National Institute for Health and Care Excellence

IP1180 – Implanting a baroreceptor stimulation device for resistant hypertension

Consultation Comments table

IPAC date: Thursday 12 March 2015

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
1	Consultee 1 Renal Association uk	**1.1**	This is an exciting device based therapy for treatment of true drug resistant hypertension which has the potential to benefit a significant number (5 to 10%) of individuals with hypertension in the UK. However, as yet there is not enough evidence to recommend its use outside research studies for the following reasons. The main RCT failed to attain primary endpoint of BP reduction from time 0 to 6 months. Moreover, this study used the first generation device (Rheos) which is a large device with leads attached to both carotid sinuses and requires invasive insertion technique. There is no RCT or large cohort study data demonstrating efficacy of the second generation device Barostim Neo which is a smaller device with unilateral lead and requires less invasive surgical procedure to insert.	Thank you for your comment.
2	Consultee 2 British Heart Foundation Charity	**1.1**	Overall the BHF agree with NICE's recommendation that more research in required into both the safety and efficacy of this treatment before this technology is used in routine treatment of resistant hypertension.	Thank you for your comment.

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3	Consultee 5 Royal College of Physicians	**1.1**	• Baroreceptor stimulation is a promising novel therapeutic avenue for treating hypertension, and trials published to date are encouraging. However, larger well-designed randomised sham-controlled trials are still required to prove its effectiveness, especially its long term effectiveness. • Its safety needs to be better defined, especially with long term follow up. • We need better data on unilateral vs bilateral stimulation; is the former as effective as the latter? (in which case, it is a simpler procedure and would be preferred.) • We need better definition of exactly what types of patients benefit most from this procedure. • In conclusion, it is premature to recommend it routinely in clinical practice. Potentially eligible patients should be entered into research trials to address the above questions.	Thank you for your comment.
4	Consultee 3 Professor of Therapeutics and Clinical Pharmacology	**1.1**	Draft guidance recently published on the NICE website states that “Current evidence on the safety and efficacy of implanting a BST device for resistant hypertension is inadequate. Therefore, this procedure should only be used in the context of research.” I find this a disappointing view. Clinically, I think that is that this position is unnecessarily restrictive and will deny patients with very limited therapeutic options an alternative that offers some possibility of controlling very high blood pressure, which has not responded to pharmacological therapy, and which poses a serious risk of morbidity and mortality. There are various points I would like to make.	Thank you for your comment. The Committee considered this comment but decided not to change the guidance.

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5	Consultee 3 Professor of Therapeutics and Clinical Pharmacology	**1.1**	I understand the Barostim neo system has now been implanted in more than 400 patients with excellent outcomes. I would hope, therefore, the risk/benefit profile of implanting Barostim neo has been demonstrated sufficient to justify its use in normal clinical practice for carefully selected patients.	Thank you for your comment. The Committee considered all the peer-reviewed published data that was identified. Procedures with a 'research only' recommendation may be reassessed when relevant new research is published.
6	Consultee 3 Professor of Therapeutics and Clinical Pharmacology	**1.1**	I urge IPAC to reconsider their draft recommendation, and consider a "special arrangements" recommendation. This will allow clinicians to meet the urgent needs of those patients who have no other therapeutic option. The evidence suggests that this therapy lowers blood pressure, has an acceptable safety profile, and maintains blood pressure reduction over a follow-up of several years. A "special arrangements" recommendation would be more consistent with previous guidance for therapies with arguably similar evidence levels, and will ensure that clinicians like me are able to offer patients, who otherwise have no therapeutic options, a therapy that could potentially avoid serious morbidity and even save lives.	Thank you for your comment. The Committee considered this comment but decided not to change the guidance.
7	Consultee 3 Professor of Therapeutics and Clinical Pharmacology	**1**	As with all relatively new procedures, there is clearly more to learn, and it is important to review the outcomes from this therapy in order to confirm that the results in everyday clinical practice are similar to those reported in clinical trials. It is my understanding that all treated patients should be enrolled in the 'European Barostim Registry, set up with the express purpose of capturing real world data. I believe this registry could be used under a "special arrangements" recommendation within the NHS, to capture the outcomes suggested in the IPAC consultation document – including survival, strokes, MI, and cardiovascular hospitalisation.	Thank you for your comment. The Committee considered this comment but decided not to change the guidance.

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8	Consultee 4 Manufacturer	**1**	Registry Although we strongly dispute that the available evidence merits a 'research only' recommendation for barostimulation therapy in resistant hypertension, we agree with the committee that more data are needed to establish more fully the optimal use of this therapy. For that reason, a European registry for barostimulation therapy - The European Barostim Registry - has been set up, to measure long-term safety and effectiveness in a real-world setting for patients with resistant hypertension. Centres treating patients are encouraged to submit data to the registry and enrolment is ongoing. To date data on more than 100 subjects have been submitted. The European Barostim Registry records key safety endpoints (adverse events related to the device and/or the procedure), key efficacy outcomes (including office and ambulatory blood pressure, death, stroke, myocardial infarction), and use of health service resources such as hospitalisation for cardiovascular events, attendance at A&E, ICU stays, and medication use. Results from the registry have not yet been published, but analyses show that the clinically relevant and statistically significant improvement shown in the clinical trials is maintained in a real-life setting. We encourage all surgeons using this procedure to submit data to the Registry, and expect these real world data to define more completely the most appropriate use of this therapy.	Thank you for your comment. The Committee considered this comment but decided not to change the guidance.

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9	Consultee 6 Specialist Adviser Clinical Hypertension Specialist European Society for Hypertension	**1.1**	I am surprised and disappointed to see that the draft recommendation for IP1180 is “Current evidence on the safety and efficacy of implanting a baroreceptor stimulation device for resistant hypertension is inadequate. Therefore, this procedure should only be used in the context of research.” Reading the three available documents (overview, consultation and the SAQ) it is clear that NICE has been misled by confused or factually incorrect answers from many of the specialist advisers. In my opinion the conclusion that there is inadequate evidence on safety and efficacy is fundamentally flawed for reasons that I shall expound below. I appreciate that the committee has to reach out to specialist advisers in order to make a more informed decision on procedures with which members of the committee are unfamiliar. However, it is frustrating that some of those specialist advisers have proffered opinions on a procedure with which they clearly have very little familiarity, since there are glaring factual errors that have confounded rather than illuminate the topic.	Thank you for your comment. The Committee considered this comment but decided not to change the guidance. Before a procedure is considered by the Committee, NICE seeks the opinion of at least two Specialist Advisers who are nominated by relevant Specialist Societies. The Committee consider all the published evidence on safety and efficacy of the procedure, alongside this advice from Specialist Advisers.

