Neurosciences and History 2016; 4(1): 43-46

The Framingham study

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ABSTRACT

The Framingham study, which was started in 1948 in the Massachusetts towns of Framingham and Newton, is one of the most important epidemiological contributions to the study of cardiovascular disease. It was later expanded to include cerebrovascular disease and other conditions. The initial study included a cohort of 5209 men and women aged 30 to 60 years. They had not yet developed symptoms of any type of cardiovascular disease, and they had no history of heart attacks or cerebrovascular accidents. Since that time, subjects have attended follow-up visits twice yearly. In 1971, the study recruited a new generation by selecting 5124 subjects among the children (and their spouses) of the initial cohort. This group was included in the Offspring Study. In 2002, a further 4095 participants forming a third-generation cohort were added. Thanks to the results from this study, the concept of risk factors was firmly established.

KEYWORDS

Epidemiology, risk factors, cardiovascular disease, cerebral circulation

One of the most important epidemiological contributions to the field of cardiovascular disease was the Framingham Heart Study, which began in 1948 in Framingham in northern Massachusetts. The design, objectives, and methodology of this study have earned their place in the history of medicine.[1-3]

As part of the Public Health Service Act, Franklin D. Roosevelt (1882-1945) and his government set up a department known as the Hygienic Laboratory, which was soon renamed the National Institute of Health. Within that department, the National Heart Institute (NHI) was created in 1949 as a special unit for the study of cardiovascular diseases.

A few years before the NHI appeared, however, Joseph W. Mountin had already formed a committee for epidemiological studies and prevention of heart disease.

To carry out its study, the committee chose two towns in Massachusetts, Framingham and Newton. The approach was different in each case: Framingham was used to study epidemiological features, whereas Newton was used to study preventive measures.

The main purpose of the Framingham study was early detection of heart disease and diagnosis of unremarkable manifestations in apparently healthy people.

Dr Gilcin F. Meadors was entrusted with organising the Framingham study. Since the recently created NHI had requested oversight of all studies of cardiovascular diseases, the Framingham study depended on that institution.

In 1948, the town of Framingham had a population of 28 000 inhabitants, of whom 10 000 fell within the age range of 30 to 60 years. The primary objective of the study was to monitor coronary artery disease and arterial hypertension in the above age group and during a 20-year period.

One of the study's limitations was that African-Americans were under-represented in the sample, making it difficult to extrapolate results to the national level.

The study subjects were initially examined in the spring of 1950; the loss rate in follow-up sessions was 2%.

In addition to completing clinical examinations, researchers recorded any diseases affecting the selected

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group, admissions to hospital, deaths, and any death and autopsy certificates.

A neurologist also participated in the study evaluating any cases of cerebrovascular disease and other neurological diseases.

Follow-up studies witnessed a rise in the number of people who moved from the 'disease-free' to the 'disease' category, and who therefore had presented clinical signs of cardiovascular disease.

More than seven years would pass before the subjects with signs of coronary artery disease were numerous enough to warrant a published study, but Dawber, Moore, and Mann published their preliminary notes in 1957.

As time went on, the number of subjects with cardiovascular disease gradually increased. In 1970, twenty years after the study was launched, the committee concluded that they had reached their targets and decided to end the study, over the objections of certain professionals. These dissenting voices plus the NHI, upon receiving private funding and support from Boston University Medical Center, were able to continue the study for another five years.

When this new stage in the study ended in 1975, the National Heart, Lung, and Blood Institute reconsidered its initial decision and signed a contract with the Boston University Medical Center in which it agreed to fund follow-up on the study population. Extending the study let scientists gather additional data on cerebrovascular accidents, peripheral artery disease, and a few non-vascular diseases in those years. In doing so, they contributed to our understanding of the natural history of cardiovascular diseases and other entities affecting elderly individuals. As time passed, the study acquired new fields of interest, including ophthalmological disease and senile deterioration processes, without changing its working methodology.

The data obtained were encoded so that they could be processed electronically. When statistical software started to become available, it was suggested that data from the project be sent to the Biometric Division of the NIH in Bethesda, Maryland.

But this suggestion led to a tug of war between the researchers collecting the data and those analysing it. The resulting climate of distrust made it difficult to run the study well, and raised questions about ownership of the data. Fortunately, the two groups were able to reach an agreement as to how the collected data was to be used.

