FirstChoice VIP CARE
by Select Health of South Carolina

Renal denervation

Clinical Policy ID: CCP.1283

Recent review date: 1/2025

Next review date: 5/2026

Policy contains: Renal sympathetic ablation; renal denervation; treatment-resistant hypertension.

FirstChoice VIP Care has developed clinical policies to assist with making coverage determinations. FirstChoice VIP Care's clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of "medically necessary," and the specific facts of the particular situation are considered, on a case by case basis, by FirstChoice VIP Care when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. FirstChoice VIP Care's clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. FirstChoice VIP Care's clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, FirstChoice VIP Care will update its clinical policies as necessary. FirstChoice VIP Care's clinical policies are not guarantees of payment.

Coverage policy

Renal denervation for treatment-resistant hypertension is investigational/not clinically proven and, therefore, not medically necessary.

Limitations

No limitations were identified during the writing of this policy.

Alternative covered services

- Medically prescribed antihypertensive therapy.
- Standard medical treatment of underlying disorders.

Background

Hypertension is largely viewed as a major modifiable risk factor associated with mortality. The sympathetic nervous system is activated in stressful or emergency situations and often referred to as the fight-or-flight response. The kidneys play a major role in the response by increasing secretion of renin to activate a chemical chain reaction that changes the hemodynamic system of the body and provides the protective physiological response needed for a person to react. The systemic effects include arterial blood vessel constriction, increased heart rate, dilated pupils, and elevation of blood pressure (Sarathy, 2021).

Sympathetic hyperactivity-mediated resistant hypertension has been associated with multiple conditions, including but not limited to stroke, obstructive sleep apnea, metabolic syndrome, myocardial hypertrophy and

heart failure, and cardiac dysrhythmias (Böhm, 2014; Hou, 2018; Sarathy, 2021). Renal injury or hypoxia can further result in systemic and renal sympathetic activity (Hou, 2018).

Renal denervation, also referred to as endovascular renal sympathetic ablation, is a minimally invasive percutaneous procedure that applies radiofrequency or focused ultrasound via a catheter inserted through the femoral artery to selectively engage the sympathetic nerve fibers surrounding the renal artery. The desired result is to interrupt the influence of the sympathetic reflexes on the kidney and systemic hemodynamics and provide a simple solution to the complex issue of hypertension (Azizi, 2023).

The procedure usually takes from 45 to 60 minutes when a single catheter is used, or less time with a multi-electrode or balloon catheter. Analgesia and sedation are required. Renal denervation has been proposed as a non-pharmacologic treatment for treatment-resistant hypertension, which is common in patients with pre-existing comorbid atherothrombotic disease and obesity, and for other sympathetically-driven conditions (Böhm, 2014).

In 2023, two renal denervation devices received pre-market approval for clinical use in the United States: Symplicity Spyral™ Renal Denervation System and Paradise® Ultrasound Renal Denervation System (U.S. Food and Drug Administration, 2023a, 2023b).”).

Findings

Guidelines:

Guidelines and consensus recommendations have consistently identified renal denervation as a potential adjunctive therapy for patients with resistant or uncontrolled hypertension, albeit with caution and calls for further evidence. Position statements from the Society for Cardiovascular Angiography and Interventions reported that modest systolic blood pressure reductions of about 10 mm Hg can yield a 20% relative risk reduction in cardiovascular events, but also noted that approximately one-third of patients do not respond meaningfully to the therapy (Swaminathan, 2023).

The American Heart Association highlighted an average systolic blood pressure reduction of about 5 to 10 mm Hg, with approximately 60% to 70% of patients achieving at least a 5 mm Hg decrease by two to three months. Longer-term data from a global registry indicated sustained reductions of approximately 16 mm Hg in office measurements and 8 mm Hg by ambulatory monitoring over three years, with serious adverse events typically under 1% and no meaningful decline in renal function (Cluett, 2024; Carey, 2018). The European Society of Cardiology Council on Hypertension and the European Association of Percutaneous Cardiovascular Interventions cited durable 24-hour blood pressure reductions of clinically meaningful magnitude over up to three years without significant renal complications (Barbato, 2023).

