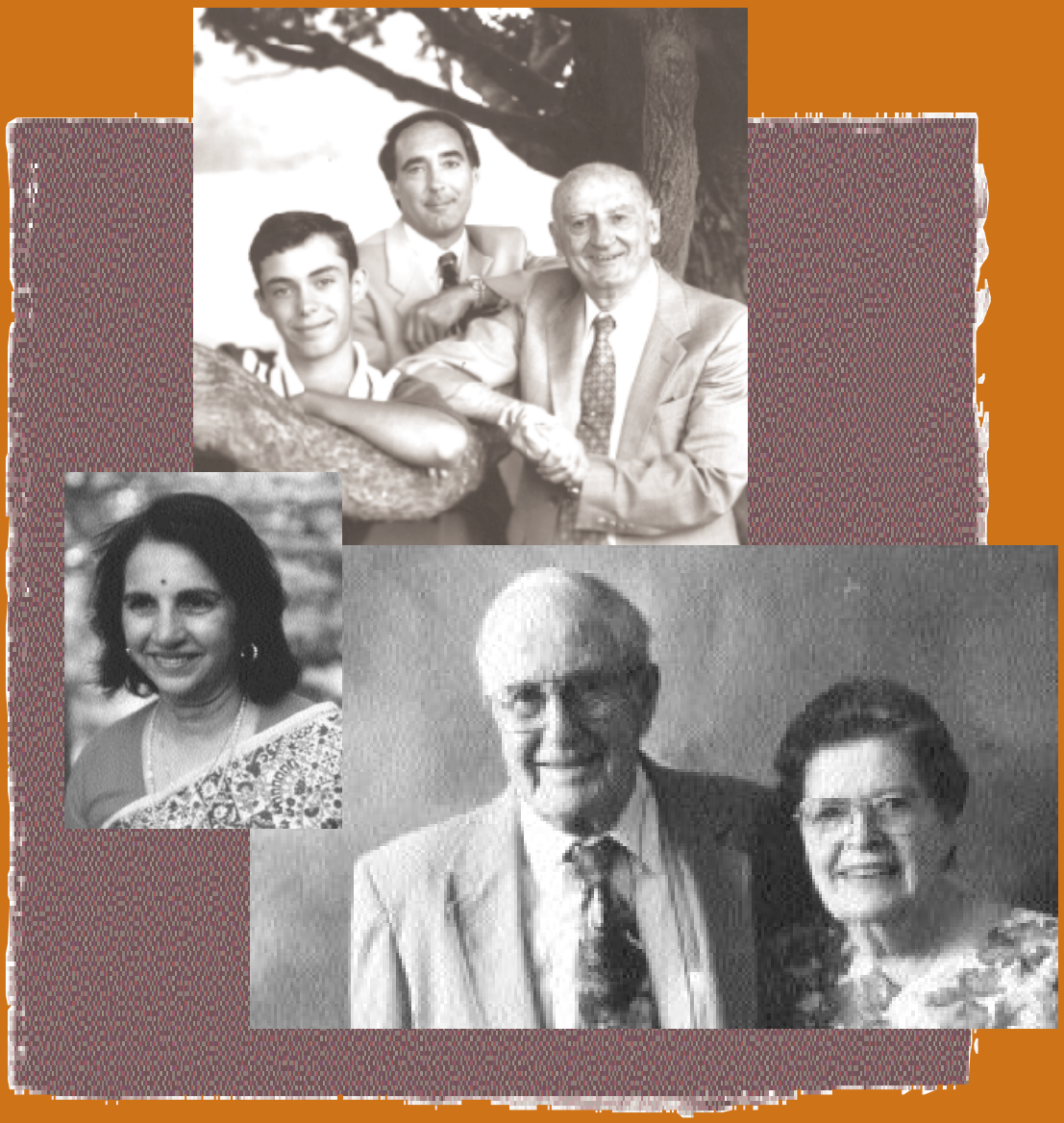
# You changed America's heart

1948-1998

**A 50th anniversary tribute to the participants in the Framingham Heart Study**



## Major moments in the Framingham Heart Study

**1948** Framingham Heart Study begins

**1956** Findings on progression of rheumatic heart disease reported

**1957** High blood pressure and high cholesterol levels shown to increase likelihood of heart disease

**1959** Some heart attacks discovered to be "silent" (causing no pain)

**1961** The term "risk factor" introduced

**1962** Cigarette smoking found to increase risk for heart disease

**1965** First Framingham report on stroke

**1967** Physical activity shown to reduce risk of heart disease. Obesity found to be associated with increased risk of heart disease.