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10	Consultee 6 Specialist Adviser Clinical Hypertension Specialist European Society for Hypertension	**1**	The fact that the second generation device has been shown to have comparable efficacy to the now superseded first generation, with a four-fold improvement in terms of safety (Hoppe 2012), demonstrates that this device should be made available, in a controlled fashion, to our patients in the UK. As an aside, due to my standing within the hypertension community in Europe, I recently had a resistant hypertensive patient referred to me from Ireland whom I had to send back to Ireland with my clinical recommendation to be treated with Barostim, since I was unable to treat him here. In addition I have a list of 15 more patients referred to me from all over the UK who would be candidates for this procedure having failed all conventional approaches to hypertension management including (in several cases) renal denervation. As mentioned earlier many of these patients experience frequent inpatient admissions spells lasting weeks due to hypertensive crises and some have had strokes whilst waiting for device therapy of hypertension. Those that are not in this category are also attending clinic very frequently to try alternative antihypertensive drugs - one such patient attended my clinic 13 times in 2012 and spent 3 months in hospital in 2013!	Thank you for your comment. Hoppe 2012 is included in table 2 of the overview (study 4).

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11	Consultee 6 Specialist Adviser Clinical Hypertension Specialist European Society for Hypertension	**1**	Whilst the barriers to novel therapies are high in the UK for very good reasons, it is equally important that when there is sufficient evidence to make a novel therapy available to patients in the UK, we ensure this happens. Responsible uptake of novel therapy by hypertension specialists (who are device agnostic as they do not perform procedures) is the best way forward here. I hope that, by drawing your attention to the errors within the specialist advice, and by providing sensible corrections, I will have provided you with information which will help you to review the current draft guidance which I do not feel would serve these patients well. It is critical that this small, but clinically in need, patient population that is currently without therapeutic option, is not denied access to a therapy that has proven itself to have sufficient safety and efficacy to be used in a limited number of specialist centres with follow up in a registry. I urge the committee not to confine this procedure to a research setting.	Thank you for your comment. The Committee considered this comment but decided not to change the guidance. Section 6 has been changed to include a comment about the difficulties in treating patients with drug resistant hypertension.

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12	Consultee 7 Consultant Vascular Surgeon	**1.1**	It is my professional opinion that there is sufficient evidence on the safety and efficacy of Barostimulation therapy to afford its use in the NHS, and that special arrangements should be made for its controlled use to treat pharmacologically resistant hypertensive patients. It should not be confined to the context of research, since there already has been substantial research conducted with this therapy, proving long term efficacy, and a perfectly acceptable safety profile with the second generation Barostim neo device, that is similar to devices already in routine use in the NHS for other indications (such as pacemakers). It is therefore appropriate for NHS patients to be able to be treated with this therapy within a carefully controlled environment such as “special arrangements” would afford, under which arrangements continued data collection and experience within the service setting could be gathered, such as within a registry.	Thank you for your comment. The Committee considered this comment but decided not to change the guidance.
13	Consultee 4 Manufacturer	**1.1**	As set out in detail in the following comments, we submit that the committee does not appear to have considered the evidence for the barostimulation procedure in its context, has been materially inconsistent in its apparent expectations of the evidence to support this procedure, and has raised unwarranted methodological concerns about the key trial [Bisognano 2011]. Applying the committee’s approach to other, arguably comparable, procedures for which IP guidance has been published, we submit that for the reasons set out in this document, ‘research only’ guidance for this procedure is unwarranted, unnecessarily restrictive, and will deny a group of patients at serious risk of harm with no effective therapeutic options an apparently safe and efficacious therapy.	Thank you for your comment. The Committee considered this comment but decided not to change the guidance.

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14	Consultee 4 Manufacturer	**1.1**	While we appreciate that the number of studies and sample sizes is not the only metric the committee would use to judge the adequacy of the evidence base, however, we submit that the quality of the evidence for barostimulation therapy which is available to the committee is high and, we submit, supports 'special arrangements' guidance for barostimulation therapy.	Thank you for your comment. The Committee considered this comment but decided not to change the guidance.
15	Consultee 4 Manufacturer	**1.1**	Inconsistency in wording compared to comparable published IP guidance There are striking differences in the wording of the draft guidance on barostimulation compared to (without limitation) the final guidance on renal denervation (IPG418). For example, the committee's approach to the available evidence, summarized in §1.1 of that guidance states: "Current evidence on percutaneous transluminal radiofrequency sympathetic denervation of the renal artery for resistant hypertension is from limited numbers of patients, but there is evidence of efficacy in the short and medium term. There is inadequate evidence on efficacy in the long term; this is particularly important for a procedure aimed at treating resistant hypertension. The limited evidence suggests a low incidence of serious periprocedural complications, but there is inadequate evidence on long-term safety. Therefore this procedure should only be used with special arrangements for clinical governance, consent, and audit or research."	Thank you for your comment. The Committee considered this comment but decided not to change the guidance.
16	Consultee 7 Consultant Vascular Surgeon	**1.2**	1.2 No comments.	Thank you for your comment.

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17	Consultee 1 Renal Association uk	**1.2**	All the studies reported so far are either sponsored by the device company or the authors have significant conflicts of interest. There is need for an adequately powered RCT (ideally independent of industry) using a second generation device (like Barostim Neo) with primary endpoint of reduction in ambulatory BP and secondary endpoints including cardiovascular events and hospitalisation. The study should also include direct testing of antihypertensive drug adherence ,like urine assay, as non-adherence is the main cause of resistant hypertension. We need to be very cautious before introducing any new device based treatment for resistant hypertension as the Symplicity HTN3 study on renal denervation has taught us.	Thank you for your comment. Section 1.2 states that further research should document patient selection in detail and specify the devices and techniques used. It also states that outcomes should include the duration of effect of baroreceptor stimulation; device durability; and the complications of hypertension, such as myocardial infarction and stroke.

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18	Consultee 4 Manufacturer	**2**	§2 of the draft guidance does not clearly identify the intended target population for barostimulation therapy. The procedure is indicated for patients whose blood pressure cannot be controlled (SBP >140/90 mm Hg despite optimal or best tolerated doses of third-line treatment [NICE CG127. Hypertension: Clinical management of primary hypertension in adults. www.nice.org.uk/guidance/cg127]. Barostimulation therapy is not an alternative to but an additional treatment to, pharmaceutical therapy. Barostimulation is recommended as a treatment option for resistant hypertension patients in the European Guidelines for the management of arterial hypertension [2013 European Society for Hypertension (ESH)/European Society of Cardiology (ESC) Guidelines for the management of arterial hypertension. Journal of Hypertension 2013;31:1281–1357. doi:10.1093/eurheartj/eht151]. To date, over 800 patients have been treated in the USA and Europe with barostimulation therapy in research and service settings, both of which have shown a statistically significant and clinically relevant improvement in blood pressure for a resistant hypertension population (Bisognano 2011, Hoppe 2012, Wallbach 2015).	Thank you for your comment. The title of the guidance states that it is for resistant hypertension and this is defined in section 2.2 of the guidance.

