The Joint UK Societies' Consensus Statement on Renal Denervation for Resistant Hypertension.

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This statement was developed with the guidance and advice from patients who had undergone this procedure at Barts and The London NIHR Cardiovascular Biomedical Research Unit and are members of the Patients and Public Engagement Group. The Joint UK Societies wish to express their thanks to Mr John Bold and Mr Anthony Henry.

This statement is intended to be read alongside NICE IP 418.
http://guidance.nice.org.uk/IPG418

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Executive Summary of Joint Societies Statement on Renal Denervation.

Background to the Joint Societies' Statement on Renal Denervation.
Renal denervation for proven resistant hypertension is a new procedure with an emerging evidence base of effectiveness and safety [1,2,3]. This Joint Societies' Consensus Statement was prepared to support the National Institute of Health and Clinical Excellence Interventional Procedure Guidance on Renal Denervation (NICE IP418) by representatives of key stakeholder societies [4].

Eligiblity for renal denervation.
We recommend that we rely upon the current evidence-base to select patients with resistant hypertension who may be eligible for this therapy. In the trials, resistant hypertension was defined as a sustained clinic systolic blood pressure of ≥ 160 mm Hg (≥ 150 mm Hg in Type 2 Diabetes) in patients on 3 or more anti-hypertensive medications [1,2,3]. This is equivalent to stage 2 hypertension which is an average clinic blood pressure >160 mm Hg and equivalent to a daytime average on ambulatory blood pressure >150 mm Hg as defined by the 2011 National Institute for Health and Clinical Excellence (CG 127) Hypertension Guideline[5]. We further recommend that to be eligible for renal denervation patients should have progressed through the medications recommended at step 4 in the NICE/British Hypertension Society Treatment Algorithm in CG 127 [5]. Confirmation of sustained raised blood pressure using ambulatory blood pressure monitoring is essential (as above). It will allow detection of a "white coat", or alerting response which may be a cause of apparently resistant hypertension.

The multi-disciplinary team of hypertension specialists and interventionalists.
The selection, treatment and follow up of patients for this intervention requires a multidisciplinary team which must include hypertension specialists who can demonstrate active involvement in the routine investigation and care of patients with resistant hypertension. They will provide detailed assessment of the eligibility of the patients to receive this procedure, excluding non-compliance, secondary causes of hypertension and ensuring that a full range of lifestyle and therapeutic options have been carefully tried. The intervention may be undertaken by interventional cardiologists or radiologists who have been trained in the procedure and are competent to manage complications such as dissection of the renal artery.

Preparing patients for renal denervation.
Preparation of patients for this therapy will entail providing a clear description of the procedure including provision of contemporary statistics on success rates/potential complications, detailed technical information regarding the procedure itself and after care. In particular loin or abdominal pain occurs in the majority of recipients during ablation and adequate peri- and post-procedural analgesia should be provided. Blood pressure typically falls gradually over time and, although uncommon, post-procedural hypotension has been noted.

Establishment of a National Registry for Renal Denervation.
The Joint Societies recommend that data on all patients undergoing this procedure in the United Kingdom must be submitted to a national registry to inform practice, generate research opportunities and permit audit of clinical effectiveness.

1. Hypertension in the UK Healthcare setting.

1.1. Prevalence of resistant hypertension.

There are 18 million adults in the UK with hypertension: of the 10 million or so receiving treatment, only about 50% have adequately controlled blood pressure (BP). Recent National Institute for Health and Clinical Excellence Guidance (CG127) defined resistant hypertension as uncontrolled BP on 3 or more antihypertensive medications [5]. Data from Primary Care in 2008 scaled up to the UK population suggests there may be 0.5m hypertensive patients who appear to be resistant to therapy. Recent recruitment to the British Heart Foundation funded PATHWAY 2 study of optimal therapy for resistant hypertension suggests that truly resistant hypertension is much less common (personal communication PATHWAY investigators). Patients with resistant hypertension who do not achieve optimal control in spite of treatment with multiple anti-hypertensive drugs remain at high risk of cardiovascular events.

1.2. The sympathetic nervous system and renal denervation in hypertension.

Chronic elevation of sympathetic nervous system (SNS) activity has been identified as an important pathological mechanism in hypertension [1]. Therapeutic renal denervation, the deliberate disruption of the nerves connecting the kidneys with the central nervous system, has been shown to be an effective means of modulating the effects of elevated SNS activity - both by reducing the efferent renal sympathetic control of kidney function (renin release, sodium excretion and renal blood flow) and by removing the renal afferent sympathetic contribution to central BP control [1,2,3]. It is important to note that denervated kidneys maintain appropriate electrolyte and volume homeostasis.

Recently percutaneous renal denervation has become possible through the development of a catheter-based radiofrequency ablation procedure resulting in selective renal sympathectomy and has been shown to be effective in lowering blood pressure in patients with resistant hypertension [1,2,3].

