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The benefits of a plant-based diet for the prevention and treatment of heart disease

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Thesis

**THE BENEFITS OF A PLANT-BASED DIET FOR THE PREVENTION AND
TREATMENT OF HEART DISEASE**

by

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DEDICATION

I would like to dedicate this work to my family, classmates, and colleagues.

ACKNOWLEDGMENTS

This thesis would not have been possible without the help of Dr. Barbara Seaton, Dr. James F. Head, and David Flynn, three people who provided endless support and assistance throughout the entire process and whose help gave me the motivation to succeed.

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ABSTRACT

Heart disease is still the number one killer in the United States. Recent research has suggested that adhering to a plant-based diet can prevent, treat, and reverse heart disease. In order to further clarify these findings, an analysis was made of the components of a plant-based diet and such dietary effects in relation to being a possible treatment for heart disease. Based on a comprehensive investigation of this area of study, an extensive body of evidence supports the finding that a whole-food, plant-based diet can significantly lower the risk of heart disease, mainly by reducing blood levels of lipids and cholesterol associated with atherosclerosis. Comparison was made between the efficacy of the plant-based diet versus more conventional approaches such as medication and surgery. Further clinical trials are needed to validate the findings of adopting this diet in the prevention and treatment of heart disease.

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LIST OF ABBREVIATIONS

ACATase	Acetyl-coenzyme A acetyltransferase
AHA	American Heart Association
Apo-A1	Apolipoprotein A1
apo-B	Apolipoprotein B
ARTS	Arterial Revascularization Therapy
CABG	Coronary artery bypass grafting
CAD	Coronary Artery Disease
CBS	Coronary bypass surgery
CHD	Coronary heart disease
CVD	Cardiovascular disease
FDA	Food and Drug Administration
HDL	High-density lipoprotein
HMG-CoA	3-Hydroxy-3-methylglutaryl-coenzyme A
ICD	International Classification of Diseases
IGT	Impaired glucose intolerance
LDL	Low-density lipoprotein
MACCE	Major adverse cardiac and cerebrovascular events
NCEP	National Cholesterol Education Program
PPAR	Peroxisome proliferator-activated receptor
PTCA	Percutaneous transluminal coronary angioplasty
PTCR	Percutaneous transluminal coronary revascularization

TSH	Thyroid-stimulating hormone
VLDL	Very low-density lipoprotein
WHO	World Health Organization

CHAPTER 1

INTRODUCTION

The heart is the powerhouse organ responsible for ensuring an adequate blood supply to all surrounding tissues. This delivery of oxygen, nutrients, and other essential cells or molecules maintains the intricate balance of reactions that sustains human life. A small threat to this system shifts the equilibrium in a direction that requires other processes to compensate at the expense of their physiological function. These adjustments initiate a waterfall of changes that can take years to surface as medical diagnoses, often when it is too late to intervene. Disruption of such an intricate system serves as the underlying cause of heart disease, as well as many, if not all, other life-threatening conditions. In ways still yet to be entirely understood, the human body houses a silent system existing in constant progression with the heart as the centerpiece for both life and death. Physiological changes to the system introduce alternative pathways that compromise the optimal functionality of the heart and blood vessels. One specific example is when circulation seeks and creates alternative routes that bypass occluded areas to supply surrounding tissues with oxygen- and nutrient-rich blood. Behind and within the system of balance is a biochemical arrangement of reactions driven by the availability of reactants that are in large part supplied from one major source: the diet.

Although current research findings and statistics lean toward conventional prevention and treatment, current research has offered a new perspective for the benefits of dietary interventions, particularly for whole food plant-based diet. A plant-based diet

consists of fruit, grains, legumes, vegetables, and little to no animal foods (i.e. dairy products). Whole foods include those that have undergone the minimal amount of processing, free of artificial and other additives that distract the body from obtaining the original nutrient composition upon digestion. An example of this distinction is seen in white bread, which has ultimately been processed to a point where the product has lost a majority of its whole wheat nutritional value. This thesis will examine the role that such an alternative diet may have in the prevention and treatment of heart disease.

Overview of heart disease

The cardiovascular system is responsible for a multitude of functions that extend well beyond the scope of this analysis; however, a brief description of cardiac physiology is called upon for references in this thesis to be understood in terms of disease. As the driving feature behind blood circulation to all tissues, the heart must be able to produce enough mechanical force to pump blood through the entire circulatory system. This force is provided by contraction of cardiac muscle within the walls of the heart. In an average lifetime, the human heart will beat about three billion times (Campbell & Campbell II, 2006). These muscle fibers also need an adequate supply of oxygen-rich blood, supplied by the coronary arteries, to meet myocardial demand. The coronary vasculature should provide the heart with sufficient blood circulation to allow the organ to function properly.

When structural changes within the blood vessels occur, such as constriction or hardening of coronary vessel walls, the heart no longer receives the necessary supply of oxygen it needs for the myocardium to contract (Klabunde, 2013). As time passes

without intervention, the heart adjusts until it can no longer meet the needs of both of its own tissues and those of the entire body, at which point myocardial ischemia causes angina, potentially leading to myocardial infarction (Kiefe, 2001). During the time it took to read the beginning of this paragraph, one human coronary artery circulation was cut off, blood flow to an area of heart muscle tissue ceased, and tissue died resulting in a heart attack. This lack of oxygen supply to cardiac muscle can quickly jeopardize the heart's ability to pump blood to peripheral vasculature, including the brain. Within seconds, cerebrovascular blood supply ceases and irreversible neurological damage occurs. By the time this page has been read, roughly four Americans will have suffered a heart attack and an additional four will have had a stroke and succumbed to heart failure. In the next day, 3,000 people in the United States will have a heart attack (Campbell & Campbell II, 2006).

An analogy of an artery as a garden hose exemplifies the effects of minimal changes to coronary vasculature. The hose is used to supply desired amounts of water (or blood) to a surface area (or heart muscle). This perfusion depends on the rate at which the water is being pumped throughout the irrigation system and valves (Peskin, 1977). If a constriction device were to decrease the diameter of the hose (or vessel), a smaller amount of water leaves the hose. Pressure builds up behind the constricted area and, if possible, the spout adjusts. Allowing for the heart and spigot as comparable structures, the heart would have to work harder to ensure that the rest of the heart and peripheral tissue area receiving enough oxygenated blood. An image of a diseased heart can be viewed as this example, similar to watering land with a small series of droplets.

When a plaque develops slowly over time, the heart and peripheral tissues have time to promote collateral circulation. Circling back to the garden hose example, if a small piece of gum were adhered to the inside of the hose wall, water would still flow past. If polluted water was run through the hose, particles would eventually stick to the gum and attract more particles until water can no longer pass by the obstruction. With time, the coronary circulation loses its ability to adjust and treatment is sought, usually when it is too late.

The purpose of describing the macroscopic changes associated with heart disease progression is to introduce the origin of these atherosclerotic changes, which comes from diet. Diet provides the building materials for atherosclerosis (Page et al., 1957). The contents and make up of an atherosclerotic plaque include protein, lipid, cholesterol and other immune system cells, most of which are supplied by what is included in the diet.

The coronary vasculature can only withstand a limited amount of plaque buildup until a vessel becomes completely occluded, at which point angina ensues. Interestingly, the accumulation of plaque that we see in these patients does not lead to the most common types of myocardial infarction. Heart attacks are usually caused by occlusions blocking less than half of the artery lumen. These smaller buildups are partially sealed by a fibrous cap that divides the plaque's contents from adjacent blood flow. In relation to the hose example, this "cap" would consist of a thin layer of debris that immediately sticks to the gum adhered inside the hose wall. Essentially, this cap represents a ticking time bomb. Its rupturing releases the contents of the plaque immediately into the heart's blood stream. Clotting grows at the site of plaque breakage within seconds, leaving no

time for collateral circulation to form. This is the major difference between those plaques that accumulate slowly over time versus occlusions that form instantaneously and why these smaller plaques are the most lethal. Unfortunately, physicians cannot predict when these plaque ruptures will occur, let alone detect them at times. Instead physicians can aim to avoid these events through preventative medication and advocating a lifestyle that poses less risk.

Classification and statistics

The International Classification of Diseases (ICD) categorizes heart diseases as those pertaining to the heart and blood vessels (National Heart, 2012). Cardiovascular diseases (CVD), as defined by the American Heart Association, include coronary heart disease (coronary artery disease and ischemic heart disease), stroke, hypertension, and rheumatic heart disease. Of these, coronary artery disease (CAD) is the most common type of heart disease (Centers for Disease Control, 2009). With heart disease being the number one killer in the United States and entire world, all related conditions are considered similarly lethal with no discrimination toward age, gender, or race (National Heart, 2012).

The most common underlying cause of cardiovascular disease is the narrowing of the coronary arteries, better known as coronary artery disease. It is also the leading cause of heart attack and stroke (National Institutes of Health, 2014). On average, one adult in the United States suffers a stroke every 40 seconds. Stroke is a leading cause of serious, long-term disability that accounts for more than half of all patients hospitalized for a

neurological disease. 600,000 United States citizens die each year, labeling heart disease responsible for 1 in every 4 deaths annually. 84 million people in the United States suffer from some form of heart disease, causing approximately 3,000 deaths each day, averaging 1 death every 40 seconds. Almost 1 out of every 3 deaths results from heart disease. An estimated 16 million United States adults have coronary heart disease (CHD). Cardiovascular disease is the cause of more deaths than cancer, chronic lower respiratory diseases, and accidents combined. The death rate for women from heart disease is eight times higher than their death rate from breast cancer, an unusually low recognized statistic (Johns Hopkins University, n.d.).

Risk factors associated with heart disease

Taking control of the factors that put one at a higher risk is the main principle behind heart disease prevention. Due to the complex combination of environmental, behavioral, and biological risk factors, a universal approach to prevention cannot be generalized. A common finding when reviewing these risk factors is that most are indeed controllable or preventable (Freedman et al., 2001). The relationship between predisposing factors versus those that can be avoided is difficult understand and apply to daily habits. This chapter calls upon a brief introduction of those factors that place people in a category at higher risk of heart disease.

An environmental risk factor often overlooked when weighing out the risk of heart disease is infection. A number of studies have shown a link between coronary heart disease and chronic bacterial and viral infection in early life (Danesh et al., 1997). The

Helsinki Heart Study showed that chronic *Chlamydia pneumoniae* infection may be a significant risk factor for the development of heart disease (Saikku et al., 1992).

Helicobacter pylorus is an acquired chronic bacterial infection found in the gastric mucous layer or adherent to the epithelial lining of the stomach, which can cause ulcers (Centers for Disease Control, 1998). Before its discovery in 1982, most stomach ulcers were mislabeled as stress- and acid-induced due to dietary habits. Since then, its eradication can be accredited to the use of antibiotic treatment. Medical advances have proven worthy in this epidemiological perspective; however, there is popular evidence for a connection between childhood *H. pylori* infection and heart disease later in life (Mendall et al., 1994). Research has uncovered a possible connection between *H. pylori* infection and heart disease through an increased number of risk factors associated with chronic inflammatory responses (Patel et al., 1995). As an environmental factor, chronic infection is one example of a possible predisposition to heart disease that cannot be entirely controlled by lifestyle choices. A steady forward progression in awareness and exposure prevention has helped minimize the changes of these diagnoses.

The prediction and prevention of heart disease also has a genetic component. Many biomarkers are used to predict the presence or predisposition of heart disease, which draws attention to the idea that a person's genome can be scrutinized for those specific genes coding for the production of these important molecules. Genetic factors cannot be controlled; however, awareness of genetic predispositions may motivate heart-healthy lifestyle changes.