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19	Consultee 4 Manufacturer	**2**	Placing guidance in clinical context There is no evidence in the draft guidance, or the overview, that the committee has considered its proposed guidance in the relevant clinical context. There is a very striking difference between the phrasing of §2.1.1 of IPG418, on percutaneous transluminal radiofrequency sympathetic denervation of the renal artery for resistant hypertension ("Hypertension is a major risk factor for cardiovascular disease and chronic renal disease. First-line treatment usually involves lifestyle changes. Antihypertensive medications (in combinations, as required) are used if hypertension persists. Sympathetic denervation of the renal artery is considered if hypertension fails to respond adequately to these measures") which explicitly recognizes the clinical context, and the phrasing of §§2.1 and 2.2 of the draft guidance on the barostimulation procedure, which would give those unfamiliar with the context no idea of the purpose or place of this therapy in clinical practice. In IPG418, the committee went even further: in §2.5.1, IPG418 says: "The Committee was mindful of the difficulties in treating patients with drug- resistant hypertension and the serious risks these patients face from uncontrolled high blood pressure. It considered sympathetic denervation of the renal artery to be a promising procedure, which might offer benefit to many patients, but a larger evidence base of well-designed trials is required." The inconsistency is striking.	Thank you for your comment. The title of the guidance states that it is for resistant hypertension and this is defined in section 2.2 of the guidance. Section 6 has been changed to include a comment about the difficulties in treating patients with drug resistant hypertension.
20	Consultee 7 Consultant Vascular Surgeon	**2**	2. Indications and current treatments No comments.	Thank you for your comment.

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21	Consultee 7 Consultant Vascular Surgeon	**3.1**	3.1 Two factual inaccuracies: - the electrode is located on 1 carotid sinus not both. - device programming allows the frequency and amplitude and pulse-width of stimulation to be adjusted.... (not just frequency and amplitude)	Thank you for your comment. Sections 3.1 of the guidance has been changed.
22	Consultee 4 Manufacturer	**3**	Correction to the description of the procedure §3.1 in the guidance states that “the device consist of an electrode placed on one or both carotid sinuses”. Since the Rheos device is obsolete this is no longer correct and should be corrected. The same applies to §3.2 which describes the Rheos device procedure.	Thank you for your comment. Sections 3.1 and 3.2 of the guidance have been changed.
23	Consultee 7 Consultant Vascular Surgeon	**3.2**	3.2 Factual inaccuracies: - the exact technique does not vary according to the type of device being used. There is only one device currently available and that is the second generation, single 2mm electrode, which is used unilaterally. “The following technique is used for a device...” that no longer exists. This procedure is no longer in use and cannot form part of an assessment on safety of the implantation of a baroreceptor stimulation device. - the electrode is not necessarily placed at the location of the highest density of baroreceptors. It is placed at the location on the carotid artery that affords the best hemodynamic response in the patient. As I understand it this is the extent of the mapping element of the procedure: to locate that position which affords the best hemodynamic response. Mapping does not necessarily locate baroreceptor density – it may do, but this is not the intention.	Thank you for your comment. Section 3.2 of the guidance has been changed.
24	Consultee 7 Consultant Vascular Surgeon	**3.3**	3.3 No comments	Thank you for your comment.

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25	Consultee 7 Consultant Vascular Surgeon	**3.4**	3.4 Same inaccuracy as above, pulse-width can also be adjusted.	Thank you for your comment. Section 3.4 of the guidance has been changed.
26	Consultee 4 Manufacturer	**4**	In respect of the evidence available on effectiveness, we submit that the guidance should be based on trials with both the Rheos and the Barostim neo devices. The development of Barostim neo device was prompted by the finding that although barostimulation therapy conferred a significant improvement in blood pressure between intervention group and sham group in the short term (SBP reduction of 9 mm Hg at 6 months, P < 0.03) and the long term (SBP reduction 35 mm Hg for the group with 12 months of therapy and 33 mm Hg for the group with 6 months of therapy) [Bisognano JD et al. Baroreflex activation therapy lowers blood pressure in patients with resistant hypertension: results from the double-blind, randomized, placebo-controlled rheos pivotal trial. Journal American College of Cardiology 2011;58(7):765-73], the device- and procedure safety profile of the Rheos device was unsatisfactory. In the barostimulation RCT, the electrode was implanted bilaterally but the majority of patients were programmed to receive unilateral stimulation, 215/295 (73%) patients who had been stimulated for six months were stimulated unilaterally while the remaining 80 (27%) patients were stimulated bilaterally.	Thank you for your comment. Bisognano JD et al., 2011, is in table 2 of the overview (study 1). The following paper was identified in the updated literature search and has been added to table 2 of the overview: de Leeuw PW, Alnima T, Lovett E et al., 2015. Bilateral or unilateral stimulation for baroreflex activation therapy. Hypertension 65: 187-192

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27	Consultee 4 Manufacturer	**4**	The mechanism of action of barostimulation therapy is the same whether stimulation is unilateral or bilateral. Baroreceptors play a vital role in regulating blood pressure providing a feedback from arterial blood pressure to the sympatho-vagal system resulting in a reduction in blood pressure [Heusser et al 2010]. The impact of both the Rheos and the neo devices on sympathetic activity has been assessed in studies measuring muscle sympathetic nerve activity. Heusser 2010 [Heusser K et al. Carotid baroreceptor stimulation, sympathetic activity, baroreflex function, and blood pressure in hypertensive patients. Hypertension. 55(3):619-25] measured acute changes in muscle sympathetic nerve activity (MSNA) in resistant hypertensive patients implanted with the Rheos system and showed that reductions in blood pressure associated with barostimulation therapy were accompanied by reductions in MSNA. When stimulation was stopped, blood pressure and MSNA returned to baseline. Gronda 2014 [Gronda E et al. Chronic baroreflex activation effects on sympathetic nerve traffic, baroreflex function, and cardiac haemodynamics in heart failure: a proof-of-concept study. European Journal of Heart Failure 2014;16:977-83] measured the chronic effects of barostimulation therapy on MSNA recordings in heart failure patients implanted with the neo system. After six months of stimulation, MSNA was reduced from 45.1 ± 7.7 to 31.3 ± 8.3 bursts/min and from 67.6 ± 12.7 to 45.1 ± 11.6 bursts/100 heartbeats.	Thank you for your comment. Heusser K, Tank J, Engeli S et al. (2010) is included in the appendix of the overview. Gronda E et al., 2014, is not included in the overview because it refers to a different indication (heart failure rather than resistant hypertension). The following paper was identified in the updated literature search and has been added to table 2 of the overview: de Leeuw PW, Alnima T, Lovett E et al., 2015. Bilateral or unilateral stimulation for baroreflex activation therapy. Hypertension 65: 187-192
28	Consultee 4 Manufacturer	**4**	These studies support that the mechanism of action of Rheos and neo are the same and effectiveness data from these two procedures can be aggregated for the purposes of developing IP guidance.	Thank you for your comment.