1.3. The technology.

Currently there is only one percutaneous renal denervation system - the *Symplicity* Catheter System (*Medtronic*). Others are in development. The *Symplicity* System is made up of a single-use, disposable catheter and a reusable radiofrequency (RF) generator. The system is used to deliver low-level radiofrequency energy through the wall of the renal artery to denervate the human kidney. The 6 French compatible *Symplicity* catheter is introduced using standard interventional techniques via the femoral artery, and is positioned in the renal artery under fluoroscopic guidance. The treatment involves delivery of relatively low-power and precisely focused two minute bursts of RF energy (8W or less) endoluminally to disrupt the surrounding renal nerves lying in the adventitia of the artery wall.

1.4. Trial evidence for renal denervation.

A proof of concept observational cohort study demonstrated that renal denervation produced significant BP lowering in a group of well treated but resistant hypertensive patients with no major safety concerns[1]. Subsequently a multicentre, randomised control trial of 106 patients was undertaken. The results of this study again demonstrated that renal denervation was both safe and efficacious with substantial BP lowering effects (average fall of 33/11 mm Hg) in patients with resistant hypertension and preserved renal function[2]. Extended follow up data on a cohort of 153 treated patients has demonstrated safety and durability of BP reduction out to 24 months[3]. Apart

from peri-procedural loin, or para-umbilical pain, which can be effectively managed with opioid analgesia and sedation there were no major complications.

2 Optimal assessment and treatment of resistant hypertension.

2.1. Definition of resistant hypertension.

Recent National Institute for Health and Clinical Excellence Guidance for Hypertension (CG127) produced in collaboration with the British Hypertension Society (BHS) defined resistant hypertension as uncontrolled BP (≥140 systolic or 90 mm Hg diastolic) on 3 or more antihypertensive medications [5]. For patients being considered for renal denervation the current evidence base only supports deployment of this therapy in those who are truly resistant and compliant with conventional therapy. This includes full lifestyle measures and pharmacotherapy following the Joint NICE/BHS Treatment algorithm specified in CG127 [5].

2.2. Recommendation of characteristics of resistant hypertensive patients to be considered for renal denervation.

To date this interventional therapy has only been studied in those with systolic BP proven to be ≥160 mm Hg and who are taking 3 or more anti-hypertensive medications. To ensure conventional approaches have been exhausted, we recommend that patients considered for renal denervation should have confirmed sustained systolic blood pressure above 160 mm Hg in the clinic setting and confirmed as above 150 mm Hg on daytime average on ambulatory BP (150 mm Hg clinic and confirmed as above 140 mm Hg ABPM for patients with Type 2 Diabetes) [1,2]. Furthermore, because the trial patients were on an average of 5 medications we recommend that patients being considered for renal denervation should have tried the medication options up to and including step 4 of the NICE/BHS algorithm, especially additional diuretic therapy [2,5](see figure 1).

It is important to note that the term “Resistant Hypertension” may include individuals who are truly resistant (with, or without secondary causes) and those who are pseudo-resistant such as those who:

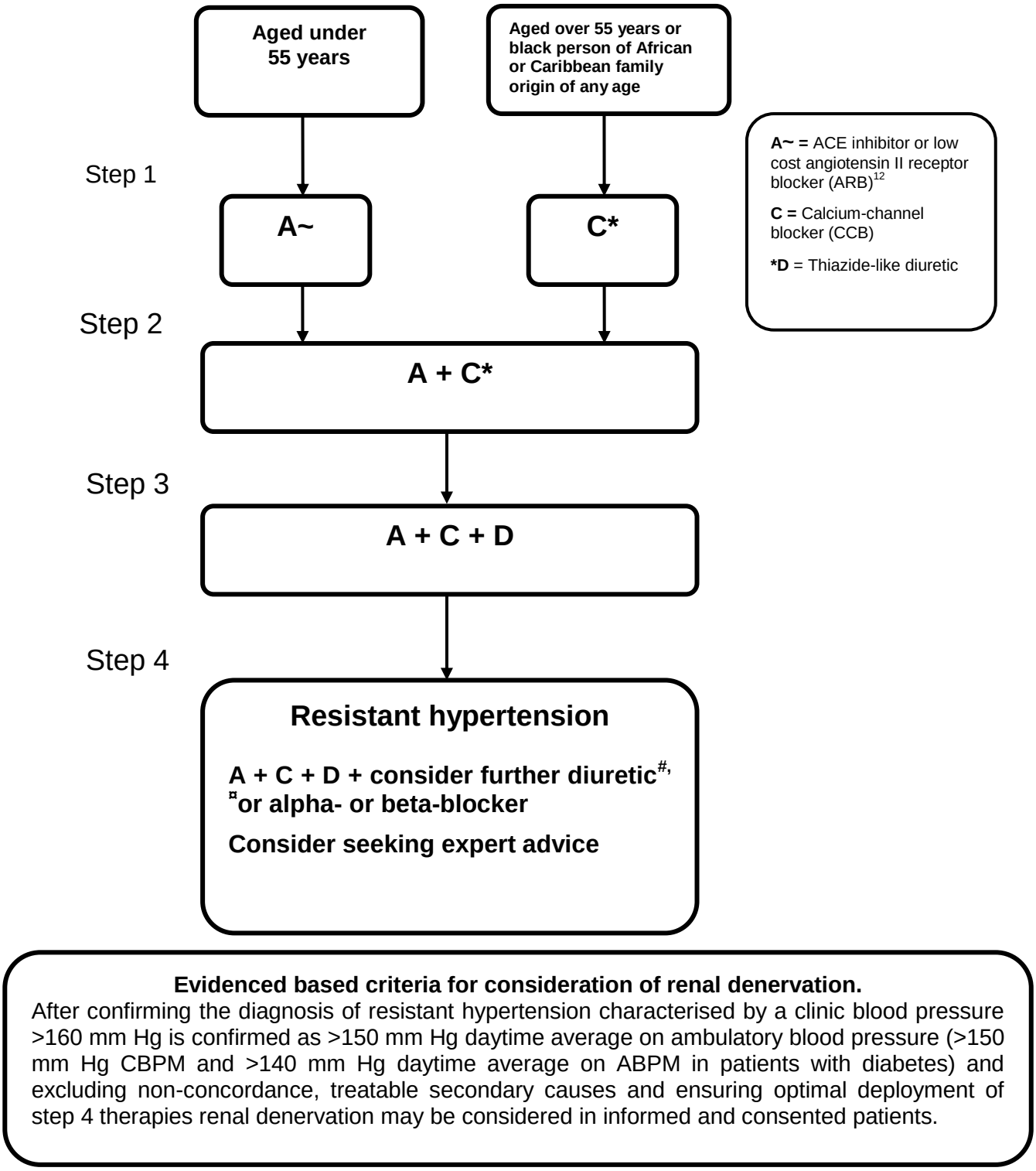
- may be non-concordant with medication,
- may be intolerant of medication,
- have white coat hypertension.

