National Institute for Health and Clinical Excellence

923 – Percutaneous transluminal radiofrequency sympathetic denervation of the renal artery for resistant hypertension

Consultation Comments table

IPAC date: Thursday 8 September 2011

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
1	Consultee 1 Chairman NICE Hypertension Guideline NHS Professional	**1**	It is very important that patients are selected appropriately and that the proceedure is done in centres with critical mass to develop expertise. in my view it is essential that an experienced hypertension specialist/centre is involved in decision making to esnure appropriate deployment of the technique.	Thank you for your comment. Section 1.3 of the guidance will be changed.
2	Consultee 2 British Society of Interventional Radiology	**1**	The British Society of Interventional Radiology welcome and support the guidance. The Society acted as specialist adviser in this process and have no further comments to add.	Thank you for your comment.
3	Consultee 3 Private Sector Professional	**1**	For use in patients with uncontrolled BP 140/90 on 4+ meds (including aceI/ARB CCB DIURETIC AT MAX DOSES). Angiographic normal renal arteries suitable for Rsd intervention Plus contraindications from Symplicity 2 trial	Thank you for your comment. Section 1.3 of the guidance will be changed, however the Committee decided not to incorporate the consultee's comments into this change. A section 2.5.1 will be added to the guidance.
4	Consultee 4 NHS Professional	**1**	This procedure has some reported short term vascular complications no more than for a coronary angiogram. The prerequisite for ongoing BP measurement should be standardised and will be costly ? maybe home monitoring and a hypertension nurse collating the data could cut the cost of follow up	Thank you for your comment. Cost-effectiveness is not within the remit of the IP programme.

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5	Consultee 5 NHS Professional	**1**	For a device based randomised controlled trial 106 pts in the Symplicity 2 trial seems a reasonable number of patients with positive results published after peer review. the incidence of complications of any signifcance is extremely low and based on similar procedures in centres performing renal arterial intervention in larger numbers is an expected finding. Access site complications were within the BSIR guidelines for femoral angiography.	Thank you for your comment.
6	Consultee 6 Manufacturer	**1**	1.1 Current evidence on limited numbers of patients shows that percutaneous transluminal radiofrequency sympathetic renal denervation for resistant hypertension (as defined in the guidelines as patients without defined secondary causes of hypertension, who fail to attain adequate blood pressure control despite compliance with a diet, exercise and at least three anti hypertensive medications, one being a diuretic, at maximum tolerable doses.) is efficacious in the short and medium term.	Thank you for your comment. It is not within the scope of NICE IP guidance to define treatment thresholds in detail. Section 1.3 of the guidance recommends a multidisciplinary referral decision, “giving consideration to the number of antihypertensive drugs that have failed to control the patient’s blood”.
7	Consultee 6 Manufacturer	**1**	There is a potential for procedural complications, but based on the limited number of patients reported, these are very uncommon. The risk of the procedure needs to be balanced by the potential patient benefit that can be predicted to come from blood pressure and therefore long-term risk reduction. Current evidence on the safety and efficacy of appears adequate to support the use of this procedure provided that normal arrangements are in place for consent, audit and clinical governance	Thank you for your comment. Section 1.1 of the guidance will be changed, but the Committee did not wish to change it along the lines of the consultee’s requested change.