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29	Consultee 4 Manufacturer	**4**	Further analyses of the findings related to stimulation mode in the barostimulation RCT (Bisognano 2011) have recently been reported by de Leeuw et al. 2015 [de Leeuw P W et al. Bilateral or unilateral stimulation for baroreflex activation therapy. Hypertension 2015;65(1):187-92]. This study was not published when the literature review was presented to the committee, and should be included in an updated overview before guidance is finalised. The de Leeuw paper reports that SBP dropped from 178 ± 23 mm Hg to 145 ± 30 mm Hg ($P < 0.001$) in the unilaterally stimulated group vs a drop from 178 ± 23 mm Hg to 155 ± 31 mm Hg ($P < 0.001$) in the bilaterally stimulated group. There was a significant drop in heart rate in the unilaterally stimulated group from 73 ± 15 to 71 ± 14 bpm ($P < 0.02$) but no significant change in heart rate in the bilaterally stimulated group (76 ± 14 to 75 ± 13 bpm). A higher percentage of patients reached a goal systolic blood pressure of ≤ 140 mmHg with unilateral than bilateral stimulation (46% vs 41%, $P = 0.003$). These observations confirm that the improved safety profile of the neo procedure is not obtained at the expense of efficacy: unilateral stimulation works at least as well as bilateral stimulation.	Thank you for your comment. The cited paper was identified in the updated literature search and has been added to table 2 of the overview.

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30	Consultee 4 Manufacturer	**4**	Long-term efficacy As for long-term efficacy, a follow-up study of patients in the barostimulation RCT [Bakris GL et al. Baroreflex activation therapy provides durable benefit in patients with resistant hypertension: results of long-term follow-up in the Rheos Pivotal Trial. Journal of the American Society of Hypertension 2012;6(2):152-8] reported a mean blood pressure reduction of 35 mm Hg at an average follow up time of 28 months. Five-year data have recently become available, although they have not yet been submitted for publication. Data from 182 patients which have reached four years of follow-up have been reported at the 2014 Journal Society of Hypertension congress and confirm a sustained effect, with average reduction of systolic blood pressure -31.3 mm Hg at four years (Journal of the American Society of Hypertension 2014;8(4S):e9–e10).	Thank you for your comment. Bakris GL et al., 2012, is included in table 2 of the overview (study 2). Conference abstracts are not normally considered adequate to support decisions on efficacy and are not generally selected for presentation in the overview, unless they contain important safety data.
31	Consultee 7 Consultant Vascular Surgeon	**4**	4 Efficacy No comments	Thank you for your comment.
32	Consultee 4 Manufacturer	**5.1**	The relevant evidence base for Barostim neo We submit that guidance on implanting a baroreceptor stimulation device for resistant hypertension should be based on the safety profile of the Barostim neo procedure since this is the only barostimulation procedure available today. This is particularly relevant to nerve injury, to which §5.1 of the draft guidance referred.	Thank you for your comment. The Committee considered this comment but decided not to change the guidance.
33	Consultee 7 Consultant Vascular Surgeon	**5**	Sections 5.1, 5.2, 5.3, 5.4 all refer to a procedure associated with implanting a baroreceptor stimulation device that no longer exists, and as such have no relevance.	Thank you for your comment. The Committee considered this comment but decided not to change the guidance.

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34	Consultee 7 Consultant Vascular Surgeon	**5**	5.5 Two of the three reported complications are with the obsolete device. 5.6 and 5.7 are with the obsolete device. 5.8 No comment.	Thank you for your comment. The Committee considered this comment but decided not to change the guidance.
35	Consultee 4 Manufacturer	**5**	Long-term safety In terms of therapy safety, long-term follow-up of patients in the barostimulation RCT [Bakris GL et al. Baroreflex activation therapy provides durable benefit in patients with resistant hypertension: results of long-term follow-up in the Rheos Pivotal Trial. Journal of the American Society of Hypertension 2012;6(2):152-8] reported 13 deaths during the 9,200 months of cumulative follow-up, none of which were related to the therapy. The barostimulation RCT reported that hypertensive crises were reduced by 40% with barostimulation [Bisognano 2011]. The long-term data from the follow up sub-study which was presented at the 2014 Journal of Hypertension Congress confirm these findings, with a rate of system- and/or procedure-related complications following one year of therapy of 0.037 per patient-year and a therapy-related safety profile showing a rate of stroke and myocardial infarction at 0.014 and 0.0050 per patient-year, respectively (Journal of the American Society of Hypertension 2014;8(4S):e9–e10).	Thank you for your comment. Bakris GL et al., 2012, is included in table 2 of the overview (study 2). Bisognano 2011 is included in table 2 of the overview (study 1). Conference abstracts are not normally considered adequate to support decisions on efficacy and are not generally selected for presentation in the overview, unless they contain important safety data.

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36	Consultee 4 Manufacturer	**5**	Device- and procedure safety of Barostim neo As for device- and procedural safety of the neo device, the Hoppe 2012 paper, included in the overview, showed that the procedure using the neo device had a 90% adverse event-free rate at 30 days post-procedure. The three complications which occurred in this 30-day period consisting of a self-inflicted wound complication, a pulse generator pocket haematoma, and discomfort in the pulse generator pocket that motivated a patient to request device repositioning. This device- and procedure safety profile is comparable to that of a pacemaker [Udo EO et al. Incidence and predictors of short- and long term complications in pacemaker therapy: the FOLLOWPACE study. Heart Rhythm 2012;9(5):728-35]. In respect of longer-term safety, 29/30 (97%) patients remained event-free over 180 months of cumulative follow-up. The one instance of a system-related complication after the perioperative period consisted of a report of intermittent pain near the pulse generator.	Thank you for your comment. The data that relate to implantation of a baroreceptor stimulation device for resistant hypertension are included in the overview.
37	Consultee 4 Manufacturer	**5**	The committee should also consider safety data on the neo device reported in a recent RCT of barostimulation in heart failure [Abraham A et al. Baroreflex Activation Therapy for the treatment of heart failure with a reduced ejection fraction. Accepted by the Journal of American College of Cardiology 2015. At the time of writing, we do not have a copy of the manuscript, but we are expecting this shortly and will be happy to provide it as soon as we receive it]. The objective of this clinical trial was to assess the safety and efficacy of barostimulation therapy with the neo device in an advanced (NYHA class III) heart failure patient population (n = 140). Although this is a different indication, the procedure is identical to that being considered by the committee, and safety data from this trial is therefore relevant.	Thank you for your comment. The cited paper refers to a different indication (heart failure rather than resistant hypertension). The NICE interventional procedures programme does not usually consider evidence for a different indication to the one being assessed.

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38	Consultee 4 Manufacturer	**5**	The primary safety objective in the Abraham trial was to determine the event-free rate of all system- and procedure-related major adverse neurological and cardiovascular events (MANCE) over six months. MANCE included cardiovascular-related death, stroke, cardiac arrest, acute myocardial infarction, acute decompensated heart failure, hypertensive crisis, severe complications of heart failure treatment, systemic and pulmonary thromboembolism, infection requiring explant of any portion of the neo system, cranial nerve damage that was permanent (not resolved within 12 months of onset) or required invasive intervention to correct, and events requiring non-elective major restorative procedures. Device and procedure safety were also assessed. The overall MANCE-free rate was found to be 97.2%. Only two system- or procedure-related MANCE events (both haematomas) occurred during the course of the study, consisting of two hematomas adjudicated as related to the procedure. The system- and procedure-related complication event-free rate was 85.9%. All but one event occurred within seven days of implant and resolved without residual side effects. Eight patients in the intervention group in this trial had hypertension (SBP > 140 mm Hg). No device- or procedure-related adverse events were reported in these subjects.	Thank you for your comment. The cited paper refers to a different indication (heart failure rather than resistant hypertension). The NICE interventional procedures programme does not usually consider evidence for a different indication to the one being assessed.

