National Institute for Health and Care Excellence

IP280/2 – Endoscopic radiofrequency ablation for gastro-oesophageal reflux disease

Consultation Comments table

IPAC date: 14 June 2013

Due to the large number of consultation comments, the comments have been organised into the following categories:

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Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
1	Consultee 1 Chief Medical Officer, Manufacturer, USA	**1**	There is strong evidence for Stretta's durability in GORD treatment at 48 months:• Reymunde, et al (2007): Mean GORD-QOL scores of 2.4 (baseline), 4.6 (36 months), and 4.3 (48 months, P < .001). The mean GORD symptom score was 2.7 (baseline), 0.3 (36 months), and 0.6 (48 months, P < .001). Daily medication usage was 100% (baseline) and 13.6% (48 months, P < .001). • Noar et al (2007): Heartburn scores decreased from 3.6 to 1.18 (P < .001); total heartburn score (GORD HRQL) decreased from 27.8 to 7.1 (P < .001), patient satisfaction improved from 1.4 to 3.8 (P < .001). Medication usage decreased significantly from 100% of patients on 2X PPI therapy at baseline to 75% of patients showing elimination of medications or only as-needed use of OTC meds at 48 months (P < 0.005). • Dughera et al (2011): Significantly improved heartburn scores, GORD-specific QOL scores, and general QOL scores at 24 and 48 months in 52/56 patients (92.8%) At each control time mean heartburn and GERD HRQL scores decreased (p = 0.001 and p = 0.003, respectively) and both mental SF-36 and physical SF-36 ameliorated (p = 0.001 and 0.05, respectively). At 48 months, 41/56 patients (72.3%) completely off PPIs.	Thank you for your comment. Reymunde (2007) and Noar (2007) are listed in appendix A of the overview and are included in the systematic review that is included in the main extraction table of the overview. Dughera (2011) is included in the main extraction table. The Committee considered this comment but decided not to change the guidance.

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2	Consultee 2 Private Sector Professional, USA	**1**	2) There is strong evidence for durability in GORD treatment at 48 months and up to Â 10 years: a. Noar et al (2007): Heartburn scores decreased from 3.6 to 1.18 (P < .001); total heartburn score (GORD HRQL) decreased from 27.8 to 7.1 (P < .001), patient satisfaction improved from 1.4 to 3.8 (P < .001). Medication usage decreased significantly from 100% of patients on 2X PPI therapy at baseline to 75% of patients showing elimination of medications or only as-needed use of OTC meds at 48 months (P < 0.005). b. Reymunde, et al (2007): Mean GORD-QOL scores of 2.4 (baseline), 4.6 (36 months), and 4.3 (48 months, P < .001). The mean GORD symptom score was 2.7 (baseline), 0.3 (36 months), and 0.6 (48 months, P < .001). Daily medication usage was 100% (baseline) and 13.6% (48 months, P < .001). c. Dughera et al (2011): Significantly improved heartburn scores, GORD-specific QOL scores, and general QOL scores at 24 and 48 months in 52/56 patients (92.8%) At each control time mean heartburn and GERD HRQL scores decreased (p = 0.001 and p = 0.003, respectively) and both mental SF-36 and physical SF-36 ameliorated (p = 0.001 and 0.05, respectively). At 48 months,41/56 patients (72.3%) completely off PPIs. d. Noar et al (2013): 10-year continuation study, long term durable response with 41% of patients off of PPI therapy at year 10, and 75% using 50% less medication compared to baseline med use of Â BID PPI. Normalization of GORD-HRQL scores sustained at 10 years in 71/99 (72%) of patients. (p<10-6). (pending publication)	Thank you for your comment. Reymunde (2007) and Noar (2007) are listed in appendix A of the overview and are included in the systematic review that is included in the main extraction table of the overview. Dughera (2011) is included in the main extraction table. Noar (2013) is a poster abstract and has been submitted for publication. The NICE IP Methods Guide highlights that efficacy outcomes from non peer-reviewed studies are not normally presented to the Committee. The Committee considered this comment but decided not to change the guidance.

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3	Consultee 3 Private Sector Professional, USA	**1**	There is strong evidence of the long-term (48 months) safety and clinical effectiveness of Stretta in the treatment of GORD. Reymunde (Gastrointest Endosc. 2007; 65:361): Mean GORD-QOL: 2.4 (baseline), 4.6 (36 mo), and 4.3 (48 mo, P < .001). Mean GORD symptom score: 2.7 (baseline), 0.3 (36 mo), and 0.6 (48 mo, P < .001). Daily medication use: 100% (baseline) and 13.6% (48 mo, P < .001). Â Noar (Gastrointest Endosc. 2007; 65:367): Heartburn scores: 3.6 (baseline) 1.18 (48 mo) (P < .001); GORD-HRQL: 27.8 (baseline) to 7.1 (48 mo) (P < .001). Patient satisfaction: 1.4 (baseline) 3.8 (48 mo) (P < .001). Medication use: 100% (baseline) 25% (48 mo) (P < 0.005). Dughera (Diagn Ther Endosc. 2011; 2011:507157): Heartburn scores, GORD-HRQL, and general quality of life scores significantly improved at 24 and 48 months in 52 out of 56 patients (92.8%) At each control time both heartburn and GERD HRQL scores decreased (p = 0.001 and p = 0.003, respectively) and both mental SF-36 and physical SF-36 ameliorated (p = 0.001 and 0.05, respectively). At 48 months, 41 out of 56 patients (72.3%) were completely off PPIs. There are no clinical trials using pH normalization (or even % reduction) as a primary endpoint. Normalization of esophageal acid exposure has been a controversial endpoint. Despite effective symptom control with PPI, ~50% of patients do not normalize acid exposure (Milkes Am J Gastroenterol 2004; 99:991) questioning how much acid control is necessary to achieve a good clinical response.	Thank you for your comment. Reymunde (2007) and Noar (2007) are listed in appendix A of the overview and are included in the systematic review that is included in the main extraction table of the overview. Dughera (2011) is included in the main extraction table. Milkes (2004) is not included in the overview because it assesses the effect of PPIs and does not include radiofrequency treatment. The Committee considered this comment but decided not to change the guidance.

