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ORIGINAL RESEARCH ARTICLE

Cost-Effectiveness of Ultrasound Renal Denervation for Resistant Hypertension in Belgium, France and The Netherlands

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Abstract

Background Endovascular ultrasound renal denervation (uRDN) with the Paradise System has emerged as an adjunctive treatment option for the management of uncontrolled resistant hypertension (rHTN). This study assesses the cost-effectiveness of uRDN for rHTN across three European countries—Belgium, France and the Netherlands.

Methods On the basis of a previously developed state-transition Markov model, we projected costs, life years (LYs) and quality adjusted life years (QALYs) with the addition of uRDN to standard of care (SoC) compared with SoC alone over patient lifetime. Analyses were based on the RADIANCE-HTN TRIO trial, which demonstrated a mean reduction in office systolic blood pressure from a baseline of 8.5 mmHg at 2 months post-uRDN among patients with rHTN. Mortality and costs data were separately sourced and applied for each country independently. Country-specific discount rates were applied to both cost and outcomes. One-way and probabilistic sensitivity analyses were conducted to assess the uncertainty surrounding the model inputs and sensitivity of the model results to changes in parameter inputs. Results were reported as incremental cost-effectiveness ratios (ICERs).

Results The base-case analyses of the models for all three countries show uRDN plus SoC results in improvement in both LYs and QALYs per patient and higher costs compared with SoC alone. The mean ICERs for each country model fall well below the respective country-specific willingness-to-pay thresholds (WTPs)—Belgium: WTP €40,000 and ICER €4426/QALY gained; France: WTP €50,000 and ICER €6261/QALY gained; and the Netherlands: WTP €20,000 and ICER €1654/QALY gained. Results were robust across scenarios and sensitivity analyses.

Conclusions The addition of endovascular uRDN offers clinicians and payers a cost-effective adjunctive treatment approach alongside hypertensive medication for the management of rHTN in the healthcare systems of Belgium, France and the Netherlands.

1 Introduction

Resistant hypertension (rHTN) represents a high burden for healthcare systems across the world [1]. rHTN is defined in Europe as a blood pressure (BP) of ≥ 140/90 mmHg despite treatment with at least three antihypertensive medications, including a diuretic, a renin-angiotensin-system blocker and a calcium channel blocker at a maximally tolerated dose [1]. People with rHTN are at a twofold increased risk of cardiovascular morbidity and mortality compared with patients responsive to treatment [2–4]. rHTN is estimated to have a prevalence across the globe of 10–15% of the treated hypertensive population [5].

Patients with rHTN have a substantial unmet need for an effective durable treatment that does not add to their burden

Key Points for Decision Makers

Together with our previous UK analysis, this three-country analysis, based on the RADIANCE-HTN TRIO trial data, suggests that endovascular ultrasound renal denervation (uRDN) is likely to be a cost-effective option for patients with resistant hypertension in Belgium, France and the Netherlands.

Treating resistant hypertension (rHTN) with the addition of endovascular uRDN instead of standard-of-care antihypertensive medications alone leads to long-term gains in life-years and quality-adjusted life-years.

Cost-effectiveness data supports international clinical guideline recommendation for the availability of endovascular uRDN as a treatment for rHTN.

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of adherence to multiple antihypertensive medications and does not lead to poorly tolerated adverse effects. Endovascular ultrasound renal denervation (uRDN) is a minimally invasive procedure that thermally ablates the sympathetic nerves that play an important role in the pathophysiology of rHTN [6–8]. The RADIANCE-HTN TRIO multicentre, randomised, sham-controlled trial of the uRDN Paradise System conducted in the USA and Europe in patients with rHTN reported a mean systolic BP (SBP) reduction at 2 months follow-up of −8.5 mmHg compared with baseline measurements [9, 10]. The strength of trial evidence has led to an update in international clinical guidelines including those of 2023 European Society of Hypertension and 2024 European Society of Cardiology [11, 12], both recommending RDN as an adjunctive treatment in patients with rHTN.

In addition to clinical effectiveness and safety, many healthcare systems require evidence of cost-effectiveness to approve funding/coverage of a healthcare technology [13]. Our analysis of the addition of uRDN plus standard of care (SoC) compared with SoC from the UK healthcare perspective, reported a base-case incremental cost effectiveness ratio (ICER) of £5600 (€6500) per quality adjusted life year (QALY) gained (95% confidence interval (CI): £5463 to £5739 [€6341 to €6661]); with a > 99% probability that the ICER is below the £20,000 to £30,000 (€23,214 to €34,821) per QALY willingness-to-pay threshold (WTP) in the UK [14].

Nevertheless, a single country economic analysis does not address the wider question of whether uRDN is a cost-effective approach to the management of rHTN in other national healthcare systems. Given between-country differences in healthcare costs, patterns of healthcare utilisation and routine clinical practice, simply extrapolating the incremental cost-effectiveness estimates from one country to another is not an appropriate methodological or policy approach [15–17].

The aim of this study was therefore to combine country specific healthcare costs and clinical data in Belgium, France and the Netherlands with data from the RADIANCE-HTN TRIO trial and our previously developed economic decision-analytic model [14] to estimate the cost effectiveness of uRDN in each of these three countries.

