Renal Denervation: A Mathematical Analysis of Technology and the Treatment of Resistant Hypertension

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Executive Summary

Given the growth of innovation in the healthcare industries, the use of technology allows for avant-garde treatment methods capable of changing healthcare. In the United States, hypertension affects 85 million people, and 12% of patients diagnosed with hypertension suffer from resistant hypertension. Resistant hypertension is a form of hypertension in which high blood pressure is difficult to treat, regardless of lifestyle changes and various pharmaceutical medications used by the patient. Renal denervation (RDN), however, provides a potential treatment for resistant hypertension. This catheter-based invasive solution uses radio frequency blasts to ablate renal sympathetic nerves and allow the blood to flow through the arteries more easily.

The average per capita Medicare spending for a patient with resistant hypertension was found to be $20,018, more than the $14,487.50 of spending for an average hypertension patient. A cost-savings model was developed with a decreasing spread rate found from a study on a comparable technology. This rate was modified to create more apt region based models, with variations of this spread rate dependent upon the Medicare funding available in each region used to develop a scaling factor for each region. It was also found that 60% of RDN treatments are successful, whereas 40% result in the patient maintaining resistant hypertension. These data were utilized to create a Markov model and to conduct a Kaplan-Meier analysis. The Markov Model predicted how the population of those with and without resistant hypertension changed over time with and without the widespread use of RDN. The Kaplan-Meier analysis found how the survival rate of those with resistant hypertension changed with RDN. The cost-savings model indicated that the annual savings per capita is $5,498.44 after ten years, and that at this point, annual total cost would be reduced by $18,054,765,559.04. The geographic analysis indicated that the areas more heavily impacted by hypertension would implement the technology sooner than lesser impacted regions. The results of the Markov model show that RDN therapy is more effective and appropriate for the resistant hypertension population than non-medicinal therapy. The Kaplan-Meier analysis also showed that individual survival rates greatly improved with RDN.

Based on these results, it is recommended that the RDN treatment be implemented in the United States. In the health sector, there would be a minimal financial burden, the only challenge involving the learning curve for healthcare professionals. As RDN advances past its negative effects to be an effective treatment for all forms of hypertension, its positive impact will be even greater. To avoid a loss in profits for pharmaceutical companies by decreased spending on hypertension drugs, these companies must develop drugs that mitigate negative effects of RDN, shifting their focus to the new technology. RDN presents a clear and cost effective solution for Medicare to pursue for patients with resistant hypertension, a condition that is currently untreatable by medication.

Technology and Disease Overview

Hypertension, or high blood pressure, is a disease caused by the force of blood pushing against the walls of blood vessels, a condition affecting approximately 85 million people in the United States. According to the American Heart Association (AHA), hypertension is defined as a blood pressure higher than 130 over 80 mmHg, with normal blood pressure being 120 over 80 mmHg. Hypertension can lead to severe complications, including heart disease, stroke, and death.

The exact causes of hypertension often cannot be pinpointed, but typically 1 in 20 cases of hypertension are brought on by another condition or medication. Chronic kidney disease (CKD) is often a cause of hypertension, because impacted kidneys are unable to filter out fluid and regulate blood pressure. Additionally, age, ethnicity, size and weight, substance use, sex, and existing health conditions can increase the chances of hypertension. The risk of high blood pressure tends to increase in individuals over the age of sixty, as arteries become narrower and stiffer over time. Being overweight and consuming harmful substances can also lead to hypertension. In males, hypertension is more common with individuals of a younger age, while the opposite is true for females. In addition to CKD, cardiovascular disease, high cholesterol, and diabetes can also lead to hypertension as people age (Nwankwo et al., 2013). Lifestyle choices such as diet and level of physical activity can also contribute to high blood pressure, and 70% of all hypertension cases are associated with individuals who are overweight and diabetic (Schlaich, 2011).

According to the National Health and Nutrition Examination Survey from 2011-2012, hypertension affected 29.1% of the adult US population. Hypertension affected 29.7% of males, compared to 28.5% of females. Additionally, the prevalence of hypertension increased with age, with younger individuals (18-39) having a 7.3% prevalence rate. Between the ages of 40 and 59, hypertension was prevalent at a rate of 32.4%, and for adults over the age of 60, hypertension affected 65% (Nwankwo et al., 2013).

Individuals with hypertension often do not manifest visible symptoms, but high blood pressure can cause sweating, anxiety, sleeping problems, and blushing. Signs of hypertension are often identified with a sphygmomanometer, or blood pressure monitor. High blood pressure is often a normal response in situations of acute stress or intense exercise, so multiple readings that indicate high blood pressure over time are necessary to diagnose hypertension. The following guidelines define the ranges of high blood pressure as per the AHA (Table 1):

	Systolic (mmHg)	Diastolic (mmHg)
Normal blood pressure	Less than 120	Less than 80
Elevated	Between 120 and 129	Less than 80
Stage 1 Hypertension	Between 130 and 139	Between 80 and 89
Stage 2 Hypertension	At least 140	At least 90

Table 1

Long-term hypertension can cause complications due to atherosclerosis, or the formation of plaque that results in the narrowing of blood vessels. This can lead to heart failure, heart attacks, aneurysms, kidney failure, stroke, amputation, hypertensive retinopathies, and death. High blood pressure that is not a result of another condition is primary hypertension. Though its causes cannot be traced back to an underlying condition, primary hypertension is brought on by multiple lifestyle and health factors. If hypertension is a complication of another condition it is secondary hypertension (MacGill, 2018). In the United States, one in three adults are diagnosed with hypertension, and while most patients have primary hypertension, 5-10% of adults suffer from secondary hypertension (Viera & Neutze, 2010).