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4	Consultee 4 Scientist and clinical surgeon, Europe	**1**	Although there is not 5-year results of Stretta (as Â already exist for Secca) Â studies provided evidence for Stretta's Â prolonged follow up to 48 months. Dughera (2011), Noar (2007) Â Reymunde (2007) All these studies revealde significant improvement of symptom, disease specyfic life quality and decrease of Â daily medication usage.There were not evidence on Â deterioration of Stretta results with the time. Long term study on Secca procedure (RF teratment of fecal incontinence) provide evidence that sphincter remodeling effect is stable and Â sustained Â up to 5 years after tratment.(Takayashi 2011)	Thank you for your comment. Reymunde (2007) and Noar (2007) are listed in appendix A of the overview and are included in the systematic review that is included in the main extraction table of the overview. Dughera (2011) is included in the main extraction table. Takayashi (2011) is not included in the overview because it refers to a different indication (faecal incontinence). The Committee considered this comment but decided not to change the guidance.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
5	Consultee 5 NHS Professional, Europe	**1**	There is Â quite strong evidence that Stretta procedure is effective in the medium term follow up studies , as shown by Reymunde (2007) and Noar (2007) ; in my personal case series Â Stretta significantly improved heartburn scores, GORD-specific QOL scores, and general QOL scores at 24 and 48 months in 52/56 patients (92.8%) At each control time mean heartburn and GERD HRQL scores decreased (p = 0.001 and p = 0.003, respectively) and both mental SF-36 and physical SF-36 ameliorated (p = 0.001 and 0.05, respectively). At 48 months, 41/56 patients (72.3%) completely off PPIs. Furthermore I have presented at the OESO conference held in Como in september 2012 my data concerning a 8 years Â long term follow up, in which 67% of patients were symptom free and off PPIs (Gut supplement Â 2012) and these data are now under sbmission for peer rewieved pubblication	Thank you for your comment. Reymunde (2007) and Noar (2007) are listed in appendix A of the overview and are included in the systematic review that is included in the main extraction table of the overview. The NICE IP Methods Guide highlights that efficacy outcomes from non peer-reviewed studies are not normally presented to the Committee. The Committee considered this comment but decided not to change the guidance.
6	Consultee 6 Private Sector Professional, USA	**1**	As a practicing surgeon in an academic medical center I have evaluated the current clinical evidence for Stretta. I feel there is adequate evidence to demonstrate satisfactory improvement in esophageal ph measurements and more than adequate evidence of treatment durability. A direct comparison to Nissen may be interesting—but not necessary, as both treatments have been well studied, and as a practitioner I am capable of selecting which patients are candidates for either. The instructions for use for Stretta give detail regarding patient selection, so I am unclear what questions remain. The mechanism of action is adequately demonstrated in clinical studies; LES compliance improvement, reduced TLESR's, increased LES wall thickness. I use Stretta and have found it to be effective and safe.	Thank you for your comment. The Committee considered this comment but decided not to change the guidance.

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7	Consultee 7 NHS professional Specialty Lead in GE	**1**	It is unclear what is considered as uncertain with regards to long term safety. Early trials showed early complications probably as a result of inexperience. This is common for all new procedural intervaentions. There is now clear long term safety data accumulated globally, mainly in the US on safety at 5 years and 10 years amongst several thousand patients. I disagree there is any evidence or reasonable doubt about liong term safety. Long term efficacy may reasonably be argued about and although the number of patients free from reflux or not using PPI therapy reduces with time this is not disproportionate to that observed in more established procedures such as nissen fundoplication. Unproven 'efficacy' is not valid.	Thank you for your comment. The Committee considered this comment but decided not to change the guidance.
8	Consultee 8 NHS Professional	**1**	There are studies Â about the long term safety up to 8 years, NICE should consider reviewing the evidence till todate and change the first statement in 1.1 section.	Thank you for your comment. The Committee considered this comment but decided not to change the guidance.
9	Consultee 9 CEO, Manufacturer, USA	**1**	There are 3 four year follow up studies, all of which conclude the symptomatic benefits are sustained through that period. Four years should constitute adequate longevity of effect. Numerous studies have demonstrated objective improvements; e.g. reduced tissue compliance, reduced acid exposure, reduced TLOSR's. It is important to note that PPI are intended to control symptoms, so the symptomatic benefit of Stretta should not be discounted.	Thank you for your comment. Reymunde (2007) and Noar (2007) are listed in appendix A of the overview and are included in the systematic review that is included in the main extraction table of the overview. Dughera (2011) is included in the main extraction table. The Committee considered this comment but decided not to change the guidance.

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10	Consultee 1 Chief Medical Officer, Manufacturer, USA	**4**	Stretta has been shown to be effective and safe in all 32 separate clinical studies and a recent meta analysis. The primary endpoint of GORD therapy has been consistently achieved, that is, a high rate of symptom control. Secondarily, a dramatic decrease or elimination of GORD medication use has been consistently shown in three separate studies to a minimum of 48 months. A recent meta analysis (Perry et al., 2012) of 18 studies and 1488 patients concluded that: 1) Stretta is very effective in GORD symptom relief, 2) Is safe and well-tolerated, 3) Stretta significantly reduces acid exposure to the oesophagus.	Thank you for your comment. Perry et al. (2012) is included in the main extraction table of the overview. The Committee considered this comment but decided not to change the guidance.
11	Consultee 5 NHS Professional, Europe	**4**	Stretta has been shown to be effective and safe in all 32 separate clinical studies and a recent meta analysis of 18 studies and 1488 patients	Thank you for your comment. A recent meta-analysis is included in the main extraction table of the overview (Perry et al., 2012). The Committee considered this comment but decided not to change the guidance.
12	Consultee 10 NHS Professional	**4**	Whilst there is an ideal aim to normalise Ph levels, this has not been used as an endpoint in the studies, particularly as the studies are comparing Stretta with medical therapy rather than surgery. It is recognised that medical therapy does not completely normalise the pH profile, and certainly does nothing to reduce the amount of reflux; all that happens is the reflux pH is altered.	Thank you for your comment. The Committee considered this comment but decided not to change the guidance.
13	Consultee 1 Chief Medical Officer, Manufacturer, USA	**2**	It is important to note that Stretta has demonstrated significant reductions in oesophageal acid exposure, but not consistent normalization. This statement equally applies to PPI medication. Stretta should not be held to a different standard than the commonly accepted first-line therapy, PPIs.	Thank you for your comment. The Committee considered this comment but decided not to change the guidance.

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14	Consultee 2 Private Sector Professional, USA	**4**	In over 32 separate clinical studies, 4 RCT trials, a recent meta analysis and a soon to be published 10 year study, Stretta has been shown to be safe and effective. Â The primary endpoint of GORD therapy, >50% normalization in GERD-HRQL scores and symptom control has been consistently achieved in all studies including at 10 years (Noar et al 2013). Â The secondary endpoint of dramatic decrease or elimination of GORD medication use has been consistently shown in three separate studies at a minimum of 48 months, which appears durable at 10 years post procedure with 75% of patients on >50% less medication and up to 41% off medication entirely. In the recent meta analysis (Perry et al., 2012) of 18 studies and 1488 patients concluded that: 1) Stretta is very effective in GORD symptom relief, 2) Is safe and well-tolerated, 3) Stretta significantly reduces acid exposure to the oesophagus. In the soon to be published 10 year trial, in 167 patients, no cases of esophageal cancer developed at 10 years and Barrett's tissue was seen to spontaneously regress.	Thank you for your comment. Noar et al. (2013) is a poster abstract and has been submitted for publication. The NICE IP Methods Guide highlights that efficacy outcomes from non peer-reviewed studies are not normally presented to the Committee. Perry et al. (2012) is included in the main extraction table of the overview. The Committee considered this comment but decided not to change the guidance.
15	Consultee 7 NHS professional Specialty Lead in GE	**4**	There is a meta analysis published in 2011 showing there to be long term efficacy and safety with Stretta. My own experience with 5 patients range from 3-18 months and due to careful pre procedure sel;ection these patients have all felt well, are off PPI and have negative salivary pepsin tests.	Thank you for your comment. A recent meta-analysis is included in the main extraction table of the overview (Perry et al., 2012). The Committee considered this comment but decided not to change the guidance.

