# A Controlled Evaluation of Mass Surveys for Tuberculosis and Heart Disease

PHILIP E. ENTERLINE, M.A., and BERNARD KORDAN, M.D.

A BASIC ASSUMPTION underlying mass casefinding programs is that those persons with disease who are detected are "better off" than they would have been had they not been detected. This assumption has never been completely tested, primarily because of the difficulty of obtaining a control group. A control group would consist of randomly selected persons participating in the casefinding program whose screening tests are positive but who are not advised of these results and are allowed to go on their way to be discovered by some other procedure, or possibly are never detected. Since casefinding programs are considered a service, a control group usually cannot be withheld deliberately, for moral and ethical reasons.

It recently became apparent that controls might be obtained for the evaluation of chest X-ray programs without raising questions of propriety or medical ethics. It has been known for some time that there are inconsistencies in interpreting chest photofluorograms (*1–3*); when two readers interpret a series of X-ray films, no matter how similar their training and orientation, some of the films will be selected as positive by one and negative by the other. This same phenomenon has been reported for interpretations of electrocardiograms (*4*) and for examinations of children for tonsillectomy (*5*), and no doubt it could be observed in the application of many medical procedures.

In casefinding programs based on a single reading of photofluorograms, it is possible to identify by reading the films at a later date persons who appear positive but who were considered negative on the first reading. This group, who would not have received any benefits from the casefinding program since their apparent abnormality was not detected, would seem to constitute a control group for testing the assumption that persons whose disease is detected are better off than they would have been otherwise. The procedure would also identify a comparable group of persons considered positive on the initial reading and negative on the second reading. This group would have received whatever benefits casefinding has to offer and would constitute the study group.

Using this procedure for selecting study and control groups, we have examined the mortality experience of X-ray survey participants during a period of approximately 3½ years as an index of the benefits of this type of casefinding program. More than 200,000 photofluorograms taken in two large-scale, commmunitywide surveys, one in Los Angeles City and County, Calif., and the other in Dallas City and County, Tex., were re-read 3 to 5 years after the completion of the surveys. Sponsoring or participating in this study were the Texas and California State Health Departments, the Dallas and Los Angeles City Health Departments, the Dallas City and County and the Los Angeles

*Mr. Enterline is chief statistician of the Heart Disease Control Program, Division of Special Health Services, Public Health Service. Dr. Kordan, now assistant clinical professor, radiology staff, University of Southern California School of Medicine, was during the time of this study chief of Radiology Services, Division of Special Health Services.*

County Tuberculosis Associations, the Los Angeles County X-ray Survey Foundation, and the Public Health Service.

The second readings of the X-ray films were done by physicians with training and orientation similar to that of the original readers. In neither instance were the readers qualified as radiologists, although they had received training in reading chest photofluorograms, with emphasis on the detection of tuberculosis.

The second readings were not in many instances done by the same physicians as those who did the first. Moreover, the conditions of the second readings were quite different from those of the first. The criteria used for classifying abnormalities on the two readings therefore probably differed. For this reason, one of us (B. K.), a radiologist, re-read all films called positive on only one of the two readings and prepared a detailed description of any abnormalities observed. He reviewed the films with the knowledge that one of two readers had considered them positive but without knowing whether it had been considered positive on the first or second reading.

In the final selection of films for the study and control groups, only the radiologist's interpretations were used. Relying on a single reader's observations provides some assurance that the same criteria were used to describe abnormalities for both groups. For example, it is possible that tuberculoma was defined somewhat differently by the first and second sets of readers. Having a third reader define tuberculoma for both the study and control groups and using only his readings in comparing the two groups tend to minimize the effect of any differences in criteria. In addition, using only the films designated positive by the radiologist increases the likelihood that the abnormalities were truly pathological. The films called positive by the radiologist are, in fact, films that have been considered positive by two out of three readers.

