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Exploring The Potential Impact Of Meditation Intervention On Stroke Trends In The United States.

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EXPLORING THE POTENTIAL IMPACT OF MEDITATION INTERVENTION ON STROKE TRENDS IN THE UNITED STATES

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ABSTRACT

Meditation has shown promise in clinical trials in reducing systolic blood pressure, one of the main causes of stroke. We explore the potential impact of expanding meditation intervention on stroke trends in the US. We developed a dynamic population simulation in which the progression of each individual is governed by a micro-simulation model. We calibrated the micro-simulation model for stroke incidence and further validated it by comparing the stroke-related mortality for each age group generated by the model with that observed in the US. We used the population simulation model to estimate the effects of mindfulness meditation intervention on stroke incidents and mortality over a course of fifteen years. Our results show that we could avert 1,016,315 stroke incidences and 250,226 stroke-related deaths over the same period which is equivalent to a yearly saving of nearly one billion dollars in health care expenditure. Our sensitivity analysis reveals that most of benefit comes from applying the intervention for individuals older than 60 years and adherence to mindfulness meditation plays the critical role in its effectiveness. Meditation intervention, if properly utilized along with the regular antihypertensive medication, could substantially alleviate the burden of stroke in the United States. For designing an effective mindfulness meditation program, policy makers may prioritize funding to the programs that aim to improve the compliance of older individuals to meditation.

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CHAPTER ONE

INTRODUCTION

This research considers the effect of mindfulness meditation on stroke incidences and stroke mortality in the United States. A stroke incidence is defined as a sudden death of brain cells due to lack of oxygen, caused by blockage of blood flow or rupture of an artery to the brain[1]. On the other hand, stroke mortality is defined as the death caused due to one or more stroke incidents. There are mainly two types of strokes, ischemic strokes and hemorrhagic strokes. In ischemic stroke blood supply to part of the brain is decreased, leading to dysfunction of the brain tissue in that area. In Hemorrhagic stroke there is bleeding within the brain tissue or it could also be defined as accumulation of blood anywhere within the cranial vault. This research is mainly focused on the former type of stroke which is the ischemic stroke.

Cardiovascular diseases accounts for more than $500 billion in health care expenditures in 2010 alone[2]. Among these cardiovascular diseases, stroke is the third leading cause of death in the United States[3], costing the country $36.5 billion annually[4]. Around 800,000 people in the United States have a stroke on average each year[4], with an annual figure of about 130,000 stroke mortality cases—one out of every 19 deaths[5]. The number of people living with stroke is projected to increase by four million by 2030[6].

Out of all the people having stroke in a given year, one third of them die over the next year, one third of them are permanently disabled and remaining one third make a

good recovery[7]. Stroke causes 4.4 million (9%) of a total of 50.5 million deaths each year throughout the world[8]. The two thirds of individuals who survive a stroke add to a large pool of prevalent stroke survivors (about 1% of the population, or 10,000 per million), of whom at least half are disabled[9], making the stroke the most important single cause of severe disability in people living in their own homes[10].

Stroke is one of the most significant healthcare problems faced by the US. The prevalence of stroke was 5.8 million among the adults age 20 and above in 2005[11]. Strokes are mainly divided as 87% ischemic, 10% are intracerebral hemorrhage, and 3% are subarachnoid hemorrhage[11]. Stroke shows a significant burden on the economy, with acute ischemic stroke accounting for the most of the cost[11]. Direct cost encompasses all expenditures from hospitalization, nursing homes, physicians and other healthcare professionals, drugs and other medical durables, and home healthcare, whereas indirect cost accounts for lost productivity due to morbidity or mortality. Stroke can be ranked among the most expensive chronic diseases such as cancer ($219.2 billion in 2007), diabetes ($174 billion in 2007), and depression ($83.1 billion in 2000)[12,13].

CHAPTER TWO

LITERATURE REVIEW

There is one line of research to improve the education of the general public which would allow them to recognize a stroke based on the knowledge of the symptoms and also allow them to quickly respond to it and seek treatment urgently[14]. For example, a study was conducted in Australia by a group with an aim to find out how patients perceive life in the first week after a stroke[15]. One of the important findings was that it is not easy to identify the symptoms of stroke just because they vary widely. One of the studies was aimed at recording the experience of stroke from a perspective of people who have just suffered one. The findings of the study were that the individual suffered loss of social and bodily controls. Alongside that the study also suggests that the meaning of recovery for an individual is getting back to a pre-stroke life and that for the professionals is regain of functionality[16]. A study from Canada trying to investigate the ideas of a professional and the patients about the stroke and recovery found out that the professionals had a rather negative view given the recovery of the patient. Also patients had unrealistic ideas about the recovery due to the information given by the professionals[17].

Rehabilitation of the stroke patients is an important part for the care of patients and for a successful recovery. A study was aimed to describe the rehabilitation process to the stroke patients and analyze whether the treatment goals and interventions could be classified. Results show that patients who do set goals and participate in the various

interventions designed to help in the recovery of the stroke patients usually are passive. This could be corrected by reeducating the staff to improve the goal setting with the patients and providing them with relevant information[18].

A study was done in the UK with the focus on facilitating stroke care planning through simulation modeling. The study concluded that, through simulation modeling they could successfully map out the elements of the care and their interdependencies. Also, that simulation modeling has the potential to support both decision making at system level and making sense for the stake holders.[19] Another research article emphasizing the use of Markov models states that, Markov models provide a means of modeling clinical problems in which the risk is continuous over time, in which events may occur more than once and when the utility of an outcome depends on when it occurs.[20] The author extends it further by mentioning that most analytic problems involve at least one of the abovementioned considerations and modeling such problems with conventional decision trees may require unrealistic simplifying assumptions. Thus, the use of Markov models aids in the development of more reliable and faithful models on clinical problems.[20]

Stroke secondary prevention lifestyle interventions are effective in terms of positive change in relation to behaviors, secondary outcomes and physiological outcomes. In terms of physiological outcomes, the interventions aiming at reducing blood pressure were found to be effective[21]. Another study aiming to find any statistical difference in two groups, the control group comprising of physical activity alone and intervention group comprising of the physical activity and lifestyle intervention. They

concluded that although there is not significant statistical difference in the two groups at a nine month follow-up, there may be potential benefits in the long term rehabilitation after stroke.[22]

Among major preventable causes of stroke, high blood pressure affects approximately one in three adults in the United States and thus hypertension control becomes one of priorities in stroke prevention[23]. Pharmacological and surgical treatment of hypertension, however, has high drug cost and the risk of adverse effects and hence there is a need to assess the long-term benefits of various lifestyle modification interventions as ambulatory alternatives to pharmacological and invasive therapies.

Among lifestyle modification interventions aimed at blood pressure control, mindfulness therapies including transcendental meditation and mindfulness-based stress reduction[24,25] have been shown to be effective in lowering both systolic blood pressure and diastolic blood pressure[26] among people with hypertension or pre-hypertension[27], as well as the "hard" outcome of mortality [28]. Meditation intervention as a low-cost, non-invasive and non-pharmacological approach holds promise for reducing the burden of illness from cardiovascular diseases. However, a 2012 study of twenty-nine integrative medicine centers and programs across the United States found that among all integrative medicine therapies these mind-body approaches are the least reimbursed by insurers and most of such services were paid for by cash from the patients[29], which signals a possible missed opportunity to lower the burden of illness from cardiovascular diseases. Thus, a model-based exploration about the long-term benefits and cost-effectiveness of meditation intervention at the population level could help us better understand the

benefits of increasing meditation intervention among people with elevated risk for cardiovascular diseases.