There is strong evidence of genetic influence on heart disease including high blood pressure and various vascular conditions (Centers for Disease Control, 2009). Due to similar environmental tendencies that may also affect the expression of these signature genes, an increased risk of developing some form of heart disease occurs just by being a product of your environment. The odds slowly shy away from one's favor when an unhealthy lifestyle is paired with medical family history, which stresses the need for those with such genetic predisposition to be aware of the risk factors that could be the tipping point for their disease onset (Centers for Disease Control, 2009).

Apart from those heart disease risk factors that are out of conscious control are a number that can be eliminated almost entirely. Adjusting years of behavioral habits is not easy, especially when the symptoms of severe heart disease are not obvious enough to make a change (Greenland & Grundy, 2001). Behavioral risk factors are studied individually and usually connected when patients follow predicted lifestyle patterns (Stampfer et al., 2000). The most important behavioral risk factors associated with 80% of heart disease are an unhealthy diet, physical inactivity, tobacco, and harmful use of alcohol. Intermediate risk factors include raised blood pressure, glucose levels, blood lipid levels, and obesity, which are also obvious signs of an unhealthy diet and lack of physical activity (World Health Organization). Many studies have shown that most people can become heart healthy by following a healthy diet and participating in an appropriate exercise program; eliminating tobacco products; and following a routine health care plan (Johns Hopkins University, n.d.).

One cardinal example of the interplay between genetic elements and a person's capacity to control lifestyle is with diabetes mellitus. The Framingham Study, a comprehensive heart disease cohort study consisting of over 5,000 participants, showed that heart disease mortality was as great for thousands of diabetic women as for diabetic men (Kannel & McGee, 1979). The cardiovascular complications caused by diabetes include stroke, peripheral arterial disease, nephropathy, retinopathy, neuropathy, and possibly cardiomyopathy. The American Heart Association strongly recommends that diabetes be considered one of the chief heart disease risk factors because of the aging of the population and an increasing prevalence of obesity and sedentary life habits in the United States that foreshadow the onset of diabetes. This organization asserts that from a cardiovascular medicine perspective, "diabetes *is* a cardiovascular disease" (Grundy et al., 1999). The Framingham Study's twenty-year surveillance linked subsequent cardiovascular disease events as prior evidence of diabetes, a two- to three-fold increase risk of atherosclerotic disease (Kannel & McGee, 1979). Atherosclerosis is widely viewed as an inflammatory disease with hypercholesterolemia being a dominant underlying risk factor (Ross, 1993). "The adverse effects of diabetes are amplified in the presence of other heart disease risk factors, many of which being modifiable" (Manson et al., 1991).

A patient presenting with only one of the behavioral risk factors for heart disease is certainly at a better standpoint than someone with multiple risk factors (Anderson et al., 1991). Metabolic syndrome, which is defined as a group of risk factors that increases the risk of cardiovascular disease, stroke, and other diseases such as diabetes, includes

risk factors such as hypertension and high blood cholesterol levels. A 2004 study found that CHD, CVD, and total mortality are significantly higher in United States adults with metabolic syndrome than in those without (Malik et al., 2004). Manifestations of metabolic syndrome and causes of underlying disease vary on a patient-to-patient basis. Awareness of all risk factors associated with heart disease permits the most dynamic and useful approach. The overall importance of these factors yields the ability to integrate their avoidances into daily lifestyle.

The relationship between diet and heart disease

The United States lead with the highest heart disease death rates across 20 different countries including most of Europe in 1955 (Jolliffe & Archer, 1959). When most of the world was unaffected by heart disease, more Americans were dying due to its cause. Those cultures with lower death rates consumed a different diet: low saturated fats and animal protein, more whole grains, fresh fruits, and vegetables (Campbell & Campbell II, 2006). Therefore, in the 1960s and 1970s, the United States diet was almost entirely animal-based while the rest of the world was eating mostly plant-based foods.

With regard to the previous discussion of genetic predisposition, these dietary differences raise concern about the role of genetics in these differing death rates. This connection between higher death rates due to heart disease and genetics is extraneous. An epidemiological study focused on heart disease incidence and diet in men of Japanese ancestry resident in Hawaii, California, and Japan. This clarified just how meaningful this connection is when it was found that Japanese men residing in Hawaii or California have

higher blood cholesterol levels and proportions of heart disease than Japanese men living in Japan (Kagan et al., 1974). A similar project's data presented with these results. In Japanese men, dietary patterns varied remarkably among the three cohorts despite their comparable genetic backgrounds. In Japan, the average man consumes 40% of the fat intake noted in Americanized cohorts. Consuming animal protein, saturated fat, and dietary cholesterol showed a positive regression of serum cholesterol levels among those in Japan (Kato et al., 1973). Within a group with the same genetic heritage, these relationships between diet and disease were still prevalent, meaning that the genetic component was not responsible. Kagan et al. ruled out the proposition that smoking habits were tied to these results. Japanese men living in Japan who reported as smokers still had lower prevalence of heart disease than with the Japanese-American residents (Kagan et al., 1974). All other results of these two studies suggested a dietary cause. Blood cholesterol showed a negative association with the consumption of complex carbohydrates, meaning that plant-based foods were accountable for lowering cholesterol levels in the Hawaii and California cohorts (Kato et al., 1973).

Evidence suggests an environmental cause for these associations, diet being the most influential factor. Decades later, dietary methods and corresponding research have all emphasized the connection between diet and heart disease. Saturated fat and cholesterol, both indicators of an animal-based diet, are strongly correlated with the disease onset and prevalence.

In 1950, American troops intervened as North Korea invaded South Korea. 30,000 American soldiers were killed in the three short years leading up to the end of the

Korean War. The United States number one killer remained uncrowned until a groundbreaking study was reported by the *Journal of the American Medical Association* in 1953. The hearts of 300 male soldiers killed in action were examined. 77.3% had “gross evidence” of heart disease, including largely visible coronary arteriosclerosis. 1 out of 20 men had arteries with plaque occluding 90% of the vessel lumen. No autopsies were performed on those suspected with cardiovascular disease, meaning that the 22 year old (average age) men were subjected to a variety of medical examinations and deemed clear upon enlisting (Enos et al., 1953). The shocking data of this study demanded and received much attention, as this surely demonstrated that heart disease can develop over a lifetime as short as 20 years. Simply stated, these men were far above average in terms of physical fitness and overall health condition. These soldiers were probably the fittest men in our country at the time and yet they were unknowingly living with diseased hearts. This and many other subsequent studies have clearly proven just how insidious heart disease is in young Americans, suggesting the reality that with age comes a scary truth. From 1971 to 1993, hospitalization rates for heart failure alone increased in patients 45-64 years old, indicating the need for attention toward this threat to middle-aged people (National Institutes of Health, 2012).

What was the cause of the disease that silently and slowly crept through the hearts of these soldiers? Looking back to dinner menus of the 1950’s, meals were heavy in meat and refined carbohydrates, and low in vegetables (Powell-Smith, 2014). After rationing food during the Second World War, people were fixed to a diet of processed and prepared “TV Dinner” meals that filled as many mouths as possible, giving women more time to

accomplish other things besides meal preparation. “People were surprised at what some meat and soup could do in the oven” (Tucson Citizen, n.d.). Conforming to a nationwide cultural cuisine may have, in retrospect, been preparing hearts for an unforeseen fate.

We see and know lifestyle as characteristic to a particular person. That lifestyle is what makes the person who they are, how they interact with others and their surroundings. What would happen if it was a lifestyle that was causing the onset of a condition, say heart disease? Would that person be able to make changes to their behavior and habits to compensate for the need to reestablish better health? Is it possible to inspire these changes upon someone who is so close to the end? “Those who maintained the healthful diet had an incidence of coronary events that was more than 80% lower. Closer adherence to a more healthful lifestyle might reduce the risk of heart disease still further (Stampfer et al., 2000). It starts and ends with a whole food diet low in fat and rich in plant-based protein.

Referring to the garden hose as an analogous system to the heart’s circulation, we can now investigate into the underlying cause of plaque growth. Simply put, the heart is responsible for distributing blood throughout the body. Blood is not just a homogenous mixture of cells that carry oxygen to peripheral tissues. Within the blood is a transportation system for nutrients, waste, and many other cells that sustain life by responding to external stimuli. As human beings, we are responsible for providing our bodies with the resources it needs to survive, whereas our bodies know exactly what to do with whatever we give it. Thousands of chemical reactions are taking place every day that utilize what we put into our blood stream. What happens when the system too much

of what it minimally requires? Excess phospholipids, cholesterol, fatty acids, proteins, and immune system cells slowly congregate in the blood stream and violà, a plaque forms. Here exists a simple cause-and-effect relationship whose reversal could be the solution to most all circumstances of heart disease.

By the end of World War II, medical science had merely seen a glimpse of what heart disease was capable of. Researchers and scientists were aware of the contents of these vicious plaques but it remained a mystery as to how and why they formed. Around the same time, the National Heart Institute¹ was formed to answer these questions by monitoring a population, now almost five generations long, of patients from Framingham, Massachusetts. The Framingham Heart Study is prestigiously known for its implementation of heart disease risk factors, including blood pressure, cholesterol, inactivity, and tobacco use. This model is still used as a prediction tool to determine if a patient will be at risk for heart disease (Campbell & Campbell II, 2006). The Framingham Heart Study raised awareness to the risk factors associated with heart disease, one factor in particular: blood cholesterol levels. This and many of the other important risk factors all point to diet as the most efficacious intervention. The Framingham Study, and the many others that followed, all opened the door to raising awareness of the world's most powerful killer. Fifty years have passed and we still have not been able to completely convince this same world that our diet is both the cause and

¹ The National Heart Institute is now referred to as the National Heart, Lung, and Blood Institute of the National Institutes of Health.

the solution. A plant-foods diet has proven its effectiveness, which is why the proceeding discussion places such an emphasis on this diet as a heart disease intervention.

CHAPTER 2

PLANT-BASED DIET OVERVIEW

An in-depth discussion on plant foods is pertinent to consider in terms of their role in human health and nutrition, heart disease being the main focus of this analysis. As the predominant harvesters of solar energy, plants are a primary source of carbon, vitamins, fiber, minerals, protein, essential fatty acids, and energy for food production. The global household has always used plant foods as a supply for energy intake. For no reason other than their nutritional value, it comes as no surprise that an increased frequency of plant food contribution to the diet has been recommended to reduce the risk of chronic Western diseases (Lindeberg, 2012). Multiple research studies have examined the benefits of consuming a whole-food plant-based diet in terms of minimizing these risks. It has been observed that whole grains, fruits, and vegetables, are all low in cholesterol and fat, making them useful in the prevention of heart disease (Andrus, 2010). Therefore, an analysis of nutrition and plant foods is called upon to examine each component in regards to the prevention and treatment of human heart disease. It is important, though, not to emphasize each component as a discrete entity but as a contribution to the overall health benefits this diet brings.

Dietary cholesterol and heart disease

Many people are aware of the associated risk between raised blood cholesterol levels and heart problems. Despite this cognizance, 100 million Americans are living with high cholesterol, one of the strongest predictors of Western disease. Money is poured into the marketing of food products and dietary supplements with the intended use of lowering cholesterol levels, yet Americans still seem to be avoiding the most important fact: these solutions are not entirely effective (Consumer Healthcare Products Association, 2014). Drug therapy has proven to considerably lower blood lipid levels. Even with the bulk of data supporting the benefits of pharmacotherapy for heart disease prevention and treatment, “Patients often express a desire to accomplish similar goals with diet alone. Except for patients with extreme cholesterol elevations, panels promote dietary therapy as an initial treatment of hyperlipidemia” (Rosenthal, 2000).

Cholesterol has two distinct origins: dietary cholesterol, distinct from blood cholesterol made by the liver, is only found in animal-based foods. A complex system of biochemical reactions use and synthesize dietary lipids and cholesterol. Blood lipid panels do not accurately report the values in dietary sources because those levels represent the lipids and cholesterol made by the body once these have been processed. Diet, however, influences the balance of these reactions, which is why blood levels can still be used as a predictive method.

