Surgical versus non-surgical interventions for vocal cord nodules (Review)

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[Intervention Review]

Surgical versus non-surgical interventions for vocal cord nodules

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ABSTRACT

Background

This is an update of a Cochrane review first published in *The Cochrane Library* in Issue 2, 2001 and previously updated in 2007 and 2009.

Vocal cord nodules are bilateral, benign, callous-like growths of the mid-portion of the membranous vocal folds. They are of variable size and are characterised histologically by thickening of the epithelium with a variable degree of inflammation in the underlying superficial lamina propria. They characteristically produce hoarseness, discomfort and an unstable voice when speaking or singing.

Objectives

To assess the effectiveness of surgery versus non-surgical interventions for vocal cord nodules.

Search methods

We searched the Cochrane Ear, Nose and Throat Disorders Group Trials Register; the Cochrane Central Register of Controlled Trials (CENTRAL); PubMed; EMBASE; CINAHL; Web of Science; BIOSIS Previews; Cambridge Scientific Abstracts; ISRCTN and additional sources for published and unpublished trials. The date of the most recent search was 9 April 2012.

Selection criteria

Randomised and quasi-randomised trials comparing any surgical intervention for vocal cord nodules with non-surgical treatment or no treatment.

Data collection and analysis

No suitable trials were identified.

Main results

No studies fulfilled the inclusion criteria.

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Authors' conclusions

There is a need for high-quality randomised controlled trials to evaluate the effectiveness of surgical and non-surgical treatment of vocal cord nodules.

PLAIN LANGUAGE SUMMARY

Surgery versus non-surgical interventions (voice therapy, medical treatment) for the resolution of vocal cord nodules

Vocal cord nodules are benign, callous-like growths on the vocal cords. Symptoms include hoarseness, throat discomfort, pain and an unstable voice when speaking or singing. They can be caused by 'voice abuse' (prolonged shouting or singing above the individual's own range) but may also be caused by infection, allergy or acid reflux.

Vocal cord nodules can be surgically removed but may also be treated with non-surgical voice therapy interventions (e.g. voice re-training, rest or hygiene advice) or medical/pharmacological treatment of underlying infections, allergy or gastroesophageal reflux.

The authors of this review sought to identify trials which compared surgical with non-surgical treatment. They found that there was not enough evidence to compare surgery to other treatment options. More research is needed.

BACKGROUND

This is an update of a Cochrane review first published in *The Cochrane Library* in Issue 2, 2001 and previously updated in 2007 and 2009.

Definition

Vocal cord nodules are bilateral, benign, callous-like growths of variable size found at the mid-part of the membranous vocal cords. They are characterised mainly by thickening of the epithelium with a variable degree of inflammatory reaction in the underlying superficial lamina propria (Nagata 1983).

Symptoms, prevalence and aetiology

Vocal nodules cause hoarseness, throat discomfort or pain, which varies with the amount of voice use. This results in an unstable and unpredictable voice, which can affect quality of life, particularly in professional voice users such as singers (Lacina 1972). The prevalence of nodules in the general population is not known but it has been reported as being the cause of hoarseness in up to 23.4% of children (Silverman 1975), 0.5% to 1.3% of ENT clinic attendances (Böhme 1969; Nagata 1983) and 6% of phoniatric clinic attendances. The prevalence of nodules in female teachers was found to be 43% of 218 cases with dysphonia, in a population of 1046 female teachers in a study in Spain (Urrutikoetxea 1995). It has been reported that teachers speak for an average of 102 minutes per eight hours (Masuda 1993). Nodules were found in 25% of hoarse singers (Lacina 1972).

