

**Supplemental Table: Evidence-base for therapies for unexplained chronic throat symptoms**

<b>Treatment options</b>	<b>Indications</b>	<b>Treatment details</b>	<b>Evidence in UCTS</b>	<b>Recommendations</b>
<b>Standard interventions</b>				
Education and reassurance	All patients	Education on ITS and multi-factorial nature, prevalence, symptom validation, reassurance re benign nature of symptoms, establish goals	No data	We suggest these strategies form the standard foundation of treatment in all patients, to support patient engagement and optimise aerodigestive health. Initial speech therapy review can seek to reinforce vocal hygiene and health, and initiate tactics to minimise phonotraumatic symptoms as the treatment plan is developed
Minimise intake of carbonated beverages and high acid content food / liquids	All patients	Educational materials and counselling	Minimal data. Weak evidence to support symptom benefit on UCTS <sup>1-3</sup>	
Ensure sufficient oral hydration	All patients	Education materials and counselling	Moderate evidence for epithelial barrier integrity and symptom benefits <sup>4-6</sup>	
Vocal hygiene education	All patients (particularly those with dysphonia)	Educational materials and counselling, initial speech therapy review	Moderate evidence for minimising laryngeal irritation and symptoms <sup>7-9</sup>	
<b>Dietary interventions</b>				
Elevate head /torso during sleep Avoid eating within 3 hours of sleep Avoid excess caffeine, alcohol, processed foods	Suspected or known GORD Patients with dysphagia	Provide educational materials and counselling or consider dietician review and education	Moderate-strong evidence supports dietary and lifestyle interventions for management of	In patients with known or suspected GORD, these are safe and simple strategies to implement and are therefore recommended in combination with standard measures, and pharmacological

Control meal portions, mindful chewing / swallowing			oesophageal symptoms of GORD. Their efficacy for presumed LPR is not well established <sup>2 10 11</sup>	therapies where indicated
<b>Psychosocial interventions</b>				
Mindfulness and meditation therapies	Co-morbid anxiety and depression	Counsel patient on purpose of treatments, potential benefits, mind-body link	Moderate, limited evidence suggests therapies supporting mental wellness and mindfulness improve symptoms in patients with UCTS. <sup>12-26</sup>	Mindfulness and meditation practices, in addition to regular exercise, have numerous reported benefits and health and wellness and may be recommended to any patient with UCTS. Approach with sensitivity and consent.
Exercise	Suspected symptom hyper vigilance	Educational materials and Link patient with resources and local providers		Specific psychotherapy or behavioural therapies may be useful tools in patients with co-morbid mental illness or significant stressors, or recalcitrant symptoms, and should involve referral to a psychologist or other mental health professional with patient consent.
Acceptance and Commitment therapies	Prominent psychosocial stressors	Refer to psychologist or other mental health provider where appropriate		
Cognitive Behavioural Therapy	Muscle tension or vocal fold movement disorders			
Hypnotherapy	Muscle tension or vocal fold movement disorders			
Patient support groups				
Exercise	Muscle tension or vocal fold movement disorders			
<b>Environmental modifications</b>				
Occupational and domestic modifications	Suspected inhaled irritant or allergy Professional voice users	Alterations in workplace/domestic activity or environment, or PPE use to minimise potential exposures	Limited data for evidence of benefit in workplace associated laryngitis	Avoidance of the suspected irritant is ideal. Appropriate PPE may be necessary, though consideration of increased vocal effort

			syndromes <sup>27-30</sup>	and airway dehydration associated with mask use must be considered Occupational physicians may be able to confirm irritant reactivity and initiate additional therapeutic strategies
		Change in work activities to reduce vocal load	Weak-Moderate evidence of benefit for dysphonia in professional voice users <sup>30-32</sup>	Vocal demand should, where possible, be reduced in patients with symptoms suspected to be related to high voice use
<b>Speech Therapy</b>				
Various interventions	All patients	Vocal hygiene, vocal retraining, behavioural modification, symptom mindfulness, swallow retraining, relaxation techniques etc.	Moderate-strong evidence supports benefit from speech therapy for a variety of UCTS <sup>7 9 13 33-41</sup>	All patients should be referred to speech therapy for assessment, education and specific therapies guided by symptoms, nasoendoscopic features and patient factors
<b>Reflux treatments</b>				
Alginates	Patients with confirmed or suspected GORD	Oral alginate suspension (Gaviscon DA) 10-20mL post meals and pre bedtime	Weak-moderate evidence of benefit in patients with GORD associated UCTS <sup>42-45</sup>	Safe, recommended in all patients with suspected LPR
PPIs	Patients with oesophageal symptoms of GORD or confirmed PPI	Pantoprazole 40mg BD or esomeprazole 40mg BD for 12 weeks*	Strong evidence for oesophageal symptoms of GORD, weak	Acid suppression therapies appear minimally effective for UCTS based on pooled data from randomised trials.