Rotterdam ischemic heart disease and stroke computer simulation (RISC) model was developed by using the data from a follow-up of 5 years from the Rotterdam study which is a cohort follow-up study of 7,983 adults aged 55 years and older. This model is a Monte Carlo Markov model designed to investigate the effects of modifying the cardiovascular disease (CVD) risk factors on the burden of CVD. The observed values fell within the 95% credibility intervals of the simulated values confirming the internal, predictive, and external validity of the simulation model; thus providing a basis for analyzing the effects of modifying cardiovascular disease risk factor by a simulation model[30]. The internal and predictive validation stands for the validation done using the data from the internal cohort study of 3,501 individuals, while the external validation means the validation was completed using the external data from an EPIC-Norfolk study which is an cohort study of 25,663 individuals. A computer simulation model was designed for the cost effectiveness analysis of cardiovascular disease prevention. This model makes it possible to compare the cost effectiveness of different interventions. The model, however, was developed in a very general sense, thus lacking a focused intervention and its cost-effectiveness[31].

In this study, we develop a simulation model to quantify the prevention potential of mindfulness meditation intervention on stroke trends in the United States. Our calibration of the simulation model is based upon data from the Centers for Disease Control and Prevention (CDC)'s online query system of "underlying causes of death"[32],

and model parameters are drawn from documented evidence about meditation and health outcomes. We then explore the comparative effectiveness of meditation interventions by examining its long-term cost-effectiveness ratio at the population level, to facilitate a relevant comparison with other prevention interventions designed to improve the cardiovascular health of the population.

Our simulation model mainly consist of producing the trend of strokes observed from 1999 to 2013 as given by the observed data by the CDC and forecasting it for the next fifteen years to get a reasonable trend of strokes in the future. Mindfulness meditation could be defined as the intentional, accepting and non-judgmental focus of one's attention on the emotions, thoughts and sensations occurring in the present moment. This research allows us to observe and examine the trend for stroke mortality and stroke incidences. This research also explores one of the main causes, systolic blood pressure, and tries to find an alternative lifestyle change solution for its reduction. Alongside that, age is another risk factor which is considered in this research.

CHAPTER THREE

METHODOLOGY

3.1. Introduction

We created a simulation model to represent a population of individuals where the evolution of each individual is governed by a micro-simulation model. A simulation model refers to a set of dynamic mathematical equations used to generate a pattern of observed data. A micro-simulation model is an agent based model which generates the stroke incidences for each individual at a time. The census year 1999 was chosen as the start year of the simulation because the data for the stroke mortality is available only from the year 1999 and onwards. We simulate the births and deaths for each individual to create a total population that resembles the age and systolic blood pressure (SBP) structure of the US population. In each calendar year, one of three major stochastic events occurs in the model: (i) each simulated individual may die due to non-stroke-related causes, according to a probability which is calculated for each age group; (ii) he/she may die due to stroke with a probability calculated based on an adapted Cox hazard model comprising age, systolic blood pressure, and the calendar year; (iii) he/she might survive the year and then moves on to the next calendar year.

We started the simulation of the US population in the census year of 1999 and calibrated the model by comparing the number of stroke-related deaths generated by the model with that observed in historical data from 1999 to 2013[32]. Calibration of the model is achieved by adapting the coefficients of the Cox equation. The original Cox equation is

developed by Philip et al and provides a simple formula for estimating the probability of stroke for specified levels of risk factors. The Cox equation mainly includes three parameters: SBP, age, and a constant. We adapted the model by changing the constant term to fit the data. Then, we used the model to predict the impact of meditation intervention on stroke mortality in the US population over a course of fifteen years through 2028. We modeled the attendance rate for meditation intervention among individuals as research shows that not everybody receiving a meditation intervention chooses to attend the teaching sessions, and we assume that these people do not benefit from meditation. Our model also simulates the adherence rate to the meditation intervention in each calendar year simulated, and we assume that the blood pressure goes back up to its natural level (intervention-free) once the individual chooses not to adhere to the practice in a given year. Next, we elaborate on micro-simulation and population simulation model development.

3.2. Overview of Micro-Simulation Model

The population model is based on an individual-based micro-simulation that replicates the probabilistic dynamics of stroke in an individual's life course. Probabilistic dynamics of the stroke is the probability of either having or not having a stroke for an individual at any given point of time. The model tracks the age and SBP of an individual on a yearly basis. While age increases by one for each calendar deterministically, SBP changes over time based on age groups, i.e., we update the SBP of an individual due to aging according to the patterns observed in the literature[33]. Aligned with literature, we

discretized age into six age groups namely 25-44, 45-54, 55-64, 65-74, 75-84, and >85 years, respectively for SBP updates[32]. The progression of each individual at a time period is based on the following three stochastic events.

First, an individual may die due to non-stroke-related causes. Non-stroke-related causes include every other cause of death except only deaths due to strokes. We estimated the probability of death in each age group from the life table (Table A.1) which provides a direct relation between age and probability of death[34]. For example, for a given age of 25 years, the probability of death is 0.00096. Life expectancy is used to confirm that the model replicates the desired outcomes. Life expectancy means that for any given age in years, what is the average period of years the individual may live, which is also obtained from the life table. For example, for a given age of 25 years, the life expectancy is 53.9 years, meaning that the individual will die when he/she is 78.9 years old.

Second, an individual may experience a stroke with a probability which is calculated based on a validated Cox hazard model[35]. The Cox hazard model equation constitutes of three main parts namely the age, the SBP, and a constant. The Cox hazard model equation in our model is (0.0485 * age + 0.0147 * SBP + 0.31), where 0.485 is the coefficient of the variable age, 0.0147 is the coefficient of the variable SBP, and 0.31 is the constant. The respective coefficients in the above equation were computed based on a trial and error focused on the successful calibration of the model. However, since we used age and SBP as risk factors in calculating the probability of stroke, we adapted the equation and calibrated the model accordingly. This necessarily means that the equation

derived from the original Cox hazard model for probability of stroke contains more than the abovementioned two variables, but the two most significant of them are the age and SBP in the equation.

After finalizing the coefficients of the variables, the probability of having a stroke is calculated in the following steps: (i) calculate the value of the random variable '*L*' which equals the value calculated using the abovementioned equation for any given values of age and SBP at a given time. The equation is stated as $L = (0.0485 * \text{age} + 0.0147 * \text{SBP} + 0.31)$; (ii) after calculating the value of *L*, we subtract 5.2529 from it and store it in another variable, say '*A*',hence, $A = L – 5.2529$. The value 5.2529 is based on the mean values for age and SBP calculated by using this mean values in the Cox hazard equation . The mean value for age is considered as 65.4 and for SBP as 139.3 form the literature which is used in the Cox hazard equation.[35] (iii) the next step involves taking the exponential of the value *A* which is stored in the variable '*B*'; (iv) after taking the exponential, we calculate a value which equals 0.9948 to the power *B*; (v) Finally, we subtract the calculated value in the step (iv) from 1.0 and the answer is the final probability of stroke for that individual at that calendar year. This probability of stroke is then used to decide whether the person has a stroke or not. This is done by comparing the calculated probability of stroke with a random number generated between zero and one. If the random number generated is greater than the probability of stroke, then the individual doesn't have a stroke and moves to the next year and his age is incremented by one. If the random number generated is less than the probability of stroke, the individual

has a stroke. Then, we check whether the person dies due to stroke or he/she doesn't, which is explained in the third step below.

Third, if an individual experiences a stroke, he/she may die due to stroke according to a probability that depends on his/her age group[32]. The probability of death in any age group is calculated based on the total number of death in that age group and total number of people in the age group in 1999.This probability is then fixed for every other year till the end of the simulation. The formula for calculating the probability of dying due to stroke is given by: $(\frac{Total\ number\ of\ death\ due\ to\ stroke\ in\ that\ age\ group}{Total\ population\ in\ the\ age\ group\ who\ had\ stroke})$.