2 Methods

a. Study Design

This study used a Markov model to extrapolate the results of the RADIANCE-HTN TRIO trial, which included patients aged 18–75 years with an office BP ≥ 140/90 mm Hg despite three or more antihypertensive medications including a diuretic [9]. All patients in the trial were treated with a single-pill triple antihypertensive combination therapy prior to their allocation to uRDN or sham control. Key baseline characteristics of the trial population have been previously reported [9] and are shown in eTable1. This economic evaluation is reported in accordance with the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) [18] and applied the perspectives of the three health care systems of Belgium, France and the Netherlands.

b. Model Structure

Consistent with the methodology used in our previously developed economic decision-analytic model [14], a state-transition (Markov) model was used to project the impact of treatment with uRDN plus SoC compared with SoC alone over a lifetime horizon. Reflective of current guidelines [11, 12] and the TRIO trial [9], SoC across the three countries included treatment with three classes of antihypertensive medication, including a diuretic, a renin-angiotensin-system blocker and a calcium channel blocker at maximally tolerated dose. The model had a 1-month cycle length with half-cycle correction incorporated. For the Belgian and Dutch models, costs were discounted at 1.5% annually and outcomes [QALYs and life years (LYs)] were discounted at 3.0% annually in order to take into account the impact of time on valuation of costs and outcomes; for the French model, costs, QALYs and LYs were discounted at 2.5% annually up to 10 years, and 1.5% annually thereafter [19–21].

The model included 11 mutually exclusive health states to represent disease progression. The health states consisted of hypertension, five types of cardiovascular events (myocardial infarction, stroke, heart failure, end-stage renal disease and chronic heart disease) and death. All patients start in the hypertension health state and move to a different health state (with different health-related quality of life and costs) when an event occurs. Death is an absorbing health state and can occur at any time. In accordance with our previous cost-effectiveness model [14], we used risk equations based on Framingham and the Prospective Cardiovascular Münster (PROCAM) study to model how patients transition through the different health states [22, 23].

All patients start in the hypertension health state and move to a different health state when an event occurs, or a specific diagnosis is established. The patient pathway through various cardiovascular events is shown in Fig. 1. In accordance with the previously developed model [14], memory for end stage renal disease (ESRD) was incorporated, and a recurrent stroke health state was included; these enable consideration of different costs and health-related quality of life for the previous ESRD status of a

patient experiencing an additional complication, and for patients who remain at risk for subsequent strokes. Also, consistent with previous modelling [14], the SBP reduction associated with uRDN was translated to a reduction of clinical events on the basis of the relative risks reported by the meta-analysis of Thomopoulos et al. (55 randomised controlled trials of antihypertensive medication in 195,267 individuals) [24]. We adapted and populated the economic model with data in late 2023 to early 2024.

c. Clinical and Health-Related Quality-of-Life Inputs

The key parameters used in the model are detailed in the data supplement (eTable 2). The model used office-based SBP from the RADIANCE-HTN TRIO trial since current cardiovascular risk equations [22, 23] and published meta-analyses of the clinical effect of changes in SBP [24] are calibrated using office SBP measurements. The baseline office SBP across both arms of the trial was 155.3 mmHg, with a mean reduction of 8.5 mmHg (and standard deviation of 19.1 mmHg) in the uRDN arm at 2 months [9, 10]. No sham intervention would be performed in real-world clinical practice, and any placebo effect would be part of the overall treatment effect observed for the intervention. Therefore, the base-case analysis assumes that no SBP reduction was associated with continuation of SoC (continued medical management for rHTN). Additional model clinical parameters were derived from literature searches and previously published models relevant to hypertension, and specifically, treatment with RDN. Health utilities for the specific health states identified were drawn from a variety of sources, including previous clinical trials and economic evaluations of cardiovascular interventions and health-related quality of life studies (eTables 3–5).

d. Cost Inputs

Hypertension-related costs and event-related costs were considered throughout the patient's lifetime. These were broken down into the following categories: procedure costs, anti-hypertensive medication costs, monitoring

