# T H E
# F R A M I N G H A M
# S T U D Y

An Epidemiological Investigation
of
Cardiovascular Disease

Sections 1 and 2

Framingham Study

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June 1968

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## Section 1



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# INTRODUCTION

In 1948 the United States Public Health Service undertook to study the factors associated with the development of atherosclerotic and hypertensive cardiovascular disease by the long-term surveillance of a sample of the adult population of Framingham, Massachusetts. The study has been reported at various stages; key findings have been presented in numerous papers--some published, some not. However, it is useful to reconsider at this time the reasons for bringing the study into being and to prepare a systematic account of the major findings. That is the purpose of this monograph.

Previous accounts, where still appropriate, will be retained. Most of the material, however, will be new. The study cohort will be uniformly characterized, using the information collected on the first 7 biennial examinations. The incidence of new cardiovascular events will be described through the first 14 years of follow-up, that is, essentially through the 8th examination.

This will not be a complete and definitive account of the Framingham study. For one thing, it will be prepared in sections, over an extended period. For another, the study is still in progress. But even if data collection had stopped, more information has already been accumulated than could be accommodated in one monograph, no matter how thick. Moreover, as differing points of view, new hypotheses, and new analytical devices become available, the data will be re-worked for new insights. In that sense, the Framingham Study can be thought of not as a unique effort, but rather as a continuing resource for the study of cardiovascular disease.

Elsewhere we have listed the people who have worked on the Framingham Study over the years. The credit for this monograph is theirs, jointly and as individuals. But, of course, special credit must go to two individuals--Dr. Thomas R. Dawber and Mr. Felix E. Moore--who together guided the destinies of the study for so long. Dr. Dawber, as director of the Study, and Mr. Moore, as senior statistician of the National Heart Institute brought together from the beginning a unique combination of medical and statistical competence. It is this melding that gives the Framingham Study its special solidity. It is their contributions over many years that, in the final analysis, make this monograph possible

# THE FRAMINGHAM STUDY

## Rationale

In 1947, when the U.S. Public Health Service began to lay plans for setting up an epidemiological study of the cardiovascular diseases, little was known of the epidemiology of hypertensive or arteriosclerotic cardiovascular disease.

The scanty epidemiological knowledge of these diseases which did exist was based either on the study of mortality statistics, often not very revealing in the investigation of long-term diseases, or on clinical studies. It was felt that the best hope for new insights lay in the study of these diseases in populations of normal composition, including both the sick and the well.

Studies using the epidemiological method have led to findings of considerable practical importance for prevention and treatment of cardiovascular diseases. Mention may be made of the studies of nutritional diseases, such as beriberi, pellagra, and scurvy, and of the infectious diseases such as syphilis, hemolytic streptococcal infections, and streptococcus viridans bacteremia. Rubella in the first trimester of pregnancy and other virus diseases have been implicated as etiological factors in congenital malformations of the heart. However, rheumatic fever and the other diseases mentioned account for only a very small proportion of the morbidity or mortality from cardiovascular disease, whereas hypertensive and arteriosclerotic cardiovascular disease account for the great bulk of deaths from cardiovascular disease.

The Framingham Study, therefore, focused on arteriosclerotic and hypertensive cardiovascular disease. These were and are the most important of the cardiovascular diseases and when the Framingham Study began the least was known about their epidemiology. As a working hypothesis it was assumed that these diseases do not each have a single cause, but that they are the result of multiple causes which work slowly within the individual. It was recognized that, for the most part, specific and unambiguous tests for precise diagnosis of the early stages of these diseases were lacking.

The study proceeded by the following plan: A probability sample of persons in the ages where arteriosclerotic and hypertensive cardiovascular disease are known to develop was selected for study. Based on as complete a clinical examination as feasible, the presence or absence of definite evidence of these diseases was determined. Persons free of overt disease would be observed over a period of years until a sizable number were found to have acquired the diseases. A search would be made for the factors which influenced the development of these diseases by classifying the population according to characteristics believed to be related to their development and looking for associated differences in disease incidence.

As one by-product of this investigation it would also be possible to study the efficiency of various diagnostic procedures in finding heart disease or their effectiveness as indicators of the subsequent development of overt heart disease. (These findings, of course, would have important bearing on the question of including tests for heart disease in mass screening programs.) A second by-product would be data on the

natural history of cardiovascular diseases, including prevalence, incidence, recurrence and survival.

The general approach was described in the original protocol in these terms :

"If it is accepted:

"That pathological change in or disordered function of the intimate structures of the cardiovascular system resulting from stresses and insults of various types is reversible up to a degree or point which is inherent in the individual, and

"That pathological or physiological change beyond that degree probably results in minute residual changes which are immeasurable by methods now available, and

"That continuous accretion of such residual changes results finally in a clinically recognizable abnormality, and

"That there is a wide variability in the individual response to many stresses and insults.

"It is hypothesized that the age of onset of degenerative cardiovascular disease is a function of three variables:

(1) Constitutional factors (including hereditary factors)

(2) Conditioning factors (including external environmental factors), and

(3) The time factor or length of time the conditioning factors must act on the constitutionally determined characteristics or interact with them to result in clinical cardiovascular disease.

"The Framingham Heart Disease Epidemiology Study is designed to measure certain selected constitutional factors and certain of the conditioning factors in a large number of 'normal' persons selected at random and to record the time during which these selected factors act and interact before clinical cardiovascular disease results."

With these aims set up, it was then necessary to define the population on which the study would be carried out. Ideally, perhaps, epidemiological investigations of cardiovascular disease should be set up in a number of widely separated areas simultaneously, so that various racial and ethnic groups will be represented, and a variety of geographic, socio-economic, and other environmental factors can be considered. The results of a study of a single area will have generality only in so far as the population of the area is representative of some larger population. Many thousands of persons should be included to allow for numerous axes of analysis, and it would be profitable to follow a cohort of individuals from birth to death. Because of the expense of examination and follow-up, however, it was not practicable to carry on studies simultaneously in several areas, nor to observe more than a few thousand persons for a limited number of years. It was not considered economicalto include persons less than **30** years old or more than **60.** Because of their great mobility young people are hard to follow, and because of the low incidence of cardiovascular disease in this group the person-years of experience required would be high. Older -persons, on the other hand, probably include so many persons who are subclinically ill that they form a poorgroup for prospective studies. It was concluded, therefore, that the

study should be set up in a single area, and that coverage would have to be limited to approximately 6,000 persons in the age range 30-59 years. This group would be observed for a period up to 20 years. A town of 25,003 to 53,000 population will supply the required number of adults, and it was felt that a town of this size would be more desirable than a larger city for the type of community approach required to secure full cooperation and coverage.

The limitation in geographic coverage clearly limits the generality of conclusions which can be reached. There is reason to believe that some communities in the United States differ considerably from the average with respect to arteriosclerosis and hypertension. On the other hand, in the white race in the United States the within-community variance in the distribution of arteriosclerosis and hypertension is probably very much greater than between-community variance, and a wide range of type-situations influencing development of these diseases may be found in any community. This presumption could only be tested, of course, by similar studies in other communities; in fact, later studies have borne it out.

In mid-1947, Dr. Vlado A. Getting, State Health Commissioner for Massachusetts, offered to cooperate with the U.S. Public Health Service in setting up the study in that state. After consideration of a number of possible areas the Town of Framingham was selected. Framingham, lying 21 miles west of Boston, is an industrial and trading center of 28,000 population. As is true of New England towns, it includes not only the built-up business and residential areas but also the outlying rural area

within the town limits. Framingham has the town-meeting form of government and the people are accustomed to and well versed in the group approach to their problems. It was in Framingham that the first communit study of tuberculosis was undertaken--z program sponsered by the National Tuberculosis Association and the Metropolitan Life Insurance Company, which began in 1917 and continued successfully for six years. This latter fact, together with an indication of interest in response to the initial approach, influenced to some extent the selection of the town.

## Early history

Up to this point in the account, the beginnings of the study may appear relatively immaculate. However, pioneering studies (and the Framingham Study was such a study) seldom arise this way. A brief history of the early beginnings may make this a little clearer.

The Heart Disease Epidemiology Study had its beginnings in October 1947 in a cooperative project of the Massachusetts State Department of Health (Dr. Vlado Getting, Health Commissioner), the Department of Preventive Medicine at the Harvard Medical School (Dr. David D. Rutstein, Chairman) and the Heart Disease Demonstration Section of the U.S. Public Health Service (Dr. Bert R. Boone, Chief). At the initiative of Dr. Joseph W. Mountin, Assistant Surgeon General, Drs. Lewis C. Robbins and Gilcin Meadors were detailed to organize a heart disease study in the Boston area. Working out of quarters at the Harvard Medical School, and with the advice and assistance of the various cooperating organizations, they canvassed opportunities for study populations. By December 1947 it was decided to initiate two programs, one to be known as the Cardiovascular Hygiene Demonstration under the direction of Dr. Robbins, the other to be known as the Heart Disease Epidemiology Study under the direction of Dr. Meadors. The first study was to be located in Newton, the second in Framingham, Massachusetts.