Results from the Framingham study provide a clearer view of the incidence of arterial and heart diseases in patients with cerebrovascular accidents and peripheral vascular disease. The cohort's limited number of African-Americans and its high percentage of subjects of Italian descent was not considered sufficient motive to refrain from extrapolating its results to the general population of the United States. This decision was based on the premise that race had little influence on the diseases examined by the study.

It was demonstrated beyond any doubt that arteriosclerosis increased with age in both sexes. As time passed, researchers observed a progressive increase in the number of people with a disease within the selected population, thus resulting in higher numbers of people in the study group.

Researchers found that coronary artery disease, especially myocardial infarction, was twice as frequent in men as in women, and appeared an average of two years earlier in men as well.

The study observed that cerebrovascular accidents of any type of pathogenesis tended to present later in life than did heart disease. Coronary artery disease presented an average of 2 years earlier than cerebrovascular disease. The sex-related difference in the incidence of myocardial infarction was not observed for cerebrovascular accidents. For peripheral vascular disease in general, and intermittent claudication in particular, researchers observed an evolutionary pattern similar to that of heart disease with regard to age of onset and the sex-related difference in incidence.

Another noteworthy finding was that myocardial infarction was an event very likely to cause an embolic cerebrovascular accident. Researchers also found myocardial infarction to be four times more frequent among subjects with no history of cerebrovascular accident than among stroke patients.

The impact of the Framingham study on medical practice was substantial. Until the 1950s, every patient who did not have clinically apparent signs of disease was considered healthy, even when anomalies were present in the vital signs or laboratory analyses. These altered vital signs were regarded as benign as long as they were bearable and caused no clinical symptoms.