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8	Consultee 6 Manufacturer	**1**	The treatment standards for patients with resistant hypertension are not well defined, and the information on renal denervation is comparable to the information on the addition of more medications to these patients. The identified risk is critical in assessing the benefit risk seen in patients who consider this therapeutic route. It is suggested that the risks of percutaneous transluminal radiofrequency sympathetic denervation of the renal artery for resistant hypertension vs uncontrolled drug trialsin this population, are entirely comparable.	Thank you for your comment. The Interventional Procedures programme at NICE assesses the safety and efficacy of new interventional procedures. It does not have a remit to determine the placement of a procedure in the pathway of care for a disease or condition. It does not assess the efficacy and safety of comparator interventions.
9	Consultee 6 Manufacturer	**1**	The reduction of blood pressure with this strategy has also been associated with a significant reduction of insulin resistance (Mahfoud, F. et. al. Circulation 2011). If confirmed, this treatment strategy is then unique in reducing cardiovascular risks by simultaneously reducing blood pressure and the risk of developing type II diabetes mellitus.	Thank you for your comment.
10	Consultee 6 Manufacturer	**1**	The complications that occurred would not be classed as either serious or common by experienced interventional cardiologists or radiologists. The intervention cannot be judged against pharmaceutical measures as, by definition, the population that this therapy is suitable for have failed to achieved control with polypharmacy and remain at high risk of adverse event from their hypertension.	Thank you for your comment. Section 1.1 of the guidance does not state that the complications are common. The Committee considered that some of the adverse events reported in the literature were serious.
11	Consultee 6 Manufacturer	**1.2**	No Change	Thank you for your comment.

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12	Consultee 6 Manufacturer	**1.3**	Patient selection should be carried out by a multidisciplinary team including a physician with expertise in hypertension and a specialist in endovascular interventions, giving due consideration to the number of antihypertensive drugs that have failed to control the patient's blood pressure and the anatomical suitability of their renal arteries, and the patients relative risk without adequate blood pressure control.	Thank you for your comment. Section 1.3 will not be changed in response to the consultee's comment but a section 2.5.1 will be added to the guidance.
13	Consultee 6 Manufacturer	**1.4**	No Change	Thank you for your comment.
14	Consultee 7 NHS Professional	**1**	I agree with the principles behind statement 1.1, though it is important that we all understand the basis for them. Special arrangements must not be used as an inappropriate barrier to treatment. I would recommend a compulsory national database, overseen by BCIS, with compulsory reporting of 30 day and 1 year outcomes, similar to the arrangements for other catheter-based cardiovascular procedures. These are special arrangements, but reasonable and proportionate ones one would not want to consider this technology out of bounds to those patients with a clear need for a new approach to their hypertension simply because of the wording of this paragraph. Equally, we cannot have the indiscriminate use of this technology without appropriate oversight. The wording, though, will affect how PCTs will approach funding discussions.	Thank you for your comment. A new section 1.5 on data collection will be added to the guidance.
15	Consultee 8 NHS Professional	**1**	Patient selection should certainly be made through a multidiciplinary effort. However, the therapy should be made avaialbe to all patients considered by the expert team to benefit from the procedure, without further special arrangement, to avoid delay in benefit to patients.	Thank you for your comment. The Committee considered this comment and decided not to change the guidance.

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16	Consultee 9 British Cardiovascular Society	**1.4**	Regarding point 1.4 Recommend that a formal comprehensive audit programme be instituted for all use of percutaneous transluminal radiofrequency sympathetic denervation of the renal artery	Thank you for your comment. A new section 1.5 on data collection will be added to the guidance.
17	Consultee 10 NHS Professional	**1**	I think that there is mounting evidence that the procedure is safe and effective. The recommendations should allow for the procedure to be carried out without such strict limitations.	Thank you for your comment. Section 1.1 of the guidance will be revised, but the main recommendation will not be changed.
18	Consultee 11 NHS Professional	**1.1**	1.1 By stressing at the outset the "potential for serious complication" the implication is that the reader should consider the procedure potentially dangerous, without putting this danger into context. Whilst the next sentence acknowledges that current evidence is that the complication rates are low, it might usefully point out that compared to other interventional cardiological and radiological procedures the reported risks to date are extremely low. Whilst I would argue for less prejudicial introductory wording I do agree with the recommendation that its implementation should be carefully controlled and monitored until larger numbers of patients have had data collected, either in registries or controlled trials.	Thank you for your comment. Section 1.1 states that serious complications are uncommon. The IP programme does not assess the efficacy and safety of comparator interventions.
19	Consultee 12 BCIS lead for NICE	**1**	BCIS are curious that this procedure requires special rather than normal arrangements for clinical governance audit and consent. Â This IPG recommendation is based upon a RCT which is evidence of a higher quality than that which usually supports procedures that require special arrangements. We suggest normal arrangements would suffice. We agree with the MDT approach.	Thank you for your comment. Section 1.1 of the guidance will be revised, but the main recommendation will not be changed.
20	Consultee 13 Chairman, Guidelines Committee, British Cardiovascular Society	**1.3**	1.3 crucially important. Â Br Hypertension Society will have a role here. Â Should not be performed without clinical input from a recognised member of BHS.	Thank you for your comment. Section 1.3 states that the MDT should include a physician with expertise in hypertension.