First-line treatments for hypertension typically involve lifestyle changes, though individuals with blood pressure higher than 130 over 80 mmHg can use medication. Drugs are usually prescribed at low doses, and patients eventually work up to taking a combination of drugs. Types of drugs prescribed depend on the patient and conditions they may have (MacGill, 2018). Despite the number and diversity of treatments for hypertension, patients with resistant hypertension typically do not respond well to the available medications. These patient's high blood pressure is difficult to treat, even after lifestyle changes, diuretics use, and using multiple blood pressure medications (American Heart Association, 2016). Additionally, patients are at a 30-50% higher risk for death, stroke, or coronary heart disease, and at a two-fold higher risk of developing new-onset heart failure, compared to patients without resistant hypertension.

In order to treat patients with resistant hypertension, innovative methods such as renal denervation (RDN) have been developed. RDN for resistant hypertension refers to a catheter-based intervention procedure that uses radiofrequency to ablate renal sympathetic nerves, reducing blood pressure in patients suffering from hypertension. The renal sympathetic nervous system moderates interactions between the brain and the kidney through a feedback loop, and therefore plays a role in hypertension. RDN functions by placing a catheter into the lumen of the renal arteries. Next, radiofrequency or ultrasound energy is applied, which causes thermal injury to the sympathetic nerves. This reduces renal sympathetic nerve activity and increases renal blood flow, therefore decreasing blood pressure. Furthermore, in humans, nerve regeneration occurs at a rate of 2 mm/day in smaller nerves and 5 mm/day in larger nerves, so for the procedure results to be retained, the RDN treatment must be repeated biennially (Bronzino, 2006). The purpose of this innovative treatment is to allow patients with "apparent treatment resistant hypertension" to reach a goal blood pressure of 120 mm Hg, according the Systolic Blood Pressure Intervention Trial. These reduced rates are reported to reduce cardiovascular events by approximately one-third, and to reduce the risk of death by one-fourth.

While theoretically, RDN is considered to be a viable solution to treat patients with resistant hypertension, there are various potential complications that may arise due to the invasive nature of the procedure. These complications may include femoral artery puncture (pseudoaneurysms, hematomas), renal artery interventions (dissections, stenosis), embolic (stroke-related) events, and renal events (acute kidney injuries, end-stage renal disease). In addition to these drawbacks of RDN, studies have also reported adverse effects due to drastic changes in blood pressure (hypo or hypertension), the procedure itself (renal artery spasms after procedure), and sedation (laryngospasms). However, despite the extensive list of potential side effects, the risks of developing life-threatening effects as a result of the procedure are fairly low. The following table (Table 2) portrays the range of rates for various adverse effects according to studies that monitored adverse outcomes within a short follow-up duration.

Adverse Effect	N Studies/N Participants	Mean Followup (in Months)	Risk Estimate
Stroke	3/1302	10	0 to 2.2%
Myocardial Infarction	3/1302	10	0 to 2%
Hospitalization	4/1455	16.5	0 to 8.5%
Mortality	4/1455	16.5	0 to 2%
Cardiovascular Mortality	2/1153	9	0.7 to 2%

Table 2

Additionally, based on 17 randomized controlled trials (RCT), the studies reported that there were no statistically significant differences in risk of stroke, heart attack, hospitalization, or mortality as a result of RDN (Shafi et al., 2016). As a result, the best way to reduce the risk of adverse effects would be to ensure all eligible patients are of good health. Because the studies do not significantly suggest that RDN increases risk of adverse effects, the most effective way to minimize risks of adverse effects would be to ensure all patients eligible for treatment undergo thorough medical background checks. Furthermore, compared to other frequently used treatment technologies, such as chemotherapy, the risks of adverse effects from RDN are much lower. For instance, in a study of 449 individuals over a course of several months, 86% reported an adverse effect of chemotherapy, compared to only 47% of 17 RCTs for RDN (Pearce et al., 2017). Given that treatment options for patients with resistant hypertension are extremely limited, RDN provides a potential viable treatment, regardless of potential adverse effects (Shafi et al, 2016).

Data Methodology

This section explains the data that were garnered through extensive research for the respective analyses and then manipulated in order to model the impact of RDN as a treatment for resistant hypertension. CMS data were also used due to their accessibility and regional specificity for a geographic analysis.

I. **Savings Analysis of RDN**: The table below (Table 3) portrays the specific data gathered and utilized to produce the cost-saving model.

Hypertension Prevalence in Adults Over 18	58%	**Average Healthcare Expenditures for RDN Treatment**	$6,811 per capita
Resistant Hypertension Prevalence	12%	**Procedure Frequency of RDN**	Biennial
Chronic Kidney Disease Prevalence	15%	**Compounding Annual Growth Rate of RDN Market**	7.5%
Average Annual Healthcare Expenditures for Resistant Hypertension	$20,018 per capita		

Table 3

The data above were manipulated and used to produce a quantitative analysis of the RDN treatment. The data were gathered from multiple research papers and studies, beyond the CMS data provided. These data were collected to determine variables for the cost-savings model. For further explanation regarding variable determination, see *Mathematics Methodology- Section I.*

II. Savings Analysis of RDN per Geographic Region

In order to perform a non-numerical analysis of RDN technology, the CMS data sets were utilized to determine the prevalence of hypertension in regions across the United States. According to the US Census Bureau, there are nine subdivisions of regions in the United States: New England, Middle Atlantic, East North Central, West North Central, South Atlantic, East South Central, West South Central, Mountain, and Pacific (US Census Bureau, 2010). The CMS data sets were utilized to determine a ratio between the average Medicare spending per capita specific to each region, and the national average. This ratio was then used to find the regional average spending per capita for resistant hypertension. The CMS data provided the most extensive and reliable figures, and were therefore used to perform this qualitative analysis.

III. Markov Model

To evaluate the change in the number of people with resistant hypertension overtime with the addition of RDN therapy, a Markov model was created as a method to predict future populations. This model would serve as a reference to determine the impact of RDN therapy on the future of healthcare. In order to construct the Markov model for comparing effectiveness of RDN Therapy to Non-Pharmaceutical Methods on treating resistant hypertension, percentage values had to first be calculated in order to be input into the initial matrix. Data sources containing probability-related information specific to the various outcomes of resistant hypertension treatment were used. The data found were then manipulated to appropriately fit the input matrix.