The purpose of the Newton program was to determine what existing knowledge of prevention, diagnosis, treatment and rehabilitation of cardiovascular disease could be applied within community health programs.

The purpose of the Framingham program, as it was originally conceived, was the development of case-finding procedures in heart disease. The potential of the Framingham program for epidemiological studies soon became apparent, however, and the program turned increasingly in that direction.

Because of the research orientation of the program, the question of including it among the activities of the National Heart Institute was raised. After a review by Dr. C.J. Van Slyke, Director of the National Heart Institute, Dr. James A. Shannon, Director for Research, and Felix E. Moore, Chief of Biometrics, the National Heart Institute arranged to accept the transfer of the Framingham Heart Disease Epidemiology Study (as it was then called) on July 1, 1949.

In the meantime operations had already begun at Framingham in a clinic located at the Framingham Union Hospital. The clinic was formally opened on October 11, 1948 but examinations had already begun by September 29. By the time the study was transferred to the National Heart Institute, more than 1500 volunteers had been examined. A large amount of the groundwork for the later study had already been laid. A community had been selected for study and community participation had been obtained. Quarters had been prepared and staff recruited. The first series of examinations had been designed and put in motion. The purposes and direction of the study had slowly hardened.

It was already understood that the general epidemiological purpose of the study was the "determination of factors influencing the development of heart disease," and that the program would require repeated examinations of the study cohort. Important assistance in this early design came from a Technical Advisory Committee which included the following members:

Edward F. Bland, M.D., in charge of follow-up program in Rheumatic Fever, Massachusetts General Hospital, Boston,

Laurence B. Ellis, M.D., Chief, Cardiology Service, Boston City Hospital.

James M. Faulkner, M.D., Cardiologist, Dean, Boston University Medical School.

Burton E. Hamilton, M.D., Chief, Cardiology Service, Boston Lying-In Hospital.

Hugh R. Leavell, M.D., Professor of Public Health Practice, Harvard School of Public Health, Boston.

Samuel A. Levine, M.D., Chief, Cardiology Service, Peter Bent Brigham Hospital, Boston.

Benedict F. Massell, M.D., Secretary, New England Heart Association; Associate Director of Research, Good Samaritan Hospital, Boston.

Loren D. Moore, M.D., First Assistant to Commissioner, Massachusetts Department of Public Health.

Samuel H. Proger, M.D., Chief of Tufts Cardiology Service, Pratt Hospital, Boston.

David D. Rutstein, M.D., Professor of Preventive Medicine, Harvard Medical School, Boston.

Other distinguished physicians, such as Howard Sprague and Conger Williams, joined this group later. The Technical Advisory Committee not only supplied technical advice but was of help in recruiting expert assistance for the study operation.

When the Framingham Study became the responsibility of the National Heart Institute a new study protocol and a sampling scheme was introduced This was the work jointly of Mr. Moore and Dr. Meadors. Both thesampling scheme, which was finally spelled out in December, 1949, and the study protocol, which was completed a month earlier, were really structural overlays on an ongoing study.

These were the beginnings. In April 1950 Dr. Thomas R. Dawber assumed direction of the study. Under his stewardship the study began a long period of growth and productivity. The formative period was by no means over but the study was now well on its way.

Community arrangements

A program which involves medical examination of large numbers of people requires the acceptance, endorsement, and support of the medical profession. The plans for the project were given the endorsement of the Massachusetts Medical Society. In Framingham the medical groups which centered around the two local hospitals offered their active support to the program as proposed. (One of the hospitals has since closed; the other continues a close cooperation with the study).

From an administrative standpoint it was necessary to secure clinic facilities and recruit a professional and technical staff. A centrally located residential building was remodeled for clinic and laboratory space, and diagnostic equipment installed. A staff was organized, including the examining physicians; a clinic nurse; x-ray, electrocardiography and laboratory technicians; statisticians; interviewing and administrative clerks; a health educator; and visiting consultants in the fields of cardiology, electrocardiography, roentgenology, pathology, and biochemistry.

As a start, a health educator was placed in the health Department with the assignment of studying the community. This meant not or-&-learning about the history, resources, and government of the town, but, more important, getting to know the people--their national origins, economic conditions, and lines of social stratification, their religious,

fraternal, and civic organizations; and their recognized and potential leaders. From this study grew plans for the appointment, by the Town Health Officer, of an Executive Committee of 15 persons for the study--a committee which was broadly representative of the various groups in the community. Parallel to, and integrated with, the lay Executive Committee there was organized a Professional Committee of physicians and dentists under the chairmanship of a cardiologist. Together, the Executive Committee and the Professional Committee accepted the following responsibilities:

1. To assist in planning a program which would be acceptable to the community as a whole.
2. To interpret the aims and objectives of the study in a way which would be understandable to all eiements of the community.
3. To bring recognized and potential leaders of the community into active participation in the organizational aspects of the study.

After analysis of the community organization requirements of the study by the Executive Committee, six sub-committees were set up: Arrangements, Publicity, Industry, Business, Civic Organizations, and Neighborhood Organization. The Arrangements Committee assisted in the operation of the study by providing clerical assistance and transportation. The Publicity Committee, composed of residents who warespecialists in the areas of press, radio, advertising, and associated fields developed a plan for publicity media to be used in placing the program before the community. The Industry, Business, and Civic Organizations Committees

brought the study to the attention of their special Publics.

Perhaps the most important of the committees, however, was the Neighborhood Organization Committee. It had been the aim that every participant in the study should come into it on the basis of an invitation from someone he knew, and in whom he had confidence, and further that the invitation should come from a person who had been through the clinic. At the start, therefore, examinations in the clinic were offered to all members of the committees and these, in turn, passed word of the study to other members of the community who were encouraged to volunteer for examination. From these volunteers a set of neighborhood committees was selected. To those committees fell the all-importart job of inviting the initial participation of the selected individuals and later stimulating cooperation in return for follow-up observation.

Use was made of standard publicity channels to inform the people about the program. However, it was discovered from sampling the opinion of persons volunteering for the study that the most valuable public information came through uord of mouth.

Sampling plan

The choice of a sampling plan for this study was dictated by a number of considerations, some of which have already been suggested. The number of cases which could feasibly be studied--6,000--was much smaller than the total adult population of Framingham. Therefore, some method had to be introduced to select persons and avoid the unknown biases of self-selection. The total sample had to be allocated in such a way as to yield the maximum information over the period that the study was to be carried out. And the plan had to be such that it would be acceptable to the community, and could be carried out through the community organization.

One important decision which had to be reached concerned the age range of the study population. Clearly, if only a very young group was studied, only a very small number would develop arteriosclerotic or hypertensive cardiovascular disease even in 10 to 20 years' time and since this is a mobile age group they would be difficult to re-examine regularly. On the other hand, in a very old group there would be too largea proportion with pre-existing cardiovascular disease. To balance these two effects, the age group 30 through 59 was selected for study. The population in this age range was approximately 10,000. If 6,000 of this group were taken into the study, with the age-sex distribution existing in the town, it could be predicted (on the'basis of the criteria of the study and tentative data available from a small volunteer group) that roughly 5,000 would be free of cardiovascular disease at the time of initial examination. Of these 5,000 it was estimated that approximately 400 would be found to have cardiovascular disease at the end of the

5th year after the initial examination, 900 at the end of the 10th year, 1,500 at the end of the 15th year, and 2,150 at the end of the 20th year. (These numbers include, of course, persons who would be dead of the disease at the end of the specified period). These numbers appeared to be large enough to insure statistically reliable findings, though it is recognized that even this number of cases would not be sufficient to carry out all of the detailed analyses which would suggest themselves in the course of the study.

There remained the problem of securing an actual listing of persons who would form the sample. Under ordinary circumstances, it would probably have been desirable to use some form of area sampling. The Town of Framingham, however, publishes annually a listing of all residents 20 years of age and over, based on a local census, and it was possible to use this list as a basis for sampling.

The Executive Committee advised that it would be desirable not to break up families--that is, if one member of a family was to be brought into the sample, all other family members resident in the same household should also be brought in, provided they were within the eligible age limits. This was arranged, and-the sample was drawn in systematic fashion from a list which was first stratified by family size and by precinct of residence (eight precincts), and then arranged in serial order by address.

The sampling ratio was two- thirds, which would yield approximately 6,600 names. This (it was thought) would be 10 per cent over the number required for the study in order to provide for losses through refusal or by movement out of the town before examination. The list of residents twenty years of age and over on January 1, 1949, served as the sampling frame for precinct 3. The list for January 1, 1950, served as the frame for the remaining 7 precincts, Each list came in two forms, an alphabetic roster and a roster by address. The declared age, name, address and precinct number was given for each person, The precinct list also specified the place of residence on the previous January 1.

As a check on the completeness of the town lists, the Bureau of the Census matched the January 1, 1950 list against a sample of persons aged 30-59 who appeared on the Framingham census schedules for April 1, 1950. Some 89 percent of those on the census schedules were found on the town list.

