Original Article

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Impact of expected blood pressure reduction on patient preferences for pharmaceutical and renal denervation treatment

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Background: Effective patient-centered care requires an adequate understanding of patient preferences for different therapeutic options. We modelled patient preference for blood pressure (BP) management by pharmaceutical or interventional treatments such as renal denervation in patients with different profiles of uncontrolled hypertension.

Methods: Modeling was based on the findings from a previously conducted quantitative discrete choice experiment (DCE). The likelihood of selecting either an interventional treatment option or additional antihypertensive medication option was calculated for three patient profiles that represent the range of patients with hypertension commonly encountered in clinical practice: treatment-naive, patients with uncontrolled BP while on one to three antihypertensive medications, and patients with drug-resistant hypertension. Variables in the preference model were treatment attributes from the DCE study: expected reduction in office SBP with each treatment, duration of treatment effect, risk of reversible drug side effects from drugs, and risk of temporary pain and/or bruising or vascular injury from interventions. Values of the variables were derived from published clinical studies or expert opinion.

Results: The model predicted that the likelihood of choosing renal denervation over initiating pharmacotherapy was 17.2% for previously untreated patients, 23.7% for patients with moderate hypertension currently on pharmacotherapy, and 41.8% for patients with drug-resistant hypertension. The dominant variable driving preference in these models was the expected BP reduction. Patient preferences for intervention are greater when drug nonadherence or increased SBP reduction at 3 vs. 1 year are included in the model. Baseline BP, drug side effects, or risks of the procedure had little influence on decisions.

Conclusion: Modeling using patient preference weights predicts that a substantial minority of patients favor an interventional treatment such as renal denervation over initiation or escalation of medications. Awareness of a patient's interest in device-based versus pharmaceutical strategies should inform the shared decision-making process for hypertension treatment.

Keywords: antihypertensive drugs, discrete choice experiment, patient preference, renal denervation

Abbreviations: BP, blood pressure; DCE, discrete choice experiment; GSR, Global SYMPLICITY Registry; RDN, renal denervation

BACKGROUND

Despite the widespread availability of effective pharmacological treatments for high blood pressure (BP), uncontrolled hypertension is a growing, major global health issue [1]. Among those treated with antihypertensive drugs, BP control depends on physician prescription of an adequate number and dose of BP medications and patient adherence to therapy [2]. For patients on pharmacological treatment regimens, there is an inverse relationship between adherence and the number of pills prescribed, especially when compounded by multiple daily dosing regimens. Adherence also depends on the time to achieve therapeutic goals, need for adjustments to the medication regimen, and adverse side effects [2]. Catheter-based renal denervation has been shown to provide sustained BP reductions in patients with hypertension with an 'always on' effect that is independent of patient adherence to antihypertensive medications [3,4].

Effective patient-centered care is fundamental to understanding patients' treatment preferences. Patient choice is associated with a greater knowledge of treatment options, improved decision-making quality, an increased rate of selecting the option that matches an individual patient's

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values, improved adherence to therapy, and improved BP control [5]. Thus, a framework of patient attitudes is valuable for physicians when engaging in an informed discussion and shared decision-making process with patients to reach personalized antihypertensive treatment options. Such shared treatment decision-making should include patients' understanding and tolerance of risk and expectations of benefit [6,7].

A number of studies in different countries have shown that a significant percentage of patients with hypertension – between 25 and 45% of those surveyed – would prefer an interventional antihypertensive treatment, such as renal denervation (RDN), rather than an increase in antihypertensive medication regimen [8–11]. Contrary to the perception of many physicians, patients' interest in the intervention does not appear to correlate with the severity of their BP, whereas the likelihood of provider referral for RDN is dependent upon both BP severity and escalating medication burden [4].

Recently, we employed a more rigorous and comprehensive methodology of a discrete choice experiment (DCE) [12] enrolling 400 patients with uncontrolled moderate hypertension (office systolic BP $\geq$140 mmHg and $<$170 mmHg) to quantify the influence of clinical factors of pharmaceutical and interventional treatments for hypertension on patient preferences [10]. The DCE surveyed patients on the expected magnitude office BP reduction weighed against the number of daily antihypertensive medications, risks of medication side effects, access site pain, and vascular injury. The magnitude of the reduction in office SBP was the most important treatment attribute recorded by respondents. Risk of access site pain did not influence patient choice. Respondents generally favored pharmaceutical intervention, however, only a 2.3 mmHg greater reduction via intervention vs. increasing medications was sufficient to offset this preference [10].

The objective of the current study is to apply the results of the DCE study to specific scenarios that reflect actual clinical circumstances commonly experienced in hypertension practice. More specifically, preference weights from the DCE study with efficacy and safety data were combined to model patient preference across the spectrum of hypertension management. The goal of this prespecified application of the DCE preference weight findings is to compare patient preferences for interventional versus pharmaceutical treatments for three typical hypertensive patient profiles, ranging from treatment-naive patients to those with drug-resistant hypertension. The profiles represent the natural pathway of disease progression commonly encountered in clinical practice.