The aetiology of vocal nodules is not known, but traditionally they are thought to be due to 'voice abuse' and psychological factors, especially in children. Other medical conditions, such as infection, allergy and reflux may also play a role (Hugh-Munier 1997). In a study of 20 adult females, voice abuse was considered to be the cause of vocal nodules (Yamaguchi 1986). The abuse was characterised by strain in the neck and shoulder region, hard glottal attack, loud voice in the chest register and singing above the individual's range. The definition of vocal abuse is however subjective, although attempts have been made to define objective deviations (Pedersen 1997; Xu 1991). The impact stress of phonation appears to be important both clinically and in laboratory models of vocal cord nodules (Jiang 1994). In boys it is recognised that nodules resolve spontaneously at puberty (Håkansson 1984; Seidner 1982).

Diagnosis

The accepted method for the diagnosis of nodules is endoscopic laryngeal examination (allowing visualisation of the vocal cords during phonation and respiration). Examination with a stroboscope gives additional information about the vibratory and closure patterns of the vocal cords and helps exclude other vocal cord pathology, for example intracordal cysts. Stroboscopy is considered a necessary preoperative examination in adults and in children it is also

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desirable but not always possible. Acoustic and aerodynamic criteria alone cannot be used for diagnosis, although improvements in certain parameters, with return towards normal values, can be taken as a sign of response to intervention (Remacle 1999). As many patients will not have had surgery, a clinical diagnosis may not have been confirmed by histological examination.

Management options

There is considerable controversy over the role of surgery in the management of vocal cord nodules. Historically, nodules were excised, but with better understanding of vocal function, more conservative non-surgical techniques have been developed and are now considered by many to be the primary treatment of choice. Rates of surgical intervention vary widely and the exact criteria for surgery are not clearly defined.

Vocal cord nodules are treated either by speech therapy techniques or by surgery (Hocevar 1997; Kuhn 1998). Exacerbating factors, such as infection, allergy and reflux, may also be treated with medical/pharmacological interventions. Non-surgical treatments are based on behaviour modification (McFarlane 1990; Murry 1992). They include vocal hygiene measures (Verdolini 1994), 'abuse' reduction and vocal retraining (Fex 1994). Occasionally no intervention is indicated and observation alone is recommended, either because the symptoms are not severe enough or because there is a strong expectation of spontaneous improvement (Nagata 1983).

Surgical removal of nodules includes excision with microsurgical instruments (Bouchayer 1988; Cornut 1989; Kleinsasser 1991; Wendler 1971) and the laser (Keilmann 1997; Remacle 1999).

A systematic review is warranted to compare the effectiveness of surgical removal of nodules with more conservative treatments.

OBJECTIVES

To assess the effectiveness of surgical versus non-surgical treatment in the management of vocal cord nodules.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials. Controlled clinical trials (trials using a control group but no adequate randomisation procedure) and quasi-randomised trials were also identified.

Types of participants

Children and adults with visually confirmed vocal cord nodules. We planned to include studies where the clinical diagnosis had been reached by examination of the vocal cords by indirect laryngoscopy, rigid or fibre-optic endoscopy or micro-laryngoscopy. Stroboscopy was not considered mandatory.

Types of interventions

Non-surgical versus surgical interventions.

Non-surgical measures included one or more of the following:

1. medical/pharmacological treatment of infections, allergy and gastroesophageal acid reflux;
2. vocal hygiene advice (including alterations in working environment);
3. reduction of 'voice abuse';
4. voice re-training;
5. voice rest;
6. observation alone.

Surgical treatment was removal of the nodules by:

1. direct microsurgical techniques;
2. indirect microsurgical techniques;
3. laser excision;
4. laser ablation.

Types of outcome measures

Primary outcomes

1. Perceptual scoring of voice quality (both by the patient and the investigator).
2. Quality of life, for example, return to singing career or other vocally demanding profession.

Secondary outcomes

1. Assessment of conditions associated with nodules (see under non-surgical types of interventions).
2. Objective assessment of the vocal cords and of vocal function in individuals with nodules:
   i) visual appearance of the vocal cords;
   ii) scoring of roughness, breathiness and overall hoarseness of the voice with perceptual measures;
   iii) acoustic measures of continuous speech or sustained vowels and phonetograms;
   iv) fundamental frequency with jitter and shimmer;
   v) aerodynamic measurements.

