

## The Framingham Heart Study: Transforming a National Health Challenge to a Strategic Global Solution

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### ABSTRACT

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Cardiovascular disease is a leading cause of preventable morbidity and mortality among the adult population worldwide. Initiated as a result of the sad events associated with the death of the US president from cardiovascular disease, the Framingham Heart Study was initiated and designed to identify the risk factors and track the natural history of cardiovascular disease. It also focuses on developing and evaluating interventions for preventing and treating cardiovascular disease.

This project is a prospective cohort study of the Framingham population supported by the National Health Act of 1948. A total of 5,209 adults were initially recruited for the study, which has spanned three generations since its inception. The researchers initially acquired and tracked data through medical history, cardiovascular-focused physical examination, laboratory tests, and follow-up visits. With time, novel methods of tracking the course of cardiovascular disease, such as wearable devices, mobile health apps, electronic health records, and biobanks, were introduced.

The study's results revealed that high blood pressure, elevated blood glucose, high blood cholesterol, smoking, diabetes mellitus, inactivity, overweight or obese, and specific genetic traits are the major risk factors for cardiovascular disease. The study established interventions to prevent and treat cardiovascular disease, which have become life-saving measures worldwide.

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### INTRODUCTION

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Cardiovascular disease (CVD) is a spectrum of conditions affecting the heart and/or blood vessels. These include coronary artery disease, hypertensive heart disease, stroke, heart failure, arrhythmias, cardiomyopathy, and peripheral arterial disease. CVD is the leading cause of preventable morbidity and mortality among adults worldwide<sup>1</sup>. Among efforts aimed at unmasking the risk factors for cardiovascular disease in the community, the Framingham Heart Study (FHS) located in the city of Framingham, Massachusetts in the United States of America is foundational and fundamental. Other laudable initiatives aiming at the exploration of risk factors for cardiovascular disease include the Global Burden of Diseases, Injuries, and Risk Factors (GBD) study launched in 1990 and the Global Burden of Cardiovascular Diseases Collaboration global extension introduced in 2020.

The sudden decline in health and the death of the 42<sup>nd</sup> President of the United States, President, Franklin D Roosevelt from heart disease and stroke in 1943 triggered the awareness of

the cardiovascular disease epidemic in the US. By 1948, President Harry Truman, the Vice-President under Franklin D. Roosevelt signed into law the National Health Act for the establishment of the National Health Institute with the mandate to explore the epidemiology of cardiovascular disease through a community-based study. A seed grant of \$500,000 was allocated for the take-off of the study which was eventually located in Framingham, Massachusetts, hence the name, Framingham Heart Study<sup>2</sup>.

The FHS is a prospective cohort study of the Framingham population, focusing on investigating and understanding the epidemiology and risk factors for cardiovascular disease.<sup>2-3</sup> This study was initiated at a time when the understanding of the cardiovascular disease was poor.<sup>4</sup> Most of the revolutionary evaluation concepts, interventions, and outcomes with regard to cardiovascular disease today are traceable to the study.

According to the 1948 US Census, the population of Framingham, Massachusetts was 28,019.<sup>5</sup> The Framingham Heart Study began in 1948 with 5,209 adult subjects from Framingham, which was about 18.6% of the town's population at that time.

Framingham was chosen as the site of the FHS because it was thought to be a representative sample of the United States population at the time. The town is a relatively affluent town with a diverse population, and it has a long history of public health research especially research in tuberculosis.<sup>6</sup> The aims and objectives of the FHS are to identify the risk factors for cardiovascular disease, track the natural history of cardiovascular disease, and develop and evaluate interventions for cardiovascular disease.<sup>3</sup> Since its inception in 1948, the FHS has had four principal investigators. The incumbent principal investigator who assumed duty in 2016 is Dr. Vasana Ramachandra. Previous principal investigators were Dr. Thomas "Ray" Dawber (1948-1975), Dr. William Kannel (1975-1994), and Dr. Jack Jukema (1994-2016).

