NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of endoscopic thoracic sympathectomy for primary facial blushing

Facial blushing is reddening of the face because of excessive blood flow to the skin. In endoscopic thoracic sympathectomy, keyhole surgery using an endoscope (a type of thin telescope) is done through a small cut in the armpit, to remove nerve tissue near the spine that controls small blood vessels supplying the skin of the face. The procedure is then repeated on the other side as necessary.

Introduction

The National Institute for Health and Care Excellence (NICE) has prepared this overview to help members of the Interventional Procedures Advisory Committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in June 2013.

Procedure name

- Endoscopic thoracic sympathectomy for primary facial blushing

Specialist societies

- Vascular Society of Great Britain and Ireland
- Society for Cardiothoracic Surgery in Great Britain and Ireland

Description

Indications and current treatment

Blushing or facial reddening is an involuntary reaction, usually as a result of a strong emotional response that stimulates the sympathetic nervous system to increase the flow of blood to the skin of the face. People with facial blushing may also have hyperhidrosis (excessive sweating).

Conservative treatment for facial blushing includes oral medications such as beta-blockers or anticholinergics. When anxiety is the cause of blushing psychological treatments such as cognitive behavioural therapy may be used.

If blushing fails to respond to conservative medical treatment or behavioural therapy, then surgical sympathectomy is an option: this can be done either by open or endoscopic approaches. Endoscopic sympathectomy is now usually the preferred technique.

What the procedure involves

The aim of endoscopic thoracic sympathectomy (ETS) for primary facial blushing is to reduce the frequency and duration of blushing by dividing the sympathetic nerves that lie along the sympathetic chain beside the vertebral column.

ETS is usually done with the patient under general anaesthesia. Small incisions are made in the axilla and an endoscope is inserted. The lung is partially collapsed; this is typically done by insufflating the chest cavity with CO_2. The sympathetic chain is visualised and the chosen part of the chain is divided by electrocautery or endoscopic scissors, or surgical clips may be applied. The extent of division varies but usually involves the part of the sympathetic chain over the second or third ribs, or both. Gas is removed from the pleural space, allowing the lung to re-expand, and the wounds are closed. The procedure is then usually repeated on the other side.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to endoscopic thoracic sympathectomy for primary facial blushing. Searches were conducted of the following databases, covering the period from their commencement to 24 June 2013: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were

also searched. No language restriction was applied to the searches (see appendix C for details of search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with primary facial blushing.
Intervention/test	Endoscopic thoracic sympathectomy.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the overview

This overview is based on 4520 patients (approximately 2544 treated for facial blushing or blushing associated with hyperhidrosis) from 1 randomised controlled trial[5] and 9 case series[1-4; 6-10]. There may be some overlap of patients.

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A.

Table 2 Summary of key efficacy and safety findings on endoscopic thoracic sympathectomy for treatment of primary facial blushing

Abbreviations used: ETS, endoscopic thoracic sympathectomy; HH, hyperhidrosis; NS, not significant; QoL, quality of life; SEM, standard error of the mean; VAS, visual analogue scale.

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Drott C (2002)[1]

Case series
Sweden
(2 centres)
Recruitment period: not reported
Study population: patients with severe facial blushing
n = 1314 (833 responded)
Age: median 34 years (range 15–74)
Sex: 55% women

Patient selection criteria: Patients with facial redness likely to be mediated by the sympathetic nervous system. (Patients with constant redness were urged to see dermatologist to exclude primary dermatological disease).

Technique: bilateral ETS with the sympathetic chain divided in most cases by electrocautery</td>
<td>Number of patients analysed: 831
Change in symptoms- facial blushing and sweating (assessed by patient on VAS)
<table>
<tr><th></th><th>Before procedure</th><th>After procedure</th></tr>
<tr><td>Facial blushing[a]</td><td>8.8 (0.05)</td><td>2.5 (0.09)</td></tr>
<tr><td>Hand sweating[b]</td><td>4</td><td>0.5</td></tr>
<tr><td>Facial sweating[b]</td><td>4</td><td>1.5</td></tr>
</table>
[a]data reported as mean (SE); the difference was significant p<0.0001; [b] extracted from graph
A decrease in facial blushing was reported in 94% of patients. Compensatory sweating remained unchanged in 67% of the patients and decreased in 15% of the patients.
Perceived feeling of blushing in different situations
<table>
<tr><th></th><th>Before procedure</th><th>At end of follow-up[a]</th></tr>
<tr><td>Socially tense situation</td><td>9.0 (0.05)</td><td>2.9(0.11)</td></tr>
<tr><td>Physical exercise</td><td>6.9(0.11)</td><td>3.3(0.10)</td></tr>
<tr><td>Temperature change</td><td>6.3(0.10)</td><td>3.5(0.10)</td></tr>
<tr><td>From alcohol intake</td><td>4.8(0.13)</td><td>2.9(0.11)</td></tr>
</table>
[a]The difference in score was significant (p<0.001) for all situations. Data reported as mean (SE).

Overall satisfaction
85% were satisfied and the remaining 15% were to some degree not satisfied.
Quality of life- ‘substantial’ improvement was reported</td>
<td>Compensatory sweating
Compensatory sweating was reported on the trunk, groin and feet (onset was median 2 months after surgery) and increased in 18% of patients.
<table>
<tr><th>Experience of compensatory sweating on the trunk (at end of follow-up)</th><th>%</th></tr>
<tr><td>No increase of trunk sweating</td><td>17</td></tr>
<tr><td>Insignificant sweating</td><td>10</td></tr>
<tr><td>Occasional non-problematic sweating</td><td>26.5</td></tr>
<tr><td>Moderately severe sweating</td><td>23.5</td></tr>
<tr><td>Pronounced sweating</td><td>17</td></tr>
<tr><td>Severe sweating/regret of procedure</td><td>6</td></tr>
</table>
Worsening of compensatory sweating (extracted from graph)
<table>
<tr><th></th><th>Before procedure</th><th>After procedure</th></tr>
<tr><td>Trunk</td><td>2</td><td>6</td></tr>
<tr><td>Groin</td><td>2</td><td>4</td></tr>
<tr><td>Feet</td><td>2.5</td><td>4</td></tr>
</table>
Gustatory sweating (assessed on VAS) increased from mean 1.8 to 3.7 (but only 3 patients considered this a problem).</td>
<td>Follow-up issues:
• 63% (833/1314) responded to questionnaire
• Non-responders: n=481; however, responses were available from 159 patients at a mean follow-up of 5 months. Of these patients, 89% were satisfied and 11% dissatisfied with the outcome. 72 had unknown addresses and 250 failed to respond.

Study design issues:
• Questionnaire (sent to patients with at least 1 year follow-up) was used to assess blushing and side effects on a VAS (range 0 to 10, with 10 indicating worst possible symptom). 14 questions assessed different types of quality of life related to consequences of facial blushing.

Study population issues:
• Indication was for facial blushing perceived as disabling by the patient.
• Pharmacological treatment had been tried by 28% of the patients prior to surgery.</td>
</tr>
</table>

Abbreviations used: ETS, endoscopic thoracic sympathectomy; HH, hyperhidrosis; NS, not significant; QoL, quality of life; SEM, standard error of the mean; VAS, visual analogue scale.

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>on the second and third ribs.