Desirable time points of outcome assessment were: short-term, one month; medium-term, six months; long-term, one to five years.

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Search methods for identification of studies

We conducted systematic searches for randomised controlled trials. There were no language, publication year or publication status restrictions. The date of the last search was 9 April 2012, following previous searches in 2009, 2007 and 2001.

Electronic searches

We searched the following databases from their inception for published, unpublished and ongoing trials: the Cochrane Ear, Nose and Throat Disorders Group Trials Register; the Cochrane Central Register of Controlled Trials (CENTRAL, *The Cochrane Library* 2012, Issue 3); PubMed; EMBASE; CINAHL; LILACS; KoreaMed; IndMed; PakMediNet; CAB Abstracts; Web of Science; BIOSIS Previews; CNKI; ISRCTN; ClinicalTrials.gov; ICTRP; Google Scholar and Google.

We updated our search strategies in 2009 and they were modelled on the search strategy for CENTRAL. Where appropriate, we combined subject strategies with adaptations of the highly sensitive search strategy designed by the Cochrane Collaboration for identifying randomised controlled trials and controlled clinical trials (as described in the *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.0.1, Box 6.4.b. (Handbook 2011)). Updated search strategies for the major databases are provided in Appendix 1; original search strategies are provided in Appendix 2.

Searching other resources

We scanned the reference lists of identified publications for additional trials and contacted trial authors where necessary. In addition, we searched PubMed, TRIPdatabase, NHS Evidence - ENT & Audiology and Google to retrieve existing systematic reviews relevant to this systematic review, so that we could scan their reference lists for additional trials. During the preparation of the original version of this review, we checked personal files of references, and attended the PEVOC III conference 1999 and the XXI conference of the Union of European Phoniatricians 1999, but no further references were obtained.

Data collection and analysis

Selection of studies

Two authors reviewed the full-text articles of the retrieved trials and applied the inclusion criteria. Any differences in opinion about which studies to include in the review were resolved by discussion between the two authors.

We identified no suitable trials for inclusion in this review. Should such trials become available the following methods will be applied.

Data extraction and management

The two authors will independently extract data from the studies using standardised data forms. We will extract data so as to allow an intention-to-treat analysis. After all the data forms are filled in, all first authors of the trials to be included and possibly included will receive a copy for comments. Where data are missing, we will write to the authors of the study requesting the missing data.

Assessment of risk of bias in included studies

The two authors will independently undertake assessment of the risk of bias of the included trials with the following to be taken into consideration, as guided by the *Cochrane Handbook for Systematic Reviews of Interventions* (Handbook 2011):

- sequence generation;
- allocation concealment;
- blinding;
- incomplete outcome data;
- selective outcome reporting; and
- other sources of bias.

We will use the Cochrane 'Risk of bias' tool in RevMan 5 (RevMan 2011), which involves describing each of these domains as reported in the trial and then assigning a judgement about the adequacy of each entry: low, high or unclear (or unknown) risk of bias. We will resolve differences by discussion.

Data synthesis

Data analysis will be by intention-to-treat. If they are of sufficient quality we will combine data to give a summary of effect, otherwise we will not combine data. We will use study quality in a sensitivity analysis. If the data permit, we will carry out analysis separately for different types of voice treatment, as well as considering surgical versus non-surgical treatment of nodules as a whole.

Study outcomes are likely to be measured in a variety of ways using several categorical variables. Data may be dichotomised if appropriate. We will seek statistical advice to determine the best way of presenting and summarising the data.

RESULTS

Description of studies

See: Characteristics of excluded studies; Characteristics of studies awaiting classification.

We retrieved a total of 244 references from the 2012 searches, which dropped to 179 after removal of duplicates. Following first-level screening for clearly irrelevant references we were left with 17 references, none of which met the inclusion criteria for the review.

