequate baseline details presented?	{yes; no; partial}
9. Are groups similar at baseline?	{yes; no; partial; not applicable}
10. Are any baseline imbalances adequately adjusted for in the analysis?	{yes; no; not applicable; unclear}
11. If the study is a x-over trial, is there an adequate wash-out period?	{yes; no; unclear; not applicable}
12. Are similar co-interventions administered?	{yes; no; unclear; not applicable}
13. Are outcome assessors blinded?	{yes; no; unclear}
14. Is compliance with treatment adequate?	{yes; no; unclear; not reported}
15. Were any sub-group analysis justified?	{yes; no; not applicable}
16 Were data collection tools shown or known to be valid for the outcome of interest?±	{yes; no; unclear}
17 Were the data collection tools known or were shown to be consistent and accurate in measuring the outcome of interest?*	{yes; no; unclear}
18 Were all study participants accounted for?	{yes; no}
19. Are data analyses appropriate?	{yes; no; partial; unclear}
20. Is analysis conducted on an ITT basis?	{yes; no; not applicable}
21. Are greater than 80% of patients included in the follow-up assessment?	{yes; no; unclear}
22. Are the conclusions supported by the results?	{comment}
23. Generalisability	{comment}
24. Inter-centre variability	{comment}
25. General comments	{comment}

± The tools are known to be valid or were shown to measure what they are intended to measure
* The tools are known to be reliable or were shown to be consistent and accurate in measuring the outcome of interest (e.g. test-retest, Cronback's alpha, interrater reliability)