Follow-up: mean 29 months

Conflict of interest/source of funding: not reported</td>
<td>and consequences of facial blushing including in the following activities was less:
avoid meetings at work (86%), avoid meeting with friends (83%), avoiding social gathering (80%), fear of being centre of attention (79%)

Positive effects of ETS (n=831)
<table>
<tr><th></th><th>% (n)</th></tr>
<tr><td>More self-confidence/calmer</td><td>35 (291)</td></tr>
<tr><td>Less heart palpitations</td><td>4.5 (37)</td></tr>
<tr><td>Less headache</td><td>0.5 (4)</td></tr>
<tr><td>Improved bowel function</td><td>0.4 (3)</td></tr>
<tr><td>Improved physical performance</td><td>0.2 (2)</td></tr>
</table>
</td>
<td>
<table>
<tr><th>Other complications</th><th>n</th></tr>
<tr><td>Cold hands</td><td>22</td></tr>
<tr><td>Impaired physical performance</td><td>11</td></tr>
<tr><td>Heart palpitations</td><td>6</td></tr>
<tr><td>Arm pain</td><td>5</td></tr>
<tr><td>Chills</td><td>5</td></tr>
<tr><td>Back or chest pain</td><td>4</td></tr>
<tr><td>Dizziness</td><td>3</td></tr>
<tr><td>Gastrointestinal disturbances</td><td>3</td></tr>
<tr><td>Headache</td><td>1</td></tr>
</table>
Quality of life- worsening of consequences of facial blushing was reported on the following :
An increased need for medication or suicidal thoughts (2% each), alcohol consumption, fear of being in centre of attention, impact on choice of profession or periodical sick leave (1% each), difficulty keeping a clear mind or avoid meetings at work (less than 1%).
</td>
<td></td>
</tr>
</table>

Abbreviations used: ETS, endoscopic thoracic sympathectomy; HH, hyperhidrosis; NS, not significant; QoL, quality of life; SEM, standard error of the mean; VAS, visual analogue scale.

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Smidfelt K (2011)[2]

Case series
Sweden
(2 centres)

Recruitment period: 1989–98
Study population: patients with facial blushing or hyperhidrosis (32% facial blushing, 7% facial blushing combined with HH, 47% palmar HH, 6% axillary HH, 3% facial HH, 6% a combination of more than 1 type of HH)

n= 3015 (data available for 1700: 536 facial blushing; 112 combination of blushing and any HH; remaining patients had HH)

Age: median 32 years (range 9–73)
Sex: 59% female
Patient selection criteria: not reported
Technique: bilateral ETS; the sympathetic chain was divided with</td>
<td>Number of patients analysed: 1700
Effect of the procedure (for all patients)
• Satisfactory and lasting effect of the procedure, or some increase in sweating or blushing over the years that patents did not consider a problem :85.1%
• Poor or no effect from the procedure: 6.9% (dominated by patients with facial blushing and axillary HH)
• Problematic recurrence of blushing or sweating: 8.1%

Effect of procedure in patients with facial blushing alone or facial blushing with HH (estimated from graph)
<table>
<tr><th></th><th>Facial blushing (n=536); %</th><th>Facial blushing and any HH (n=112); %</th></tr>
<tr><td>No change, satisfactory</td><td>50</td><td>60</td></tr>
<tr><td>Some increase (but no problem)</td><td>20</td><td>20</td></tr>
<tr><td>Recurrence</td><td>15</td><td>10</td></tr>
<tr><td>Poor/no effect</td><td>15</td><td>10</td></tr>
</table>
Overall satisfaction
• 80.0% (1360/1700) of all patients were very satisfied, satisfied or semi-satisfied; 6.5% of all patients were dissatisfied (110/1700).

• 73.5% of patients with facial blushing were very satisfied, satisfied or semi-satisfied. In multiple logistic regression analysis, women were more satisfied than</td>
<td>Postoperative compensatory sweating (in all patients)
<table>
<tr><th>Degree of compensatory sweating</th><th>Number of patients (n=1700) %(n)</th><th>% satisfied with the procedure</th></tr>
<tr><td>None</td><td>20 (340)</td><td>92.7</td></tr>
<tr><td>Insignificant</td><td>5.6(95)</td><td>98</td></tr>
<tr><td>Troublesome</td><td>17.6 (299)</td><td>97.3</td></tr>
<tr><td>Annoying</td><td>24.1 (409)</td><td>91.4</td></tr>
<tr><td>Severe</td><td>21.6 (367)</td><td>68.9</td></tr>
<tr><td>Incapacitating/regret having the procedure</td><td>11.2 (190)</td><td>10.4</td></tr>
</table>
There was a significant difference in the prevalence of compensatory sweating between men and women (85.4% versus 76.2%, p<0.001).

Over time, 60% reported unchanged, 16.4% decreased and 23.6% increased compensatory sweating.

The main side-effects expressed in free-text comments in the questionnaire were: dry hands (3.7%), gustatory sweating (3.6%), cold hands (1.5%), low pulse rate (0.5%) and reduced stamina (0.4%).

Regret of having had the procedure
• 13.5% (230/1700) of all patients regretted having the procedure
• Approximately15% of patients with facial blushing and facial blushing with HH regretted having the procedure (data estimated from graph).</td>
<td>There may be some overlap with patients included in Drott (2002)[1].
Follow-up issues:
• A total of 3015 patients were treated by ETS during the study period; an address was available for 2639 patients, for whom 387 letters were returned as undeliverable.
• The response rate was 56.4% of the total number of patients and 75.5% of those who presumably received the questionnaire.
Study design issues:
• Retrospective study.
Study population issues:
• The proportion of women was higher among the responders compared with non-responders (59.1% versus 46.3%, p<0.001) and the proportion of non-Scandinavians was smaller (3.5% versus 19.3%, p<0.001).
Other issues:
• Study noted that an interim survey showed 7.8% (96/1235) regretted the procedure at mean 3.7 years after the procedure.
• Where reported, results have been presented specifically for patients with</td>
</tr>
</table>

Abbreviations used: ETS, endoscopic thoracic sympathectomy; HH, hyperhidrosis; NS, not significant; QoL, quality of life; SEM, standard error of the mean; VAS, visual analogue scale.			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
electrocautery and the ganglia were not dissected. The nerve was divided over the second rib in 136 (8%), the second and third ribs in 748 (44%), the second to fourth ribs in 663 (39%) and the second to fifth ribs in 153 (9%) patients. Follow-up: **mean 14.6 years** Conflict of interest/source of funding: none	men in the facial blushing group (odds ratio 2.9, 95% CI 2.03 to 4.06). **Quality of life** 68.6% of patients with facial blushing stated that the procedure had improved their quality of life.		facial blushing. The presentation of data therefore differs slightly to that in table 2 for ETS for primary hyperhidrosis of the upper limb (IP 295).

Abbreviations used: ETS, endoscopic thoracic sympathectomy; HH, hyperhidrosis; NS, not significant; QoL, quality of life; SEM, standard error of the mean; VAS, visual analogue scale.

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Rex LO (1998)[3]
Case series
Sweden
Recruitment period: 1989–96
Study population: patients with facial blushing and HH
n=1152 (244 facial blushing, 785 palmar HH; 93 axillary HH; 30 facial HH)
Age: mean 35 years (range 15–67) (patients with facial blushing)
Sex: 59% female
Patient selection criteria: patients who had undergone ETS for facial blushing, palmar, axillary or facial HH.
Technique: Under general anaesthesia, ETS was performed by transection of the sympathetic chain where it overlies the second and third rib.
Follow-up: mean 8 months(patients with facial blushing)
Conflict of interest/source of funding: not reported.</td>
<td>Number of patients analysed: 244 (for efficacy outcomes)

Symptom improvement (assessed on VAS) –data estimated from graph.
Preoperative rating for facial blushing: 8.5
Postoperative: 2.5
The difference in pre- and postoperative ratings of symptoms was reported to be significantly different; p<0.0001

Effect rate (defined as percentage of patients who had a reduced VAS rating of their symptom after surgery) was 96% in patients with facial blushing.