METHODS

A model was designed to predict the likelihood of patients with elevated SBP opting for either adding an antihypertensive medication or undergoing an interventional procedure. The model included three different patient profiles along the progression of hypertension: untreated, moderate hypertension; uncontrolled hypertension (office SBP $\geq$140 mmHg) despite treatment with one to three antihypertensive medications; and uncontrolled, resistant hypertension taking more than three antihypertensive medications. The estimated preference weights for each attribute from the DCE study were applied to efficacy and safety outcomes based on published data or expert opinion wherever published data was not available. The model included each treatment attribute in the original DCE study [12]: interventional or pharmaceutical treatment; number of daily antihypertensive medication pills; reduction in office SBP (mmHg); duration of treatment effect; risk of drug-related side effects; risk of access site pain and/or bruising at the site of vascular access for an interventional treatment, and risk of vascular injury (including renal artery stenosis) with interventional treatment. The weight of the influence of each of these treatment attributes on patient preferences and how changes in the levels affected those preferences were also extrapolated from the previously reported DCE study [12].

Predicted outcomes

Meta-analyses report placebo-adjusted reductions in office SBP for commonly used antihypertensive drugs (e.g. angiotensin converting-enzyme inhibitors, angiotensin receptor blockers, amlodipine, hydrochlorothiazide, and beta-blockers) ranging from 5.2 to 11.2 mmHg [13,14]. However, as patients in actual care experience absolute and not placebo-adjusted BP reductions, we used data on absolute office SBP reductions, which have been reported in trials across these classes of oral antihypertensive medications to range from 6.4 to 14.2 mmHg [15–18]. Given the inherent differences in clinical studies including patient inclusion/exclusion criteria, variable antihypertensive drug dosing and drug classes, we critically evaluated antihypertensive medication efficacy and arrived at a consensus assumption of a 10 mmHg absolute reduction with the addition of a single drug therapy in the model.

The expected reductions in absolute office SBP with RDN treatment in the patient profiles were based on the published results from the clinical trials: SPYRAL HTN–OFF MED Pivotal trial [19] for the 9.2 mmHg SBP reduction in untreated patients with moderate hypertension and SPYRAL HTN–ON MED trial [20] for the 9.9 mmHg SBP reduction in the treated patients with moderate hypertension. A subgroup from the Global SYMPLICITY Registry (GSR) DEFINE trial [21] of patients with office SBP greater than 140 mmHg and treated with at least three medications including a diuretic, informed the 17.3 mmHg expected treatment effect for the profile of patients with drug-resistant hypertension.

The risk of reversible side effects from antihypertensive drugs reported in the literature are incomplete and, whenever available, report widely varying values often because of lack of a common definition. The expert consensus was to assume a 10% risk of reversible side effects from drug therapy. This is also the midpoint among the values presented to participants in the original DCE analysis [22]. For interventional therapies, the risks of temporary and reversible pain and/or bruising, and of vascular injury were based on the SPYRAL HTN clinical program (Table 1).

Sensitivity analyses

To study how patient preferences might vary with different expected efficacy and safety treatment outcomes, we performed several sensitivity analyses on the profile of the

TABLE 1. Patient types extracted from the SPYRAL OFF MED and SPYRAL ON MED studies and the Global SYMPLICITY Registry and assumptions of efficacy and safety with the treatment alternatives

	Profile 1: patients with hypertension, treatment-naive (no AH medication)		Profile 2: patients with uncontrolled hypertension, treated with 1, 2, or 3 AH medications		Profile 3: patients with severe uncontrolled hypertension, treated with ≥3 AH medications including a diuretic	
Profile based on study	SPYRAL HTN–OFF MED [19]		SPYRAL HTN–ON MED [20]		Global SYMPLICITY Registry DEFINE[a] [21]	
Uncontrolled HTN	0 medication		1–3 medications		3+ medications	
Mean baseline office SBP (mmHg) in study	163 mmHg		163 mmHg		170 mmHg	
Treatment option	Renal denervation (no AH medication)	Drugs (Start 1 AH medication)	Renal denervation (no change in AH medication)	Drugs (Increase AH medication +1)	Renal denervation (no change in AH medication)	Drugs (increase AH medication +1)
Expected absolute office SBP reduction	−9.2 mmHg [19]	−10 mmHg	−9.9 mmHg [20]	−10 mmHg	−17.3 mmHg [21]	−10 mmHg
Risk of reversible drug side effects	0%	10%	10%	10%	10%	10%
Risk of temporary pain and/or bruising	13%	0% (N/A)	13%	0% (N/A)	20%[a]	0% (N/A)
Risk of vascular injury	0.3%	0% (N/A)	0.3%	0% (N/A)	20%[a]	0% (N/A)
Duration of effect of intervention	1 year	0 (N/A)	1 year	0 (N/A)	1 year	0 (N/A)

AH, antihypertensive.
[a]Profile based on subgroup of patients with severe hypertension (office SBP >150 mmHg, ≥3 medications including diuretic).

patient with moderate hypertension on drug treatment. These sensitivity analyses include evaluating the impact of incomplete drug adherence, evaluating the impact of duration of SBP reduction, varying the risk of drug side-effects, varying the risk of pain and/or bruising and of risk of vascular injury from interventional treatment. All sensitivity analyses varied the values of efficacy and safety outcomes within the lowest and highest values used in the original DCE study (detailed in Table 2); these low and high values were agreed upon in consultation with the Food and Drug Administration (FDA) based on clinical trials and expert opinion of both pharmacotherapy and with RDN [14,15,19–21,23].