Once the probability of death due to stroke is calculated, it is compared with a random probability generated between zero and one. If the random probability is less than the probability of death due to stroke then the person dies due to stroke and he is removed from the simulation after collecting of all the statistics related to the individual.

To calibrate the micro-simulation model, we compared the number of stroke incidences produced by the model with that observed from historical data in the US. Pursuant to this goal, we created the US population in 1999, ran the simulation model for a year, and computed the total number of stroke incidences in each group. This computed incidences were compared to the actual observed data and through the process of trial and error the model was calibrated: see Figure 3.1.

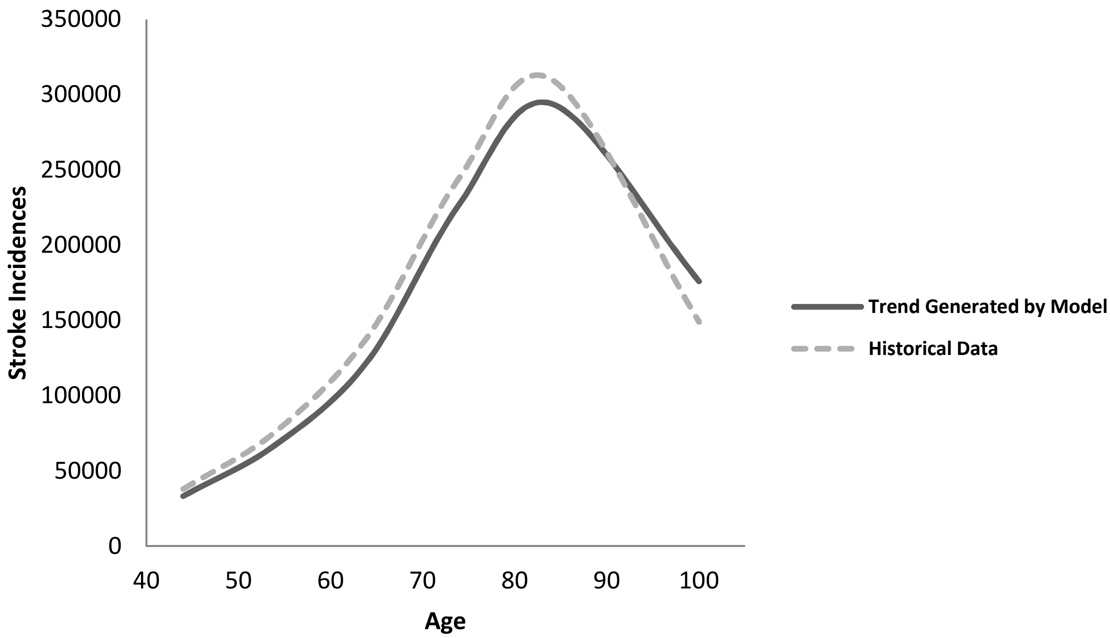

Figure 3.1. Calibration of micro-simulation model

Note: Figure 3.1 shows the trend generated by the model as well as the original expected trend for the stroke incidences.

We further validated the model by comparing the stroke mortality in each age group reported in historical data with that generated by the model. For the validation process the term stroke mortality stands for the total number of deaths in each age group, which is compared with the actual observed stroke mortality. The model was automatically validated for the stroke mortality meaning the trend for the stroke mortality as observed in the historical data is very close to the model generated trend as seen in Figure 3.2. The validation process increases the confidence on reliability of the model in generating results representing the real trends.

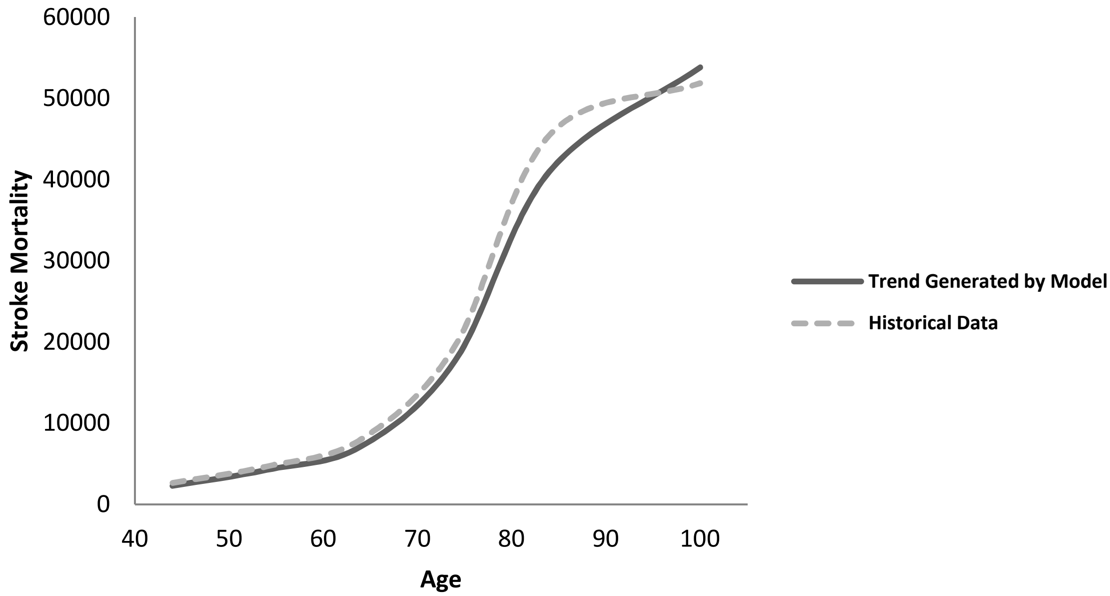

Figure 3.2. Validation of micro-simulation model

Note: Figure 3.2 shows the trend generated for the model as well as the original expected trend for the stroke mortality. We used data from 1999 for the model calibration.

In order to capture the real-life impact of mindfulness meditation on individuals, we simulated two more characteristics for each individual: attendance and adherence to mindfulness meditation practice. We define attendance rate as the probability that an individual ever attends a mindfulness meditation program during the course of his/her life. Due to lack of significant evidence for the attendance rate of mindfulness meditation in the US, we assume that the attendance rate of individuals follows a normal distribution with mean 0.5 and standard deviation 0.04[36]. We truncated the normal distributions of these rates at 0% and 100% and we assume that attendance rates do not change over time.

We decide whether a person attends the mindfulness meditation intervention at the very start when the person is just introduced into the simulation. The following few steps are to be followed to decide if a person attends or does not attend the intervention practice**:** (i) Calculate a random probability between zero and one; (ii) Calculate the probability of attending the mindfulness mediation intervention by using the abovementioned normal distribution; (iii) Compare the random probability generated with the calculated probability of attendance and if the random probability is smaller than the calculated probability of attendance, then the person will attend the mindfulness mediation intervention. The mindfulness mediation intervention effect is considered for a person only when he turns age 50 or higher.

Also, we define adherence as the probability that an individual, who has already attended a mindfulness meditation program, complies with the intervention. We assume that the adherence of individuals follows a normal distribution with mean 0.66 and standard deviation 0.04[36]. We also truncated the normal distributions of this rate at 0% and 100% same as the attendance rate and we also assume that adherence rate does not change over time. Based upon our meta-regression of meditation's impact on blood pressure and patient age[37], we assume that if an individual attends a mindfulness meditation and complies with it in a period, his/her SBP reduction will follow an age-dependent dosage. However, if an individual does not comply with the intervention in a period, his/her SBP returns to its natural SBP level. In order to have the natural SBP of each individual in all time periods, we keep track of the SBP progression of each individual in an intervention-free setting. The decision as to who adheres to the

intervention follows the same exact way as the attendance for the intervention by just changing the attendance rate in the steps by adherence rate.