This matrix considers the probabilities of of progressing from resistant hypertension to being treated, maintaining resistant hypertension post-treatment, progressing from not having hypertension to having resistant hypertension, and not having resistant hypertension before and after the time period. The following table (Table 4) depicts the data that were researched, recorded, and manipulated to produce the matrix for the Markov model. An in-depth explanation of the data manipulation can be found under *Mathematics Methodology- Section III.*

Progressing from Resistant Hypertension to Successful Treatment	60%	**US Population over 65**	49.2 million
Maintaining Resistant Hypertension Post-Treatment	40%	**Prevalence of Hypertension Among Adults over 65**	75%
Increase in Population with Hypertension (2005-2015)	11% (12% of this value was resistant hypertension patients)		

Table 4

IV. Kaplan-Meier Analysis

To determine how total lifespan of those with resistant hypertension is immediately changed due to the addition of RDN, a Kaplan-Meier analysis was run. Data regarding death by natural causes and non-hypertension related causes were ignored, and the remaining data points were kept. Since the population over 65 is most affected by hypertension, the survival rate of those older than 65 was calculated. To run the calculations for a year-by-year change, age-based population data was required. This included the populations of each age, death rates by hypertension, and mortality rates for each age group. These data were acquired for every age from 65 to 80. Additionally, data regarding the percent of people in each age group with hypertension, and percent of successful hypertension treatments were used. Based on these data, the probability for a person dying from hypertension for each age was calculated. The rates varied slightly age-by-age, in an increasing manner.

Mathematics Methodology

I. Individual Variable Determination and Manipulation

All variables required were created from outside research and data manipulation. For descriptions regarding the sources and types of data used to determine the variables, please see the *Data Methodology section*. The variables below were used in the models and determined accordingly:

<u>Population Eligible to Receive RDN</u> = *Population of Adults with Hypertension × 0.12 × 0.85*

Of the population of adults with hypertension, resistant hypertension has a prevalence rate of 12% (Pimenta & Calhoun, 2012). However, in order to be treated with RDN, the patient must be free of any chronic kidney problems, and given that 15% of people have chronic kidney disease, this suggests that 85% of patients with resistant hypertension are eligible for RDN (Center for Medicare and Medicaid Services, 2012).

<u>Average Annual Healthcare Expenditures for Hypertension Patients</u> = *$20, 011 per capita*

The average annual health care expenditures for patients with resistant hypertension was found to be $20,018 per capita (Jancin, 2015).

<u>Average Annual Healthcare Expenditures for Resistant Hypertension Patients Undergoing RDN</u> = *$6,811 per capita*

RDN treatment for resistant hypertension costs $6,811 per capita per year (Weber et al., 2018).

<u>First-Year Savings</u> = *Average Annual Healthcare Expenditures for Hypertension Patients - Average Annual Healthcare Expenditures for RDN Treatment*

Based on the cost values per capita per year for both treatment options, the first-year savings can be calculated by subtracting the cost per capita per year of RDN treatment from the average annual expenditure for patients with resistant hypertension. This value represents the first-year savings, assuming that the patient can stop relying on pharmacology, given that the RDN treatment is effective.

<u>Intermediate Year Savings</u> = *Average Annual Healthcare Expenditures for Hypertension Patients*

As a result of the sympathetic nerves regrowing over time, RDN is not a permanent solution. The procedure must be repeated every other year in order to maintain optimal blood pressure, therefore, assuming that all patients undergo the procedure in the same year, the intermediate year savings are equal to the average annual expenditures for patients with hypertension (Krawczyk-Ozog et al., 2016).

Average Year Maximum Savings = $\frac{(First-Year\ Savings + Intermediate\ Year\ Savings)}{2}$

Based on the savings for a given intermediate year, the average of a year in which every person had to receive the therapy and a year in which every person had undergone the therapy the previous year, is used to find the average year's maximum savings once the therapy is fully implemented.

Predicted Market Growth Rate = $\frac{20}{2n}\%$, *where n is equal to years since implementation*

According to the technological spread rate for 64-slice computed tomography, because both technological innovations are similar in their targeted markets, it is assumed that the spread rate of RDN can be modeled using the same rate that was found for the 64-slice CT technology (Ladapo et al., 2009).

Maximum Savings = *Average Year Savings After Ten Years × Population Eligible to Receive RDN*

The maximum savings from implementing RDN can be calculated by multiplying the average year savings value by the 58% of the population diagnosed with hypertension, 12% of high BP patients with resistant hypertension, and 85% of resistant hypertension patients eligible for RDN treatment.

RDN Effectiveness = *60%*

The probability of progressing from resistant hypertension to being treated was 60%, and maintaining resistant hypertension even after treatment was 40% (Kandzari, et. al., 2018).

Increase in Resistant Hypertension Patients over 6 months = *Number of People Diagnosed with Hypertension over 6 months × Percent of Hypertension Cases that are Resistant*

Over the course of 2005 to 2015, there was an 11% increase in the population of patients with hypertension (0.55% over 6 months), only 12% of which was resistant hypertension (American Heart Association, 2018). Therefore, on average, there was a 0.066% chance of progressing from not having resistant hypertension to having it, and a 99.934% chance of not being diagnosed with resistant hypertension over a 6 month period

People over 65 with Resistant Hypertension = *Number of People over 65 with Hypertension × Percent of Hypertension Cases that are Resistant*

There are 49.2 million people over the age of 65 in America (Census Bureau, 2017). The starting value of those with resistant hypertension was 4.428 million; 75% of all adults over 65 have hypertension, and 12% of that 75% have resistant hypertension (Chobanian, 2004; Pimenta & Calhoun, 2012).

People over 65 without Resistant Hypertension = *Number of People Over 65 - Number of People Over 65 with Resistant Hypertension*

The initial number of people above 65 without Resistant Hypertension was calculated to be the difference of 49.2 million and 4.428 million.

