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ORIGINAL ARTICLE

# Patient Preferences for Pharmaceutical and Device-Based Treatments for Uncontrolled Hypertension: Discrete Choice Experiment

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**BACKGROUND:** Discrete choice experiment is a survey method used to understand how individuals make decisions and to quantify the relative importance of features. Using discrete choice experiment methods, we quantified patient benefit–risk preferences for hypertension treatments, including pharmaceutical and interventional treatments, like renal denervation.

**METHODS:** Respondents from the United States with physician-confirmed uncontrolled hypertension selected between treatments involving a procedure or pills, using a structured survey. Treatment features included interventional, noninterventional, or no hypertension treatment; number of daily blood pressure (BP) pills; expected reduction in office systolic BP; duration of effect; and risks of drug side effects, access site pain, or vascular injury. The results of a random–parameters logit model were used to estimate the importance of each treatment attribute.

**RESULTS:** Among 400 patients completing the survey between 2020 and 2021, demographics included: 52% women, mean age 59.2±13.0 years, systolic BP 155.1±12.3 mm Hg, and 1.8±0.9 prescribed antihypertensive medications. Reduction in office systolic BP was the most important treatment attribute. The remaining attributes, in decreasing order, were duration of effect, whether treatment was interventional, number of daily pills, risk of vascular injury, and risk of drug side effects. Risk of access site pain did not influence choice. In general, respondents preferred noninterventional over interventional treatments, yet only a 2.3 mm Hg reduction in office systolic BP was required to offset this preference. Small reductions in office systolic BP would offset risks of vascular injury or drug side effects. At least a 20% risk of vascular injury or drug side effects would be tolerated in exchange for improved BP.

**CONCLUSIONS:** Reduction in systolic BP was identified as the most important driver of patient treatment preference, while treatment-related risks had less influence. The results indicate that respondents would accept interventional treatments in exchange for modest reductions in systolic BP compared with those observed in renal denervation trials.

**Key Words:** ablation techniques ■ antihypertensive agents ■ autonomous denervation ■ hypertension ■ patient preference ■ renal artery ■ sympathetic nervous system

Against the background of a high prevalence of uncontrolled hypertension (HTN)[1] and growing recognition of medication nonadherence,[2] there are an increasing number of studies evaluating renal denervation (RDN) and alternative interventional technologies for the treatment of HTN. In addition to clinically meaningful and sustainable reductions in blood pressure (BP) after RDN in randomized trials,[3–8] studies have demonstrated achievement of targeted BP measures with fewer medications or reduced dosages compared with a control group.[9,10]

Patient-reported symptoms, outcomes, and preferences are important in assessing the benefits and risks of antihypertensive therapy; yet, they are rarely incorporated

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## WHAT IS KNOWN

- Renal denervation is an interventional procedure that has been shown to safely lower blood pressure in patients with uncontrolled hypertension in randomized sham-controlled clinical trials. However, further investigation is needed to better understand patient preferences for an interventional procedure compared with antihypertensive medications.
- Discrete choice experiment is a survey-based preference assessment method commonly used to quantify how individuals value selected features of hypothetical treatment options.

## WHAT THE STUDY ADDS

- This is the first discrete choice experiment study to examine patient preferences for hypertension treatments involving interventional and/or oral antihypertensive treatments.
- A discrete choice experiment survey was conducted with 400 patients with physician-documented uncontrolled hypertension on 0 to 3 antihypertensive medications.
- Reduction in systolic BP was identified as the most important driver of patient treatment preference in this DCE, whereas treatment-related risks had less influence.
- Results determined that patients in the survey were willing to accept interventional treatment in exchange for reductions in office systolic blood pressure smaller than those reported in randomized sham-controlled clinical trials of renal denervation.

## Nonstandard Abbreviations and Acronyms

| | |
|---|---|
| **BP** | blood pressure |
| **DCE** | discrete choice experiment |
| **HTN** | hypertension |
| **RDN** | renal denervation |
| **SBP** | systolic blood pressure |

into trials evaluating pharmaceutical or device-oriented strategies. An individual's interest in treatment for HTN is conditioned by an understanding of the clinical benefit of lowering BP, symptoms, or adverse events associated with either uncontrolled HTN or medications, and physician endorsement.[11]

Considering the potential of RDN to lower BP and medication burden, and the potential for procedure-related adverse events, assessing patient preference for alternatives to traditional pharmaceutical and lifestyle interventions is essential. In recent surveys of patients with HTN, approximately one-third preferred RDN over escalation of medications for BP control.[11,12] Notably, preference for device-based therapy among patients may be highest among those not taking medications and may be independent of BP severity.[11] Such observations not only inform clinical practice and development of guidelines, but rigorously developed quantitative patient preference information may also be used as valid scientific evidence to aid the Food and Drug Administration in regulatory decision making.[13–15]

A discrete choice experiment (DCE) is a survey-based preference assessment method commonly used to quantify how individuals value selected features of hypothetical treatment options. DCE enables quantitative estimates of risk tolerance, including the maximum acceptable risks of a treatment that patients are willing to accept in exchange for a given treatment benefit and the minimum level of treatment benefit required to offset a specific treatment-related risk. We applied DCE to (1) quantify patients' preferences for attributes of interventional and pharmaceutical treatments for HTN that include both efficacy and risks of treatment-related adverse events, and (2) examine the trade-offs that individuals with uncontrolled HTN are willing to make among different treatment attributes when choosing among varied treatment options.

# METHODS

Because of the sensitive nature of the data collected for this study, requests to access the dataset from qualified researchers trained in human subject confidentiality protocols may be sent to Medtronic at vanessa.debruin@medtronic.com.