Sources of dietary cholesterol include meats, poultry, egg yolks, and whole milk products. The United States daily cholesterol recommendation is less than 300 mg (Centers for Disease Control, 2012). The liver synthesizes blood cholesterol. Low-

Density Lipoprotein (LDL), labeled “bad cholesterol,” differs from High-Density Lipoprotein (HDL) or “good cholesterol,” which is responsible for removing fat from the body. Epidemiological research attests to the role of HDL as a marker inversely and independently associated with the risk of developing heart disease (Miller & Miller, 1975). Increasing physical activity, decreasing alcohol intake, quitting cigarette smoking, and losing weight can elevate HDL (Goldbourt et al., 1997). Drugs such as fibric acid derivatives or niacin have the same effect (Strisower et al., 1968). Ongoing pharmaceutical trials are currently testing whether raising HDL will improve heart disease prognosis (Goldbourt et al., 1993). An increased emphasis has been placed on heart disease risk as a guide to cholesterol therapy (Grundy et al., 1993).

The human body is capable of maintaining an intricate balance of chemical reactions that synthesize and utilize blood cholesterol until this system of equilibrium is influenced by the excess dietary cholesterol. Blood cholesterol levels, however, do not always represent dietary cholesterol levels, despite their chemical similarities. Dietary fat and cholesterol do not always turn into body fat and blood cholesterol. How, then, do we take control of the processes that allow blood cholesterol levels to fluctuate? Consuming plant foods with low to absent dietary cholesterol minimizes the risk of disturbing this system of stability.

In the late 1950s, The Chicago Western Electric Study investigated and identified those risk factors associated with heart disease. 1,900 middle-aged men were subjected to three separate examinations. Upon initial review and measurement of diet and blood cholesterol, no therapeutic changes were suggested. One- and 20-year follow up exams

were subsequently performed. Each subject's diet score was calculated and adjusted to incorporate dietary intake of cholesterol, saturated fatty acids, and polyunsaturated fatty acids. Results showed a positive association between diet score and cholesterol after all three exams. The Western Electric Study made the conclusion that lipid composition of the subjects' diet scores affected serum cholesterol concentration and risk of coronary death in middle-aged American men (Shekelle et al., 1981).

An important association was found between animal foods and an increased blood cholesterol level, while an opposite association was linked to plant-based foods and lowered blood cholesterol (Campbell & Campbell II, 2006). Various studies have attempted to clarify these clinically relevant associations. A study replaced animal protein with soybean foods in a low-lipid, low-cholesterol diet for subjects with stable type II (non-genetic) hyperlipoproteinemia. After 8 short weeks of the adjusted regimen, plasma cholesterol was reduced by 23.1% and 25.3% in male and female subjects, respectively. No notable changes in plasma triglycerides, HDL cholesterol, or body weight were recorded, further supporting the new diet's efficacy (Descovich et al., 1980). These results deemed this method of dietary intervention as appropriate for outpatient treatment and further supported the correlation between a plant-based diet and lowering cholesterol; however, the mechanism of action is not entirely known.

Investigators collected and analyzed mortality data for more than 50 diseases in rural mainland China. Blood, urine, food, and dietary data were collected and analyzed for an assortment of nutritional, viral, hormonal, and toxic chemical factors (Campbell et al., 1998). In southwestern China, the prevalence of Western diseases followed trends

associated with high blood cholesterol but at much lower levels. There, any value larger than 127 mg/dL is considered to be high, whereas in America the normal average is 215 mg/dL (Heiss et al., 1980). In China, the normal average blood cholesterol is 94 and 80 mg/dL in males and females. These numbers are more than half the United States average, which is why it comes as no surprise for death rates from CHD in America to be 17 times higher than China.

To emphasize the protective effects of low blood cholesterol, during a 3-year period, no one died from heart disease before the age of 65 among over 400,000 subjects in southwestern China (Campbell et al., 1998). Further, Dr. William Castelli, the director of the renowned Framingham Heart Study, reports that he has rarely seen a patient die from heart disease with blood cholesterol levels under 150 mg/dL (Hubert et al, 1983). What does this mean and how can we use these reports to understand why the United States is still suffering from its number one killer? The answer lies within the vast differences between American and southwestern Chinese diets. Americans average a daily animal protein intake of 70 grams. This number completely overshoots the average 7 grams per day consumed in China. A number of conclusions can be made when relating cholesterol to heart disease within the parameters set by dietary resources. Nutritional methods have been proven to decrease LDL cholesterol from 0% to 37%. However, heart disease risk may be more significantly impacted than predicted from dietary changes alone (Rosenthal, 2000). Non-pharmacologic measures yield impressive results. Understanding the difference between blood and diet cholesterol is the underlying issue of concern in relation to awareness of the seriousness of these dietary and disease

associations. Multiple studies have indicated just how important these relationships are, which in turn emphasizes the need to implicate dietary changes conducive to low-cholesterol intake with plant- instead of animal-based foods. The China Study marked undiscovered territory for epidemiological research, redefining the interpretation of heart disease statistics. With cholesterol on the front line, a new cohort of heart disease prevention and treatment can be sought through the implementation of a whole food, plant-based diet.

Soy foods as cholesterol-lowering agents

Soybean has been an established crop in Western countries for less than a century. The Western American diet now uses soybean in baby formula, meat products, baked goods, and dairy products. Most soy protein is found as flour, concentrate, or isolate added into mixed-food systems. Many know soybean for its positive nutritional profile and protein quality, accounting for roughly 2.1% of daily protein intake in America (Erdman & Fordyce, 1989). The composition of soybean foods include not only protein but lipid, carbohydrates, fiber, water, minerals (calcium, iron, magnesium, phosphorus, zinc), and vitamins (B-6, folacin, niacin, riboflavin, thiamine).

Soy products present a number of health benefits: an abundant source of nutrients, inhibition of harmful proteases, food allergy alternatives, fiber enhancement, and mineral bioavailability. Soybean foods have also been noted for their involvement in lipid metabolism, glucose intolerance and dietary caloric reduction. Of these, the hypocholesterolemic effect of soy protein is the main advantage in regards to heart

disease. The hypolipidemic effects of vegetable proteins have been examined in both animal and human studies. Soy protein is not the only vegetable with cholesterol-lowering capabilities; however, this plant has received a majority of the attention from the many studies of this kind (Erdman & Fordyce, 1989). The most significant decrease in cholesterol levels has been found among hypercholesterolemic patients (Sirtori, 1983). The protein component of soy is thought to be responsible for its cholesterol-lowering capabilities (Erdman & Fordyce, 1989).

Researchers observed a cholesterol-lowering response when vegetable protein was substituted for animal protein in a low-fat, cholesterol-free, semi-purified diet (Wilcke et al., 1979). Significant reduction in cholesterol levels in healthy women with normal lipid profiles has also been observed (Carroll et al., 1978). A similar study was conducted with hypercholesterolemic men who were divided into two groups. One group conformed to a conventional diet of low cholesterol, animal-based protein and dairy products while the experimental group substituted soy for animal products. Serum cholesterol in the experimental plant diet group decreased by 13% and serum triglycerides were lowered by 23%. No change in HDL cholesterol was observed; however, LDL cholesterol exhibited a 17% decrease (Carroll et al., 1978). Similar results were found by Sirtori et al. in his studies of type II hyperlipoproteinemic and hypercholesterolemic patients. This cholesterol-lowering result was seen with or without 500 mg/day of cholesterol administration (Sirtori et al., 1977).

The abundance of attention toward soy products as cholesterol-lowering compounds served as an incentive to clarify the mechanism of action. Understanding

these pathways can therefore allow the opportunity to manipulate, interrupt, or mimic those processes that deal with the pool of materials available for the proliferation of atherosclerotic growth. Animal studies have shown the most promise in terms of elucidating the mechanism of action. Soy protein consumption has shown improvement of very low-density lipoprotein (VLDL) catabolism when compared to casein (a source of animal protein). Soy consumption yields a smaller fraction of dietary lipid uptake and less deposition in the body as excess fat or atheromatous plaques. Dietary soy protein may also increase biliary excretion of cholesterol, reduce cholesterol biosynthesis and increase fecal steroid excretion (Erdman & Fordyce, 1989).

Other projects aimed to find a connection between soy protein's structure and function by studying the individual amino acid components. An animal study concluded that the amino acid arginine counteracted the hypercholesterolemic effects of other essential amino acids. Soy is an abundant source of arginine (Carroll & Kurowska, 1995). Another animal study claimed that the lysine-arginine ratio could be related to cholesterol-lowering effect of protein sources. Soy and plant protein sources, compared to animal, have a low lysine-arginine ratio (Kritchevsky et al., 1981).

Numerous studies have focused on clarifying the mechanism of action associated with the cholesterol-lowering effect of soy products. Sirtori and Lovati (2001) noted that the soy protein activates LDL receptors in the human liver. This finding provides a mechanism by which plasma cholesterol reduction is distinct from other diets and lipid-lowering drugs. Female rats were given a 1.2% cholesterol diets of animal-based protein and immediately observed an increase in VLDL cholesterol. When the animal protein

was substituted with soy, opposing effects were recorded for both VLDL and total cholesterol. Next, both diets were analyzed to determine the site of action with liver receptor proteins. Normal VLDL-receptor binding was found in rats when soy protein was consumed, while no binding occurs with an animal protein diet. HMG-CoA reductase activity decreased in both groups with a greater value for the soy diet. 7 α -hydroxylase and acyl-coenzyme A acetyltransferase (ACATase) activity are significantly increased with casein but were in a normal range for soy protein (Sirtori et al., 1984). This study presented marked evidence for changes in hepatic receptor regulation caused by altering diet between animal- and plant-based protein sources. A similar study confirmed these results in humans when Huff et al. concluded that soy protein can increase the catabolism of VLDL cholesterol (Huff et al., 1984).

The bigger picture illuminates the connection between raised cholesterol and heart disease. Circling back to the makeup of atheromatous lesions and coronary plaque, cholesterol and corresponding lipids are found within these structures that so heavily influence the physiology of diseased coronary vasculature. Plant foods contain no cholesterol. By substituting or replacing animal protein with plant protein, soybean in particular, one can decrease the amount of cholesterol made by the body. Saturated fat and dietary cholesterol both raise blood cholesterol, but not nearly as much as animal foods do (Campbell & Campbell II, 2006). Hence, advocating the minimization of animal foods can yield significant outcomes for those affected by raised blood cholesterol levels. Making this type of lifestyle change is most important for those who fall into the category of genetic predisposition for heart disease.

The power of plant protein

Protein, Greek *proteios* for “of prime importance,” has been linked to meat since the 19th century. When most people think of protein, they think of solely animal foods. Some have even claimed protein consumption as a symbol of civilization itself. The rich consumed meat, the poor ate plant-based foods. It was wrongly assumed that lower classes were inept because of their dietary habits. Protein, a vital component of the human body, exists as enzymes, hormones, tissue structures, and transport molecules. Without these, life could not function properly or even at all. Our bodies replenish worn down protein through our diet, meaning that we are responsible for the types of protein we put into our bodies.

The association between protein quality and amino acid composition was first shown by Willcock and Hopkins in 1906 (Food History, 2012). The definition of protein quality is based on the amino acids a protein provides when broken down that are reused to build tissues to sustain life. A protein source of high quality donates a noticeable variety of individual amino acids to rebuild. The rebuilding process is slowed down if one particular amino acid is missing. Interestingly enough, the tissue of perfect protein quality is human flesh; animal flesh comes as a close second in diet regimens. The best amino acid match for animal flesh is found in egg yolk and milk. Individually, plants do not always have the right amino acids amounts to be considered of high quality but do as a collective group. Low quality protein permits the slow and steady synthesis in the healthiest type (Campbell & Campbell II, 2006).