Success Rate of Non-Pharmaceutical methods to treat Resistant Hypertension = *0.6923%*

Based on the type of diet necessary to accomplish the needed drop in blood pressure in the 6 months, only 0.6923% historically were able to accomplish this (LaMeaux, 2019; Searing, 2018). This means that of people with Resistant Hypertension, 99.3077% will not be treated after the time period.

Death by each age group over 65 = $(Total\ people\ who\ died\ at\ age\ [X])\ (\frac{Hypertension-related\ deaths}{Total\ deaths})$

Number of people who died at each age was found, then multiplied by 0.149 to find the number of people who died each year from hypertension-related deaths. 0.149 is equal to Hypertension-related death/Total deaths (410,000/2,744,248) (United States Census Bureau, 2017).

II. Cost-Saving Model

The final calculation of savings over time was calculated using the decreasing annual growth rate. The model is as follows:

Savings Spread (Year One) = *First-Year Savings × 0.2*

Savings Spread (Year Two) = *Average Year Maximum Savings × 0.3*

Savings Spread (All Consequent Years) = *[Savings Spread (of Previous Year)] (1+* $(\frac{0.20}{2n})$ *)*

This value is compounded until reaching a value at which the savings per capita increased by less than $1.00. The time taken for the value to compound to this represents the time it would take for the technology to be optimally implemented, as all further increases would be marginal.

This same method was used for individual American regions, based on the US Census Bureau, to determine how recommendations would vary based on geographic locations. The population total and maximum savings for each region varied but the same 20% decreasing spread rate was applied.

III. Markov Model

A Markov model was created to evaluate the effectiveness of RDN therapy by predicting the probability of future states, based on current hypertensive conditions.

Input Value Determination for Markov Model

The RDN therapy matrix created for the Markov model utilized the probabilities of progressing from resistant hypertension to being treated, maintaining resistant hypertension post-treatment, progressing from not having hypertension to having resistant hypertension, and not having resistant hypertension before and after the time period. The time period was 6 months, because that was calculated as the optimal time period for RDN therapy to be most effective. The diagram (Figure 1) and table (Table 5) below show the matrix inputs and potential outcomes for the RDN therapy Matrix.

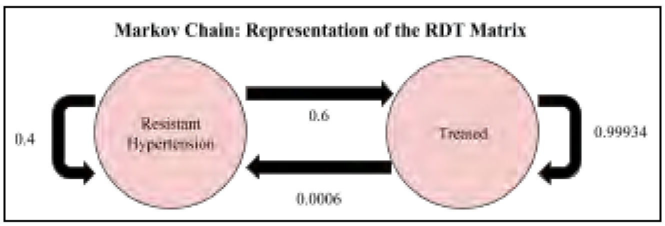

Figure 1

	Resist	Not	Initial (millions)
Resist	0.4	0.00066	4.428
Not	0.6	0.99934	44.772

Table 5

The non-pharmaceutical method matrix created, utilized the probabilities of progressing from resistant hypertension to being treated, maintaining resistant hypertension even after treatment, progressing from not having hypertension to being diagnosed with resistant hypertension, and not having resistant hypertension before and after the time period. The time period was 6 months again. Much of the methods involved diet restrictions (Calhoun, et. al., 2008). The rest of the values are consistent from the previous matrix. The diagram (Figure 2) and table (Table 6) below show the initial matrix inputs for the non-pharmaceutical method Matrix.

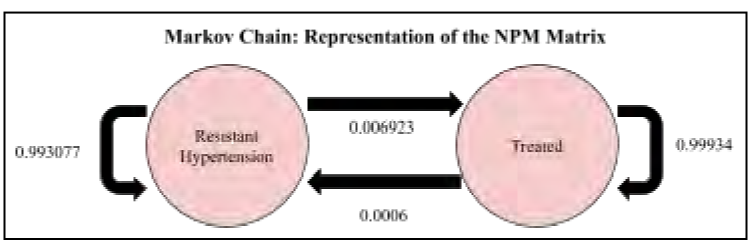

Figure 2

	Resist	Not	Initial (millions)
Resist	0.993077	0.00066	4.428
Not	0.006923	0.99934	44.772

Table 6

IV. Kaplan-Meier Analysis

A Kaplan-Meier analysis was used to estimate the survival of post-RDN treatment patients. Data used included the number of people dying every year due to resistant hypertension, and how that would change if RDN is used. This then showed the change in survival rate for patients over 65 if RDN was used. The variables used are explained in detail earlier in the section.

Results

I. Cost-Saving Model

The initial nationwide cost-savings model was used to find the savings accumulated through this program after ten years, after which the spread rate would have decreased to marginal levels. The savings per capita ten years after implementation was found to be $5,498.44. This value indicates that by implementing RDN therapy, on an average year, the cost of treatment for hypertension is reduced by $5,498.44 per person eligible for treatment. This value is impactful, given the relatively large impacted population of 3,283,616 people, which equates to approximately 1% of the American population.

Furthermore, the cost-saving model also functions to determine the amount of time it will take for the the RDN therapy to be fully implemented. The therapy is considered fully implemented when the net savings value increases by less than one dollar per capita the next year. Given the ten year savings value, full implementation of the RDN treatment would lead to $18,054,765,559.04 saved annually, given that 3,283,616 people will be impacted by the implementation of this technology. Taking into account the decreasing annual spread rate, as well as the change in population over time, this technology would take ten years in order to be implemented optimally, assuming Medicare funding was divided evenly between states. The following graph (Figure 3), shows the projected change in savings per capita over time, as the technology and program is implemented across the United States.