Overall satisfaction (in patients with facial blushing)- at end of follow-up.
<table>
<tr><th></th><th>%</th></tr>
<tr><td>Totally satisfied</td><td>85</td></tr>
<tr><td>Dissatisfied to some extent</td><td>13</td></tr>
</table>
</td>
<td>Complications (unclear which of the adverse events were in patients with facial blushing)
<table>
<tr><th></th><th>% (n/1152)</th></tr>
<tr><td>Compensatory sweating</td><td>59.8% (numbers not reported</td></tr>
<tr><td>Gustatory sweating</td><td>28% (numbers not reported)</td></tr>
<tr><td>Pneumothorax (needing intercostal drainage)</td><td>1.0% (12)</td></tr>
<tr><td>Haemothorax</td><td>0.3% (4)</td></tr>
<tr><td>Horner’s syndrome</td><td>0.4% (5)</td></tr>
<tr><td>Pulmonary embolus (detected 3 weeks after procedure; uneventful recovery)</td><td>n=1</td></tr>
<tr><td>Contusion of the long thoracic nerve (no further details available)</td><td>n=1</td></tr>
<tr><td>Chronotropic insufficiency needing pacemaker (in patient with history of myocardial infarction)</td><td>n=1</td></tr>
</table>
Regret:
2% of patients with facial blushing (n=244) regretted the operation.</td>
<td>There may be some overlap of patients included in Drott (2002)[1] and Smidfelt (2011)[2].

Follow-up issues:
• Questionnaires sent to 1152 patients and study reported response rate was 90%.

Study design issues:
• Questionnaires sent to all patients who had been operated on between 1989 and 1996.
• Blushing rated by patients on VAS (scores range from 0 to 10, with 10 indicating most exaggerated blushing). Questions related to overall satisfaction rates took into account any complications and side effects.
Other issues:
• Study reported efficacy results separately for blushing and HH; only the results for facial blushing group are reported here.</td>
</tr>
</table>

Abbreviations used: ETS, endoscopic thoracic sympathectomy; HH, hyperhidrosis; NS, not significant; QoL, quality of life; SEM, standard error of the mean; VAS, visual analogue scale.

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Licht PB (2006)[4]
Case series
Denmark (2 centres)
Recruitment period: 1999–2004
Study population: patients with disabling isolated facial blushing (as defined by patient)
n=180 (T2 sympathectomy: n=101; T2-T3 sympathectomy: n=79.
Age: median 37 years (range 16–67)
Sex: 72% female

Patient selection criteria: patients with isolated facial blushing

Technique: Bilateral ETS on T2 or T2-T3.

Follow-up: median 20 months
Conflict of interest/source of funding: not reported</td>
<td>Number of patients analysed: 173

Treatment outcome (%[n])
<table>
<tr><th></th><th>Excellent</th><th>Satisfactory</th><th>Some effect</th><th>No effect</th></tr>
<tr><td>T2 (n=95)</td><td>50 (47)</td><td>23 (22)</td><td>17 (16)</td><td>10 (10)</td></tr>
<tr><td>T2-T3 (n=78)</td><td>62 (48)</td><td>14 (11)</td><td>15 (12)</td><td>9 (7)</td></tr>
</table>
There was no significant difference in the effect of the operation between the two extents of sympathectomy.

Symptom recurrence
Symptom recurrence was reported in 4 patients after 1 month to 1 year; all patients subsequently underwent reoperation with good results.

.</td>
<td>Complications
<table>
<tr><td></td><td></td></tr>
<tr><td>Compensatory sweating[a]</td><td>88% (153); located on the back (77%), abdomen (68%), lower extremities (42%) and chest (10%)</td></tr>
<tr><td>Gustatory sweating[b]</td><td>30%(52)</td></tr>
<tr><td>Dry hands[b]</td><td>26% (actual number not reported)</td></tr>
<tr><td>Horner’s syndrome - unilateral (resolved after 2 days)</td><td>1</td></tr>
<tr><td>Pneumothorax (needing chest drain)</td><td>1</td></tr>
<tr><td>Mild pain (reported 2 to 20 months after procedure)</td><td>2.3%(4)</td></tr>
</table>
[a]Compensatory sweating was significantly more frequent after T2-T3 sympathectomy: 95% (74) compared to after T2 sympathectomy: 83% (79); (relative risk 1.14 [95% CI 1.03 to 1.27; p=0.02]). 25% (35) of the patients noted they had to change clothes during the day because of this side effect.
[b]There was no difference between the 2 extents of sympathectomy.
No conversion to open technique was needed, haemothorax or operative mortality observed.
Regret
10% (18) of patients regretted the operation because of side effects (n=1), lack of effect from the operation (n=7) or both (n=10). There was no significant association between the extent of sympathectomy and regretting the operation.</td>
<td>Follow-up issues:
96% (173/180) responded to questionnaires.

Study design issues:
• Patients identified from a database of those treated by ETS over a 6 year period. Patients with palmar or axillary HH were excluded from analysis.
• Questionnaires assessed professional and social disability (very much; some or none) from symptoms before surgery and effect of operation on blushing (excellent, satisfactory, some effect, or no effect).

Study population issues:
• Social and professional disability from blushing (before surgery):
– Social (n=173): ‘very much’ in 94% (162) and ‘some’ 6% (11).
– Professional (n=171): ‘very much’ 91% (157); ‘some’ 8% (13); and ‘none’ 1% (1).</td>
</tr>
</table>

Abbreviations used: ETS, endoscopic thoracic sympathectomy; HH, hyperhidrosis; NS, not significant; QoL, quality of life; SEM, standard error of the mean; VAS, visual analogue scale.

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Licht PB (2012)[5]
Randomised Controlled Trial
Denmark (2 centres)
Recruitment period: 2005–2011
Study population: patients with isolated facial n=100 (R2: n=48; R2-R3: n=52)
Age: median 29 years (range 18–56)
Sex: 73% female
Patient selection criteria: isolated emotional facial blushing with underlying disease ruled out.
Technique: Transection of the sympathetic chain at the level of the second and third ribs. All procedures were completed by visual re-inflation of the lung with manual ventilation to prevent pneumothorax.
Follow-up: 12 months
Conflict of interest/source of funding: not reported</td>
<td>Number of patients analysed: 93
Treatment outcome
<table>
<tr><th></th><th>Excellent</th><th>Satisfactory</th><th>Some effect</th><th>No effect</th></tr>
<tr><td>R2 (n=42)</td><td>52.4 (22)</td><td>33.3 (14)</td><td>11.9 (5)</td><td>2.4 (1)</td></tr>
<tr><td>R2-R3 (n=51)</td><td>54.9 (28)</td><td>29.4 (15)</td><td>11.8 (6)</td><td>3.9 (2)</td></tr>
</table>
No significant difference between the 2 extents of sympathectomy.
QoL (12 months; n=87) (baseline and follow-up scores not reported).
QoL increased significantly in all social and mental domains: total score (p=0.001), social functioning (p<0.001), general mental health (p=0.001), role emotional (p=0.009) and vitality (p=0.05).
No significant differences in any physical domains between the 2 extents of sympathectomy.