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We added one study to the 'Characteristics of excluded studies' table (a randomised controlled trial comparing vocal therapy with vocal hygiene in patients with voice disorders including nodules). One reference is awaiting assessment as no abstract was available and we are currently unable to obtain the full text of the paper ('Characteristics of studies awaiting classification').

From the 2009 update searches a total of 356 references were retrieved: 312 of these were removed in first-level screening (i.e. removal of duplicates and clearly irrelevant references), leaving 44 references for further consideration. We identified no studies which met the inclusion criteria for the review. We added a further three studies to the 'Characteristics of excluded studies' table. All were randomised controlled trials which comprised or included a proportion of vocal cord nodules patients, however none compared a surgical with a non-surgical intervention.

In 2007 a total of 295 studies were identified through electronic searching for the previous update of this review. For the original review, handsearching of more than 250 pre-1966 papers was also carried out. From the full search results, we obtained 18 full-text papers for further evaluation. Of these 10 were not relevant to the review, and the remaining eight were excluded. Details of the excluded studies, with reasons for exclusion, can be found in the table of 'Characteristics of excluded studies'. Again all excluded studies were randomised controlled trials and all, or a proportion of, the participants in each trial had vocal cord nodules. The studies were excluded because they compared different surgical techniques (e.g. microspot CO_2 laser versus excision), different regimens of voice therapy (e.g. traditional voice therapy versus transnasal flexible laryngoscopy assisted voice therapy) or other interventions for nodules (e.g. acupuncture). We identified no randomised controlled trials which compared surgical with non-surgical interventions and therefore no studies met the inclusion criteria for this review.

Risk of bias in included studies

Not applicable.

Effects of interventions

No studies were found which satisfied the inclusion criteria for this review.

DISCUSSION

We used a comprehensive search strategy for the review. We excluded no studies due to language. While we made several attempts to identify unpublished works, it is still possible that some studies will have been missed. However, the absence of eligible studies for review was not due to restricted selection criteria.

We identified a large number of studies describing either the aetiology, methods for diagnosis or treatment of vocal cord nodules. A major problem highlighted by these descriptive studies is the lack of consensus on the definition of vocal cord nodules and relationship with possible aetiological factors. Not all patients with vocal nodules are symptomatic and some may like the quality of voice that the nodules give them. Out of 65 asymptomatic singing students Lundy found two with nodules diagnosed with videostroboscopy (Lundy 1999). Malmgren et al did not find a strong association between the patient's and speech therapist's perception of the voice after treatment and the size or change in size of the vocal nodules (Malmgren 1990). This raises the question of whether the endoscopic appearance of vocal cords is actually an appropriate outcome measure in spite of it being one of the most widely used. A variety of other outcome measures were used to assess the effectiveness of the interventions, many of which were subjective and there was often no reference to validation. Some studies used psychological and quality of life measures, and a few used perceptual measures and objective voice measurements. There were problems with many of the studies considered for this review in that they had methodological and statistical errors such as inconsistent definitions of key variables, inadequate sample size, no confidence limits, short or missing follow-up, too many separate endpoints and missing data.

Although it is taught that vocal cord nodules form as a result of 'voice abuse', this is increasingly recognised as being a being a rather simplistic view. Firstly nodules have a heterogenous appearance ranging from diffuse swellings where the histological abnormality seems to be more concentrated in the superficial lamina propria to tiny discrete whitish lesions representing focal epithelial thickening. These various types may not necessarily have the same aetiology or prognosis and further studies need to be performed to determine the causative factors now that the lesions can be better visualised with newer imaging techniques.

Secondly, the point at which nodules become pathological may depend on the individual's perception of their voice and the demands on their voice. As with any organ it is possible to improve its physical performance with training and optimisation of the environment in which it is expected to function. However, there are likely to be physical limits to the sound production (in terms of stamina, pitch range, loudness, timbre and fine control) based on the anatomical and physiological limitations of the individual's vocal apparatus. It may be necessary to recognise that the vocal demands are in fact too great for the individual, or the individual's larynx, in their chosen working environment (the amount of background noise or vocal cord irritation from a pollutant). These factors may be as important as, if not more important than, the intervention itself in determining the success of a treatment.