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16	Consultee 4 Scientist and clinical surgeon, Europe	**4**	Based on the recent literature reviev Stretta appear effective and safe in all avaiable clinical studies . RF GORD therapy has been shovn to be effective it the symptom control and patients improvemnet. Â The Perry's Â meta analysis (2012) covered of 18 studies and 1488 patients confirmed Â that Â Stretta is safe, Â well tolerated and Â very effective in GORD symptom reliefe. Stretta significantly reduces acid exposure to the oesophagus and significantly improve patients live quality.	Thank you for your comment. Perry et al. (2012) is included in the main extraction table of the overview. The Committee considered this comment but decided not to change the guidance.
17	Consultee 3 Private Sector Professional, USA	**4**	Several studies have shown significant reduction but not consistent normalization of esophageal acid exposure after Stretta. In a meta-analysis of 11 studies comprising 364 patients over a mean follow-up period of 11.9 months, esophageal acid exposure decreased from a mean of 10.29%+/-17.8% to 6.51%+/-12.5% (P=0.0003) (Surg Lap Endoscopy Perc Tech 2012; 22: 283-288). Â However, refractory GERD symptoms may not always reflect the acidity of the refluxate but may be due to increased refluxate volume, esophageal distensibility and individual sensitivity to acid (Clin Outcomes Manag. 2000; 7:29; Clin. Gastroenterol. Hepatol. 2004; 2(8):656; Gut 2012; 61:1501-1509). Indeed, visceral analgesics, such as a tricyclic antidepressants, selective serotonin uptake inhibitors, or trazodone, are used as adjunctive tools in the management of PPI-refractory GERD patients.	Thank you for your comment. These results are presented in section 4.1. The Committee considered this comment but decided not to change the guidance.

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18	Consultee 3 Private Sector Professional, USA	**4**	Stretta could be effective in decreasing esophageal sensitivity to acid. This has been suggested by controlled clinical trials showing improvement of symptoms and decrease in PPI use despite the lack of normalization of esophageal acid exposure, as well as experimentally, by decreasing esophageal inflammation and sensitivity to acid perfusion (Bernstein's test) (Dig Dis Sci. 2007; 52: 2170-7). Stretta also decreases GOJ compliance, which in turn contributes to symptomatic benefit by decreasing refluxate volume. (Am. J. Gastroenterol. 2012;107: 222-30). Therefore, Stretta may be considered as an "endoscopic pain modulator" and should be considered in patients with refractory symptoms despite PPIs, as well as in patients with hypersensitive esophagus and functional heartburn (Gut 2012; 61:1340-1354). Further, it does not preclude any other alternative (repeat Stretta, PPI addition or fundoplication) and is the least expensive alternative to medical therapy. Today more than ever, clinicians will benefit from the addition of Stretta to the treatment armamentarium for their GERD patient.	Thank you for your comment. The Committee considered this comment but decided not to change the guidance.
19	Consultee 6 Private Sector Professional, USA	**4**	My professional assessment of Stretta data mirrors that of the Society of American Gastrointestinal Endoscopic Surgeons (SAGES) recent Clinical Spotlight Review, as well as the conclusion reached in the 2011 meta-analysis. There is adequate long term evidence of both subjective and objectively measured improvements.	Thank you for your comment. The SAGES review is included in the overview under 'Existing assessments of this procedure'. A recent meta-analysis is included in the main extraction table of the overview (Perry et al., 2012). The Committee considered this comment but decided not to change the guidance.

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20	Consultee 9 CEO, Manufacturer, USA	**4**	There is strong evidence of sustained symptom and ph control, and long term quality of life improvements. The meta analysis of 18 studies and 1400 patients clearly demonstrates Stretta's effect and benefit.	Thank you for your comment. The consultee is referring to Perry et al. (2012), which is included in the main extraction table of the overview. The Committee considered this comment but decided not to change the guidance.
21	Consultee 11 NHS Professional	**Notes**	This technique has a crucial role in the spectrum of management of oesophageal reflux and faecal incontinence. Â The literature is vast and shows that it is effective and safe. Â It is also endoscopic or day case, with minimal invasion. Â The tablets are expensive and sometimes do not work. Â Surgery is risky, fails and may recur. Â an intermediary is essential. Â The technology for faecal incontinence is often the only available treatment (internal anal sphincter) or provides an intermediate treatment for moderate incontinence. Â Low risk and effective. Much has been discussed about mechanism. Â it is clearly not just burning and scarring. Â there is clear evidence that there must be a more physiological effect. Â burning fragile muscular sphincters such as the LOS and internal anal sphincter just would nit work. Â Lesser insults lead to damage. Â The literature is clear on this. Â Even if the exact mechanism is not proven this should not deter so long as effective and safe. Â There are many examples where true effect cannot be explained ie sacral nerve neuro-modulation. Â Many established treatments evolve, almost by chance. It is essential that NIiCE endorses this treatment modality as safe and effective. Â Many patients at present with no option and por quality of life rely on this.	Thank you for your comment. The Committee considered this comment but decided not to change the guidance.

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22	Consultee 12 AUGIS Council - adviser on reflux therapy Specialist Adviser	**1**	I would prefer to see a recommendation for further controlled clinical trials (and not observational registry)	Thank you for your comment. The Committee considered this comment but decided not to change the guidance.
23	Consultee 8 NHS Professional	**6**	Given the procedure been done in more than 15,000 patients worldwide, based on current evidence NICE should positively look in to this as an adjunct to the current GORD management in UK. There is a need in the guidance to address 'who' should do the procedure, on pragmatic grounds, it should be done by endoscopicts (medical and surgical) who regularly perform therapeutic upper GI endoscopies.	Thank you for your comment. The Committee considered this comment but decided not to change the guidance.
24	Consultee 10 NHS Professional	**1**	These are standard NICe recommendations fopr any new procedures, and seems appropriate to ensure adequate governance arrangements.	Thank you for your comment.
25	Consultee 11 NHS Professional	**1**	reasonable. Â this must occur then for all medication treatment.	Thank you for your comment.
26	Consultee 12 AUGIS Council - adviser on reflux therapy Specialist Adviser	**4**	paragraph 4.1 is very important - the sham study showed no significant changes in acid reflux (measured by pH monitoring at 3 or 6 months post procedure). Â The efficacy of this device is questionnable, and most of the other studies are observational, not controlled and no objective help in assessing cost - effectiveness.	Thank you for your comment. Cost-effectiveness is not part of the remit of the IP Programme.
27	Consultee 2 Private Sector Professional, USA	**1**	1) The term ablation is incorrect. Â No ablation takes place using RF energy. Â Tissue remodeling occurs from application of RF, but nothing is destroyed, and there is no scientific evidence to suggest destruction.	Thank you for your comment. The Committee considered this comment but decided not to change the guidance.
28	Consultee 13 Professor of Gastroenterology, France	**1**	No negative long term effect has been reported regarding esophageal motility (many physicians fear the development of achalasia-like esophageal dysmotility after Stretta)	Thank you for your comment.