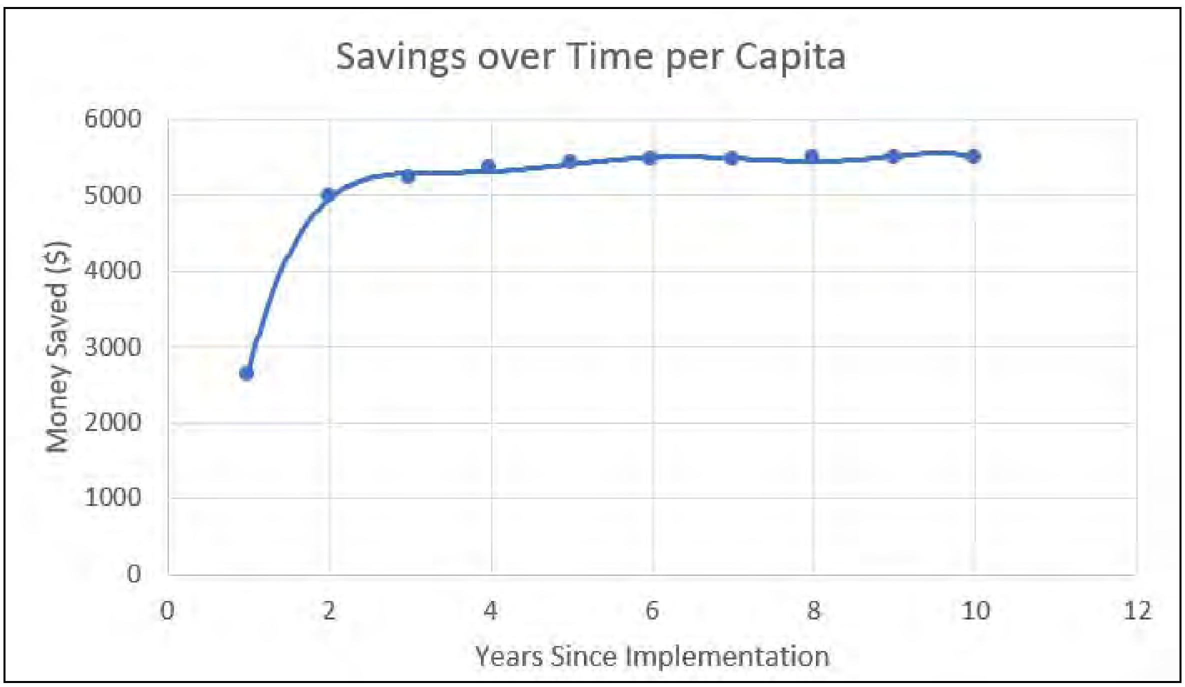

Figure 3

II. Geographic Regional Analysis

A regional analysis of the savings per capita was conducted, with varying growth rates based on the Medicare funding average per capita of each state. The regional divisions were based on US Census data. The division of the regions can be seen below (Figure 4):

Figure 4

This Medicare average funding for each region was compared in a ratio to the national average, in order to develop a factor by which to multiply the given 20% decreasing spread rate. The greatest of these factors was 1.9 for the Middle Atlantic region while the lowest was 0.37 for the Mountain region. The per capita Medicare funding by the states was used to represent the importance of bringing new treatment technology to government funded hospitals. The results show that, unsurprisingly, the Middle Atlantic region, comprising of New York, New Jersey, and Pennsylvania had the highest spending and as such would implement the technology the fastest. These low factors for the Mountain, New England, West North Central, and East South Central regions mean that, assuming additional Medicare spending is not allocated to fund implementation, the technology would be slower to develop. The technology will be implemented in the most affected areas–the South Atlantic, East North Central, and Middle Atlantic– in a very short timeframe. This is representative of areas that are more heavily afflicted by hypertension wanting to implement the technology sooner than lesser impacted regions. The graph below (Figure 5) depicts the change in savings over time per capita specific to each region. The plateauing lines represent the spread rate reaching a marginal level.