Sample response

At the outset a blanket invitation was issued to any town resident in the age range 20 to 70 to come to the clinic for examination. Initial expectations, based on the great rush of volunteers at the beginning, was for a nonresponse not in excess of **10** per cent, so a sample roster of approximately 6,600 men and women who were in age range 30-59 on January 1, 1950, was expected to yield the desired 6,000 examinees. As originally listed the sample consisted of 6,587 names, which was reduced to 6,510 after correction for duplication of names and removal of persons found to be outside the eligible age limits. The number 6,510 appears in a report published in 1957. Since then, three more duplicates have been found in the nonrespondent group, thus reducing the total drawn sample to 6,507. In the end, only 4,494 or 68.8 per cent of the drawnsample came to the study clinic for examination in spite of many and varied appeals to nonrespondents.

For women in each of the age groups under 45 the response rate was around 75 per cent; for men in these age groups it was around 66 per cent. For men or women aged 55 or over the response rate was around 60 per cent. Furthermore, response varied according to the section of town, which presumably means that it varied according to socioeconomic characteristics. From one precinct tc another response ranged from 57 to 73 per cent for men and from 64 to 76 per cent for women.

The volunteer community workers who made all of the contacts with the persons drawn in the sample were asked to secure reasons for non-response. The reasons they reported are of uncertain validity. However, before the end of the initial examination period, 6.5 per cent of the persons in the sample had moved from Framingham and 1.1 per cent were dead. Of the 6,015 persons in the sample alive and resident in Framingham at the end of the initial examination period, 74.3 per cent had been examined in the clinic. The initial examinations, which were originally planned for a much shorter period, extended from September, 1948, through August, 1952, with a handful of respondents coming in even later.

It seems clear that there was differential response to the invitation to participate according to health status. Since participation required a visit to the clinic, the moribund and bedridden were included among the nonrespondents. The 1 per cent of the sample (74 persons) who were reported as nonrespondent on this account seems a reasonable percentage for this age group. For the age group 45 to 64 the U.S. National Health Survey reported a figure of 1 per cent for "confined to house" and 1 per cent for "unable to get around alone" in the second quarter of 1957.

Because of the structure of community organization about which the Framingham study was originally built, which included complete dependence on volunteer canvassers, there was no systematic attempt to secure reports on health status. Except for a small number of refusals attributed to incapacity by the canvassers and a scattering of information from relatives in the study, there is no direct evidence available on the health status of nonrespondents.

If we were to repeat this study we would take all possible steps to secure some minimal data on reported health status and past utilization of medical services by means of interviews in the home by trained interviewers in advance of invitation to examination. With this information some estimate of the relation of assumed health status to the refusal rate could be secured. This is the procedure which has been followed in several subsequent studies.

In the absence of more direct evidence on the health status of nonrespondents we are left dependent on the evidence of subsequent mortality for inferences concerning differentials in the health status of respondents and nonrespondents to the initial examination. Not all of the mortality information is usable, however. Of the 1 per cent of the sample not examined at the clinic who died during the period between September, 1948, and December, 1952 (54 men and 23 women), it: is not now possible to establish with certainty how many were alive at the date

when they should normally have been examined and how many had died before that date. Consequently, it does not appear that there is any appropriate basis for comparing this mortality with the 34 daaths among respondents (25 men and 9 women) which occurred during the same period.

If we were to set up another study of this sort in which the period over which the initial cohort was to be examined was a lengthy one, we would propose that an examination date be set up in advance for each individual in the cohort and that on or very near that date the status of the prospective examinee be recorded in at least the following terms: Zxamination completed, examination refused, person moved prior to examination date, and person dead prior *to* examination date.

Lacking this kind of information, the earliest mortality experience cannot be used for a comparison of respondent with nonrespondent. However, it seems reasonable to compute mortality rates for the years 1951 and 1952 alone, since the disinclination or incapacity to respond becomes less ambiguous toward the end of the period of canvassing. For the nonexamined group the mortality during this period was double that for the examined group. For men, this contrast was equally evident *for* both cardiovascular and for noncardiovascular deaths. For women this is not true; none of the deaths in the nonexamined group were from cardiovascular causes.

The strength of the health differential between respondents and the various classes of nonrespondents may be judged from subsequent mortality experience. As expected, the level of mortality varies according to the reason given for nonresponse. It was least for those who had moved and greatest for those incapacitated. What is of more moment, there is as yet no clear indication that mortality in the respondent and nonrespondent groups is converging. This is rather surprising. If those who failed to join the study because of illness had been only the terminally ill, this group would have died during the first years of the study. With the passage of time mortality in the respondent and nonrespondent groups might be expected to converge, just as mortality in insured groups tends to rise toward the level of mortality in ths general population. It need not be anticipated that mortality in the respondent group would rise completely to the level of mortality in the nonrespondent group, for if there were substantial differences between the two groups mortality among the respondents might remain below that for nonrespondents indefinitely. However, the differential ought to become less. It has not. (This discussion is based on mortality through 1957. An evaluation of more current mortality is now underway).

Later mortality

A preliminary examination of data through 1966 indicates that mortality in the respondent sample has remained what it was. It is still lower than that for the general population. There is no suggestion that it is rising.

Originally this low mortality represented the effect of selection. Through 1953, mortality in the total drawn sample was essentially the same as that for the town of Framingham. If it was lower in the respondent part of the sample, it was correspondingly higher in the non-respondent part. This initial difference between respondent and non-respondent mortality can reasonably be explained by the presumption that persons who were seriously ill were less likely to appear for examination than persons who were well. This is clear for those 74 non-respondents who initially declared themselves to be ill. They have had and continue to have a high mortality. However, among the persons who gave no reason for not appearing fcr examination, or simply declined to come in, there must also have been some who were seriously ill, for this group also had an excess mortality at the beginning.

The excess mortality for the non-respondent sample was quite large for the years 1950-1952. This was a period when the first examination cycle was still in progress--a period, that is, when it was difficult to specify whether a person didn't come in because he 'had already died or didn't come in and then died. By June 1952, however, the initial examination cycle was essentially complete; that is, the non-respondent group alive was defined without ambiguity. Excess mortality in the non-respondent sample remained great through 1952 and 1953.

In 1954, however, mortality dropped in the non-respondent group to a level only slightly greater than that for the town as a whole and remained at that level. Thus, in the non-respondent group selective bias seems to have become a minor influence by 1954. Since selective bias in the respondent group is simply the reverse side of selective bias in the non-respondent group, it is difficult to see how the initial process of self-selection can account for a continued low mortality in the respondent sample group.

The issue, however, is clouded by questions about the completeness of mortality follow-Up. About 14 percent of the respondent sample still alive at Exam 8 were no longer returning for examination, and it is conceivable that a few deaths are missed in this group. The effect of such loss, however, would be trivial at worst. With the non-respondent sample the case is somewhat different. It seems fairly obvious that there is a serious deficiency in mortality reporting for the 426 persons in the non-respondent group who moved from Framingham before the middle of 1952. Thus, for the years 1964-1966, four deaths were reported for this group whereas 20.0 deaths would have been expected on the basis of general mortality. This raises the possibility that there has also been a deficiency in mortality reporting for the non-respondent sample who moved from Framingham after the middle of 1952. Clearly, this is not possible to assess from internal evidence alone; and a special program for evaluating this will have to be undertaken.

A note on the tables included with this discussion may be in order. Logically it might be argued that expected mortality should use mortality for the town of Framingham as the standard. This has a number of

difficulties. Appropriate populations for computing rates are not easy to come by. There should be some allowance made for institutional populations in Framingham. This has been done for 1950 but not for later years. As the study cohort ages it becomes necessary to compute age-specific death rates over age 70, and population estimates are not available for this. Hence it was felt that the U.S.. white death rates might serve as a better standard. They appear to be very similar to those for Framingham town. They are readily available. What is more, as time passes it becomes increasingly moot whether characteristics of the town and the Study populations should agree. The town population in 1966 is not the same as the town population in 1950, when the sample was drawn. The sample: in turn, includes a number of people who are no longer town residents.