Protein quality is tested by monitoring subsequent overall growth after consumption, hence why animal protein presents with a higher efficiency ratio than plants. The major concern with this conclusion is the equation of growth rate and overall health. This perspective encourages the consumption of animal foods. Mixtures of plant protein foods provides a sufficient source of amino acids to meet human physiological requirements (Young & Pellett, 1994). The complex metabolic systems housed in the body are capable of deriving all essential amino acids from low quality plant protein, meaning that a diet of plant foods alone can provide a complete and well-balanced source of amino acids. Soy protein, for example, is of such high quality that it can suffice as the sole protein source in the human diet (Erdman & Fordyce, 1989). Contributing to more than half of the world's per capita protein supply, plant protein foods are scrutinized for their amino acid content, human amino acids requirements, and dietary protein quality (Young & Pellett, 1994).

Plant antioxidants

A considerable amount of attention has been brought toward antioxidants due to recent findings. As chief defenders of lipid oxidation of LDL cholesterol, antioxidants may be responsible for interrupting the formation of atheromatous plaques known to be affiliated with heart disease. Eliminating this method of atherogenesis is crucial, especially in patients with high levels of LDL cholesterol, regardless of its cause.

A remarkable feature possessed by plants is their ability to perform photosynthesis. This produces antioxidants; therefore, these molecules can only be

derived from plant sources. The presence of antioxidants in animal tissue can only be seen upon consumption of plant material and accumulation of these molecules. The powerful process of photosynthesis has a tendency to create unwanted byproducts that can threaten the integrity of plant cell walls if not for the protection of antioxidants. These form a shield against electrons and free radicals, as well as against their damaging effects. Although animal species are incapable of housing this energy-forming process, humans still produce free radicals. Even at low levels, free radicals can have very damaging risks to tissues.

Exposures and production of free radicals slowly decrease animal tissue rigidity and compromise tissue function, similarly related to the effects of aging. Also with age, free radicals instill uncontrolled damage to artery walls, which is pertinent to this analysis. Plants have evolved to prevent the detrimental effects of this process to their own structures. Unlike their surroundings, humans do not possess a protective mechanism against this undesirable effect. Instead, protection is sought directly or indirectly by consuming foods with antioxidants such as ascorbic acid (vitamin C) and vitamin E. Fortunately, antioxidants undergo similar behavior in both plants and animals, therefore defending against free radical damage.

An association has been made to explain the basis of the “oxidative-modification hypothesis” behind atherosclerosis. This proposition claims that atherogenesis is initiated by oxidation of the lipid molecules in LDL cholesterol. Another name for this process is lipid peroxidation (Diaz et al., 1997). Antioxidants do exactly what their name implies: they are anti-oxidation agents. Investigations have shown an inverse relationship between

the consumption of fruit and esophageal cancer. For example, vitamin C has demonstrated an effect against heart disease and stroke. In postmenopausal women, consumption of foods rich in vitamin E was inversely associated with the risk of heart disease mortality (Kushi et al., 1996). The same study demonstrated that women can lower their risk of heart disease without taking vitamin supplements. These benefits can come from lifestyle and dietary changes alone.

A progression of studies reported negative findings associated with antioxidant therapy, which subsequently overshadowed the original eagerness in this field of research (Jialal et al., 2001). Apo-A₁ (apolipoprotein A1), a component of HDL cholesterol, holds responsibility in the efflux of fat from body tissues via liver excretion. The resulting removal of fat from arterial wall white blood cells reduces the chances of these cells becoming overloaded with lipid, dying, and contributing to the growth of atheromatous plaques that occlude vessel walls. Therefore, apo-A₁ (along with HDL cholesterol) is one of the body's preventative mechanisms against heart disease. A genetic defect in this protein product has shown to be directly correlated with heart disease prevalence (Dastani et al., 2006).

Antioxidants support animal tissue health in numerous ways. Minimizing the damage caused by free radicals reduces the risk of plaque formation (atherosclerosis) as well as hardening of vessel walls, both being responsible for the physiological changes associated with heart disease. If antioxidants can only be obtained from plant foods, this leads directly to advocating increased consumption for the prevention, treatment, and even reversal of heart disease. Despite allegations from negative trials, the global effects

of dietary antioxidants remain unscathed. The fact that antioxidants can only be found in plant-based material further supports the emphasis of a diet high in plant foods for not just heart disease but overall health.

Other data suggest a favorable inclination toward antioxidant therapy as an alternative to lipid-lowering medication. A study conducted by Cheung et al administered an antioxidant “cocktail” of vitamins E and C, β -carotene, and selenium. This mixture was given to patients already taking statin drugs. Results indicated a considerable dampening response of the apo-A₁-HDL_{2C} response compared with subjects taking just lipid-lowering drugs (Cheung et al., 2001). This feedback thus offered a mechanism by which antioxidants reduce blood lipid levels. A lack of antioxidant efficacy in the aforementioned clinical trials suggested that antioxidant-vitamin combinations of dosages exceeding dietary recommendations should not be used for the prevention and treatment of heart disease. Physicians should warn patients that the use of antioxidants could be harmful, particularly in co-administration with lipid-lowering drugs (Kuller, 2001). With respect to the topic at hand, the results of this study and those that followed lead to the conclusion that antioxidant treatment should be administered through dietary means that exclude the use of lipid- and cholesterol-lowering agents. This does not belittle the benefits of antioxidants but rather emphasizes the power of diet alone in the prevention and treatment of heart disease.

Dietary fiber approach

The consumption of dietary fiber is recognized for its anti-cancer effects, leaving little attention for the idea that this diet may also prevent heart disease. Fiber gives rigidity and structure to plant cell walls. These complex carbohydrates are, like antioxidants, only found in plant foods. In the human body, fiber is rarely completely digested but still vital for good health due to its resistance to hydrolysis by human enzymes. This resistance allows fiber to travel further along the gastrointestinal tract to draw water into the intestines. Undigested fibers have a tendency to attract and collect substances that include potential carcinogens. Constipation-based diseases usually come from a lifestyle with low fiber diet (Campbell & Campbell II, 2006). Dietary fiber introduces few if any calories and, creates the sensation of satiety, thus suppressing appetite. Some short-term diets praise the incorporation of dietary fiber for these reasons as it satisfies hunger while simultaneously minimizing the overconsumption of calories (Jampolis, 2012).

In addition to its numerous overall health benefits, crude fiber in the diet has been shown to support the hypothesis that it can protect against hyperlipidemia and heart disease. Animal experiments suggest that an increase in dietary fiber may be responsible for decreasing the reabsorption of bile salts, increasing fecal excretion of these salts, and therefore lowering levels of serum lipids. A decrease in circulating lipid levels minimizes the likelihood of arterial plaque formation and continued progression of heart disease. In addition, a low-fat/high-fiber diet shows a permanent increase in plasma fibrinolytic activity and a decrease in coagulant activity (Marckmann et al., 1993).

Another study reviewed the long-term intake of dietary fiber and risk of heart disease among women. Their hypothesis supported the observation that, particularly for cereal foods, a high intake of fiber, especially soluble fiber, decreased LDL cholesterol and had little or no effect on HDL cholesterol levels. The effect of soluble fiber on serum cholesterol was modest and could not account for a substantial reduction in heart disease incidence. This study also found that fiber-filled diets also may have other beneficial physiological effects such as increased insulin sensitivity and lower triglyceride levels, giving more reason to replaced refined forms of starch with whole-grain products (Wolk et al., 1999).

To summarize the importance of dietary fiber and its affects against heart disease, it is imperative to note similar findings in The China Study. As previously mentioned, a statistically significant difference was noted between the incidence of heart disease in southwestern China and the United States. The average fiber intake in China was found to be three times higher than in America: 34 mg per day versus 18 mg per day in the United States (Campbell & Campbell II, 2006). These findings clarified and supported the association with a reduced prevalence and occurrence of heart disease in China compared to America, denoting that such an association should not be overlooked in the realm of heart disease awareness.

Phytochemicals

The favorable effects of fruits and vegetables on heart health cannot always be attributed to nutrients such as vitamins and minerals. Phytochemicals have taken the lead

in the marathon against heart disease with their well-known anti-atherosclerotic effects. Three classes of molecules in particular have raised a substantial amount of attention in this area of study. The American Heart Association lists plant sterols, flavinoids, and sulfur-containing compounds as phytochemicals with astounding epidemiological worthiness (Howard & Kritchevsky, 1997).

Knowledge in the area of plant sterols has recently flourished, making it an important feature of this thesis' argument. Plant sterols differ from cholesterol by the presence of an ethyl or methyl ring substitution or unsaturated side chain. Predominant forms of plant sterols have been recently found in Western diets in nearly equal amounts to dietary cholesterol (Miettinen et al., 1990). Sterols and mixtures of soy sterols have been studied for their hypocholesterolemic effect (Lees et al., 1977). Previous studies found that the administration of one particular sterol, β -sitosterol, to cholesterol-fed chickens or rabbits lowered cholesterol and the formation of atheromatous plaques (Pollak & Kritchevsky, 1981). The mechanism of action was found to involve the inhibition of cholesterol absorption, even though the plant sterols themselves are poorly absorbed (Tilvis & Miettinen, 1986). Consuming just one gram of β -sitosterol remarkably reduced cholesterol absorption by 42% in a meal of 500 mg of cholesterol (Mattson et al., 1982). This decrease in plasma cholesterol is most likely due to an increase in LDL receptor activity. It was noted that the decline in plasma cholesterol was less than the decrease in absorption, meaning a compensatory increase in cholesterol synthesis must have occurred (Howard & Kritchevsky, 1997).

It was found that a different form of β -sitosterol, stiostanol, showed an ability to reduce intestinal absorption of cholesterol and serum cholesterol more effectively than the original target compound but at much lower doses (Heinemann et al., 1986). Another study exhibited the cholesterol-lowering effects of plant sterols in a population of patients with mild hypercholesterolemia with a mean one-year reduction in cholesterol of approximately 10%. The new form of sitostanol used was not absorbed and therefore did not interfere with the absorption of fat-soluble vitamins, further minimizing that concern (Miettinen et al., 1995).

Fruits, vegetables, nuts, and seeds have an element in common: flavonoids. Tea, onions, soy, and wine are all good sources of these compounds whose intake has been inversely associated with heart disease risk. Multiple studies have all presented evidence in favor of this conclusion. The Zutphen Elderly Study found that “in vitro, flavonoids inhibit oxidation of LDL and reduce thrombotic tendency, but their effects on atherosclerotic complications in human beings are unknown” (Hertog et al., 1993). 1.85% of subjects died from heart disease with an intake of 0 to 19 mg per day. This number was higher than the 0.78% heart disease deaths among those whose flavinoid consumption was more than 29.9 mg per day (five to six cups of coffee). Some flavonoids have properties similar to those of antioxidants, supporting this effect on atherogenesis. A supporting study found that red wine inhibited LDL oxidation (Frankel, Kanner et al., 1993). Other studies have shown flavinoids to reduce the aggregation of platelets and adhesion, most likely linking this positive effect to the reduced risk of heart disease (Gryglewski et al., 1987).

What do garlic, onion, and leeks all have in common? Each of these possesses naturally-occurring sulfur-containing compounds that have been linked to the reduction in cholesterol and atherosclerosis. Since ancient times, garlic has been used as a pharmacological agent. Recent studies suggest that just one half clove of garlic each day can lower serum cholesterol levels by almost 10% (Warshafsky et al., 1993). Feeding the same amount of garlic to rabbits exhibited similar results (Jain & Konar, 1978). By inhibiting cholesterol synthesis, garlic has fought for its esteemed cholesterol-lowering effect (Sendl et al., 1992). Other sources have found garlic to inhibit platelet aggregation (Samson, 1982), lower coagulation time (Bordia et al., 1975), and lower blood pressure (Mansell & Reckless, 1991). Stampfer et al (2000) have commented that “part of the effect of diet and lifestyle is mediated through improvements in lipid levels and blood pressure.”