This means a rigorous clinical assessment of these patients by a hypertension specialist is needed to confirm true resistance. There is currently no trial evidence for treatment of those who are pseudo-resistant.

3. Clinical assessment of patients with resistant hypertension:

This should be carried out by specialist clinical teams with extensive experience of the assessment and management of severe primary and secondary hypertension. Assessment involves careful history and examination and there are a number of important considerations when assessing patients with resistant hypertension:

Figure 1. Adapted summary of antihypertensive treatment from the NICE CG127 Hypertension Guideline[4] indicating the criteria by which patients with hypertension resistant to step 4 therapies may be considered for renal denervation.



* A CCB is preferred but consider a thiazide-like diuretic if a CCB is not tolerated, or the person has oedema, evidence of heart failure or a high risk of heart failure.

Consider a low dose of spironolactone, or higher doses of a thiazide-like diuretic.

¤Spironolactone does not have a UK marketing authorisation for this indication. Informed consent should be obtained and documented.

3.1. Procedure for verifying that blood pressure is uncontrolled.

We recommend confirming that BP has been appropriately measured, according to the recommendations of NICE and the BHS in CG 127 [5]. This is important because BP readings can be spuriously elevated if the BP cuff size is too small for the patient's arm circumference. The BHS www.bhsoc.org provides guidance on appropriate cuff sizes.

In patients with clinic BP >160 mm Hg (150 mm Hg clinic BP in patients with type 2 diabetes) we recommend that resistance to therapy is confirmed using 24 hour ambulatory blood pressure monitoring. In accordance with NICE and BHS guidance we recommend use of daytime average > 150 mm Hg (140 mm Hg in patients with Type 2 Diabetes) with a minimum of 14 daytime readings for quality assurance [5]. This will enable identification of patients with an exaggerated BP response in the clinic setting, i.e. so-called "white coat hypertension". Although not as robust as ABPM, a series of home BP measurements could be used if ABPM was not available (follow recommendations in CG127).

3.2. Ensure conventional therapy is optimised.

We recommend that treatment is optimised including the deployment of agents indicated according to step 4 of the BHS/NICE treatment algorithm adapted from CG127 (see figure 1). This includes ensuring use of the maximum recommended and tolerated dosages. If not, then the treatment regimen should be revised and the patient should be reassessed before consideration of renal denervation.

3.3. Ensure patient concordance with therapies.

It is important to confirm patient concordance with lifestyle and pharmacotherapy (see NICE Guidance CG127). This is not always resolved by direct enquiry but may be established by measuring the BP response to directly observed ingestion of therapy in the clinic. This is followed either by 24 hour APBM or a series of home BP measurements over the following 24 hours to establish the BP response to definitive treatment to help confirm resistance or not. This assessment may be facilitated by confirming regular collection of prescriptions from primary care.

3.4. Patients intolerant of medications.

Hypertension is asymptomatic in 75% of people and although the medications are well-tolerated some patients experience unacceptable side effects. Beyond the NICE Treatment algorithm above there is no way presently to personalise medicine selection, or predict side effects. In people experiencing unacceptable side effects the use of half standard dose of several medicines is associated with lower rates of side effects and should be considered. Alternative strategies include tablet splitting of the lowest or half standard doses which may be efficacious and better tolerated or greater effort on lifestyle measures [6].