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29	Consultee 7 NHS professional Specialty Lead in GE	**1**	The points to make in the wording of this statement are; Reflux does not just constitute acid reflux. Patients may also experience biliary reflux or have symptoms of visceral hypersensitivity. The LES may be lax in reflux disease but the condition is also contributed Â to by poor or inco-ordinate gastric emptying and hiatus hernia. There is no evidence that the technology described causes a scar in the esophagus but rather remodelling and altered esophageal relaxation.	Thank you for your comment. The lay description that is presented in the consultation document will be removed from the final guidance document. The lay description in the overview will be amended.
30	Consultee 2 Private Sector Professional, USA	**2**	GERD is a complex disease that results from caustic reflux of acidic, weakly acidic or non-acidic gastric contents into the oesophagus. Until recently the exact mechanism of heartburn was not well understood. Previously, it was thought that the predominant mechanism of action causing disease was acid penetration of the esophageal mucosa as the sole cause of heartburn manifestations. However, research performed over the past several years looking at not only mucosal receptors but also the molecular response to stimulation of these receptors, revealed an indirect cascade of action in which acid and other caustic-sensing receptors cause release and activation of both neural and non-neural chemokine pathways leading directly to a decline in cell integrity, as well as the development of inflammation, pain, and compromised motility. Stretta effectively addresses underlying mechanisms of GORD by reducing TLOSRs and therefore may effective treat the basic mechanism of action of disease, by reducing amount of caustic reflux.	Thank you for your comment. The Committee considered this comment but decided not to change the guidance.

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31	Consultee 13 Professor of Gastroenterology, France	**3**	In our current study, we also expect an effect of Stretta in patients with refractory symptoms not related to GERD because we assume a decrease in esophageal sensitivity (hypersensitivity is present in patients with functional heartburn). Having an effect on esophageal acid exposure does not exclude an effect on esophageal sensitivity. Moreover, Stretta inhibits the occurence of TLESRs which is a vago-vagal reflex elicited by the stimulation of sub-cardial receptors. Therefore, there should be -at least in part- some kind of denervation. I agree that it is a matter of concern for people. But most patients with refractory symptoms don't have esophagitis (they have either NERD or no reflux at all) and will not develop esophagitis on the long term.	Thank you for your comment. Section 3.1 of the guidance has been changed.
32	Consultee 5 NHS Professional, Europe	**3**	The notion of fibrosis as the cause of the Stretta effect is purely conjectural and has been disproven in clinical studies. Several putative mechanisms could explain Stretta's clinical effectiveness. Increased gastric yield pressure, increased thickness of the LOS muscle, decreased distensibility of the GOJ without fibrosis, decreased GOJ compliance and decreased TLOSRs	Thank you for your comment. Section 3.1 of the guidance has been changed.
33	Consultee 7 NHS professional Specialty Lead in GE	**3**	The role of RFA on dennervation is speculative and without basis in science or fact. The treatment applied in RFA is at the muscular rather than mucosal layer. The only effect the anti-reflux endpoints of stretta might produce are increased LESP and increased proximal gastric emptying, subsequent reduction in visceral sensitivity is much more likely to be secondary to fewer reflux episodes then some dennervation effect.	Thank you for your comment. Section 3.1 of the guidance has been changed.

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34	Consultee 10 NHS Professional	**3**	Whilst the mechanism of action is not entirely clear, it appears to cause augmentation of the lower oesophageal sphincter. There is no evidence that it causes 'narrowing' ie striuctures, or denervation. These comments should be removed from the guidance as they are mere supposition and misleading	Thank you for your comment. Section 3.1 of the guidance has been changed.
35	Consultee 9 CEO, Manufacturer, USA	**3**	Study confirmed mechanisms of action are, in addition to thickening of the LOS, reduced TLOSR's--which are principally responsible for GORD, and reduced tissue compliance. Stretta reduces reflux, regardless of the contents ph. Besides healing oesophageal erosions and the subsequent reduction of acid sensitivity that accompanies healing of these erosions, there is no evidence of any sort of denervation. There is strong evidence noted in several studies there is no denervation.	Thank you for your comment. Section 3.1 of the guidance has been changed.

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36	Consultee 1 Chief Medical Officer, Manufacturer, USA	**3**	Strong evidence exists to support symptomatic improvement after Stretta is attributable to a decrease in oesophageal acid exposure and not to desensitization. Desensitization is completely unsubstantiated conjecture based on the false assumption that Stretta relies on tissue destruction for treatment effect. Clinical data completely refutes this conclusion. Studies have also noted an improvement in oesophagitis, which is impossible in a desensitized oesophagus still exposed to acid.• Sholten (2007), a “normal” oesophagus is less sensitive to acid• Arts (2007), no direct correlation between symptom scores and esophageal sensitivity to acid perfusion, improvement of symptom scores was related to improvement of esophageal acid exposure• Liu (2011), Stretta healed erosions• Triadafilopolous (2004), changes in GORD-HRQL and heartburn severity correlated to changes in acid exposure • Richards (2003), 80% of patients with complete response to Stretta, no longer taking PPIs normalized pH scores, and no evidence of esophagitis• DiBaise (2002), reduction in the number of TLOSRs, no adverse effect on abdominal vagal function, no significant change in any esophageal motility parameter	Thank you for your comment. Section 3.1 of the guidance has been changed. Scholten (2007) is not included in the overview because it does not assess radiofrequency treatment. Arts (2007), Triadafilopoulos (2004), Richards (2003) and DiBaise (2002) are included in appendix A of the overview.