The results of the first reading, the second reading, and the radiologist's review are shown in table 1. The first and second readings were made at about the same level of suspicion: 7,644 films (3,670+3,974) were considered positive at the time of the surveys, and 7,612 films (3,974+3,638) were considered positive on the second reading. The percentages of the positive films confirmed by the radiologist were about the same for the two readings, 87.5 for the first and 85.0 for the second.

The percentage confirmation for the second reading excludes 379 of the Los Angeles films not read by the radiologist. These films were not read because the names of the persons, essential for obtaining mortality information, were not legible on the photofluorograms. Since the entire file of records for 1,700,000 persons examined in this survey was in alphabetical order, it was virtually impossible to identify individuals from the film number (which was legible). Omission of these films should not bias the study results since the illegibility of the name was due to poor positioning of the survey records in the photo-identifier of the X-ray machines, a circumstance

**Table 1. Results of re-reading 70 mm. photofluorograms taken in two communitywide chest X-ray programs**

| Survey area | Total films re-read | Positive on first reading only | | Positive on both readings | Positive on second reading only | |
|---|---|---|---|---|---|---|
| | | Total | Confirmed by radiologist [1] | | Total | Confirmed by radiologist [2] |
| Both surveys | 208, 555 | 3, 670 | 3, 179 | 3, 974 | [3] 3, 638 | 2, 772 |
| Los Angeles | 108, 409 | 1, 883 | 1, 647 | 2, 207 | [3] 1, 964 | 1, 488 |
| Dallas | 100, 146 | 1, 787 | 1, 532 | 1, 767 | 1, 674 | 1, 284 |

[1] The study group, that is, persons given the "benefits" of casefinding.
[2] The control group, that is, persons from whom the benefits of casefinding were withheld.
[3] 379 of these films were not reviewed by the radiologist.

**Table 2. Type and activity of tuberculosis noted by radiologist**

| Type and activity | Los Angeles | | | | Dallas | | | |
|---|---|---|---|---|---|---|---|---|
| | Study group | | Control group | | Study group | | Control group | |
| | Number | Percent | Number | Percent | Number | Percent | Number | Percent |
| All tuberculosis | 1,017 | 100.0 | 732 | 100.0 | 407 | 100.0 | 241 | 100.0 |
| Healed primary | 64 | 6.3 | 38 | 5.2 | 0 | 0 | 1 | 0.4 |
| Minimal, probably active | 22 | 2.2 | 8 | 1.1 | 17 | 4.2 | 10 | 4.1 |
| Minimal, activity undetermined | 172 | 16.9 | 87 | 11.9 | 50 | 12.3 | 38 | 15.8 |
| Minimal, probably inactive | 708 | 69.6 | 549 | 75.0 | 136 | 33.4 | 125 | 51.9 |
| Tuberculoma | 50 | 4.9 | 45 | 6.1 | 204 | 50.1 | 65 | 27.0 |
| Other and suspected | 1 | .1 | 5 | .7 | 0 | 0 | 1 | .4 |

that should not be correlated with variables under study.

The names of all persons whose films were considered positive by the radiologist were checked against the files of the death certificates maintained by the State health departments of California and Texas. In this way death rates were derived for the study and the control groups. Care was taken to provide the same information for each group in checking against files of death certificates. The mortality rates derived from this procedure covered approximately a 4½-year period for Los Angeles and a 2½-year period for Dallas.

Despite the fact that about the same percentages of films were probably positive on the first and second readings, the kinds of disease in the study and control groups were, in the opinion of the radiologist, somewhat different. Since the probability of death within stated intervals varies from one disease to another, the mortality experience is presented separately for each suspected disease grouping.

### Tuberculosis Suspects

A description of the films that the radiologist believed showed evidence of tuberculosis appears in table 2. The differences in the type and activity of tuberculosis in the two groups are important to the study insofar as they affect the mortality experience of persons with suspected tuberculous lesions.