Figure 1 -1

DEATH RATES BY AGE & SEX: FRAMINGHAM STUDY, 1953-1966

**Sample respondents**

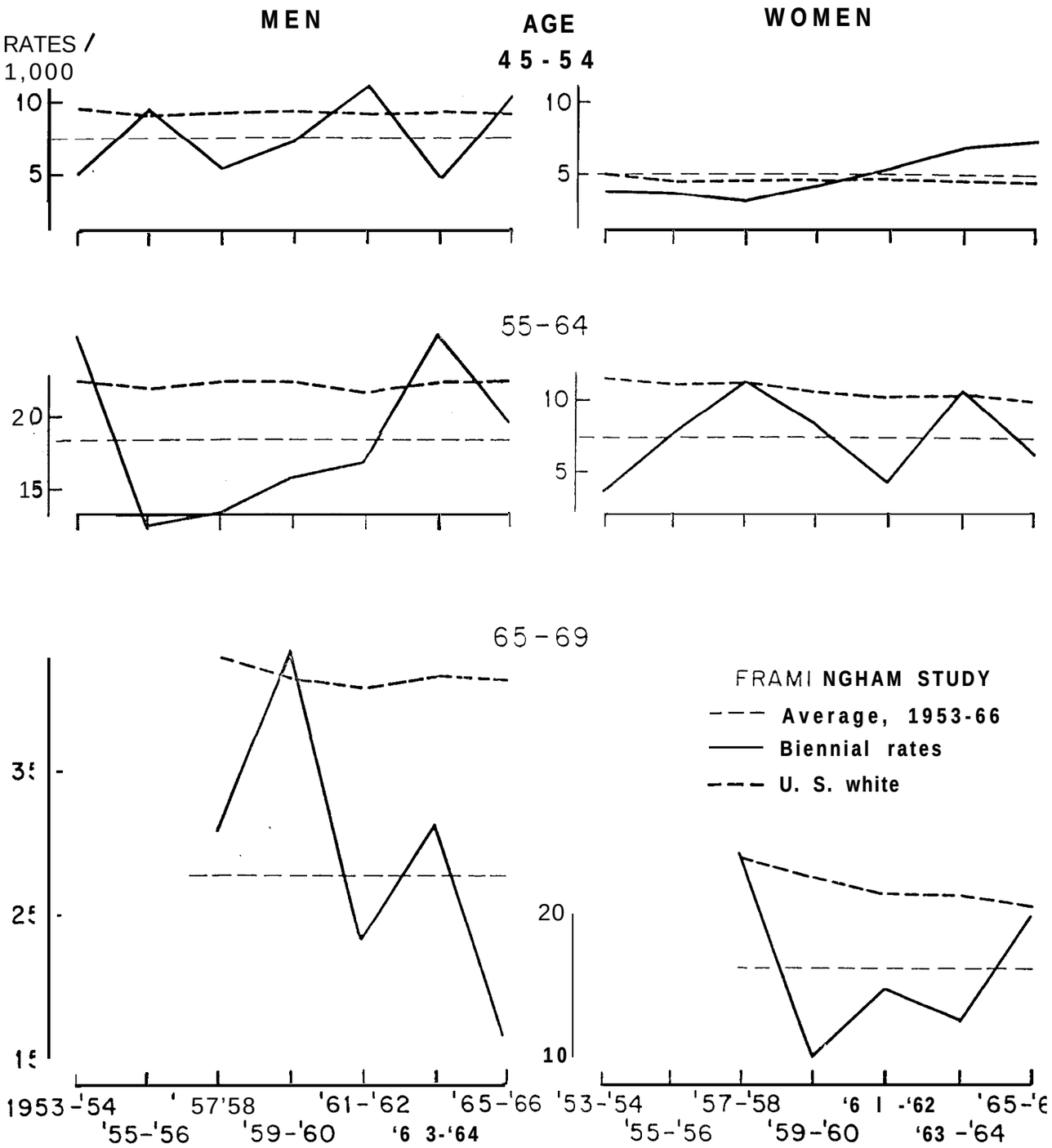
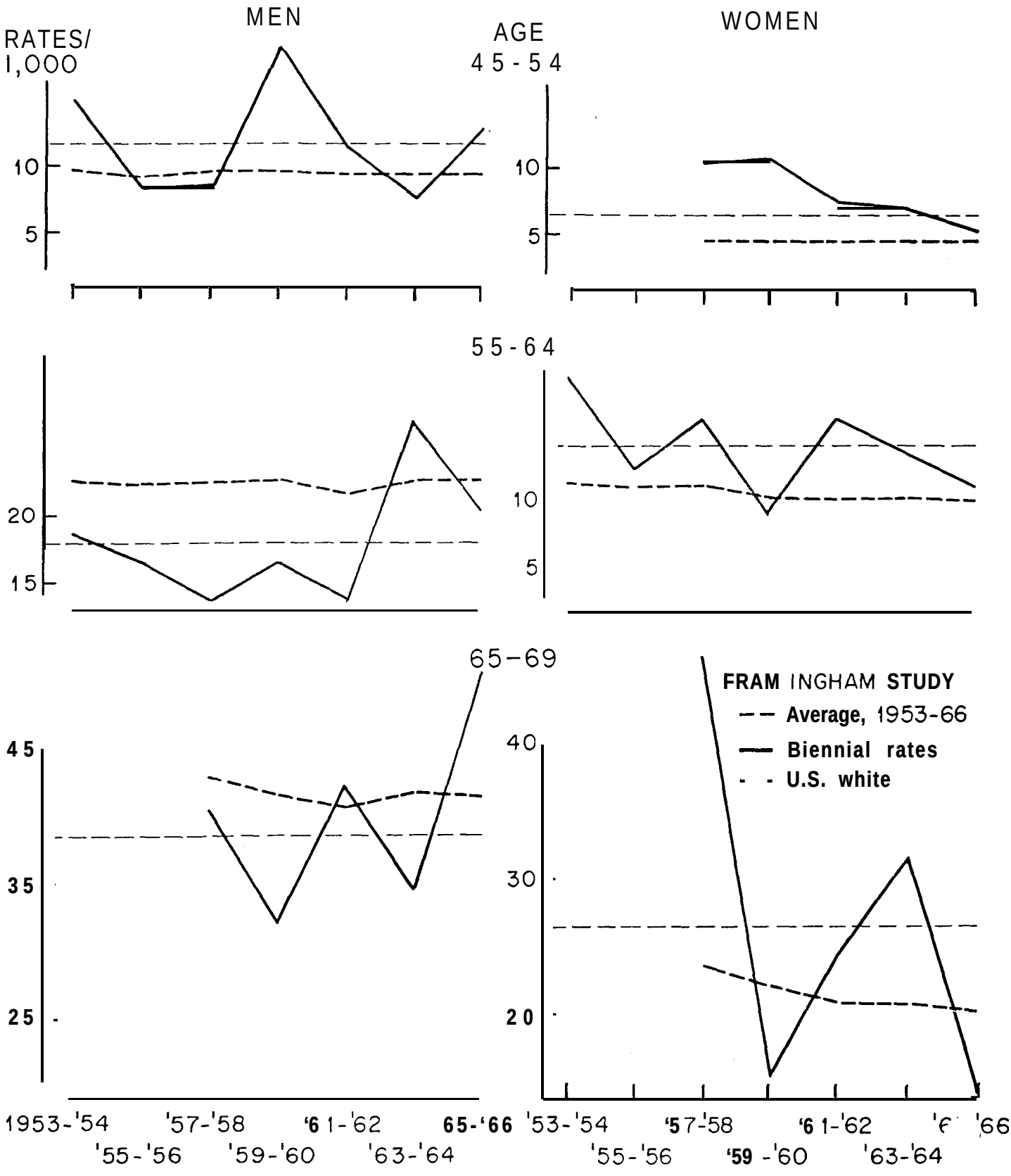


Figure 1-2

DEATH RATES BY AGE & SEX: FRAMINGHAM STUDY, 1953- 1966
Sample Non-respondents



Volunteers--the SX group

At the end of the first examination round there were in the files records for a large group of volunteers not in the drawn sample. Because the number of sample respondents had fallen short of expectations, it was decided to recall some of the volunteers as a supplement to the regular study group. The 1951 town list of residents was used as a roster. Those volunteers whose names were missing from the list were considered as moved and no further effort was made to trace them. Those on the list were asked to return if they fell within the proper age range. The resultant group included a slightly larger proportion of women than the respondent sample--57.8 as against 54.7 per cent--but was not especially different in age structure.

It was at first planned to reexamine only those volunteers "normal" on their initial examination. This plan, however, was not rigorously followed. While 13 people were eliminated for hypertensive or coronary heart disease, these omissions modified the clinical characteristics of the group only trivially.

The volunteer group was, as noted, drawn from people who had already been examined once at the clinic and were requested to return for re-examination. Some 3 per cent refused to do so, while 12 per cent were unavailable because they had moved out of Framingham. In contrast, 9 per cent of the sample group who received the first examination refused to take the second examination and 2 per cent were unavailable for the second examination because they had moved from Framingham.

It should be noted in evaluating these figures that no effort was made to bring into the study those people who had moved out of Framingham before they could be scheduled for examination, either from the sample or volunteer group. This was a deliberate policy to maximize follow-up, so that in a sense, part of the follow-up was bought at the expense of nonresponse. To a degree, this is also true for the Framingham residents who refused to be examined. While a few of these might have come in had greater persuasion been used, they would almost surely have returned for clinic re-examination less frequently than the presentgroup of respondents.

Clearly this is not the ideal procedure for defining a sample. It would have been possible, for example, to hedge against a high level of nonresponse by drawing a supplementary sample at the outset and holding it in reserve until the need for it became apparent. The procedure actually used of adding a supplement of volunteers is another mark of the conceptual and operational difficulties that beset a pioneer enterprise.