Regulatory bodies have taken more conservative positions. The National Institute for Health and Care Excellence advised that percutaneous transluminal renal sympathetic denervation be performed only with specific governance, consent, and audit arrangements due to uncertainties in long-term benefit (NICE, 2023). Hypertension Canada did not recommend routine use, as the device was not approved in Canada, and advised that the procedure be limited to controlled clinical investigations (Hiremath, 2020).

Systematic Reviews:

A number of systematic reviews and meta-analyses have quantified the blood pressure-lowering effects of renal denervation, though effect sizes and consistency have varied. A meta-analysis of second-generation sham-controlled trials (n=1622) found statistically significant reductions in 24-hour ambulatory systolic blood pressure by -3.72 mm Hg (95% CI -5.44 to -2.00; $p<0.001$) and daytime systolic blood pressure by -4.10 mm Hg (95% CI -5.84 to -2.37; $p<0.001$). Reductions in office systolic blood pressure were also statistically significant in this analysis (-6.04 mm Hg, 95% CI -11.31 to -0.78; $p=0.024$), though the effect was less pronounced than for

ambulatory measures; nighttime reductions did not reach statistical significance (Dantas, 2024). Another quantitative review of 15 randomized studies (n=2581) also reported statistically significant reductions in systolic and diastolic blood pressure across ambulatory, office, and home measurements (Mufarrih, 2024). A comprehensive systematic review analyzing 25 randomized controlled trials (16 included, n = 2268) demonstrated clinically meaningful reductions in office and ambulatory systolic blood pressure across multiple subgroups (Sharp, 2024). Similarly, a meta-analysis focusing on ultrasound-based renal denervation reported mean systolic and diastolic reductions of approximately 2 to 4 mm Hg across office, daytime, nighttime, and home measurements (Maia, 2024).

Other syntheses have yielded more mixed results. A systematic review and meta-analysis of six studies (n=989) found no statistically significant difference in 24-hour ambulatory or office blood pressure compared to sham, with low certainty of evidence (Ahmed, 2023). Earlier systematic reviews and meta-analyses offered inconsistent support for renal denervation in treatment-resistant hypertension (Fadl Elmula, 2015; Shafi, 2016) and for related conditions such as Type 2 diabetes and obstructive sleep apnea (Pan, 2015; Shantha, 2015). A Cochrane review reported low- to moderate-quality evidence that did not clearly support long-term benefits (Coppolino, 2017). Additional meta-analyses published subsequently confirmed that renal denervation could safely reduce blood pressure compared to sham, but noted challenges with medication adherence and the need for improved trial design (Agasthi, 2019; Cheng, 2019; Liu, 2019; Lobo, 2019).

Randomized Controlled Trials and Device-Specific Evidence:

Randomized controlled trials have shown varied results, influenced by population characteristics, procedural techniques, and study design. The foundational SYMPLICITY trials established early evidence for renal denervation. SYMPLICITY HTN-1 (n=45) and SYMPLICITY HTN-2 (n=106) reported significant short- to medium-term office-based systolic blood pressure reductions, though these effects were smaller or inconsistent when assessed with ambulatory monitoring (Krum, 2014; Esler, 2014). The larger, sham-controlled SYMPLICITY HTN-3 trial (n=535) met safety endpoints with a major adverse event rate of only 1.4%, but failed to demonstrate statistically significant differences in blood pressure reduction compared to the sham group (Bakris, 2014; Bhatt, 2014). These studies indicated that baseline blood pressure, patient characteristics such as ethnicity and renal function, and technical proficiency might affect outcomes, prompting calls for improved trial designs and methodology (Lobo, 2015; White, 2014).