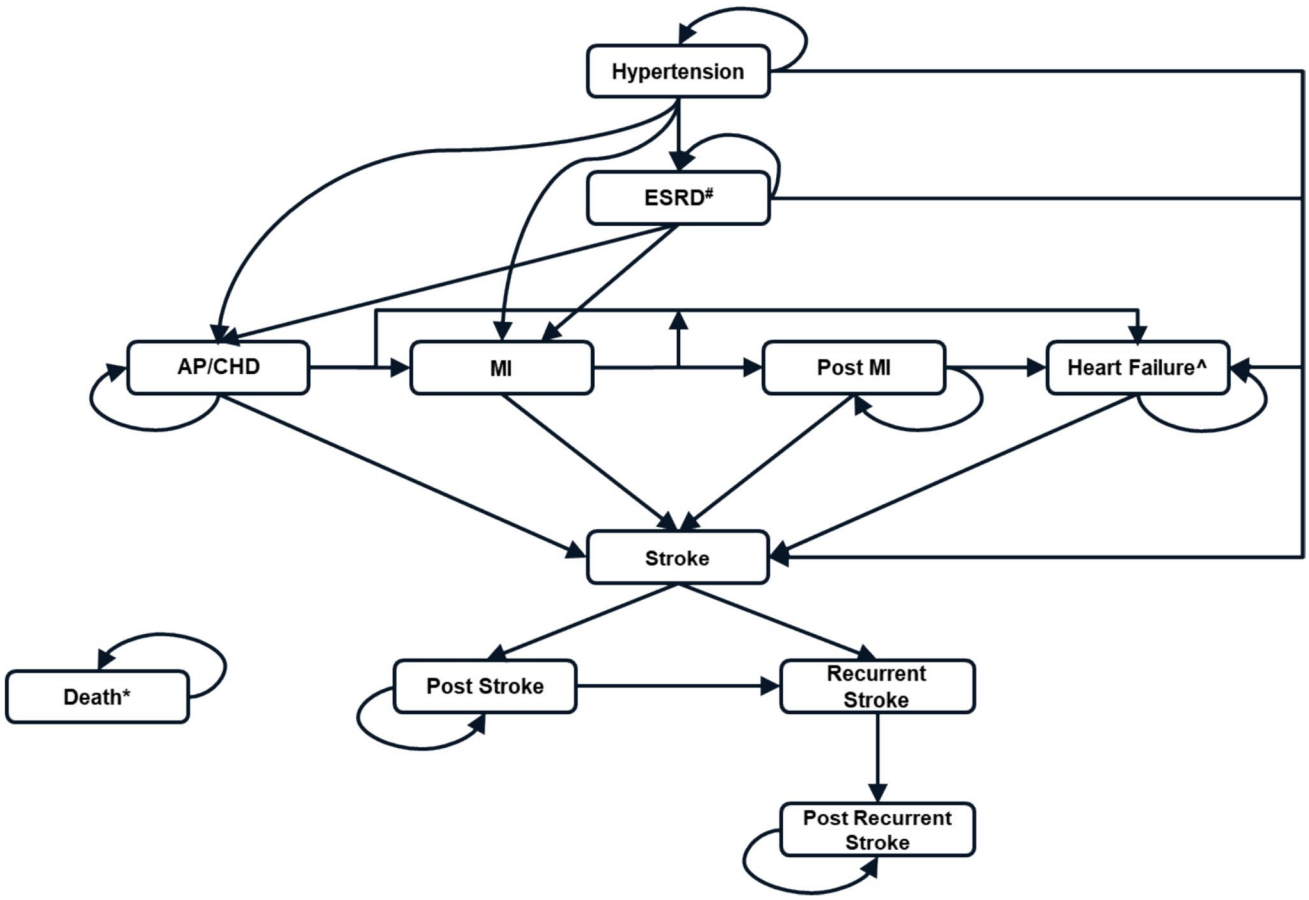


Fig. 1 Schematic of cost-effectiveness model structure. *AP* angina pectoris, *CHD* coronary heart disease, *ESRD* end-stage renal disease, *MI* myocardial infarction. *Death is an absorbing health state that can be entered at any given time. #A memory has been incorporated to track ESRD status throughout the model time horizon. ^A memory has been incorporated to track heart failure status in stroke patients

costs, cardiovascular event costs, drug acquisition, drug administration, resource use, cardiovascular events and treatment-related adverse events. Details on the resources and their unit costs, for each country, are presented in eTables 6–9. The procedural cost for uRDN (including all cost components associated with the one-off provision of the uRDN system plus procedural components and hospital treatment costs) was assumed to be €8500 in all three countries. Whilst this is higher than the assumed cost in our previously published UK economic evaluation [14], we wished to take a conservative position with respect to the impact of recent cost inflation, exchange rates and inter-country procedural cost variability. When required, costs were inflated to 2023 levels using country-specific inflation indices.

e. Data Analysis

Results were reported as ICERs. This was done by calculating the ratio of the difference in mean costs and mean change in LYs and QALYs between uRDN plus SoC and SoC alone. To provide full insight into the robustness of the results, a 95% CI around the ICER has been calculated. The box method was applied as a simplified method to calculate this interval to avoid additional complexity [25].

One-way sensitivity analysis and probabilistic sensitivity analysis (PSA) were conducted to assess the uncertainty surrounding the model inputs and sensitivity of the model results to changes in parameter inputs. One-way sensitivity analysis was performed using realistic minimum and maximum individual model inputs (one at a time); for all model parameters, the minimum and maximum plausible values for univariate analysis were defined as the lower and upper 95% CIs. For the PSA, all parameters were varied simultaneously, and results were recorded for 1000 iterations, which was sufficient to provide stable results from the model. The majority of variables were assumed to have a normal distribution, with the exception of proportions, probabilities and utility estimates, which were all varied using a beta distribution. Gamma distributions were applied for hazard ratios.

In addition, several scenario analyses were used to explore the impact of the model's validity. For insight into the cost-effectiveness of uRDN in real-world conditions, we used the 12-month results of the ACHIEVE study, which included patients treated with the uRDN system ($n = 96$) [26]. The ACHIEVE observational study demonstrated a 15.0 mmHg reduction in mean office SBP at 12-month follow-up. The mean baseline office SBP in ACHIEVE was 176 mmHg versus 155.3 mmHg in the RADIANCE-HTN TRIO trial [9]. A scenario in which the sham-subtracted SBP reduction of 5 mmHg from the sham-controlled RADIANCE-HTN TRIO trial was used to further test the cost-effectiveness based on conservative assumptions.

