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The Impact of the Framingham Study on Evidence Based Medicine

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INTRODUCTION

Longitudinal research studies have led to important changes in how medicine has been practiced over more than 70 years.[1] Prior to the inception of the Framingham Heart Study, chronic conditions like hypertension were not totally understood and were not necessarily treated. The Framingham Study was proposed following the death of President Franklin D Roosevelt in 1945. At that time, it was believed high blood pressure should not be controlled in an older individual and was a perfectly normal part of the aging process.[2]

Shortly thereafter, the next president, Harry Truman, approved an allocation of funding for a government grant to study cardiovascular disease. The purpose of the grant was to study coronary artery disease and determine the factors contributing to the disease's development. Framingham, MA was chosen as a site due to its geographical proximity to cardiologists affiliated with Harvard University in Boston, MA.[3]

The Framingham Study was one of the first studies to recruit a patient population and follow them, along with their biological relatives, throughout their lives.[4] The inception of this study was also motivated by the increase in deaths due to cardiovascular disease in the early part of the twentieth century in the United States. By the 1940s fifty percent of the deaths of Americans were due to cardiovascular disease.[2]

The Framingham Study differed from earlier studies in that prior studies had retrospectively reviewed data from community registries and not from screened volunteers. The prospective design of the Framingham Study was made up of three multi-generational cohorts and has contributed over time to advances in the treatment of cardiovascular disease including improvements in the understanding, following, and treatment of hypertension and hypercholesterolemia[4]. The data that has been amassed from this study is still contributing to changes in the treatment of chronic and inherited disease states such as hypertension and hypercholesterolemia.

DISCUSSION

The Framingham Heart Study is a longitudinal cohort study, composed of three generations of original participants, that has focused on epidemiological methods as well as technological advances that have improved the practice of evidence-based medicine over time.[4] Prior to this study the only entity that was following morbidity and mortality of cardiovascular disease were insurance companies.[2]

The initial focus of the study was to determine the natural history of heart disease. [2] The Framingham Study has had a significant impact over time with the development of methods to better treat and to better understand inherited diseases that affect cardiovascular morbidity and mortality. These include a better understanding of the impact of high blood pressure, high cholesterol, and diabetes, involving risk factors such as smoking, obesity, and physical inactivity. [1]

Major risk factors were identified for hypertension and hypercholesterolemia, and these factors formed the basis for the 10-year and 30-year risk prediction algorithms[4] used in routine practice today. Establishing hypertension, hyperlipidemia, diabetes, and tobacco as risks for cardiovascular disease led to targeted study and reduction of said risk factors and significantly lower incidence of disease. [1,4]

The data obtained from the Framingham Study, and research studies that built upon that data, have demonstrated that benign essential hypertension, or rising blood pressure in older adults, was not a normal compensatory response to forcing blood through aging arteries.[4] Atherosclerosis was found to be an arterial abnormality rather than a normal part of aging and is impacted by the combined effects of genetics, lifestyle, and environmental outcomes. This solidified the relationship between higher cholesterol levels and the increased risk of cardiovascular disease as well. [5]

Prior to the first report of the Joint National Committee on Detection, Evaluation and Treatment of Hypertension in 1977[4], the standard of practice suggested that diastolic blood pressure was more important than the systolic measurement, particularly in the elderly. Analysis of the data from the Framingham Study showed that the risk of coronary heart disease morbidity was greater when associated with higher systolic pressure and had a stronger association with cardiovascular disease mortality than with diastolic blood pressure. Twenty years after President Roosevelt's death the study data dispelled the erroneous beliefs concerning hypertension and cardiovascular disease or the lack of importance of lowering systolic blood pressure as well as treating labile hypertension. [2,5]

Another contribution of the Framingham Study was the discovery of the etiology of heart failure and the establishment of criteria to diagnose and treat it. Before the data was gathered in 1966 there were no criteria to analyze heart failure. By 1971, the major and minor criteria were developed and the leading cause of heart failure was determined to be hypertension. With the advent of newer interventions to treat heart failure, including beta blockers and ACE inhibitors the mortality associated with heart failure decreased from 70% in 1950 to 59% in 1999 for men and similarly from 57% to 45% for women. [2]