The aforementioned plant sulfur compounds have raised attention for their anti-atherosclerotic effects apart from the previously described advantages of a plant- and fruit-based diet. A reduction in growth of atheromatous plaques significantly reduces the negative effects of heart disease. Any ambiguities in the studies surrounding these compounds call upon the need for additional research into their classes of micronutrients. Being unable to target those mechanisms of action responsible for these results also indicates the necessity of a well-balanced, whole food plant-based diet low in fat for the prevention and treatment of heart disease.

Summary

Evidence for the efficacy of a plant-based diet in the prevention and treatment of heart disease has yielded promising results. Studies of cholesterol, a major component of heart disease, have demonstrated just how valuable dietary interventions can be for minimizing associated risk factors. Soybean, among many other plant foods, has been studied for its hypocholesterolemic effect. Unique to plant sources, antioxidants possess the capability to prevent and potentially reverse the formation of atherosclerotic plaques responsible for the cardiovascular mutations chargeable for the lethality of heart disease. The consumption of dietary fiber has also been efficacious in this regard. Phytochemicals, including plant sterols, sulfur compounds, and flavinoids, exhibit remarkable evidence for heart health due to their anti-atherosclerotic effects. A whole food, plant-based diet takes advantage of the benefits provided by these results. As a supplement to other necessary behavioral and lifestyle changes, dietary measures present with the utmost importance in regards to heart disease. The benefits of a heart-healthy diet are not restricted to one body system, but extend beyond the confines of cardiovascular health as a means that encompasses overall well-being.

CHAPTER 3
COMPARISON PLANT-BASED DIET AND CONVENTIONAL TREATMENT
EFFICACY

This chapter focuses on comparison between dietary and conventional approaches to heart disease prevention and treatment. For the purposes of this chapter, these approaches will be classified into pharmaceutical and procedural subcategories. The comprehensiveness of this topic extends well beyond the outlook of the present analysis; nonetheless, understanding the overall purpose of these interventional methods is a key resource in order to compare their efficacy to that of a plant-based diet. When lifestyle changes no longer suffice, heart disease treatment is sought in the form of pharmaceutical regimens that aim to lower blood pressure, cholesterol and lipid levels, blood clotting, and reduce the overall burden placed on the diseased heart (National Heart, Lung, and Blood Institute, 2011). When these treatments are inefficient in maintaining or minimizing the diseased state, invasive surgical procedures are sought. These include angioplasty and coronary artery bypass graft surgery. The following includes a brief overview of each conventional approach as it pertains to the comparison of its efficacy versus dietary changes.

Pharmacological interventions for heart disease

The Framingham Heart Study introduced primary risk factors associated with heart disease. These include age, blood pressure, cholesterol, diabetes, and tobacco use.

Due to proven efficacy, drug therapy has been recommended to lower blood pressure and blood lipid levels as methods to prevent and treat heart disease (Stampfer et al., 2000). It has been demonstrated that heart disease-free survival is directly associated with blood cholesterol and inversely with HDL cholesterol levels. Research has reported a relatively unreliable association between coronary mortality and fatty acid profiles. This relationship was found to be mediated by the dietary-blood cholesterol interaction (Goldbourt et al., 1993). Various guidelines have been using these risk factors to measure and predict risk for over 50 years, including the United States National Cholesterol Education Program (NCEP) Adult Treatment Panel III, European Societies guidelines, British guidelines, and Sheffield table. These programs assess risk in order to determine the necessity for lipid-lowering pharmaceutical regimens.

A cross-sectional evaluation of 58 men and 42 women concluded that all dietary guidelines have noticeable differences and therefore should be used with caution (Broedl et al., 2003). This same study reported that dietary guidelines differ in terms of a common selection and assessment of risk factors. Dietary recommendations are deemed controversial if a threshold level of risk at which drug therapy is sought cannot be agreed upon. This disagreement is the root of what may be considered “unjustified financial burden and side effects” that may no longer balance the benefits of these lipid-lowering drugs. The Munster Heart Study calculator bases its evidence on an entirely different epidemiological dataset that includes triglyceride concentration and family history; however this method of risk assessment can only be applied to male patients between the ages of 40 and 65 (Assmann et al., 2002).

Another noteworthy inconsistency across these agencies is the argument that they “do not provide the same recommendation for the same patient” (Broedl et al., 2003). Patients estimated to be at risk of heart disease based on one set of guidelines were considered to be at low risk by another. Relaying these guidelines at random to a selection of physicians as standards of risk assessment may therefore create the illusion that risk is being assessed consistently where in actuality an inconsistency exists across the board that plays out as serious results in a clinical setting. This example of conflicting recommendations is just one way in which the pharmacologic management of heart disease may be lacking and represents the need to reevaluate the overall advantages of such therapy if risk assessment is so unpredictable among agencies.

A conflicting system of risk classification can only lead to more confusion for both the prescriber and patient. However effective these drugs may be, current research has indicated that the population of patients prescribed to these medications may not necessarily need them to lower their risk of heart disease. The alternative to this lipid-lowering regimen, changing dietary habits, shows promise as no findings have suggested the reevaluation of such a recommendation. The results of a similar risk assessment profile would be clear: all patients should and will benefit from a heart-healthy diet of plant-based foods. There are no significant negative side effects caused by the implementation of a plant foods diet, not to mention the additional benefits of this diet in terms of its positive nutritional profile. Finding a common ground for heart disease risk assessment may be difficult, which is why it is crucial to seek an alternative treatment in the form of diet that utilize natural remedies opposed to pharmaceutical.

Instead of discrediting the idea of pharmaceutical treatment altogether, a study has identified the lipid-lowering effects of encapsulated plant sterol esters. This study concluded that “plant sterol ester capsules are effective in improving lipid profiles among hypercholesterolemic subjects at the minimum dosage recommended by the Food and Drug Administration (FDA)” (Acuff et al., 2007). Significantly positive lipid profile improvements were noted after just 3 weeks of administration. LDL cholesterol was lowered by 7% and HDL cholesterol increased by 9%. This report suggests consuming a diet low in saturated fat and cholesterol in combination with the capsule regimen. Alternatively, consuming foods with high levels of plant sterol esters should have a similar effect. This connection recognizes the usefulness of the study’s findings, while suggesting the need for similar studies to be conducted with a plant sterol diet instead.

Cholesterol-lowering medication

A diet rich in plant sterols or sterol esters has been shown to reduce levels of LDL cholesterol. Findings from a meta-analysis of 41 trials reveal that consuming 2 grams per day of stanols or sterols reduced LDL cholesterol by 10%. Synergistic and additive effects were seen with the combination of cholesterol-lowering medications and adhering to a high-sterol, low-fat, low-cholesterol diet to lower LDL cholesterol up to 20%. Hence, adding plant sterols to the diet was more effective than doubling the statin dosage (Katan et al., 2003). Additional benefits from this dietary change included stable and unaffected levels of vitamins such as plasma levels of vitamin A, D, and E.

The difficult part of staying true to a diet rich in plant sterols is consuming enough to meet the daily recommendation. Just one-half cup of wheat germ contains 0.2 grams of phytosterol. That same portion of wheat bran contains only half the amount of sterol content but also includes 9-13 grams of fiber, nearly half the daily recommendation of 25 grams and 38 grams for men and women, respectively. Nuts and legumes, however, are a better source of plant sterols. Peanuts have 0.1 grams in just a one-ounce serving, while other nuts including cashews and walnuts only supply roughly 0.03 to 0.04 grams (Busch, 2014). Devaraj et al. (2004) concluded that the consumption of sterol-enriched orange juice can lower LDL cholesterol levels. This finding suggests that similar products could be incorporated into the diet and yield similar effects. According to a different study, the impact of increased serum concentrations of plant sterols on cardiovascular risk was unclear, which is why these researchers set out to clarify these associations. Their review and meta-analysis did not reveal any confirmation of an association between serum concentrations of plant sterols and risk of heart disease (Genser et al., 2012). Metabolic studies have shown that plasma plant sterol levels correlate with dietary cholesterol absorption and inversely with markers of whole body cholesterol synthesis (Tilvis & Miettinen, 1986). Plasma plant sterol levels allow a complex relationship with known heart disease risk factors, positively correlated with serum cholesterol and LDL cholesterol levels and inversely related to Body Mass Index (BMI) and fasting glucose and insulin levels (Wilund et al., 2004). Any unique role of plant sterols as opposed to cholesterol in atherogenesis remains to be proven (Sehayek & Breslow, 2005). This, however, should not be mistaken for evidence against the use of

plant sterols as a preventative mechanism against heart disease. The overall lipid-lowering effect of a plant-based diet still proves efficacious.

The last three decades have seen a remarkable surge in the popularity of statins, or cholesterol-lowering, drugs for their efficacy in preventing cardiovascular outcomes due to disproportionate cholesterol production. For a lack of discrete biochemical description, these drugs prevent the function of cholesterol-synthesizing enzymes and possess other anti-inflammatory and antioxidant effects including the stabilization of atherosclerotic plaques (Kapur & Musunuru, 2008). Recently, statins have been linked to their newly-explored peroxisome proliferator-activated receptor (PPAR)-activating property that could potentially be mediating the valued cardiovascular protective “pleiotropic” effects of statins that include anti-fibrotic properties (Balakumar & Mahadevan, 2012). The overall benefit and safety of cholesterol-lowering statins has proven their efficacy as prevention or treatment of heart disease.

Diabetes medication

A well-known connection has been established between heart disease risk and diabetes. For this reason, the indirect pharmacologic management of heart disease is needed with diabetic treatment. There is a lack of data on the significance of the diabetes-associated risk factors for heart disease. This is seen especially for the role of lipid levels, as LDL cholesterol is often not elevated in these diabetic patients (Cowie et al., 1994). The Strong Heart Study set out to evaluate heart disease risk factors in a cohort of diabetics and to compare the importance of dyslipidemia and LDL cholesterol in

determining heart disease risk in diabetic patients. Diabetic subjects had lower LDL cholesterol levels with elevated triglyceride levels and lower HDL cholesterol, otherwise known as dyslipidemia. The National Cholesterol Education Program established the blood cholesterol level target to be 130 mg/dL. However, it has been found that levels of LDL cholesterol that fall below this marker are strong predictors of heart disease probability in diabetic patients (Howard et al., 2000). Just a 10 mg/dL increase in LDL cholesterol was associated with a 12% increase in heart disease risk.

According to the World Health Organization (WHO), more than 60% of diabetic patients die from heart disease, meaning that macrovascular complications are the leading cause of morbidity and mortality in diabetics (World Health Organization, 1994). Compared to non-diabetic patients, diabetics have a significantly higher risk of heart disease (National Diabetes Information Clearinghouse, 2013). Risk of heart disease mortality in diabetic individuals may be as high as that in non-diabetics with previous myocardial infarction (Haffner et al., 1998). It has been postulated that in diabetes, the dyslipidemia, rather than elevated LDL cholesterol, is the predominant lipoprotein determinant of atherosclerosis (Reaven, 1987). In The Strong Heart Study, triglycerides were a significant univariate predictor of cardiovascular events in diabetic women (Howard et al., 2000).