## Discrete Choice Experiment

The DCE method is a survey method that is increasingly used to assess preferences for attributes of products or items, including medical treatments.[16] We used DCE to quantify benefit–risk preferences because it can simultaneously evaluate multiple treatment features that vary between interventional and pharmaceutical HTN treatments.[17–19] In a DCE survey, respondents evaluate a series of treatment choice pairs, with treatments characterized by varying attribute levels regarding mode, efficacy, and risks. Respondents' choices among treatments depend on their relative preferences for attribute levels. The analysis of choices yields preference weights that describe how each attribute level influences the likelihood of choosing a treatment profile. The preference weights are used to calculate conditional, relative attribute importance, which describes the magnitude of the influence that differing attribute levels have on treatment choice. Preference weights also provide insights into the maximum acceptable risk acceptable in exchange for a treatment benefit, and the minimum acceptable benefit required in exchange for a level of treatment-related risk.[14,20]

The study was designed in collaboration with the US Food and Drug Administration and followed Food and Drug Administration guidelines for Patient Preference Information studies conducted for benefit–risk assessment and guidelines prepared by the International Society for Pharmacoeconomics and Outcomes Research.[18,21–23]

## Survey Development

From RDN clinical trial end points, safety events, and HTN-related outcomes recognized to be salient for clinicians and patients,[5–7,24,25] 7 attributes were identified (Table 1): (1) whether the treatment was interventional or pharmaceutical; (2) number of daily BP pills; (3) reduction in office systolic blood pressure (SBP); (4) duration of effect; (5) risk of drug-related side effects; (6) risk of access site pain and/or bruising at the site of vascular access for an interventional treatment; and (7) risk of vascular injury (including renal artery stenosis due to interventional treatment). Attribute levels were selected within the ranges observed for clinical trials of HTN treatments. Treatment efficacy was defined as a reduction in office SBP from the respondents' current SBP and included the information that sustained reductions in office SBP reduce the risks of cardiovascular events, although absolute or relative risk reductions were not specified.

In a series of HTN treatment choice questions, respondents chose between 2 hypothetical treatments involving interventional or pharmaceutical therapies that were characterized by specific attributes and levels. Example HTN treatment choice questions are shown in Figure 1. Respondents were asked to consider their own BP and the context of existing therapy, if applicable, at the time of the survey. Respondents were subsequently offered the choice of no HTN treatment at all after each treatment choice question. If patients chose "no treatment" as their preference, this was defined as not taking any medications or interventional procedures. The survey was administered during the coronavirus-19 pandemic, during which restrictions on healthcare access (including elective surgical procedures) were imposed and varied by locality. Respondents were asked to choose HTN treatments as if all restrictions and safety concerns due to coronavirus-19 were removed and asked whether they felt they could successfully make this assumption when making choices.

To pretest the questionnaire, interviews were conducted among 28 patients with physician-confirmed uncontrolled HTN. The semistructured interviews were used to assess whether pretest participants understood the relationship between reduction of BP and reduction of stroke, myocardial infarction, and renal failure, the attribute descriptions and wording, and the pictograms used to communicate side-effect risk. The interviews also explored participants' tolerance for the risks of treatment-related side effects to inform the risk levels included in the DCE. The questionnaire was iteratively revised based on pretest findings until the interviews indicated that the questionnaire was clear. The final questionnaire also included items to measure respondent characteristics, including HTN and treatment history, health status, and socioeconomic and demographic characteristics.

The attribute levels used to describe the pairs of hypothetical HTN treatments presented in the choice questions were determined by an experimental design.[23] SAS statistical software (version 9.4) was used to generate a design with 96 treatment choice questions. To avoid presenting more choice tasks than respondents could reasonably answer in a DCE survey, the experimental design was divided into 8 blocks of 12 questions. Each respondent was randomly assigned to 1 block of treatment choice questions. To avoid having later questions systematically affected by learning and fatigue,[28,29] the order of the questions in each block was randomized for each respondent.