3.5. Medications that elevate blood pressure level.

It is important to exclude consumption of other medications that may be contributing to their resistant hypertension. Various drugs, including herbal remedies, either prescribed, available over the counter, or illicit, can interfere with the action of BP-lowering drugs, or directly contribute a pressor effect. These drugs are listed tabulated below. Enquiry about concomitant medications is an important part of the evaluation of resistant hypertension.

Concomitant medications/drugs that may contribute to the development of resistant hypertension.
Oral contraceptive Pill
Non-steroidal anti-inflammatory drugs (NSAIDs)
Sympathomimetic agents (e.g. decongestants in proprietary cold remedies)
Immunosupressants – Corticosteroids, Cyclosporine
Erythropoietin
Migraine therapy: ergot derivatives, triptans
Drug abuse (e.g. cocaine, amphetamines)
Excess liquorice ingestion
Herbal remedies (e.g. ephedra also known as ma huang)

3.6. Exclude secondary causes of hypertension.

Comprehensive exclusion of secondary causes of hypertension is mandatory prior to renal denervation. Even if a careful history and evaluation has been previously undertaken when hypertension was first diagnosed, the sudden emergence of resistant hypertension in a patient previously well controlled may signal a new secondary cause on a background of previous primary hypertension.

Renal denervation should not be used to treat resistant hypertension due to a secondary cause where a known alternative remedy exists as there is no trial data on this group of patients.

4. Selection for renal denervation.

Following the assessment and therapeutic strategy outlined above a truly resistant patient may be considered for renal denervation if they fulfil the following criteria:

- Sustained clinic BP >160 mm Hg confirmed to be greater than 150 mm Hg daytime average on ambulatory BP recording (equivalent to a clinic blood pressure ≥ 150 mm Hg and confirmed by a daytime average >140 mm Hg on ABPM in patients with Type 2 Diabetes).
- In the trials an estimated GFR >45ml/min/1.73m^2 was used [1,2]. If patients with lower estimated GFRs are considered for this procedure then this should be in consultation with a nephrologist.
- On three or more medications and with proven deployment of step 4 therapies from the NICE CG127 Treatment algorithm for hypertension [5].
- Exclusion of non-concordance.
- Exclusion of white coat hypertension.
- Exclusion of secondary causes.
- Suitable renal artery anatomy: usually 1 main renal artery to each kidney >20 mm in length and >4 mm in diameter without significant stenosis or other abnormality.
- Patient is fully informed and has given written and verbal consent to treatment.

Adequate pre-procedural imaging of the renal artery should be undertaken. If available previous imaging should be reviewed and further imaging performed if considered appropriate by the Interventionalist who is considering performing renal denervation. There are cases where two renal arteries supplying a single kidney have been treated. In the event of a second artery to a

single kidney being treated its diameter and length should meet the criteria above. In the Symplicity HTN-2 trial, patients with pre-existing renal artery stenting were excluded.

5. Patient care and the renal denervation procedure.

Any institution carrying out the procedure should have in place:

1. A process for determining suitability for renal denervation including a multi-disciplinary team and specified care pathway. The multi-disciplinary team must include hypertension specialists who can demonstrate active involvement in the routine investigation and care of patients with resistant hypertension, interventional cardiologists and/or radiologists trained in the procedure and competent to manage complications such as dissection of the renal artery. Renal specialist advice should also be available.
2. Written protocols for procedural care, including contingency plans to cope with any of the complications of the procedure.
3. Commitment and capability to include data in a National Registry.
4. Local agreement from relevant clinical governance committee.

6. Pre-Procedure care of the patient.

Patient materials including key elements of consent and lay descriptions of the procedure are included for use in appendix 2.

After appropriate patient selection as detailed above, patients undergoing renal denervation should be counselled for the procedure. A full explanation of the procedure and associated risks should be included. These risks include:

- Most patients experience loin or para-umbilical pain during the ablation and this is minimised and in many cases prevented by administration of conscious sedation and analgesia both before and during the procedure.

- Complications of femoral arterial puncture requiring invasive treatment (1:200 needing repair or have major bleeding).

- Significant renal artery dissection requiring treatment is very rare.

- Risk of failure to respond to renal denervation in 10-15% of cases.

- Risk of post-procedure hypotension (approximately 1%).

Patients with conscious sedation should be fasted for four hours and well-hydrated before the procedure and have an intravenous cannula inserted.

Before the procedure the patient should have analgesic and sedative premedication (usually with midazolam and opiate with anti-emetics) according to local procedures.

7. The renal denervation procedure.

Renal artery anatomy must be fully delineated prior to selection for renal denervation, using Competerised Tomography (CT) or Magnetic Resonance (MR) imaging.

Renal denervation should be performed in an interventional angiography suite with ECG, haemodynamic and oxygen saturation monitoring and full cardiovascular resuscitation facilities.