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39	Consultee 7 Consultant Vascular Surgeon	**5.9**	5.9 - Excessive lowering of blood pressure is completely avoidable due to the ability to program the device. If excessive lowering of blood pressure were to occur, this would be due to user error and would not be a potential safety concern of the device. It is expected that clinicians would properly utilise any medical device in use in the NHS in accordance with the instructions for use for that device. - Orthostatic hypotension is incredibly unlikely, and has never been seen to the best of my knowledge. The mechanism of action of the baroreceptor stimulation device is not to control blood pressure per se, but rather to regulate the autonomic nervous system by down-regulating sympathetic tone and up-regulating parasympathetic tone. This means that the baroreflex remains intact and remains capable of reacting to external stimuli.	Thank you for your comment. Section 5.9 lists theoretical adverse events that were described by Specialist Advisers.
40	Consultee 4 Manufacturer	**6**	Methodological issue in Bisognano 2011 §6.1 of the draft guidance on barostimulation notes that in the Bisognano 2011 RCT, a fall in blood pressure was observed after screening and before stimulation started. We submit that the committee's apparent concern, which was expressed also at the discussion at IPAC's meeting on 11 December 2014, is misplaced. Blood pressure is highly variable and this observation appears to be regression to the mean. Regardless of the fall in blood pressure prior to stimulation, the results of the Bisognano RCT show a mean fall in SBP of 9 mm Hg at six months in the intervention group vs the sham group, which is both statistically ($P < 0.03$) and clinically significant.	Thank you for your comment. Section 6.1 of the guidance has been changed.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
41	Consultee 7 Consultant Vascular Surgeon	**6**	6.1 - Reductions in blood pressure before stimulation began could be attributed to any of the following: mechanical response due to the original lead design (now obsolete), placebo/Hawthorne effect, regression to the mean. - most of the available evidence was related to bi-lateral stimulation. This is not the case. My understanding is that many of the patients in the barostimulation RCT are only receiving therapy unilaterally, although implanted bi-laterally.	Thank you for your comment. Section 6.1 of the guidance has been changed to clarify that most patients had bilateral implantation.
42	Consultee 4 Manufacturer	**General**	As a result of combining these two distinct procedures in a single piece of guidance, we submit that the draft guidance is fundamentally flawed. We understand that the committee is currently developing two separate pieces of guidance on retinal implants (#915 Insertion of an epiretinal prosthesis system for retinitis pigmentosa and #1252 Insertion of a sub-retinal implant for retinitis pigmentosa) after considering what may be a similar situation. As #1252 is guidance in development at an early stage of the process, no documents have yet been published in relation to the sub-retinal implant, and we have not been party to the committee's discussion to comment further on this, but on the basis of the information we have, this seems relevant to the committee's approach to developing guidance on barostimulation. The Rheos device is no longer available, and guidance on a procedure using this device is therefore unnecessary and confusing. The implant procedure involving the Rheos device was significantly more invasive than that using Barostim neo, as described in the studies that the committee has reviewed. The evidence is that the relevant procedure (implanting Barostim neo) has a different (and more favourable) safety/efficacy profile than the other procedure (implanting Rheos).	Thank you for your comment. The IP programme issues guidance on procedures rather than individual devices.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
43	Consultee 2 British Heart Foundation Charity	**General**	Hypertension is a significant risk factor for cardiovascular disease, which can increase the risk of a heart attack or a stroke and can result in heart failure. It is estimated that over a quarter of adults in the UK have hypertension and as many as half of them are not receiving treatment for the condition. The area of this consultation is therefore of significant interest to the BHF. We therefore welcome the opportunity to respond to NICE's consultation on implanting a baraceptor stimulation device to treat resistant hypertension.	Thank you for your comment.
44	Consultee 3 Professor of Therapeutics and Clinical Pharmacology	**General**	Re.: Proposed IPAC response on baroreceptor stimulation therapy (BST) with Barostim Neo Last year I provided a report for IPAC about a new procedure for the implantation of a BST device in patients with drug-resistant hypertension, a condition I see fairly frequently in our tertiary referral centre, as the Head of a European Society of Hypertension (ESH) Hypertension Excellence Centre based in Edinburgh. This condition puts patients at very high risk of cardiovascular events, can be hard to manage for those intolerant of treatment, and, in some patients, further medical treatments are not an option. Since renal denervation therapy failed to show benefit, in properly randomized and blinded studies rightly mandated by FDA, there has been no alternative except for BST, which has shown efficacy in reliable studies (where the timing of activation of the device can be regulated so that patients are fully blinded to treatment).	Thank you for your comment.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
45	Consultee 3 Professor of Therapeutics and Clinical Pharmacology	**General**	1. The procedure: In the draft guidance the committee has considered two different procedures: implantation of the Rheos system and the Barostim neo. I commented on the procedure for implanting the Barostim neo, not for implanting (the now obsolete) Rheos. Although the Barostim neo is a second generation device for stimulating the baroreceptors in patients with resistant hypertension, considering the procedure for implanting the obsolete Rheos device would be like considering the safety profile of the first generation cardiac pacemakers when assessing the safety and efficacy of newer and safer pacemakers which rendered those original devices obsolete – this makes no sense. I believe there is good evidence in the literature demonstrating that the efficacy of Barostim neo is comparable to that of the Rheos device in reducing blood pressure in patients with resistant hypertension. The development of the Barostim neo is a product development which delivers the same therapy but with an improved safety profile (as was the case with cardiac pacemakers). For these reasons, the committee's review of the efficacy of the barostimulation procedure should encompass the clinical results from the Barostimulation RCT that utilised the first generation device, but the review of safety should be based the risk profile of the only device now available, the Barostim neo.	Thank you for your comment All the evidence on the procedure 'Implanting a baroreceptor stimulation device for resistant hypertension' was presented to the Committee, regardless of which device was used. Most of the evidence, including the RCT, related to the first generation device.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
46	Consultee 3 Professor of Therapeutics and Clinical Pharmacology	**General**	2. European guidelines The British Hypertension Society (of which I am a Fellow) is affiliated with the European Society of Hypertension (ESH) and has participated fully in the development of ESH guidelines (J Hypertens 2013;31:1281–1357), which take the view that baroreceptor stimulation may be considered in cases of ineffective treatment with drugs. BST is indicated for patients with very high blood pressure, which has not been controlled despite optimal medical treatment, in whom a full workup has confirmed true drug resistant hypertension. For the patient population identified above, which we have identified in the British Heart Foundation funded PATHWAY trials, there are no other therapeutic options, and lowering their blood pressure by 10-15 mm Hg over a four year period would reduce their risk of coronary heart disease by ~20%, reduce their risk of stroke by ~40%, associated with a 25% reduction in cardiovascular mortality, and a 13% reduction in all-cause mortality (Am Heart J 1999;138:211-9). This, though, is a conservative estimate, because the evidence would suggest that BST achieves a far greater average reduction of blood pressure of ~30mmHg.	Thank you for your comment.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
47	Consultee 4 Manufacturer	**General**	Clinical context: unmet need Most hypertension can be controlled using pharmacotherapy but a small minority are resistant to pharmaceutical therapy. These patients are at high risk of morbidity and mortality from cerebrovascular, cardiovascular, cardiac, and renal events (particularly stroke, myocardial infarction, heart failure, and renal failure) while their blood pressure remains substantially elevated despite optimal medical therapy. These patients have no effective therapeutic options, with the possible exception of renal artery denervation (the efficacy of which is currently being investigated following negative results from a recent RCT). If the draft guidance is confirmed, these patients will continue to be at high risk of serious mortality and morbidity. The risk rises with increasing blood pressure. An evidence review of RCTs found that an average reduction of 12 to 13 mm Hg in systolic blood pressure (SBP) over four years of follow-up was associated with a 21% reduction in coronary heart disease, 37% reduction in stroke, 25% reduction in total cardiovascular mortality and 13% reduction in all-cause mortality rates [He J, Whelton PK. Elevated systolic blood pressure and risk of cardiovascular and renal disease: overview of evidence from observational epidemiologic studies and randomized controlled trials. American Heart Journal 1999;138:211-9]. Barostimulation is intended for patients with severe (Grade 2) blood pressure.	Thank you for your comment.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
48	Consultee 4 Manufacturer	**General**	The inclusion criteria in the 265 patient barostimulation randomized sham-controlled trial was a systolic blood pressure (SBP) of at least 160 mm Hg: patients in the trial had an average baseline SBP of 169 mm Hg [Bisognano JD et al. Baroreflex activation therapy lowers blood pressure in patients with resistant hypertension: results from the double-blind, randomized, placebo-controlled rheos pivotal trial. Journal American College of Cardiology 2011;58(7):765-73]. The average blood pressure in the Hoppe trial of barostimulation therapy was an SBP of 172 mm Hg [Hoppe UC et al. Minimally invasive system for baroreflex activation therapy chronically lowers blood pressure with pacemaker-like safety profile: results from the Barostim neo trial. Journal of the American Society of Hypertension 2012;6(4):270-6]. Patients at these blood pressure levels have a particularly high risk of debilitating cardiovascular morbidity such as stroke, myocardial infarction, renal disease and heart failure as well as cardiovascular mortality: for example, a patient with SBP of 160 mm Hg is at 35% higher risk of stroke and 29% higher risk of myocardial infarction than a patient with SBP of 140 mm Hg [Rapsomaniki E et al. Blood pressure and incidence of twelve cardiovascular diseases: lifetime risks, healthy life-years lost, and age-specific associations in 1·25 million people. Lancet 2014;383:1899-911].	Thank you for your comment. Bisognano JD et al., 2011, is in table 2 of the overview (study 1) Hoppe UC et al., 2012, is in table 2 of the overview (study 4)