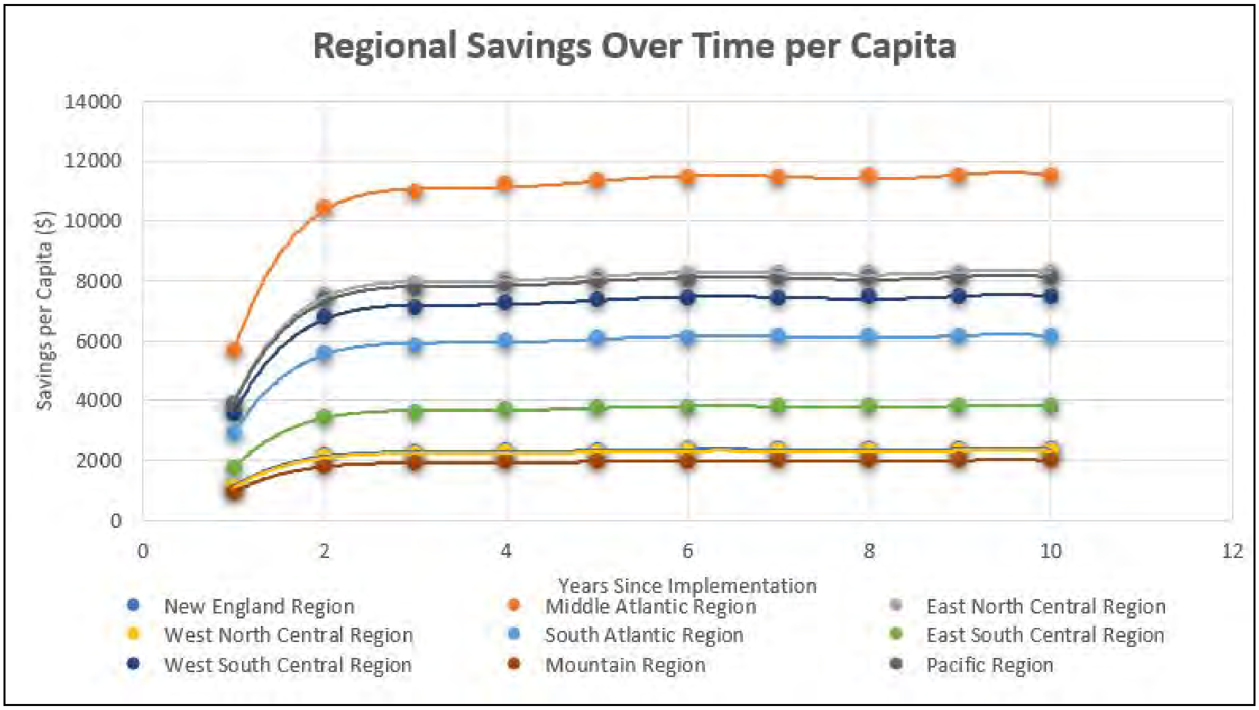

Figure 5

III. Markov Model

Based on the probability of RDN therapy effectively treating resistant hypertension versus the non-pharmaceutical method, the higher success rate implies that RDN therapy is more effective. However, the Markov Model was constructed to showcase how the demographic most likely to be diagnosed with resistant hypertension (individuals above the age of 65) would concretely be impacted by both forms of therapy, and whether there would be a significant difference between both treatment forms (Chobanian, 2004). Over the same time period for effective RDN therapy (6 months), it was calculated that 0.066% of people would develop resistant hypertension. The Markov model was run on Excel, and it was found that after one cycle of RDN therapy, the number of people above the age of 65 with resistant hypertension would drop from 4.428 million people to 1.801 million, with 2.627 million people having successful treatments (Table 7). In comparison, non-pharmaceutical method would drop the number of people with resistant hypertension to 4.427 million people, with 0.001 million people successfully being treated (Table 8).

Renal Denervation Therapy					
	Resist	Not	Initial (millions)	After 6 months (10^6)	Net Change (10^6)
Resist	0.4	0.00066	4.428	1.80074952	2.62725048
Not	0.6	0.99934	44.772	47.39925048	-2.62725048

Table 7

Non-medicinal Therapy					
	Resist	Not	Initial (millions)	After 6 months (10^6)	Net Change (10^6)
Resist	0.99308	0.00066	4.428	4.426894476	0.001105524
Not	0.00692	0.99934	44.772	44.77310552	-0.001105524

Table 8

Based on the results of the Markov model, aside from cost-efficiency, the RDN treatment option is a more effective and appropriate treatment for patients diagnosed with resistant hypertension, compared to the non-medicinal therapies available to treat patients. The purpose of this model is to determine the effectiveness of the RDN therapy beyond the cost, but rather based on the probability of a successful treatment. The model takes into account the various potential outcomes and predicts the probability of a certain outcome, based on the current state of the patient.

Furthermore, the purpose of the Markov model is to provide a randomly changing system, in which the change in the frequency of resistant hypertension diagnosis is accounted for. During the same cycle length that RDN therapy is conducted to successfully treat 60% of patients, there are more people being diagnosed with resistant hypertension. The Markov model takes this into account, providing accurate figures of outcomes for patients after six-months, according to individuals that were treated successfully and unsuccessfully, and adjusts this number according to the number of people free of resistant hypertension that eventually developed the disease.

The Markov model extended over a five-year time period further showcased the difference between the RDN therapies and non-pharmaceutical method's effectiveness in treating patients with resistant hypertension. Because treated patients could no longer develop resistant hypertension, this number was subtracted from the total amount of people treated to solve for subsequent treatment cycles. The following graphs (Figures 6 & 7) show the changes in the numbers of people with and without resistant hypertension, based on the treatments they undergo (RDN therapy and non-pharmaceutical method).

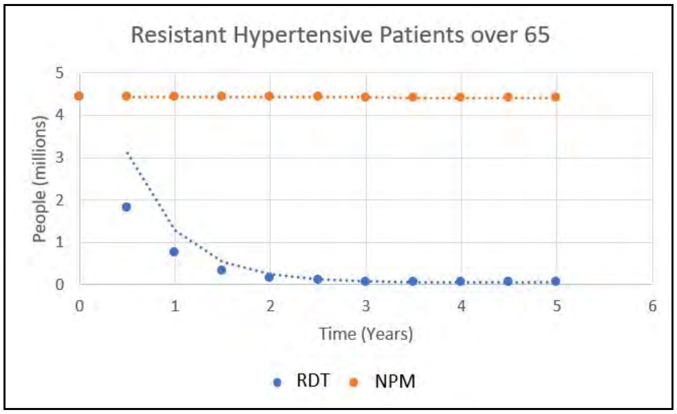

Figure 6

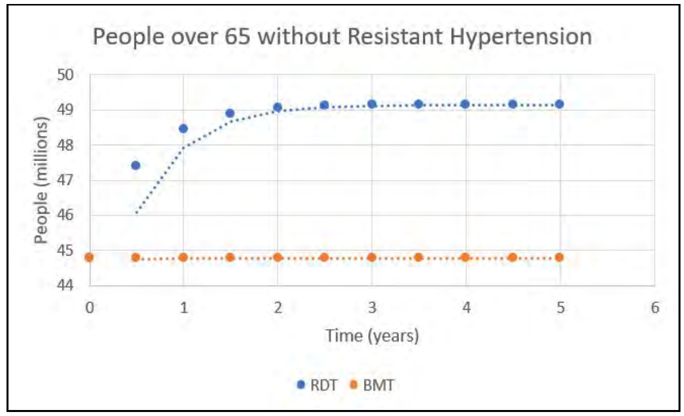

Figure 7

IV. Kaplan-Meier Analysis

Kaplan-Meier analysis was run to showcase the impact of renal denervation on an individual, rather than a whole population, as analyzed by the Markov model. This program was run using the "Survival" package in R and programmed in R Studio. This analysis was conducted for determining survival rates, but was isolated to resistant hypertension to show the direct increase in life-expectancy on the average person over 65 due to RDN. The x-axis conveys years after 65, and how the survival rate changes. The y-axis shows the survival rate itself. In real life, the survival rate does not start at 100% for age 65, but for this analysis, to portray the differences in the survival rates over time, the starting point does not matter.