For the Los Angeles films, the differences

**Table 3. Number of tuberculosis suspects and deaths [1] observed in Los Angeles and Dallas, by age and sex**

| Age | Study group | | | | Control group | | | |
|---|---|---|---|---|---|---|---|---|
| | Male | | Female | | Male | | Female | |
| | Suspects | Deaths | Suspects | Deaths | Suspects | Deaths | Suspects | Deaths |
| All ages | 620 | 23 | 804 | 18 | 456 | 30 | 517 | 23 |
| 15–24 | 46 | 0 | 52 | 0 | 29 | 0 | 24 | 0 |
| 25–34 | 88 | 2 | 114 | 0 | 50 | 0 | 45 | 0 |
| 35–44 | 114 | 2 | 151 | 2 | 68 | 0 | 79 | 0 |
| 45–54 | 123 | 5 | 193 | 5 | 99 | 3 | 86 | 2 |
| 55–64 | 136 | 6 | 166 | 4 | 96 | 13 | 119 | 7 |
| 65–74 | 85 | 8 | 103 | 4 | 78 | 8 | 113 | 6 |
| 75 and over | 28 | 0 | 25 | 3 | 36 | 6 | 51 | 8 |

[1] Excluding 3 deaths due to violence.

were slight. Because of a slightly greater percentage of probably active lesions in the study group, its mortality rate would probably be somewhat higher than that of the control group. It is to be expected that persons with lesions detected in a casefinding survey would have a lower mortality rate (because of the medical and nursing care subsequently provided) than those whose lesions are not detected. Thus, the presence of a greater percentage of probably active lesions in the study group would tend to minimize the difference in mortality between these two groups, and would make conservative any estimates regarding benefits to tuberculous individuals resulting from discovery in chest X-ray surveys. It was decided, therefore, not to make adjustments for differences in the types of tuberculosis included in the study and control groups in Los Angeles.

For the same reason, no adjustment will be made for an even more important difference in types of abnormalities present in the study and control groups in Dallas. Here the difference was due almost entirely to the preponderance of tuberculomas in the study group, and the presence of these would tend to raise the death rate in this group.

The number of tuberculosis suspects and the number of deaths among them for the study and control groups are given in table 3. Adjusted death rates for broad age groups are shown in figure 1. The death rates within these broad age groups have been adjusted for age (10-year groupings), sex, and race (white and nonwhite) differences between the study and control groups. The adjustment was made by the direct method using a standard population consisting of the sum of the study and control group populations. Because the number of

**Figure 1. Mortality experience for tuberculosis suspects: percentages adjusted for age-sex-race differences within age groupings.**