Recurrence
‘Mild’ recurrence of facial blushing was reported in 30% (28) within the first year and was less severe than before the procedure.</td>
<td>
<table>
<tr><th>Side effect</th><th>R2 % (n)</th><th>R2-3 % (n)</th></tr>
<tr><td>Compensatory sweating[a]</td><td>95 (40)</td><td>90 (46)</td></tr>
<tr><td>Gustatory sweating</td><td>36 (15)</td><td>39 (20)</td></tr>
<tr><td>Dry hands</td><td>63 (26)</td><td>69 (35)</td></tr>
</table>
No significant difference between the 2 extents of sympathectomy
[a]occurred predominately on the back and the trunk. Severe in 37%.

Permanent unilateral Horner’s syndrome was reported in 1 patient who had undergone R2 sympathectomy.

Regret
Regretting the operation was reported in 10% (4) of patients in the R2 group and 16% (8) of the patients treated by R2-R3 sympathectomy (no significant difference).</td>
<td>Follow-up issues:
93% responded to questionnaires.5 patients did not return questionnaires and 2 were lost to follow-up (unrelated to procedure).

Study design issues:
• Study is a randomised trial comparing sympathectomy at different levels.
• Randomisation was on 1:1 basis and web based. Questionnaires assessing effect of operation, QoL (Short Form 36), and patient satisfaction.

Other issues:
• Median duration of disabling facial blushing was 12 years (range 2 to 46 years)
• Study refers to rib levels instead of vertebral levels at which the nerve was interrupted.</td>
</tr>
</table>

Abbreviations used: ETS, endoscopic thoracic sympathectomy; HH, hyperhidrosis; NS, not significant; QoL, quality of life; SEM, standard error of the mean; VAS, visual analogue scale.

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Coveliers H (2011)[6]
Case series
The Netherlands
Recruitment period: 1994–2006
Study population: patients with excessive blushing or upper limb HH
n=73 (36% (26) facial blushing or rubeosis; 4%(3) had combined facial blushing and HH palmaris and 1 had facial blushing and axillary sweating; 64% of had HH as primary complaint)
Age: mean 30 years (range 15–58)
Sex: 62% female
Patient selection criteria: failure of conservative treatment with topical agents, oral medication, iontophoresis, botox injections or psychological treatment.
Technique: bilateral ETS transecting the sympathetic chain at level T2-T4 and lower one third of the Stellate ganglion.
Follow-up: median 93 months
Conflict of interest/source of</td>
<td>Number of patients analysed: varied by timing

Success rates (in patients with facial blushing)

<table>
<tr><th>Timing</th><th>Outcome</th><th>% (n)</th></tr>
<tr><td>Short-term (6 weeks)</td><td>Success</td><td>81 (21)</td></tr>
<tr><td></td><td>No success</td><td>19 (5)</td></tr>
<tr><td>Long-term</td><td>Success</td><td>71 (17)</td></tr>
<tr><td></td><td>No success</td><td>29 (7)</td></tr>
</table>
Long-term satisfaction (in patients with facial blushing)
Satisfied: 42% (10)
Not satisfied: 58% (14)</td>
<td>Compensatory sweating[a] (in patients with facial blushing)
<table>
<tr><th></th><th>% (n)</th></tr>
<tr><td>Intolerable</td><td>4 (1)</td></tr>
<tr><td>Hardly tolerable</td><td>21 (5)</td></tr>
<tr><td>Tolerable</td><td>54 (13)</td></tr>
<tr><td>None</td><td>21 (5)</td></tr>
</table>
Timing: compensatory sweating was present within 1 month in half of all patients and stabilised during the 18 months after the operation in all patients; [a]occurred mainly at the axillae, trunk and groin in all patients.

Complications (unclear if any of these were in patients with facial blushing)
<table>
<tr><th></th><th>n</th></tr>
<tr><td>Pneumothorax (needed tube drainage)</td><td>7</td></tr>
<tr><td>Prolonged chest wall pain (for more than 3 months)[a]</td><td>6</td></tr>
<tr><td>Horner’s syndrome (partial or full)</td><td>3</td></tr>
<tr><td>Palpitations</td><td>1</td></tr>
<tr><td>Brachial plexus lesion[b]</td><td>1</td></tr>
</table>
[a] persistent neuralgic chest pain attributed to size of trocar used at the fifth intercostal space; [b]the ‘partial but persistent’ brachial plexus apraxia was attributed to poor positioning of the patient and undue traction to the arm during the procedure.</td>
<td>Follow-up issues:
85% response rate to questionnaires.

Study design issues:
Retrospective review
• Standardised questionnaire was developed to assess outcomes.
• Compensatory sweating assessed using Hyperhidrosis Disease Severity Scale graded in order of severity from 1 to 4, with higher score indicating intolerable sweating interfering with daily activities.
Study population issues:
• Medication usage was reported in 46% of patients with facial blushing (unclear if reporting concomitant use or previous history).</td>
</tr>
</table>

Abbreviations used: ETS, endoscopic thoracic sympathectomy; HH, hyperhidrosis; NS, not significant; QoL, quality of life; SEM, standard error of the mean; VAS, visual analogue scale.			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
funding: not reported			

Abbreviations used: ETS, endoscopic thoracic sympathectomy; HH, hyperhidrosis; NS, not significant; QoL, quality of life; SEM, standard error of the mean; VAS, visual analogue scale.

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Lardinois D (2002)[7]
Case series
Switzerland
Recruitment period: 1996–98
Study population: patients with facial blushing or HH.
n=37 (32% facial blushing, 52% HH or 16% both)
Age: mean 34 years (range 18–67)
Sex: 51% female
Patient selection criteria: patients referred with disabling facial blushing interfering with work or social activities.
Technique: Under general anaesthesia, a transaxillary approach was used and the sympathetic chain was divided over the ribs II–V. The procedure was repeated on the contralateral side.
Follow-up: mean 30 months (in patients with facial blushing)
Conflict of interest/source of funding: not reported</td>
<td>Number of patients analysed: 18
Symptom relief in patients with facial blushing
<table>
<tr><th></th><th>Preoperative</th><th>Follow-up</th><th>p value</th></tr>
<tr><td>Blushing</td><td>9.1 (1.7)</td><td>4.0 (2.3)</td><td><0.0005</td></tr>
<tr><td>Cardiac palpitations</td><td>4.5 (1.4)</td><td>1.2 (0.8)</td><td><0.008</td></tr>
<tr><td>Anxiety</td><td>4.2 (2.5)</td><td>2.2 (1.1)</td><td><0.04</td></tr>
</table>
Data reported as mean (SEM)
Age, sex or follow-up time were not associated with degree of relief of symptoms.

Overall satisfaction
Overall satisfaction and improvement in lifestyle was reported in 94.5% (17/18) of patients with facial blushing alone or with HH.
Recurrence of moderate facial and neck blushing (in stressful situations) on 1 side of face was reported in 1 patient 8 weeks after the procedure (chain was divided from only T2-T4 in this patient).