Based on the Kaplan-Meier analysis, the probability of survival from hypertension-related causes decreases with age, however, patients that have undergone consistent resistant hypertension treatment are less likely to die due to hypertension as they get older. This Kaplan-Meier curve compares the likelihood of survival between patients that have been treated with RDN and those that have not received treatment for their resistant hypertension. While both curves initially follow a similar trend, as patients increase in age, the survival of patients void of RDN treatment steeply drops. The curve (Figure 8) represents a cumulative probability of survival, and approximately after age 70, the probability of survival for patients with regular RDN treatment exceeds that of untreated patients.

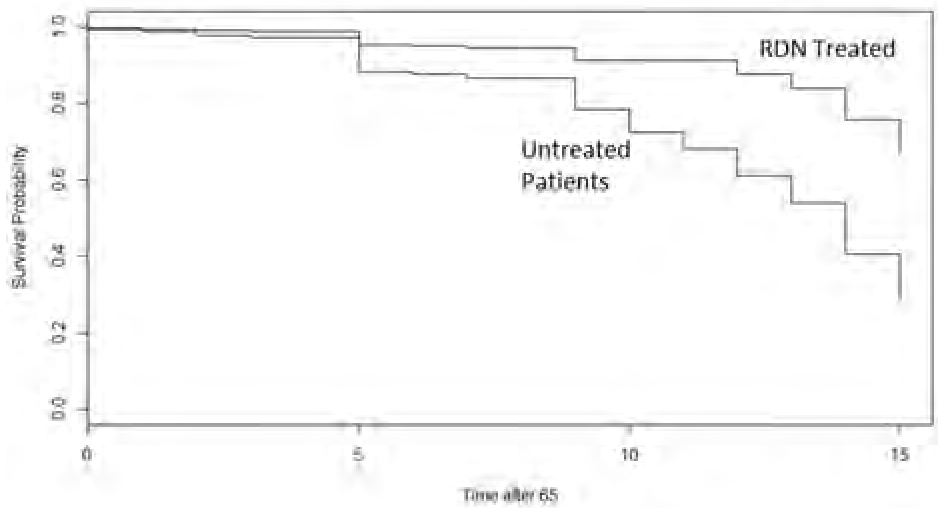

Figure 8

The analysis also provided statistics on the changes of survival rate for every year. As time increased, the confidence intervals decreased. Standard Deviation also increased as time passed. These two were negligible between those who underwent RDN and those who didn't. The main difference came at the number of people who had died cumulatively at each age, and the probability that they survive. Table 9 shows an excerpt of the values up to 5 years after 65 for those with resistant hypertension who did not use RDN. The full tables have values up to 15 years after 65.

time	n.risk	n.event	survival	std.err	lower 95% CI	upper 95% CI
0	991	7	0.993	0.00266	0.988	0.998
1	901	4	0.989	0.00344	0.982	0.995
2	822	8	0.979	0.00480	0.970	0.988
3	737	4	0.974	0.00546	0.963	0.984
5	575	54	0.882	0.01284	0.857	0.908

Table 9

Table 10 shows an excerpt of the values for those with resistant hypertension who did use RDN.

time	n.risk	n.event	survival	std.err	lower 95% CI	upper 95% CI
0	991	3	0.997	0.00175	0.994	1.000
1	901	2	0.995	0.00234	0.990	0.999
2	822	3	0.991	0.00313	0.985	0.997
3	737	2	0.988	0.00366	0.981	0.996
5	575	21	0.952	0.00850	0.936	0.969

Table 10

Conclusions and Recommendations

I. Healthcare

Given the increasing prevalence of information technology and innovation in the medical field, health organizations such as hospitals are constantly faced with decisions regarding capital allocation. As a result, many hospital health systems struggle with making investment decisions regarding new technologies, as technological investments have become more difficult to evaluate, due to increases in complexity (Coye & Kell, 2004). The main challenges faced by the healthcare industry when deciding whether or not to implement new technology are the financial investment and the learning curve (USC Price).

While the financial requirement to implement new technology often serves as a burden for hospitals, RDN uses radiofrequency ablation to destroy the tissue in the renal artery, which requires a multi-electrode ablation catheter, an endovascular catheter, and a guiding catheter, as well as a device capable of administering radiofrequency pulses (Thukkani & Bhatt, 2013). According to the Bureau of Industry and Security, catheters of all sizes and types and ultrasound and X-ray machines are considered basic medical supplies, so the majority of the technology necessary is already possessed by hospitals (Bureau of Industry and Security, 2014). However, as with most medical technology, the mechanisms used for RDN will continue to improve. The overall idea of denervation involves catheter ablation to kill the outer adventitial layers of renal arteries, so changes will include improvements to catheters used to deliver radiofrequency energy, drugs, and ultrasound-guided intervention techniques. For instance, new catheter designs such as multi-electrode catheters, balloon-based catheters, and basket catheters are just a handful of attempts to simplify and improve the procedure (Fornell, 2013). For the procedure to continue to increase in effectiveness, all that remains is ablation technology that is actively improving, for which the purchasing spread is modeled in the cost savings model (Fornell, 2018).

When deciding whether or not to implement a new technology, hospitals must consider the effectiveness of the technology, and whether or not it is worth training the medical staff to adopt this new technology. In this case, the opportunity cost for training medical professionals would be the procedures that they could perform in the time it takes for training. According to the model, as the technology is implemented, the average spending per capita will decrease by $5,498.44 for every individual eligible for treatment. As this technology is implemented, 3,283,616 people are impacted, and $18,054,765,559.04 are saved annually. This significant decrease in spending for resistant hypertension treatment suggests that the technology implementation is worth the training that health professionals may need to undergo. Furthermore, the results of the Markov model indicated that the RDN treatment is a more effective treatment, compared to the non-medicinal therapies, with a 60% success rate in RDN procedures. The following table (Table 11) shows the changes that will result from implementing the RDN technology.