**1970** High blood pressure shown to increase risk of stroke

**1971** Framingham Offspring Study begins

**1974** Diabetes, its complications and association with development of cardiovascular disease described

**1976** Menopause shown to increase the risk of heart disease in women

**1977** Effects of triglycerides, LDL and HDL cholesterol on cardiovascular disease risk described

**1978** Atrial fibrillation shown to increase the risk of stroke

**1981** Filter cigarettes shown to offer no protection against coronary heart disease

Major Framingham report on relationship of diet to heart disease

**1983** Framingham reports on epidemiology of mitral valve prolapse

**1987** Fibrinogen shown to increase risk of heart disease

**1988** High levels of HDL cholesterol shown to be associated with reduced risk of death

Isolated systolic hypertension shown to increase risk of heart disease

Cigarette smoking shown to increase risk of stroke

**1993** Mild isolated systolic hypertension shown to increase risk of heart disease

Major report on survival after diagnosis of heart failure

**1994** Enlarged left ventricle shown to increase risk of stroke

Lipoprotein (a) implicated as possible risk factor for heart disease

Risk factors for atrial fibrillation described

Apolipoprotein E shown to be possible risk factor for heart disease

**1995** Omni Study of minorities begins

**1996** Homocysteine implicated as risk factor for heart disease

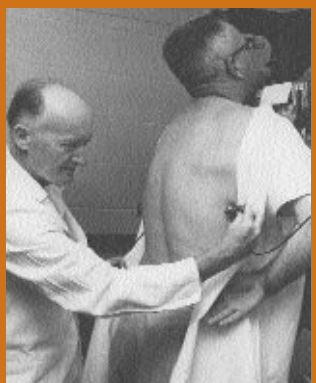
Progression from hypertension to heart failure described

**1997** Cumulative effects of smoking, high blood pressure and high cholesterol on the risk for atherosclerosis reported

Impact of an enlarged left ventricle on risk for heart failure in asymptomatic individuals investigated

**1998** New models developed to predict risk of coronary disease

Association of gene with risk of hypertension in men reported



This report is dedicated to you, the participants in the Framingham Heart Study, who have given the world the gift of knowledge. By volunteering your time, loyalty and good will during the past 50 years, you have shaped our understanding of the many interrelated factors that cause and prevent cardiovascular disease. In so doing, you have helped to save millions of lives.

## Thanks to you...

~ high cholesterol, high blood pressure, smoking, obesity and diabetes were identified as "risk factors"– a term coined by the Study – for cardiovascular disease.

~ we heard the groundbreaking news that we could modify these risk factors.

~ physicians began to practice preventive medicine, checking for risk factors, questioning their patients about lifestyle and encouraging positive changes.

~ we learned that sickness and health result from a complex mix of nature and nurture.

~ genetic causes for risk factors are being discovered.

~ we gained new perspectives on many other diseases, including cancer, arthritis, osteoporosis, eye disease, hearing problems and dementia.

~ we learned that we can do our part, as a society, to promote healthier lifestyles for longer lives.

1948

## NO STONE UNTURNED: Framingham residents help solve mysteries of cardiovascular disease

Sherlock Holmes and his sidekick Dr. Watson left no stone unturned as they painstakingly gathered evidence and searched for patterns in solving a mystery. Epidemiology is similar to detective work, as scientists slowly unravel the mysteries behind who gets sick, and why.

Deriving its meaning from the word "epidemic," epidemiology before 1948 dealt primarily with outbreaks of infectious diseases. That year, scientists at the U.S. Public Health Service were concerned about a non-infectious disease that had become the nation's number-one killer: heart disease.

For answers they looked to Framingham, Massachusetts, setting in motion the Framingham Heart Study, which would become one of the most important epidemiological studies in the annals of American medicine.

"The more than 10,000 Framingham citizens who have participated in the Study are as responsible for its major impact on the lives of individuals and families as the medical professionals who have devoted their careers to this research," says director Daniel Levy, M.D. "They have helped to create a national treasure in their own backyard."

### Watching and waiting

William B. Kannel, M.D., M.P.H., who directed the Study from 1966 to 1979, says, "We pioneered a novel approach in epidemiology. First, we dealt with a non-infectious disease and second, we looked at the relationship between lifestyle and disease. In 1948 it was very unusual

Singer-songwriter Vaughn Monroe was on stage at the Meadows on Route 9, singing "Yi-pi-yi-ay, yi-pi-yi-o...ghost riders in the sky," while men and women enjoyed their steak dinners in the smoke-filled room. "The Meadows was the first big nightclub and banquet hall in town," says Framingham Heart Study participant Victor Galvani. "You could go there for dinner, or for dancing, or to attend a large gathering, like a ball or wedding reception." The Meadows was built and partly owned by Monroe, who broadcast his famous "Camel Caravan," sponsored by Camel cigarettes, from there in the 1940s and '50s.

Plans would soon be made for Shoppers World, which would open in 1951. Designed to look from the air like a flying saucer, Shoppers World would became a prototype for a generation of indoor malls. Because gas was cheap and abundant and many people had cars, Shoppers World was advertised as a "homemaker's dream," and even included a kiddie playground.