More recent trials have examined novel technologies, particularly the Paradise Ultrasound Renal Denervation System. The RADIANCE-HTN SOLO, TRIO, and RADIANCE II trials demonstrated significant reductions in daytime ambulatory systolic blood pressure at two months compared to sham, with a pooled difference of -5.9 mm Hg (95% CI -8.1 to -3.8; $p<0.001$) across the three cohorts (Azizi, 2018, 2019, 2021, 2022, 2023; Kirtane, 2023). These reductions persisted at six months, sometimes with fewer antihypertensive medications. However, the REQUIRE study (n = 143) in Japan and South Korea did not find a significant difference at three months compared to sham, potentially due to unexpected blood pressure reductions in the control group (Kario, 2022). Ongoing RCTs (SPYRAL HTN-OFF MED Pivotal and SPYRAL HTN-ON MED Expansion) are designed to address prior limitations and clarify the efficacy of renal denervation (Böhm, 2020).

Other Study Types:

Observational studies and registries have generally reported durable blood pressure reductions and favorable safety profiles. Data from global registries have shown sustained office-based systolic blood pressure reductions of approximately 16 mm Hg and ambulatory reductions of about 8 mm Hg over three years, with serious adverse events typically under 1% and no meaningful renal function deterioration (Cluett, 2024; Lee, 2019; Rodriguez-Leor, 2020; Naduvathumuriyil, 2020). Cost-effectiveness analyses, such as one by Geisler (2012), suggested potential economic value if these blood pressure reductions translate into fewer cardiovascular events. However,

without definitive evidence linking renal denervation to improved long-term outcomes (e.g., stroke, myocardial infarction, heart failure), cost-effectiveness remains theoretical.

In 2025, we reorganized the findings section thematically and by evidence type. No Policy changes were warranted.

References

On December 6, 2024, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were “renal denervation,” “ablation,” “sympathectomy,” and “treatment resistant hypertension.” We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

Agasthi P, Shipman J, Arsanjani R, et al. Renal denervation for resistant hypertension in the contemporary era: A systematic review and meta-analysis. *Sci Rep.* 2019;9(1):6200. Doi: 10.1038/s41598-019-42695-9.

Ahmed M, Nudy M, Bussa R, Filippone EJ, Foy AJ. A systematic review and meta-analysis of all sham and placebo controlled trials for resistant hypertension. *Eur J Intern Med*. 2023;113:83-90. Doi: 10.1016/j.ejim.2023.04.021.

Azizi M, Mahfoud F, Weber MA, et al. Effects of renal denervation vs sham in resistant hypertension after medication escalation: Prespecified analysis at 6 months of the RADIANCE-HTN TRIO randomized clinical trial. *JAMA Cardiol*. 2022;7(12):1244-1252. Doi: 10.1001/jamacardio.2022.3904.

Azizi M, Sanghvi K, Saxena M, et al. Ultrasound renal denervation for hypertension resistant to a triple medication pill (RADIANCE-HTN TRIO): A randomised, multicentre, single-blind, sham-controlled trial. *Lancet (London, England)*. 2021;397(10293):2476-2486. Doi: 10.1016/s0140-6736(21)00788-1.

Azizi M, Saxena M, Wang Y, et al. Endovascular ultrasound renal denervation to treat hypertension: The radiance II randomized clinical trial. *JAMA*. 2023;329(8):651-661. Doi: 10.1001/jama.2023.0713.

Azizi M, Schmieder RE, Mahfoud F, et al. Endovascular ultrasound renal denervation to treat hypertension (RADIANCE-HTN SOLO): A multicentre, international, single-blind, randomised, sham-controlled trial. *Lancet (London, England)*. 2018;391(10137):2335-2345. Doi: 10.1016/s0140-6736(18)31082-1.