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37	Consultee 2 Private Sector Professional, USA	**3**	3.1 Â The goal of RF therapy is to cause remodeling of the sphincter to reduce TLOSR's and reflux thereby reducing symptoms. . Strong evidence exists to support symptomatic improvement after Stretta is attributable to decreased Â oesophageal acid exposure and not desensitization. Desensitization is completely unsubstantiated conjecture as there is no nerve destruction. Patients continue to have symptomatic GORD immediately after the procedure and for several week s after Clinical data completely refutes this conclusion with studies showing: a. Sholten (2007), a "normal" oesophagus is less sensitive to acid b. Arts (2007), no direct correlation between symptom scores and esophageal sensitivity to acid perfusion, improvement of symptom scores related to improvement of esophageal acid exposure Liu (2011), Stretta healed erosions c. Triadafilopolous (2004), changes in GORD-HRQL and heartburn severity correlated to acid exposure d. Richards (2003), 80% of patients with complete response no longer taking PPIs normalized pH scores, and no evidence of esophagitis e. DiBaise (2002), reduction in the number of TLOSRs, no adverse effect on abdominal vagal function, no significant change esophageal motility	Thank you for your comment. Section 3.1 of the guidance has been changed. Scholten (2007) is not included in the overview because it does not assess radiofrequency treatment. Arts (2007), Triadafilopoulos (2004), Richards (2003) and DiBaise (2002) are included in appendix A of the overview. Liu (2011) is included in the main extraction table of the overview.
38	Consultee 6 Private Sector Professional, USA	**3**	The concept of reduced acid sensitivity as a result of Stretta treatment is pure hypothesis, with the exception that Stretta has been shown to heal esophageal erosions, and it is widely accepted that normal tissue is less sensitive to acid exposure than ulcerative tissue. Further, studies of Stretta have addressed the issue of "denervation" and have concluded that no such effect exists. Further discussion of hypothesis in the presence of study conclusions refuting this conjecture is not scientifically sound.	Thank you for your comment. Section 3.1 of the guidance has been changed.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
39	Consultee 4 Scientist and clinical surgeon, Europe	**3**	Several studies Â elucidates the mechanisms of Â RF treatment. Symptomatic improvement after Stretta was related to a decrease in oesophageal acid exposure but not to LES desensitization. Â Â Â Â Â Â Â Â Â Â Â Â Â RF application does not produces desinsetisation. Our study on RF treatment of fecal incontinence (Secca) revealed Â increased anorectal sensitivity after baloon distension and increased theremo/ electro sensitivity after RF Â (Herman R. 2013 ASCRS Â).In double-blind sham-controlled Â study Arts shoved that LES after RF application responds to the sildenafil . It Â relaxes smooth muscle by blocking type 5-PDE,eliminating distal esophageal contractions and LES pressure. After sildenafil , GEJ compliance after Stretta was normalized to pre-Stretta level. This rules out GEJ fibrosis Â as an underlying mechanism. Studies confirmed that nonablative RF Â treatment Â relies on tissue remodeling not tissues destruction and fibrosis. Our experimental tissues study shoved increase diameter and number of SM fibers within IAS after RFand increase of Conexin 43 activity. Study Â revealed the increase in fiber typ I in EAS and no increase in EAS dystrophin activity (Herman R. 2013.SAGES).	Thank you for your comment. Section 3.1 of the guidance has been changed. Arts (2012) is included in the main extraction table of the overview.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
40	Consultee 3 Private Sector Professional, USA	**3**	The main aim of GORD treatment should be rapid and sustained achievement of comprehensive symptom resolution, because this is associated with marked improvement -often normalization- in health-related quality of life (Revicki et al 1999). The other primary aims are to heal esophageal mucosal damage if it is present and to prevent relapse of erosive esophagitis in the hope that this will reduce the development of complications. Adequate treatment of GERD should either prevent repeated reflux of gastric contents into the esophagus or reduce the damaging effect of gastric acid. Symptom relief has been demonstrated consistently in all 32 peer-reviewed published Stretta studies, which include, four RCTs and one meta-analysis. As the primary intention of pharmacologic therapy in the treatment of GORD is symptom relief, that same standard would logically apply to radiofrequency treatment of GORD. In addition to significant improvements in symptom control and quality of life, Stretta has also been shown to consistently and durably reduce medication use (Sholten (Ther Clin Risk Manag. 2007 June; 3(2): 231–243).	Thank you for your comment. The Committee considered this comment but decided not to change the guidance. Scholten (2007) is not included in the overview because it does not assess radiofrequency treatment.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
41	Consultee 1 Chief Medical Officer, Manufacturer, USA	**6**	Mechanisms demonstrated in numerous clinical studies explain Stretta's effectiveness. Increased gastric yield pressure, increased thickness of the LOS muscle, decreased distensibility of the GOJ without fibrosis, decreased GOJ compliance and decreased TLOSRs. • Utley 2000, augmented gastric yield pressure by 75%• Kim 2003, inhibits triggering of TLOSRs• Arts 2011, decreased GOJ compliance, altered LOS neuromuscular function–no fibrosis• Tam 2003, significant effects on LOS function and improvement in antireflux barrier Improvement after Stretta has also been attributed to a decrease in oesophageal acid exposure, not desensitization. Desensitization is unsubstantiated conjecture based on the false assumption that Stretta relies on tissue destruction for treatment effect. Clinical data refutes this conclusion. Studies have also noted an improvement in oesophagitis, which is impossible in a desensitized oesophagus exposed to acid. Undocumented conjecture of the denervation, or burning/fibrosis theory following Stretta should be abandoned. Available data on alterations in GOJ physiology should be noted to accurately inform physicians.	Thank you for your comment. The Committee considered this comment but decided not to change the guidance. Utley (2000) and Kim (2003) are not included in the overview because they are animal studies. Arts (2012) is included in the main extraction table of the overview. Tam (2003) is included in appendix A of the overview.
42	Consultee 5 NHS Professional, Europe	**6**	Symptomatic improvement after Stretta is attributable to a decrease in esophageal acid exposure and not to esophageal desensitization or nerve damage. In fact, studies have also noted an improvement in oesophagitis, which would not be possible in a desensitized lower oesophagus that was still exposed to acid.	Thank you for your comment. The Committee considered this comment but decided not to change the guidance.
43	Consultee 10 NHS Professional	**6**	There is no evidencve that the treatment causes denervation. This should be removed from the guidance	Thank you for your comment. The Committee considered this comment but decided not to change the guidance.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
44	Consultee 2 Private Sector Professional, USA	**6**	Characterizations that desensitization is a mechanism of action are irresponsible and unsubstantiated by the literature, and based upon a false assumption that tissue destruction is the mechanism of action. In fact, while some RF devices ablate (cardiac), the Stretta device is carefully engineered to prevent tissue destruction. Undocumented conjecture of denervation, or burning/fibrosis caused by Stretta should be abandoned in light of evidence to the contrary and only raise the specter of motive and integrity. More notably, studies demonstrate consistent improvement in oesophagitis, making it impossible to invoke desensitization as the etiology for improvement. Â There are a plethora of studies that demonstrate the mechanisms of action, including: Â increased gastric yield pressure, increased LOS muscle thickness, increased LOS pressure, decreased distensibility of the GOJ without fibrosis, decreased GOJ compliance and decreased TLOSRs.• Utley 2000, augmented gastric yield pressure by 75%• Kim 2003, inhibits triggering of TLOSRs• Arts 2011, decreased GOJ compliance, altered LOS neuromuscular function–no fibrosis• Tam 2003, effects on LOS function and improvement in antireflux barrier Taken as the sum of all actions, this results in a demonstrated decrease in oesophageal acid exposure resulting from fewer TLOSRs, thereby limiting V1 receptor activation that is responsible for tissue destruction and symptoms of reflux.	Thank you for your comment. Utley (2000) and Kim (2003) are not included in the overview because they are animal studies. Arts (2012) is included in the main extraction table of the overview. Tam (2003) is included in appendix A of the overview. The Committee considered this comment but decided not to change the guidance.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