### PROSPERITY SPURS SILENT EPIDEMIC

Amid the postwar prosperity symbolized by places like the Meadows and Shoppers World, however, was a silent epidemic: heart disease. Scientists from the U.S. Public

to ask how the lifestyles of people who suffered from heart disease differed from those who did not." The Study had another feature that made it unusual for its time: it included women.

***"It is of the highest importance in the art of detection to be able to recognize, out of a number of facts, which are incidental and which are vital."*** Sherlock Holmes in "The Reigate Puzzle," by Sir Arthur Conan Doyle

The first cohort included 5,209 healthy residents between 30 and 60 years of age. In 1971, 5,124 sons and daughters (and their spouses) of the original cohort were recruited for the Offspring Study. Today, approximately 500 (and growing) members of Framingham's minority communities are participating in a new facet known as the Omni Study. Each participant is given an extensive medical examination every two to four years.

Committed to their perception of heart disease in the United States as a true epidemic, scientists

Health Service chose Framingham to help them find out why. They assembled an executive committee of citizens and a medical committee of local physicians to serve as advisors for the project. These groups helped persuade healthy men and women to undergo detailed physical examinations every two years while scientists waited to see who developed heart disease, and who did not.

Chairing the executive committee at the start was Walter Sullivan, a teacher who became an attorney the following year. He and his wife, Katie, agreed to participate. Their four grown children later joined the Offspring Study, returning to Framingham over the years, from far and wide, for their checkups.

Victor Galvani, a young attorney who had returned in 1946 from four years of service in the Army, was also a member of the executive committee. His wife, Louise, whom he married in 1949, joined the Study in 1971 along with their son, Paul. Sullivan and Galvani are the only executive committee members still living.

"We were like a storefront," says Sullivan. "We gave the scientists a picture of the community. When they asked for our opinions on their plans, we'd usually say 'that sounds great.' We all felt that we were involved in something good."

looked carefully at biologic and environmental factors, recording not just the participants' blood pressures, electrocardiograms (EKG) and blood chemistry tests, but finding out what they ate and drank, whether or not they smoked and how much exercise they got. Mostly, they waited.

Why Framingham? "The government remembered Framingham's participation in a major study of tuberculosis in 1918," says Walter Sullivan, a member of the original cohort. "When this opportunity was offered to the town, it looked to many of us that it would be very beneficial." Other advantages included Framingham's proximity to Boston's major medical centers, the presence of several large employers and the support of a well-informed and highly cooperative medical community.

### One river, many tributaries

The Study took time. "When you start out with a population free of disease and must wait for

Slowly, people began to sign on. "Some people were reluctant," says Evelyn Langley, another original member who was then the mother of three young children and president of the PTA at the Woodrow Wilson School. "Early on, they were afraid the researchers would learn too much about their private lives and their families." Langley was recruited by the principal, and went door to door herself, persuading others to join.

Galvani says some people signed on because they were getting a bargain. "What an exam you got!" he says. "That was the biggest selling point. People would tell each other about how they were examined, for how long. The exams were much more thorough than what I was used to."

In those days, bacon and eggs was a common breakfast, exercise clubs were unheard of and many people smoked cigarettes. "In 1948, we paid little attention to diet," says Sullivan. "We ate what we wanted. My wife and I smoked. We ate meat twice a day. As a lawyer in solo practice, I worked every day until I finished. Never exercised.

"My wife and I already had our 25th exam," says Sullivan. "All through the years there were many changes. Sometimes we had our hearing and eyesight tested. Once I had a

the development of this disease in sufficient numbers to permit evaluation of the causative factors under consideration, there is a considerable lapse of time during which no conclusions are possible," wrote Thomas R. Dawber, M.D., the Study's first director.

In the solving of a mystery, one clue leads to another, then another and another; one question, instead of yielding easy answers, may lead to more questions. Similarly, as they witnessed the unfolding of heart disease over the years, the investigators found several, interrelated causes. (See "Risk factors," page 10.)

"When any kind of medical research project is undertaken, its findings must be corroborated elsewhere," says Claude Lenfant, M.D., director of the National Heart, Lung, and Blood Institute, which has supported the Study throughout its history. "The research in Framingham worked both ways. Not only were their findings corroborated by other studies; discoveries made by other scientists were corroborated in Framingham. By observing the presence of cardiovascular disease, Framingham identified a serious problem and laid the foundation for many other clinical investigations over the years that would be dedicated to finding solutions."

In time their investigations reached beyond the cardiovascular system, as they began to use the same methods to explore other diseases that appeared in their once-healthy subjects, such as cancer and arthritis. Now that most original participants are over 80 years of age, there is ample opportunity to study problems of older persons

psychological interview. But the core of the exam remained the same. Surrounding it were different things when the Study decided to go off in one direction or another."

Now Framingham is a famous study, and this reality has not gone unnoticed by the participants. "When we visit our daughter and her family in England and tell people where we're from, they ask about the Framingham Heart Study," says Sullivan.