The same patient profile (moderate hypertension on drug treatment) was used as a baseline to assess incomplete drug adherence as most studies of drug adherence are in patients taking multiple medications. Although poor drug adherence is a known problem with antihypertensive drugs, both the definition as well as reported rates of drug adherence vary in the literature; many patients are partially adherent (not taking all medications every day) rather than entirely nonadherent [24]. Moreover, there are no definitive studies reporting the effect of drug nonadherence on office BP or drug side effects. Thus, we used a simple linear model of reduced drug use on efficacy and safety, assuming 20% nonadherence and an associated 20% reduction in both drug effects on SBP and the risk of side effects.

The original DCE reported that safety outcomes did not have a major impact on patient choice. We thus evaluated the impact of maximum and minimum values for both drug and interventional safety used in the DCE study on calculated preference choices. To assess safety, we utilized the patient profile of moderate hypertension without antihypertensive drugs as clinical trials on drug safety are typically conducted in participants who are not already on drug treatment.

TABLE 2. Assumptions for sensitivity analyses

Sensitivity analysis	Point estimates for sensitivity analyses
Efficacy	
Reduced drug adherence[a]	
Patient profile	Office SBP ≥150 mmHg and prescribed 1–3 antihypertensive medications
Reduction in office SBP (mmHg)	20% reduction from base case
Risk of reversible drug side effects	20% reduction from base case
Increased duration of effect to 3 years for intervention group[b]	3 years [21,25] and associated office SBP reductions at 3 years of -18 mmHg
Safety	
Patient profile	Treatment-naive; untreated, office SBP ≥150 mmHg
Risk of drug side effects	1%
Best case scenario	
Worst case scenario	20%
Risk of temporary pain and/or bruising with interventional treatment	1%
Best case scenario	
Worst case scenario	20%
Risk of vascular injury with interventional treatment	1%
Best case scenario	
Worst case scenario	20%

[a]Assumes 20% nonadherence.
[b]Actual absolute office SBP reductions at 3 years in the ON MED pilot and Global Symplicity Registry are −20.9 and −16.5 mmHg, respectively. The office SBP value of −18 mmHg was chosen as it is within the range of the two studies and is the maximum reduction the model allows.

In addition, we varied the assumed duration of effect of RDN. Unlike drugs which may require increase in dose and/or number of drugs over time, published data both in clinical trials and in registries [21,25] support the finding of an increase in treatment effect with RDN over 3 years. Although there are some reports with longer treatment effects reported in literature [26,27], absolute SBP reduction at 3 years is best supported by published literature and was used in this sensitivity analysis.

As a final sensitivity analysis, we evaluated the impact of sham/placebo-adjusted SBP reduction in addition to absolute SBP reduction as an input into the model.

RESULTS

Respondent characteristics

A complete description of the survey respondents has been previously published [22]. Briefly, 400 adults met the eligibility criteria and completed the DCE survey between October 2020 and March 2021. Eligibility criteria included being between 20 and 80 years of age with an office SBP at least 140 mmHg, office DBP at least 90 mmHg, and prescribed 0–3 antihypertensive medications. Patients were excluded if they had prior experience with RDN. Among the respondents, 52% were women, with a median age of 59 years. The mean office SBP was 159 mmHg. The mean age, prescribed number of antihypertensive medications, proportion by race and ethnicity were broadly consistent with the US population with hypertension [28,29].

Patient profiles

Three patient profiles were constructed representing different stages of hypertension corresponding to what practitioners commonly encounter in clinical practice: treatment-naive patients, as a proxy for those who have been recently diagnosed with high BP (moderate hypertension, untreated); patients whose BP is uncontrolled while on one to three antihypertensive medications (moderate hypertension, treated), and patients with drug-resistant hypertension [defined in this study as uncontrolled hypertension (office SBP $\geq$140 mmHg) despite three or more antihypertensive medications, including a diuretic] [30]. Expected safety and efficacy outcomes of interventional therapy or added medication for patients in these three profiles were obtained from published data or, when not available from published data, using the expert clinical opinion of the authors (A.P., M.W., and D.K.). The outcomes were then used as an input in the model and weighted according to the strength of each attribute in the underlying DCE as detailed in the original publication [22]. The outcome was an estimate of the likelihood of patients opting for each of the treatment options. Table 1 summarizes the patient profiles and assumptions. The DCE was conducted on a mixed population of patients, 91.8% ($n = 367$) of whom were on one to three antihypertensive drugs and 8.3% ($n = 33$) who were not on any antihypertensive medications. For the modeling, the impact of treatment attributes on patients' preferences were assumed to be the same for each of the three profiles evaluated.