45	Consultee 6 Private Sector Professional, USA	**6**	The mechanism of action is adequately demonstrated in clinical studies; LES compliance improvement, reduced TLESR's, increased LES wall thickness. There is no evidence of any kind to support denervation. The concept of reduced acid sensitivity as a result of Stretta treatment is pure hypothesis, with the exception that Stretta has been shown to heal esophageal erosions, and it is widely accepted that normal tissue is less sensitive to acid exposure than ulcerative tissue. Further, studies of Stretta have addressed the issue of "denervation" and have concluded that no such effect exists. Further discussion of hypothesis in the presence of study conclusions refuting this conjecture is not scientifically sound. Clinical studies show a beneficial effect of Stretta on esophageal and gastric motility, with improvements noted in gastroparesis. Short term complications as noted, are negligible. 48 month follow up studies indicate no subsequent complications of any type. Ten year follow up data indicates a sustained beneficial effect and no long term complications.	Thank you for your comment. 10 year follow up data has been reported by Noar et al. (2013) in a poster abstract and has been submitted for publication. The NICE IP Methods Guide highlights that efficacy outcomes from non peer-reviewed studies are not normally presented to the Committee. The Committee considered this comment but decided not to change the guidance.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
46	Consultee 7 NHS professional Specialty Lead in GE	**6**	This is not the case. As with all new technology that is correctly applied, because ongoing research is being undertaken this does not imply we dont know any of the mechanisms by which STRETTA improves symptoms in refluxers. There is a reduction in interprandial LER, increased, LEwall thickness and LES compliance as shown in clinical papers. I would add that there are no clinical papers or case reports supporting dennervation ior esophageal cancer. If this is to be considered a balanced review of the medical evidence it is clear that in a low risk population, without barretts or large hiatus hernia STRETTA has evidence of 10 Â year safety and efficacy data and a meta analysis of a large group of treated patients supporting its use.	Thank you for your comment. 10 year follow up data has been reported by Noar et al. (2013) in a poster abstract and has been submitted for publication. The NICE IP Methods Guide highlights that efficacy outcomes from non peer-reviewed studies are not normally presented to the Committee. A recent meta-analysis is included in the main extraction table of the overview (Perry et al., 2012). The Committee considered this comment but decided not to change the guidance.
47	Consultee 3 Private Sector Professional, USA	**6**	Strong evidence suggests that symptomatic improvement after Stretta is attributable to a decrease in esophageal acid exposure and not to esophageal desensitization or nerve damage. In fact, studies have also noted an improvement in oesophagitis, which would not be possible in a densensitized lower oesophagus that was still exposed to acid (Liu, World J Gastroenterol 2011). Oesophageal acid sensitivity depends on multiple factors, including esophageal exposure to hydrogen ions, mucosal permeability, number and activation state of acid-sensitive nerve endings, and central processing of incoming sensory information.	Thank you for your comment. Liu et al. (2011) is included in the main extraction table of the overview. The Committee considered this comment but decided not to change the guidance.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
48	Consultee 3 Private Sector Professional, USA	**6**	One criticism of Stretta has been the theoretical concern that it induces partial desensitization of the oesophageal body through ablation of sensory nerve endings rather than a reduction in oesophageal acid exposure. In fact, the available clinical data completely refutes this conclusion. It is ironic that on one hand, visceral analgesics are accepted in the management of refractory GORD without concerns about desensitization and on the other Stretta is criticized as potentially harmful. Nevertheless, Arts (Dig Dis Sci. 2007;52:2170-7) evaluated the effect of Stretta on symptoms, acid exposure, and sensitivity to esophageal acid perfusion in 13 patients with PPI-dependent GERD. Six months after Stretta, the symptom scores were significantly improved (12.5+/-2.0 to 7.5+/-2.1; P<0.05), seven patients no longer needed daily PPI, and acid exposure was significantly decreased (11.6%+/-1.6% to 8.5%+/-1.8% of time pH<4; P<0.05). The time needed to induce heartburn during acid perfusion (as a measure of esophageal sensitivity) decreased from 9.5+/-2.3 to 18.1+/-3.4 min (P=0.01), and five patients became insensitive to 30-min acid perfusion, versus none at baseline (P=0.04). However, esophageal acid perfusion occurred through a midoesophageal infusion port, whereas radiofrequency energy delivery involved only a narrow area around the LES. As esophageal acid sensitivity is not limited to this small region, it seems less likely that sensory nerve ablation sufficiently explains the changes.	Thank you for your comment. Arts et al.(2007) is included in appendix A of the overview. The Committee considered this comment but decided not to change the guidance.
49	Consultee 11 NHS Professional	**6**	this is simlplistic. Â there is an increasing literature trying to explain the mechanism. Â it is clear that it work well, and many treatments in established practice are still not fully explained as to mechanism of action. Â many established treatments devlop almost by chance.	Thank you for your comment. The Committee considered this comment but decided not to change the guidance.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
50	Consultee 9 CEO, Manufacturer, USA	**6**	As noted previously, study findings are that Stretta reduces tissue compliance without fibrosis, increases LOS wall thickness, and reduces refluxate by reducing TLOSR's.	Thank you for your comment.
51	Consultee 4 Scientist and clinical surgeon, Europe	**6**	Numerous studies revealed mechanisms of RF tissue remodeling (Stretta/Secca). Studies shoved : increased thickness of the LOS muscle, gastric yield pressure, decreased distensibility of the GOJ without fibrosis, decreased GOJ compliance an TLOSRs.(Utley 2000,Kim 2003,Arts 2011,Tam 2003). Study on treatment of fecal incontinence(Secca) revealed the increased in anal pressure and anorectal sensitivity to baloon distension and theremo/electrosensitivity(HermanR.M.2013 ASCRS).Nonablative RF Â treatment relies on tissue remodeling not tissues destruction.Experimental tissues study shoved increase in diameter and numer of muscle fibers within IAS Â after RF, and increase of Conexin 43 and SM actin.Study revealed the increase in fiber typ I EAS Â and no increase in EAS dystrophin activity(Herman R.M 2013.SAGES,DDW).There are ANY study supporting the theory of LES Â denervation, its Â termal ablation and subsequent fibrosis, as well as Â mucosa damage after RF . Therefor-based on also on my personale experiences all this undocumented speculation on RF induced sphincters „termal laesions” and „fibrosis” after Stretta or Secca Â procedure should not be distributed.	Thank you for your comment. Utley (2000) and Kim (2003) are not included in the overview because they are animal studies. Arts (2012) is included in the main extraction table of the overview. Tam (2003) is included in appendix A of the overview. The Committee considered this comment but decided not to change the guidance.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
52	Consultee 13 Professor of Gastroenterology, France	**2**	As far as I know, only a minority of studies have included patients with refractory symptoms, and that's why we are currently performing such a study in France. Most studies to date have included patients doing well on PPIs but wanted to get rid of these medecines. It may be useful to identify the few studies in patients with refractory symptoms to advocate the use of Stretta in this situation.	Thank you for your comments.