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
49	Consultee 4 Manufacturer	**General**	These patients also have a risk of hypertensive crises: episodes with large elevations in SBP or DBP (180 mm Hg or 120 mm Hg, respectively) which are associated with organ damage, such as major neurological changes, hypertensive encephalopathy, cerebral infarction, intracranial haemorrhage, acute LV failure, acute pulmonary oedema, aortic dissection, renal failure, or eclampsia. Hypertensive crises may be life-threatening, and demand urgent admission for assessment and treatment to lower blood pressure within hours, in order to minimise further end-organ damage, and reduce the risk of life-threatening events such as myocardial infarction, encephalopathy and intracerebral or subarachnoid haemorrhage.	Thank you for your comment.
50	Consultee 4 Manufacturer	**General**	Apparent inconsistency in IP reviews for comparable therapies Although this guidance is not a comparison of this procedure against other therapies for hypertension, the committee should demonstrate how its expectations, regarding evidence on the safety and efficacy of the procedure, have taken account of the risk of mortality and morbidity resulting to patients who might otherwise be offered this therapy and have a significant unmet clinical need with a very poor prognosis.. The guidance itself and/or the associated documentation should include enough information on this to allow readers to understand the committee's thinking.	Thank you for your comment. Section 6 of the guidance has been changed.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
51	Consultee 4 Manufacturer	**General**	This is particularly important given some previous IP guidance in which it appears that the committee's expectations of the evidence base seem to have been rather different in relation to the guidance. A very brief, limited, search for some procedures that had certain characteristics in common with barostimulation, identified several anomalies. For example, without limitation: (a) IPG418. Percutaneous transluminal radiofrequency sympathetic denervation of the renal artery for resistant hypertension. January 2012. Evidence quoted in the guidance document was based on one RCT (not-blinded) (n = 100) and one case series (n = 153). The committee's guidance for that procedure was 'special arrangements'; (b) IPG477. Transcranial magnetic stimulation for treating and preventing migraine. January 2014. Evidence quoted in the guidance document was based on one RCT (n = 164) and two case series (n = 51, n = 27). The committee's guidance for that procedure was 'special arrangements'; (c) IPG452. Occipital nerve stimulation for intractable chronic migraine. April 2013. Evidence quoted in the guidance document was based on two RCTs (n = 157, n = 67) and one case series (n = 25). The committee's guidance for that procedure was 'special arrangements'; (d) IPG307. Intramuscular diaphragm stimulation for ventilator-dependent chronic respiratory failure due to neurological disease. July 2009. Evidence quoted in the guidance document was based on three case series (n = 50, n = 26, n = 6).	Thank you for your comment. The requirements of evidence for guidance development vary according to clinical context and practical issues posed by research questions that need to be addressed. The Committee's comments on the available evidence are at section 6.1. As well as the quantity of evidence, in making a decision on each procedure, the Committee takes account of factors including the risks and benefits of the procedure, the nature of the indication and its effect on patients and the availability of other treatments.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
52	Consultee 4 Manufacturer	**General**	We note also that the committee has previously issued 'special arrangements' guidance while explicitly stating that the evidence is less than the committee would have wanted. For example, the committee states in IPG418 "there is evidence of efficacy in the short and medium term. There is inadequate evidence on efficacy in the long term; this is particularly important for a procedure aimed at treating resistant hypertension. The limited evidence suggests a low incidence of serious periprocedural complications, but there is inadequate evidence on long-term safety". In IPG307, the committee states: "The evidence on … raises no major safety concerns; however, current evidence on its efficacy is inadequate in quantity". We suggest that the committee appears to have different expectations of the evidence base for barostimulation therapy than of some other therapies that are not wholly dissimilar, in clinical situations no less pressing than in these examples. The reasons for this are not at present evident.	Thank you for your comment. The Committee consider all the published evidence on safety and efficacy of the procedure, alongside advice from Specialist Advisers. The Committee's comments on the available evidence are at section 6.1. As well as the quantity of evidence, in making a decision on each procedure, the Committee takes account of factors including the risks and benefits of the procedure, the nature of the indication and its effect on patients and the availability of other treatments.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
53	Consultee 4 Manufacturer	**General**	The draft guidance covers two distinct procedures The Interventional Procedures Process Guide states that NICE produces guidance about whether interventional procedures used for diagnosis or treatment work well enough and are safe enough for use in the NHS. In the case of barostimulation therapy, IPAC has drafted guidance which relates to two different procedures as if they are a single procedure. Key differences in the procedure for the Rheos device and the Barostim neo device are substantial, as noted in §3.2, §3.3, and §6.1 of the draft guidance.	Thank you for your comment. The NICE Interventional Procedures Programme assesses procedures rather than devices. The Interventional Procedures Methods Guide (section 5.3) states: *The technology of devices may advance rapidly. This means that both efficacy and safety outcomes reported in the published literature may not accord with 'current practice' using technologically more advanced devices; further technological progress may alter outcomes still further.The Committee is mindful of these issues; it makes recommendations based on the available evidence, bearing in mind that it is evaluating the procedure rather than a specific device.* More information is available at: https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-interventional-procedures/The-interventional-procedures-programme-methods-guide.pdf