Azizi M, Schmieder RE, Mahfoud F, et al. Six-month results of treatment-blinded medication titration for hypertension control after randomization to endovascular ultrasound renal denervation or a sham procedure in the RADIANCE-HTN SOLO trial. *Circulation*. 2019;139(22):2542-2553. Doi: 10.1161/circulationaha.119.040451.

Bakris GL, Townsend RR, Liu M, et al. Impact of renal denervation on 24-hour ambulatory blood pressure: results from SYMPLICITY HTN-3. *J Am Coll Cardiol.* 2014;64(11):1071-1078. Doi: 10.1016/j.jacc.2014.05.012.

Barbato E, Azizi M, Schmieder RE, et al. Renal denervation in the management of hypertension in adults. A clinical consensus statement of the ESC council on hypertension and the European Association of Percutaneous Cardiovascular Interventions (EAPCI). *Eur Heart J*. 2023;44(15):1313-1330. Doi: 10.1093/eurheartj/ehad054.

Bhatt DL, Kandzari DE, O'Neill WW, et al. A controlled trial of renal denervation for resistant hypertension. *N Engl J Med.* 2014;370(15):1393-1401. Doi: 10.1056/NEJMoa1402670.

Böhm M, Linz D, Ukena C, Esler M, Mahfoud F. Renal denervation for the treatment of cardiovascular high risk-hypertension or beyond? *Circ Res.* 2014;115(3):400-409. Doi: 10.1161/circresaha.115.302522.

Böhm M, Townsend RR, Kario K, et al. Rationale and design of two randomized sham-controlled trials of catheter-based renal denervation in subjects with uncontrolled hypertension in the absence (SPYRAL HTN-OFF MED pivotal) and presence (SPYRAL HTN-ON MED expansion) of antihypertensive medications: A novel approach using Bayesian design. *Clin Res Cardiol.* 2020;109(3):289-302. Doi: 10.1007/s00392-020-01595-z.

Carey RM, Calhoun DA, Bakris GL, et al. Resistant hypertension: Detection, evaluation, and management: A scientific statement from the American Heart Association. *Hypertension.* 2018;72(5):e53-e90. Doi: 10.1161/HYP.0000000000000084.

Cheng X, Zhang D, Luo S, Qin S. Effect of catheter-based renal denervation on uncontrolled hypertension: A systematic review and meta-analysis. *Mayo Clin Proc*. 2019;94(9):1695-1706. Doi: 10.1016/j.mayocp.2019.07.005.

ClinicalTrials.gov. A study of the ReCor Medical Paradise system in clinical hypertension (RADIANCE-HTN). ClinicalTrials.gov identifier NCT02649426. https://www.clinicaltrials.gov/study/NCT02649426?cond=hypertension&term=Radiance&rank=2. Last updated August 29, 2022.

ClinicalTrials.gov. RADIANCE II Pivotal Study: A study of the ReCor Medical Paradise System in stage II hypertension (RADIANCE-II). ClinicalTrials.gov identifier NCT03614260. https://www.clinicaltrials.gov/study/NCT03614260?cond=hypertension&term=Radiance&rank=3. Last updated June 22, 2023.

ClinicalTrials.gov. Renal denervation on quality of 24-hr BP control by ultrasound in resistant hypertension (REQUIRE). ClinicalTrials.gov identifier NCT02918305. https://www.clinicaltrials.gov/study/NCT02918305?term=NCT02918305&rank=1. Last updated November 19, 2021.

Cluett JL, Blazek O, Brown AL, et al. Renal denervation for the treatment of hypertension: A scientific statement from the American Heart Association. *Hypertension*. 2024;81(10):e135-e148. Doi: 10.1161/HYP.0000000000000240.

Coppolino G, Pisano A, Rivoli L, Bolignano D. Renal denervation for resistant hypertension. *Cochrane Database Syst Rev*. 2017;2:Cd011499. Doi: 10.1002/14651858.CD011499.pub2.