A further contribution of the Framingham Study was the identification and treatment of atrial fibrillation as a risk for stroke. In 1978, it was reported that chronic atrial fibrillation was associated with a greater risk for stroke. This evidence precipitated further study for use of anticoagulation or antiarrhythmic agents in participants with a diagnosis of chronic atrial fibrillation. In turn, the use of anticoagulants became the standard of care for patients with chronic atrial fibrillation.[2]

One of the greatest contributions of the Framingham Study to the practice of evidence-based, or preventative, medicine is the concept of the risk factor. This concept was fundamental to the prevention of cardiovascular disease through the findings of the effects of tobacco, unhealthy diet, physical inactivity, obesity, elevated cholesterol levels, elevated blood pressure levels, and diabetes mellitus on cardiovascular disease. The study contributed to the shift in the second half of the twentieth century from treating established cardiovascular disease to preventing cardiovascular disease for those at risk. The data revealed risk factors, or comorbidities, which included hypertension, hypercholesterolemia, and diabetes mellitus. These risk factors were first outlined in 1961 resulting in the first risk profile in 1976 and culminating in the 10-year risk estimate in 1998. [2]

The data collected continues to be shared and analyzed and now includes genetic information to assess the novel risk factors. Samples including whole blood and lymphoblastoid cell lines; and DNA, through the Emerging Risk Factor Collaboration; as well as single nucleotide polymorphisms, through the SNP Health Assoc Resource, and the Candidate Gene Assoc Resource; have been made available for researchers to identify and characterize risk factors that correlate to the health outcomes reported by the study participants. This work has led to the identification of SNPs for traits to better understand hypertension, lipids, endothelial function, valvular calcifications, and carotid atherosclerosis.

The success of the Framingham Study is not only the contribution of the initial study design but that it was able to continue longitudinally beyond the first participants. In addition to the original cohort in 1948, their children in 1971, and their grandchildren in 2002, were enrolled and continued to be followed. Furthermore, to expand the ethnic diversity of research subjects, two additional cohorts were recruited in 1994 and 2003. [2] The data was retrieved over a more than 70-year period of time and continues to be a resource to both clinical and research practitioners now and in the future.[6,7]

CONCLUSION

The Framingham Heart Study has advanced the practice of evidence-based medicine by following several cohorts of successive generations of participants. The Framingham Study has been the only longitudinal cohort study to identify, as well as evaluate, cardiovascular disease risk factors over three generations. [1]

Originating in 1948 the focus was to determine the natural history of heart disease. This study has had a significant impact over time with the development of methods to better treat and to better understand inherited diseases that affect cardiovascular morbidity and mortality.[2] These include a better understanding of the impact of high blood pressure, high cholesterol, and diabetes, involving risk factors such as smoking, obesity, and physical inactivity.[4]

Over this period of time, several cohorts were established including the original cohort in 1948, their children in 1971, and their grandchildren in 2002. Since the original cohorts were made up of mostly white western European participants, in 1994 and 2003 two additional cohorts were initiated to reflect the ethnic diversity in the area of recruitment.

The collection and storage of DNA and other samples from the Framingham Study participants has allowed for the analysis of genomic data using current technologies, as well as future analyses for improving understanding and outcomes. The combination of genetic data and comprehensive epidemiological longitudinal data from the multi-generational Framingham Study cohorts provides a powerful tool for assessing risk factors and their overall impact on lifestyle and longevity.

Understanding the combined effect of genetics, lifestyle, and environmental factors on cardiac morbidity and mortality continues to be the legacy of the Framingham Study. The data will enable researchers to continue to make progress in the better understanding and treatment of cardiovascular disease to continue to improve the prognosis for genetically inherited diseases over time.[1,6,7]

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