Uneventful wound healing with excellent cosmesis was reported in 97.3% (36/37) of all patients (at 3-month follow-up).</td>
<td>Complications (in patients with blushing)
Motor aphasia developed in 1 patient because of multiple pulmonary thromboembolism and cerebrovascular insult related to patent foramen ovale (crossed embolism); treated by anticoagulants and needing hospitalisation for 10 days. Sequelae of aphasia were still present 6 months after procedure.
Compensatory sweating
<table>
<tr><th></th><th>Preoperative</th><th>Follow-up</th><th>p value</th></tr>
<tr><td>Trunk
44% (8/18)</td><td>3.0 (0.5)</td><td>4.5 (1.1)</td><td>NS</td></tr>
<tr><td>Feet
67% (12/18)</td><td>2.6 (0.7)</td><td>5.9 (1.2)</td><td><0.004</td></tr>
</table>
Data reported as mean (SEM). The patients did not consider these side effects as significant.
Worsening of symptoms (in patients with facial blushing)
• in 1 patient who regretted the operation
• in 1 patient 6 months after the procedure.
Complications (all patients): 13%(5/37) (including cerebral emboli [2.6%]described above)
<table>
<tr><th>Complications</th><th>%</th></tr>
<tr><td>Intraoperative bleeding</td><td>2.6 (did not need transfusion)</td></tr>
<tr><td>Pneumothorax</td><td>2.6 (did not need drainage; patient needed hospitalisation)</td></tr>
<tr><td>Horner’s syndrome</td><td>5.2 (in 2 patients with unilateral Horner’s syndrome, clinical signs were transient and disappeared 14 and 18 weeks after the procedure)</td></tr>
</table>
There was no 30-day mortality or conversion to an open procedure.</td>
<td>Study design issues:
• Prospectively enrolled patients.
• Relief of symptoms and compensatory sweating assessed by 10-point VAS (0, no symptom; 10, worst possible symptom).</td>
</tr>
</table>

Abbreviations used: ETS, endoscopic thoracic sympathectomy; HH, hyperhidrosis; NS, not significant; QoL, quality of life; SEM, standard error of the mean; VAS, visual analogue scale.

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Adair A (2005)[8]

Case series
UK
Recruitment period: 1998–2001
Study population: patients with facial blushing
n=120
80 responded (59 facial blushing: 12 isolated; 47 patients had associated HH; 21 patients HH only)
Age: range 8–52 years (9 patients under 16 years)
Sex: 59% female

Patient selection criteria: not reported

Technique: bilateral ETS T2-T3

Follow-up: mean 20 months

Conflict of interest/source of funding: not reported</td>
<td>Number of patients analysed: 59
Severity score
(in 59 patients with facial blushing)
Reduced from a mean score of 78 (SD 32) to 26 (SD 27.6) after the procedure; this difference was significant, p<0.001.

Symptom resolution
29% (17/59) of patients reported complete resolution of facial blushing. 11 reported no change in symptoms.
In patients with facial blushing alone (n=12), all reported improvement with 4 patients reporting complete resolution.

Quality of Life (in 59 patients with facial blushing)

<table>
<tr><th>Rating</th><th>% (n)</th></tr>
<tr><td>Overall QoL much better</td><td>63 (37)</td></tr>
<tr><td>Some improvement</td><td>15 (9)</td></tr>
<tr><td>No change</td><td>8 (5)</td></tr>
</table>
Overall QoL was reported as being ‘much better’ in all 9 children.</td>
<td>Worsening of symptoms and QoL (in patients with isolated facial blushing or blushing associated with HH)
• worsening of symptoms was reported in 1 patient.
• worsening of QoL was reported in 14% (8) of patients.

Complications (in patients with isolated facial blushing or blushing associated with HH)
<table>
<tr><th>Complications</th><th>% (n)</th></tr>
<tr><td>Compensatory sweating[a] (most commonly affected areas were back and chest)</td><td>91 (54)</td></tr>
<tr><td>Gustatory sweating[a]</td><td>32 (19)</td></tr>
<tr><td>Chest pain [b]</td><td>88 (52)</td></tr>
<tr><td>Needing chest drain (no further details)</td><td>8.5 (5)</td></tr>
<tr><td>Horner’s syndrome (transient)</td><td>3.4 (2)</td></tr>
</table>
[a]onset of sweating varied between 24 hours and 12 months, most commonly starting at 4 weeks after the procedure
[b]ranging from 24 hours to 6 weeks in all patients.

No postoperative mortality or no major complications needing surgical intervention were observed.</td>
<td>Follow-up issues:
• 67% (80/120) response rate

Study design issues:
• Questionnaire assessed facial blushing before and after the procedure (VAS; score range 0–100).
• Questions on postoperative complications (pain, Horner’s syndrome or pneumothorax) and overall QoL assessed on a 5-point Likert scale.</td>
</tr>
</table>

Abbreviations used: ETS, endoscopic thoracic sympathectomy; HH, hyperhidrosis; NS, not significant; QoL, quality of life; SEM, standard error of the mean; VAS, visual analogue scale.			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
Kwong KF (2005)[9] **Case series** USA Recruitment period: 1992–2003 n=**202** Age: mean 29 years (range 9–65); Sex: 52% female Technique: ETS (at high T2 for facial blushing) was done using electrocautery. ETS was synchronous (194), staged (1), or done on one side alone (2). Follow-up: **mean 13 months** Conflict of interest/source of funding: not reported	**Chylothorax** (identified 'early'; needing reoperation): n=1 (unclear if this was in a patient with facial blushing). **Horner's syndrome** (unilateral): n=2 (in patients with facial blushing; 1 subsequently underwent blepharoplasty). Additional complications (unclear if in patient with facial blushing): • Hyperaesthesia at the incision: n=3; • Pleural effusion(asymptomatic): n=1; and • Pneumothorax: n=1.		**Study design issues:** • •Retrospective review **Study population:** • Patients with facial blushing (21), HH (175), Raynaud's (3) digital ischaemia (2) and reflex sympathetic dystrophy (1). • Patients offered procedure were intolerant of or had failed medical therapy.
Jeganathan R (2008)[10] **Case series** UK Recruitment period: 1994–2006 Age: mean 29 years (range 10–66 years); Sex: 69% female n=**163** ;Technique: ETS at high T2 division Follow-up: **mean 51 months** Conflict of interest/source of funding: not reported	Complications (unclear if in patients with facial blushing): • **Bleeding** (leading to conversion to a minithorocotomy at end of procedure): 1 patient • **Chronic wound pain** (>6 months): 0.6% • Pneumothorax (needing chest drain): 4% • Compensatory sweating (most frequently on trunk): none: 22.1%; mild: 52.8%; moderate:22.7%; severe: 2.4% • Gustatory sweating: 7.4%		**Study design issues:** • Data entered prospectively. • Definition of blushing was based on patient's perspective regarding the severity of the complaint **Study population**: • Patients with facial blushing (isolated 5%; with facial HH 10%) who had failed to respond to adequate medical treatment and were referred for surgery.

Efficacy

Symptom resolution

A case series of 120 patients (80 patients responded; 12 patients with isolated facial blushing) reported complete resolution in 33% (4/12) of patients with isolated facial blushing at a mean follow-up of 20 months[8].

A case series of 3015 (with 1700 patients who responded to questionnaire; 648 patients with facial blushing or blushing with hyperhidrosis) reported that 85% of patients had a satisfactory and lasting effect of the procedure, or some increase in sweating or blushing that they did not consider a problem, at a mean follow-up of 15 years (absolute number not reported)[2].

Improvement in severity of symptom

In a case series of 1314 patients with facial blushing (833 patients responded; 831 analysed), mean symptom improvement score (assessed on visual analogue scale (VAS), scores from 0 to 10, with 10 indicating worst possible symptom) decreased from 9 before the procedure to 3 after the procedure in patients with facial blushing at a mean follow-up of 29 months; this difference was significant ($p < 0.0001$) [1].

In a case series of 1152 patients (244 patients with facial blushing) mean symptom improvement score (assessed on visual analogue scale (VAS), scores from 0 to 10, with 10 indicating worst possible symptom) decreased from 9 before the procedure to 3 after the procedure in patients with facial blushing at a mean follow-up of 8 months; this difference was significant ($p < 0.0001$)[3] (data estimated from graph).