Thirdly there are no gold standards in objective outcome measures of voice treatment and often there is poor correlation between the more objective and subjective measures of assessment. The aims of

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treatment need to be carefully defined, e.g. resolution of nodules on endoscopic examination, improvement in levels of impairment, activity and participation, acoustic, perceptual and aerodynamic measurements. Whatever measurements are chosen they must be as objective as possible, but also have real relevance to patients.

There is evidence from non-randomised intervention studies (Holmberg 2001; Verdolini 1994; Yamaguchi 1986) that both speech therapy techniques and surgery (Bouchayer 1988; Keilmann 1997; Wendler 1971) are effective. However it is not clear how patients should be selected. Although speech therapy is first-line treatment, there is no consensus as to which of the techniques employed by speech therapists are most effective nor for how long they should be used. The techniques range from improving vocal hygiene, behaviour modification and 'abuse' reduction, to vocal retraining and psychological support. It is likely that more than one factor usually requires intervention and that this should be individualised. Future studies would benefit from attempts at quantifying or at least defining each of these factors.

There is a general consensus that surgical treatment of the nodules should aim at removing the minimum amount of mucosa from the vocal cord. Whether cold surgical techniques are better than laser treatment has not been determined with certainty but with newer instruments the surgical result is more likely to be dependent on the skill and experience of the surgeon rather than the tool.

The role of postoperative voice therapy is unclear with some claiming that recurrence is more likely without it. The chance of recurrence is likely to depend on compliance with pre-operative instructions in speech therapy techniques, anatomical, physiological, environmental and psychological factors. Some are likely to be cured with or without postoperative voice therapy and some will suffer further recurrence in spite of it.

There is no doubt that vocal nodules are a difficult condition to study and treat when the aetiology is not fully understood. In addition there are no robust objective measures of vocal function and there are many variables that can affect the outcome of an intervention. More patient-orientated outcome measures are being developed and their value is being slowly defined.

AUTHORS' CONCLUSIONS

Implications for practice

There is no evidence from randomised controlled trials on which to base reliable conclusions about the comparative effectiveness of surgical versus non-surgical interventions for the management of patients with vocal cord nodules.

Implications for research

There is a need for a carefully designed prospective randomised controlled study to determine which patients should be selected for primary voice therapy and which would benefit from surgery. Although voice therapy is usually chosen as primary treatment it may not necessarily be the most cost-effective way of managing this condition. Voice therapy usually requires a prolonged period of treatment while surgery potentially removes the causative lesions restoring the anatomical configuration of the vocal folds. However, there are potential risks of surgery and failures have been reported if the underlying causative factors are not addressed. In addition, it may be that patients would rather explore the more conservative approaches before submitting themselves to surgery. It may be important to determine patient views before investing in such a study.

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* *Indicates the major publication for the study*