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21	Consultee 1 Chairman NICE Hypertension Guideline NHS Professional	**2.1**	Patients with true drug resistant hypertension in whom white coat hypertension has beene excluded and BP levels confirmed on ABPM, and in whom all treatment options have been exhausted - I see this as a Step 5 treatment option according to the forthcoming NICE treatment algorithm that should be offered by specialist centres - the thought of this being offered by practitioners without experuence in the assessment and treatment of complex hypertension is worrisome	Thank you for your comment. Section 1.3 states that the MDT should include a physician with expertise in hypertension. NICE anticipates that referring clinicians will use authoritative standards that are current at the time of selecting patients for treatment.
22	Consultee 3 Private Sector Professional	**2.1**	Uncontrolled BP (as per symplicity trial indications)	Thank you for your comment. The indication for this procedure is 'resistant hypertension'. Section 2.1.1 will be changed.
23	Consultee 5 NHS Professional	**2.1**	This is insufficient. The indications for this treatment modality are poor blood pressure control while compliant with at least three antihypertensive agents. Â It is clearly not a first or second line treatment. for resistant hypertension there would seem to be a good evidence base for use given certain anatomical constraints.	Thank you for your comment. Section 2.1.1 will be changed and a section 2.5.1 added to the guidance.
24	Consultee 6 Manufacturer	**2.1.1**	Hypertension is a major risk factor for cardiovascular disease (including stroke and myocardial infarction) and for chronic renal disease. First-line treatment usually involves lifestyle changes, such as diet modification and exercise. Combinations of antihypertensive medications may be introduced for the management of hypertension. As provided in the British Hypertension Society Guidelines, patients whose hypertension remains uncontrolled whilst on 3 or more medications are termed 'resistant', and it is these patients with on-going high level of CV risk that are considered for this new procedure.	Thank you for your comment. Section 2.1.1 will be changed and section 2.5.1 added to the guidance. Please see also response to comment no. 6.

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25	Consultee 6 Manufacturer	**2.1.1**	Resistant hypertension is defined in the guidelines as patients without defined secondary causes of hypertension, who fail to attain adequate blood pressure control despite compliance with a diet, exercise and at least three anti hypertensive medications, one being a diuretic, at maximum tolerable doses.	Thank you for your comment. Please see also response to comment no. 6.
26	Consultee 7 NHS Professional	**2.1**	Needs re-phrasing. Resistant hypertension is a phrase associated with a particular sub-group of difficult to control hypertensives, rather than anyone who persists following lifestyle measures. It should read: Combinations of anti-hypertensive medications should then be introduced for persistant hypertensives. For those resistant to combination drug therapies, specialist advice should be sought and other strategies considered, within the framework of those specialist services. It is worth pointing out here that the prognosis of drug-resistant hypertension is bad and in the worst subset of patients, worse than many cancers.	Thank you for your comment. Please see also response to comment no. 6.
27	Consultee 10 NHS Professional	**2.1**	fair	Thank you for your comment.
28	Consultee 11 NHS Professional	**2.1**	No comment	Thank you for your comment.
29	Consultee 12 BCIS lead for NICE	**2.1**	We suggest a definition of resistant hypertension is inserted in to section 1.3 or 2.1 (patients without a secondary cause who fail to attain adequate control of blood pressure despite compliance with lifestyle measures and at least 3 anti-hypertensive medications, one being a diuretic, at maximumum tolerated doses). Such patients are at high risk of adverse CV events and of the side effects Â of polypharmacy and require frequent medical attention.	Thank you for your comment. Please see also response to comment no. 6.