Impaired glucose intolerance (IGT) increases the risk of developing Type 2 diabetes. Diet and exercise interventions can decrease the incidence of diabetes among subjects with IGT (Pan et al., 1997). Diabetes is listed as a medical condition with similar standing to heart disease. For this reason, the association should be taken seriously as a

probability factor (Khavandi et al., 2013). Reducing the prevalence of these cases therefore reduces the risk and progression of cardiovascular complications affiliated with diabetes. With diet as one of the main factors associated with the origin of type 2 diabetes, its management is essential in maintaining a metabolic profile that reduces the risk of diabetes and therefore heart disease. A low-fat vegan diet has been shown to improve glycemic and lipid control in type 2 diabetic patients (Barnard et al., 2006). The connection between a plant-based diet and diabetes yields valuable for heart disease prevention as well, further clarifying the need to emphasize such a diet for its benefits to overall health.

Procedural interventions for heart disease

Various surgical procedures aim to ease the heart's stress and restore coronary circulation. "Since the early 1990s, with significant improvement in the procedural success, there has been a concomitant reduction in the need for emergency coronary artery bypass graft surgery" (Singh et al., 2002). Although this improvement in numbers presents a positive outlook for the heart disease community from a procedural standpoint, these are only temporary fixes. These findings account for successful procedures and do not take into consideration those ending in patient death. Each of these procedures poses relatively lethal risks that are weighed upon before making such an impactful medical decision (Johnson et al., 2013). Alternative interventions seek to treat the underlying lifestyle that is responsible for the heart's disease state. These behavioral and nutritional changes can be, if not more, just as successful as the previously mentioned surgical

procedures, which rationalizes the interest in a whole food plant-based diet for the prevention and treatment of heart disease.

A myriad of situations emphasize the need for conventional approaches to heart disease that involve surgical procedures. It is important to recognize the difference between the inevitably necessary and potentially preventable cases. Those preventable cases highlight the situations that could have been avoided through the implementation of lifestyle changes. However effective this approach may seem, it is important to separate the two in terms of argument when a patient's disease phenotype no longer possesses the life-sustaining capabilities. Thus, the effectiveness of such surgical procedures cannot always be compared to those of preventative measures unless the origin of the disease is noted. For example, childhood early-onset cases of heart disease cannot always be prevented and treated with a diet regimen; therefore, these procedures are necessary to save a life. However, implementing this diet after such a procedure may be life-saving in regards to avoiding the recurrence of what may be a subsequent disease state.

Both conventional and up-and-coming dietary methods have noteworthy advantages, as well as serious disadvantages. Overall, conforming to an approach built around the awareness and implementation of dietary habits conducive to a heart-healthy lifestyle yields more benefit than harm. This chapter placed importance in advocating such regimens with the disclosure of severe cases that undeniably require conventional treatment. Understanding the pathological progression of heart disease at a microscopic level permits the understanding of how these interventions bring benefit; however, this thesis presents only the minimally required background information permitted by the

focus of this topic. Dietary and procedural methods are set apart according to their measure of effectiveness. Recognizing the existence and necessity of both interventions as distinct methods of prevention and treatment is important in clarifying the misinterpretation that one should be chosen over the other. The initiative of this chapter was to stress the need for more emphasis on dietary intervention as the best choice for heart disease prevention and how these methods could potentially reduce the need for conventional approaches associated with limited effectiveness and risk.

Coronary Artery Bypass Graft Surgery

The heart can only handle so much stress after compensating for its diseased coronary vessels. Angina and infarction result from overburdened muscle tissue no longer being able to pump blood throughout its own vasculature. The location, type, and extent of coronary artery disease are assessed before surgical procedures are planned. Coronary bypass surgery (CBS) is more effective than medical treatment in the relief of myocardial ischemia and angina. “Patients with chronic, stable angina assigned to CBS have an improved survival if they have left main CAD, three-vessel CAD with normal or impaired left ventricular function, proximal left anterior descending CAD that is part of two-vessel CAD, or two- or 3-vessel CAD with a positive exercise test for ischemia” (Rahimtoola, 1985).

Coronary artery bypass grafting (CABG) is a surgical procedure that attempts to restore blood flow to the heart’s tissues by passing over the diseased artery or arteries. A section of healthy artery or vein is removed from the patient’s peripheral vasculature

(usually chest, leg, or arm) and grafted to create a new route, or bypass, allowing the heart to regain its required circulation to supply its own tissues. This in turn allows the heart to distribute blood to the rest of the body. Although this procedure sounds ideal, bypass surgery poses a number of risks both during and after the procedure. Even if the procedure is an immediate success, long term outcomes depend on a number of factors that are generally determined by the patient's adherence to a modified lifestyle built around the prevention of recurring symptoms. Bypass surgery does not cure cardiovascular disease (Cleveland Clinic, 2014). Decreasing risk factors after surgery is key, especially in terms of conforming to a lifestyle that is built around a drastically different diet. If, however, this diet was followed much earlier than these types of procedural interventions might not have been necessary.

Mechanical versus surgical intervention

The Arterial Revascularization Therapies Study (ARTS) conducted in 2005 compared the freedom from major adverse cardiac and cerebrovascular events (MACCE) at one and five year intervals in a randomized trial between patients who underwent CABG surgery or vessel stenting procedures. Results found that the mortality rates did not statistically differ for these procedures. Other events, including infection, were not considered in this particular study. The incidence of repeated revascularization was much higher in the stent group, corresponding to a higher MACCE occurrence for those who opted against surgery. An event-free survival rate of 58.3% and 78.2% was found in the stent and CABG groups, respectively (Serruys et al., 2005).

Earlier studies comparing balloon percutaneous transluminal coronary angioplasty (PTCA) versus CABG demonstrated comparable results in terms of the aforementioned parameters. Post-CABG patients presented less need for repeat procedures and fewer episodes of angina than post-PTCA patients. A similar study conducted in 2001 compared percutaneous transluminal coronary revascularization (PTCR) with stent implantation to CABG in patients with multiple-vessel CAD. This study concluded that PTCR with stent implantation yielded better survival and reduced occurrence of MI than CABG surgery, significantly decreasing early complications. Like ARTS, the PTCR group in this study had a higher rate of repeat revascularization procedures (Rodriguez et al., 2001).

Negative aspects of surgical intervention

Mechanical interventions for heart disease provide a number of benefits; however, in comparison to dietary and lifestyle changes, these solutions are in some cases more definitive than the data warrant. In 1990, approximately 380,000 bypass operations were performed (Marwick, 1994). Of those, more than 1 of every 50 died due to complications, including heart attack, respiratory complications, bleeding complications, infection, high blood pressure, and stroke (Gersh et al., 1997). During the procedure, the blood vessels surrounding the heart are clamped shut, allowing plaque to release from the inner vessel walls and carry debris to the cerebral vasculature. This interrupts and momentarily seizes blood flow to parts of the brain, which may cause “mini strokes” to occur, an unintentional and undesirable side effect resulting in permanent neurological

damage. Compared to before and after bypass surgery, the intellectual capability is impaired in 79% of patients who present with cognitive dysfunction within a week of the procedure (Shaw et al., 1986).

Most bypass operations are performed to relieve chest pain or angina. Roughly 70-80% of post-operative patients remain pain-free for one year, meaning that the results do not always last (Cameron et al., 1995). Within three years after the procedure, up to one-third of patients will experience recurring chest pain (Gersh et al., 1997). Within ten years, one-half of these people will die, have a heart attack, or experience recurring pain (Kirklin et al., 1989). Other studies have shown that only a specific population of heart disease patients will actually postpone death after bypass surgery, stating that there was no correlation between bypass success and minimized probability of experiencing subsequent heart attacks (Forrester & Shah, 1997).

Bypass surgery is targeted toward the largest, visible occlusions detected with imaging techniques. However, these buildups are not the cause of heart attacks. As previously mentioned, heart attacks occur when less than half of the artery's diameter has been occluded. This means that the surgery cannot treat the most lethal part of the disease, it only (sometimes temporarily) relieves the chest pain caused by the larger plaques. Angioplasty procedures are similarly effective. This procedure aims to re-open an occlusion by spreading the vessel apart with a balloon. By pushing the plaque back, it allows more blood to flow past while also posing the risk of releasing plaque contents into the bloodstream. 1 out of 16 patients experience what is known as "abrupt vessel closure" that can lead to heart attack, emergency bypass operation, or death (Gersh et al.,

1997). 40% of those re-opened vessels will constrict and close within 4 months of the surgery (Hirshfeld et al., 1991). Again, angioplasty can successfully relieve chest pain. It cannot, however, do anything to fix those smaller undetected occlusions potentially responsible for subsequent heart attacks.

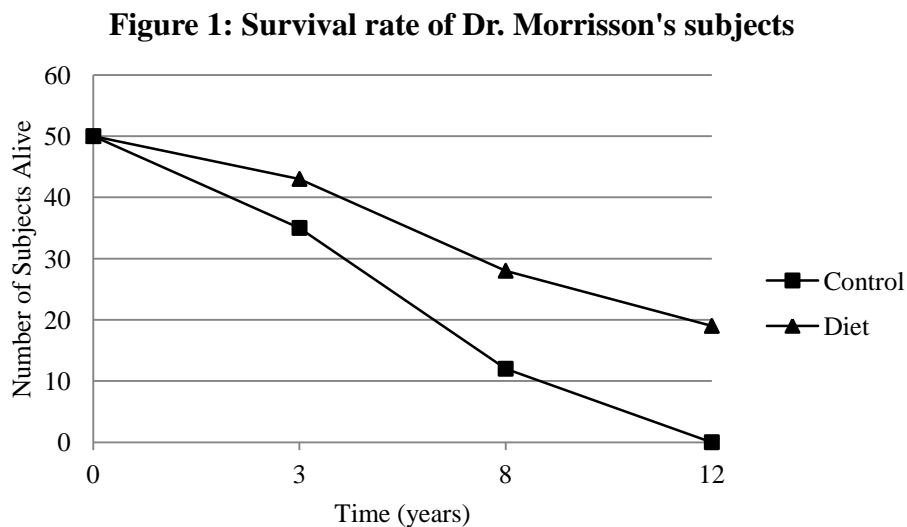
Bypass surgery and angioplasty procedures do not address the actual cause of heart disease, nor do they prevent heart attacks or prolong life for any but those in severe states. Despite their immediate effectiveness, both interventions have no means to prevent or treat heart disease like dietary methods can. Therefore, it is necessary to discuss the benefits and usefulness for a plant-based diet more thoroughly.

Evidence for plant-based treatment of heart disease

Little has changed in the past century for the management of heart disease. The epidemiology of this disease is provocative: “Three-quarters of the humans on this planet have had no heart disease [in the last 100 years], a fact strongly associated with diet” (Esselstyn, 2008). This thesis has demonstrated the benefits of a plant-based diet as a method of prevention; however, this section focuses on said diet as a method of treatment. “Medical, angiographic, and surgical interventions treat only the symptoms of heart disease. A fundamentally different approach to treatment is necessary” (Esselstyn, 2008).

In 1946, Dr. Lester Morrison led an innovative study of 100 patients with coronary arteriosclerosis (i.e. heart attack survivors). Half were instructed to consume a diet low in fat, cholesterol, and animal-based foods. These subjects were asked to

consume a small amount of meat twice a day: two ounces of cold roasted lamb for lunch and two ounces of lean meats for dinner. Permitted foods included “cream soups, pork, fat meats, animal fats, whole milk, cream, butter, egg yolks, breads and desserts containing butter, whole eggs, and whole milk” (Morrison, 1960). The other half were not given any dietary suggestions or restrictions. Figure 1 shows that eight years later, twelve of the 50 (24%) subjects consuming an unrestricted diet were still alive while 28 (56%) of the experimental group remained. Twelve years later, 19 of the 50 patients in the first group survived, a survival rate of 38%. Of the 50 patients in the control group, there were no survivors. The fact that these subjects were able to delay or prevent death draws attention to the idea that a plant-based diet could potentially treat heart disease. Dr. Morrison’s trial did not cure heart disease but it showed that making dietary changes can alter the course of the disease even after it has caused a heart attack.