It cannot be said that all the conceptual issues have ever been clearly resolved. With the passage of time the distinction between sample and SX has been dulled and the two groups are usually merged. This can be defended, of course. In a prospective study disease experience is referred back to the defined characteristics of the study group and these are as easily obtained for volunteers as for sample persons. The reason for drawing a sample, however, is partly a concern for the hidden role of undefined characteristics, and partly an interest in getting as wide a range of characteristics as the population contains. Despite these defects, the Framingham Study sample did bring into the study per-

sons who would not have come in at their own initiative and, as a consequence, may be presumed to include a wider and more representative human population than could have been obtained by relying exclusively on volunteers.

Sources

This introductory section includes excerpts from the following two reports, as well as some supplementary material:

Dawber, T.R., Meadors, G.F. and Moore, F.E.: Epidemiological approaches to heart disease: The Framingham Study. Amer. J. Public Health 41:279-286, March 1951.

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Table 1-1. Response by Age and Sex
Framingham Study: Drawn Sample

| Age and Sex | Total | Examined | Not Examined | Per Cent Examined |
|---|---|---|---|---|
| Both Sexes | 6,532 | 4,494 | 2,038 | 68.8 |
| Men | 3,086 | 2,036 | 1,050 | 66.0 |
| 30-34 | 628 | 417 | 211 | 66.4 |
| 35-39 | 529 | 385 | 144 | 72.8 |
| 40-44 | 540 | 358 | 182 | 66.3 |
| 45-49 | 461 | 301 | 160 | 65.3 |
| 50-54 | 481 | 314 | 167 | 65.4 |
| 55-59 | 447 | 261 | 186 | 58.4 |
| Women | 3,446 | 2,458 | 988 | 71.3 |
| 30-34 | 670 | 506 | 164 | 75.5 |
| 35-39 | 625 | 466 | 159 | 74.6 |
| 40-44 | 576 | 438 | 138 | 76.0 |
| 45-49 | 566 | 391 | 175 | 69.1 |
| 50-54 | 538 | 367 | 171 | 68.1 |
| 55-59 | 471 | 290 | 181 | 61.6 |

Age is the "declared age" in the lists from which the sample was drawn. Included in these totals are 25 respondents who were found to be out of the age range on examination and who for that reason were dropped from the study group.

Table l-2. Response and Nonresponse by Reason
Framingham Study: Drawn Sample

| Response and Reason | Number of Persons | Percent of Drawn Sample | Percent of Nonrespondentr |
|---|---|---|---|
| Total | 6,532 | 100.0 | ----- |
| Examined | 4,494 | 68.8 | ----- |
| Not examined | 2,038 | 31.2 | 100.0 |
| Moved from Framingham | 426 | 6.5 | 20.9 |
| Died | 74 | 1.1 | 3.6 |
| Ill or incapacitated | 74 | 1.1 | 3.6 |
| Refused | 1,464 | 22.4 | 71.8 |

**See** footnote to Table 1.

Table 1-3. Deaths and Age-Adjusted Death Rates by Sex: Specified Groups

| Age Span, Time Period, and Population Group | Number of Deaths | | Age-Adjusted Death Rate | |
|---|---|---|---|---|
| | Men | Women | Men | Women |
| Ages 30-59 years, 1950-1952 | | | | |
| Massachusetts | 20,701 | 12,735 | 7.7 | 4.3 |
| Framingham (town) | 109 | 55 | 7.3 | 3.4 |
| Study sample | 67 | 30 | 7.3 | 3.0 |
| Ages 35-64 | | | | |
| Massachusetts, 1954-1956 | 27,554 | 16,629 | 11.0 | 5.8 |
| Framingham (town), 1953-1956 | 197 | 125 | 10.3 | 5.8 |
| Study sample, 1953-1957 | 125 | 71 | 8.9 | 4.3 |
| Respondents | 76 | 36 | 8.2 | 3.2 |
| Nonrespondents | 49 | 35 | 10.4 | 6.9 |
| Refused | 43 | 29 | 11.9 | 7.3 |
| Moved | 4 | 3 | 4.6 | 3.6 |
| Incapacitated | 2 | 3 | 14.8 | 11.9 |
| Study volunteers, 1953-1957 | 11 | 11 | 7.3 | 5.2 |

Death rates are on an annual basis per 1,000 population and are age-adjusted by the direct method using the enumerated population of Massachusetts in 1950 as the standard. Framingham rates for 1950-1952 are corrected for the institutional population.

Table 1-4. Death rates by age and sex for Framingham sample and town and U.S. white population: 1950-1952, 1953-1956 (rates per 1,000)

1950-1952

| Age and Sex | Framingham[1] | U.S. White | Framingham Sample |
|---|---|---|---|
| Men | | | |
| 35-44 | 2.5 | 3.8 | 2.8 |
| 45-54 | 11.9 | 9.8 | 12.9 |
| 55-59 | 18.2 | 18.9 | 15.9 |
| Women | | | |
| 35-44 | 1.5 | 2.3 | 1.6 |
| 45-54 | 4.9 | 5.4 | 3.7 |
| 55-59 | 7.6 | 10.0 | 6.1 |

1953-1956

| Age and Sex | Framingham[2] | U.S. White | Framingham Sample |
|---|---|---|---|
| Men | | | |
| 35 -44 | 2.8 | 3.4 | 3.6 |
| 45-54 | 9.4 | 9.2 | 8.5 |
| 55-64 | 20.5 | 22.2 | 18.1 |
| Women | | | |
| 35-44 | 1.8 | 2.0 | 1.8 |
| 45-54 | 5.0 | 4.8 | 3.2 |
| 55-64 | 11.8 | 11.5 | 9.0 |

1 Corrected by deleting populations in VA hospital and women's reformator

2 Uncorrected

Table 1- 5. Mortality experience of total drawn sample Framingham Study, 1953-1966

| | Male | | Female | |
|---|---|---|---|---|
| Year | A | E | A | E |
| 1953 | 25 | 29.5 | 17 | 18.0 |
| 1954 | 31 | 29.5 | 11 | 18.3 |
| 1955 | 23 | 31.2 | 10 | 19.1 |
| 1956 | 27 | 34.0 | 25 | 21.1 |
| 1957 | 25 | 37.6 | 19 | 23.2 |
| 1958 | 25 | 39.8 | 35 | 24.4 |
| 1959 | 27 | 42.2 | 24 | 25.8 |
| 1960 | 50 | 45.0 | 20 | 27.4 |
| 1961 | 39 | 47.1 | 29 | 29.2 |
| 1962 | 47 | 50.8 | 28 | 31.8 |
| 1963 | 50 | 55.2 | 34 | 34.6 |
| 1964 | 48 | 57.2 | 40 | 36.8 |
| 1965 | 48 | 60.7 | 32 | 38.9 |
| 1966 | 54 | 65.1 | 40 | 43.0 |
| 1953-1966 | 519 | 624.9 | 364 | 391.6 |

Note: A - actual number of deaths; E - expected number of deaths Expected deaths based on age-sex specific death rates for U.S. white population.

Table 1-6. Mortality experience of sample persons taking Exam 1 (S and volunteers (SX): Framingham Study, 1953-1966

| | S | | | | SX | | | |
|---|---|---|---|---|---|---|---|---|
| | Male | | Female | | Male | | Female | |
| Year | A | E | A | E | A | E | A | E |
| 1953 | 10 | 19.1 | 9 | 12.5 | 2 | 3.1 | - | 2.4 |
| 1954 | 23 | 19.4 | 5 | 12.8 | 2 | 3.2 | 3 | 2.4 |
| 1955 | 13 | 20.5 | 7 | 13.4 | 2 | 3.5 | 6 | 2.6 |
| 1956 | 19 | 22.3 | 13 | 14.7 | 5 | 3.8 | 1 | 2.7 |
| 1957 | 16 | 24.5 | 6 | 16.2 | 2 | 4.1 | 2 | 3.1 |
| 1958 | 15 | 26.0 | 25 | 17.3 | 5 | 4.3 | 2 | 3.2 |
| 1959 | 15 | 27.6 | 15 | 18.1 | 6 | 4.4 | 2 | 3.4 |
| 1960 | 32 | 29.7 | 12 | 19.3 | 6 | 4.7 | 4 | 3.7 |
| 1961 | 24 | 30.7 | 16 | 20.6 | 5 | 4.9 | 2 | 3.8 |
| 1962 | 32 | 33.4 | 17 | 22.4 | 4 | 5.3 | 3 | 4.2 |
| 1963 | 32 | 36.3 | 23 | 24.5 | 1 | 5.8 | 3 | 4.6 |
| 1964 | 30 | 37.7 | 25 | 26.1 | 5 | 6.0 | 2 | 4.8 |
| 1965 | 28 | 40.1 | 22 | 27.8 | 1 | 6.4 | 3 | 5.3 |
| 1966 | 36 | 42.9 | 29 | 30.7 | 3 | 7.0 | 7 | 5.7 |
| 1953-1966 | 325 | 410.2 | 224 | 276.4 | 49 | 66.5 | 40 | 51.9 |

Note: A - actual number of deaths; E - expected number of deaths
Expected deaths based on age-sex specific death rates for U.S. white population