"We may have been reluctant back then," says Langley, "but today people say, 'I'd give my right arm to be in the Study!'"

such as osteoporosis and dementia. "The fact that Framingham today explores not just cardiovascular disease but many other diseases as well makes it a unique, living textbook of medicine," says Lenfant.

### Three phases of detective work

Levy divides the Study into three phases. "The first 30 years were devoted to traditional epidemiology," he says. "Scientists took meticulous measurements of everything they saw. All they had to go on were clinical observations and early tests such as the electrocardiogram and chest x-ray. As they watched disease develop, they counted up events. For example, they saw that obese people, individuals with high blood pressure and high cholesterol levels, and people who smoked were more likely to develop heart disease.

"During the second era, which began in the late 1970s, new technologies came into play and tools for observation became more refined," says Levy. "Researchers could use echocardiography to measure the heart's function as well as its form. Exercise stress tests, Holter monitors and carotid artery ultrasound also offered clearer pictures of the cardiovascular system and its functions.

"The third phase, which began in the late 1980s, is focused on molecular genetics. We are keeping Framingham on the cutting edge of efforts to locate the genes responsible for clinical risk factors and disease. We are now investigating the

## 1971

**D**owntown Framingham was vibrant, anchored by Dennison Manufacturing, where a variety of paper goods were made, and the General Motors (GM) plant. Three movie theaters enlivened the community. Shoppers filled the stores and the streets. GM employees could buy shoes at Kiley's on their lunch break, or after work. Owned and operated by Framingham Heart Study participants Florence and William Kiley, the shoe store on Kendall Street was taken over by their son, Bill, after they died in 1969.

When Bill and his sisters Janice and Karen Kiley were recruited for the Offspring Study in 1971, they eagerly agreed because they wanted to continue the work their parents had begun.

Today, Karen Kiley LaChance, 53, a local realtor, has been in the Study half her life. "I was 27, still single, and probably dressed in bell-bottoms when I went in for my first exam," she says. Since then, LaChance has participated in the core study as well as osteoporosis and arthritis studies.

*continued on page 12*

possibility of enrolling a third generation of participants, which would vastly increase our opportunity to study the role genes play in common diseases," Levy says.

### "They have taught us"

In Framingham, the participants applaud the investigators, and the investigators praise the participants. "The whole atmosphere here has always been gracious and welcoming. Once in a while when we get reports there is a personal note attached, thanking us for coming in," says Sullivan.

In a recent interview published in the *Journal of the American Medical Association*, William P. Castelli, M.D., who directed the Study from 1979 to 1995 and now serves as medical director of the Framingham Cardiovascular Institute, credited Dawber, the Study's first director, with setting the stage for participant appreciation. "He emphasized that we weren't doing the participants a favor by taking care of them, they were doing us a favor by getting involved in the Study," said Castelli. "He got us to understand that these men and women were giving of their time to help us and to help the world. This Study is their gift to the rest of the world; they have taught us."

### Administration of the Framingham Heart Study

In 1948, the Framingham Heart Study was initiated by the U.S. Public Health Service, and was the brainchild of Assistant Surgeon General Joseph Mountin, M.D., an ardent advocate of epidemiological approaches. Gilcin F. Meadors, M.D., a young Public Health Service officer, was charged with organizing the Study.

That year, the National Institute of Health (NIH) was expanded to encompass several institutes, each devoted to the study of particular diseases. The National Cancer Institute was established first, followed by the National Heart Institute in 1949. The Framingham Heart Study was transferred to the Heart Institute, now known as the National Heart, Lung, and Blood Institute, and remains under its direction today. Since 1970 the Framingham Heart Study has been closely affiliated with Boston University School of Medicine.

### Framingham Heart Study directors

Thomas R. Dawber, M.D., 1949-1965

William B. Kannel, M.D., M.P.H., 1966-1979

William P. Castelli, M.D., 1979-1995

Daniel Levy, M.D., 1995-present

# A DAY AT THE CLINIC

Having fasted since 8:30 the night before, Karen LaChance arrives at the Framingham Heart Study, a small brick building downtown on Thurber Street, at 8:30 a.m., and is greeted by project coordinator Marian Bellwood. She puts on a robe in the changing room and locks up her clothes and valuables. LaChance knows she will be there for four hours, and has taken the time off from her job as a local realtor.

Like most other Framingham Heart Study participants, LaChance uses medical terminology quite comfortably as she describes each procedure she is prepared to undergo.

"Over the 27 years I've been coming here," she says, "the visits have included different types of tests as new technologies entered the picture. Most of the core tests have remained the same."

Today, LaChance's visit will include the following experiences and procedures.

~ Blood will be drawn and later tested in the lab for cholesterol levels. White blood cells will be separated out for DNA testing.

~ A urine sample will be analyzed for glucose and protein.

~ She will be given a beverage of methionine and orange juice that, two hours later, will reveal the level of homocysteine in her blood.