3.3. Overview of Population Simulation Model

We extend the individual micro-simulation model described above by running multiple, unique, simultaneous copies of the model to represent a population of individuals and to simulate the effect of applying a variety of intervention scenarios. What makes every year unique is that the starting population for every year of the iteration is based on the ending population of the last year. In addition to the population , we add new individuals at each age period to the first age group of the population, i.e., the 25-44 age group. We set the birth rate to 0.012 which is the rate observed in the US over the past two decades[38]. The birth rate is kept the same for every year through the simulation which necessarily does not mean that the model adds the same constant number of people every time, since the population added into the 25-44 age group follows a Binomial distribution. We consider the integral expected value of this distribution by multiplying the birth rate with the total population of the previous year.

At each time period, the micro-simulation model simulates the probability of having a stroke event for each individual in the population. The model is, therefore, able to produce the number of stroke incidences and mortality as well as life expectancy. We used the population simulation model to estimate the number of stroke incidences and mortality for the next fifteen years and investigated the impact of implementing a variety of mindfulness meditation interventions on stroke trends.

To calibrate the population simulation model, we first created the US population (greater than 25 years old) in 1999 according to the same age and SBP distribution observed in the data. This necessarily means that a population of 176,826,619 people is first created. The difference between the micro-simulation model and the population model is that in micro simulation model we simulate the population for year 1999 by one individual at a time, while in the population model we generate all the people for year 1999 concurrently and then the progression of each individual is governed by the micro-simulation model.

We repeated the abovementioned steps for all the years till 2013 and gathered the statistics related to the stroke incidences and stroke mortality. Then, we compared the number of stroke-related deaths from 1999 to 2013 generated by the model with that of the observed statistics in the historical data. A decreasing trend exists in the stroke mortality after the year 1999. This was later explained with the help of literature review that a drug named statin was introduced in the late 1990's. We considered the impact of statin on SBP and consequently on stroke trends since there is evidence that statin has had a significant impact on stroke trends after 1999. For example, a randomized trial concluded that reductions in the systolic and diastolic blood pressure occurred with the use of statin and these modest effects may contribute to the reduction in the risk of stroke along with some other cardiovascular diseases[39]. In particular, they showed that the effect of statin is significant in people with an elevated blood pressure[40]. We assume that the population above 50 years of age uses statin after 1999 and reduces the blood pressure by 2.4 mm Hg[39].

The mindfulness meditation intervention is then applied to individuals with age greater than 50 years and SBP greater than 140 mm of Hg. Note that the mindfulness meditation intervention could only be applied to individuals who have already attended the mindfulness meditation practices and also adhere to it. If an individual adheres to the meditation intervention, the SBP of the individual reduces given by the equation,

$$\text{Reduction in SBP} = -0.058 * \text{age} - 2.149.$$ [37]

Here the age stands for the age of the individual at that particular instance. In particular, the equation implies that more the age of the individual, greater will be the effect of mindfulness meditation which is supported by the literature[37]. Apart from this mindfulness meditation has shown reduction in SBP as high as 3.8 mm of Hg.[27]

Once the intervention is applied, the SBP of that particular individual is reduced and thereafter the SBP is updated every year accordingly, given that the person adheres to the intervention every year. For example, if the SBP of a person is 152 mm of Hg and the age is 55 years and he adheres to the intervention, then the SBP will be reduced based on the equation given above, which will come down to 146.61 mm of Hg. Now, say for instance, the next year he does not adhere to the mindfulness meditation intervention, then his/her SBP goes back up to the natural SBP. Natural SBP denotes the SBP of an individual without any kind of intervention effect on it.

This process works in the very same way as prescription medicines would work. For example, if a person takes medication to reduce the SBP, then his/her SBP is controlled by it as long as he/she is taking those medications as prescribed. If, however, the person stops taking the medication, then the SBP will shoot up. Also, if the person

decides to take the medication again, then the SBP will decrease to the controlled state again. Pursuant to this goal, individuals have two SBP's at any given point of time in the simulation. One is the natural SBP which is the normal SBP without any interventions, and the other is the actual SBP which is the SBP after applying the intervention. Note that the two SBP's are only assigned to those individuals who attended the mindfulness meditation intervention. For those individual who do not attend any kind of mindfulness meditation intervention, we keep track of natural SBP only.

After all the computations, the statistics relating to each person are recorded. These statistics mainly include what is the final age, how many years the person lived, did the individual suffer any strokes in his life and if yes then how many, what was the reason of the death of the individual, whether it was because of stroke or because of the reasons other than strokes. All this are recorded for every individual in the population. On death of an individual we remove him from the total population and update the population accordingly.

CHAPTER FOUR

RESULTS

Figure 4.1 shows the result of the population simulation model calibration where we compare the number of stroke-related deaths from 1999 to 2013 generated by the model with that observed in historical data. Note that since the model is stochastic, to provide stable estimates, we repeat each simulation 50 times to attain stable results and report the average of results.

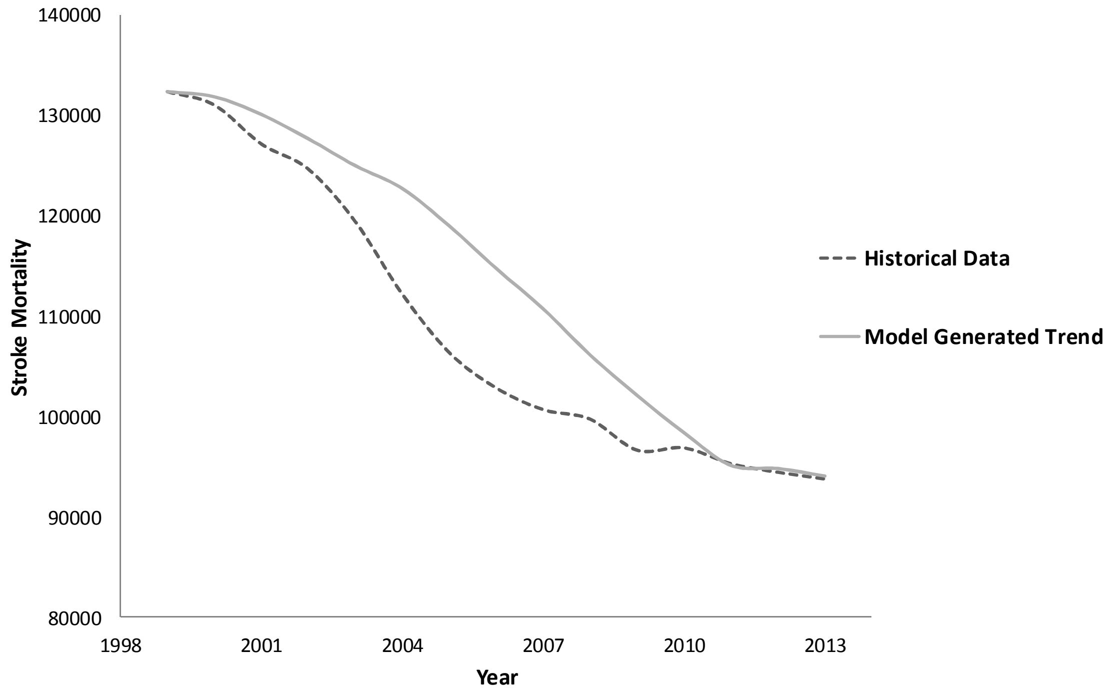

Figure 4.1 Calibration of population model

Note: Figure 4.1 shows the trend generated for the model as well as the original expected trend for the stroke mortality for the population model.