Around the same time Dr. Morrison was making his advancements in heart disease research, another group conducted a similar study using more than three times the number of patients. 351 patients (with myocardial infarction or angina pectoris) were placed on a diet low in fat and cholesterol. Those that abided by their instructed diet were found to die or have recurring events (heart attack or chest pain) at a rate four times lower than those subjects who did not make the change (Lyon et al., 1956). Similar results were found in subsequent studies (Table 1) (Jolliffe et al., 1959). These studies showed that heart disease was not caused by old age and that even patients with advanced disease can prolong their life simply by adjusting their dietary habits to consume a plant-based diet.

Table 1: Monthly serum cholesterol determinations and heart disease conditions after 6 months adherence to prudent diet (Jolliffe et al., 1959)

	Time (months)			Coronary Disease*
	0	3	6	
Serum Cholesterol (mg per 100 mL)	350	313	288	NC
	346	298	287	NC
	339	268	273	NC
	325	307	300	NC
	318	273	240	NC
	318	244	230	NC
	308	285	242	NC
	308	289	270	NC
	307	263	260	NC
	305	270	245	C
	304	302	320	C
	300	250	272	NC
	299	275	243	NC
	296	295	290	NC
	294	250	215	NC
	293	250	258	NC
	Average	313.125	277	264.5625

*NC = no coronary disease under the criteria of the New York Heart Association. C = coronary disease under the criteria of the New York Heart Association.

These breakthroughs introduced diet and environmental factors as the focal points for heart disease, fat and cholesterol being the most important. The new attention paid to these two dietary components was misguided. What remained unreported was the fact that fat and cholesterol were indicators of the consumption of animal-based foods. As previously mentioned, plant-based foods are essentially low in fat and possess cholesterol-lowering capabilities. Across 20 countries, heart disease death rates for men (age 29 to 55 years) is directly related to animal protein consumption (Jolliffe & Archer, 1959), showing that the more animal protein consumed, the more heart disease prevails. Animal studies have revealed that feeding rats, rabbits, and pigs animal protein (casein) will increase their cholesterol levels, while feeding them plant protein (soy) has the opposite effect (Raaij et al., 1983). Human studies have also yielded the same effect with even greater cholesterol-lowering effects (Descovich et al., 1980). Fat, cholesterol, and animal protein are all linked to heart disease, which brings truth to the reasoning that animal-based foods, not just these isolated nutrients, are responsible for causing heart disease. Identifying the effects of the removal of these nutrients brings clarity to the idea of such a diet being a means to treat heart disease.

In 1985, Dr. Caldwell Esselstyn chose to study the effects of a whole food, plant-based diet on patients with heart disease. He implemented a minimal amount of cholesterol-lowering drugs in addition to an extremely low-fat, plant foods diet. When the study began, the only goal was to reduce the 22 subjects' cholesterol levels below 150 mg/dL. Excluding the five who dropped out, the 17 subjects had all sought Dr. Esselstyn's care after surviving the previous eight years of suffering from 29 coronary

events including angina, bypass procedures, heart attacks, strokes, and angioplasty. The experimental diet avoided oils, meat, fish, and dairy products (excluding skim milk and non-fat yogurt). Five years into the program, it was advised to completely remove the latter two (Esselstyn et al., 1995). Biweekly, for five years, patients were met with to record their weight, blood pressure, and blood cholesterol. A unique aspect of this study was that these patients gathered frequently to discuss the trial, share stories and advice. Another unusual feature was that both Dr. Esselstyn and his wife participated, upholding a certain level of involvement and support for these patients. This particular cohort was not a double-blind study and did not use a control group.

Before the program began, the average subject's blood cholesterol was measured to be 246 mg/dL. During the next few years, this number dropped to 132, past the hypothesized target (Esselstyn, 2008). LDL cholesterol levels significantly decreased along with the number of coronary events. Eleven years later, exactly one coronary event occurred among those 17 patients remaining in the trial. This event occurred in a patient who allegedly strayed from the dietary restrictions during two of those years (Esselstyn et al., 1995). This particular patient, after avoiding the diet, experienced angina and subsequently resumed the diet, soon being relieved of all previous pain (Esselstyn, 2008).

The most impressive result of this study was not the elimination of heart disease, but that their disease was reversed. 70% of these subjects' clogged arteries were seen to re-open. Upon angiographic examination of eleven people, an average blockage reduction of 7% was seen during the first five years, increasing the blood flow by 30%. A 7% mean decrease of arterial stenosis was the first and largest of its kind. The 30% flow increase

represents the difference between the presence and absence of angina. It was reported that this study was the longest study of minimal fat nutrition used in combination with pharmacologic therapy conducted thus far (Esselstyn, 2008).

The results of this study were impressive enough to influence another physician to make this dramatic life change. At 44 years old and with overall good health, this physician suffered a heart attack. After just 32 months of Dr. Esselstyn's program and without cholesterol medication, the physician was able to reverse his condition and lower his blood cholesterol to 89 mg/dL. Figure 2 shows that narrowing of a coronary artery from this patient is reversed following implementations of a plant-based diet. The final and most interesting aspect of this study was the willingness of those patients who left the study to share their statuses. As last reported in 1995, these people had suffered a combined total of ten new coronary events since their dissociation from the program (Esselstyn et al., 1995). Then as of 2003, only one person remained alive.

Figure 2: Coronary artery before and after consuming a plant-based diet



Coronary angiograms of the distal left anterior descending artery before (left) and after (right) 32 months of a plant-based diet without cholesterol-lowering medication, showing profound improvement (Caldwell B. Esselstyn, 2001).

The Lifestyle Heart Trial was another noteworthy story of how heart disease can be treated with lifestyle changes alone. 28 patients were placed on an experimental treatment plan: all were assigned to stay in a hotel room for the first week and asked to eat a low-fat (10% of calories coming from fat), plant-based diet for at least a year. The acceptable food list included fruits, vegetables, and whole grains. Patients had no limit to how much food they could eat as long as it was from this list. Animal foods were prohibited, except for egg whites and one cup per day of non-fat milk or yogurt (Ornish et al., 1990). Unlike the previously mentioned trials, this one required the practicing of stress management, meditation, breathing exercises, and relaxation exercises for at least

one hour each day. Exercise was required for three hours per week. No drugs, surgery, or technology was used during this trial and patients met twice a week for support.

The results of these findings were impressive. Average total cholesterol decreased from 227 mg/dL to 172 mg/dL and LDL cholesterol decreased from 152 mg/dL to 95 mg/dL. The frequency, duration, and severity all dropped by 91%. A correlation was found between closer adherence to the diet and positive results. Arterial sclerosis dropped by almost 4% and 82% of the subjects presented with regression of their initial heart disease state (Ornish et al., 1990). In the 20-person control group, chest pain worsened in all aspects by 165%. Cholesterol levels increased and degree of arteriosclerosis was raised by 8%. However, weight loss was not mentioned as a contributing factor to the overall benefits of this study, which seems to be an omission.

CHAPTER 4

DISCUSSION

This thesis has provided an in-depth account of the benefits of a plant-based diet in the prevention and treatment of heart disease. With the heart as the dominating force responsible for the survival of the human body, its health is undoubtedly critical. When the coronary vasculature is compromised by events such as atherosclerosis, heart disease sets in and a multitude of physiological changes occur. Medical research has evolved to offer a variety of methods to approach heart disease, medications and procedures being the most popular. Dietary management of heart disease stands as a conservative method of heart disease intervention. Despite its lack of attention within the field of cardiovascular medicine, the emphasis of a heart-healthy diet of plant-based foods is recognized for its significant advantages and overall health benefits. According to the research presented in this thesis, the most notable means for this evidence is the capability of dietary methods alone in preventing and often reversing atherogenesis. As the central basis for heart disease rationale, reducing the growth of atheromatous plaques is the most effective treatment.

During the Framingham Heart Study, thousands of permanent residents (both men and women) were tracked over a 26-year period in Framingham, Massachusetts. The primary objective of analysis in this particular cohort was to identify the primary risk factors indicative of heart disease (Hubert et al, 1983). A strong connection was made between the prevalence of diabetes as a predecessor to heart disease (Benjamin et al.,

1994). Obesity, particularly in women, was also identified as a primary risk factor. According to the research by Hubert et al., the most effective method of obesity prevention is through dietary changes, permitting only minimal consumption of animal-based saturated fat and cholesterol. A single geographic location cohort study may limit the universal credibility of these results. Conducting a study with multiple cohorts from different ancestries would clarify the overall applicability of these prevention methods. Similar methods were followed during the China Study, which proved that these primary risk factors do exist across all ancestries.

According to Segelken, an animal-based diet is directly responsible for “Western diseases” (i.e. obesity and allergies), cancer, and other medical conditions. A plant-based diet can prevent, treat, and reverse these diagnoses. Apolipoprotein B (apo-B, a form of so-called bad blood cholesterol) consumed in excess has been linked to heart disease and animal food consumption while showing an inverse relationship with a plant food diet. An association between consuming lower levels of green vegetables and heart disease concludes that the effects of an animal versus plant food diet is mediated through LDL cholesterol levels (Segelken, 2001). This claim has two parts: green vegetable consumption and apo-B. The China Study represented the green vegetable variable with a diet survey measuring grams of green vegetables consumed per day and a questionnaire recording how many times per year green vegetables were consumed(Minger, 2012).

Table 2: Correlations with green vegetable intake reported by the China Study
(Minger, 2012)

	Diet survey Green vegetable intake (average grams/day)	Questionnaire Green vegetable intake (times eaten/year)
Myocardial infarction and coronary heart disease	+5	-43
Hypertensive heart disease	-4	-36
Stroke	-8	-36

Upon examination of the total quantity of green vegetables consumed (in terms of weight) (Table 2), there are only weak negative associations for two cardiovascular conditions, and a slightly positive association for heart attacks (myocardial infarction) and coronary heart disease (Minger, 2012). Some geographical regions have strong parallels with heart disease; however year-round green vegetable consumption is only an indicator of geography. The frequency, not quantity, of greens consumption seems to be protective of heart disease and stroke. Therefore, green vegetables probably are not the true protective factor. Positive correlations with apo-B and the following are true: myocardial infarction and coronary heart disease (+37), hypertensive heart disease (+35), and stroke (+35). A negative association does, in fact, exist between plant-based protein and apo-B (-37). In addition, there is a positive association with non-fish animal-based protein and apo-B (+25) as well as fish protein (+16) (Minger, 2012). Therefore, aside from the green vegetable portion of his discovery, The China Study's conclusion about apo-B (bad or LDL cholesterol) is statistically significant. However, there are ambiguities with the implications of this finding. The conclusions presented by The China Study associate plant protein and heart disease with a protective relationship.

Table 3: Correlations with heart disease reported by The China Study (“The China Study,” n.d.)

	Animal protein	Fish protein	Plant protein (from the China Study’s “diet survey”)	Plant protein (from the China Study’s “food composite analysis”)
Myocardial infarction and coronary heart disease	1	-11	25	21
Hypertensive heart disease	25	-9	-10	0
Stroke	5	-11	-3	12

As reported in Table 3, fish protein seems to be protective for each form of heart disease studied. Animal protein is neutral for coronary heart disease/heart attacks and stroke but associates positively with hypertensive heart disease. Plant protein is positively correlated with heart disease from a “food composite” standpoint. No significant distinction between protective or disease-causing effects of animal-based protein versus plant protein. Using the data from Table 3 alone, fish protein has the greatest protective effect.

This part of the China Study was a three-day survey that, when repeated at a later date, yielded similar results for each county. This could have been solely due to geography. Future studies should track and estimate greens intake on a long-term basis to validate these conclusions. Campbell is correct in highlighting the positive correlation between some heart diseases and apo-B. Relaying this into the conclusion that animal foods cause heart disease—and green vegetables and plant protein protect against—is questionable. A follow-up study should be held to answer the question of what factors cause both apo-B and heart disease risk to increase together.