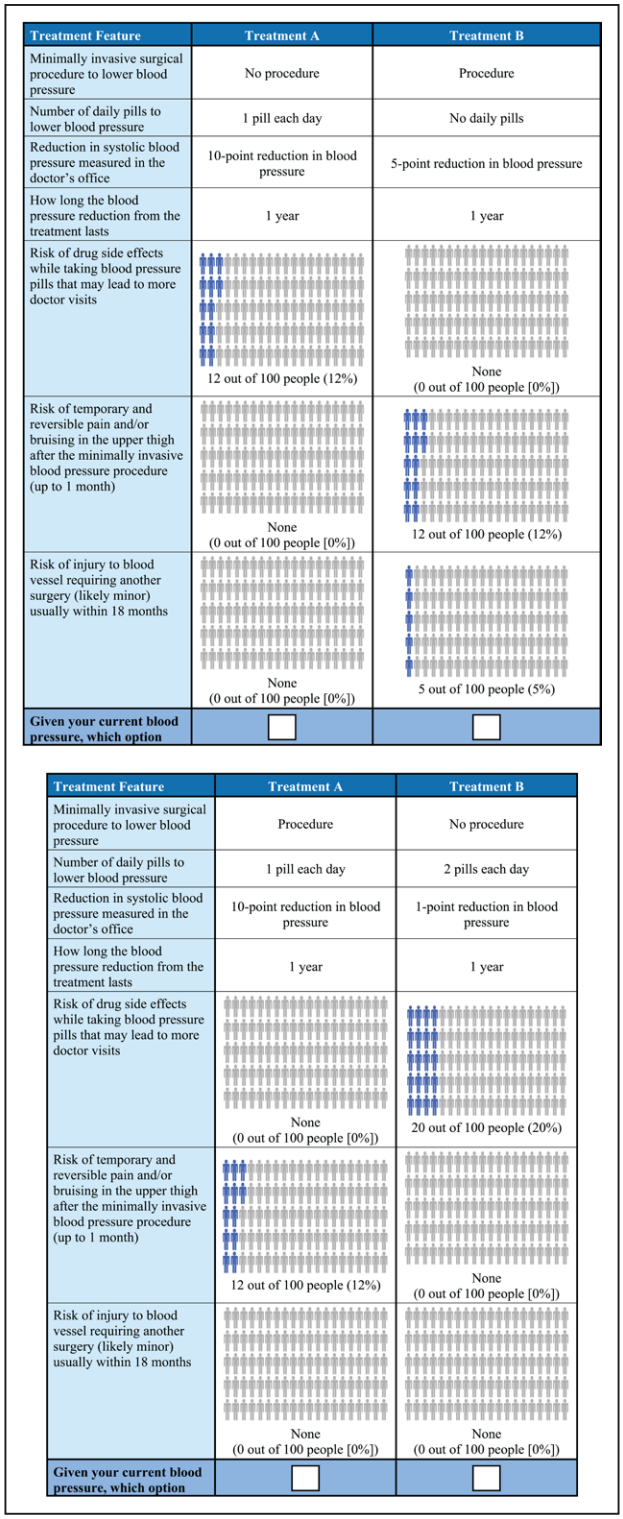


**Figure 1. Two example choice questions.**

The survey included questions to assess respondent engagement, comprehension, and response consistency to evaluate data quality. Ten questions evaluated whether respondents understood and remembered the attribute descriptions and other information in the survey. One treatment choice question included a superior treatment choice (ie, better efficacy and lower risks than the alternative) to evaluate respondents'

attention to attribute levels when answering treatment choice questions. A scope test evaluated respondents' attention to risk levels when answering treatment choice questions.[26,27,30] The scope test was performed to ensure respondents were attentive to the actual attribute levels rather recoding the levels as "low" or "high" when making treatment choices. Additional details on the scope test are provided in Supplemental Methods and Tables S1 and S2. To examine whether survey respondents were trading between all attributes when making treatment choices, the data were examined for attribute dominance (ie, whether survey respondents always chose the treatment with the better level of 1 particular attribute)[31,32]

## Data Collection

Survey respondents were recruited primarily through physicians identified by an independent organization specializing in patient research, including recruiting and data collection (Global Perspectives, Norfolk, England). In addition, patients were recruited using online panels and social media, with eligibility confirmed by the individual's physician.

Inclusion criteria confirmed by the patient's physician were: age, 20 to 80 years; English-speaking resident of the United States; diagnosis of HTN with office SBP ≥ 140 mm Hg and office diastolic BP ≥ 90 mm Hg; and prescription of 0 to 3 oral antihypertensive medications limited to a thiazide-type diuretic, dihydropyridine calcium-channel blocker, angiotensin-converting enzyme/ or angiotensin receptor blocker, and/or beta blocker. BP and medication requirements were modeled after inclusion criteria of contemporary RDN trials.[5,6] Exclusion criteria were: eGFR < 45 mL/min/1.73 $m^2$, prior experience with RDN or other interventional treatments for HTN; chronic oxygen use; and history of cognitive impairment, dementia or Alzheimer disease. In addition, sampling quotas were imposed to recruit a sample that was distributed across 4 US census regions and reflective of the US population with HTN regarding age, sex, race and ethnicity, and number of classes of oral antihypertensive medications.[33,34]

The study protocol was assessed by an independent ethics committee and determined to be exempt from review. All pretest participants and survey respondents provided informed consent.

## Statistical Analysis

A random-parameters logit regression model was used to analyze the treatment choice data and estimate the attribute-level preference weights (details in Supplemental Methods). The model included effect-coded variables for each attribute level in Table 1. The estimated parameters on each attribute level are referred to as preference weights. A 2-sided chi-squared test

**Table 1. Attributes and Levels for the Discrete Choice Experiment Survey**

| Attribute | Attribute levels | |
|---|---|---|
| Interventional treatment | Procedure | |
| | No procedure | |
| Number of oral antihypertensive pills per day | No daily pills | |
| | 1 pill each day | |
| | 2 pills each day | |
| | 3 pills each day | |
| Reduction in office systolic BP | 1-point (1 mm Hg) reduction in BP | |
| | 5-point (5 mm Hg) reduction in BP | |
| | 10-point (10 mm Hg) reduction in BP | |
| | 18-point (18 mm Hg) reduction in BP | |
| Duration of effect | 1 y | |
| | 3 y | |
| | 10 y | |
| Risk of reversible drug side effects such as fatigue/drowsiness or dizziness, frequent urination, swollen ankles, sexual problems, persistent cough, or acute kidney injury due to oral antihypertensive medication | None (0 out of 100 people [0%]) | |
| | 4 out of 100 people (4%) | |
| | 12 out of 100 people (12%) | |
| | 20 out of 100 people (20%) | |
| Risk of temporary and reversible pain and/or bruising at the site of vascular access for interventional treatment | None (0 out of 100 people [0%]) | |
| | 4 out of 100 people (4%) | |
| | 12 out of 100 people (12%) | |
| | 20 out of 100 people (20%) | |
| Risk of vascular injury, including narrowing of the artery to the kidney | *Narrow* range:* None (0 out of 100 people [0%]) | *Wide* range:* None (0 out of 100 people [0%]) |
| | 1 out of 100 people (1%) | 5 out of 100 people (5%) |
| | 5 out of 100 people (5%) | 20 out of 100 (20%) people |

BP indicates blood pressure.