In our base case analysis, where we assume that the mindfulness meditation intervention is applied for individuals with a SBP of greater than 140 mm Hg and all parameters are set to the baseline values, our results show that we could avert 1,016,315 stroke incidences and 250,226 stroke-related deaths over the course of fifteen years. Figure 4.2(A) shows the prediction for the number of stroke incidences over a course of fifteen years for two scenarios: (i) mindfulness meditation intervention is not implemented, and (ii) mindfulness meditation intervention is implemented at baseline.

Similarly, Figure 4.2(B) shows the number of stroke-related mortality for the abovementioned scenarios. We also estimated the monetary saving that could be achieved by considering the mindfulness meditation intervention. The average cost of care for a patient up to 90 days after stroke is approximately $15,000[41]. Therefore, based on our baseline assumptions on model parameters, a yearly saving of nearly one billion dollars is achievable due to this intervention. The breakdown of the costs of stroke for both short and long term could be seen in the Figure A.1 in the Appendix B. Note that the breakdown of the stroke is by the type of expense. Also the literature for the cost burden for ischemic stroke could be found in the Table A.2 and Table A.3 in Appendix C.

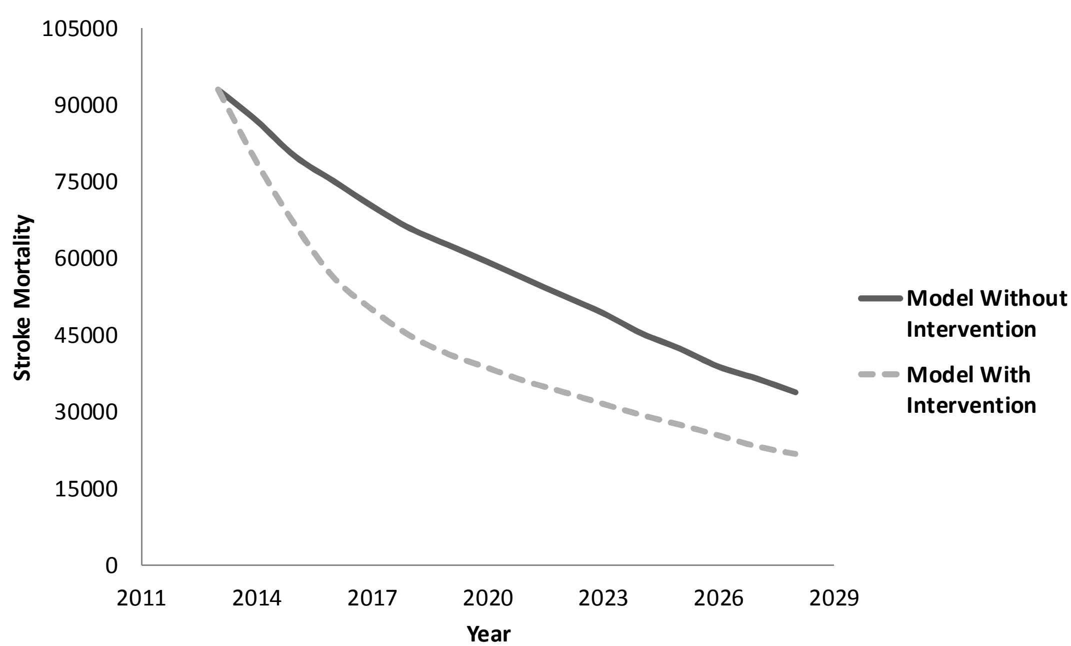

Figure 4.2(A) Reduction in stroke incidence by applying the intervention

Note: Figure 4.2(A) depicts the results of applying the intervention on stroke incidence trends. In particular, the solid line shows the stroke incidence in an intervention-free setting and the dotted lines shows that in a setting where the intervention is implemented. Results show an improvement of 23.75% in the reduction of stroke incidences.

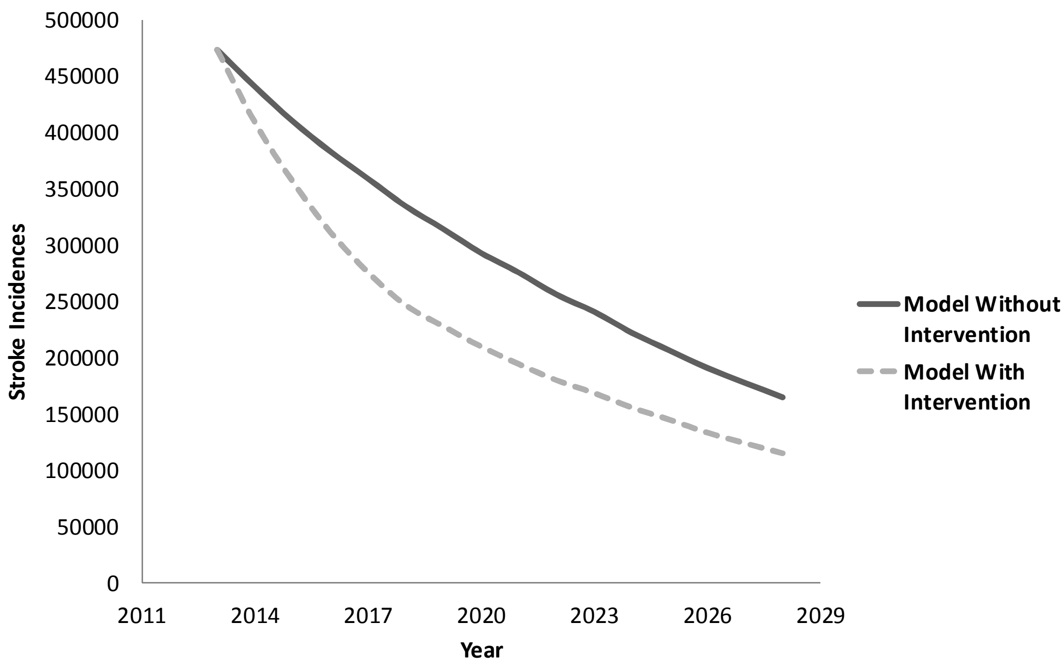

Figure 4.2(B). Reduction in stroke mortality by applying the intervention

Note: Figure 4.2(B) compares the predicted number of stroke-related mortality produced by the model in two scenarios. The solid line shows the number of stroke-related deaths in an intervention-free setting and the dotted line shows that in a setting where the mindfulness meditation intervention is applied. The results are reported over a period from year 2013 to 2028. Results show an improvement of 28.88% in the reduction of stroke mortality.

We conducted a variety of one-way and two-way sensitivity analysis to investigate the robustness of our results as well as identify the key factors on outcomes

by perturbing the model parameters. Table 4.1 reports the results of the sensitivity analysis. In the base case, we applied the intervention to individuals with a SBP of greater than 140 mm Hg. In one sensitivity analysis, we considered two other thresholds for applying the intervention, namely, 150 and 160 mm Hg. Our results show that by increasing the intervention initiation threshold to 150 mm Hg, the number of stroke incidences averted and the number of deaths averted, compared to the base case, would reduce by 29.42% and 27.15%, respectively. Similarly, by increasing the intervention initiation threshold to 160 mm Hg, the number of stroke incidences averted and the number of deaths averted, compared to the base case, would reduce by 78.03% and 79.27%, respectively. Recall that in our base case, the intervention is applicable to all adult age groups. In a sensitivity analysis, we applied the intervention to a variety of age groups. In particular, we assumed that the intervention is applied to individuals older than 40, 50, and 60 years old, and our results show that, compared to the base, there is not a significant difference in the number of stroke incidences and stroke-related deaths. This shows that the most benefit comes from applying the intervention for individuals older than 60 years. We changed the expected value of attendance rate from 25% to 75% and did not observe a significant difference among outcomes compared to the base. However, when we varied the expected value of the adherence rate from 25% to 90%, we observed a substantial change in the results. In particular, if the average adherence rate drops to 25%, the number of stroke incidences averted and the number of deaths averted, compared to the base case, would decrease by 39.84% and 41.11%, respectively. Moreover, if the average adherence rate increases to 90%, the number of stroke

incidences averted and the number of deaths averted, compared to the base case, would increase by 8.20% and 9.9%, respectively.