In a case series of 37 patients (18 with facial blushing), mean symptom relief scores (assessed on VAS, 0 to 10, with 10 indicating worst possible symptom) improved from 9 at baseline to 4 at a mean follow-up of mean 30 months; this difference was significant ($p < 0.0005$)[7].

Symptom recurrence

A case series of 180 patients with isolated facial blushing reported symptom recurrence (1 month to 1 year after the procedure) in 2% (4/173) of patients; all 4 patients subsequently underwent reoperation with good results[4].

Patient satisfaction

The case series of 3015 patients (1700 patients responded to questionnaire; 648 patients with blushing or blushing with hyperhidrosis) reported satisfaction rates of 74% in patients with facial blushing (n=536) at a mean follow-up of 15 years (absolute number not reported). Fifteen per cent of patients (with facial blushing; data estimated from graph) were dissatisfied or regretted having had the procedure in this case series[2].

In the case series of 1152 patients, with 244 patients with facial blushing, 85% of patients with facial blushing reported to be totally satisfied [3].

Quality of life
In the case series of 80 patients, with 59 patients with facial blushing (isolated or in association with hyperhidrosis), quality of life (assessed on a 5-point Likert scale) was reported to be 'much better' in 63% (37/59) of patients, 'some improvement' in 15% (9/59) of patients and 'no change' in 8% (5/59) of patients[8].

Safety

Safety events in patients with facial blushing
Horner's syndrome
Horner's syndrome on one side of the face was reported in 10% (2/21) of patients with facial blushing in a case series of 202 patients (1 patient underwent blepharoplasty; no further details) and in 1 patient in the case series of 180 patients (this resolved after 2 days)[9,4].

Pneumothorax
Pneumothorax (needing a chest tube) was reported in 1 patient in the case series of 180 patients[4].

A chest drain was needed postoperatively (no further details provided) in 9% (5/59) of patients in the case series of 80 patients (59 with facial blushing)[8].

Compensatory sweating
Compensatory sweating was reported in 88% (153/173) of patients in the case series of 180 patients[4].

Compensatory sweating (assessed using Hyperhidrosis Disease Severity Scale; scores range 1 to 4, with higher score indicating intolerable sweating interfering with daily activities) was reported to be 'intolerable' in 4% (n=1) , 'hardly tolerable' in 21% (n=5), 'tolerable' in 54%(n=13) of patients with facial blushing in a case series of 73 patients (denominator unclear). Compensatory sweating was present within 1 month in half of all patients [6].

Severe compensatory sweating on the trunk and regret associated with having the procedure was reported in 6% of patients in the case series of 831 patients at mean follow-up of 29 months[1]. Compensatory sweating that was 'incapacitating'and regret associated with having the procedure was reported in 11% (190/1700) of patients with facial blushing or hyperhidrosis at a mean follow-up of 15 years[2].

Gustatory sweating
Gustatory sweating was reported in 30% (52/173) of patients with facial blushing in the case series of 180 patients and in 32% (19/59) of 59 patients with either isolated facial blushing or blushing with hyperhidrosis in the case series of 80 patients[4,8].

Worsening of symptoms
Worsening of symptoms was reported in 1 patient and worsening of quality of life was reported in 14% (8/59) of patients with isolated facial blushing or blushing with hyperhidrosis (n=59) in the case series of 80 patients[8].

Regret
In the case series of 1152 patients, with 244 patients with facial blushing, 13% of patients were 'dissatisfied to some extent' and 2% regretted the operation (absolute number not reported)[3].

In the case series of 180 patients, 10% (18/180) of patients regretted the operation because of side effects (n=1), lack of effect (n=7) or both (n=10)[4]. A randomised controlled trial (comparing sympathectomy of the second versus the second and third thoracic ganglia) of 100 patients with isolated facial blushing reported that overall 13% (12/93) of the patients regretted the operation (reasons not reported) at a mean follow-up of 12 months; there was no significant difference between the groups treated by different extents of sympathectomy[5].

Motor aphasia
Motor aphasia developed in 1 patient with facial blushing in a case series of 37 patients. This was because of multiple pulmonary thromboembolism and cerebrovascular insult (treated by anticoagulants and needed hospitalisation for 10 days) and sequelae of aphasia were still present 6 months after the procedure[7].

Safety events: unclear if the following events occurred in patients with facial blushing
Brachial plexus lesion
Brachial plexus lesion (partial but persistent) was reported in 1 patient in the case series of 73 patients(this was attributed to poor positioning of patient and undue traction to the arm during the procedure; no further details) [6].

Haemothorax
Haemothorax was reported in less than 1% of patients (4/1152) in the case series of 1152 patients (timing unclear)[3].

Bleeding
Bleeding (leading to conversion to a minithorocotomy) was reported in 1 patient in a case series of 163 patients[10].

Chylothorax
Chylothorax (needing operation) was reported in 1 patient in a case series of 202 patients [9].

Pulmonary embolus
Pulmonary embolus (detected 3 weeks after the procedure with uneventful recovery) was reported in less than 1% of patients (1/1152) in the case series of 1152 patients[3].

Validity and generalisability of the studies

- The evidence included is mainly from case series. Two of the studies were conducted in the UK.
- Most of the studies use data from patient questionnaires, so there may be some recall bias. Response rates for questionnaires ranged from 56%[2] to 96%[4].
- Most of the studies included patients with blushing with co-existing hyperhidrosis.
- Studies included both adults and children.
- In some studies, it was unclear if the adverse events reported were in patients with facial blushing.

Existing assessments of this procedure

An Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP-S) report published in 2009 concluded: 'A lack of high quality randomised trial evidence on ETS means that it is difficult to make a judgement on the safety and effectiveness of this technique. There is potentially a number of safety issues associated with this procedure. ASERNIP-S suggests that a full systematic review including all available comparative and case series information, together with clinical input, should be undertaken to provide an up-to-date and comprehensive assessment of the safety and effectiveness of ETS'[11].

The findings by Swedish Council on Health Technology Assessment (1999) SBU Alert 'show that poor evidence is available about ETS as regards side effects, risks, and short-term effects. There is no scientific evidence demonstrating the long-term results of the method or its cost effectiveness in relation to other methods.

If the results from pilot studies are confirmed by current randomised studies, the method may prove to be a valuable alternative for patients in whom problems persist after traditional therapies have been unsuccessful. Until further notice, the method should be used only in a controlled way within the framework of scientific studies. An assessment should be carried out addressing treatment benefits in

relation to the risks for side effects, direct healthcare costs, and socioeconomic effects'[12].

Related NICE guidance

Below is a list of NICE guidance related to this procedure. Appendix B gives details of the recommendations made in each piece of guidance listed.

Clinical guidelines

- Social anxiety disorder: recognition, assessment and treatment. NICE clinical guideline 159 (2013). Available from www.nice.org.uk/guidance/CG159

Specialist advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their specialist society or royal college. The advice received is their individual opinion and does not represent the view of the society.