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30	Consultee 13 Chairman, Guidelines Committee, British Cardiovascular Society	**2.1**	Should only be considered when BP is not controlled on multiple therapies.	Thank you for your comment. Section 2.1.2 of the guidance will be changed.
31	Consultee 14 NHS Professional	**2.1**	The indications section should include a statement that for a minority of patients, pharmacological and lifestyle changes do not adequately control blood pressure. It is in such cases that renal denervation might be considered as an adjunct to pharmacological therapy to reduce blood pressure.	Thank you for your comment. Section 2.5.1 of the guidance will be changed and a 2.5.1 added to the guidance.
32	Consultee 1 Chairman NICE Hypertension Guideline NHS Professional	**2.2**	OK	Thank you for your comment.
33	Consultee 15 NHS Professional	**2.2**	there are also alternative energy sources in early laboratory trial like ultrasound.	Thank you for your comment. This guidance is only concerned with the use of radiofrequency energy, since this was the procedure notified to NICE.
34	Consultee 3 Private Sector Professional	**2.2**	Procedure is simlar to renal stent procedure. Access obtained via femoral artery. Renal artery is engaged with a guide catheter and enal ablation catheter is advanced. The catheter is connected externally to a power source to deliver RF energy (similar to cardiac ablation for arrhythmias). Short low energy pulses are applied for 2 minutes and 4-6 runs to each kidney artery in different positions along artery. Patients may feel mild discomfort at this time so consciuous sedation is tooped up with morphine or fentanyl. The procedure is performed in both renal arteries at same visit.	Thank you for your comment. This is only intended to be a brief summary of the procedure.

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35	Consultee 3 Private Sector Professional	**2.2**	Following procedure sheath is removed and manual pressure is applied. Patient is observed for 4 hours or overnight. Then allowed home (similar to any PCI or cardiac ablation procedure). Anticoagulation is also similar with iv heparin given at beginning. Changes in BP do not become apparent until clinical follow up, usually after several months	Thank you for your comment. This is only intended to be a brief summary of the procedure.
36	Consultee 5 NHS Professional	**2.2**	brief but to the point.	Thank you for your comment.
37	Consultee 6 Manufacturer	**2.2.1**	No Change	Thank you for your comment.
38	Consultee 6 Manufacturer	**2.2.2**	The procedure is carried out with the patient under local anaesthesia with conscious sedation, and procedural anticoagulation medication is given. A radiofrequency catheter is introduced via the femoral artery and advanced sequentially into each renal artery under fluoroscopic control. The catheter is connected to a generator which delivers low-power radiofrequency energy in 2-minute applications to each renal artery at 4–6 points along its length, in a spiral pattern.	Thank you for your comment. This is only intended to be a brief summary of the procedure.
39	Consultee 7 NHS Professional	**2.2**	This is a bit restrictive. Strategies are altered according to anatomy and patient.	Thank you for your comment. This is only intended to be a brief summary of the procedure.
40	Consultee 8 NHS Professional	**2.2**	The procedure should be carried out in a setting where endovascular renal artery intervention takes place routinely, to ensure provision of adequate imaging and endovascular intervention equipments for the procedure.	Thank you for your comment. Section 1.3 of the guidance states that the multidisciplinary team should include a specialist in endovascular interventions and will be changed to include facilities for stenting.
41	Consultee 10 NHS Professional	**2.2**	fair	Thank you for your comment.
42	Consultee 11 NHS Professional	**2.2**	No comment	Thank you for your comment.
43	Consultee 12 BCIS lead for NICE	**2.2**	No comments.	Thank you for your comment.