The dispersive electrode should be attached to the patient's lower limb. Atropine and intravascular nitrate therapy should be readily available.

Standard interventional techniques are used to access the femoral artery.

Angiography may be performed allowing the renal artery anatomy to be further defined and the treatment targets identified. Multiple renal arteries can be treated but it is not recommended to treat arteries of less than 4 mm in diameter.

Heparin is administered in doses sufficient to maintain anticoagulation during the procedure. ACT monitoring is recommended.

A guide catheter or sheath is placed in the renal artery and intra-arterial nitrate is delivered into the artery.

The denervation catheter is then introduced through the guide catheter and placed in the artery. The denervation catheter electrode is positioned in contact with the vessel wall at the desired location using fluoroscopic guidance. With the available technology, the generator is pre-programmed with an automated algorithm to provide the desired power level and duration of treatment. The generator is activated by the operator and treatment is delivered to the site.

Multiple treatments at positions along the renal artery are performed. Each individual treatment last for two minutes and are performed distal to proximal along the renal artery in a helical pattern. It is recommended that 4-6 treatments are delivered to each renal artery.

In accordance with the current evidence RF energy should not be delivered in the immediate area of a branch artery or within 0.5 cms of the ostia of the renal artery.

The catheter is then removed from the guide, cleaned and then used to treat the other kidney in the same fashion.

Delivery of RF energy is almost always accompanied by pain in the abdomen and loin and regular re-administration of analgesia and sedation may be required throughout the procedure to minimise patient discomfort.

The femoral sheath is removed as per standard interventional practice with haemostasis either by manual compression or by a closure device.

8. Post-procedure care of the patient.

After the procedure the patient should be carefully monitored with regular measurement of BP (as per registry requirement). The overwhelming majority of patients with successful procedures show a gradual decline in BP over the succeeding weeks and months. Occasionally there may be significant early drops in BP requiring modification of antihypertensive medication but most patients should be discharged on their usual medication. For the majority of patients this improves control of BP but thus far it is rare that patients have been able to reduce use of anti-hypertensive drugs. Up to 15% of those treated in the Symplicity Programme did not respond to therapy but the precise reason for this and how to predict it remain an area of research. Patients may be treated either as day cases or kept in for one night depending on local protocols.

It is rare for patients to experience post procedure pain. However, there is one case of loin pain post-procedure. All patients should be encouraged to report pain and simple analgesia can be used as appropriate.

Patients should have an early out-patient review with their hypertension specialist.

9 UK Registry for renal denervation.

We recommend that a UK Registry for Renal Denervation be established and hosted at the National Institute for Cardiovascular Outcomes Research, which has a track record of developing, hosting and fostering research across a range of UK registries. www.ucl.ac.uk/nicor/

This is supported by the Joint Stakeholder Societies who have contributed to this consensus statement.

This Registry will be designed to facilitate development of metrics of Clinical Effectiveness and Outcomes. In addition it is envisaged that the Registry will enable the UK to undertake Observational Cohort and Randomised Controlled Trial Research to establish the role of this procedure in settings beyond the current indications above. It will be managed by a steering group comprising representatives of stakeholder societies.

10 Commissioning principles and guidelines.

- The technology is at an early stage of development and it is not yet possible to establish the number of patients that might benefit from the procedure with any certainty.
- Widespread commissioning is not currently justified without further efficacy and safety data in larger groups of patients.
- However, resistant hypertension is a significant problem for many patients and results in considerable mortality, morbidity and healthcare costs.
- There is a clinical case for offering renal denervation to a selected group of patients within the NHS. Careful selection of patients with truly resistant hypertension for whom no other therapeutic option exists is required.

- We strongly recommend commissioning a limited volume of activity to establish an initial UK experience and to assist in the collection of further data to assess better the safety and efficacy of the procedure. At present, this would be best suited to inclusion in a national specialist commissioning strategy.

- There should be a sensible geographic distribution of centres that are commissioned (so that there are no regional or post code differences in access to this technology). Criteria are suggested below that will help commissioners identify providers who should be supported.

- The selection of appropriate patients is demanding and requires specialist input from teams with experience in the management of resistant hypertension. Commissioned centres should have a multidisciplinary team which includes hypertension specialists and interventional cardiologists/radiologists.

- Patients should not be selected by any individual specialty. Patient evaluation and selection must be through a structured MDT process to include hypertension specialists and two or more interventional radiologists/cardiologists with the appropriate skills and interests.

- There should be formal training of the team which should include:

    a. Didactic theoretical training.

    b. A visit to an experienced centre to observe renal denervation.

    c. Support for the initial cases at any site by a proctor or clinical specialist.

    d. Simulator training if available.

- All activity must be captured via centralised data collection via a Joint Societies national database hosted by NICOR. A suggested dataset for collection is detailed in appendix 1.

Centres wishing to undertake renal denervation for resistant hypertension would need to demonstrate:

1. Significant experience in the management of resistant hypertension.
2. High volume interventional radiology/cardiology experience.
3. A written protocol for the renal denervation procedure including contingency plans for the management of any complications.
4. Availability of high quality CT/MR imaging.