A patient-level simulation component explored the impact of modelling a heterogeneous patient population, which can cause biased results when there is a nonlinear relationship between risk factors and cardiovascular event risks (Jensen's inequality) [27]. The simulation model uses random sampling to create a virtual patient cohort based on defined patient characteristics and the correlation between them, as found in the RADIANCE-HTN TRIO trial (eTables 1 and 25). Each patient from the cohort is then run through the model's existing Markov structure. The results are averaged to achieve an overall cohort result to compare with the base-case deterministic results.

3 Results

a. Base-Case Results

As shown in Table 1, base-case analyses for all three countries indicate uRDN plus SoC results in a mean improvement in LYs and QALYs per patient compared with SoC over a lifetime horizon. Higher mean costs are associated with uRDN plus SoC compared with SoC alone. The ICERs for each country model fall well below the respective WTP thresholds. The breakdown of model results detailing specific downstream event rates and averted events, in addition to costs associated with individual events, are shown in eTables 13–24.

b. Sensitivity Analyses

The results from one-way sensitivity analysis indicate that the model's findings are insensitive to uncertainty around individual parameter estimates. Figure 2 presents the tornado diagrams of the most influential parameters for the Belgian, French and Dutch models, respectively. In each model, the relative risks applied to the intervention arm baseline cardiovascular risks, and the mortality and utility of stroke, were each shown to be some of the most influential parameters. The PSA results, based on 1000 iterations (Fig. 3), shows there is > 99% probability of the uRDN system being cost-effective in each country according to the respective country-specific willingness-to-pay thresholds (€40,000 for Belgium [28], €50,000 for France [29] and €20,000 for the Netherlands [20]) (eFigs. 1–3).

c. Scenario Analyses

The results of the model scenarios, shown in Table 2, are consistent across all three countries in terms of the direction of change observed from the base-case ICER. Applying relative risks from the meta-analysis by Ettehad et al. [30] and hazard ratios by Rahimi et al. [31] (scenarios 1 and 2, respectively) results in an increased ICER in all countries. The model results are robust when making alternative assumptions around the model's structure (scenarios 3–5), with these having a minimal impact on the model ICERs. When the inputs observed in the real-world ACHIEVE study were added to the models (scenario 6), for all countries, it resulted in a reduced ICER. Results of the patient-level simulation (scenario 7) show consistency with the base-case deterministic results, and sham-subtracted SBP reduction of −5 mmHg (scenario 8) results in an increased ICER. Reducing the time horizon from a lifetime to 20 years (scenario 9) results in an increased ICER. Notably, in all scenarios across each country, ICERs remain below the respective WTP thresholds.

4 Discussion

Contemporary high quality randomised trials demonstrated the safety and effectiveness of RDN in terms of clinically meaningful SBP reductions in people with rHTN, defined as uncontrolled BP and treatment with at least three antihypertensive medications [8, 9]. Despite the recent approval of uRDN by the United States Food and Drug Administration (FDA) [10] and a recommendation for the use of RDN from international clinical society guidelines [11, 12], uncertainty around value for money may act as a barrier to patient access [32]. In our analysis, we therefore chose to examine the cost-effectiveness of RDN across three European countries (Belgium, France and the Netherlands) that formally consider cost-effectiveness to inform their coverage decisions around access to health technologies. On the basis of the assumption that the decrease at 2 months would be sustained, our results show that the addition of uRDN to SoC compared with SoC alone, resulted in a range of country base-case mean ICERs from €1654 to €6261/QALY. Over patient lifetime, our economic modelling showed a > 99% probability that uRDN is cost-effective across all three countries on the basis of their specific WTP thresholds. Given the differences in intercountry healthcare treatment costs, it was anticipated that there would be some variation in ICERs across the three countries. Whilst small in this three-country analysis, these differences support the importance of country-specific estimations of cost-effectiveness, especially in the context of different country's WTPs. The variation in ICERs between the three European country models could be attributed to a combination of factors. First, cost differences as the result of different prices of goods and services, and different treatment practices used in each country. Second, different sources used to derive country costs, which varied in their transparency in their reporting. Third, each model was based on country-specific population mortality. Fourth, country-specific data from the ERA-EDTA registry [39] were used