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
54	Consultee 6 Specialist Adviser Clinical Hypertension Specialist European Society for Hypertension	**General**	The inaccuracy and marginal relevance of many of the SA comments should lead the committee to worry about placing reliance on these comments. When the specialist adviser responses are so compromised, it is not surprising that the overview and draft guidance are confounded. The most obvious error has been to confuse a procedure that no longer exists (implanting the Rheos device which is no longer available) with the current procedure to implant the Barostim neo. As noted in my own questionnaire, “Targeting the baroreflex with device therapy is clearly novel but there is a literature to support the use of this treatment and increasing evidence of safety given that the device is now in its second generation iteration which is unilateral, easier to insert and can be done under conscious sedation.”	Thank you for your comment. Before a procedure is considered by the Committee, NICE seeks the opinion of at least two Specialist Advisers who are nominated by relevant Specialist Societies. This advice is considered alongside published evidence,

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
55	Consultee 6 Specialist Adviser Clinical Hypertension Specialist European Society for Hypertension	**SAQ**	Factual errors amongst the questionnaires include: *'Still "experimental" and devices changing'* o No longer experimental – CE mark granted for Barostim neo in 2011 after 10 years of research, and multiple publications. o 4 years on from the CE mark, more than 400 patients treated in European Society of Hypertension Centres of Excellence. o There is only one baroreceptor stimulation device available today and it remains unchanged since the CE mark. *'Few published studies to date of any size so difficult to assess'* o 1 RCT, 1 cohort study, 4 case series + various smaller studies *'Manufacturers updating devices'* o There is only one manufacturer with a stable device in excess of 4 years. I am not aware of any plans to update the Barostim neo	Thank you for your comment. The Specialist Adviser Questionnaires (SAQs) contain the opinions of Specialist Advisers and are not part of NICE recommendations. These opinions are considered by the Committee alongside published evidence on efficacy and safety.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
56	Consultee 6 Specialist Adviser Clinical Hypertension Specialist European Society for Hypertension	**SAQ**	*'Little performed in UK presently to my knowledge but potentially a reasonable patient base if successful'* o Although available in all EU since CE mark in 2011, and part of the European Society for Hypertension (ESH)/European Society of Cardiology (ESC) guidelines for the management of arterial hypertension (Journal of Hypertension 2013;31:1281–1357.doi:10.1093/eurheartj/eht151), to the best of my knowledge no UK patients have been treated to date *'Disorders of rhythm- bradycardia due to vagal stimulation and bradypnoea (reduced breathing rate) due to vagal stimulation'* o There is no evidence to suggest that vagal stimulation is a potential complication when implanting the baroreceptor stimulation device that is currently available. *'The reporting of adverse events has been very limited and it is often not really mentioned'* o This is a very biased statement. The limited reporting of adverse events with this procedure may reflect that there were only a limited number to report. Event-free rate of 90% at 1 month (Hoppe 2012), and 97% at 180 month cumulative follow up.	Thank you for your comment. The Specialist Adviser Questionnaires (SAQs) contain the opinions of Specialist Advisers and are not part of NICE recommendations. These opinions are considered by the Committee alongside published evidence on efficacy and safety.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
57	Consultee 6 Specialist Adviser Clinical Hypertension Specialist European Society for Hypertension	**SAQ**	*'Will it work long term'* *o* Depends what is meant by long term, but there are now published results to four years showing that it still works, and data being presented out to 6 years, and case reports of the therapy still working 11 years post-procedure. I think it is important to recognise that reduction in left ventricular hypertrophy has been demonstrated at 12 months which supports the longer term efficacy of the device (Bisognano 2011) *'Is it safe long term'* *o* As above, with no procedure or device related adverse events long term. After the perioperative period, there has been one report of intermittent pain near the pulse generator which subsequently resolved. *'It is expensive but could be important for a very small number of refractory hypertensive patients'* *o* Expense is outside IPAC's remit. o I think it is also worth pointing out that a 40% reduction in hospital admissions for hypertensive crises was demonstrated (Bisognano 2011). These are exceedingly costly to the NHS as patients are admitted to ICU/HDU settings for parenteral antihypertensives and often spend weeks in hospital. Several of my patients waiting for baroreflex activation have spent cumulatively more than 6 months in hospital in the past 3 years with uncontrollable blood pressure as well as having cardiovascular events such as strokes. I think the cost of this to the NHS is far greater than a baroreceptor implantation which could actually end up as a cost saving to the NHS.	Thank you for your comment. The Specialist Adviser Questionnaires (SAQs) contain the opinions of Specialist Advisers and are not part of NICE recommendations. These opinions are considered by the Committee alongside published evidence on efficacy and safety.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
58	Consultee 6 Specialist Adviser Clinical Hypertension Specialist European Society for Hypertension	**SAQ**	*'This type of procedure will need to be carried out as a combined procedure between a vascular surgeon and a cardiologist in order to ensure patient safety during the dissection and exposure of the carotid bifurcation. This could cause conflict as it is likely that specialists in other healthcare systems (e.g. US) would be carrying out the entire procedure independently. Because of this, consultants in the UK may think that they should be carrying out the entire procedure independently but this would not be safe in my opinion.'* *o* This is a very surprising and wholly unjustifiable comment. Hypertension specialists around Europe are routinely treating their patients with this therapy: the procedure is carried out by a single surgeon, who is usually a vascular surgeon. Some clinicians performing the procedure are heart surgeons or neurosurgeons, but the most common is a vascular surgeon. My plan in [redacted] is for the vascular surgeon to undertake the procedure which can now be done under conscious sedation – I do not see the need for the cardiologist to be involved at all.	Thank you for your comment. The Specialist Adviser Questionnaires (SAQs) contain the opinions of Specialist Advisers and are not part of NICE recommendations. These opinions are considered by the Committee alongside published evidence on efficacy and safety.