Clinical scenarios related to patient profiles

The baseline clinical characteristics of the patient population in the original DCE were average age 59 years and office SBP 155 mmHg. Figure 1 shows the predicted likelihood of uncontrolled patients with each profile, opting for antihypertensive drug or an interventional treatment such as RDN using the applied model. Pharmacological treatment was the most likely choice across all three profiles. For the profile of previously untreated patients with moderate hypertension, the likelihood of choosing an interventional therapy such as RDN instead of initiating pharmacotherapy was 17.2%. For the second profile of patients with moderate hypertension currently on pharmacotherapy, the likelihood of opting for the interventional treatment (while maintaining the current medication regimen) compared with increasing the number of pills was 23.7%. For patients with drug-resistant hypertension, the likelihood of choosing an interventional treatment versus adding an additional antihypertensive medication was 41.8%.

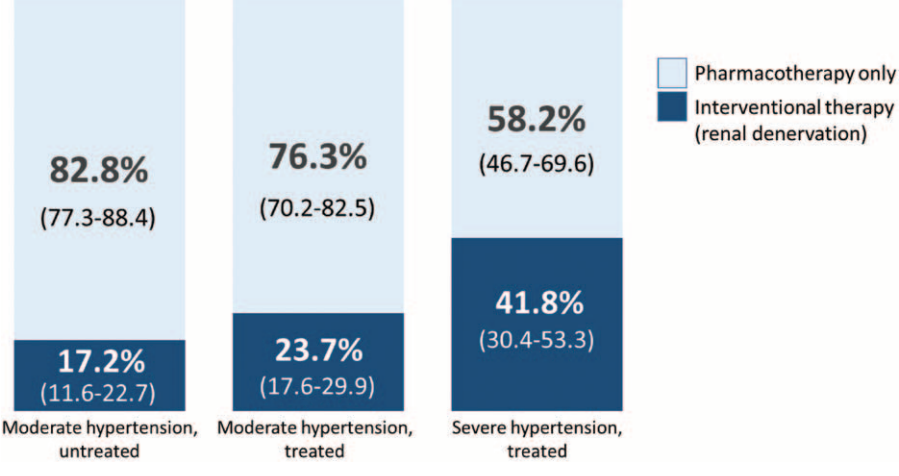

FIGURE 1 Predicted likelihood of patients with different levels of hypertension opting for adding pharmacotherapy (light) or interventional treatment (dark), for different patient profiles. Numbers in brackets indicate 95% confidence intervals. Model inputs used base case assumptions as detailed in Table 1.

TABLE 3. Sensitivity analysis of efficacy changes in the predicted likelihood of a patient population with treated mild-to-moderate hypertension preferring an intervention or additional pharmacotherapy, respectively

Variable	Likelihood of preferring treatment option (95% confidence interval)	
	Intervention with maintained medications	Added drug
Base case (moderate hypertension with drug therapy)	23.7% (17.6–29.9)	76.3% (70.2–82.5)
Efficacy		
Increased duration of interventional treatment effect from 1 year to 3 years		
Office SBP reduction after interventional therapy at 3 years	58.3% (48.5–68.2)	41.7% (31.8–51.5)
Reduced adherence to pharmacotherapy		
20% reduction in in efficacy and safety from base case	43.2% (34.8–51.6)	56.8% (48.4–65.2)

Assumptions and references are shown in Table 1.

Sensitivity analyses

The assumptions used in the sensitivity analyses using the patient profile of treated moderate hypertension are shown in Tables 1 and 2. The outcomes are listed in Tables 3 and 4. Reduced adherence to drug therapy, with an associated reduction in the expected SBP change and reduced risk of side effects from pharmacotherapy, increased the likelihood of choosing the interventional option. The likelihood of opting for interventional therapy was also positively affected by a greater assumed duration of the treatment effect of the intervention. Increasing the duration of interventional efficacy from 1 to 3 years increased the likelihood of choosing the interventional treatment option over an increase in drugs, from 23.7 to 58.4%. This increased preference is driven by the greater SBP reduction of RDN reported at 3 years with no change in drug efficacy (Table 3).

Safety had less impact on preferences. Doubling the assumed risk of drug side effects to 20% minimally impacted the likelihood of opting for drugs, changing from 83 to 77%. Varying the assumed risks with interventional therapy changed the likelihood of patients preferring this option by less than 4 percentage points (Table 4). In a confirmatory analysis, the case-based scenarios were also modeled in the treatment-naive moderate hypertension profile using sham-adjusted SBP reductions (4.9 mmHg) for the intervention and placebo-adjusted reductions (−5.1 mmHg) for drug therapies. There was no relevant impact on patient preference, with 22.7% (16.7–28.6) likelihood of preferring interventional therapy and 77.3% (71.4–83.3) likelihood of opting for added drugs. In an exploratory analysis, which included the option of no treatment, the likelihood of patients opting for this alternative was less than 5% for all three patient profiles.