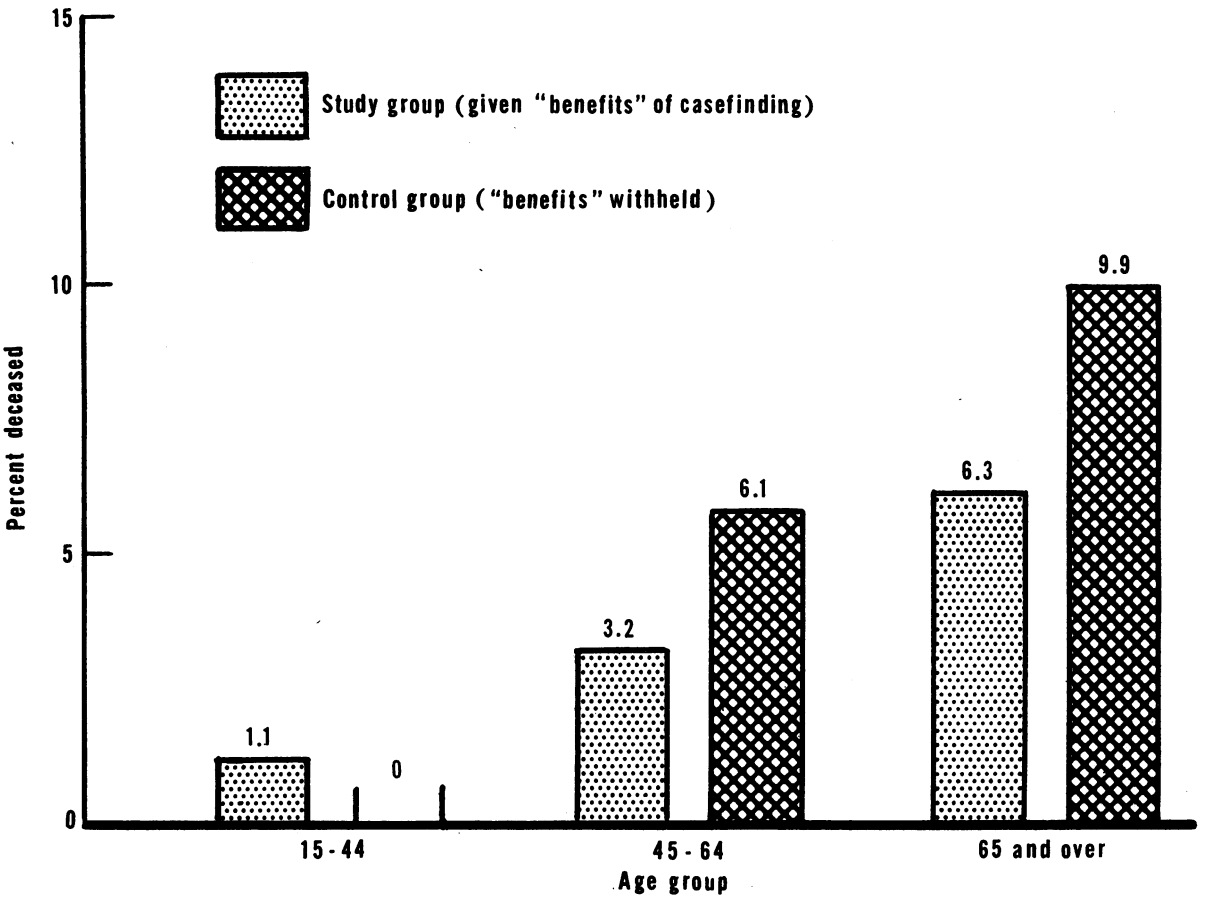

**Table 4. Cause of death for tuberculosis suspects, Los Angeles and Dallas**

| Cause of death | Total | Study group | Control group |
|---|---|---|---|
| All causes | 97 | 43 | 54 |
| Tuberculosis | 1 | 1 | 0 |
| Malignant neoplasms | 19 | 13 | 6 |
| Cardiovascular disease [1] | 62 | 21 | 41 |
| Vascular lesions of C. N. S. | 8 | 1 | 7 |
| Diseases of the heart | 52 | 18 | 34 |
| Arteriosclerotic heart disease | 40 | 13 | 27 |
| Hypertension with heart disease | 6 | 2 | 4 |
| Other heart disease | 6 | 3 | 3 |
| Other cardiovascular disease [1] | 2 | 2 | 0 |
| Accidents, suicide, homicide | 3 | 2 | 1 |
| All other causes | 12 | 6 | 6 |

[1] Includes 1 death from cardiovascular syphilis.

deaths is very small, the Los Angeles and Dallas data have been combined. The results for the combined groups appear to be approximated when each city-county group is considered separately.

In the age groups 45–64 and 65 and over, persons with X-ray evidence of tuberculosis who were given the "benefits" of casefinding had considerably lower death rates than those who were not. The difference in the age group 45–64 is statistically significant at the 5 percent level, using a one-tailed test of the hypothesis that the death rates were the same ($P=0.0274$). Whether the absence of deaths in the control groups aged 15–44 has meaning or is due to the small number (295) of persons in these groups cannot be determined. The age-sex-race-adjusted death rate for all ages was 3.13 per 100 for the study group during the 2½- to 4½-year period, or about a third lower than the comparable rate of 4.73 per 100 for the control group. This difference is statistically significant at the 5 percent level (one-tailed test, $P=0.0262$).