Mr Mark McCarthy, Mr Isaac Nyamekye, Mr Rajiv Vohra (Vascular Societies of Great Britain and Ireland); Mr Pala Rajesh (Society for Cardiothoracic Surgery in Great Britain and Ireland)

- All specialist advisers perform this procedure regularly; 1 specialist adviser stated that they usually carry out this procedure for hyperhidrosis or for digital ischaemia.
- Two specialist advisers considered this procedure to be established practice, 1 considered this a minor variation and 1 considered this definitely novel and of uncertain safety and efficacy.
- Comparators include best medical therapy and open sympathectomy.
- Key efficacy outcomes: symptom improvement (blushing and redness of face, decreased sweating of scalp), absence of symptoms, dry hands and face, and patient's perception of improvement of symptoms.
- Adverse events reported in literature: bleeding, chylothorax, harlequin face, Horner's syndrome, post thoracoscopy chronic pain, recurrent blushing, transient truncal hyperhidrosis, and wound infection.
- Anecdotal adverse events: air embolism, arm ischaemia, compensatory sweating, haemothorax, pneumothorax and post thoracoscopy chest wall pain.

- Theoretical adverse events: bleeding (needing thoracotomy), death, dry hands and visceral injury.
- One specialist adviser stated this procedure is likely to be carried out in most or all district general hospitals, 2 stated fewer than 10 specialist centres and 1 noted in a minority of hospitals.
- The potential impact of this procedure on the NHS, in terms of numbers of patients eligible for treatment and use of resources, was considered to be minor by 3 specialist advisers and moderate by 1 specialist adviser.

Patient commentators' opinions

NICE's Public Involvement Programme sent 53 questionnaires to 3 NHS trusts for distribution to patients who had the procedure (or their carers). NICE received 12 completed questionnaires.

The patient commentators' views on the procedure were consistent with the published evidence and the opinions of the specialist advisers. The problem of compensatory sweating was reported and a minority of patients reported regret at having had the procedure.

Issues for consideration by IPAC

There were no ongoing trials identified.

References

1. Drott C, Claes G, and Rex L. (2002) Facial blushing treated by sympathetic denervation--long lasting benefits in 831 patients. Journal of Cosmetic Dermatology 1:115-9.

2. Smidfelt K, Drott C (2011) Late results of endoscopic thoracic sympathectomy for hyperhidrosis and facial blushing. British Journal of Surgery 98: 1719–24

3. Rex LO, Drott C, Claes G et al. (1998) The Boras experience of endoscopic thoracic sympathicotomy for palmar, axillary, facial hyperhidrosis and facial blushing. European Journal of Surgery, Acta Chirurgica, Supplement 23-6

4. Licht PB, Ladegaard L, and Pilegaard HK. (2006) Thoracoscopic sympathectomy for isolated facial blushing. Annals of Thoracic Surgery 81:1863-6.

5. Licht PB, Pilegaard HK, and Ladegaard L. (2012) Sympathicotomy for isolated facial blushing: a randomized clinical trial. Annals of Thoracic Surgery 94:401-5.

6. Coveliers H, Atif S, Rauwerda J et al. (2011) Endoscopic thoracic sympathectomy: long-term results for treatment of upper limb hyperhidrosis and facial blushing. Acta Chirurgica Belgica 111:293-7.

7. Lardinois D and Ris HB. (2002) Minimally invasive video-endoscopic sympathectomy by use of a transaxillary single port approach. European Journal of Cardio-Thoracic Surgery 21:67-70.

8. Adair A, George ML, Camprodon R et al. (2005) Endoscopic sympathectomy in the treatment of facial blushing. Annals of the Royal College of Surgeons of England 87:358-60.

9. Kwong KF, Cooper LB, Bennett LA et al. (1066) Clinical experience in 397 consecutive thoracoscopic sympathectomies. Annals of Thoracic Surgery 80:1063-6.

10. Jeganathan R, Jordan S, Jones M et al. (2008) Bilateral thoracoscopic sympathectomy: results and long-term follow-up. Interactive Cardiovascular and Thoracic Surgery 7:67-70.

11. Watt A, Cameron AL, Maddern GJ. Evidence essential: Endoscopic thoracic sympathectomy. ASERNIP-S report No. 71 Adelaide, South Australia: ASERNIP-S, August 2009

12. Hjalmarsson A. Endoscopic Transthoracic Sympathectomy (ETS). Alert 1999. Online, available from http://www.sbu.se/en/Published/Alert/Endoscopic-transthoracic-sympathectomy-ETS/ [accessed 12 September 2013] (translation of version 1 published on August 30, 1999. The latest version of this report published in 2002 is not available in English)

Appendix A: Additional papers on endoscopic thoracic sympathectomy for primary facial blushing

The following table outlines the studies that are considered potentially relevant to the overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Article	Number of patients/follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Black SA, Taylor FG, Russell MH et al. (2008) Thorascopic sympathectomy performed using laser. Annals of the Royal College of Surgeons of England 90:142-5.	n=123 (8 facial blushing) Follow up=range 6-120 months	Complications included bleeding (2), pulmonary oedema (1) and failed procedure (2). Four patients were very satisfied, 1 reasonably satisfied and no improvement in 1 patient.	Larger studies included in table 2.
Centre for Clinical Effectiveness. Endoscopic thoracic sympathectomy for treating facial blushing Southern Health/Monash Institute of Public Health, Melbourne, 2001.	n= 4 studies Follow up= unclear	Benefits or side effects associated with endoscopic thoracic sympathectomy for treating facial blushing have not been properly evaluated.	Relevant studies included in this summary are in table 2 or Appendix A.
Drott C, Claes G, Rex L et al (1998) Successful treatment of facial blushing by endoscopic transthoracic sympaticotomy British Journal of Dermatology 138:639-43	n=244 Follow up= mean 8 months	Overall 85% of the patients were satisfied with result and 15% were to some degree dissatisfied, mainly due to insufficient effect, but only 2% regretted the operation.	Larger studies included in table 2. There may be some overlap of patients included in Drott (2002)[1] study table 2.
Fibla JJ, Molins L, Mier JM et al. (2009) Effectiveness of sympathetic block by clipping in the treatment of hyperhidrosis and facial blushing. Interactive Cardiovascular and Thoracic Surgery 9:970-2.	n=110 (15 facial blushing and in 1 facial blushing associated with hyperhidrosis) Follow up= 12 months	One patient with facial blushing needed reintervention (additional clip). Complications were reported in 5.5% (3) of patients, pneumothorax in 1 patient and persistent air leaks in 2 other patients.	Larger studies included in table 2.
Fischbacher C. Sympathectomy for facial blushing. In Bazian Ltd (ed) STEER: Succinct and Timely Evaluated Evidence Reviews 2003; 3(4). Wessex Institute for Health Research & Development. University of Southampton.	n= 3 studies	The evidence based on three case series provide very limited evidence that sympathectomy improves blushing. Side effects were common.	Review. Relevant studies included in this review are in table 2 or Appendix A.
Garcia Franco CE,	n= 58 (18 blushing [8	Efficacy was improved in	Larger studies included