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44	Consultee 13 Chairman, Guidelines Committee, British Cardiovascular Society	**2.2**	OK	Thank you for your comment.
45	Consultee 1 Chairman NICE Hypertension Guideline NHS Professional	**2.3**	The efficacy data has always looked surprisingly good. The amount of data is limited and is relatively short ter. The RCT did not include a sham control and this is bening done in an ongoing US study which will be interesting. The most reliable data is for ABPM and the difference in SBP of 8mmHg is less impressive than the office BP data. Future studies must include ABPM data pre and post proceedure. The technique looks promising but much more data is needed	Thank you for your comment.
46	Consultee 16 NHS Professional	**2.3**	The efficacy of this procedure is based on observations and one poorly controlled study. Â No “placebo procedure” group was included and, thus, the magnitude of benefit in blood pressure reduction is exaggerated. Â This interpretation is compounded by inappropriate statistical analysis. Â Instead of comparing before and after in each group, differences in responses between the groups should be compared. Â The 24 hour ambulatory blood pressure data is probably the most reliable (least unreliable) and suggests only a modest beneficial effect from the procedure of 8/6 mmHg. Â These findings do not support widespread adoption of this procedure.	Thank you for your comment. NICE does not analyse results of studies, but simply presents the results to IPAC as they are reported. These are then included in the guidance.
47	Consultee 3 Private Sector Professional	**2.3**	Consistent reductions in BP have been observed as has safety albeit at few years follow up.	Thank you for your comment.
48	Consultee 5 NHS Professional	**2.3**	2.3.4 This may be the case but this is an IPG assessing use of the device in hypertension control. There may be additional benefits which are secondary but i am not sure of the relevance to this.	Thank you for your comment. This is the opinion of Specialist Advisers asked to comment on the procedure and will not be changed.

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49	Consultee 6 Manufacturer	**2.3.1**	A randomised controlled trial (RCT) of 106 patients treated by renal artery denervation (n = 52) or unchanged medical therapy (n = 54) reported an average change from baseline in blood pressure measurements of -32/-12 mmHg and +1/0 mmHg respectively at 6-month follow-up (p < 0.001 for both systolic blood pressure [SBP] and diastolic blood pressure [DBP] in the treatment group compared with p = 0.83 for SBP and p = 0.77 for DBP in the control group). The primary endpoint was difference in office BP response between groups; the 33/11 mmHg difference was highly statistically and clinically significant (p<0.0001) Correction of data given in IPG	Thank you for your comment. Only 100 of the 106 patients were assessed for the primary endpoint at 6 months. Section 2.3.1 will be changed.
50	Consultee 6 Manufacturer	**2.3.3**	No Change Additional supporting comment - Muscle sympathetic nerve recordings in a patient with ESRD who underwent native kidney denervation for hypertension have remained substantially reduced to normal for 33 months post procedure (citation)	Thank you for your comment.
51	Consultee 6 Manufacturer	**2.3.4**	The Specialist Advisers listed potential theoretical key additional efficacy outcomes as reduction in cardiovascular morbidity and mortality, improvement in the parameters of renal function, and regression in left ventricular mass. Reduction in measured insulin resistance could also be deemed useful.	Thank you for your comment. This section lists only the stated opinions of Specialist Advisers asked to comment on the procedure and will not be changed.
52	Consultee 6 Manufacturer	**2.3.4**	These additional measures stray from the essence of an IPG which is to evaluate what is presented – ie: the technology is safe and reduces BP post procedure. The inclusion of these measures is not needed in an IPG. Reduction of measured insulin resistance - two separate reports confirm this later finding, one using gold standard euglycemic insulin clamp, the second using calculated insulin resistance index.	Thank you for your comment. This is the opinion of Specialist Advisers asked to comment on the procedure and will not be changed.