*The study included an assessment of respondents' sensitivity to absolute differences in risks,[26,27] known as a scope test. Respondents were randomly assigned to 1 of the 2 ranges of the risk of vascular injury: narrow or wide.

was used to evaluate differences between preference weights. Statistical analyses were conducted using Stata Version 16 (StataCorp LP, College Station, Tex.) and NLOGIT (version 5). The estimated parameters on each attribute level were rescaled as follows. The difference between the largest and smallest parameter within each attribute was calculated. These differences were summed across attributes and the sum scaled to 100. The parameters corresponding to each attribute were scaled accordingly.

The preference weights were used to calculate 3 measures of benefit–risk preferences. First, the preference weights were used to calculate the conditional relative importance of each attribute, defined as the difference between the preference weights corresponding to the most and least preferred levels of an attribute and represented as a percentage of the sum of the importance of all attributes.

Second, the preference weights were used to calculate 2 measures of risk tolerance: the maximum acceptable risk and minimum acceptable benefit.[14,20] Maximum acceptable risk is the level of treatment-related risk that offsets a specific change in another attribute's levels. For example, an improvement in BP reduction increases the likelihood of choosing a treatment, which is reflected in a higher log-odds preference weight for the more preferred level. The increase in the treatment-related risk that exactly offsets that change in likelihood of treatment choice is the maximum acceptable risk. The maximum acceptable risk estimates were censored at a 20% risk of each adverse event to avoid extrapolation outside of the risk range in the DCE design. Minimum acceptable benefit is the level of reduction in office SBP that offsets an undesirable change in another treatment attribute, such as increased treatment-related risk. Each minimum acceptable benefit calculated should be interpreted as being in addition to a 1 mm Hg reduction, the minimum office SBP change evaluated for this attribute. Both measures reflect the tolerance for risk assuming respondents switch from their current treatment to another treatment, and do not reflect the tolerable level of risk for a HTN treatment over opting-out of treatment.

Finally, the predicted probability of choosing among a set of treatments, each with a specific benefit-risk profile was calculated using the sum of preferences-weighted treatment attributes. In this analysis, the probability of selecting an interventional treatment over no HTN treatment is calculated for interventional treatments, with the highest treatment risks in the study and varying levels of office SBP reduction based on meta-analyses.[35,36]

## RESULTS

Between October 2020 and March 2021, 505 adults were either referred by physicians or identified from online panels and social media. Of these, 400 adults (79%) met the eligibility criteria, consented, and completed the survey. The majority of respondents (n=346; 86.5%) were recruited through physicians, and 54 (13.5%) individuals were recruited via online panels or social media.

Selected respondent characteristics are summarized in Table 2 (additional characteristics are reported in Tables S3 and S4). Approximately one-half (52%) of the sample consisted of women, the median age was 59 years, and more than one-half of the sample had a diagnosis of HTN for >5 years. Average office SBP was 155 mm Hg. Overall, the average age, average number of classes of oral antihypertensive medications, and proportion of the sample by sex, race, and ethnicity were similar to the broader US population with HTN.[33,34]

**Table 2. Respondent Characteristics**

| | Respondents (N=400) |
|---|---|
| Age (y) | 59.2±13.0 |
| Women (%) | 206 (51.5%) |
| Race or ethnicity | |
| White | 269 (67.3%) |
| Black or African American | 59 (14.8%) |
| Hispanic or Latino | 36 (9.0%) |
| Asian | 20 (5.0%) |
| Other | 16 (4%) |
| History of hypertension (y) | |
| ≤5 | 171 (42.8%) |
| 6–10 | 111 (27.8%) |
| >10 | 118 (29.5%) |
| Highest level of education completed | |
| Less than high school degree | 10 (2.5%) |
| High school degree or equivalent | 101 (25.3%) |
| Technical school or some college education | 122 (30.5%) |
| 4-year college degree | 115 (28.8%) |
| Graduate degree | 52 (13.0%) |
| Baseline prescribed oral antihypertensive pills* | 1.8±0.9 |
| 0 | 33 (8.3%) |
| 1 | 133 (33.3%) |
| 2 | 129 (32.3%) |
| 3 | 105 (26.3%) |
| Office blood pressure* (mm Hg) | |
| Systolic blood pressure | 155.1±12.3 |
| Diastolic blood pressure | 95.2±5.3 |

Data are presented as mean ± standard deviation or n (%).

*These screening questions were completed by either the recruiting physician from Global Perspectives' network of physicians or the respondent's physician if recruited through other methods (online panels or social media) using a case report form provided by Global Perspectives.

### Response Consistency

The majority of respondents (72%) answered all 10 of the comprehension questions correctly (responses in Table S5). Nearly all (92%) respondents selected a superior treatment over an inferior alternative, and the sample passed the scope test (detailed in Supplemental Methods), indicating that respondents understood the quantitative levels of vascular injury risk.

The analysis of attribute dominance indicated that over one-half of the sample (n=232; 58%) of respondents made choices based on a single attribute. Although we

can identify respondents with dominant preferences, we cannot determine whether respondents made their treatment choices on the basis of 1 attribute to simplify the choice tasks (which may bias preference estimates) or whether these choices are an accurate representation of strong preferences for that attribute. Two sets of analysis were conducted to evaluate these possibilities. First, whether respondents with dominant preferences for 1 or more attributes were more likely to answer questions incorrectly or choose the no treatment alternative was evaluated by calculating the correlation between dominance and (1) the number of comprehension questions that the respondents answered correctly and (2) the number of times the respondent selected the opt-out (ie, no treatment) alternative. Second, an evaluation of whether respondents who dominated on systolic BP reduction (n=128; 32%) or whether the treatment involved an intervention (n=144; 36%) were more likely to answer comprehension questions incorrectly or choose the opt-out alternative was performed. None of the correlation coefficients in these analyses were statistically significant, and the correlation coefficients indicated very low levels of correlation (see Tables S6–S9 in Supplemental Materials for details). Thus, respondents with dominant preferences were neither more likely to answer comprehension questions incorrectly nor more likely to select the opt-out alternative. These findings therefore suggest that dominance may reflect true preferences.