Table 1 Base-case cost-effectiveness results

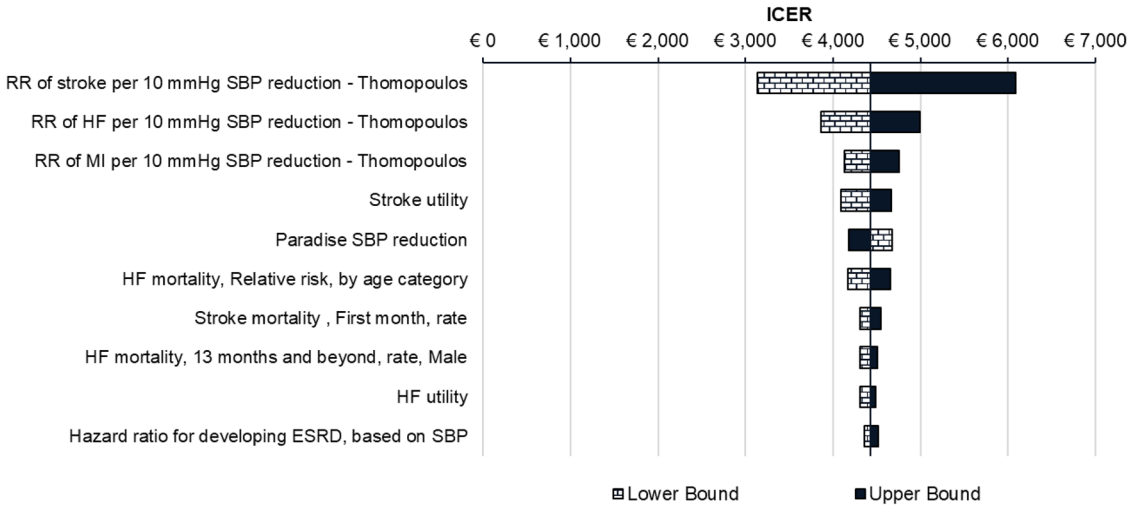
Treatment	LYs	QALYs	Costs	ΔLYs	ΔQALYs	ΔCosts	ICER (€/LY)	ICER (€/QALY)
Belgium								
SoC alone	17.94	14.17	€44,087	1.22	0.97	€4291	€3528	€4426
uRDN + SoC	19.15	15.14	€48,378					
France								
SoC alone	17.43	13.77	€48,795	1.18	0.9	€5897	€4996	€6261
uRDN + SoC	18.61	14.71	€54,692					
The Netherlands								
SoC alone	17.94	14.18	€55,478	1.21	1.0	€1594	€1321	€1654
uRDN + SoC	19.15	15.15	€57,072					

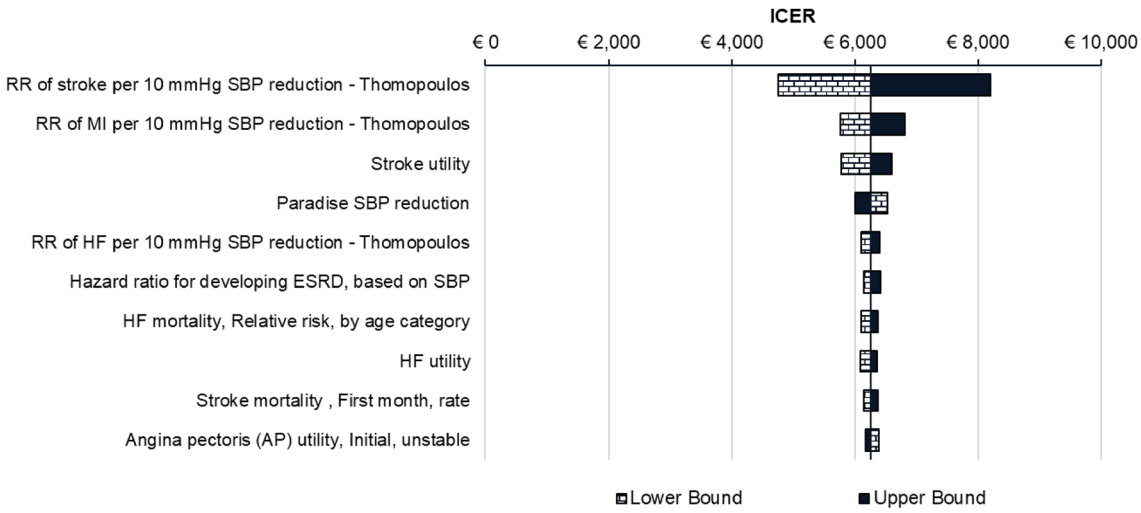
ICER incremental cost-effectiveness ratio, *LY* life year, *QALY* quality-adjusted life year, *uRDN* ultrasound renal denervation, *SoC* standard of care

Δ indicates the difference between uRDN plus SoC versus SoC alone

Discounting: QALYs and life years are discounted at 1.5% annually and costs are discounted at 3.0% annually for Belgium and the Netherlands; for France, costs, QALYs and LYs were discounted at 2.5% annually up to 10 years, and 1.5% annually thereafter

Willingness-to-pay thresholds: €40,000 for Belgium, €50,000 for France and €20,000 for the Netherlands