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53	Consultee 7 NHS Professional	**2.3.4**	Section 2.3.4 should clearly be removed.	Thank you for your comment. This is the opinion of Specialist Advisers asked to comment on the procedure and will not be changed.
54	Consultee 8 NHS Professional	**2.3**	There is early evidence for improvement in glucose intolerance and sleep apnoea following the procedue and this should be considered to be included in the list of additional efficacy outcpoomes.	Thank you for your comment. This is the opinion of Specialist Advisers asked to comment on the procedure and will not be changed.
55	Consultee 10 NHS Professional	**2.3**	effective and safe	Thank you for your comment.
56	Consultee 11 NHS Professional	**2.3**	2.3.4 The Specialist Advisers have suggested reasonable additional outcome measures that should, in time, be reported once larger series of patients have been studied over longer periods of time. However, this technique does seem to offer the potential for very significant reductions in blood pressure for patients who have largely "failed" pharmacological and lifestyle interventions. Would it not also be reasonable to highlight that the potential morbidity/mortality consequences of allowing hypertension to remain uncontrolled are considerable (ie: there are risks associated with NOT undergoing a potentially therapetic procedure)?	Thank you for your comment. A new section 2.5.1 will be added to the guidance.
57	Consultee 12 BCIS lead for NICE	**2.3.1**	In 2.3.1 the p value for SBP and DBP is not 0.001 but 0.0001.	Thank you for your comment. Section 2.3.1 of the guidance will be changed.
58	Consultee 13 Chairman, Guidelines Committee, British Cardiovascular Society	**2.3**	Long term F/U mandatory.	Thank you for your comment. Section 1.4 of the guidance states that further research should include the long-term effect of the procedure on blood pressure. A new section 1.5 on data collection will be added.
59	Consultee 1 Chairman NICE Hypertension Guideline NHS Professional	**2.4**	This is a key issue - acute complications are low but may be more common in less experienced hands. Longer term safety, especially the integrity of the renal artery will be important to evaluate	Thank you for your comment. The guidance recommends more research into adverse events at section 1.4..

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60	Consultee 3 Private Sector Professional	**2.4**	A similar procedural risk to angiography procedures is observed. Again emphasizes patient selection appropriately qualified doctors with renal intervention experience performing procedure who are aware of possible complications and how to treat them similarly appropriate BP doctor involvement is critical for withdrawing BP meds and dealing with any risks associated with this.	Thank you for your comment. Section 1.3 contains recommendations for patient selection.
61	Consultee 4 NHS Professional	**2.4**	Would it be sensible to set up govenrance that the procedure should only be performed in centres that have access to renal stenting	Thank you for your comment. Section 1.3 of the guidance will be changed.
62	Consultee 5 NHS Professional	**2.4**	access site complications are common to all vascular procedures. back pain, bradycardia and paraethesia seem to be procedure specific. theoretical longterm risks need to be considered but at two years there is no evidence of renal artery stenosis in patients treated and this should offer some reassurance. clearly audit and long term follow up will be required but on current evidence the procedure appears as safe as many other vascular interventions for which no RCT is available!	Thank you for your comment.
63	Consultee 6 Manufacturer	**2.4.1**	No Change	Thank you for your comment.
64	Consultee 6 Manufacturer	**2.4.2**	Additional comment - sudden hypertensive crisis is recognised as a possibility with this clonidine	Thank you for your comment.
65	Consultee 7 NHS Professional	**2.4.2**	2.4.2 Nausea and oedema is unclear(oedema of what?)	Thank you for your comment. The site of oedema was not reported in the paper.
66	Consultee 7 NHS Professional	**2.4.3**	2.4.3 These are the consequences of femoral access and are part and parcel of any arterial access procedure. It is worth considering that percutaneous coronary intervention, performed on over 80,000 patients a year in this country, is associated with similar issues.	Thank you for your comment.

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67	Consultee 6 Manufacturer	**2.4.3**	Each of the following minor periprocedural events was reported in 1 patient treated by renal artery denervation in the RCT of 106 patients: femoral artery pseudoaneurysm (treated by manual compression), paraesthesia (requiring extended hospital stay), back pain (resolved after 1 month) and transient intraprocedural bradycardia (treated with atropine). Complications due to access site should not be considered as related to the procedure specifically as the method of access is proven, routine and common to many high volume catheterisation laboratory procedures (coronary & renal artery stenting, etc)	Thank you for your comment. The complications listed are those reported in the literature.
68	Consultee 6 Manufacturer	**2.4**	Correction of data and making the point that access site complications are not due to the renal denervation procedure itself rather the access method which is a standard technique common to many interventional vascular procedures.	Thank you for your comment. The complications listed are those reported in the literature.
69	Consultee 6 Manufacturer	**2.4.4**	Delete this comment as unnecessary The inclusion of this comment seems excessive. To report the need for over the counter pain relief as minor complication that affected 0.007% of the study seems unnecessarily alarmist	Thank you for your comment. The patient had bilateral flank pain for several months after the procedure.