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59	Consultee 6 Specialist Adviser Clinical Hypertension Specialist European Society for Hypertension	**SAQ**	*'Totally untested and given the recent rapid uptake of renal denervation before efficacy was proven this procedure should be tested prior to widespread adoption, including long-term efficacy.'* o As will be apparent to the committee, "Totally untested" is either ill-informed or unreasonably biased. – 1 blinded RCT, 1 cohort study, 4 case series + other publications. Approx 1000 patients treated with barostimulation, half of which with the current available system. o The reference to an unrelated therapy is prejudicial and unhelpful to the committee when assessing barostimulation. o Efficacy is already demonstrated up to six years. o The intention is for a controlled use within a registry setting amongst Hypertension Centres of Excellence, under "special arrangements".	Thank you for your comment. The Specialist Adviser Questionnaires (SAQs) contain the opinions of Specialist Advisers and are not part of NICE recommendations. These opinions are considered by the Committee alongside published evidence on efficacy and safety.
60	Consultee 6 Specialist Adviser Clinical Hypertension Specialist European Society for Hypertension	**SAQ**	*'The requirement to cannulate vessels for baroreceptor mapping means that radiological imaging would be required and this then necessitates the use of either a mobile C-arm in theatre or hybrid theatre.'* o This response indicates a total misunderstanding of the procedure, and is extremely unhelpful. Baroreceptor mapping does not require cannulation of the vessels and radiological imaging is not required. Mapping is performed via electrical stimulation, and remains extra-vascular. It is frustrating that certain specialist advisors are clearly guessing what the procedure involves, rather than performing the appropriate research to discover what it does entail.	Thank you for your comment. The Specialist Adviser Questionnaires (SAQs) contain the opinions of Specialist Advisers and are not part of NICE recommendations. These opinions are considered by the Committee alongside published evidence on efficacy and safety.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
61	Consultee 6 Specialist Adviser Clinical Hypertension Specialist European Society for Hypertension	**SAQ**	*'Uncertain long term efficacy and safety. Short device battery life'* o Same comments as above. Safety and efficacy now published to 5 years (Bakris et al. ASH 2014 presentation "Baroreflex Activation Therapy safely reduces blood pressure for at least five years in a large resistant hypertension cohort" with abstract in JASH 8(4S) (2014) e9-e10) with 6 years expected to be presented/published later this year. o Battery life is now shown to be an average of 4.9 years, and my understanding is that this should increase to 6 years with an algorithm improvement. *'As with all new devices the initial studies have large effect sizes'* o This portmanteau statement is unsupported by references, is wrong, and does not appear to be relevant.	Thank you for your comment. The Specialist Adviser Questionnaires (SAQs) contain the opinions of Specialist Advisers and are not part of NICE recommendations. These opinions are considered by the Committee alongside published evidence on efficacy and safety.
62	Consultee 6 Specialist Adviser Clinical Hypertension Specialist European Society for Hypertension	**SAQ**	*'It is not a common procedure - I know of only one centre in the UK that are doing it'* *o* This comment is ill-informed. There are no centres in the UK performing this procedure, due to the requirement to have an IPAC review. This procedure has been performed in over 1000 patients to date.	Thank you for your comment. The Specialist Adviser Questionnaires (SAQs) contain the opinions of Specialist Advisers and are not part of NICE recommendations. These opinions are considered by the Committee alongside published evidence on efficacy and safety.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
63	Consultee 6 Specialist Adviser Clinical Hypertension Specialist European Society for Hypertension	**SAQ**	*'There are two devices and it is unclear which one will work best. It is also still a very new and novel procedure so more evidence is needed about its long term safety and efficacy.'* o This comment is ill-informed and incorrect. There is only one device. More evidence is desirable, but given the evidence already available this should be collected in a real-world setting such as a registry rather than being confined to formal research studies	Thank you for your comment. The Specialist Adviser Questionnaires (SAQs) contain the opinions of Specialist Advisers and are not part of NICE recommendations. These opinions are considered by the Committee alongside published evidence on efficacy and safety.
64	Consultee 6 Specialist Adviser Clinical Hypertension Specialist European Society for Hypertension	**SAQ**	*'It might be helpful to get information from those actually doing it e.g.* [redacted] *in* [redacted]*.'* *o* This comment is ill-informed. [redacted] is a neuroscientist and a collaborator of mine and has certainly not performed the procedure.	Thank you for your comment. The Specialist Adviser Questionnaires (SAQs) contain the opinions of Specialist Advisers and are not part of NICE recommendations. These opinions are considered by the Committee alongside published evidence on efficacy and safety.
65	Consultee 3 Christison Professor of Therapeutics and Clinical Pharmacology	**Note**	Finally, I should say I have no financial relationship with the company that manufactures the device, or other relevant conflict of interest.	Thank you for your comment.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
66	Consultee 7 Consultant Vascular Surgeon	**Note**	I feel compelled to comment on the recently published IPAC recommendations for IP1180, Implanting a baroreceptor stimulation device for resistant hypertension. I am an experienced vascular surgeon based in [redacted] and have been co-ordinating with [redacted] with a view to starting to treat our pharmacologically resistant hypertension patients with the Barostim neo. I notice that "the advisory committee particularly welcomes comments on the provisional recommendations and the identification of factual inaccuracies, as well as the provision of additional relevant evidence, with bibliographic references where possible."	Thank you for your comment.

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
67	Consultee 7 Consultant Vascular Surgeon	**General**	It has clearly caused confusion, both amongst the committee and the advisors whose opinions were sought by the committee, that there used to be a different procedure to implant a now obsolete baroreceptor stimulation device. As outlined above, the safety concerns around this procedure (that no longer exists) are irrelevant when considering the risk/benefit profile of the current, and only available, CE marked baroreceptor stimulation device. Furthermore, in terms of implanting this device, the procedure is arguably safer than a carotid endarterectomy, which is routinely performed in the NHS, since the implant remains extra-vascular. I would urge the committee to reconsider their recommendation in light of the inaccuracies highlighted above, and to consider allowing patients, who would otherwise have no therapeutic option, to be treated with this baroreceptor stimulation device under "special arrangements".	Thank you for your comment. The Committee considered this comment but decided not to change the guidance. The Interventional Procedures Methods Guide (section 5.3) states: *The technology of devices may advance rapidly. This means that both efficacy and safety outcomes reported in the published literature may not accord with 'current practice' using technologically more advanced devices; further technological progress may alter outcomes still further.The Committee is mindful of these issues; it makes recommendations based on the available evidence, bearing in mind that it is evaluating the procedure rather than a specific device.* More information is available at: https://www.nice.org.uk/Media/Default/About/what-we-do/NICE-guidance/NICE-interventional-procedures/The-interventional-procedures-programme-methods-guide.pdf