Table l-7. Mortality experience of sample persons not taking Exam 1 (SR): Framingham Study, 1953-1956

| Year | SR - Total | | | | SR - Refused | | | | SR - Moved | | | | SR - Ill | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Male | | Female | | Male | | Female | | Male | | Female | | Male | | Female | |
| | A | E | A | E | A | E | A | E | A | E | A | E | A | E | A | E |
| 1953 | 15 | 10.4 | a | 5.5 | 13 | a.2 | 5 | 4.3 | 2 | 1.9 | 1 | 0.9 | | 0.3 | 2 | 0.3 |
| 1954 | a | 10.1 | 6 | 5.5 | 7 | a.0 | 4 | 4.3 | 1 | 1.9 | 1 | 0.9 | | 0.2 | 1 | 0.3 |
| 1955 | 10 | 10.7 | 3 | 5.7 | a | a.4 | 3 | 4.4 | 1 | 2.0 | - | 1.0 | 1 | 0.3 | | 0.3 |
| 1.956 | a | 11.7 | 12 | 6.4 | 7 | 9.2 | 10 | 4.9 | | 2.2 | 1 | 1.1 | 1 | 0.3 | 1 | 0.4 |
| 1957 | 9 | 13.1 | 13 | 7.0 | 9 | 10.3 | 12 | 5.4 | | 2.4 | 1 | 1.2 | | 0.4 | | 0.4 |
| 1958 | 10 | 13.8 | 10 | 7.1 | 10 | 10.7 | 7 | 5.5 | | 2.7 | - | 1.2 | | 0.4 | 3 | 0.4 |
| 1959 | 12 | 14.6 | 9 | 7.7 | 10 | 11.3 | 6 | 6.0 | 1 | 2.9 | 1 | 1.3 | 1 | 0.4 | 2 | 0.4 |
| 1960 | 18 | 15.3 | 8 | a.1 | 14 | 11.9 | 6 | 6.3 | 4 | 3.0 | 1 | 1.4 | | 0.4 | 1 | 0.4 |
| 1961 | 15 | 16.4 | 13 | 8.6 | 12 | 12.8 | 12 | 6.7 | 2 | 3.2 | | 1.5 | 1 | 0.4 | 1 | 0.4 |
| 1962 | 15 | 17.4 | 11 | 9.4 | 12 | 13.5 | 11 | 7.2 | 3 | 3.5 | | 1.7 | | 0.4 | | 0.5 |
| 1963 | 18 | 18.9 | 11 | 10.1 | 14 | 14.6 | 9 | 7.7 | 3 | 3.9 | 1 | 1.9 | 1 | 0.4 | 1 | 0.5 |
| 1964 | la | 19.5 | 15 | 10.7 | 17 | 15.0 | 15 | a.2 | 1 | 4.1 | | 2.0 | | 0.4 | | 0.5 |
| 1965 | 20 | 20.6 | lo | 11.1 | 17 | 15.6 | a | 8.5 | 1 | 4.5 | | 2.1 | 2 | 0.5 | 2 | 0.5 |
| 1966 | 18 | 22.2 | 11 | 12.3 | 13 | 16.8 | 9 | 9.3 | 1 | 4.9 | 1 | 2.4 | 4 | 0.5 | 1 | 0.6 |
| 195 3-1966 | 194 | 214.7 | 140 | 115.2 | 163 | 166.3 | 1.17 | 88.7 | 20 | 43.1 | a | 20.6 | 11 | 5.3 | 15 | 5.9 |

Note: A - actual number of deaths; E - expected number of deaths
Expected deaths based on age-sex specific death rates for U.S. white population

Table I-8. Deaths from Specified Causes According to Response and Sex Framingham Study: Drawn Sample, 1951-1952

| Sex and Cause* | Total | Examined | Not Examined |
|---|---|---|---|
| Men | 52 | 22 | 30 |
| Cardiovascular | 29 | 13 | 16 |
| Cancer | 11 | 3 | 8 |
| Accidents | 3 | 1 | 2 |
| All other | 9 | 5 | 4 |
| Women | 17 | 7 | 10 |
| Cardiovascular | 4 | 4 | -- |
| Cancer | 9 | 3 | 6 |
| Accidents | 1 | -- | 1 |
| All other | 3 | -- | 3 |

* The cause groups are defined by category number of the Sixth Revision of the International List, Cardiovascular diseases are List numbers 330-334, 400-468; Cancer, List numbers 140-205; Accidents, List numbers E800-E962.

For men the annual death rates per 1,000 population for 1951-1952 were 6.6 (examined) and 11.1 (not examined); for women they were 1.7 (examined: and 3.7 (not examined).

Table 1- 9. Deaths and death rates (per 1,000) by age, sex, and broad cause groups Framingham Study, 14-year follow-up

| Sex/Age | All Causes | | Cardiovascular Disease | | | | | | | | Cancer | | Other Causes | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Total | | CHD | | CVA | | Other CV | | | | | |
| | Number | Rate | Number | Rate | Number | Rate | Number | Rate | Number | Rate | Number | Rate | Number | Rate |
| Men | | | | | | | | | | | | | | |
| 45-54 | 85 | 7.8 | 45 | 4.1 | 35 | 3.2 | 5 | 0.5 | 5 | 0.5 | 22 | 2.0 | 18 | 1.6 |
| 55-64 | 147 | 18.6 | 93 | 11.8 | 65 | a.2 | 12 | 1.5 | 16 | 2.0 | 25 | 3.2 | 29 | 3.7 |
| 65-69 | 50 | 31.3 | 24 | 15.0 | 18 | 11.3 | 5 | 3.1 | 1 | 0.6 | 14 | 8.8 | 12 | 7.5 |
| 70-74 | 18 | 50.8 | 10 | 28.2 | 6 | 16.9 | 2 | 5.6 | 2 | 5.6 | 2 | 5.6 | 6 | 16.9 |
| Women | | | | | | | | | | | | | | |
| 45-54 | 64 | 4.6 | 14 | 1.0 | 3 | 0.2 | 5 | 0.4 | 6 | 0.4 | 27 | 1.9 | 23 | 1.7 |
| 55-64 | 76 | 7.5 | 35 | 3.4 | 18 | 1.8 | 6 | 0.6 | 11 | 1.1 | 27 | 2.6 | 14 | 1.4 |
| 65-69 | 36 | 16.3 | 21 | 9.5 | 9 | 4.1 | 6 | 2.7 | 6 | 2.7 | 9 | 4.1 | 6 | 2.7 |
| 70-74 | 12 | 25.1 | 7 | 14.6 | 6 | 12.6 | - | 0.0 | 1 | 2.1 | 1 | 2.1 | 4 | 8.4 |

Note: Classification of cause of death based; on physician review.
Deaths are for sample respondents and volunteers (S + SX)

Source: Section 6 of the monograph'

Framingham Study

Section 2

2a. Introduction

2b. Repeated examination

2c. Loss due to moving, disability and refusal

Tables

1. Number of surviving in cohort and number receiving examination at each of the first 8 examinations: Framingham Study

2. Number of persons according to examination status at Exam 7 and at Exam 8: Framingham Study

3. Number of persons according to examination status at Exam 7 and at Exam 8 and the number of biennial examinations received: Framingham Study

4. Number and per cent of persons receiving Exam 7 and Exam 8 by sex and age at Exam 1: Framingham Study

5. Number of persons not receiving Exam 8 according to last biennial examination received: Framingham Study

6. Number of persons lost to examination after moving from Framingham who developed new CHD within the 14-year follow-up: Framingham Study

7. Number of persons lost to examination while still resident in Framingham who developed new CHD within the 14-year follow-up: Framingham Study

a. Examination dates for specified subjects: Framingham Study, Exams l-7

June 1968

## FOLLOW-UP

The study design required that persons in the cohort be called back for re-examination at two-year intervals. Originally the possibility of annual examinations was considered. Fortunately, this plan was never tried: the initiation of biennial examinations proved difficult enough. The first examination series began on September 29, 1948. The second series got under way with scattered examinations early in 1951 but did not begin in earnest until May of that year, more than two and a half years after the first series had begun.

Eventually a procedure was set up for regularizing callback, and this went into effect early in 1953. Each person was assigned an anniversary date. Ordinarily the anniversary date was the date of the first examination but in order to even out the workload, it was sometimes slightly different. Every two years after his anniversary date a person is due for his next examination. For persons who come in at some irregular interval the rule is to number. the examination according to the nearest scheduled visit. This allows a period from a year before the scheduled date to a year after for any examination, but most visits come relatively close to being on schedule.

Repeated examination

While there are other sources of information for the study, the chief one is the clinic examination. It is only on this basis that repeated observations of personal characteristics can be made; and a standard examination is also the only means for obtaining uniform information on clinical status. Thus, adequacy of follow-up must be judged primarily by the rate at which the cohort returns for examination.