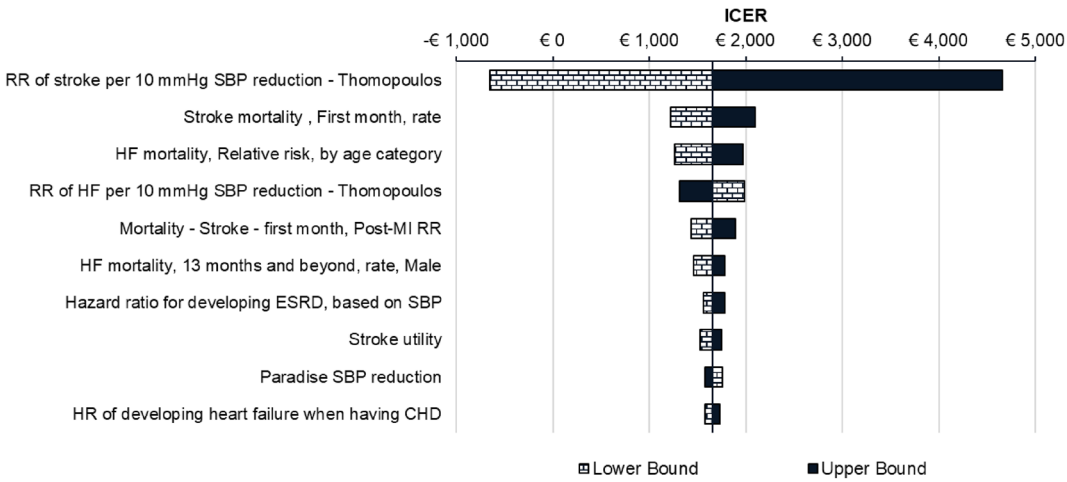


Fig. 2 **A** Tornado diagram for uRDN plus SoC versus SoC alone: Belgium. **B** Tornado diagram for uRDN plus SoC versus SoC alone: France. **C** Tornado diagram for uRDN plus SoC versus SoC alone: the Netherlands. *CHD* coronary heart disease, *ESRD* end-stage renal disease, *HF* heart failure, *ICER* incremental cost-effectiveness ratio, *MI* myocardial infarction, *RR* relative risk, *SBP* systolic blood pressure, *SoC* standard of care

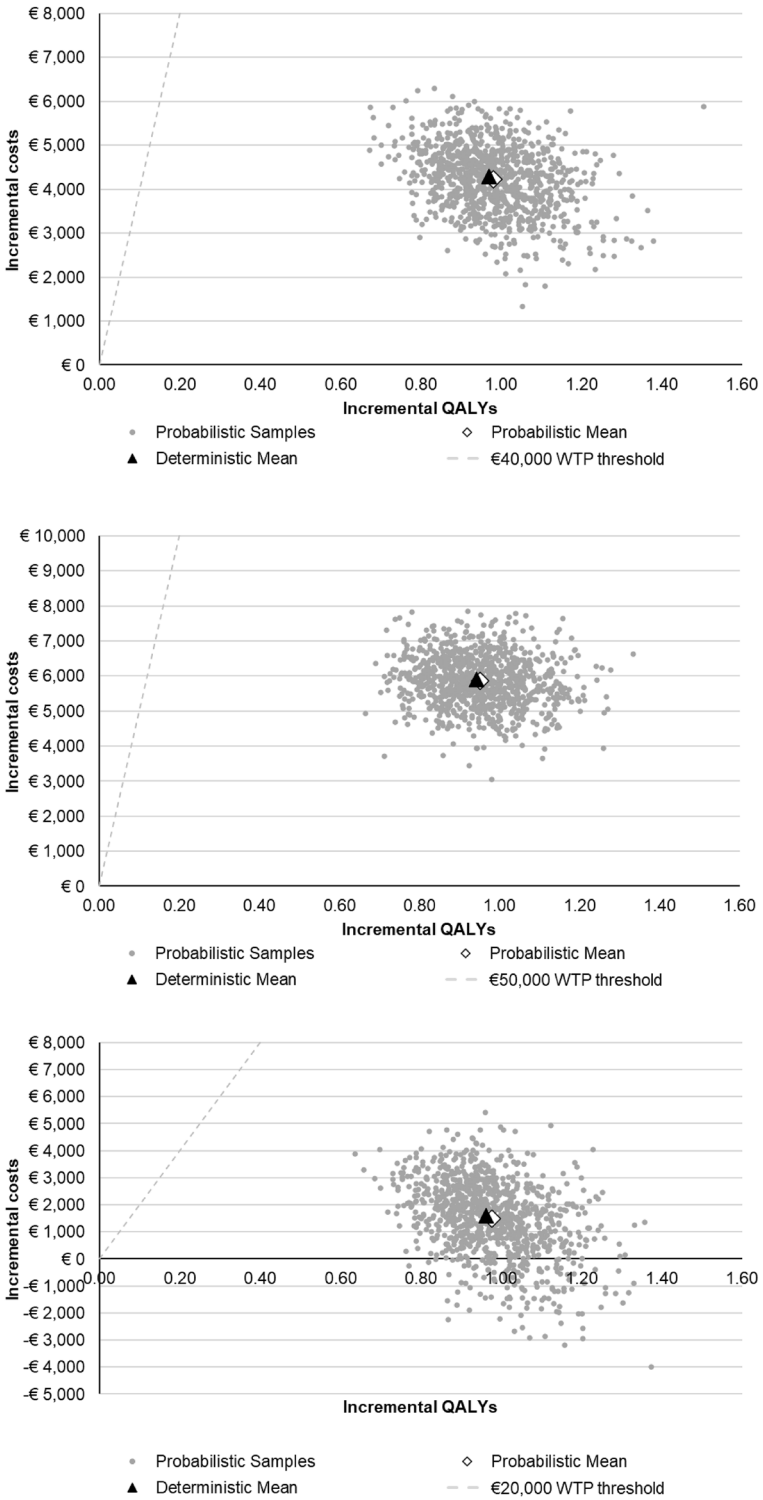


Fig. 3 **A** Probabilistic sensitivity analysis with 1000 iterations of uRDN plus SoC versus SoC alone: Belgium. **B** Probabilistic sensitivity analysis with 1000 iterations of uRDN plus SoC versus SoC alone: France. **C** Probabilistic sensitivity analysis with 1000 iterations of uRDN plus SoC versus SoC alone: the Netherlands. *QALY* quality-adjusted life-year, *SoC* standard of care, *WTP* willingness-to-pay