Only one of the deaths observed among the tuberculosis suspects was coded to tuberculosis as the underlying cause (table 4). Two-thirds were ascribed to cardiovascular disease. Death rates for all causes were as high as or higher than the expected rate, based on death rates observed in the United States in 1950, in all age groups except 65 and over. Considering that all persons in this study were in sufficiently good health to participate in a communitywide chest X-ray program (suggesting that the expected deaths might be somewhat lower than for the United States as a whole) and that the procedures used in matching survey records with death certificates probably caused an understatement of the true death rates, the abnormalities discovered on the X-ray films undoubtedly had an effect on the mortality experience.

Any reduction in death rates among those suspected of having disease would, of course, be the result of medical and nursing care given them. In both Los Angeles and Dallas, followup of tuberculosis suspects was fairly complete. While data were not obtained spe-

**Table 5. Type and degree of cardiovascular abnormality noted by radiologist**

| Type and degree of enlargement | Los Angeles | | | | Dallas | | | |
|---|---|---|---|---|---|---|---|---|
| | Study group | | Control group | | Study group | | Control group | |
| | Number | Percent | Number | Percent | Number | Percent | Number | Percent |
| All cardiovascular abnormalities | 654 | | 811 | | 534 | | 587 | |
| Cardiac enlargement (percent) | 412 | 100.0 | 564 | 100.0 | 325 | 100.0 | 363 | 100.0 |
| 10–20 (minimal) | 298 | 72.3 | 357 | 63.3 | 223 | 68.6 | 245 | 67.5 |
| 20–40 (moderate) | 94 | 22.8 | 159 | 28.2 | 87 | 26.8 | 93 | 25.6 |
| 40 or more (marked) | 20 | 4.9 | 48 | 8.5 | 15 | 4.6 | 25 | 6.9 |
| Other cardiovascular abnormalities [1] | 242 | | 247 | | 209 | | 224 | |

[1] Without heart enlargement.

cifically on the extent of followup and treatment given the study group in this report, it is known that for all tuberculosis suspects referred, a final diagnosis was received by the health department on 90 percent in Los Angeles and on 81 percent in Dallas.

### Cardiovascular Disease Suspects

The readings for the films in which the radiologist found evidence of a cardiovascular abnormality are shown in table 5. For films from Los Angeles there was a greater degree of heart enlargement in the control group than in the study group. Thus, a higher mortality rate might be expected in the control group even if there were no benefits derived from casefinding. This difference in degree of heart enlargement was associated with a difference in the age distribution of the Los Angeles population and was compensated for by an age adjustment of the death rates.

Table 6 gives the number of cardiovascular suspects and the number of deaths for the study and control groups, and figure 2 shows death rates for broad age groups. As in figure 1, the rates have been adjusted for age, sex, and race differences in the two populations. Of the total 213 deaths observed none was due to tuberculosis; 156, or 75 percent, were due to cardiovascular-renal disease (table 7).

In each age group death rates were lower for those persons with suspected cardiovascular abnormalities given the benefits of casefinding than for the corresponding control group. None of the differences is statistically significant, however. The age-sex-race-adjusted death rate for all ages in the group of cardiovascular suspects given the benefits of discovery in a chest X-ray program was 7.16 per 100, or

**Figure 2. Mortality experience for cardiovascular disease suspects: percentages adjusted for age-sex-race differences within age groupings.**