53	Consultee 5 NHS Professional, Europe	**2**	Although effective, proton pump inhibitors provide incomplete control of reflux symptoms in up to 40% of patients. A partial response can occur because these drugs do not address an incompetent sphincter or prevent reflux. Consequently, some patients seek alternative treatment if their quality of life is compromised. Failure of the PPI treatment to resolve GORD-related symptoms has become the most common presentation of GORD among Â gastroenterologists. Stretta is a valuable option for such refractory patients who are not willing to undergo surgery (fundoplication).Potential candidates for Stretta would be those with GORD who have persistent heartburn and/or regurgitation despite escalating doses of PPI (refractory GORD), patients with GORD who are symptomatic because they cannot tolerate PPIs (2% of PPI users), those who desire to stop drug therapy and those who do not wish antireflux surgery Â or are poor surgical candidates.	Thank you for your comment. The Committee considered this comment but decided not to change the guidance.
54	Consultee 8 NHS Professional	**2**	It is more appropraite to insuniate a statement that it has got a role in patients who are not keen or not fit for surgery (in indicated cases as mentioned). The procedure is not appropriate for patients with more than 3 cms hiatus hernia and very low lower sphincter pressure (less than 5 mmHg)	Thank you for your comment. The Committee considered this comment but decided not to change the guidance.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
55	Consultee 10 NHS Professional	**2**	Stretta is an ideal treatment for patients in the 'therapeutic ap'; that is the 45-50% of reflux patients who remain dissatisfied with medication alone, and may not have seve3re enough reflux to undergo surgical intervention.	Thank you for your comment. The Committee considered this comment but decided not to change the guidance.
56	Consultee 4 Scientist and clinical surgeon, Europe	**2**	Since GERD is rather complex disease caused by different Â refluxes and disturbed mechanisms of LES competency there is Â actually no single treatment covering all these mechanisms . Radiofrequency treatment (Stretta) effectively influences several underlying mechanisms of GORD (such as TLOSRs, LES competency) therefore it may be utilized in different patients despite the underlying mechanism of GERD. It may Â be also used in refractory patients who are not interested or willing to underwent Â major anti-reflux surgery. Stretta has been found as the Â noninvasive procedure which may be used if Â medical therapy failed medical Â and surgical intervention is not indicated or possible. Stretta appeared effective in significant reductions in oesophageal acid exposure, but not its normalization and therefore may require PPI medication .	Thank you for your comment. The Committee considered this comment but decided not to change the guidance.
57	Consultee 1 Chief Medical Officer, Manufacturer, USA	**2**	GERD is a complex disease caused by any number of types of reflux (acidic, weakly acidic or non-acidic) into the oesophagus. Since Stretta effectively addresses several underlying mechanisms of GORD (such as TLOSRs) it does not discriminate to the type of reflux, it may be utilized in those refractory patients who are not interested in pursuing anti-reflux surgery. As such, Stretta provides an invaluable adjunct in the treatment of GORD that spans the “gap” between PPI responders and surgical candidates.	Thank you for your comment. The Committee considered this comment but decided not to change the guidance.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
58	Consultee 3 Private Sector Professional, USA	**2**	Overall, GORD is a complex disease caused by various types of reflux (acidic, weakly acidic or non-acidic) into the esophagus. Since Stretta effectively addresses several underlying mechanisms of GORD (such as TLOSRs) it does not discriminate to the type of reflux, it may be utilized in those refractory patients who are not interested in pursuing anti-reflux surgery. There is unquestionably an unmet need for the many sufferers of GORD, particularly the refractory ones, where Stretta has been shown to offer significant improvements by both objective and subjective criteria. As such, Stretta provides an invaluable adjunct in the treatment of GORD that spans the "gap" between PPI responders and surgical candidates. As the precise physiologic dysfunction exhibited by GORD sufferers is not completely understood, multiple therapeutic modalities – used alone or even in combination -may contribute to symptom control. The abundance of clinical data on Stretta confirms: 1) tissue destruction and creation of fibrosis does not occur; 2) symptom control in PPI dependent patients occurs consistently; 3) a variety of functional improvements occur in the distal esophagus including improved acid sensitivity and tissue compliance; and 4) the procedure is exceedingly safe and reproducible. Stretta is safe, effective, durable, repeatable if necessary, and it does not preclude any other alternative (repeat Stretta, PPI addition or fundoplication).	Thank you for your comment. The Committee considered this comment but decided not to change the guidance.
59	Consultee 6 Private Sector Professional, USA	**2**	Lifestyle modifications, medications, and anti-reflux surgery successfully treat a large portion of reflux sufferers. However, there is a clear unmet need in the refractory GERD sufferer. A safe, effective, same day treatment such as Stretta adds an important alternative treatment to the current offering.	Thank you for your comment. The Committee considered this comment but decided not to change the guidance.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
60	Consultee 12 AUGIS Council - adviser on reflux therapy Specialist Adviser	**3**	The use of this device is limited to patients with small hiatal hernias and excludes patients with Barrett's oesophagus. Â This is not clear from this paragraph.	Thank you for your comment. The Committee considered this comment but decided not to change the guidance.
61	Consultee 11 NHS Professional	**2**	fine	Thank you for your comment.
62	Consultee 9 CEO, Manufacturer, USA	**2**	The population of refractory GORD sufferers (estimated at 30-40% of all GORD sufferers)compared to the number of GORD surgical procedures done each year (a small fraction of potential candidates), indicates a significant need for safe and effective alternatives such as Stretta.	Thank you for your comment.
63	Consultee 2 Private Sector Professional, USA	**3**	3.2 Â It is the length of the esophagus from incisors to gastro-oesophageal junction that is measured.	Thank you for your comment. Section 3.2 of the guidance will be changed.
64	Consultee 11 NHS Professional	**3**	fine	Thank you for your comment.
65	Consultee 8 NHS Professional	**3**	Worth metioning it is a day case.	Thank you for your comment. The Committee considered this comment but decided not to change the guidance.
66	Consultee 11 NHS Professional	**4**	Fine. Â the expense of ppi should not be under-estimated.	Thank you for your comment.
67	Consultee 13 Professor of Gastroenterology, France	**5**	I don't understand why adding the risk of cancer. GERD per se is a risk factor of cancer. No data support this assumption since there is no evidence of esophagitis worsening or Barrett's esophagus development related to the procedure. Regarding the risk of perforation, as far as I know peforations occurred in the very beginning of the development of the device.	Thank you for your comment. Section 5.4 is the opinion of the Specialist Advisers. The Committee considered this comment but decided not to change the guidance.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
68	Consultee 10 NHS Professional	**5**	I am unclear as to how the theoretical risk of increased cancer risk was arrived at; if anything it potentially could reduce the risk as it reduces the amount of mucosal damage. The relationship between reflux and cancer risk is a complex one, and indeed there is suggestion that medical therapy is associated with increasing the risk (Prof T R DeMeester). Again this statement is supposition and misleading- it should be removed from the guidance	Thank you for your comment. Section 5.4 is the opinion of the Specialist Advisers. The Committee considered this comment but decided not to change the guidance.
69	Consultee 6 Private Sector Professional, USA	**5**	From my own use of Stretta, from discussions with many of my peers who also use Stretta, from the conclusions of the dozens of Stretta published studies, and from the available reports of complications such as the FDA, I concur with the findings that Stretta is very safe. The complications that are noted in the draft guidance generally took place before 2001, when the treatment protocol called for more energy and treatment sites. When this was changed in 2001, complications diminished significantly. I believe the suggestion of any increased risk of esophageal cancer is entirely without merit and should be retired from the conversation immediately. The manufacturers IFU calls exclusively for treatment of non-erosive disease sufferers. This population itself is in the low risk category for esophageal cancer.	Thank you for your comment. Section 5.4 is the opinion of the Specialist Advisers. The Committee considered this comment but decided not to change the guidance.