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70	Consultee 7 NHS Professional	**2.4.5**	This should be altered as it implies that pain during the procedure is rare. It is not, though it is readily managed. Any surgical procedure would induce pain if it is not managed properly, and with renal denervation, analgesia and sedation can manage this. Renal artery perforation is a theoretical severe complication and if this is to be included, it would be important to incorporate incidence from previously performed procedures. With over 500 procedures worldwide, we should ask the company for the incidence. The vast disparity in incidence and seriousness between periprocedural pain and renal artery perforation means these two should not be grouped together. Theoretical adverse events are meaningless without context or projected incidence. Paracetamol over the counter is associated with a worse list than this.	Thank you for your comment. Section 2.4.5 is the opinion of the Specialist Advisers and will not be changed.
71	Consultee 6 Manufacturer	**2.4.5**	The Specialist Advisers listed anecdotal adverse events as transient pain from the delivery of radiofrequency energy and renal artery perforation. They considered theoretical adverse events to include late stenosis or promotion of atheroma in the renal artery in the long-term, sodium depletion and hypotension. Although these are theoretical concerns, both the non-randomized study and the randomized study evaluated renal artery safety peri-procedurally and at 6-months with CT and MRA imaging, and in no instance did these evaluations surface any cause for concern.	Thank you for your comment. Section 2.4.5 is the opinion of the Specialist Advisers and will not be changed.
72	Consultee 6 Manufacturer	**2.4.5**	Renal artery perforation has never been observed nor has late stenosis. Atheroma promotion has never been observed and is a theoretical concept unsupported by the imaging follow-up from the HTn-2 and HTN-2 trials and the commercial clinical experience.	Thank you for your comment. Section 2.4.5 describes the opinions of Specialist Advisers asked to comment on the procedure in question. Renal artery perforation was not listed by the Specialist Advisers as having occurred so will be removed from the guidance.

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73	Consultee 8 NHS Professional	**2.4.5**	Although risks are small the procedure should best be performed only by experts in renal artery intervention, with established experience in renal artery catheter manipulation, stent placement and angioplasty. Renal artery perforation could potentially be catastrophic and expertise in placement of covered stents renal artery sould be available at the time of procedure.	Thank you for your comment. Renal artery perforation was not listed by the Specialist Advisers as having occurred so will be removed from the guidance.
74	Consultee 9 British Cardiovascular Society	**2.4**	Recommend that that the audit programme is essential and comprehensive rather than advisory	Thank you for your comment. NICE cannot make an audit programme mandatory in Interventional Procedures guidance, but will support its implementation by providing an audit tool, for local use, when the guidance is published. .
75	Consultee 10 NHS Professional	**2.4**	relatively safe	Thank you for your comment.
76	Consultee 11 NHS Professional	**2.4.5**	2.4.5 Is it justified for Specialist Advisors speculations, for which as I understand it there is no current evidence, to be included in a NICE document, even if it is provisional guidance? Again, this seems to lead the reader to be concerned about safety for which there is no current justification. For completeness should not the complications/side effects of the pharmacological limbs of these trials also be reported?	Thank you for your comment. All Interventional Procedures Guidance contains the opinions of Specialist Advisers, who are nominated by their professional organisation. Adverse events that occurred in the study control group will be added to section 2.4.2 of the guidance.
77	Consultee 12 BCIS lead for NICE	**2.4**	The adverse events in the treatment group need to be balanced by the adverse effects in the control group (2 TIAs and 1 coronary stent for angina).	Thank you for your comment. Adverse events that occurred in the study control group will be added to section 2.4.2 of the guidance.
78	Consultee 13 Chairman, Guidelines Committee, British Cardiovascular Society	**2.4**	OK	Thank you for your comment.