## Preference Weights

The attribute with the strongest influence on treatment choices was the reduction in office SBP (Figure 2). The remaining attributes had lower relative importance and, in decreasing order, were: duration of effect; whether treatment was interventional; number of daily pills; risk of vascular injury; and risk of drug side effects. Further, Figure 2 shows that all improvements in SBP reductions (patients preferring 5 mm Hg reduction over 1 mm Hg reduction, 10 mm Hg over 5 mm Hg, etc.) had a greater influence on treatment choice than any other change in attribute levels.

None of the relative preference weights for any level of the risk of temporary pain and bruising were statistically significantly different than any other (Figure 3), indicating that, on average, the different levels of the risks of access site pain and bruising did not influence treatment choices. The preference weight on the no treatment variable indicates that respondents preferred the treatments in the survey compared with no treatment. Within each attribute, the preference weights for most attribute levels were statistically significantly different from one another with 95% confidence interval, indicating that respondents differentiated between the levels, on average, when making treatment choices. Raw data of the preference weights are included in Table S10.

The preferences are well ordered (Figure 3), as better clinical outcomes were preferred. More specifically, larger BP reductions were preferred to smaller BP reductions, longer duration of effect was preferred to shorter duration of effect, fewer daily pills were preferred to more daily pills, and lower risks of vascular injury were preferred to higher risks.

## Maximum Acceptable Risk and Minimum Acceptable Benefit

The maximum acceptable risk of drug-related side effects and vascular injuries exceeded 20% for every possible improvement in BP reduction, every possible improvement in duration of effect in the study design, and for a noninterventional rather than an interventional treatment (all other attributes assumed to be held constant). In addition, the maximum acceptable risk of drug-related side effects exceeded 20% for every possible reduction in the number of BP pills per day in the study design. The maximum acceptable risk of vascular injury exceeded 20% only for reducing the number of BP pills per day from 3 to none. Respondents were less tolerant of vascular injury risks in exchange for other changes in the number of pills, as detailed in Table S11.

For minimum acceptable benefit, respondents would require that treatment reduce office SBP by anything >0 mm Hg in exchange for bearing an increase in the risks of drug-related side effects by 20% and 1.1 mm Hg [95% CI, 0.6–1.6] in exchange for bearing an increase in the risks of vascular injury by 20% (assuming all other attributes are held constant). If all other attributes were equal, respondents would prefer to avoid interventional treatments for HTN, yet only a 2.3 mm Hg reduction in office SBP, on average, [95% CI, 1.7–2.9] was required to offset this preference.

# DISCUSSION

Despite the availability of efficacious pharmacological treatments, HTN remains the leading global cause of death and disability,[37] and BP control rates are not achieved in nearly 60% of all individuals with HTN[1] irrespective of treatment. Interventional therapies, such as catheter-based RDN, have demonstrated consistent and clinically meaningful reductions in BP.[3–7,9,38,39] Accordingly, a DCE assessment of patient preference for alternatives to traditional pharmaceutical and lifestyle interventions is essential to align treatments with patient values in the shared decision-making process. As the first DCE inclusive of both pharmaceutical and interventional therapies for HTN, the findings of this study are: (1) respondents prioritized BP reduction over all other attributes and prefer receiving treatment over no treatment; (2) procedural safety and drug-related side effects did not substantially influence preference