	responsive GORD		evidence for UCTS <sup>1 46-50</sup>	Use only to control oesophageal symptoms. Use beyond this based on pH impedance data or other factors should be under the guidance of a gastroenterologist
H2 antagonists	Patients with oesophageal symptoms of GORD or confirmed PPI responsive GORD	H2 receptor antagonist daily (i.e. Nizatidine)	Strong evidence for oesophageal symptoms of GORD, limited data for UCTS	As above
Prokinetics	Not indicated	Not indicated	No evidence	Not recommended
<b>Allergy treatment</b>				
Oral antihistamines	Co-morbid respiratory allergy or demonstrated sensitivity to inhaled allergens	Loratadine 10mg daily for 4 weeks OR Cetirizine 10mg daily for 4 weeks	Weak evidence of benefit for patients with UCTS and AR <sup>51-56</sup>	The use of allergy treatments for UCTS has been minimally studied. In patients with previously undetected allergy, a trial of leukotriene antagonist +/- oral antihistamine is reasonable until further dedicated data is available to guide recommendations.
Leukotriene antagonists	Co-morbid respiratory allergy or demonstrated sensitivity to inhaled allergens	Montelukast	Weak evidence of benefit for patients with UCTS and AR <sup>55-61</sup>	In patients with Asthma or AR, optimise control of these conditions, and consider trial of additional agents to assess impact on UCTS.
Immunotherapy	Steroid inhaler dependent asthma Severe AR	Refer to immunology for opinion and treatment initiation / supervision	Weak evidence of benefit for patients with UCTS and Asthma <sup>53 62 63</sup>	In patients with Asthma or AR, optimise control of these conditions, and consider trial of additional agents to assess impact on UCTS. Use of steroid inhalers is associated with dysphonia and should be considered a potential symptom precipitant. Immunotherapy may be a useful

consideration in this case.

### Neuromodulators

Gabapentin	All patients*	300mg daily, titrated every 1-2 weeks to a maximum of 1200mg daily. Cease if no benefit after 6 weeks or adverse effects outweighing benefit	Moderate evidence of benefit for UCTS, particularly globus sensation, chronic cough and dysphonia <sup>9 39 64-67</sup>	A 4-6 week trial of neuromodulating therapies is reasonable for patients with recalcitrant symptoms, or where sensory dysregulation or hyper-vigilance is strongly suspected. May also be beneficial in some patients with aerodigestive motor tension or movement aberrations. Psychosomatic stressors or co-morbidity may be a relative indicator, but this requires further investigation. Ensure no contraindication to treatment and adequate monitoring for adverse effects. Informed consent is required.
Amitriptyline		10mg nocte titrated to a maximum of 40mg nocte . Cease if no benefit after 6 weeks or adverse effects outweighing benefit	Moderate evidence of benefit for UCTS, particularly globus sensation, chronic cough and dysphonia <sup>38 67-70</sup>	

### Invasive treatments

Botox injections	Dysphonia Globus Cough	Specific injection targets depending on symptom profile	Limited-moderate evidence of benefits for sensory and motor dysfunction related symptoms <sup>38 71-75</sup>	Botox injections may be of value in specific instances, depending on patient factors, symptoms, and specific factors on naso-endoscopy, manometry or functional swallow assessments. Refer to an otolaryngologist for consideration in
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Anti-reflux surgery	Objective reflux burden and recalcitrant symptoms	Surgical fundoplication or similar	Moderate evidence for benefit in GORD associated UCTS <sup>47 76-83</sup>	patients with recalcitrant symptoms Reserve for patients with high reflux burden and morbid symptoms. Limited utility of pH-Impedance data for predicting symptom response. Refer to UGI for consideration
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