Various pharmaceutical regimens aim to prevent, alleviate, and reverse symptoms of heart disease. Each medication subtype presents a distinct approach; however, a number of biochemical pathways integrate and bring forward different thoughts as to how efficacious these can be in relation to others. Overall, there are many different ways to interpret and integrate the results of research findings in a way that creates confusion when these results are put to practice in a patient setting. It is important to appreciate the complexity of heart disease and how it fits into its associations with a multitude of related diagnoses. The overall message from clinical trials cannot be elucidated into one clear recommendation because of the complexity of this disease and its subsets. This discussion concludes with an emphasis to recognize those areas of uncertainty and bring attention to the idea that an alternative solution, through dietary methods, may in fact be the most efficient approach when the diagnosis and treatment are unclear.

In the midst of the clinical inconsistency for heart disease treatment, two pharmaceutical regimens appear to be the most straightforward: cholesterol and diabetic drugs. These two treatments represent situations where there is an inevitable need for medical intervention in collaboration with significant dietary changes. At this point it is necessary to reiterate the distinction between the main finding of this thesis and the inevitable settings that call upon conventional drug treatment. It is also pertinent to focus on the fact that these regimens are most successful when structured with diets low in fat, cholesterol, and animal-based foods. Katan et al (2003) found that adhering to this diet in combination with cholesterol-lowering drugs was more efficient than doubling statin doses. Additive benefits were seen in plasma levels of various vitamins, thereby further

demonstrating the significant efficacy of this dual-method, which could potentially result in the declination of a patient's dependency on these medications. However, there are circumstances in which a patient may require pharmacological treatment indefinitely due to genetic predisposition.

According to the research discussed in previous sections of this thesis, pharmacological treatment can only do so much and will eventually lose their effectiveness if dietary restrictions are not met. These treatments cannot function if the body's nutrient supply is overwhelmed with excess materials that build up and continue to contribute to progressive plaque formation. Surgical strategies are sought when such cases persist past the point where pharmaceutical intervention is maximally efficacious. Resorting to surgery exposes the patient to a number of additional risks that often times could have been avoided through diet alone. Clinical research shows how effective procedures such as coronary bypass may be, yet little attention is drawn toward the similar efficacy of dietary methods. Morrison's study demonstrated that cutting back on animal-based foods alone can increase survival rate by 38% in patients with severe coronary arteriosclerosis. His study also reported a 0% survival rate for those who continued to consume animal foods without dietary intervention by the twelfth year (Morrison, 1960). The major breakthrough of this and its associated studies was the introduction of dietary cholesterol and fat as consequences of animal food consumption. This relationship was further clarified when Jolliffe and Archer (1959) reported a direct association between animal protein consumption and heart disease across twenty countries.

The many studies that followed all reported the same conclusions: consumption of animal protein increased cholesterol levels while consuming plant-based proteins had the opposite effect. With cholesterol being one of the most influential factors associated with heart disease progression, these results uncovered a relationship between consuming plant-based foods and the reduction of heart disease risk. Esselstyn pioneered his 1985 study to observe the effects of a plant foods diet in patients with severe heart disease. Blood cholesterol dropped well below the target levels, while LDL cholesterol also demonstrated a noticeable decrease. The most significant result of Esselstyn's study was the alleged reversal of heart disease. Approximately 70% of patient's arteries re-opened and blood flow was increased by 30%. These results were the first of their kind. Until that time, researchers were only able to postulate and prove the relationship between diet and heart disease. Not only did Esselstyn's research validate this correlation but he was able to use this association to treat and reverse the diagnosis.

A number of behavioral and lifestyle changes come hand-in-hand with post-operative care that go beyond the scope of this thesis; however, it is noteworthy to mention their significance in relation to the topic at hand. These results present an opportunity to misinterpret the true evidence they provide. On the surface, these trials simply tells us that patients with multiple-vessel disease will have better odds if they undergo surgery and will reduce the risk of subsequent medical procedures if they choose against stenting. Upon further analysis of this report, there is a question as to why repeated revascularization is needed. The answer stems from the failure to adjust behavioral and lifestyle changes that drew attention to and created the symptoms assessed

prior to surgical intervention. One potential explanation that merits further investigation is that patients who underwent revascularization or stenting did not comply with the recommended post-operative changes set forth to prevent such events from recurring.

The National Heart, Lung, and Blood Institute's 2012 Morbidity & Mortality Report concludes that heart disease has and still is the number one killer showing no preference for age, gender, ethnicity, or race. Age-adjusted death rates for heart disease have dropped. Downward trends in the morbidity and mortality rates are generally misleading. In order to appreciate the meaning of these data, one must recognize the high numbers initially reported. Heart disease accounted for over 400,000 deaths per 100,000 people, almost half of the deaths in 2008. By supporting the usefulness of these data, conscious minds are delegating an unnecessary amount of attention to the pseudo solution of conventional heart disease treatment: both pharmacological and procedural. The United States Department of Agriculture has stated that Americans consume "significantly more meat and added fat than we did 30 years ago" (Information Plus, 1999).

The number of those succumbing to heart disease is the same as it was three decades ago (T. Campbell & Campbell II, 2006). "Much effort has focused on the pharmacologic management of hypertension and blood lipid levels and on improved therapy for acute myocardial infarction and congestive heart failure. These treatments have proven benefit but are costly, may have side effects, and require medical intervention" A great deal of attention has been given to the success of drug therapy as treatment for high blood pressure and blood lipids. Similar efforts are put toward research

for improving therapeutic agents for acute myocardial infarction and congestive heart failure. However efficacious these treatments may be, it comes at an economic cost. Advocators should take into consideration those serious side effects associated with administration (Stampfer et al., 2000). America spends the most money per person on health care services, making the United States the world's top spender. Despite this investment, nearly half of the country's citizens are living with a health problem that requires weekly drug administration (T. Campbell & Campbell II, 2006). The benefits of integrating a heart-healthy diet are noteworthy from both a health standpoint as well as economic.

Each year, over one million heart surgeries are performed (Ornish, 1998). Physician care and hospital services for heart disease patients cost \$78.1 billion in 2002, not including the cost of drugs or home care (National Institutes of Health, 2012). The average cost for an angioplasty procedure and for coronary bypass are \$31,000 and \$46,000, respectively (Ornish, 1998). Alternatively, the cost of a one-year program initiated by Dr. Ornish is \$7,000. Using this program can, therefore, cut costs by an average of \$30,000 per patient. Despite the obvious benefits of cutting such costs, this idea still remains an issue from a healthcare standpoint. Currently, the United States healthcare system is set up to financially benefit from chemical and surgical treatments.

Advertisements and publications are constant reminders to maintain a "heart-healthy diet;" however, this ideal diet is described inconsistently throughout media and literature (Cleveland Clinic, 2013). It is important to know why this information dominates and why people are grossly mistaken in how they investigate diet and disease,

how media promotes health, and how medicine treats illness. If heart disease is the number one killer, it comes as no surprise to be overwhelmed with the plethora of resources that tell us how and why we should pay more attention to its awareness and prevention. The larger the information pool, the larger the chance of being misinformed. Substantial evidence supports each individual risk factor associated with heart disease, yet only a small sample is known in regards to their combined effects (Stampfer et al., 2000).

The World Health Organization is an advocate of a healthy diet and promotes behavioral risk factor awareness. Similarly, the Centers for Disease Control suggest maintaining a healthy diet but do not define what that healthy diet consists of. There is a misrepresentation of how a healthy diet is to be followed, which may be the reason why people have such a hard time attaining it. Campbell and Campbell II (2006) make the point that “This isn’t because the research hasn’t been done. We know an enormous amount about the links between nutrition and health. The real science has been buried beneath a clutter of irrelevant or even harmful information—junk science, fad diets and food industry propaganda”

Conclusion

Heart disease has and will continue to be the nation's number one killer until dietary methods are recognized as the most effective prevention and treatment. With atheromatous plaques being the physical gateway to the disease's physiological progression, interrupting their growth is the most effective way to approach onset of disease. Based on the research discussed, understanding that diet provides the building materials for this process is pertinent in recognizing the various mechanisms involved in prohibiting the disease. This thesis presented the means by which heart disease develops and overviewed the abounding advances made by clinical research to reach a universal method of treatment. A majority of sources can agree upon the sole origin of heart disease; however, exclusive preventative measures are not clearly disclosed. This lack of agreement and consistency draws attention toward the inevitable recognition of diet as both the source and solution.

Within the biomedical research field, emphasis has been placed on a whole food plant-based diet as the most efficient dietary method for the prevention and treatment of heart disease. The nutritional benefits of plant foods include cholesterol-lowering capabilities, protein quality, and abundant source of antioxidants, fiber, and phytochemicals. Each of these elements presents a unique approach as to how plant foods contribute toward the treatment of heart disease. Although a number of studies aim to elucidate each element individually, it is necessary to recognize the benefits of plant foods for their positive nutritional profile with respect to how all of these facets work together to prevent and treat disease.

A number of studies have been conducted to assess the use of dietary soybean products as cholesterol-lowering agents. Research shows strong evidence to support the hypothesis that substituting soy for animal protein displays similar results. As a mediator of lipid metabolism, incorporating soy into daily diet demonstrates an example of how heart disease can be avoided without pharmaceutical intervention. Alternative studies have shown that plant-based protein sources offer sufficient protein quality when substituted for animal foods, discrediting any previous allegations that consuming only plant foods does not provide adequate dietary protein. Plant foods also possess an additional mechanistic approach to lipid metabolism through antioxidants. Reducing free radical damage sets itself on the forefront of heart disease prevention by limiting oxidative processes that damage tissues, including coronary vasculature. Dietary fiber studies have delineated this component of plant products as capable of protecting against hyperlipidemia and consequently the plaque formation associated with heart disease. Phytochemicals are established as having anti-atherosclerotic properties that present similar results. Plant products offer a variety of methods to prevent, treat, and even reverse heart disease. This appreciation finds greater meaning when the efficacy of a plant-based diet is compared to that of animal foods and conventional methods of treatment.

Surgery and pharmaceutical intervention have been considered the predominant approach to heart disease for decades. Within the last fifty years, research has offered new ways to understand the various components of this disease that make it such a difficult diagnosis to treat. Procedural mediation offers a number of immediate benefits

but cannot ultimately cure heart disease. What sets dietary methods apart from these approaches is the ability to not only treat but reverse these conditions. Neither surgery nor drugs have been able to demonstrate these kinds of results, which is why more emphasis needs to be placed on diet as the ultimate and only way to truly treat heart disease.

Research has provided medicine with the information it needs to implement change. An abundant number of clinical trials have proven successful ways to both treat and prevent the nation's leading cause of death. The biggest challenge now is utilizing this knowledge on a global scale. Dr. Dean Ornish has already begun by advocating the Multicenter Lifestyle Demonstration Project (or simply the Lifestyle Project). This lifestyle intervention program has been trained to professionals at eight different locations. Subjects are eligible if they have heart disease severe enough to require surgical intervention. Instead, these people have the option of taking part in the one-year program previously described. Pioneered in 1993, this program was already covered by 40 insurance plans by 1998 (Ornish, 1998).

Controlling the intake of any one nutrient will not treat or prevent heart disease. Simply eating right can make significant contributions toward extending life expectancy and reducing mortality. An abundance of research has shown that heart disease can potentially be reversed with diet alone in a significant number of patients. Understanding the scientific evidence behind good nutrition not only improves health but the global medical community. The confusion and misguidance of prescription advertising that this misunderstanding causes can be dangerous. Advocating diet as an intervention for heart

disease is just one example of how it can drastically improve overall health. The future of cardiovascular research has a great deal of progress to make in regards to this area of study but will significantly benefit by starting with the implementation of a plant-based diet for the prevention and treatment of heart disease.

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