Along with the abovementioned scenarios, some other scenarios were also included in the sensitivity analysis, one of them being the optimistic setting and the other one being pessimistic setting. In the pessimistic setting, we considered the lower values for the adherence rate and attendance rate. The adherence rate for the pessimistic setting was fixed at 25% and the adherence rate was fixed at 25%. On the other hand, in the optimistic setting, we considered the upper values of the adherence rate and the attendance rate. The adherence rate was fixed at 90% and the attendance rate was fixed at 75%. The results for the optimistic setting show that the number of deaths averted would increase by 8.69% and the number of strokes averted would increase by 10.16%. The results for the pessimistic setting show that the number of deaths averted would decrease by 40.51% and the number of strokes averted would decrease by 41.81%. Our two-way sensitivity analysis also confirms the significance of individual's adherence in the effectiveness of the intervention. This observation suggests that for designing an effective mindfulness meditation program, policy makers may prioritize funding to the programs that aim to improve the compliance of individuals to meditation.

Table 4.1. Sensitivity Analysis

Scenarios	Number of Total Deaths Averted	Number of Total Strokes Averted
Base Intervention	250226	1016315
SBP_{150}	182292	717294
SBP_{160}	54974	210673
Age_{40}	249177	1016032
Age_{50}	249018	1015918
Age_{60}	247738	1015232
$Attendance_{25\%}$	248624	1014371
$Attendance_{75\%}$	251366	1017045
$Adherence_{25\%}$	150520	598477
$Adherence_{90\%}$	270768	1116955
$Attendance_{75\%}$ & $Adherence_{90\%}$	271977	1119671
$Attendance_{25\%}$ & $Adherence_{25\%}$	148853	591312

This table reports the statistics relating to the stroke incidences and stroke mortality for a variety of scenarios. In the base case, all individuals in the model are considered for the intervention. SBP_{150} denotes that intervention is applied to only those individuals whose SBP is more than or equal to 150 mm of Hg. Age_{40} denotes that the people only above 40 years of age are considered for the intervention. $Attendance_{25\%}$ is used to specify that the attendance for intervention is set to 25% and $Adherence_{25\%}$ shows that the adherence to intervention is set to 25%. With the increase in SBP above which we apply intervention the number of stroke deaths averted reduces. Similarly, with the increase in age the stroke mortality increases that is the death due to stroke reduces. As

we decrease the adherence rate or attendance rate the stroke mortality increases. The effect of adherence is larger than attendance according to the results. The important factors are the adherence and SBP because they show a much larger impact on the model in terms of stroke mortality.

CHAPTER FIVE

CONCLUSION

Summary

Mindfulness meditation is one of the emerging lifestyle techniques that addresses multiple risk factors of cardiovascular diseases, including elevated blood pressure. This research uses a simulation model to explore stroke mortality among the US population above 25 years of age. A hypothetical meditation intervention with an attendance rate of 50% and adherence rate of 66% among people with systolic blood pressure greater than 140 mm Hg averts approximately 250,226 deaths over a course of fifteen years. This outcome is very sensitive to the adherence rate we assumed: at an adherence rate of 25% the number of stroke deaths averted drops to nearly 150,520 over a course of fifteen years and if we assume the adherence rate is 75%, the number of stroke deaths averted increases to around 270,768.

To the best of our knowledge, this study is the first model-based projection of a hypothetical diffusion of meditation practice among people at elevated risk for cardiovascular diseases. The micro-simulation nature of our model makes it easy to estimate what the total benefits of meditation diffusion will look like for a defined subset of the US population. For example, a state government agency or an insurance company interested in curbing stroke-related costs and productivity losses can easily take a subset of our simulated US population and explore the extent to which a meditation promotion program could help with their goals. As the mortality benefits of meditation as simulated in our model is mediated through a decrease of systolic blood pressure, this model can

also be adapted to simulate the mortality benefit of any intervention proven to lower systolic blood pressure (e.g., physical activity, fasting, pharmacological intervention, surgical intervention, etc.).

Limitations

This study has several limitations. Our model is limited in that it only simulates one aspect of hypertension: systolic hypertension. A more comprehensive model of stroke mortality needs to include the diastolic blood pressure and its response to health interventions as well. Also, the projected health benefits based upon our model results are likely to be an underestimation of the total health improvement attainable through an increase in the uptake of meditation practice, since meditation improves health related quality of life [42] in addition to its mortality benefits and its benefits on mortality reduction is not limited to stroke mortality. We considered age and SBP to represent each individual in the population and did not consider other characteristics such as gender and race which might have impact on results.

Future Research

To have a more comprehensive quantification of what meditation can do to improve population health, future models need to add in other types of evidence-based mortality benefits from meditation, as well as adding in the components of health-related

quality of life. We can also incorporate more characteristics for the individuals, for example, considering gender, race, multiple interventions of medication and their effects on the systolic blood pressure. We could also include the effect on diastolic blood pressure, mainly because even though not major but diastolic blood pressure has some effect on the strokes.

APPENDICES

Appendix A

Table A.1. Life table for the total population: United States, 1999.

Age	Proportion dying during age interval	Number living at beginning of age interval	Number dying during age interval	Stationary population in the age interval	Stationary population in this and all subsequent age intervals	Life expectancy at beginning of age interval
	q_x	l_x	d_x	L_x	T_x	e_x
0–1	0.00706	100,000	706	99,383	7,672,728	76.7
1–2	0.00053	99,294	53	99,268	7,573,344	76.3
2–3	0.00036	99,241	36	99,223	7,474,077	75.3
3–4	0.00027	99,205	27	99,192	7,374,853	74.3
4–5	0.00022	99,178	21	99,167	7,275,662	73.4
5–6	0.00020	99,157	20	99,147	7,176,494	72.4
6–7	0.00019	99,137	19	99,127	7,077,347	71.4
7–8	0.00018	99,118	18	99,109	6,978,220	70.4
8–9	0.00016	99,101	16	99,093	6,879,111	69.4
9–10	0.00014	99,084	14	99,077	6,780,018	68.4
10–11	0.00013	99,070	12	99,064	6,680,941	67.4
11–12	0.00013	99,058	13	99,052	6,581,876	66.4
12–13	0.00017	99,045	17	99,037	6,482,824	65.5
13–14	0.00026	99,029	25	99,016	6,383,787	64.5
14–15	0.00038	99,003	37	98,985	6,284,771	63.5
15–16	0.00051	98,966	50	98,941	6,185,787	62.5
16–17	0.00063	98,916	62	98,885	6,086,846	61.5
17–18	0.00073	98,854	72	98,818	5,987,961	60.6
18–19	0.00079	98,782	78	98,742	5,889,143	59.6
19–20	0.00084	98,703	82	98,662	5,790,401	58.7
20–21	0.00088	98,621	87	98,578	5,691,739	57.7
21–22	0.00092	98,534	91	98,489	5,593,161	56.8
22–23	0.00096	98,443	94	98,396	5,494,672	55.8
23–24	0.00097	98,349	95	98,302	5,396,276	54.9
24–25	0.00096	98,254	94	98,207	5,297,974	53.9
25–26	0.00095	98,160	94	98,113	5,199,767	53.0