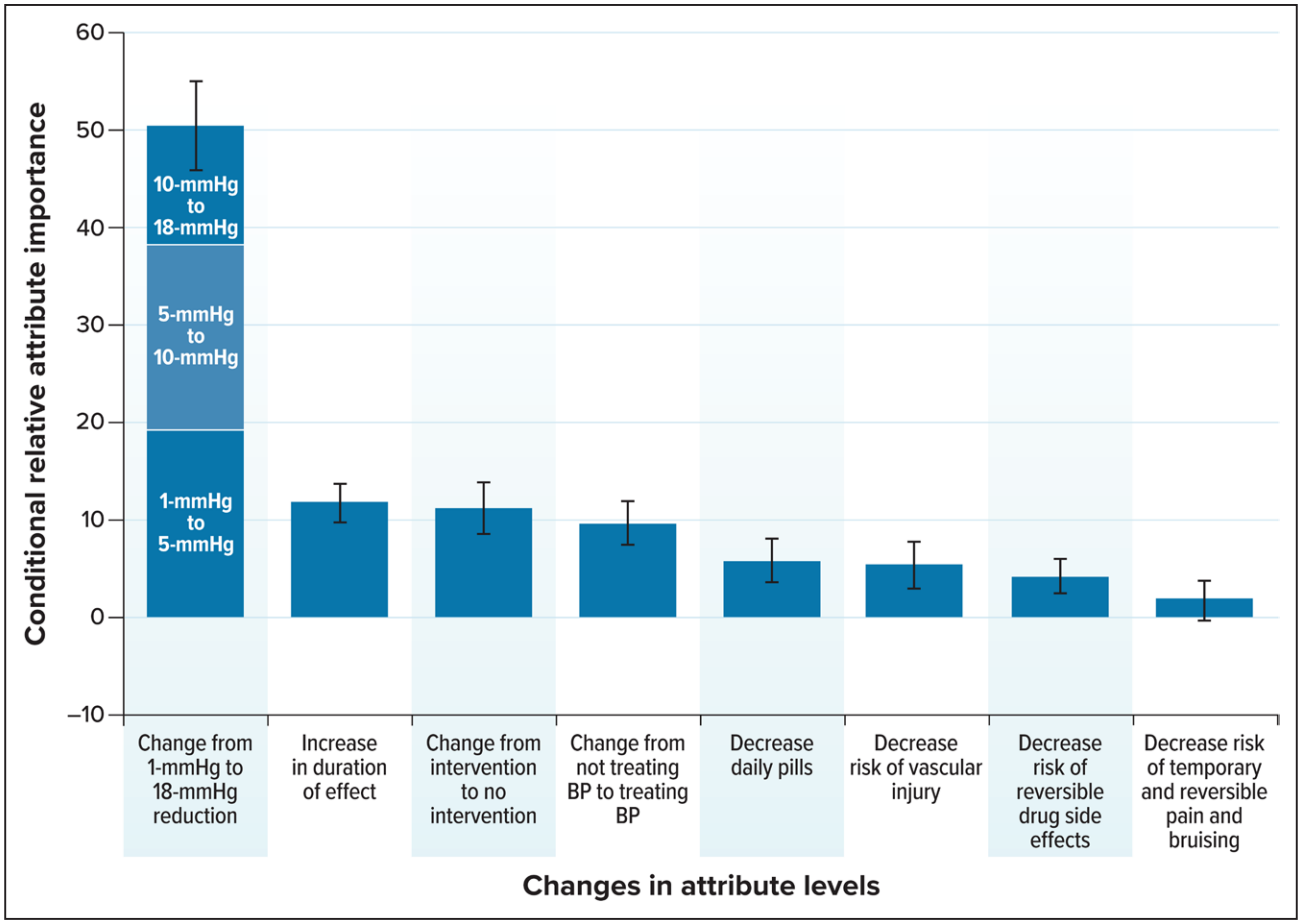


**Figure 2. Conditional relative importance.**
BP indicates blood pressure. The conditional relative importance is the difference between the preference weights on the most influential attribute level and the least influential attribute level. These differences are summed across attributes, and the sum is scaled to 100. The conditional importance of each attribute is a percentage of this total. The vertical bars surrounding each relative importance weight estimate denote the 95% confidence interval around the point estimate (computed by the delta method).

for effective treatment; (3) an estimated 2.3-mm Hg reduction in SBP was required to shift patient preference in favor of interventional therapy; and (4) patients' tolerance for risk was higher and expectation for benefit was lower than what has been observed in recent randomized sham-controlled trials of RDN.

Inclusion criteria were purposely matched with those of recent randomized, sham-controlled RDN trials[40] but also intended to represent a contemporary US population with HTN regarding age, race and ethnicity, as well as number and classes of oral antihypertensive medications. Approximately one-half of participants were women, the average SBP was 155 mm Hg, and more than half were prescribed 2 to 3 antihypertensive medications. Additionally, pretesting was performed to refine the survey prior to data collection to improve comprehension of the nature of treatments and treatment-related risks. This was also validated by the comprehension questions and response consistency.

In general, reduction in office SBP had a greater influence on treatment choice than on duration of BP lowering effect, number of daily pills, risk of drug-related side effects, and even risk of vascular injury. However, the results indicate that the risks of treatment-related adverse events were less influential than treatment efficacy. In fact, the maximum acceptable risk of drug-related side effects or vascular injury exceeded 20% for every possible improvement in BP reduction or duration of effect, most reductions in the number of BP pills per day, and for a noninterventional rather than an interventional treatment. Notably, this level of risk far exceeds observed procedural adverse event rates in randomized controlled trials of RDN.[5–7,25]

Preference for interventional treatment similarly increased with the magnitude of the BP reduction. As an example, Figure 4 illustrates the predicted probability of choosing an interventional treatment (without medications) over no HTN treatment when the interventional treatment has the maximum levels of the risks of procedure-related side effects included in the survey. The predicted probability of choosing an interventional treatment with these characteristics would be 6.9% if the office SBP reduction was 2.5 mm Hg. The probability increases with the reduction in office SBP, with 76.5% predicted