Dantas, C.R., De Oliveira Macena Lôbo, A., De Almeida, A.M. et al. Systematic review and meta-analysis of second-generation sham-controlled randomized trials of renal denervation therapy for patients with hypertension. *High Blood Press Cardiovasc Prev. 2024;* 31, 669–676. Doi:10.1007/s40292-024-00675-9.

Esler MD, Böhm M, Sievert H, et al. Catheter-based renal denervation for treatment of patients with treatment-resistant hypertension: 36 month results from the SYMPLICITY HTN-2 randomized clinical trial. *Eur Heart J.* 2014;35(26):1752-1759. Doi: 10.1093/eurheartj/ehu209.

Fadl Elmula FE, Jin Y, Yang WY, et al. Meta-analysis of randomized controlled trials of renal denervation in treatment-resistant hypertension. *Blood Press.* 2015;24(5):263-274. Doi: 10.3109/08037051.2015.1058595.

Geisler BP, Egan BM, Cohen JT, et al. Cost-effectiveness and clinical effectiveness of catheter-based renal denervation for resistant hypertension. *J Am Coll Cardiol.* 2012;60(14):1271-1277. Doi: 10.1016/j.jacc.2012.07.029.

Hiremath S, Sapir-Pichhadze R, Nakhla M, et al. Hypertension Canada's 2020 evidence review and guidelines for the management of resistant hypertension. *Can J Cardiol.* 2020;36(5):625-634. Doi: 10.1016/j.cjca.2020.02.083.

Hou H, Zhao Y, Yu W, et al. Association of obstructive sleep apnea with hypertension: A systemic review and meta-analysis. *J Glob Health.* 2018;8(1):010405. Doi: 10.7189/jogh.08.010405.

Kario K, Yokoi Y, Okamura K, et al. Catheter-based ultrasound renal denervation in patients with resistant hypertension: The randomized, controlled REQUIRE trial. *Hypertens Res*. 2022;45(2):221-231. Doi: 10.1038/s41440-021-00754-7.

Kirtane AJ, Sharp ASP, Mahfoud F, et al. Patient-level pooled analysis of ultrasound renal denervation in the sham-controlled RADIANCE II, RADIANCE-HTN SOLO, and RADIANCE-HTN TRIO trials. *JAMA Cardiol*. 2023;8(5):464-473. Doi: 10.1001/jamacardio.2023.0338.

Krum H, Schlaich MP, Sobotka PA, et al. Percutaneous renal denervation in patients with treatment-resistant hypertension: Final 3-year report of the Symplicity HTN-1 study. *Lancet.* 2014;383(9917):622-629. Doi: 10.1016/s0140-6736(13)62192-3.

Lee CK, Wang TD, Lee YH, et al. Efficacy and safety of renal denervation for patients with uncontrolled hypertension in Taiwan: 3-year results from the global SYMPLICITY registry-Taiwan (GSR-Taiwan). *Acta Cardiol Sin.* 2019;35(6):618-626. Doi: 10.6515/acs.201911_35(6).20190826a.

Liu LY, Lin PL, Liao FC, et al. Effect of radiofrequency-based renal denervation: The impact of unplanned medication change from a systematic review and meta-analysis. *Acta Cardiol Sin*. 2019;35(2):144-152. Doi: 10.6515/acs.201903_35(2).20181231a.

Lobo MD, de Belder MA, Cleveland T, et al. Joint UK societies' 2014 consensus statement on renal denervation for resistant hypertension. *Heart.* 2015;101(1):10-16. Doi: 10.1136/heartjnl-2014-307029.

Lobo MD, Sharp ASP, Kapil V, et al. Joint U.K. societies' 2019 consensus statement on renal denervation. *Heart*. 2019;105(19):1456-1463. Doi: 10.1136/heartjnl-2019-315098.