26–27	0.00095	98,066	93	98,020	5,101,654	52.0
27–28	0.00096	97,973	94	97,926	5,003,635	51.1
28–29	0.00098	97,879	96	97,831	4,905,708	50.1
29–30	0.00102	97,783	99	97,734	4,807,877	49.2
30–31	0.00106	97,684	103	97,632	4,710,143	48.2
31–32	0.00111	97,581	108	97,527	4,612,511	47.3
32–33	0.00117	97,473	114	97,416	4,514,985	46.3
33–34	0.00124	97,359	121	97,298	4,417,569	45.4
34–35	0.00133	97,238	129	97,173	4,320,270	44.4
35–36	0.00142	97,109	138	97,040	4,223,097	43.5
36–37	0.00151	96,971	146	96,898	4,126,057	42.6
37–38	0.00161	96,825	156	96,747	4,029,159	41.6
38–39	0.00173	96,669	167	96,585	3,932,412	40.7
39–40	0.00187	96,501	180	96,411	3,835,827	39.8
40–41	0.00201	96,321	194	96,224	3,739,416	38.8
41–42	0.00217	96,127	208	96,023	3,643,193	37.9
42–43	0.00234	95,918	224	95,806	3,547,170	37.0
43–44	0.00253	95,694	242	95,573	3,451,364	36.1
44–45	0.00274	95,452	262	95,321	3,355,791	35.2
45–46	0.00299	95,190	284	95,048	3,260,470	34.3
46–47	0.00325	94,906	309	94,752	3,165,422	33.4
47–48	0.00353	94,597	334	94,430	3,070,671	32.5
48–49	0.00381	94,263	359	94,084	2,976,240	31.6
49–50	0.00409	93,905	384	93,713	2,882,156	30.7
50–51	0.00439	93,521	410	93,316	2,788,443	29.8
51–52	0.00473	93,111	440	92,891	2,695,127	29.0
52–53	0.00512	92,670	474	92,433	2,602,237	28.1
53–54	0.00557	92,196	514	91,939	2,509,804	27.2
54–55	0.00610	91,682	560	91,403	2,417,864	26.4
55–56	0.00673	91,123	613	90,816	2,326,462	25.5
56–57	0.00742	90,510	672	90,174	2,235,645	24.7
57–58	0.00816	89,839	733	89,472	2,145,471	23.9
58–59	0.00892	89,105	795	88,708	2,055,999	23.1
59–60	0.00971	88,311	857	87,882	1,967,291	22.3

60–61	0.01058	87,453	925	86,991	1,879,409	21.5
61–62	0.01157	86,528	1,001	86,028	1,792,418	20.7
62–63	0.01265	85,527	1,082	84,986	1,706,390	20.0
63–64	0.01383	84,445	1,168	83,861	1,621,404	19.2
64–65	0.01509	83,277	1,257	82,649	1,537,543	18.5
65–66	0.01641	82,020	1,346	81,348	1,454,894	17.7
66–67	0.01782	80,675	1,437	79,956	1,373,546	17.0
67–68	0.01941	79,238	1,538	78,469	1,293,590	16.3
68–69	0.02123	77,699	1,649	76,875	1,215,121	15.6
69–70	0.02323	76,050	1,766	75,167	1,138,246	15.0
70–71	0.02528	74,284	1,878	73,345	1,063,079	14.3
71–72	0.02739	72,406	1,983	71,414	989,735	13.7
72–73	0.02970	70,423	2,091	69,377	918,320	13.0
73–74	0.03229	68,332	2,207	67,228	848,943	12.4
74–75	0.03518	66,125	2,326	64,962	781,715	11.8
75–76	0.03824	63,799	2,440	62,579	716,753	11.2
76–77	0.04145	61,359	2,543	60,087	654,174	10.7
77–78	0.04502	58,816	2,648	57,492	594,086	10.1
78–79	0.04914	56,168	2,760	54,788	536,595	9.6
79–80	0.05395	53,408	2,881	51,967	481,807	9.0
80–81	0.05950	50,526	3,006	49,023	429,840	8.5
81–82	0.06578	47,520	3,126	45,957	380,816	8.0
82–83	0.07287	44,394	3,235	42,777	334,859	7.5
83–84	0.08066	41,159	3,320	39,499	292,082	7.1
84–85	0.08913	37,839	3,373	36,153	252,583	6.7
85–86	0.09777	34,467	3,370	32,782	216,430	6.3
86–87	0.10700	31,097	3,327	29,433	183,648	5.9
87–88	0.11683	27,769	3,244	26,147	154,215	5.6
88–89	0.12725	24,525	3,121	22,965	128,067	5.2
89–90	0.13827	21,404	2,960	19,925	105,103	4.9
90–91	0.14989	18,445	2,765	17,062	85,178	4.6
91–92	0.16210	15,680	2,542	14,409	68,115	4.3
92–93	0.17489	13,138	2,298	11,989	53,706	4.1
93–94	0.18824	10,841	2,041	9,820	41,717	3.9

94–95	0.20212	8,800	1,779	7,911	31,896	3.6
95–96	0.21651	7,021	1,520	6,261	23,986	3.4
96–97	0.23138	5,501	1,273	4,865	17,724	3.2
97–98	0.24668	4,228	1,043	3,707	12,860	3.0
98–99	0.26237	3,185	836	2,767	9,153	2.9
99–100	0.27839	2,350	654	2,022	6,386	2.7
100+	1.00000	1,695	1,695	4,363	4,363	2.6

<u>Appendix B</u>

The Breakdown of Direct Costs of Stroke (Short Term and Long Term) by Type of Expense.

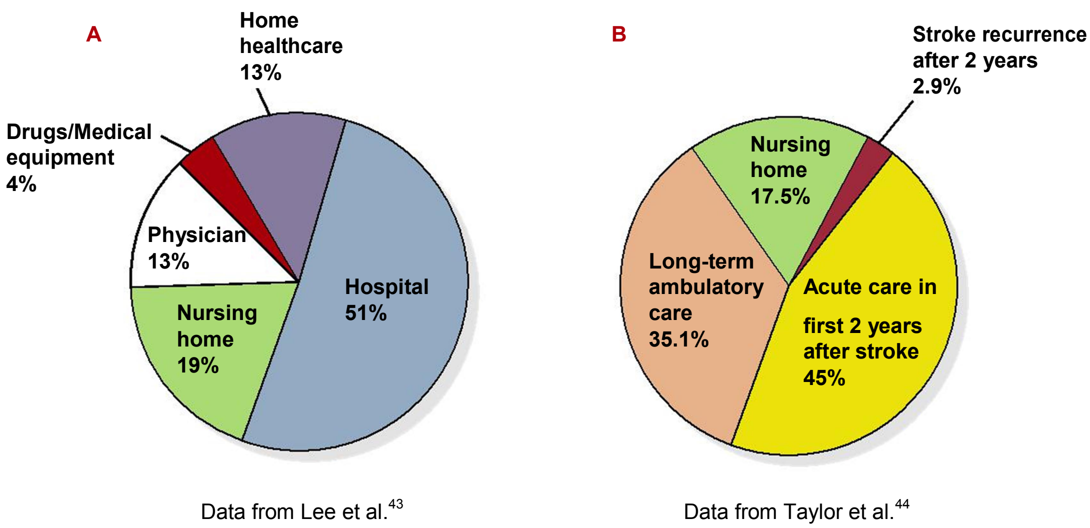

Figure A.1. The Breakdown of direct costs of stroke by type of expense.

Appendix C

Cost Burden of Ischemic Stroke.

Table A.2. Summary of Studies Reporting Average per Patient Direct Costs of Short-Term Care for Stroke.