for each model to derive end-stage renal morbidity and mortality risks. Fifth, country-specific antihypertensive usage was applied. Finally, different annual discount rates were applied to costs and outcomes for each country.

Other economic evaluations of RDN modalities in the era of contemporary randomised controlled trials have been reported [8, 9]. The first and only previously published cost-effectiveness analysis of uRDN was conducted by our group [14] and was based on the Markov model used in the present study. Undertaken from the perspective of the UK National Health Service, we reported a mean base-case ICER with uRDN in rHTN of £5600 (€6500) per QALY

Table 2 Cost-effectiveness results of scenario analyses for uRDN plus SoC versus SoC alone

Scenario		Δ LYs	Δ QALYs	Δ Costs	ICER (€/LY)	ICER (€/QALY)
Belgium						
1	Applying RRs from Ettehad et al. [30]	0.78	0.62	€5576	€7134	€8935
2	Applying HRs from Rahimi et al. (BPLTTC) [31]	0.66	0.53	€5803	€8746	€10,903
3	Heart failure baseline risk based on Khan et al. [38]	1.11	0.89	€4271	€3843	€4810
4	Recurrent stroke excluded	1.18	0.95	€4131	€3513	€4337
5	ESRD memory excluded	1.22	0.97	€4293	€3529	€4427
6	Using 12-month data from the ACHIEVE study [26]	1.46	1.14	€1076	€736	€946
7	Patient-level simulation	1.93	1.60	€4194	€2171	€2622
8	Sham-subtracted effect size (−5 mmHg)	0.70	0.56	€6044	€8586	€10,778
9	Time horizon of 20 years	0.47	0.43	€3932	€8322	€9224
France						
1	Applying RRs from Ettehad et al. [30]	0.76	0.61	€6354	€8388	€10,492
2	Applying HRs from Rahimi et al. (BPLTTC) [31]	0.64	0.52	€6378	€9951	€12,381
3	Heart failure baseline risk based on Khan et al. [38]	1.08	0.86	€5278	€4901	€6124
4	Recurrent stroke excluded	1.14	0.93	€5619	€4925	€6072
5	ESRD memory excluded	1.18	0.94	€5867	€4970	€6228
6	Using 12-month data from the ACHIEVE study [26]	1.40	1.1	€3559	€2538	€3262
7	Patient-level simulation	1.00	0.77	€3924	€3906	€5077
8	Sham-subtracted effect size (−5 mmHg)	0.68	0.54	€6945	€10,167	€12,748
9	Time horizon of 20 years	0.46	0.42	€4760	€10,269	€11,399
The Netherlands						
1	Applying RRs from Ettehad et al. [30]	0.77	0.62	€3617	€4671	€5837
2	Applying HRs from Rahimi et al. (BPLTTC) [31]	0.66	0.53	€4861	€7406	€9208
3	Heart failure baseline risk based on Khan et al. [38]	1.10	0.88	€821	€746	€931
4	Recurrent stroke excluded	1.17	0.95	€2664	€2284	€2813
5	ESRD memory excluded	1.21	0.96	€1648	€1367	€1711
6	Using 12-month data from the ACHIEVE study [26]	1.45	1.1	−€ 5652	Dominant	Dominant
7	Patient-level simulation	1.52	1.24	€4458	€2932	€3603
8	Sham-subtracted effect size (− 5 mmHg)	0.70	0.56	€4529	€6490	€8128
9	Time horizon of 20 years	0.47	0.43	€2230	€4705	€5217

ACHIEVE TrAnsCatHeter Intravascular Ultrasound Energy deliVery for rEnal Denervation, *BPLTCC* Blood Pressure Lowering Treatment Trialists Collaboration, *ESRD* end-stage renal disease, *HR* hazard ratio, *ICER* incremental cost-effectiveness ratio, *LYs* life-years, *QALYs* quality-adjusted life-years, *RRs* relative risks, *SoC* standard of care, *uRDN* ultrasound renal nerve denervation

Δ indicates the difference between uRDN plus SoC versus SoC alone

Discounting: QALYs and life years are discounted at 1.5% annually and costs are discounted at 3.0% annually for Belgium and the Netherlands; for France, costs, QALYs and LYs were discounted at 2.5% annually up to 10 years, and 1.5% annually thereafter