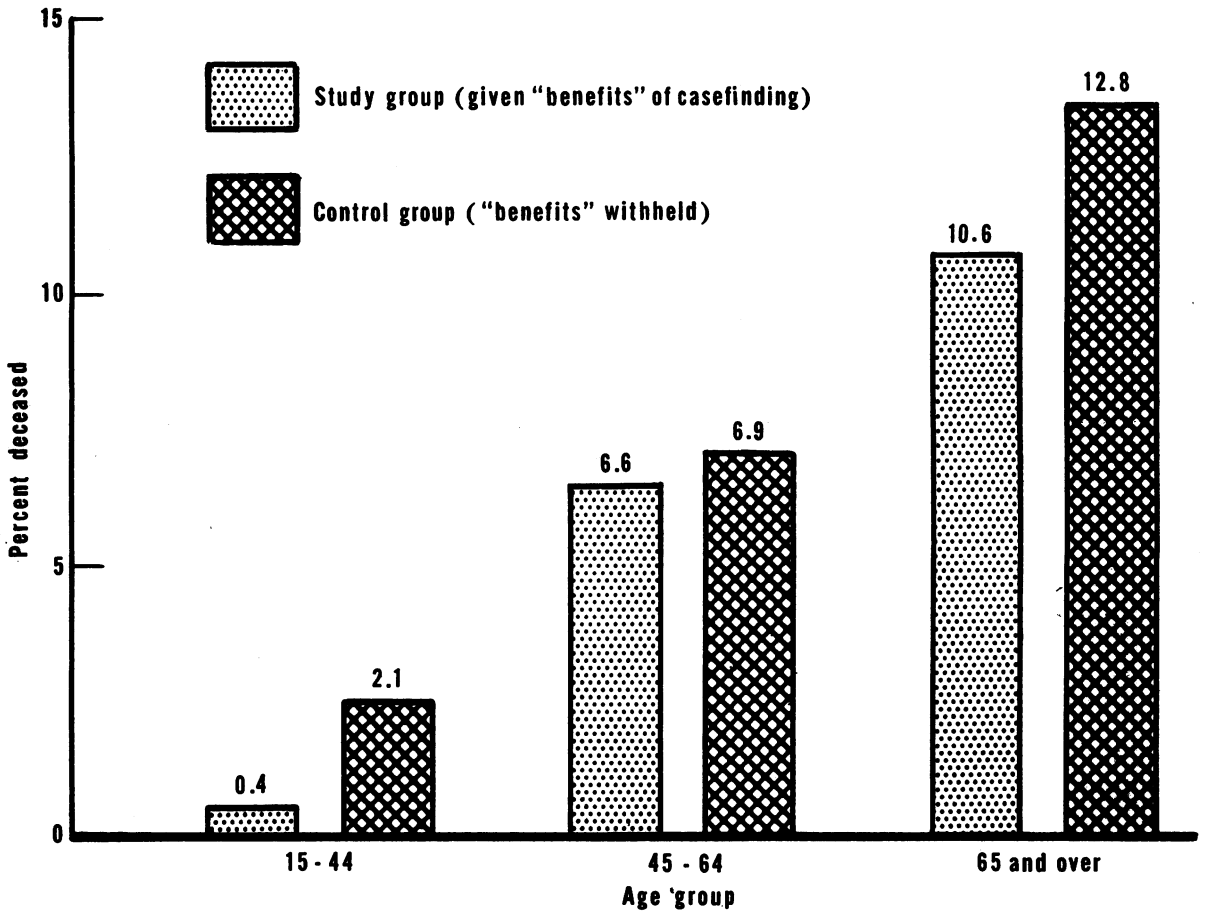

**Table 6. Number of cardiovascular disease suspects and deaths [1] observed in Los Angeles and Dallas, by age and sex**

| Ages | Study group | | | | Control group | | | |
|---|---|---|---|---|---|---|---|---|
| | Male | | Female | | Male | | Female | |
| | Suspects | Deaths | Suspects | Deaths | Suspects | Deaths | Suspects | Deaths |
| All ages | 480 | 42 | 760 | 40 | 497 | 67 | 905 | 60 |
| 15–24 | 17 | 0 | 27 | 0 | 6 | 0 | 16 | 0 |
| 25–34 | 21 | 0 | 50 | 0 | 19 | 1 | 36 | 0 |
| 35–44 | 42 | 1 | 72 | 0 | 27 | 1 | 62 | 2 |
| 45–54 | 85 | 6 | 188 | 8 | 88 | 9 | 180 | 3 |
| 55–64 | 148 | 17 | 202 | 10 | 144 | 22 | 235 | 11 |
| 65–74 | 110 | 10 | 174 | 15 | 143 | 23 | 266 | 23 |
| 75 and over | 57 | 8 | 47 | 7 | 70 | 11 | 110 | 21 |

[1] Excluding 4 deaths due to violence.

about 15 percent lower than the comparable rate of 8.39 per 100 for the group of cardiovascular suspects overlooked in the survey. This difference is not statistically significant (one-tailed test, $P=0.1190$).

Again, any benefit to persons suspected of having a cardiovascular abnormality would presumably result from medical and nursing care. In Los Angeles, a followup program was established for cardiovascular suspects. Of those considered abnormal on a confirmatory 70 mm. X-ray, a diagnostic report was obtained by the health department on 78 percent (*6*). As with the tuberculosis suspects, data were not obtained specifically on the extent of followup and treatment given the study group used in this report. In Dallas, persons with abnormal photofluorograms were referred to their physicians for diagnosis and treatment, but no intensive followup was made by the health department to obtain diagnostic reports.

**Table 7. Cause of death for cardiovascular disease suspects, Los Angeles and Dallas**

| Cause of death | Total | Study group | Control group |
|---|---|---|---|
| All causes | 213 | 86 | 127 |
| Malignant neoplasms | 29 | 13 | 16 |
| Cardiovascular disease [1] | 156 | 57 | 99 |
| Vascular lesions of C. N. S. | 36 | 13 | 23 |
| Diseases of the heart | 116 | 42 | 74 |
| Rheumatic heart disease | 7 | 2 | 5 |
| Arteriosclerotic heart disease | 86 | 31 | 55 |
| Hypertension with heart disease | 13 | 6 | 7 |
| Other heart disease | 10 | 3 | 7 |
| Other cardiovascular disease [1] | 4 | 2 | 2 |
| Accidents, suicide, homicide | 4 | 4 | 0 |