5. A business plan commitment from the hospital management team to support the programme, along with local Healthcare Governance arrangements.
6. Commissioner agreement for a designated number of procedures.
7. Catheter laboratory availability to support the programme.
8. Implementation team made up of at least two operators (interventional radiologists/cardiologists) who are dedicated to the programme.
9. An MDT to be made up of: hypertension specialist (s) with experience in managing resistant hypertension and interventional cardiologist(s)/radiologists with experience of the renal denervation procedure. There should be access to nephrologists and vascular surgery.
10. Demonstrable compliance with national data submission to the Registry hosted by NICOR and overseen by the stakeholder societies.

11. Research areas for renal denervation.

A number of new applications have been proposed for renal denervation. At this time the Joint Societies' view is that they remain research questions. In some cases there are preliminary data from observational studies or limited case series but further definitive evidence based on randomised controlled trials are needed before statements relating to use could be formulated.

There may sometimes be special cases on the basis of individual need or compassionate grounds. These should be evaluated under the usual procedures for clinical governance in such settings.

References:

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Appendix 1. Patient materials:

Renal artery denervation.

You are being invited to have a procedure called renal artery denervation. This is a very new procedure. Recent research shows that this can be an effective treatment for people with very high blood pressure (hypertension) which has been difficult to control with normal medications. However, our understanding of how renal artery denervation works is not complete, and the long-term effects (beyond about three years) are not known. Because of this we think it important you spend a few minutes reading this information leaflet carefully and discuss it with others if you wish.

Why have you been invited to have renal artery denervation?
You have very high blood pressure even though you are taking a powerful combination of blood pressure lowering tablets. This high blood pressure is putting you at an increased risk of suffering a stroke, heart attack, or other vascular event. The team of doctors involved in your care think that you may benefit from renal denervation. So far the patients who seem to benefit are those with a systolic (the 'top' number) blood pressure greater than 160mmHg despite treatment with three or more medications.

What is the background to this procedure?
High blood pressure is one of the most common and preventable causes of premature heart disease, kidney disease and stroke in the UK. About 1 in 4 adults and more than half of those over 60 years old are affected.

The cause of the majority of cases of high blood pressure is not fully understood and is generally described as 'essential hypertension'. A number of different factors are known to be important, including an increase in salt retention and a reduction in kidney blood flow partly affected by nerves involved in 'stress' responses (the sympathetic nervous system).

What is standard treatment for high blood pressure?
The standard treatment for high blood pressure in the United Kingdom is a combination of drugs/medicines, plus lifestyle changes such as reducing salt in the diet, increasing exercise and losing weight where appropriate.

Despite treatment, in about half the patients taking medication for high blood pressure their blood pressure will be higher than desirable.

There are a number of possible reasons for this which include:

1. Inadequate drug treatment (not enough, or types of medicines used that might not be the best in your case).

2. Not taking the tablets regularly or in the amounts suggested by your doctor.

3. "Special" causes of high blood pressure, so called secondary hypertension.

Before having the renal denervation procedure done, both you and your blood pressure doctor should be convinced that none of these other causes could explain how difficult your blood pressure is to control.

Renal denervation will **not** allow you to stop taking drugs to lower your blood pressure: you will almost certainly need to continue taking your current drug treatment after the procedure.

A variety of tests will have been done already to best exclude these other potential causes. Your doctor will know about the drug treatment you are prescribed, but you know best how faithfully you take your tablets. Your doctor may ask for you to come to clinic to have a witness watch you take your tablets and measure your blood pressure over a few hours to make sure that you really are taking your pills and to assess their effectiveness.

If you have any problems with taking your tablets regularly please discuss them with your doctor. This is really important because controlling your blood pressure with drugs has proved to be very safe and effective over the last 50 years. Good blood pressure control with drugs prevents many heart attacks, strokes and deaths.

Renal artery denervation has been shown to be effective at lowering blood pressure in two medical trials in appropriately selected patients. Whether this treatment is appropriate for all patients is not clear. NICE, the body that advises doctors on treatments in England and Wales, has recommended that where renal artery denervation is carried out as a treatment for high blood pressure, the results should be collected, for research, to assess safety and check outcomes. No separate guidelines have been issued for Scotland. We would like you to agree to share some of your information on how you get on with the procedure with a UK registry. Your details will all be anonymised and any personal information will be kept confidential according to normal NHS rules. You can choose not to have your data on the National Registry.

What does renal artery denervation involve?

Most people have two kidneys, each of which is supplied with blood through an artery (the renal artery). On the outside of these renal arteries are very fine nerves (renal sympathetic nerves) which carry signals between the kidney and the brain. These are the nerves we are trying to interrupt. Kidneys seem to work perfectly well doing their normal job, removing waste products and excess water from the body, without these nerves- as they do in patients with transplanted kidneys. We have known for many years that cutting these nerves can reduce blood pressure but it has not been practical to do this until very recently.