DISCUSSION

The patient profiles evaluated in this study represent populations across the spectrum of hypertension that physicians encounter in everyday practice, and for which outcome data are available for RDN and drug therapies. The baseline clinical characteristics were comparable to the populations enrolled in the trials of RDN: the SPYRAL HTN-ON MED trial [20], the SPYRAL HTN-OFF MED PIVOTAL trial [19], the Global SYMPLICITY Registry (GSR) DEFINE study [21], the RADIANCE-HTN SOLO trial [31], the RADIANCE-HTN TRIO trial [32], and RADIANCE II trial [33] are broadly representative of the characteristics of patients with hypertension in the USA [28,29]. This analysis indicates that a substantial minority of patients of all types were in favor of novel interventional therapies to reduce BP. Nonetheless, in our model, the likelihood of a hypothetical patient with elevated SBP opting for the intervention increased along the spectrum of hypertension, from 17% in treatment-naive patients to 42% of patients with drug-resistant hypertension. These findings align with a number of recent non-DCE surveys, which reported that a sizeable minority of patients with hypertension prefer an interventional treatment alternative, such as RDN, over medications [8,9,11,22].

TABLE 4. Analysis of safety changes in the predicted likelihood of a patient population with treated mild-to-moderate hypertension preferring an intervention or additional pharmacotherapy, respectively

Variable	Likelihood of preferring treatment option (95% confidence interval)	
	Intervention with maintained medications	Added drug
Base case (moderate hypertension untreated)	17.2% (11.6–22.7)	82.8% (77.3–88.4)
Safety		
Risk of drug side effects		
Reduce risk to 1%	17.2% (12.2–22.2)	82.8% (77.8–87.8)
Increase risk to 20%	23.1% (16.1–30.0)	76.9% (70.0–83.9)
Risk of temporary pain and bruising with intervention		
Reduce risk to 1%	21.2% (15.5–26.9)	78.8% (73.1–84.6)
Increase risk to 20%	23.2% (16.6–29.7)	76.8% (70.3–83.4)
Risk of vascular injury with intervention		
Reduce risk to 1%	22.5% (16.0–29.0)	77.5% (71.0–84.0)
Increase risk to 20%	15.8% (10.1–21.4)	84.2% (78.61–89.9)

Assumptions and references are shown in Table 1.

To our knowledge, this is the first model of hypertension treatment preferences of patients based on a DCE to include interventional therapies [10]. A recent DCE analysis from China indicated that patients put the greatest value on healthcare services that generated good treatment effects, but the study did not differentiate between treatments and patient's hypertension profile [34]. A greater preference for interventional treatment in patients with higher BP is in agreement with their expected treatment effect (BP reduction), which improves with the increased level of a patient's baseline BP [35]. The magnitude of SBP reduction was the main driver in the DCE utilized for the model. Thus, over the course of a patient's progression of disease development and management, a higher BP would increase the expected efficacy and subsequent preference for an interventional option.

The proportion of treatment-naive patients open to intervention (17%) is notable and overall in agreement with that has been reported in other non-DCE studies using different methodologies [8,9]. As has been recently emphasized in a clinical consensus statement, some patients with hypertension are unwilling or unable to take antihypertensive drugs or increase their medication burden, especially if they have associated comorbid conditions [36].

In the sensitivity analyses, the greatest observed effects on patient choice were associated with variables linked to SBP-reduction, for example, the magnitude of efficacy, an increased duration of interventional treatment effect, and the impact of reduced medication adherence. In contrast, varying the assumed safety risks with an intervention had only a minor impact on predicted likelihoods. Even large deviations in safety assumptions reduced the likelihood for the treatment option by only a few percentage points. These findings are in accordance with the patient preferences reported in the original DCE [22].

Due to the impact of medication adherence on drug efficacy, we examined the influence of nonadherence on treatment choice in the sensitivity analysis. The multifactorial nature of nonadherence and the lack of standardized definitions of the condition render modeling medication nonadherence speculative. It is well established that escalating medications, especially when combined with multiple daily doses, is a major barrier to adherence [37–39]. Another reason to evaluate the impact of medication adherence is the 'always-on' effect of RDN in durable blood pressure reductions throughout the 24 h day, differentiating the therapy from drug therapy [3,4]. For this analysis, we assumed a uniform 20% reduction in drug effect on SBP and risk of side effects to model partial medication nonadherence. Even these modest assumed reductions had a major negative impact on the preference for medications over intervention. This suggests that reductions in efficacy outweigh the improved safety risk in patient preferences.

An interventional treatment effect of only 1 year is likely a conservative estimate for RDN, as sustained and even progressive reductions in SBP 3 years after RDN have been reported [21,23,25,40]. Extending the assumed interventional treatment effect from 1 to 3 years greatly increased the likelihood of patients preferring an intervention because of this increased treatment effect over time. Other reports indicate that the BP-lowering effect may last for at least 9 years [26,27,41], although more evidence from extended follow-up of patients undergoing RDN is needed to verify this finding. This long-term effect is in contrast to pharmacotherapy, which has a reported waning effectiveness over 5–10 years [42] and requires strict adherence, thus necessitating drug dose and/or number escalation.