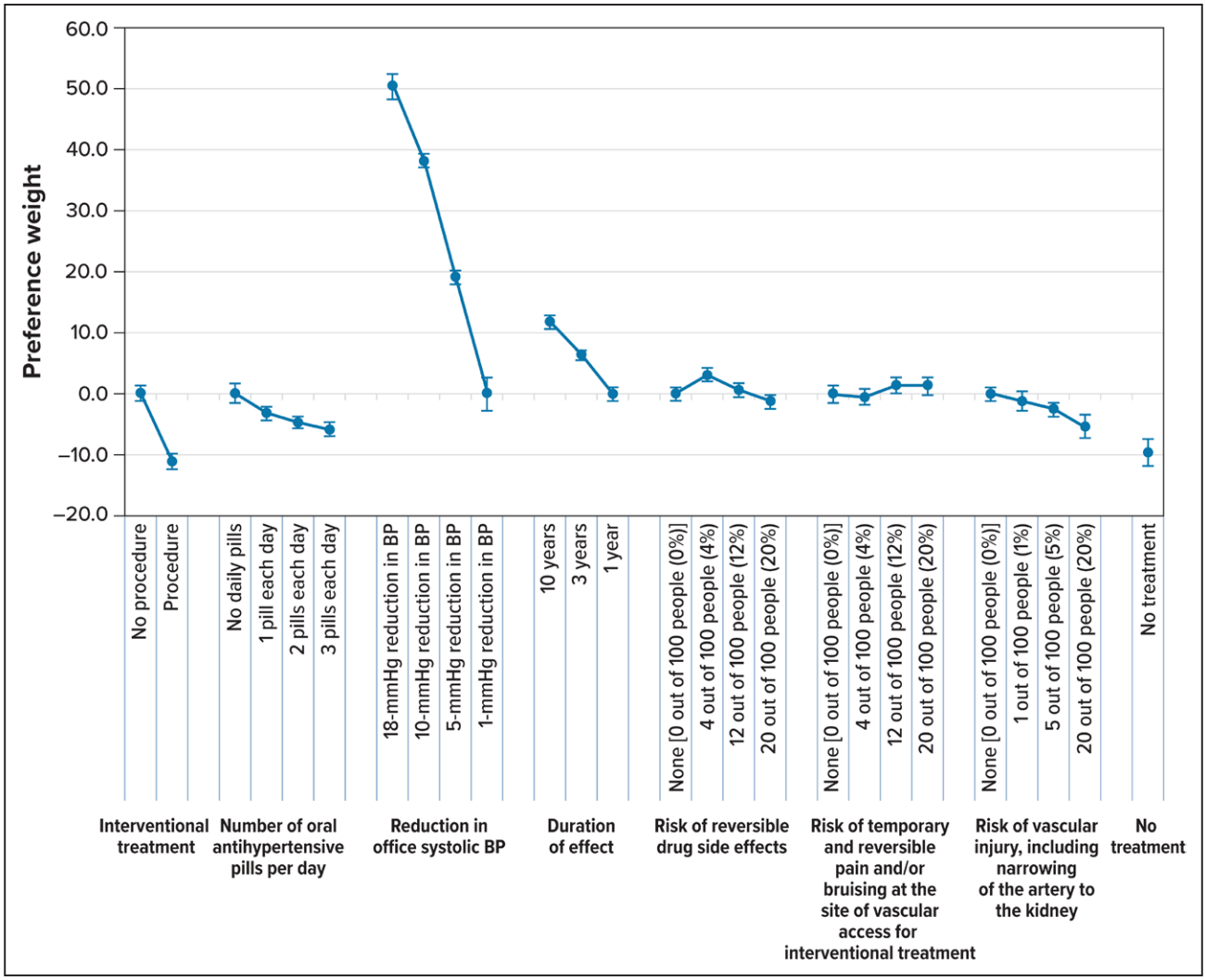


**Figure 3. Preference weights for treatment attributes.**
BP indicates blood pressure. The vertical bars surrounding each mean preference weight denote the 95% confidence interval about the point estimate. The estimated parameters on each attribute level were rescaled as follows. The difference between the largest and smallest parameter within each attribute was calculated. These differences were summed across attributes, and the sum scaled to 100. The parameters corresponding to each attribute were rescaled relative to this sum. Rescaled preference weights are plotted in the positive and negative quadrants for attributes in which changes between levels were perceived by respondents to be advantageous or disadvantageous, respectively. The vertical distance between preference weights within an attribute describe the relative importance of changes in attribute levels, which is a measure of how much that parameter influences choice.

to choose an interventional treatment with a 10 mm Hg reduction.

The fact that treatment-related risks of AEs had less influence on treatment choices than on treatment benefits is consistent with the results of other quantitative preference research on treatments for HTN. In a DCE study of preferences for attributes of oral antihypertensive medications among people with type 2 diabetes, de Vries et al found that the treatment effect on BP was the most important attribute when choosing a drug, followed by the risk of adverse drug events.[41] In a best-worst scaling study of adults with HTN in the United States, treatment outcomes related to cardiac event-risk reduction due to BP reduction were more important to respondents than adverse events related to antihypertensive therapy.[42]

Recent studies from Western Europe and the United States applied rating scales to assess patients' willingness to consider RDN, and direct questions to elicit a choice between RDN and pills only.[11] Schmieder et al[11] reported that 38% to 47% of patients whose most recent SBP was 140 mm Hg or higher were willing to consider RDN. These responses were largely independent of baseline BP and number of medications. Herein, we found that patients had a higher preference for interventional treatment associated with greater office SBP reduction (Figure 4). Furthermore, Schmieder et al[11] found that preference for RDN was highest among those not taking medications, yet in the present study, preferences for interventional therapy were driven by the potential for BP reduction and durability, but not by treatment-related risks. Importantly, unlike prior studies