~ Measurements of height, weight and blood pressure will be obtained. Skin folds will also be measured with a caliper, particularly the upper arms, waist and thighs.

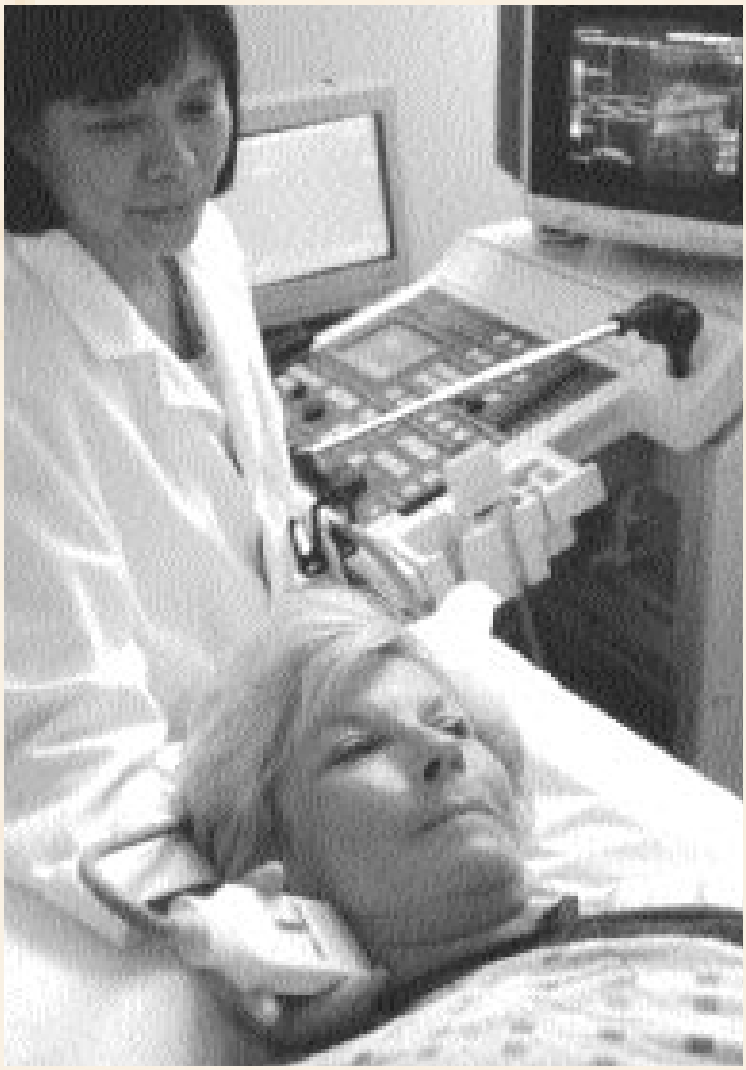
~ She will be examined by a physician.

~ An electrocardiogram (EKG), a test that measures the electrical activity of the heart, will be administered.

~ LaChance will also be given an echocardiogram, which uses ultrasound to create moving pictures of the heart. "With this test you lie on your side, the technician holds a microphone to your chest, and you can see your heart beating on a computer screen," she says.

- Another ultrasound test will show blood flow in the carotid arteries in the neck.
- A pulmonary function test, which LaChance describes as the most exhausting feature of her visit, will show lung capacity. "They put a clothespin on your nose and ask you to inhale as deeply as you can, through your mouth. Then you blow with all your might into a hose-like device. You exhale as hard and as long as you can, until you are coughing out air. Then they coach you to repeat the process one or two more times."

Last but not least, LaChance will be interviewed by one of the researchers and asked about her lifestyle. "They ask questions such as 'do you smoke, drink, take any medications,'" she says. "Often, there is paperwork to take home, in which we must give detailed information about dietary habits and activity levels.



"What I appreciate most about the staff is that they never make judgments. They don't comment if you've gained a little weight, for example. They are there to gather evidence, not to criticize."

Information from LaChance's visit, like all her previous ones and those of her parents and siblings, will become part of the vast body of knowledge that is the Framingham Heart Study. Her records will be added to, and compared with, records from her former visits. They may be compared with the records of her parents, at the same age. Other information, such as reports from her own physician or records of hospitalizations, will be merged with the Framingham data. This prospective information-gathering will enable researchers to differentiate certain risk factors and conditions, should a cardiovascular event occur in the future.

## RISK FACTORS

# Study holds lifestyle partly responsible for sickness and health

The Framingham Heart Study investigators often had to work backwards. They waited for disease to develop; when it did, they looked back to see what those participants had in common, and how they differed from their friends and neighbors who remained disease-free. After only four years, with 34 cases of heart attack, investigators pinpointed high cholesterol, high blood pressure (hypertension), obesity and abnormalities of the electrocardiogram as important factors in the development of cardiovascular disease. Over the years, these clinical findings were studied in greater depth, their causes were identified, other risk factors were added and their relationships were explored.