Of the original cohort of 5,209 persons, 4,678 were still alive at the time they were scheduled for Exam 8 (Table 1). Of these, 4,030 or 86.1 percent took Exam 8. (The comparable figure for Exam 7 was 87.2 percent; the net loss on successive examinations is now very low). Another 42 persons who had missed Exam 8 returned for a later examination by the end of 1966 (Table 2). On the basis of past experience this number can be expected to more than triple with additional follow-up. (By 3/20/68 the total had reached 91.)

A large number of people take every possible examination (Table 3). Some 3,597 persons took all of'the first 7 examinations; 3,436 took all of the first 8. This is 74.9 percent and 73.5 percent, respectively, of the surviving cohort. These figures, high as they are, actually represent an understatement of the measure of cooperation. Because of a delay in calling back the SX group (non-sample volunteers) for their second examination, 237 volunteers were rescheduled so late for Exam 2 that it was felt impolitic to ask them to come in shortly after for their regularly scheduled third examination. When allowance is made for this group there were 79 and 78 percent with a complete examination

series through Exams 7 and 8, respectively.

There has been, as anticipated, a difference between the sample and SX groups in their rates of re-examination. Of the former, 84.9 percent of the survivors received Exam 8. Of the latter, 93.7 percent received Exam 8. The SX group were volunteers in the first place, and thus more likely to cooperate; in defining the SX group only those volunteers who returned for a second examination when requested were retained. By contrast, the greatest loss in the sample was suffered at Exam 2. Some 385 persons still alive at that time did not take this examination; 184 of them never returned for a later examination.

By Exam 8, 531 persons in the original cohort had died. As might be anticipated, the number of deaths has mounted with each successive examination. Nearly 2 percent of those alive at Exam 6 died before they were scheduled for Exam 7. In the next two years mortality loss was 2.6 percent. Losses between succeeding examinations can be expected to increase rapidly.

Deaths constitute both a loss and a gain to follow-up. When reckoning the number who will be available for future observations, they constitute a loss. On the other hand, death is one of the end points of the study. Moreover, knowing a person to be dead provides a firm assurance that the person is not and will not be lost to follow-up. With the living it is sometimes difficult (particularly for those missing some examinations) to be certain whether one of the clinical endpoints has been reached.

The 648 persons not taking Exam 8 even though they were alive at the time it was due, took a varying number of earlier examinations. Some

84 took the preceding 7 examinations but missed the eighth; 121 took Exam 1 and never returned. A number varying between 74 and 101 missed 2, 3, 4, or 5 examinations.

It is surprising to find that where the person remains alive the likelihood of re-examination is about the same in one age-sex group as another (Table 4). It is also a little surprising to note that "essentially permanent" loss to follow-up for reasons other than death has been relatively constant from one examination to another (Table 5). The clear exception to this is a greater than average loss just after the first examination. The other apparent exception, for those receiving Exam 7 but not 8, includes some persons who are not permanently lost to follow-up but will return when additional time has elapsed, or have already returned.

Loss due to moving, disability and refusal

There were 606 persons in the cohort who, though still alive when scheduled for their eighth examination, did not appear for examination, then or (up to the end of 1966) later. Perhaps 10 percent of this group can be expected to return at some future time; the remainder, not.

Of these 606 persons, 355 still lived in Framingham. This includes some people who could not come in for examination and some who would not. What the proportion were of each is impossible to say. It is clear, however, that there were some persons with serious disability in this group. One evidence of this is the fact that nearly 23 percent of those who have died missed their last scheduled examination while alive. This is substantially greater than the comparable figure for those still alive.

The fact that a person fails to appear for re-examination does not mean that he is completely lost to follow-up. Considerable efforts are made to keep track of his clinical status by various forms of community surveillance. Still, nothing short of re-examination provides the same assurance. For those persons who have moved from the area, uncertainty about their clinical status may be fairly high.

On the other hand there is no direct evidence that loss to examination has lead to any substantial loss of information about the appearance of new cardiovascular disease. Tables 6 and 7 indicate, in fact, that the incidence reported after loss to examination is only slightly less than might be expected had these people continued to take repeated examinations.

Tables 6 and 7 are intended to compare CHD experience among those persons whose examination series lapsed with the CHD experience for the

total population. Table 6 gives counts for people who moved from Framingham and, presumably for that reason, did not return for examination afterwards. Table 7 gives counts for people who stopped coming in for examinations while still resident in Framingham and who never returned.

There is a slight deficit in CHD incidence in both these groups even while they were taking examinations. This is, in part, accounted for by the fact that a person who is already dead cannot "move" or "refuse", so that cases of CHD first manifest at death are not included in counts before "loss".

On a priori grounds one would assume that persons who moved out of Framingham were likely to be healthier than average at the time that they moved, and that persons who stopped coming while still resident in Framingham would include some persons who were seriously, even terminally, ill. However, both those who moved and those who didn't had fewer cases of CHD reported after they stopped taking examinations than would be expected on the basis of the total cohort's experience.

Taking the reckonings in Tables 6 and 7 at face value, loss to examination has resulted in a 3 percent deficit in the reports of CHD incidence in the 14 years since the study began. Since a clinic examination was required for the diagnosis of AP this fact would be sufficient to explain the entire deficit in CHD incidence after loss to examination. It is obvious that failure to return for examination has not as yet introduced any serious bias in the counts of new CHD.

Table 1. Number surviving in cohort and number receiving examination at each of the first 8 examinations: Framingham Study

| Exam | Number Surviving | Number Examined | | |
|---|---|---|---|---|
| | | Total | Sample | Voluntee: |
| 1 | 5,209 | 5,209 | 4,469 | 740 |
| 2 | 5,177 | 4,792 | 4,052 | 740 |
| 3 | 5,125 | 4,416[1/] | 3,935 | 481[1/] |
| 4 | 5,073 | 4,541 | 3,843 | 698 |
| 5 | 4,990 | 4,421 | 3,750 | 671 |
| 6 | 4,895 | 4,259 | 3,593 | 666 |
| 7 | 4,803 | 4,191 | 3,551 | 640 |
| 8 | 4,678 | 4, 030 | 3,402 | 628 |

1/ The indicated drop is an artifact arising from the arbitrary decision that volunteers would not be followed if they did not take Exam 2. Some 237, however, were recalled so late for Exam 2 that they were not called in for Exam 3.

Table 2. Number of persons according to examination status at Exam 7 and at Exam 8: Framingham Study

| | Both | Sample | Volunteers |
|---|---|---|---|
| Total Receiving Exam 1 | 5,209 | 4,469 | 740 |
| Examined, Exam 7 | 4,191 | 3,551 | 640 |
| Not Examined, Exam 7 | 1,018 | 918 | 100 |
| Alive, Exam 7 | 612 | 569 | 43 |
| Took later exam * | 132 | 107 | 25 |
| Did not take later exam * | 480 | 462 | 18 |
| Resides in Framingham | 276 | 265 | 11 |
| Resides outside Framingham | 204 | 197 | 7 |
| Dead, Exam 7 | 406 | 349 | 57 |
| Took last possible exam before death | 317 | 274 | 43 |
| Missed last possible exam before death | 89 | 75 | 14 |
| Examined, Exam 8 | 4,030 | 3,402 | 628 |
| Not Examined, Exam 8 | 1,179 | 1,067 | 112 |
| Alive, Exam 8 | 648 | 606 | 42 |
| Took later exam * | 42 | 30 | 12 |
| Did not take later exam * | 606 | 576 | 30 |
| Resides in Framingham | 355 | 337 | 18 |
| Resides outside Framingham | 251 | 239 | 12 |
| Dead, Exam 8 | 531 | 461 | 70 |
| Took last possible exam before death | 410 | 354 | 56 |
| Missed last possible exam before death | 121 | 107 | 14 |

* Covers experience through 1966.

Table 3. Number of persons according to examination status at Exam 7 and at Exam 8 and the number of biennial examinations received: Framingham S

EXAM 7

| Number of Exams Received | Received Exam 7 | | | Did Not Take Exam 7 | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | Alive or Dead | | | Alive at Exam 7 | | |
| | Both | S | SX | Both | S | SX | Both | S | SX |
| 1 | | - | - | 198 | 198 | - | 140 | 140 | - |
| 2 | 16 | 16 | - | 172 | 155 | 17 | 104 | 99 | 5 |
| 3 | 27 | | | | | | 99 | | |
| 4 | 52 | 27 48 | 4· | 167 162 | 145 142 | 22 20 | 90 | 88 82 | 11 8 |
| 5 | 93 | | | | | | 92 | | |
| 6 | 406 | 189 87 | 217 6 | 177 142 | 148 130 | 12 29 | 87 | 84 76 | 16 3 |
| 7 | 3597 | 3184 | 413 | | - | - | | - | - |
| Total | 4191 | 3551 | 640 | 1018 | 918 | loo | 612 | 569 | 43 |