70	Consultee 11 NHS Professional	**5**	there is no reason in my opinion to mention cancer, this is defensive and could be placed on all treatmenst. Â it serves no purpose as there is no evidence.	Thank you for your comment. Section 5.4 is the opinion of the Specialist Advisers. The Committee considered this comment but decided not to change the guidance.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
71	Consultee 7 NHS professional Specialty Lead in GE	**5**	The deaths reported were in early series, operators not following best application of the technology. Subsequently all Stretta users receive training from designatated centres before obtaining equipment to undertake the RFA. The review presented mirrored my own concerns when RFA was presented, I then reviewed outcomes only after 5 year safety data made it clear that primarily it was a safe technology with apparent efficacy. there is now 10 year data presented at DDW 2013 demonstrating long term safety. Reference to adverse events in this report is unfairly weighted to the early studies and again my argument would be that a similar finding would be likely when studying other new technologies. I am startled by the suggestion of an increased risk of esophageal cancer with this procedure. This is unscientific and scaremongering and I am surprised that based on no clinical evidence whatsoever this has found its way into the provisional guidelines of NICE.	Thank you for your comment. Section 5.4 is the opinion of the Specialist Advisers. The Committee considered this comment but decided not to change the guidance.
72	Consultee 9 CEO, Manufacturer, USA	**5**	There have been more than 15,000 Stretta procedures done, including approximately 3000 patients treated in clinical studies. The complication rate for Stretta is less than 1%, making it technically safer than an upper GI endoscopy. All 32 studies in the literature state that Stretta is safe. There is no evidence of any kind to suggest RF for GORD increases oesophageal cancer risk. There is 10 year data available for Stretta of 100 patients that examines, among other factors, oesophageal cancer occurrence in the study population. There is zero occurrence.	Thank you for your comment. Section 5.4 is the opinion of the Specialist Advisers. The Committee considered this comment but decided not to change the guidance.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
73	Consultee 5 NHS Professional, Europe	**5**	According to the literature available data Stretta is a very safe and feasible procedure, with minimal incidence of side effects that are usually selflimiting . In our personal experience we described only one case of transient severe gastroparesis, probably due to a misinbterpretation of manometric data of the patients. We emphasise that esophageal manometry has to be performed in ALL patiets who are candidates to Stretta and manometric data have to be evaluated by a physician fully experieced in this exam	Thank you for your comment. Section 5.3 reports 1 case of prolonged gastroparesis.
74	Consultee 1 Chief Medical Officer, Manufacturer, USA	**5**	All 32 studies have demonstrated that Stretta is a safe and well-tolerated treatment for GORD. The total number of patients (2,774) treated in these 32 studies and the exceedingly low complication rates noted in each, as well as the fact that any noted complications were minor and transient, mirrors the reported complication rate on the FDA MAUDE website (<1%). Both numbers are relevant as clinical studies are typically conducted by more experienced users, but FDA reported complications would include non-expert users. To date, more than 15,000 Stretta procedures have been performed globally without serious sequelae attributable to the device. The 3 deaths noted on the FDA MAUDE website clearly exonerate the device as the cause of patient expiration.	Thank you for your comment. The Committee considered this comment but decided not to change the guidance.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
75	Consultee 2 Private Sector Professional, USA	**5**	In my personal experience of having performed over 1500 Stretta procedures, I have seen only 2 complications of minor self-limited bleeding from the cardia due to premature stoppage of PPI therapy which required no transfusion or intervention. Â In the 10 year study data which we are reporting there are no additional complications either in the short or long term. Perforations reported in the first year of introduction were due to operator error from balloon over-inflation distention and non-compliance with protocol. Manufacturer introduction of angiographic pressure relief valves and standardization of technique and training methodology has eliminated all subsequent complications. Â The FDA MAUDE website reports complication rates of <1%, and the 3 deaths noted on the FDA MAUDE website clearly exonerate the device as the cause of patient expiration. Â To date, more than 15,000 Stretta procedures have been performed globally without serious sequelae attributable to the device.	Thank you for your comment. The Committee considered this comment but decided not to change the guidance.
76	Consultee 3 Private Sector Professional, USA	**5**	All studies with 2,774 patients have demonstrated that Stretta is a safe and well-tolerated treatment for GORD. Â Most of the reported complications were minor and transient and occurred early after the introduction of the procedure into the market. The FDA MAUDE website reports a rate of <1% and the 3 deaths noted on the FDA MAUDE website clearly exonerate the device as the cause of death	Thank you for your comment.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
77	Consultee 4 Scientist and clinical surgeon, Europe	**5**	Avaiable studies clearly demonstrated that Stretta is a safe and well-tolerated treatment for GORD.The significant number of patients treated Â (2,774 in 32) studies revealed very Â low complication rates noted . All Â observed Â complications were minor and transient,mostly self-limited Studies shoved that early reported serious complication Â were not related to the procedure itself.	Thank you for your comment. The Committee considered this comment but decided not to change the guidance.
78	Consultee 12 AUGIS Council - adviser on reflux therapy Specialist Adviser	**5**	Even 3 deaths is quite a lot for a relatively new procedure. Â The European operative mortality for anti reflux surgery (highly effective) Â is 0.08%. Â To be of equivalent safety the denominator of observational studies would need to be 5,000 procedures with 3 deaths.	Thank you for your comment. The Committee considered this comment but decided not to change the guidance.
79	Consultee 8 NHS Professional	**5**	It is worth highlighting that documented complication rate is less than 1% (recent metaanlysis 2012, Perry etal)	Thank you for your comment. The Committee considered this comment but decided not to change the guidance.
80	Consultee 12 AUGIS Council - adviser on reflux therapy Specialist Adviser	**6**	Agreed	Thank you for your comment.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
81	Consultee 12 AUGIS Council - adviser on reflux therapy Specialist Adviser	**2**	Because of the perceived incomplete symptom relief for GORD sufferers using medication (proton pump inhibitors) and because of concerns over dependance on life long medication there is a strong motivation to introduce alternatives to medication for GORD symptoms. As a result there are at least 3 other new technologies being marketted for GORD, none of which has been assessed in adequate controlled clinical trials. None have had comparison ot the established surgical procedures of laparoscopic anti reflux surgery. These devices include the LINX magnetic bead device (subject of NICE guidance already) the Endostim electrical stimulation of the lower oeosphageal sphincter and the Esophyx endoscopic plication device. Â NICE could use this opportunity to establish a standard of research with controlled trials prior to giving guidance to the general use of these devices.	Thank you for your comment.
82	Consultee 13 Professor of Gastroenterology, France	**Notes**	I am part of a clinical study with the device funded by the French Ministery of Health. We receive technical support from the manufacturer	Thank you for your comment.
83	Consultee 2 Private Sector Professional, USA	**Notes**	I have worked teaching the procedure around teh world and have received money for travel expenses from the manufacturer	Thank you for your comment.