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79	Consultee 17 NHS Professional	**2.4**	The reports of serious complications in the first studies must be taken within their clinical context. The occurence of renal artery dissection was rare, and certainly less common that seen with coronary arteries and coronary stenting, a procedure that is undertaken routinely. All Doctors undertaking the procedure will (or should be) extremely well versed on the assessment and management of iatrogenic arterial dissection - therefore this will be a complication that should have only mild or modest clinical sequelea for the patient - it does not indicate a serious adverse event.	Thank you for your comment.
80	Consultee 13 NHS Professional	**2.4**	2.4.2. One of the serious adverse events outlined is not specific to renal denervation therapy - stopping clonidine abruptly would precipitate a hypertensive crisis in a medically treated patient. 2.4.3. Access site complications are not specific to renal denervation therapy, rather they are common to any interventional procedure.	Thank you for your comment. The complications are described as they are reported in the literature. Hypertensive crisis after clonidine will be removed from the guidance.
81	Consultee 3 Private Sector Professional	**General**	symplicity 2 trial of patients with uncontrolled hypertension on multiple meds shows that RSD significantly reduces BP by 30+ mmHg. This is despite meds so impact for patients for stroke prevention CV disease management is enormous and a cost benefit is likely as many patients eend up coming off tablets after 6-12 months. Results are durable and procedure is safe in appropriately skilled endovascular hands (interventional cardiology, radiology, vascular surgery). Patients in Symplicity trials are the only patients tested with this technology although some german operators have tested this in patients who have uncontrolled Bp and are unable to tolerate tablets.	Thank you for your comment.

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82	Consultee 3 Private Sector Professional	**General**	Outside of these patients i do not believe that RSD should be used at present. Its introduction is likley to have enormous public health benefit but we should rememember that patient selection is critical as there is no evidence to support RSD in all BP patients. In Ireland where i am a cardiologist we are facing challenge of waiting for more clinical data yet when we faced a similar unknown with TAVI an opportunity was made to pilot innovative technology in clinical practice and to establish data in this way. RSD has a major advantage over TAVI in both cost and patient length of stay.	Thank you for your comment. NICE will support discussions with interested groups and manufacturers about the establishment of an appropriate register.
83	Consultee 4 NHS Professional	**General**	I have in the past received travel sponsorship and hospitality from medtronic	Thank you for your comment.
84	Consultee 6 Manufacturer	**General**	Medtronic feel that the context of this review has been from the perspective of a pharmaceutical as opposed to an interventional one and too much note has been taken of procedural complications common to any technique that requires femoral vascular access. The group of patients for whom this therapy intended is the population with resistant hypertension who remain at risk of significant adverse events while their blood pressure remains uncontrolled (*patients without defined secondary causes of hypertension, who fail to attain adequate blood pressure control despite compliance with a diet, exercise and at least three anti hypertensive medications, one being a diuretic, at maximum tolerable doses*) The risks and benefits of the procedure should be assessed in this context. The evidence in this patient population is sufficient for normal arrangements.	Thank you for your comment. The Committee considered this comment and decided not to change its final recommendation.

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85	Consultee 6 Manufacturer	**General**	The detailed response to the IPG which follows addresses a number of concerns within the current IPG wording which backs up the points made above. • The patient selection and definition of who is the target group for this therapy • The relative risk when compared to multiple medications and inadequate blood pressure control alone • Corrections around the numbers and findings of the trials referred to in the IPG Corrections and context of adverse events including rebuttal of theoretical risks	Thank you for your comment.
86	Consultee 11 NHS Professional	**General**	I was Deputy National Director for Heart Disease at the Dept of Health (2007-11) and as part of this role have chaired, and continue to chair, a "New Cardiovascular Procedures Steering Group" which has representation from DH, National Commissioners, Specialist surgical and cardiological societies, NICE and the MHRA. The Steering Group aims to help stakeholders understand the potential place of new technologies and and set standards for implementation where appropriate.	Thank you for your comment.