EXAM 8

| Number of Exams Received | Received Exam 8 | | | Did Not Take Exam 8 | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | Alive or Dead | | | Alive at Exam 8 | | |
| | Both | S | SX | Both | S | SX | Both | S | SX |
| 1 | | - | - | 184 | 184 | - | 121 | 121 | - |
| 2 | 14 | 14 | - | 175 | 158 | 17 | 101 | | 5 |
| 3 | 13 | 13 | - | 169 | 150 | 19 | 98 | 90 | 8 |
| 4 | 25 | | 3 | 161 | 142 | 19 | 82 | 77 | 5 |
| 5 | 53 | 22 48 | 5 | 178 | 157 | 21 | 88 | 80 | 8 |
| 6 | 92 | 78 | 14 | 151 | 129 | 22 | 74 | 65 | v |
| 7 | 397 | 190 | 207 | 161 | 147 | 14 | 84 | 77 | 7 |
| 8 | 3436 | 3037 | 399 | - | - | - | - | - | - |
| Total | 4030 | 3402 | 628 | 1179 | 1067 | 112 | 648 | 606 | 42 |

Note : S - sample, SX - volunteers

Table 4. Number and per cent of persons receiving Exam 7 and Exam 8 by sex and agt at Exam 1: Framingham Study

| Age at Exam 1 | Number Receiving Exam 7 | Number Receiving Exam 8 | Per cent of Specified Age-Sex Group | | | |
|---|---|---|---|---|---|---|
| | | | Of All Persons at Entry | | Of Survivors at Exam | |
| | | | Exam 7 | Exam 8 | Exam 7 | Exam 8 |
| Men | 1,811 | 1,741 | 77.5 84.9 | 74.5 82.4 | 87.0 87.1 | 85.0 86.5 |
| 29-34 | 332 | 322 | | | | |
| 35-39 | 380 | 376 | 86.2 | 85.3 | 89.4 | 89.3 |
| 40-44 | 343 | 333 | 81.5 | 72.9 | 87.5 | 87.9 |
| 45-49 | 274 | 261 | 70.0 | 66.2 | 87.0 | 85.9 |
| 50-54 | 261 | 247 | 62.8. | 57.4 | 85.0 84.4 | 83.1 86.4 |
| 55-62 | 221 | 202 | | | | |
| Women | 2,380 | 2,289 | 82.8 | 79.7 87.2 | 87.5 | 85.9 |
| 29-34 | 397 | 396 | 87.4 | | 89.6 | 89.4 |
| 35-39 | 493 | 479 | 84.4 | 82.0 | 86.6 | 85.8 |
| 40-44 | 438 | 413 | 85.5 | 80.7 | 88.7 | 85.2 |
| 45-49 | 379 | 363 | 84.2 | 80.7 | 89.2 | 86.k |
| 50-54 | 338 | 333 | 78.8 | 77.6 | 86.0 | 87.2 |
| 55-62 | 335 | 305 | 75.5 | 68.7 | 84.4 | 80.7 |

Table 5. Number of persons not receiving Exam 8 according to last biennial examination received:

Framingham Study

| Last Biennial Exam | Persons Receiving Exam 1 | | | Alive at Exam 8 | | | Dead At Exam 8 | | |
|---|---|---|---|---|---|---|---|---|---|
| | Total | Sample | Volunteers* | Total | Sample | Volunteers* | Total | Sample | Volunteers* |
| Total not taking Exam 8 | 1,179 | 1,067 | 112 | 648 | 606 | 42 | 531 | 461 | 70 |
| Exam 1 | 184 | 184 | | 121 | 121 | - | 63 | 63 | |
| Exam 2 | 132 | 115 | 17 | | 59 | 5 | 68 | 56 | 12 |
| Exam 3 | 130 | 119 | 11 | 71 | 69 | 2 | 59 | 50 | 9 |
| Exam 4 | 134 | 114 | 20 | 62 | 54 | 8 | 72 | 60 | 12 |
| Exam 5 | 169 | 157 | 12 | 74 | 72 | 2 | 95 | 85 | 10 |
| Exam 6 | 156 | 136 | 20 | 75 | 69 | 6 | 81 | 67 | 14 |
| Exam 7 | 274 | 242 | 32 | 181 | 162 | 19 | 93 | 80 | 13 |

* Volunteers had to return for their second biennial examination in order to be included in the cohort. These examinations are all considered Exam 2, although in some instances the examination was more than 3 years after Exam 1.

Table 6. Number of persons lost to examination after moving from Framingham who developed new CHD within the lb-year follow-up: Framingham Study

| Exam at which loss first recorded | Number developing new CHD in exam interval | | | | | | | | Number with Pre-existing CHD | Total Number Lost |
|---|---|---|---|---|---|---|---|---|---|---|
| | Total | 1-2 | 2-3 | 3-4 | 4-5 | 5-6 | 6-7 | 7-8 | | |
| 2 | 4 | | 1 | 1 | 1 | - | - | 1 | 1 | 47 |
| 3 | 1 | - | - | - | | | 1 | - | | 36 |
| 4 | 1 | - | - | - | | 1 | - | - | | 32 |
| 5 | 3 | - | - | - | | 1 | 2 | - | | 33 |
| 6 | 4 | | 1 | 2 | 1 | | | | 1 | 40 |
| 7 | 1 | | | | 1 | - | - | - | | 34 |
| a | 3 | 1 | - | - | | | 2 | - | 1 | 55 |

| Losses between Exams 2 and 8 | Number of CHD Events Before Loss | After Loss |
|---|---|---|
| Actual | a | 9 |
| Expected * | 10.5 | 14.9 |
| **Losses between Exams 3 end 7** | | |
| Actual | 5 | 5 |
| Expected * | 6.9 | 10.7 |

* Expected numbers obtained by applying age-sex- exam-specific rates for total cohort to the population lost at each examination.

Note: Covers experience through 1966

Table 7. Number of persons lost to examination while still resident in Framingham who developed new CHD within the 14-year follow-up: Framingham Study

| Exam at which loss first recorded | Number developing new CHD in exam interval | | | | | | | | Number with Pre-existing CHD | Total Number Lost |
|---|---|---|---|---|---|---|---|---|---|---|
| | Total | 1-2 | 2-3 | 3-4 | 4-5 | 5-6 | 6-7 | 7-8 | | |
| 2 | 10 | - | 2 | 1 | 1 | - | 3 | 3 | 2 | 104 |
| 3 | 5 | 2 | | 1 | 1 | - | - | 1 | 1 | 51 |
| 4 | 4 | - | 2 | 1 | | | | 1 | | 56 |
| 5 | 3 | - | | 1 | | 2 | - | - | 1 | 38 |
| 6 | 4 | - | | 1 | | | 2 | 1 | 1 | 52 |
| 7 | 5 | 1 | | | | 2 | 1 | 1 | | 46 |
| 8 | 8 | 1 | 1 | 2 | 2 | - | 2 | | 2 | 104 |

| Losses between Exams 2 and 8 | Number of CHD Events Before Loss | After Loss |
|---|---|---|
| Actual | 17 | 22 |
| Expected * | 20.5 | 29.8 |
| **Losses between Exams 3 and 7** | | |
| Actual | 9 | 12 |
| Expected * | 11.4 | 16.6 |

* Expected numbers obtained by applying age-sex-exam specific rates for total cohort to the population lost at each examination.

Note : Covers experience through 1966

Table 8

Examination dates for specified subjects: Framingham Study, Exams 1-7

| Type and Record Number | Anniversary Date | Exam 1 | Exam 2 | Exam 3 | Exam 4 | Exam 5 | Exam 6 | Exam 7 |
|---|---|---|---|---|---|---|---|---|
| Sample | | | | | | | | |
| 0001-2292 | 09/48-12/49 | 09/48-11/49 | 05/51-01/52 | 02/53-11/53 | 11/54-11/55 | 12/56-01/58 | 10/58-12/59 | 09/60-01/62 |
| 2297-3776 | 12/49-10/50 | 11/49-11/50 | 01/52-10/52 | 11/53-11/54 | 11/55-11/56 | 12/57-10/58 | 12/59-10/60 | 12/61-10/62 |
| 3777-4837 | 10/50-05/51 | 11/50-04/51 | 10/52-02/53 | 10/54-05/55 | 10/56-06/57 | 09/58-05/59 | 10/60-06/61 | 09/62-05/63 |
| 4838-5916 | 05/51-03/52 | 04/51-03/52 | 02/53-03/54 | 05/55-02/56 | 06/57-03/58 | 05/59-03/60 | 06/61-03/62 | 05/63-02/64 |
| 5917-6447 | 03/52-06/52 | 03/52-08/52 | 03/54-06/54 | 02/56-06/56 | 03/58-06/58 | 03/60-06/60 | 03/62-06/62 | 02/64-05/64 |
| sx (volunteers) 0004-3973 | 09/48-11/50 | 10/48-12/50 | 01/52-10/52 | 06/53-11/54 | 02/54-11/56 | 12/56-10/58 | 06/58-11/60 | 09/60-10/62 |

Note: Persons are to be examined at 2-year intervals after their anniversary date (generally the date of their first examination). However, a leeway of a year earlier or later is allowed. The Exam I dates are the actual examination dates, except for the last group, where a few stragglers were examined through 4/53. The dates for Exams 2-7 cover the actual examination dates of the large majority of persons in each group (all except the extreme 2 percent).