The new method of renal artery denervation uses a special wire fed up inside the artery from the groin. High frequency energy is used to heat the wall of the artery from the inside and this heating slowly kills the fine nerves that run along the outside of the artery.

The procedure is usually done under local anaesthetic and conscious sedation, which is a sedative drug(s) that makes you feel quite drowsy and relaxed but not asleep. After injection of local anaesthetic into the skin of your groin over the femoral artery (the main artery to your leg) a tube will be fed into the artery and through this a catheter (fine tube) is advanced into the renal artery under X-ray control. A dye is injected through the catheter to confirm the position inside the artery. A special wire is then fed through the catheter and high frequency energy delivered to heat the wall of the artery from the inside. The right amount of energy is used to make sure that the artery wall does not get too hot and damage the artery itself. Each of your arteries takes about 8-10 minutes to treat.

Pain and pain control.
During the energy bursts to the nerves many patients feel some pain or discomfort in the back or loin area. You will have been given powerful pain killers in advance and more will be given if necessary so that the discomfort is minimised. Your team will ask you how it feels during the treatments to make sure you get enough pain-killer. In a way the pain is a sign that the wire is in the right place, because it comes from the same nerves that we are trying to destroy. This discomfort usually passes quite quickly once the treatment has been completed.

Is renal artery denervation safe?
This is a fairly new technique and the information available so far indicates it is very safe. No-one has died and there has been no documented lasting damage to a kidney. The commonest side effects include bruising at the groin and on the abdomen or loin.

Other rare but potentially more serious side effects that have been described are:

1. Damage to the renal artery. One case has been reported and this can usually be dealt with by placing a stent in the damaged artery (like an internal scaffold or spring to keep it open).
2. Persistent abdominal pain lasting beyond the time of the procedure.
3. Low heart rate which usually settles.
4. Large drop in blood pressure. This may require you to stay in hospital for a few days to sort out your medication.
5. Damage to the artery in the groin. This occurs about 1% of the time and can require you to need a blood transfusion or rarely a small procedure or operation to the artery.

Other possible side effects that have not been seen with renal denervation, but which can occur after any procedure where an artery is catheterised include an allergic reaction to the x-ray dye, or the x-ray dye can damage kidney function. Very rarely the groin artery is damaged so badly that the leg is threatened.

Potential side effects from renal denervation that have NOT been seen yet, but might be seen in future, include narrowing of the renal artery, loss of the kidney(s), loss of water and salt control in the body and blood in the urine.

Your doctor will discuss these potential side effects with you in more detail.
There is an additional risk associated with the exposure to a small amount of radiation required for performing the renal artery denervation procedure. As part of everyday living everyone is exposed to naturally occurring background radiation and receives about 2 millisievert (mSv) each year. The effective dose from the renal artery denervation procedure is approximately 6.5mSv, comparable to that received from many other diagnostic medical x-ray procedures. This extra radiation therefore represents an additional risk of lifetime fatal cancer of 1 in 3,000. The normal lifetime risk of fatal cancer is currently 1 in 5 so it can be seen that the extra risk with the renal artery denervation procedure is very small.

What do the steps I have to go through for the renal denervation procedure?

Tests and imaging that is needed.
Your doctor will already have extensively investigated you for other causes of hypertension with a variety of scans and blood tests. These will include tests of the heart and kidneys.

You will require a CT scan or MRI scan of your kidney arteries to make sure you are suitable for this procedure. Prior to your admission your team of doctors will discuss this with you and check that all has been done and that they are in agreement that renal denervation is an appropriate option for you.

Admission to hospital.
Usually you will come in to the hospital ward on the day of the procedure. The procedure will be undertaken by a specially trained doctor (either an interventional radiologist or cardiologist). Following the procedure you will have to lie flat for a couple of hours and if all is well, go home later on the same day. You will be followed up in the clinic by your blood pressure specialist and initially stay on all your medications.

Patients may stay in hospital overnight following the procedure. If there are any clinical concerns regarding kidney function, high or low blood pressure, the hospital stay may be extended until the supervising doctor is satisfied that the patient is ready to be discharged from hospital (routine practice).

Finally, thank you for taking the time to read this information leaflet.

Appendix 2: Data requirements for inclusion in The UK Renal Denervation registry.

The Dataset Working Group will establish the core dataset adapting principles from similar registries providing NHS Clinical Effectiveness data and a Research Working Group will establish a dataset for areas of research endeavour aiming for maximal data capture.

The principles of working here parallel closely those for TAVI and other CV interventional procedures.

The Joint Societies will work with NICOR to establish a database for use in all hospitals providing this treatment.

This section will be updated in subsequent issues.

Appendix 3. Affiliations and disclosures.