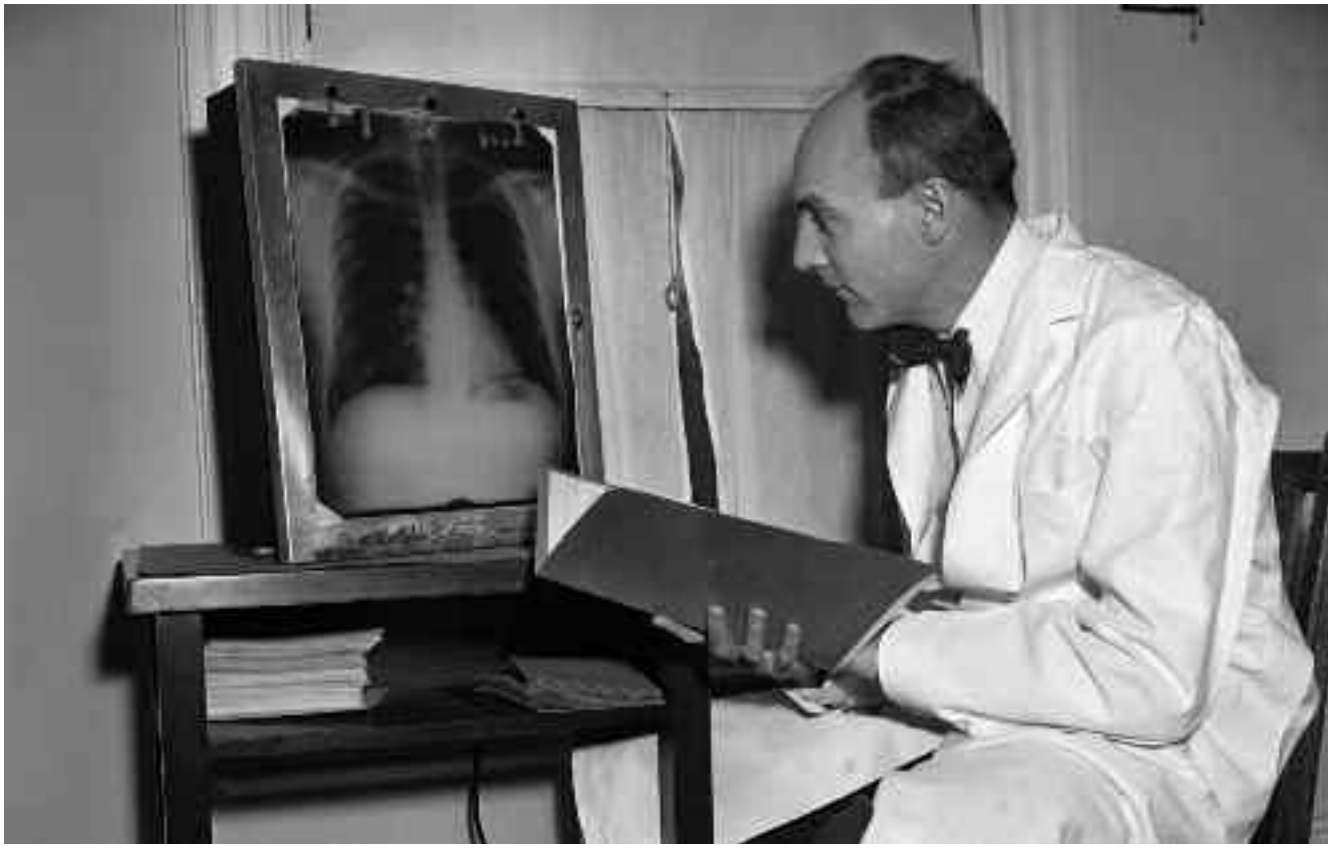

Figure 1. Thomas Royle Dawber (1913-2005), director of the Framingham study from 1949 to 1966.

Long-term follow-up on the natural history of arteriosclerosis was the key to establishing new criteria for normal health. A healthy individual came to be defined as one who not only showed no clinical manifestations, but who was also unlikely to develop them based on a lack of so-called benign changes.

As well as a revised definition of a healthy person, medical practice also gained the concept of risk factors for diseases.

One of the earliest known and most important risk factors was arterial hypertension, which plays a major role in the development of cardiovascular disease. The practical result of this discovery was that drugs and low-sodium diet were introduced to control hypertension. It has now known that these measures have contributed to decreasing the incidence of myocardial infarction and cerebrovascular accidents.

A high cholesterol reading also came to be recognised as a risk factor, and measures were applied to lower cholesterol.

Smoking had been regarded as closely linked to a higher incidence of lung cancer since the early twentieth century. In addition, the Framingham study showed smoking to be associated with higher frequency of coronary artery disease and therefore listed tobacco use as a statistically proven risk factor. Similar considerations have led to the application of measures intended to control body weight and promote regular physical exercise. In myocardial infarction and other circulatory diseases in general, such measures are effective for both prevention and rehabili-

tation. The concept of 'ideal weight' became widespread at this time.

Another of the study's key contributions was that it demonstrated, through statistics, that diabetes was related to heart and circulatory disease; hyperglycaemia was identified as a risk factor.

The Framingham study was designed in order to assess and demonstrate which personal and environmental factors promoted early development of arteriosclerosis. The study's conclusions, including statistical confirmation of the value of the risk factors that were identified, were widely accepted, and they are applied in clinical practice as a matter of course.

Cerebrovascular disease occupies a large part of the practice of clinical neurology, as well as having a tremendous social impact. With this in mind, the American Heart Association, in collaboration with the American Academy of Neurology and the American Neurological Association, decided to present a bimonthly journal exclusively covering all problems directly or indirectly related to cerebral circulation. The selected editor-in-chief was Dr Clark H. Millikan (1915-2011), a highly acclaimed neurologist in the field of cerebrovascular disease.

The journal was named *Stroke*, and its first issue was published in January 1970. In his editorial, Millikan explained the need for the journal in the following words:

> Hundreds of professional journals crowd the shelves of medical libraries; teachers and investigators have trouble enough digesting these overwhelming amounts of information while the practicing physician has time to look at only a fraction of the journals available.[5]

At present, *Stroke. A Journal of Cerebral Circulation* is the world's leading publication on cerebrovascular accidents.

Conclusion

The Framingham study is an example of teamwork, and its numerous extensions and expansions are a testimony to the enthusiasm and dedication of the researchers who came together to carry it out. It fulfilled its stated objective, which was to use statistics to confirm diverse impressions and opinions on the risk inherent to presenting metabolic changes and abnormal vital signs. The study was fundamental for establishing the concept of 'risk factor'.

Conflicts of interest

The author has no conflicts of interest to declare.

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