| All other causes | 24 | 12 | 12 |

[1] Includes 1 death from chronic nephritis.

## Other Diseases

There were too few cases in any other disease category to make analysis productive. There were, for example, only 411 photofluorograms on which the presence of a tumor was suspected by the radiologist. Of these, 231 were detected in the X-ray surveys but not on re-reading, and 7, or 3 percent, died during the followup period. Of 180 missed in the survey but detected on re-reading, 7, or about 4 percent, died.

## Discussion

Theoretically, it was possible in this study to make the study and control groups identical (except for chance variation) by exact matching of all factors that could cause bias between the first and second film readings. These factors were the abnormalities appearing on the film itself and the person's age, sex, and race. Since no other information was available to

the readers, no other factors could influence their decision on a particular film. Differences in age-sex-race distributions were compensated for by adjustment of the death rates, while effects of differences in criteria for classifying abnormalities among film readers were minimized by having the films reviewed independently and classified by a third reader.

Even with exact matching of the study and control groups, another factor that might affect the observed death rates is the mobility of the populations. Only files of death certificates in California and Texas were checked; hence, differences in death rates might have been due to a greater tendency for persons in the study group than for persons in the control group to die in another State. To check on this possibility, death rates observed during the first calendar year following the chest X-ray programs were compared for the study and control groups. Since death certificates for persons living in a State less than a year are allocated to the State of previous residence, the first year's mortality experience should be relatively free of bias due to departure from the State. It was found that differences in death rates during the first year were of about the same magnitude for the tuberculosis suspects and for the cardiovascular disease suspects as differences for the entire followup period. It would appear, therefore, that the lower death rate reported in the study group was not due to a larger out-migration of that group.