Name	Affiliation	Disclosures
Prof Mark Caulfield	Barts and The London NIHR Cardiovascular Biomedical Research Unit and the William Harvey Research Institute, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, London EC1M 6BQ.	President of the British Hypertension Society 09-11. NICE Guideline Development Group for Hypertension CG127. Symplicity HTN 2 investigator. Co-organiser of 1st UK renal denervation symposium (Unrestricted educational grant from Medtronic) Honoraria from Medtronic for speaking at Proctorship day and advise on Health Economics
Dr Mark A. de Belder	Consultant Cardiologist, The James Cook University Hospital, Marton Road, Middlesbrough, TS4 3BW	President of the British Cardiovascular Intervention Society.
Dr Trevor Cleveland	Consultant Vascular Radiologist, Sheffield Vascular Institute, Sheffield Teaching Hospitals NHSFT, Northern General Hospital, Sheffield S5 7AU.	Chair, Communications Committee, British Society of Interventional Radiology.
Dr David Collier	Barts and The London NIHR Cardiovascular Biomedical Research Unit and the William Harvey Research Institute, (as above)	None
Prof John Deanfield	The National Institute for Cardiovascular Outcomes Research, University College London	Director of NICOR
Prof Huon Gray	Consultant Cardiologist, Wessex Regional Cardiac Unit, University Hospital Southampton, Southampton. SO16 6YD	Deputy National Director for Heart Disease (2007-11), and Member of Executive Board, National Institute for Cardiovascular Outcomes Research.

Name	Affiliation	Disclosures
Dr Charles Knight	Director of Cardiovascular Clinical Academic Unit, Barts and The London NHS Trust, London Chest	Secretary of the British Cardiovascular Society 2009-11.
Dr Mel Lobo	Barts and The London NIHR Cardiovascular Biomedical Research Unit and Barts and The London NHS Trust.	Symplicity HTN 2 investigator. Co-organiser of 1st UK renal denervation symposium (Unrestricted educational grant from Medtronic) Honoraria from Medtronic for speaking at Proctorship day
Dr Matthew Matson	Barts and The London NIHR Cardiovascular Biomedical Research Unit and Barts and The London NHS Trust.	Honoraria from Medtronic for speaking at Proctorship day
Prof Jon Moss	Interventional Radiology Unit, Gartnavel General Hospital, Glasgow G12 OYN	Symplicity HTN 2 investigator
Prof Neil Poulter	International Centre for Circulatory Health, Imperial College, London	Past President British Hypertension Society Chair of British Hypertension Society Information and Guidelines Working Party
Dr Iain Simpson	Consultant Cardiologist, Wessex Regional Cardiac Unit, University Hospital Southampton, Southampton SO16 6YD	President-Elect of the British Cardiovascular Society
Dr Charles Tomson	Consultant Renal Physician, North Bristol NHS Trust, Southmead Hospital, Bristol, BS10 5NB.	President of the Renal Association
Prof Bryan Williams	Cardiovascular Sciences University of Leicester & NIHR Cardiovascular Biomedical Research Unit, Glenfield Hospital, Leicester, LE3 9QP	Chairman NICE Guideline Development Group for Hypertension CG127 2010-11.

Appendix 4 – Supporting Educational Materials for Health Professionals.

This originated from a Joint Societies Meeting following the 1st UK Renal Denervation Symposium followed by drafting with meetings on 15th and 30th November 2011 to keep in step with production of a NICE Interventional Procedure Guidance. To view presentations from the 1st UK Renal Denervation Symposium these are hosted on the British Hypertension Website. If you press ctrl and right click on the You Tube icon this takes you direct to the presentations alternatively visit http://www.bhsoc.org

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1st UK Symposium on Renal Denervation

Royal College of Physicians, London
Wednesday 5th October 2011

Session	Title	Speaker	Link
1	Introduction	**Prof Mark Caulfield and Dr Mel Lobo**	You Tube
1	Hypertension Epidemiology and Current Treatment Challenges	**Prof Francesco Cappuccio**	You Tube
1	Hypertension for Primary Care	**Prof Mark Caulfield**	You Tube
1	Resistant Hypertension and the Role of the Sympathetic Nervous System	**Prof Bryan Williams**	You Tube
1	Renal Denervation - Fundamentals of the procedure	**Dr Charles Knight**	You Tube
1	Renal Denervation Tips and Tricks	**Matthew Matson**	You Tube
1	Session 1 Panel		You Tube
2	Autonomic Nervous System Assessment Pathophysiology and Pre-Clinical Clinical Trial Data	**Prof. Murray Esler**	You Tube
2	RDN Clinical Trials Review and Q & A	**Dr Mel Lobo**	You Tube
2	Other Potential Indications for RDN	**Prof Murray Esler**	You Tube
2	Session 2 Panel		You Tube
3	Renal denveration in clinical practice Patient selection and post-operative medical management	**David Collier Manish Saxena and Fred Quatromini**	You Tube
3	Difficult Cases and Potential Complications	**Horst Sievert Ann-Kathrin Ziegler Ilona Hofmann**	You Tube
3	Session 3 Panel		You Tube

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Appendix 5. The following websites host the statement:

http://www.bhsoc.org/docs/Joint-UK-Societies-Summary-on-Renal-Denervation.pdf

http://www.bcs.com/pages/news_full.asp?NewsID=19792021

http://www.bsir.org/content/BSIRPage.aspx?pageid=787