Maia JG, Kelly FA, Gonçalves OR, de Moraes FCA, de Sousa MG, Consolim-Colombo FM. Efficacy and safety of ultrasound renal denervation on office blood pressure of patients with resistant arterial hypertension: A systematic review and meta-analysis. *High Blood Press Cardiovasc Prev*. 2024;31(6):657-667. Doi:10.1007/s40292-024-00671-z.

Mufarrih SH, Qureshi NQ, Khan MS, et al. Randomized Trials of Renal Denervation for Uncontrolled Hypertension: An Updated Meta-Analysis. *J Am Heart Assoc*. 2024;13(16):e034910. Doi:10.1161/JAHA.124.034910.

Naduvathumuriyil T, Held U, Steigmiller K, et al. Clinical benefits and safety of renal denervation in severe arterial hypertension: A long-term follow-up study. *J Clin Hypertens (Greenwich).* 2020;22(10):1854-1864. Doi: 10.1111/jch.14005.

National Institute for Health and Care Excellence. Percutaneous transluminal renal sympathetic denervation for resistant hypertension. Interventional procedures guidance [IPG754]. https://www.nice.org.uk/guidance/ipg754/chapter/1-Recommendations. Published March 1, 2023.

Pan T, Guo JH, Teng GJ. Renal denervation: A potential novel treatment for type 2 diabetes mellitus? *Medicine (Baltimore).* 2015;94(44):e1932. Doi: 10.1097/md.0000000000001932.

Rodriguez-Leor O, Segura J, García Donaire JA, et al. Renal denervation for the treatment of resistant hypertension in Spain. The Flex-Spyral Registry. *Rev Esp Cardiol (Engl Ed).* 2020;73(8):615-622. Doi: 10.1016/j.rec.2019.08.001.

Sarathy H, Cohen JB. Renal denervation for the treatment of hypertension: Unnerving of underappreciated? *CJASN.* 2021;(16):1426-1428. Doi: 10.2215/CJN.03070221.

Shafi T, Chacko M, Berger Z, et al. Renal denervation in the Medicare population [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US). https://www.ncbi.nlm.nih.gov/books/NBK390551/. Published July 2016.

Shantha GP, Pancholy SB. Effect of renal sympathetic denervation on apnea-hypopnea index in patients with obstructive sleep apnea: A systematic review and meta-analysis. *Sleep Breath.* 2015;19(1):29-34. Doi: 10.1007/s11325-014-0991-z.

Sharp ASP, Sanderson A, Hansell N, et al. Renal denervation for uncontrolled hypertension: A systematic review and meta-analysis examining multiple subgroups. *J Hypertens*. 2024;42(7):1133-1144. Doi:10.1097/HJH.0000000000003727.

Swaminathan RV, East CA, Feldman DN, et al. SCAI position statement on renal denervation for hypertension: patient selection, operator competence, training and techniques, and organizational recommendations. *J Soc Cardiovasc Angiogr Interv*. 2023;2(6). Doi:10.1016/j.jscai.2023.10112.

U.S. Food and Drug Administration. Premarket approval (PMA): Paradise® ultrasound renal denervation system. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P220023. Last updated November 16, 2023. (a)

U.S. Food and Drug. Premarket approval (PMA): Symplicity Spyral™ Renal Denervation System. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P220026. Last updated December 15, 2023. (b)

White WB, Turner JR, Sica DA, et al. Detection, evaluation, and treatment of severe and resistant hypertension: Proceedings from an American Society of Hypertension Interactive forum held in Bethesda, MD, U.S.A., October 10, 2013. *J Am Soc Hypertens.* 2014;8(10):743-757. Doi: 10.1016/j.jash.2014.06.005.

Policy updates

11/2016: initial review date and clinical policy effective date: 2/2017

1/2018: Policy references updated.

1/2019: Policy references updated and policy ID changed.

1/2020: Policy references updated.

1/2021: Policy references updated.

1/2022: Policy references updated.

1/2023: Policy references updated.

1/2024: Policy references updated.

1/2025: Policy references updated.