The fact that the control group was sent a negative report creates certain misgivings in making inferences as to the expected reduction in mortality for the tuberculosis suspects. While this report stated simply that the film "appeared satisfactory" and recommended an annual chest X-ray film, it may have deferred diagnosis and thus have worked to the disadvantage of the individual involved. There is no way of estimating the importance of this factor from the available data. If it exists, it may be offset by the imperfect matching for pathology between the study and control groups. As was noted above, this imperfect matching should have made the estimate of a third reduction in mortality conservative.

The problem of the negative notification is probably not so important for the cardiovascular disease group, since the chest X-ray surveys used for this study were not generally publicized as casefinding devices for heart disease. Thus, receipt of a negative notification was not likely to be interpreted as absence of heart disease.

Whether estimates derived here of the extent to which individuals are better off as the result of participating in chest X-ray programs apply to all those identified in these programs or only to those persons with obscure or equivocal lesions is problematical. It might be argued that, if the benefits in casefinding accrue largely because the disease found is in an early stage, and therefore is readily amenable to treatment, one would expect that persons with the very type of lesion with which this study is concerned would receive the greatest benefit.

This argument is probably more valid for cardiovascular disease than for tuberculosis. Under current treatment procedures for tuberculosis it is likely that nearly all clinical cases detected in a chest X-ray program benefit and that, in terms of averting death in the immediate future, persons with advanced disease benefit more than those with minimal disease.

From a statistical standpoint evidence of any benefit derived from the discovery of cardiovascular disease on chest X-ray surveys is weak. For tuberculosis, on the other hand, the results seem fairly conclusive. Possibly even larger differences in death rates would have been observed if it had been possible to reduce the study groups to the somewhat smaller number who actually received medical care and if appropriate control groups could have been identified for comparison. The study groups used here were, of course, diluted by some persons who were either considered essentially negative when a confirmatory film was taken or who were not kept under medical observation and treatment for other reasons.


## Summary

A study was undertaken to test the assumption that persons with disease who are detected in casefinding programs are "better off" than they would have been had they not been detected.

A study group and a control group were constructed on the basis of a second reading several years later of 208,555 70 mm. photofluorograms taken in two communitywide chest X-ray surveys. This second reading made possible the identification of 3,638 persons considered negative at the time of the survey but positive when the films were re-read and 3,670 persons considered positive at the time of the survey and negative when the films were re-read. Of those considered negative at the time of the survey but positive on second reading, a reviewing radiologist considered 3,179 as positive (control group). Of those considered positive at the time of the survey but negative on second reading, he considered 2,772 as positive (study group). The mortality experience of these two groups was then compared.

For persons whose chest X-ray films showed evidence of tuberculosis, the death rate was about a third lower in the study group than in the control group ($P=0.0262$). For persons whose chest X-ray films showed evidence of cardiovascular disease, the death rate was about 15 percent lower in the study group than in the control group ($P=0.1190$).

These differences may be considered rough estimates of the benefits of chest X-ray programs.

*Mimeographed copies of a more detailed report of this study, including additional tables, are available from Philip E. Enterline, Heart Disease Control Program, Division of Special Health Services, Public Health Service.*

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## New Division at National Institutes of Health

A Division of General Medical Sciences, headed by Dr. G. Halsey Hunt, has been formed at the Public Health Service's National Institutes of Health. The new division will administer research grants in the basic sciences and other fields, support training in the same fields through fellowships and training grants to colleges, and administer the Center for Aging Research. The first two functions have been transferred from the Division of Research Grants; the third from the National Heart Institute.

In line with these changes, the Division of Research Grants will study and evaluate all research grant and fellowship programs at the National Institutes of Health. It will continue to review, for all institutes and divisions, applications for grants and fellowship awards, and continue to process and pay grant and award funds. Dr. Ernest M. Allen will continue as chief of the Division of Research Grants.