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CHARACTERISTICS OF STUDIES

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Behrman 2008	ALLOCATION: randomised controlled trial PARTICIPANTS: women with a recent (within 3 months) diagnosis of bilateral, fairly symmetric, mid-membraneous, benign free-edge vocal fold lesions (mainly nodules) INTERVENTIONS: vocal hygiene education versus voice production therapy
Benninger 2000	ALLOCATION: randomised controlled trial PARTICIPANTS: patients (18 years and older) with vocal cord nodules, polyps, mucous retention cysts or polypoid degeneration of the vocal fold(s) INTERVENTIONS: microspot CO_2 laser excision versus microdissection
Carding 1998	ALLOCATION: randomised controlled trial PARTICIPANTS: patients with non-organic dysphonia (including minor laryngeal lesions such as insignificant vocal cord oedema, non-fibrous nodules, chronic laryngitis and dysphonia plica venticularis (false cord phonation) INTERVENTIONS: direct (voice) therapy versus indirect therapy versus no treatment
Gillivan-Murphy 2006	ALLOCATION: randomised controlled trial PARTICIPANTS: teachers with self reported voice/throat symptoms, some with nodules diagnosed following video-endoscopic examination INTERVENTIONS: vocal function exercises plus vocal hygiene education versus no treatment
Hörmann 1999	ALLOCATION: randomised controlled trial PARTICIPANTS: 44 adult patients with benign lesions of the vocal fold such as polyps, Reinke's oedema or vocal cord nodules not amenable to conservative treatment INTERVENTIONS: conventional phonosurgery versus laser surgery
Mashima 2003	ALLOCATION: randomised controlled trial PARTICIPANTS: 72 patients with voice disorders, including 31 with vocal cord nodules INTERVENTION: conventional voice therapy versus remote voice therapy delivered via a real-time audio-video monitoring system
Ragab 2005	ALLOCATION: randomised controlled trial PARTICIPANTS: 50 patients with benign superficial vocal cord lesions (20 vocal cord nodules) INTERVENTIONS: cold knife versus radiosurgical excision
Rattenbury 2004	ALLOCATION: randomised controlled trial PARTICIPANTS: 50 patients with muscle tension dysphonia (patients with minor vocal cord lesions, e.g. minor vocal cord nodules, were included) INTERVENTIONS: traditional voice therapy versus transnasal flexible laryngoscopy (TFL) assisted voice therapy

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(*Continued)*

Rodriguez-Parra 2011	ALLOCATION: randomised controlled trial PARTICIPANTS: 42 patients with voice disorders (vocal nodules, polyps, angiomatous polyps, Reinke's oedema and hypotonic dysphonia) INTERVENTIONS: vocal therapy versus vocal hygiene
Wang 2005	ALLOCATION: randomised controlled trial PARTICIPANTS: 80 patients with vocal cord nodules INTERVENTIONS: acupuncture versus Chinese herbs versus Western medicine
Yiu 2006	ALLOCATION: randomised controlled trial PARTICIPANTS: 54 patients (female) with dysphonia associated with benign pathological changes (13 nodules) INTERVENTION: acupuncture versus placebo (sham acupuncture)
Zhu 2005	ALLOCATION: randomised controlled trial PARTICIPANTS: patients with vocal nodules or vocal cord polyps INTERVENTION: surgery (not specified in abstract) versus surgery plus Jinsangsanjie pills (traditional Chinese medicine)

Characteristics of studies awaiting assessment *[ordered by study ID]*

Lin 2010

Methods	
Participants	
Interventions	
Outcomes	
Notes	No information - no abstract available. Currently unable to access full text

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DATA AND ANALYSES

This review has no analyses.