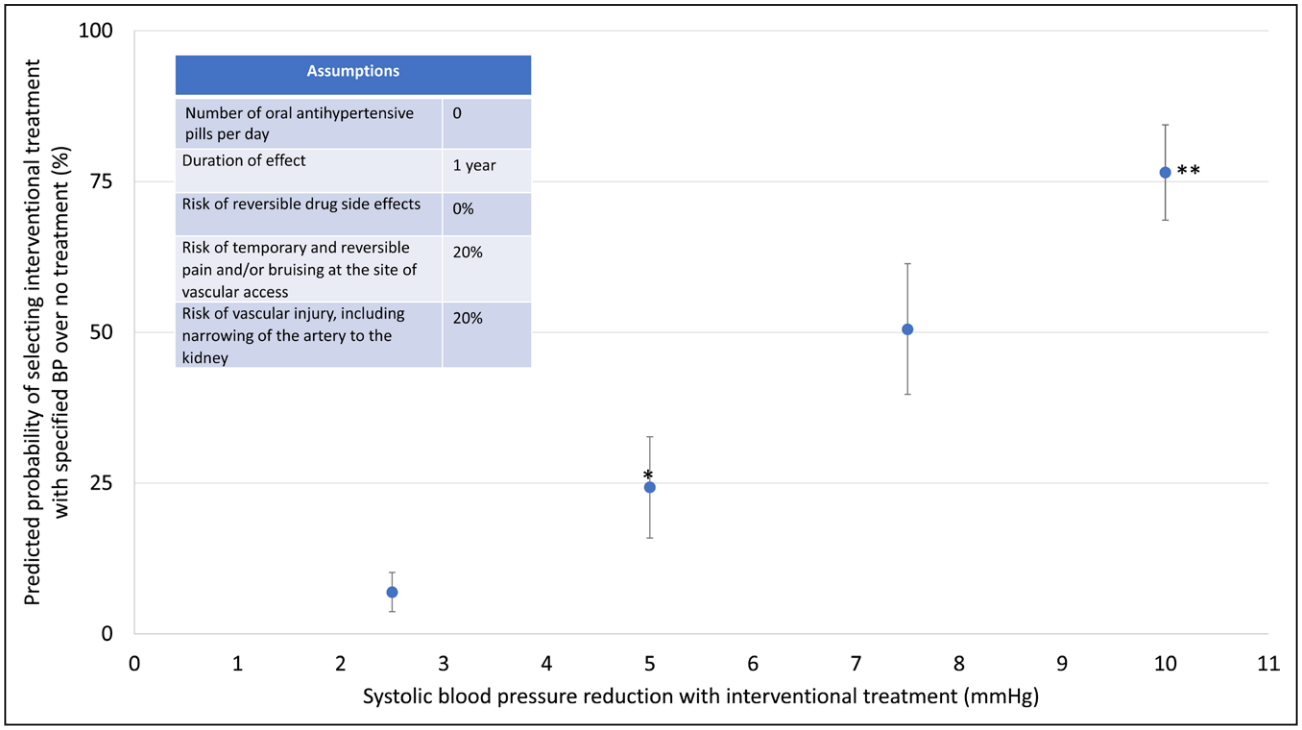


**Figure 4. Sensitivity analysis: predicted probability of choosing an interventional treatment compared with no treatment based on degree of BP reduction.**

Plotted is the predicted probability of choosing an interventional treatment (without concomitant oral antihypertensive therapy) over no HTN treatment when the interventional treatment has the maximum levels of the risks of procedure-related side effects included in the survey. The predicted probability of choosing an interventional treatment would be 6.9% if the office systolic BP reduction was 2.5 mm Hg. The predicted probability increases to 24.3% would choose an interventional treatment with a 5 mm Hg reduction, and 76.5% are predicted to choose an interventional treatment with a 10 mm Hg reduction. BP indicates blood pressure; and HP, hypertension. *5 mm Hg reduction based on Rahimi et al.[35] **10 mm Hg reduction based on Ettehad et al.[36] The vertical bars surrounding each point estimate denote the 95% confidence interval about the point estimate.

eliciting choices among RDN and other treatments on the basis of direct questioning and with few details about treatment attributes,[11,43] this DCE elicited preferences for interventional and pharmaceutical HTN treatment by detailing the benefit and risks, with outcomes based on existing clinical trials evidence[5,6]

## LIMITATIONS

The DCE method limited the total number of attributes that could be assessed for a given treatment. Therefore, selected attributes were those considered most important to individuals with uncontrolled HTN, inclusive of both efficacy and safety. Physician endorsement of a procedure was not included, which has been shown to influence patients' decision making.[11] Estimates of absolute or relative reduction in clinical events associated with lowering BP were not provided because the association may differ for each individual. However, as confirmed in the pretest, respondents demonstrated a high level of comprehension regarding the clinical benefits of improving BP control. In the survey, respondents were given the choice of "no treatment," with an explanation that their BP or health risks would not change. Because stopping antihypertensive pharmacologic treatments would likely increase BP or risk of events, this explanation could have been misleading and result in underestimation of respondents' interest in HTN treatment. Preferences regarding pill intake also did not include single pill combination therapy, although preference weighting related to number of daily pills was generally similar compared with attributes such as extent of BP reduction and durability. In addition, although there were 400 respondents recruited using commonly accepted approaches,[14,23] it is possible those surveyed do not necessarily represent a true indication of the hypertensive population in the United States. Finally, this survey was conducted during the coronavirus-19 pandemic, and the influence of the pandemic on perceptions related to seeking health care is uncertain. However, the majority of respondents demonstrated an ability to answer the treatment choice questions in the survey as if related safety concerns and restrictions were resolved (Table S12).

## CONCLUSIONS

Patient preferences for treatment are highly relevant and have implications regarding how recommendations

are made by healthcare providers, received by patients and endorsed by payers. Using a DCE to quantify preferences for both pharmaceutical and interventional therapies to treat uncontrolled HTN, respondents prioritized BP reduction over all other attributes, and procedural safety and drug-related side effects did not substantially offset preference for an effective therapy. Furthermore, relatively small reductions in BP were sufficient to offset patients' preference for interventional treatments, such as RDN, over pharmacological treatments.

## ARTICLE INFORMATION

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Dr. Weber is a consultant for Medtronic, ReCor, Ablative Solutions, Johnson & Johnson, and Urovant.

Christine Poulos is a full-time employee of RTI Health Solutions, an independent, nonprofit research organization, which received funding pursuant to a contract from Medtronic to conduct the study that is the subject of this article. Josh Coulter was a full-time employee of RTI Health Solutions at the time of the study.

Dr. Cohen is a consultant for Medtronic and owns stock and stock options in Medtronic.

Ms. DeBruin and Ms. Jones are employees of Medtronic.

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### Supplemental Material

Supplemental Methods.
Scope Test: Description of Test, Results, and Figure Summarizing Results.
Tables S1–S12.

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