RDN is recommended in the latest guidelines from the European Society of Hypertension 'as a treatment option in patients an eGFR greater than 40 ml/min/1.73 m^2 who have uncontrolled BP despite the use of antihypertensive drug combination therapy, or if drug treatment elicits serious side effects and poor quality of life' with a Class II recommendation and Level of Evidence B [43]. It has a strong recommendation (Class I) for RDN in a shared decision-making process after patients have received objective and complete information [43]. It is widely known that greater patient participation in medical care is associated with improved outcomes in chronic diseases [44]. The outcomes from our model will help treating physicians by estimating different patients' interest in hypertension treatment options with guidance toward individualized, shared-decision management process.

This study has several limitations. The weight of patient preferences were based on the results from the original DCE and are subject to the limitations of that type of study, such as the required restriction to seven treatment attributes [22]. Patients in the original DCE may not fully represent those patients that were characterized in the profiles used in the current model [22]. The definition of uncontrolled office SBP in the DCE was at least 150 mmHg, which is higher than the 140 mmHg used in clinical practice guidelines [43]. SBP reduction with drugs often results in diminishing efficacy with increasing numbers of baseline medication [45], although this is not a consistent finding. This treatment effect was not evaluated in this study as the 10 mmHg SBP reduction was used in all three scenarios regardless of antihypertensive classes. The model does not include other parameters such as cost and access to care that may influence patient decision-making in the real-world. The impact of comorbidities and the option of adding two antihypertensive drugs at low dose or in combination in a single pill were also not assessed. Further, the assumptions of the degree and impact of nonadherence is a simplification of the effects on efficacy and safety. Medication nonadherence is a complicated issue, and there is a wide scope for variations in these assumptions. Finally, the duration of interventional treatment effect that was evaluated has strong data at 1 year but is less well supported at 3 years. However, these estimates are based on the available published RDN data and provide insight into what may be an important long-term treatment effect for RDN.

In conclusion, this modeling study indicates that the likelihood of an individual with uncontrolled hypertension opting for an interventional treatment ranges from 17 to 42% in common clinical presentations of hypertension. Patient preference is mostly driven by the magnitude of the expected degree of BP reduction while the safety of intervention and drug therapy side effects have little if any impact on preference. Preference for an interventional treatment such as RDN was increased by nonadherence to prescribed drug therapy and by an increased treatment

effect from 1 to 3 years based on evidence from RDN studies. Awareness of patient interest in interventional treatment options and the outcomes of these sensitivity analyses will aid physicians in their discussions with patients on hypertension management, whether the patients are treatment-naive, have moderate hypertension, or have drug-resistant hypertension.

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Conflicts of interest

A.P. reports personal consulting from Medtronic, ReCor, Ablative Solutions, Merck, Recordati, Boehringer Ingelheim, and Astra Zeneca. M.A.W. has received consulting fees from Medtronic, ReCor, Ablative Solutions, Johnson & Johnson, and Urovant. C.P. is a full-time employee of RTI Health Solutions, an independent, nonprofit research organization that has received funding pursuant to a contract with Medtronic to conduct the study. S.A.C. is a consultant for consultant for Medtronic, and owns Medtronic stock options. V.D.B. is an employee of Medtronic. D.E.K reports institutional research/grant support from Biotronik, Orbus Neich, Teleflex, Medtronic, and Ablative Solutions; and personal consulting honoraria from Medtronic, Ablative Solutions, and DeepQure.