### Framingham Heart Study coins a phrase

In 1948, illness was viewed by many in the same light as accidents. People who developed cancer or heart disease were unlucky. They did not cause it, any more than they could cause an accident of nature.

By coining the expression "risk factor," the Framingham Heart Study helped to change the practice of medicine. Suddenly, individuals could influence their health status. Kannel says, "We were able to tell people, 'Your life is in your own hands. You personally can reduce your risk for heart attack.'" Just as important, the Study influenced physicians to place greater emphasis on prevention, as well as on detecting and treating risk factors in their earliest stages.

Today, the lessons learned in Framingham are common knowledge. In fact, it's hard to remember a time when cholesterol and other risk factors were not considered to be problems.

Victor Galvani, a member of the original cohort, remembers that time. "I grew up in an Italian household," he says. "We ate plenty of cold cut dishes and other heavy foods. We made no effort at all to modify our eating habits."

### Study focused on strokes, too

The term "cardiovascular," which has always been the focus of research in Framingham, pertains to the heart and blood vessels. Thus, the Study has also devoted much of its research to the prevention of stroke. "Most of what we know today about risk factors for heart disease and stroke came out of Framingham," says Philip A. Wolf, M.D., a neurologist specializing in stroke who has been principal investigator of the Framingham Heart Study contract since 1989.

"Stroke is a more complex event than a heart attack," explains Wolf. "About 13 percent of strokes are caused by a hemorrhage, or bleeding, in the brain. This type is usually very severe. The rest are infarcts caused by a clot in an artery anywhere in the brain, or an embolism, which is a clot elsewhere in the body that travels to the brain. Many of the same risk factors that lead to heart attacks lead to strokes."

Philip A. Wolf, M.D.

In addition, Framingham researchers found that atrial fibrillation, a rhythm disturbance in the heart, is a major risk factor for stroke. "Because the upper chamber of the heart is not pumping properly with this condition, clots can form that travel to the brain," says Wolf. Another finding was that individuals whose heart muscle appears thickened and enlarged when measured by ultrasound are at increased risk for stroke.

### Normal does not mean ideal

With regard to both cholesterol levels and blood pressure, a key lesson learned in Framingham is that no line divides safety from danger. Rather, in both cases, there is a continuum, a gray area that

becomes dangerous when genetics or additional risk factors come into play. And where scientists once recommended "normal" values, they are now recommending "ideal" values, which means even lower numbers.

### Interactions among risk factors: nature vs. nurture

Not only do risk factors for cardiovascular disease tend to run in families; they tend to work together to cause disease, each one bolstered by the others. For example, high levels of cholesterol deposit plaque on the walls of the arteries (atherosclerosis), forcing the blood through a narrow passageway that can become blocked; this problem is compounded by hypertension or high blood sugar.

Above all, Framingham taught us that both nature and nurture are involved in the development of cardiovascular diseases. Genes plays a permissive role, making some people more susceptible than others to certain risk factors.

***"In solving a problem of this sort, the grand thing is to be able to reason backwards. That is a very useful accomplishment, and a very easy one, but people do not practice it much."*** Sherlock Holmes in "A Study in Scarlet"

Taking into account the way risk factors interact with one another to promote heart disease, Framingham researchers have developed a new score sheet that can help predict a person's risk for angina, heart attack or death from heart disease. By incorporating information on multiple factors, the score sheet gives a simple estimate of an individual's likelihood for developing heart disease in the next 10 years.

### Risk factors identified by the Framingham Heart Study

#### High cholesterol

It was in Framingham that cholesterol became a villain in the story of heart disease. This fat-like substance, which is needed by cells, can build up inside the arteries and lead to heart attack or stroke. Cholesterol travels through the blood stream in several forms including low-density lipoprotein (LDL) and high-density lipoprotein (HDL). LDL is "bad cholesterol" because it deposits extra cholesterol on the walls of the arteries. HDL is "good cholesterol" because it removes cholesterol from the arteries. Today, Framingham investigators are searching for genetic causes of HDL and LDL levels.

Another lipoprotein, Lp(a), is now thought to cause harm, as well. Unlike LDL, Lp(a) does not appear to promote fatty buildup in the arteries. Instead, its damage may come from preventing the breakup of clots.

#### Hypertension

In 1948 it was thought that high blood pressure (hypertension) was necessary to force blood through the stiffened arteries of older persons and that it was a normal part of aging.

Blood pressure readings are given in two numbers, one over the other, like a fraction. The top number (systolic) measures blood pressure as the heart contracts; the bottom number (diastolic) measures blood pressure as the heart relaxes.

Framingham researchers dispelled these myths. Hypertension is a disease in itself, they said, and if left untreated it can lead to heart attacks and strokes. Another Framingham finding is that elevation of systolic pressure is just as dangerous as elevation of diastolic pressure.