People Impacted	Savings per Capita	Maximum Annual Savings	Number of Successful Treatments in a 6-Month Cycle
3,283,616	$5,498.44	$18,054,765,559.04	2.627 million Note: this is assuming that all individuals with resistant hypertension undergo treatment simultaneously

Table 11

Given the relatively light financial burden resulting from the implementation of this technology, the primary challenge faced by hospitals is ensuring that healthcare professionals have an extensive understanding of the technology and procedure. Additionally, taking into account the impact that the technology will have on the future of healthcare, it is advisable for hospitals to begin to adopt the technology. This change can best be adapted by training radiologists specialized in ultrasound-guided interventions that are familiar with ultrasound and catheter based treatments to perform the RDN procedure, and purchasing new catheters consistent with modern ablation technology. By training radiologists, only 1.2% of physicians will require training, therefore the training group is fairly refined, and ensures that training is only required for professionals that need it (Professionals in Diagnostic Radiology, 2017). Potential risks associated with the procedure are risks with the performance of the treatment. These risks, however, can be avoided by certifying that all professionals are sufficiently familiar with the technology and patients are in peak medical condition.

II. Medicare

Medicare will be heavily impacted by RDN, due to the very substantial per capita savings that stem from preventing wasted expenses on patients with resistant hypertension. The goal of Medicare should be full implementation everywhere possible, so as to reap the maximum benefits from the newfound technology. While accruing additional costs for the agency would be expensive, it would result in long term benefit. The net savings of the full implementation of the technology across the country, as earlier discussed, would be $18,054,765,559.04. This would be very substantial savings, as of 2018 the entire Medicare budget was only $625 Billion (Amadeo, 2019). It is encouraged for Medicare to subsidize the regions with the lowest spending, primarily the Mountain, West North Central, New England, and East South Central regions. The net gains of implementing the technology and training the necessary personnel far outweighs the cost of implementation. Beyond this, the equity of providing the technology and training to every part of the country, even the less well funded portions, would serve to boost the name of Medicare as a force of equality.

III. Pharmaceutical Companies

As RDN becomes more widespread, the need for drugs to reduce blood pressure drops dramatically. Currently, $42.9 billion dollars are being spent annually on hypertension medical bills, $20.4 billion of which are spent on pharmaceutical drugs. This comes out to an average of $744 per year per patient with hypertension, with several outliers (Davis, 2013). $2.5 billion of these costs are for patients with resistant hypertension.

Pharmaceutical companies, on average, make a profit margin of 12.5% on drugs sold, with the biggest companies making a profit margin of over 40% (Slovak, 2018). Many of these companies have room to sustain a loss of profit for a short while. In the short run, the drugs will be a lower price to get rid of excess supply, but eventually the companies will decrease supply and increase prices to maintain the level of profitability (Warner, 2016). In order for these companies to maintain their level of profitability without any major effects on operations, these companies will have to adjust their manufacturing process to decrease costs to keep up with the lower price care that RDN incurs. However, the best strategy would be for the pharmaceutical companies to invest into innovating drugs that mitigate negative effects of RDN, maintaining a strong hold on the hypertension drug manufacturing market while capitalizing on the new innovation within the industry.

IV. Economy

Although the medical industry will be most affected by the introduction of RDN, other factors within society as a whole will also be heavily impacted. RDN can significantly extend the life of those it impacts, as heart attacks are the number one cause of death in the US and world, with several other diseases caused by hypertension on the top 10 list (Nichols, 2017).

With longer lifespans, the number one aspect of society affected is the economy. As described earlier, Medicare is the part of the US economy most influenced, but other aspects have more widespread effects in the US and global economies. Historically, countries with improved lifespans and high fertility rates are negatively affected, as the large population becomes a strain on the countries' resources and income distribution. On the other hand, countries with improved lifespans and low fertility rates are economically much better off (Sunde & Cervellati, 2012). During the mid-20th century, there were several major medical innovations, from vaccinations to surgical advancements, that rapidly increased the lifespan of individuals. An increase of lifespan by 1%, on average, increased global population by 1.5%. However, the GDP per capita did not increases significantly in developing nations due to high fertility rates (Acemoglu & Johnson, 2006). This can be seen below (Figure 9).

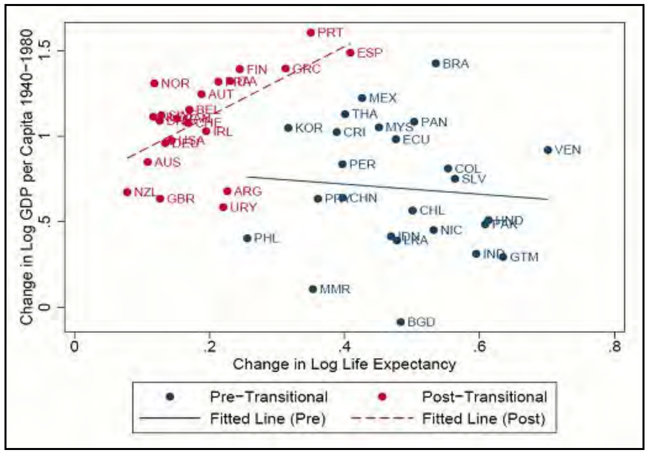

Figure 9

On average, those with hypertension have a 15 year shorter lifespan, so when the 8 million people affected by resistant hypertension no longer face this diminished lifespan, the average increases from 78.69 to 79.06 (Census Bureau, 2018; Tinker, 2017; Patel, 2000). This means that the population will increase by 0.7% and GDP per capita by $4.036, as GDP per capita increases $1 for ever 33 days longer lifespan, all as a result of the spread of RDN (Hossain, 2013).

Even though this directly won't increase economic activity, there will be a chain reaction of economic activity, from higher disposable incomes for more spending to lower poverty rates for the elderly as they can work till an older age (Ravilous, 2011).

RDN can be used to treat all forms of hypertension, but due to the numerous risks, only treating resistant hypertension has enough benefits to make up for the risks. However, as RDN becomes more widespread, the technology will improve at an increasing rate, reducing the risks. The main recommendation for society, from an economics perspective, would be to quickly embrace this new technology to allow it to advance to treat all forms of hypertension. As over a third of people in the US have hypertension, the benefits of RDN become more widespread, with much greater impacts in Medicare, healthcare, the economy, and more.

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