REFERENCES

1. NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in hypertension prevalence and progress in treatment and control from 1990 to 2019: a pooled analysis of 1201 population-representative studies with 104 million participants. *Lancet* 2021; 398:957–980.
2. Burnier M, Egan BM. Adherence in hypertension: a review of prevalence, risk factors, impact, and management. *Cir Res* 2019; 124:1124–1140.
3. Kandzari DE, Townsend RR, Bakris G, Basile J, Bloch MJ, Cohen DL, *et al*. Renal denervation in hypertension patients: proceedings from an expert consensus roundtable cosponsored by SCAI and NKF. *Catheter Cardiovasc Interv* 2021; 98:416–426.
4. Schmieder RE, Mahfoud F, Mancia G, Azizi M, Böhm M, Dimitriadis K, *et al*. European Society of Hypertension position paper on renal denervation 2021. *J Hypertens* 2021; 39:1733–1741.
5. Stacey D, Légaré F, Lewis KB. Patient decision aids to engage adults in treatment or screening decisions. *JAMA* 2017; 318:657–658.
6. US Food and Drug Administration. Factors to consider when making benefit-risk determinations in medical device premarket approval and de novo classifications. 2019. Available at: https://www.fda.gov/media/99769/download. (Accessed 3 April 2020)
7. European Medicines Agency. Engagement framework: EMA and patients, consumers and their organisations. 2022. Available at: https://www.ema.europa.eu/documents/other/engagement-framework-european-medicines-agency-patients-consumers-their-organisations_en.pdf. [Accessed 20 December 2023]
8. Schmieder RE, Högerl K, Jung S, Bramlage P, Veelken R, Ott C. Patient preference for therapies in hypertension: a cross-sectional survey of German patients. *Clin Res Cardiol* 2019; 108:1331–1342.
9. Schmieder RE, Kandzari DE, Wang T-D, Lee Y-H, Lazarus G, Pathak A. Differences in patient and physician perspectives on pharmaceutical therapy and renal denervation for the management of hypertension. *J Hypertens* 2021; 39:162–168.
10. Kandzari DE, Weber MA, Poulos C, Coulter J, Cohen SA, DeBruin V, *et al*. Patient preferences for pharmaceutical and device-based treatments for uncontrolled hypertension: discrete choice experiment. *Circ Cardiovasc Qual Outcomes* 2022; 16:e008997.
11. Kario K, Kagitani H, Hayashi S, Hanamura S, Ozawa K, Kanegae H. A Japan nationwide web-based survey of patient preference for renal denervation for hypertension treatment. *Hypertens Res* 2022; 45:232–240.
12. Soekhai V, de Bekker-Grob EW, Ellis AR, Vass CM. Discrete choice experiments in health economics: past, present and future. *Pharmacoeconomics* 2019; 37:201–226.
13. Blood Pressure Lowering Treatment Trialists' Collaboration. Effect of antihypertensive drug treatment on long-term blood pressure reduction: an individual patient-level data meta-analysis of 352,744 Participants from 51 large-scale randomised clinical trials. *medRxiv* 2021.
14. Canoy D, Copland E, Nazarzadeh M, Ramakrishnan R, Pinho-Gomes A-C, Salam A, *et al*. Antihypertensive drug effects on long-term blood pressure: an individual-level data meta-analysis of randomised clinical trials. *Heart* 2022; 108:1281–1289.
15. ONTARGET Investigators: Yusuf S, Teo KK, Pogue J, Dyal L, Copland I, *et al*. Telmisartan, ramipril, or both in patients at high risk for vascular events. *N Engl J Med* 2008; 358:1547–1559.
16. Heran BS, Wong MM, Heran IK, Wright JM. Blood pressure lowering efficacy of angiotensin converting enzyme (ACE) inhibitors for primary hypertension. *Cochrane Database Syst Rev* 2008; 2008:CD003823.
17. ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group. The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial. Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker vs diuretic: the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). *JAMA* 2002; 288:2981–2997.
18. Julius S, Kjeldsen SE, Brunner H, Hansson L, Platt F, Ekman S, *et al*. VALUE trial: Long-term blood pressure trends in 13,449 patients with hypertension and high cardiovascular risk. *Am J Hypertens* 2003; 16:544–548.
19. Böhm M, Kario K, Kandzari DE, Mahfoud F, Weber MA, Schmieder RE, *et al*., SPYRAL HTN-OFF MED Pivotal Investigators. Efficacy of catheter-based renal denervation in the absence of antihypertensive medications (SPYRAL HTN-OFF MED Pivotal): a multicentre, randomised, sham-controlled trial. *Lancet* 2020; 395:1444–1451.
20. Kandzari DE, Böhm M, Mahfoud F, Townsend RR, Weber MA, Pocock S, *et al*., SPYRAL HTN-ON MED Trial Investigators. Effect of renal denervation on blood pressure in the presence of antihypertensive drugs: 6-month efficacy and safety results from the SPYRAL HTN-ON MED proof-of-concept randomised trial. *Lancet* 2018; 391:2346–2355.
21. Mahfoud F, Mancia G, Schmieder RE, Ruilope L, Narkiewicz K, Schlaich M, *et al*. Cardiovascular risk reduction after renal denervation according to time in therapeutic systolic blood pressure range. *J Am Coll Cardiol* 2022; 80:1871–1880.
22. Kandzari DE, Weber MA, Poulos C, Coulter J, Cohen SA, DeBruin V, *et al*. Patient preferences for pharmaceutical and device-based treatments for uncontrolled hypertension: discrete choice experiment. *Circ Cardiovasc Qual Outcomes* 2023; 16:e008997.
23. Mahfoud F, Kandzari DE, Kario K, Townsend RR, Weber MA, Schmieder RE, *et al*. Long-term efficacy and safety of renal denervation in the presence of antihypertensive drugs (SPYRAL HTN-ON MED): a randomised, sham-controlled trial. *Lancet* 2022; 399:1401–1410.
24. Vrijens B, Vincze G, Kristanto P, Urquhart J, Burnier M. Adherence to prescribed antihypertensive drug treatments: longitudinal study of electronically compiled dosing histories. *BMJ* 2008; 336:1114–1117.
25. Bhatt DL, Vaduganathan M, Kandzari DE, Leon MB, Rocha-Singh K, Townsend RR, *et al*., SYMPLICITY HTN-3 Steering Committee Investigators. Long-term outcomes after catheter-based renal artery denervation for resistant hypertension: final follow-up of the randomised SYMPLICITY HTN-3 Trial. *Lancet* 2022; 400:1405–1416.
26. Sesa-Ashton G, Nolde JM, Muente I, Carnagarin R, Lee R, Macefield VG, *et al*. Catheter-based renal denervation: 9-year follow-up data on safety and blood pressure reduction in patients with resistant hypertension. *Hypertension* 2023; 80:811–819.
27. Al Ghorani H, Kulenthiran S, Recktenwald MJM, Lauder L, Kunz M, Götzinger F, *et al*. 10-year outcomes of catheter-based renal denervation in patients with resistant hypertension. *J Am Coll Cardiol* 2023; 81:517–519.
28. Bress AP, Tanner RM, Hess R, Colantonio LD, Shimbo D, Muntner P. Generalizability of SPRINT Results to the U.S. Adult Population. *J Am Coll Cardiol* 2016; 67:463–472.
29. Muntner P, Carey RM, Gidding S, Jones DW, Taler SJ, Wright JT, *et al*. Potential US population impact of the 2017 ACC/AHA high blood pressure guideline. *Circulation* 2018; 137:109–118.