### Smoking

Before Framingham, smoking was not accepted as a bona fide cause for heart disease. The Study soon demonstrated that smokers were at increased risk of having a myocardial infarction or dying suddenly. Further, the risk was found to be related to the number of cigarettes smoked each day, and smoking cessation could halve the risk for people who stopped, compared with those who continued.

### Obesity

Obesity was found to contribute to cardiovascular disease by itself, and more importantly, to promote other major clinical risk factors. Framingham research demonstrated a protective effect on the heart from even low levels of exercise. It was also learned that both men and women who "weight cycled" (repeatedly lost and gained weight) were at increased risk of cardiovascular disease.

### Diabetes

Impaired glucose tolerance was shown by Framingham scientists to be a contributor to cardiovascular disease. People with Type II diabetes (which appears in middle or old age primarily

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### Lessons for baby boomers

Today, many Offspring Study participants, most of whom are baby boomers, are still young enough to reap the rewards of the Study's findings. "The biggest thing the Framingham Heart Study taught us, and the world, is the danger of cholesterol," says Offspring participant Bob Fair. LaChance says the greatest lessons are "the importance of a balanced, low-fat diet, the benefits of exercise and the dangers of smoking."

LaChance works out on a treadmill at her health club, runs 12 miles a week and follows a low-fat diet. She quit smoking in 1984, and credits the study for the fact that her lifestyle is healthier than that of her parents. "As we were growing up, our family ate meat every day," she says.

among overweight people) are twice as likely to develop cardiovascular disease, and people with high blood sugar, who have not yet developed diabetes per se, are 1.5 times as likely to do so. People with Type II diabetes are also more likely to have high overall cholesterol, low levels of HDL and hypertension.

### New risk factors

High levels of the amino acid homocysteine may promote heart disease, stroke and a reduced flow of blood to the hands and feet. Researchers believe that homocysteine may contribute to the buildup of fatty substances in the arteries. Levels of the amino acid are related partly to a genetic mechanism and partly to diet.

Viruses and other infectious agents also may harm blood vessel walls, starting the atherosclerotic process. Framingham researchers are investigating whether cytomegalovirus (CMV), chlamydia and *H. pylori,* a bacterium that causes stomach ulcers, influence the development of coronary disease.

Fibrinogen, a substance that promotes blood clotting, was also identified as a risk factor.

### Cardiovascular disease in women

From the beginning, the Framingham Heart Study compared the risk factors of men and women. Investigators had observed that in women, cardiovascular disease occurred later in life, and wanted to know why. Today, more women die from cardiovascular disease than from any other cause, including all cancers combined, which underscores the importance of continued research.

Framingham taught us that while men begin to suffer from coronary artery disease earlier in life than women do, women are more likely to die from coronary complications once they are affected. Framingham also taught us that Type II diabetes is more prevalent in women than in men, and is for women a particularly potent risk factor for cardiovascular disease.

"We had a lot of comfort foods, such as stews and casseroles. If we had chicken, it went in the deep fryer. We drank Pepsi and had cupcakes for dessert. My parents smoked and never exercised," she says, "partly because it just wasn't done, and partly because they couldn't afford to take up golf or other activities."

James Fair, a fourth-grade teacher, says his meals while growing up featured canned foods. "We ate a lot of Franco-American spaghetti," he says. "I thought vegetables came in cans." He points out, however, that the fast pace of his own life, and the lives of his peers, sometimes counteracts the benefits of greater knowledge. "We may be more knowledgeable than our parents, but they were more relaxed and content," he says. "We are too busy to apply our knowledge."

1995

## FAMILY MATTERS
### Multigenerational aspect of study offers genetic goldmine

Since 1971, Framingham researchers have been able to compare the physiologic functions and disease rates of the original participants, at a specific age, with those of their children at the same age. Today, advances in genetics enable researchers to probe more deeply into reasons why parents and their children have similar or different disease profiles.

After years of observation, Framingham Heart Study scientists learned that the answer to their original question, "Why do some people develop cardiovascular disease while others do not?" only partially has to do with lifestyle and traditional risk factors. Some answers are tangled up in DNA.

Researchers began collecting blood samples for genetic research in the late 1980s, and now have approximately 5,000 samples. Researchers are also scanning samples from 1800 members of the largest Framingham Heart Study families (parents, children, aunts, uncles and cousins), looking for genes that control the major risk factors for heart disease and other conditions.

"Framingham offers an unparalleled opportunity for genetic research," says Richard Myers, Ph.D., a genetic epidemiologist at Boston University who oversees this segment of research in Framingham. "Because we have such a rich base of blood samples from families, we can examine the DNA of individuals who have certain risk factors, and compare it with samples from individuals who do not. This helps us narrow down the region where the responsible gene may be located."

On Oct. 22, 1994, during a visit to Framingham High School where the Elementary and Secondary Education Act was signed into law, President Clinton told students and other supporters that "our diversity in America is a goldmine of opportunity."