Willingness-to-pay thresholds: €40,000 for Belgium, €50,000 for France and €20,000 for the Netherlands

gained, and > 99% probability that it is below the WTP of £20,000 to £30,000 (€23,214 to €34,821) per QALY. Another evaluation of cost-effectiveness of the catheter-based radiofrequency RDN procedure for the management of uncontrolled hypertension patients was reported from a UK perspective and was based on the SPYRAL HTN-ON MED trial (RDN in the presence of antihypertensive medication) over a 10-year patient time horizon [33]. The authors reported an ICER of £13,482 per QALY gained with 100% probability of being cost-effective at a WTP of £20,000 per QALY. Kandzari et al. used a US Medicare perspective and undertook two base-case analyses using either the SPYRAL HTN-ON MED or SPYRAL HTN-OFF (RDN in the absence of antihypertensive medication) trials, with reported base-case (using RDN versus sham BP difference) ICERs of US $32,732 and US $25,521 per QALY, respectively [34]. The authors of this latter analysis did not report the probability of cost-effectiveness remaining under an acceptable WTP threshold for the USA (e.g., US $50,000/QALY) when reporting their PSA analyses. However, all three publications consistently stated that RDN was cost-effective within a broad range of scenarios and sensitivity analyses.

This new analysis has several strengths and important implications for clinical practice and healthcare policy. First, the three-country analysis allowed the consistency of uRDN cost-effectiveness across different health systems to be investigated. Rather than indirectly extrapolating the ICER from our original UK healthcare perspective analysis [14] to Belgium, France and the Netherlands, this analysis sourced and applied country-specific clinical and cost data to the model to generate de novo ICERs, which were then interpreted in the context of the WTP of each country. That there is now consistent evidence of cost-effectiveness of uRDN across four European countries is an important perspective for health technology agencies and payers in making coverage decisions. The European Union Health Technology Assessment Regulation (HTAR) became effective from January 2025 and aims to improve the access of innovative technologies for patients and reduce unnecessary duplication of health technology assessment resources by utilising centralised single Joint Clinical Assessments (JCA) on behalf of European member states. Our multi-country approach to cost-effectiveness based on a single economic model using country-specific clinical and cost data illustrates the potential efficiency of a centralised approach to economic analysis. Second, this economic model incorporates several significant updates compared with previous economic models applied to RDN. In particular, translation of SBP reduction to clinical events using the meta-analysis and meta-regression of Thomopoulos et al. [24] from 55 antihypertensive trials in 195,267 hypertensive patients, the inclusion of utility values for stroke, and incorporation of a memory function to better capture the impact of end-stage renal disease are all significant improvements. Third, this analysis and its conclusions were robust across all scenarios and sensitivity analyses, which tested a range of different modelling assumptions and the probabilistic uncertainty in the model data parameters. For example, the base-case analysis is conservatively based on the uRDN arm of a tightly controlled sham-controlled trial. In general, sham-controlled trials of renal denervation have shown more modest BP reductions when compared with those seen in real-world registries, including the ACHIEVE study of uRDN. Real-world registries of RDN show treatment effect sizes in rHTN as high as a SBP reduction of 20 mmHg [26].

However, there are limitations with this analysis. First, the modelling centrally depends on the assumption that the reduction in SBP observed with uRDN at 2 months predicts a reduction in the risk of downstream cardiovascular and renal events. However, it must be noted that SBP reduction is accepted as a surrogate endpoint by clinicians and regulators, and it is widely accepted that a 5mmHg reduction in SBP in response to treatment in the long-term is associated with a 10% reduction in major cardiovascular events [35]. Furthermore, BP is listed in the US FDA table of surrogate endpoints to support marketing applications [36], and meta-regression analyses of randomised trials of antihypertensive trials have shown BP to be a valid surrogate endpoint for clinical events, including stroke prevention [37]. It is important that future analyses assessing the validity of SBP as a surrogate endpoint are updated to include RDN trials alongside current data from trials of antihypertensive drugs. As with previous economic analyses, our model assumes the durability of the uRDN therapeutic effect on SBP. This is supported by data from long-term follow-up showing a reduction of SBP with RDN for up to 10-years. Given the lack of formally published WTP thresholds in Belgium and France, we used thresholds applied in previously used country-specific economic evaluations of medical technologies [28, 29]. Similarly, we needed to use cardiovascular event health state utilities primarily sourced from populations in other geographical settings.

5 Conclusions

Current clinical and society guidance indicate that uRDN is an effective and safe adjunctive treatment approach alongside hypertensive medication for the management of rHTN. Findings from this analysis suggest uRDN adds meaningful clinical benefit at incremental cost, thus, it is a cost-effective intervention for patients with rHTN in the Belgian, French and Dutch healthcare systems. Our analysis demonstrates ICERs that all fall well below the various WTP per QALY thresholds and support adoption of uRDN in the countries studied.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s41669-025-00574-2.

Declarations

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Data Availability Statement The authors confirm that the data supporting the findings of this study are available within the article and its supplementary materials.

Ethics Approval Not applicable.

Consent to Participate Not applicable.

Consent for Publication (from Patients/Participants) Not applicable.

Code Availability The cost-effectiveness model was developed in Microsoft Excel 365 (Microsoft Corporation, Redmond, WA, USA). Any additional information about model programming is available from the corresponding author upon request.

Author Contributions The economic model was updated by K.M. and R.S.T., and K.M. wrote the first draft of this manuscript. All authors revised and contributed to subsequent versions of the manuscript, and the final version was approved by all authors.

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