APPENDICES

Appendix 1. Updated search strategies - 2009 onwards

CENTRAL	PubMed	EMBASE (Ovid)	CINAHL (EBSCO)
#1 MeSH descriptor Granuloma, Laryngeal explode all trees #2 MeSH descriptor Vocal Cords explode all trees #3 (voice or vocal* or laryn* or phono*):ti #4 MeSH descriptor Granuloma explode all trees #5 nodul* or callus* or thickening* or lesion* or granuloma #6 (#2 OR #3) #7 (#4 OR #5) #8 (#6 AND #7) #9 (#1 OR #8)	#1 "Granuloma, Laryngeal"[Mesh] #2 "Vocal Cords"[Mesh] #3 (vocal* [ti] OR voice [ti] OR laryn* [ti] OR glotti* [ti] OR phono* [ti]) #4 #2 OR #3 #5 "Granuloma"[Mesh] #6 (nodul* [tiab] OR callus* [tiab] OR thickening* [tiab] OR lesion* [tiab] OR granuloma* [tiab]) #7 #5 OR #6 #8 #4 AND #7 #9 #1 OR #8	1 larynx granuloma/ 2 larynx injury/ 3 vocal cord/ 4 (vocal* or voice or laryn* or phono*).ti. 5 granuloma/ 6 (nodul* or callus* or thickening* or lesion* or granuloma*).tw. 7 3 or 4 8 5 or 6 9 7 and 8 10 1 or 2 or 9	S1 (MH "Vocal Cords") S2 TI vocal OR voice OR laryn* OR phono* S3 (MH "Granuloma+") S4 TX nodul* or callus* or thickening* or lesion* or granuloma* S5 S1 or S2 S6 S3 or S4 S7 S5 and S6
Web of Science	**BIOSIS Preview (Ovid)**	**CAB Abstracts (Ovid)**	**ISRCTN**
#1 TI=(vocal OR voice OR laryn* OR phono*) #2 TS=(nodul* or callus* or thickening* or lesion* or granuloma*) #3 #2 AND #1	1 (vocal* or voice or laryn* or phono*).ti. 2 (nodul* or callus* or thickening* or lesion* or granuloma*).tw. 3 1 AND 2	1 (vocal* or voice or laryn* or phono*).ti. 2 (nodul* or callus* or thickening* or lesion* or granuloma*).tw. 3 granuloma/ 4 2 or 3 5 1 and 4	(voice OR vocal OR laryn% OR phono%) AND (lesion% OR granuloma% OR callus% OR nodul%)

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Appendix 2. Original search strategies

CENTRAL	MEDLINE (Dialog DataStar)	EMBASE (Dialog DataStar)
1. VOICE DISORDERS explode all trees (MeSH) 2. GRANULOMA LARYNGEAL single term (MeSH) 3. VOCAL CORDS [pa] single term (MeSH) 4. vocal* NEAR (nodul* OR callus* OR thickening* OR lesion* OR granuloma*) 5. voice NEAR (nodul* OR callus* OR thickening* OR lesion* OR granuloma*) 6. laryn* NEAR (nodul* OR callus* OR thickening* OR lesion* OR granuloma*) 7. glotti* NEAR (nodul* OR callus* OR thickening* OR lesion* OR granuloma*) 8.1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7	1. VOICE-DISORDERS#.DE 2. GRANULOMA-LARYNGEAL.DE 3. VOCAL-CORDS-PA.DE 4. (vocal$2 OR voice OR laryn$4 OR glotti$1) NEAR (nodul$4 OR callus$2 OR thickening$1 OR lesion$1 OR granuloma$5) 5. 1 OR 2 OR 3 OR 4	1. VOCAL-CORD-DISORDER.DE 2. (vocal$2 OR voice OR laryn$4 OR glotti$1) NEAR (nodul$4 OR callus$2 OR thickening$1 OR lesion$1 OR granuloma$5) 3.1 OR 2

WHAT'S NEW

Last assessed as up-to-date: 9 April 2012.

Date	Event	Description
24 April 2012	New citation required but conclusions have not changed	We identified no studies which met the inclusion criteria for the review. One further study was excluded
9 April 2012	New search has been performed	New searches run.

HISTORY

Protocol first published: Issue 1, 2000

Review first published: Issue 2, 2001

Date	Event	Description
25 November 2009	New search has been performed	New searches were run in November 2009. We identified no studies eligible for inclusion. Three further studies were excluded

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(*Continued*)

30 October 2008	Amended	Converted to new review format.
18 July 2007	New citation required but conclusions have not changed	New searches were run in January 2007. No new studies were found for inclusion

CONTRIBUTIONS OF AUTHORS

Mette Pedersen: protocol development, trials searching, quality assessment of trials, data extraction, data analysis, review development.

Julian McGlashan: protocol development, trials searching, quality assessment of trials, data extraction, data analysis, review development.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- None, Not specified.

External sources

- None, Not specified.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Should studies eligible for inclusion be identified in future updates of this review we will now use the new Cochrane 'Risk of bias' tool for quality assessment (Handbook 2011).

INDEX TERMS

Medical Subject Headings (MeSH)

*Vocal Cords; Laryngeal Diseases [*therapy]

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MeSH check words

Humans

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