Framingham had a population of 64,989 then, and 11,464 were minorities. The Latino population was highest among those, with 5,291 residents. Once a homogeneous, white middle-class suburb, this town had become more like a city, with an ethnic patchwork that included African Americans and new immigrants from Latin America and Asia.

### OMNI STUDY BEGINS

Early the following year, the Framingham Heart Study began recruiting its minority population for the "Omni Study."

When 5,209 people were chosen for the Study in 1948, a random sampling was taken. Because few minorities were living in the town at the time, no conclusive information about specific minority groups could be culled.

The Omni Sudy, with its narrower focus, would help health officials understand how and if heart, lung and

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### Combing chromosomes for culprits

Genetic research involves separating white blood cells from red, then extracting DNA. Linkage studies are then used to identify a region or locus "linked to," or potentially involved in, a specific disease. Framingham researchers are currently studying the genetic markers spaced evenly along the chromosomes to find an association between a chromosomal region and the manifestation of a particular disorder.

***"My dear Watson, you as a medical man are continually gaining light as to the tendencies of a child by the study of the parents. Don't you see that the converse is equally valid. I have frequently gained my first real insight into the character of the parents by studying their children."***

Sherlock Holmes in "The Adventure of the Copper Beeches"

For example, researchers are working to identify regions of chromosomes that appear to contain a gene that protects some individuals from developing heart disease, as well as a gene that puts other individuals at greater risk. The first gene causes high levels of HDL, or "good cholesterol." The second causes high levels of LDL, or "bad cholesterol."

A variation in the ACE (angiotensin converting enzyme) gene may be an important contributor to hypertension in men. Using molecular linkage techniques, researchers examined 1,044 pairs of siblings from the Framingham Offspring Study and found the ACE variant gene in 30 percent of the men and women. Men with the ACE variant had a 59 percent increased risk for hypertension. No relationship between the gene and hypertension in women was found.

Although the region containing the ACE gene was implicated, the researchers could not tell for sure whether this gene or another nearby gene is responsible for raising blood pressure. They must now conduct finer chromosomal mapping to pinpoint the position of the responsible gene.

### Genetic discoveries yield more effective treatments

Myers warns against a fatalistic approach to genetics. "It's important for people to realize that if they suffer from a disease that runs in their family, they can still do something about it. Diseases with genetic components are very treatable; hypertension treatment is a good example. Genetics may empower physicians to tailor treatments to an individual expression of a disease, and empowers individuals to lower their risk by lifestyle changes." Myers emphasizes that the work in Framingham has only begun to scratch the surface of genetic research opportunities. The most exciting findings are yet to come.

## BEYOND HEARTS

The Framingham Heart Study began primarily as an investigation of coronary heart disease, the most common form of cardiovascular disease. Soon the Study broadened its focus to other forms of cardiovascular disease, and over the years has also provided key insights into the epidemiology of stroke, heart failure, peripheral arterial disease and arrhythmias.

Today, the loyal participation of two generations of Framingham residents has allowed scientists to observe the development of other diseases as well. Although cardiovascular and lung disease remains at the center of the Study and this core work is supported by the National Heart, Lung and Blood Institute, other major research efforts have piggybacked onto Framingham. They include investigations of cancer, dementia, arthritis, diabetes, kidney disease, osteoporosis, eye disease and hearing disorders.

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blood diseases exist disproportionately in some groups, see if risk factors associated with these diseases are the same or different among minorities than among the other two cohorts, and find out if the so-called Americanization of some minorities had become detrimental to their health.

"It is important that the Study reflect the diversity of Framingham," says Levy. "This diversity gives us a chance to observe, and compare, the risk factor levels and unfolding of certain diseases in various groups."

Jeannie Nakano, 49, who is of Asian descent, enrolled in the Study in response to a newspaper ad. "Framingham is the only longitudinal study I know of, and being part of it seemed like a worthy cause," she says. "All my life I've been aware that many health statistics, even height and weight charts, are based on homogeneous populations, and do not apply to me. I wanted to do my part to make sure future studies more accurately reflect the American population."

Nakano also signed up for the same reasons the original participants signed up in 1948: a good deal. "My reasons were not entirely altruistic," she says. "At my age, I am more concerned about my health. I wear bifocals. Things are changing. These exams will give me a complete picture over the years."

*"We approached the case, you remember, with an absolutely blank mind, which is always an advantage. We were simply there to observe and to draw inferences from our observations."*

Sherlock Holmes in "The Adventure of the Cardboard Box"

This brochure was supported by the Friends of the Framingham Heart Study through an unrestricted grant from Pfizer Pharmaceuticals Group and Parke-Davis.

Copywriting: Cleary Communications, Design: Schenkel/Stegman Communications Design, Photography: Tony Rinaldo and archives, Public relations and project management: Wanger Associates

**The Framingham Heart Study is a research study of the National Heart, Lung, and Blood Institute, and is operated in collaboration with Boston University.**