Perez-Cajaraville J, Guillen-Grima F et al. (2011) Prospective study of percutaneous radiofrequency sympathicolysis in severe hyperhidrosis and facial blushing: efficacy and safety findings. European Journal of Cardio-Thoracic Surgery 40:e146-e151.	surgical sympathectomy vs 10 radiofrequency ablation]) Follow up= mean 12 months (surgical sympathectomy group); mean 14 months (radiofrequency ablation group).	41% of patients treated by surgery compared against 28% treated by radiofrequency ablation (p=0.004). There was a greater improvement in quality of life in patients treated by surgery compared against RFA.	in table 2.
Jaffer U, Weedon K, and Cameron AE. (2007) Factors affecting outcome following endoscopic thoracic sympathectomy. British Journal of Surgery 94:1108-12.	n= 110 (facial blushing, sweating or flushing ; palmar hyperhidrosis) Follow up=unclear	For patients with predominantly facial symptoms (n=51), the median overall satisfaction score was 7, median change in facial symptoms was -15 (n=43) and compensatory sweating in patients with facial symptoms (n=43) was significantly worse in other body areas compared to patients treated for palmar sweating.	Larger studies included in table 2.
Krasna MJ, Xiaolong J, Sonett J et al. (2004) Thoracoscopic sympathectomy. Surgical Laparosocpy, Endoscopy and Percutaneous Techniques 10(5): 314-8	n= 34 (1 facial blushing) Follow up= range 1 month to 7 years	The patient with facial blushing was symptom-free for 1.5 years after the procedure.	Larger studies included in table 2.
Malmivaara A, Kuukasjarvi P, Autti-Ramo I et al. (2007) Effectiveness and safety of endoscopic thoracic sympathectomy for excessive sweating and facial blushing: a systematic review. International Journal of Technology Assessment in Health Care 23:54-62.	n= 15 studies (1 study in patients with facial blushing)	The evidence for endoscopic thoracic sympathectomy is weak due to a lack of randomised trials The intervention leads to severe immediate complications and in some of the patients and to persistent side-effects for many of the patients.	1 study included in this systematic review related to facial blushing (a foreign-language publication).
Neumayer C, Zacherl J, Holak G et al. (2003) Experience with limited endoscopic thoracic sympathetic block for hyperhidrosis and facial blushing. Clinical Autonomic Research 13:Suppl 1:.I/52-I/57	n=94 (21 facial blushing) Follow up= median 5 months	All patients with facial blushing treated by sympathectomy at level T2 had resolution of symptoms. Recurrence was reported in 1 patient 4 months after the procedure.	Larger studies included in table 2.
Neumayer C, Panhofer P, Jakesz R et al. (2005)	n= 57(33 facial blushing)	All patients with facial blushing treated by	Larger studies included in table 2.

Surgical treatment of facial hyperhidrosis and blushing: Mid-term results after endoscopic sympathetic block and review of the literature. European Surgery - Acta Chirurgica Austriaca 37 (3): 127-36.	Follow up= mean 20 months	sympathectomy at level T2 had resolution of symptoms. Recurrence was reported 1 month after the procedure in 1 patient and 4 months after the procedure. In another patient; compensatory sweating also increased in this patient.	
Rajesh YS, Pratap CP, and Woodyer AB. (2002) Thoracoscopic sympathectomy for palmar hyperhidrosis and Raynaud's phenomenon of the upper limb and excessive facial blushing: a five year experience. Postgraduate Medical Journal 78:682-4.	n= 26 (3 facial blushing) Follow up= mean 29 months	In 1 patient who underwent surgery for excessive facial blushing, a lack of facial sweating on the operated side was reported.	Larger studies included in table 2.
Reisfeld R, Nguyen R, Pnini A (2002) Endoscopic thoracic sympathectomy for hyperhidrosis: experience with both cauterization and clamping methods. Surgical Laparoscopy, Endoscopy and Percutaneous Techniques 12: 255-67	n=1312 (301 facial sweating or blushing) Follow up= mean 23 months	92.7% of patients with facial symptoms only subgroup (n=124) were satisfied and 1.6% were very unsatisfied. There was no recurrence.	Larger studies are included in table 2.
Yilmaz EN, Dur AH, Cuesta MA et al. (1996) Endoscopic versus transaxillary thoracic sympathectomy for primary axillary and palmar hyperhidrosis and/or facial blushing: 5-year-experience. European Journal of Cardio-Thoracic Surgery 10:168-72.	n= 28 (15 facial blushing with or without hyperhidrosis) Follow up= range 0 to 30 months	Efficacy for blushing was 93.3%. One patient had blushing after the procedure. Complications included unilateral transient Horner's syndrome, pneumothorax, and neuralgia.	Larger studies included in table 2.

Appendix B: Related NICE guidance for endoscopic thoracic sympathectomy for primary facial blushing

Guidance	Recommendations
Clinical guidelines	**Social anxiety disorder: recognition, assessment and treatment. NICE clinical guideline 159 (2013)** **1.6 Interventions that are not recommended to treat social anxiety disorder** 1.6.1 Do not routinely offer pharmacological interventions to treat social anxiety disorder in children and young people. 1.6.2 Do not routinely offer anticonvulsants, tricyclic antidepressants, benzodiazepines or antipsychotic medication to treat social anxiety disorder in adults. 1.6.3 Do not routinely offer mindfulness-based interventions or supportive therapy to treat social anxiety disorder. 1.6.4 Do not offer St John's wort or other over-the-counter medications and preparations for anxiety to treat social anxiety disorder. Explain the potential interactions with other prescribed and over-the-counter medications and the lack of evidence to support their safe use. 1.6.5 Do not offer botulinum toxin to treat hyperhidrosis (excessive sweating) in people with social anxiety disorder. This is because there is no good-quality evidence showing benefit from botulinum toxin in the treatment of social anxiety disorder and it may be harmful. 1.6.6 Do not offer endoscopic thoracic sympathectomy to treat hyperhidrosis or facial blushing in people with social anxiety disorder. This is because there is no good-quality evidence showing benefit from endoscopic thoracic sympathectomy in the treatment of social anxiety disorder and it may be harmful.

Appendix C: Literature search for endoscopic thoracic sympathectomy for primary facial blushing

Databases	Date searched	Version/files	No. retrieved
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	24/06/2013	Issue 6 of 12, June 2013	29
Database of Abstracts of Reviews of Effects – DARE (CRD website)	24/06/2013	Issue 6 of 12, June 2013	11
HTA database (CRD website)	24/06/2013	Issue 6 of 12, June 2013	3
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	24/06/2013	Issue 6 of 12, June 2013	92
MEDLINE (Ovid)	24/06/2013	1946 to June Week 2 2013	157
MEDLINE In-Process (Ovid)	24/06/2013	June 21, 2013	8
EMBASE (Ovid)	24/06/2013	1974 to 2013 Week 25	263
CINAHL (NLH Search 2.0 or EBSCOhost)	24/06/2013	N/A	17
BLIC (Dialog DataStar)	24/06/2013	N/A	0

Trial sources searched on 20 June 2013

- Current Controlled Trials *meta*Register of Controlled Trials – *m*RCT
- Clinicaltrials.gov
- National Institute for Health Research Clinical Research Network Coordinating Centre (NIHR CRN CC) Portfolio Database

Websites searched

- National Institute for Health and Care Excellence (NICE)
- Food and Drug Administration (FDA) - MAUDE database
- French Health Authority (FHA)
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- Conference search
- Evidence Updates (NHS Evidence)
- General internet search

MEDLINE search strategy

1	Blushing/
2	blush*.tw.
3	((flush* or red*) adj4 (face* or facial*)).tw.
4	or/1-3
5	Sympathectomy/
6	(Sympathect* or sympathicot*).tw.
7	(sympathet* adj4 denervat*).tw.
8	endoscopy/
9	endoscopes/
10	(endoscopy or Endoscopic or endoscop*).tw.
11	thoracoscopy/
12	Thoracic Nerves/
13	Thoracic Surgical Procedures/
14	(thoracoscopy or thoracic* or thorac*).tw.
15	(ETS or EBS).tw.
16	((block* or interrupt* or burn* or cut* or remov* or destroy* or resect* or clamp* or clip* or transect* or ablat*) adj4 (gangli* or nerv* or sympath*)).tw.
17	or/5-16
18	4 and 17
19	animals/ not humans/
20	**18 not 19**