30. Whelton PK, Carey RM, Aronow WS, Casey DE, Collins KJ, Dennison Himmelfarb C, *et al.* 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: Executive Summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension* 2018; 71:1269–1324.
31. Azizi M, Schmieder RE, Mahfoud F, Weber MA, Daemen J, Davies J, *et al.*, RADIANCE-HTN Investigators. Endovascular ultrasound renal denervation to treat hypertension (RADIANCE-HTN SOLO): a multicentre, international, single-blind, randomised, sham-controlled trial. *Lancet* 2018; 391:2335–2345.
32. Azizi M, Sanghvi K, Saxena M, Gosse P, Reilly JP, Levy T, *et al.*, RADIANCE-HTN investigators. Ultrasound renal denervation for hypertension resistant to a triple medication pill (RADIANCE-HTN TRIO): a randomised, multicentre, single-blind, sham-controlled trial. *Lancet* 2021; 397:2476–2486.
33. Azizi M, Saxena M, Wang Y, Jenkins JS, Devireddy C, Rader F, *et al.*, RADIANCE II Investigators and Collaborators. Endovascular ultrasound renal denervation to treat hypertension: the RADIANCE II Randomized Clinical Trial. *JAMA* 2023; 329:651–661.
34. Yu X, Bao H, Shi J, Yuan X, Qian L, Feng Z, *et al.* Preferences for healthcare services among hypertension patients in China: a discrete choice experiment. *BMJ Open* 2021; 11:e053270.
35. Schmieder RE, Schmidt ST, Riemer T, Dechend R, Hagedorn I, Senges J, *et al.* Disproportional decrease in office blood pressure compared with 24-h ambulatory blood pressure with antihypertensive treatment: dependency on pretreatment blood pressure levels. *Hypertension* 2014; 64:1067–1072.
36. Barbato E, Azizi M, Schmieder RE, Lauder L, Böhm M, Brouwers S, *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; 44:1313–1330.
37. Hill MN, Miller NH, DeGeest S. Adherence and persistence with taking medication to control high blood pressure. *J Am Soc Hypertens* 2011; 5:56–63.
38. Burnier M. Drug adherence in hypertension. *Pharmacological Research* 2017; 125:142–149.
39. Osterberg L, Blaschke T. Adherence to medication. *N Engl J Med* 2005; 353:487–497.
40. Mahfoud F, Mancia G, Schmieder RE, Ruilope L, Narkiewicz K, Schlaich M, *et al.* Outcomes following radiofrequency renal denervation according to antihypertensive medications: subgroup analysis of the Global SYMPLICITY Registry DEFINE. *Hypertension* 2023; 80:1759–1770.
41. Vogt A, Dutzmann J, Nußbaum M, Hoyer D, Tongers J, Schlitt A, *et al.* Safety and efficacy of renal sympathetic denervation: a 9-year long-term follow-up of 24-h ambulatory blood pressure measurements. *Front Cardiovasc Med* 2023; 10:1210801.
42. Jaeger BC, Bress AP, Bundy JD, Cheung AK, Cushman WC, Drawz PE, *et al.* Longer term all-cause and cardiovascular mortality with intensive blood pressure control: a secondary analysis of a randomized clinical trial. *JAMA Cardiol* 2022; 7:1138–1146.
43. Mancia G, Kreutz R, Brunström M, Burnier M, Grassi G, Januszewicz A, *et al.* 2023 ESH Guidelines for the management of arterial hypertension. The Task Force for the management of arterial hypertension of the European Society of Hypertension Endorsed by the European Renal Association (ERA) and the International Society of Hypertension (ISH). *J Hypertens* 2023; 41:1874–2071.
44. Greenfield S, Kaplan SH, Ware JE, Yano EM, Frank HJ. Patients' participation in medical care: effects on blood sugar control and quality of life in diabetes. *J Gen Intern Med* 1988; 3:448–457.
45. SPRINT Research Group. Wright JT, Williamson JD, Whelton PK, Snyder JK, Sink KM, *et al.* A randomized trial of Intensive versus Standard Blood-Pressure Control. *N Engl J Med* 2015; 373:2103–2116.