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#### RESEARCH METHODOLOGY

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The Framingham Heart Study is a long-term, prospective cohort study of residents of the city of Framingham, Massachusetts. The study began in 1948 with 5,209 adult subjects from Framingham and is now on its third generation of participants. This type of study involves monitoring a group of people over a period of time to observe how they develop cardiovascular disease and also how they respond to certain interventions.<sup>3</sup> The participants are a representative sample of the United States population, and the researchers have collected a wealth of data on the participants' health. The researchers collect a wealth of data on the participants' health, including information on their medical history, lifestyle habits, and genetic information at intervals over a period of time.<sup>2,3</sup>

The study has used a variety of methods to track the health of the participants over the years. The researchers collected detailed medical histories from the participants, including information on their past and current medical conditions, medications, and lifestyle habits. Periodic medical examinations are conducted on the participants including measurements of their height, weight, and cardiovascular examination. The researchers conducted a variety of laboratory tests on the participants, including blood sugar, blood cholesterol, urine tests, and electrocardiograms (ECG). Imaging tests done for the participants include; Chest X-rays, echocardiograms, and magnetic resonance imaging (MRI) scans. Moreover, the researcher established biobanks for the genetic analysis of urine.<sup>7</sup>

The new methods used for tracking the health status of the participants include; wearable devices such as smartwatches, and fitness devices to track physical activity, heart rate, and sleep patterns. Mobile health apps are also used for tracking dietary patterns, weight, and blood pressure. Plasma level of homocysteine was also explored as a possible risk factor for cardiovascular disease.<sup>8</sup>

The researchers also explore the participant's electronic health records to track information on their medical visits, prescriptions, and the result of their investigations. FHS spans 3 generations of the White population and 2 cohorts comprising of racial and ethnic minority groups. For health status monitoring, the researchers conducted follow-up visits with the participants every 2 years for the original cohorts and 4-7 years for the offspring, 3rd generation, and omni cohorts. The essence of follow-up is to track individual's health over a period with a view to identifying risk factors for cardiovascular disease.<sup>9</sup>

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#### RESULTS AND DISCOVERIES

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The Framingham heart study has identified a number of risk factors for cardiovascular disease, including high blood pressure, high cholesterol, smoking, obesity, physical inactivity, diabetes mellitus, and family history.<sup>10-12</sup> Through this study, the Framingham risk score<sup>13</sup> was developed to predict the risk of developing coronary artery disease and also to assist in taking proactive measures to prevent the occurrence of complications. Through FHS, risk calculators were developed to predict the risk of cardiac disease in individuals without symptoms. Framingham criteria for diagnosis of heart failure<sup>14</sup> was formulated. The major criteria are paroxysmal nocturnal dyspnoea, neck vein distention, rales, radiographic cardiomegaly, acute pulmonary edema, S3 gallop, increased central venous pressure (>16 cm H<sub>2</sub>O at right atrium), hepatojugular reflux, weight loss >4.5 kg in 5 days in response to treatment. Minor criteria are bilateral ankle oedema, nocturnal cough, dyspnoea on ordinary exertion, hepatomegaly, pleural effusion, decrease in vital capacity by one-third from maximum recorded, tachycardia (heart rate >120 beats/min). The diagnosis of congestive heart failure is made with a minimum of 2 major criteria or the presence of 1 major criterion and 2 minor criteria.

Through the FHS, a risk factor for atrial fibrillation was developed<sup>15</sup>. FHS established that age, sex, body-mass index, systolic blood pressure, treatment for hypertension, PR interval, clinically significant cardiac murmur, and heart failure were associated with increased risk of development of atrial fibrillation. The FHS has identified a number of genes that are associated with an increased risk of heart disease. These include Apolipoprotein E (APOE), low-density lipoprotein (LDL) receptor, Proprotein convertase subtilisin/kexin type 9 (PCSK9), and C-reactive protein (CRP).<sup>16</sup> APOE gene codes for

a protein that helps to transport cholesterol in the blood. Individuals with certain variants of the APOE gene are at an increased risk of developing cardiovascular disease. The LDL receptor helps to remove LDL cholesterol from the blood. People with mutations in the LDL receptor gene are at an increased risk of developing heart disease. PCSK9 helps to break down the LDL receptor. People with mutations in the PCSK9 gene have lower levels of LDL cholesterol and are at a lower risk of developing heart disease. The study facilitated the development of lifestyle changes to prevent heart disease.<sup>17</sup> FHS also Study has shown that medications, such as statins and blood pressure medications, can help to prevent complications and treat heart disease. These findings have helped to improve the treatment of cardiovascular disease.<sup>18</sup>

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#### CONCLUSION

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In conclusion, the FHS is an exemplary multigenerational community research with great and positive impact, not only on the Framingham community but also on millions of people worldwide. The study established interventions to prevent and treat cardiovascular disease and these have become life-saving measures across the globe.

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