Study	Years of Data Collection (Dollar Years Reported)	Design	Patients	Mean Cost (Hospitalization)	Mean Cost (Hospitalization)	Mean LOS
Katzan 2007[45]	1991-1997 (costs adjusted to 2000 dollars)	Retrospective cohort study (greater Cleveland area)	11,286 Medicare patients admitted for first stroke (635 with pneumonia)	$6272 without pneumonia; $21,173 with pneumonia	$7842 without pneumonia; $26,470 with pneumonia	7.6 days without pneumonia; 18.6 days with pneumonia (median LOS)
Qureshi 2007[46]	1990-1991 and 2000-2001(all costs reported in 2001 dollars)	Retrospective database analysis (US all-payer inpatient care databases)	(approx)1.13 million admissions in 1990-1991; (approx)1.26 million admissions in 2000-2001 (both periods, for ischemic stroke)	1990-1991: $13,700 2000-2001: $16,200	1990-1991: $16,655 2000-2001: $19,695	1990-1991: 9.5 days 2000-2001: 5.3 days
Reed 2001[47]	1998	Retrospective data for all patients admitted to 137 community hospitals	18,740 patients with ischemic cerebral infarction	$5837	$7710	5.9 days
Caro 2000[48]	1996 (Costs reported in 1996 dollars)	Cost data extracted from 2 prospective 12-week international trials (1 in the United States and Canada)	593 US patients with acute ischemic stroke	$7461	$10,238	9 days (median)
Gillum 2001[49]	1997-1999	Retrospective analysis of administrative database	10,880 patients with ischemic stroke	$18,000	ND	7.7 days
Samsa 1999[50]	1991	Retrospective analysis of Medicare claims files	49,333 Medicare patients hospitalized with cerebral infarction in 1991 (4947 with previous stroke in the past 4 years)	Initial hospital cost: $7091 (first stroke); $6939 (recurrent stroke)	Initial hospital cost: $11,209 (first stroke); $10,969 (recurrent stroke)	Initial LOS 10.9 days (first stroke); 11.6 days (recurrent stroke)

Diringer 1999[51]	1996	Prospective data collection at a tertiary care academic medical center with a stroke management team	191 patients consecutively admitted with acute ischemic stroke	$4408 (median hospital cost per discharge)	$6049 (median hospital cost per discharge)	6 days (median)
Fagan 1998[52]	Costs reported in 1996 dollars	Markov model estimating costs per 1000 patients treated with rt-PA vs 1000 untreated patients (NINDS rt-PA Stroke Trial)	Data at 10 days poststroke: 307 placebo and 310 rt-PA	Initial hospitalization: $14,923 (placebo) and $14,121 (rt-PA)	Initial hospital-ization: $20,478 (placebo) and $19,377 (rt-PA)	12.4 days (placebo) and 10.9 days (rt-PA)
Newell 1998[53]	1995 and 1997	Retrospective analysis of medical record and financial databases in a 22-county region (northern Mississippi, Alabama, and Tennessee)	356 patients with ischemic stroke in 1995, 399 patients in 1997	1995: $7111 1997: $6246	1995: $10,046 1997: $8379	1995: 9.9 days 1997: 7.2 days
Holloway 1996[54]	1992	Retrospective analysis of administrative and billing data from 5 academic medical centers	908 patients with ischemic cerebral infraction	Mean cost per admissions: $9882 (median $6824)	Mean cost per admission: $15,165	10.8 days
Alberts 1996[55]	1993-1994 (baseline period)	Retrospective analysis of administrative data from the neurology service at a tertiary care hospital	262 stroke patients discharged from neurology service	Mean total charges per case: #23,149 (median $10,234)	ND	9.2 days (Median 7.0 days)
Leibson 1996[56]	1987-1989 (Costs adjusted to 1989 dollars)	Retrospective analysis of Rochester (Minnesota) Stroke Registry	241 patients with confirmed first stroke (hospitalized)	Short-term care activity (inpatient and outpatient) in first 30 days poststroke: mean $13,343 (median $8619)	Short-term care activity (inpatient and out-patient) in first 30 days poststroke: mean $23,168	Not specified
Monane 1996[57]	1982-1995	Observational retrospective, consecutive case series (large tertiary care hospital in Massachusetts)	745 patients age >= 65 years admitted with ischemic stroke	Median total charges: $8740	ND	7 days (median)
Wentworth 1996[58]	1990-1994	Retrospective cost analysis (acute stroke unit opened in 1990)	414 Medicare patients with stroke	1990: $14,076 1994: $10,740	1990: $23,187 1994: $15,603	1990: 7 days 1994: 4.6 days

LOS indicates length of stay; ND, not determined; NINDS, National Institute of Neurological Disorders and Stroke; rt-PA, recombinant tissue plasminogen activator.

[a]Costs were converted to 2008 dollars using the Consumer Price Index inflation calculator (http://www.bls.gov/data/inflation_calculator.htm).

Table A.3. Summary of Studies Reporting Average per Patient Direct Costs of Stroke in the Longer Term (More than 30 Days post stroke)

Study	Years of Data Collection	Design	Patients	Stroke Type	Mean Cost (Time Frame Covered)
Kind 2008[59]	2000	Retrospective analysis of administrative data (southern and eastern United States)	9463 Medicare patients (>=65 years) with 0 bounce-backs to hospital within 30 days of stroke	Acute ischemic stroke	30-365 days poststroke 50th percentile: $9767 10th and 90th percentiles: $1667–$35,854
Lee 2007[43]	1997	National random sample of Medicare beneficiaries	9131 Medicare patients	Ischemic stroke	$39,396 (from initial event through 4 years)
Sloss 2004[60]	1995-1998	Claims data from US managed care organizations	108 patients with commercial insurance and 113 patients with Medicare experiencing secondary stroke	Ischemic stroke	$10,267 for commercial insurance or $16,280 for Medicare (180-day attributable costs: 70% to 80% of costs were incurred in first 30 days)
Samsa 1999[50]	1991	Retrospective analysis of Medicare claims files	49,333 Medicare patients hospitalized with cerebral infraction in 1991 (4947 with previous stroke in past 4 years)	Ischemic Stroke	Costs per patient-month: First strokes (recurrent strokes): months 1–3, $3368 ($3315) months 4–12, $1361 ($1700) months 13–24, $1168 ($1580)
Fagan 1998[52]	1996 Cost reported in dollars	Markov model estimating costs per 1000 patients treated with rt-PA vs 1000 untreated patients (NINDS rt-PA Stroke Trial)	Data at 1 year poststroke: 294 placebo and 298 rt-PA	Acute ischemic stroke	Cost at 1 year: $29,810 (pla-cebo) and $29,207 (rt-PA) Total cost (short-term plus long-term care): $62,716 (placebo) and $58,461 (rt-PA)
Lipscomb 1998[61]	1991-1993	Analysis of data from a national sample of Medicare patients hospitalized for ischemic stroke	21,546 Medicare patients	Ischemic Stroke	Mean Medicare costs following discharge from index hospitalization: 1 month: $4207 36 months: $694
Leibson 1996[56]	1987-1989	Retrospective analysis of Rochester (Minnesota) Stroke Registry	292 patients with confirmed first stroke	All types (ischemic and hemorrhagic)	Mean Medicare costs following discharge from index hospitalization: 1 month: $4207 36 months:

					$694
Taylor 1996[44]	1990 (estimates in 1990 dollars)	Computer-simulation model	NA	Ischemic stroke	Year 1 annual direct cost: $20,574 (age <65 years) $15,102 (age ≥85 years) Year 2 annual direct cost: $7825 (age <65 years) $4629 (age ≥85 years) Mean lifetime cost per person: $90,981

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