*Is it possible to find characteristics relating to health conditions which the general public can recognize so that high-risk groups can be identified? If this can be done, members of such groups can perhaps be examined earlier for cancer or other serious diseases. This study reports some preliminary findings in this direction.*

# SOME PRELIMINARY FINDINGS ON PHYSICAL COMPLAINTS FROM A PROSPECTIVE STUDY OF 1,064,004 MEN AND WOMEN

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THE STUDY I am about to describe was undertaken with two objectives in mind: (1) One objective was to obtain clues as to the etiology of various types of cancer. (2) The other objective was to find better means of identifying "high-risk" groups on the basis of characteristics which can be recognized by the general public. By "high-risk group" I mean a group of people that differs from the general population in that a larger percentage of them either have serious disease at the present time or are destined to develop serious disease during the next several years. While cancer is the disease of primary interest in this study, we are also interested in other diseases for reasons which will be explained later. I shall confine my remarks to the second of these two objectives.

The effectiveness of therapy for cancer depends largely upon prompt treatment. This in turn depends upon getting people with cancer to their doctor for diagnosis before the disease has advanced beyond a localized stage. Since it is not feasible to give medical examinations to everyone at frequent intervals, we must give major consideration to those persons who are most likely to have undiagnosed cancer.

The teaching of the "seven cancer danger signals" has been very useful in this respect. These physical complaints were named "cancer danger signals" because they can be produced by cancer; so in some instances they are indicative of the presence of cancer. However, they can also be produced by other serious diseases. Thus they identify a "high-risk group" of persons who should seek medical attention immediately.

Unfortunately, there are two factors which somewhat limit the usefulness of the danger signals as now taught: (1) Cancer often does not produce major complaints until it has advanced to an incurable stage. (2) Once a person with a complaint, such as severe coughing, sees his doctor and is told that he does not have cancer, he may tend to disregard that complaint in the future being under the impression that in his case it is unimportant.

Several years ago, it occurred to me that these two difficulties might be partially overcome by a different approach to the problem. Instead of merely looking for complaints which are produced by cancer (and which may not appear until the cancer is advanced), perhaps we should look for complaints which

**Table 1—Distribution of Subjects Enrolled in Study**

| Age | Male | Female | Total |
|---|---|---|---|
| <30 | 2,295 | 4,311 | 6,606 |
| 30-34 | 10,743 | 19,061 | 29,804 |
| 35-39 | 18,518 | 36,901 | 55,419 |
| 40-44 | 32,452 | 75,057 | 107,509 |
| 45-49 | 97,482 | 118,464 | 215,946 |
| 50-54 | 96,412 | 107,310 | 203,722 |
| 55-59 | 74,114 | 82,942 | 157,056 |
| 60-64 | 54,009 | 61,504 | 115,513 |
| 65-69 | 37,643 | 44,885 | 82,528 |
| 70-74 | 21,522 | 27,369 | 48,891 |
| 75-79 | 10,294 | 14,415 | 24,709 |
| 80+ | 5,956 | 10,345 | 16,301 |
| Total | 461,440 | 602,564 | 1,064,004 |

appear before the occurrence of diagnosable cancer. If this turns out to be feasible, then we could give frequent medical examinations to persons having the highest risk of developing cancer.

These possibilities are suggested by the fact that most known causes of cancer, both in man and in experimental animals, produce other biological changes long before the occurrence of cancer. These changes may produce recognizable physical complaints. Furthermore, it seems likely that certain host factors, such as hormone disorders, increase susceptibility to some types of cancer, and these disorders produce symptoms. Two examples will serve to illustrate my point.

Various histologic changes are invariably found in the lungs of persons with lung cancer, and they almost certainly arise years before the appearance of invasive carcinoma.[1-3] These changes can produce symptoms such as coughing and shortness of breath; when far advanced they produce serious disease even if cancer does not develop.

Abnormal bleeding or discharge from the vagina can be produced by uterine cancer and so is called a "danger signal" of this disease. In a prospective study of uterine cancer in Toledo, we found that the complaint frequently occurs long before the appearance of diagnosable cancer.[4] Thus women with this complaint constitute a "high-risk" group requiring annual or semi-annual medical and cytological examinations.

With these thoughts in mind, the present study was designed in the hope of finding factors predictive of the later occurrence of diagnosable cancer. Some such factors might perhaps bear no resemblance to symptoms produced by cancer; they might be related to the occurrence of diseases other than cancer. From a practical standpoint, it would be most desirable to find factors which are highly predictive of serious disease in general rather than some single disease. Danger signals are only screening devices which may be used by the general public; diagnosis is a task for the physician.

## Design of Study

The design of this study was to request a large number of people to fill out questionnaires containing questions on personal factors which might be related either to the etiology of cancer or to the probability of the occurrence of cancer; to trace them annually for six years and obtain copies of death certificates of those who died; and to ask surviving subjects to fill out questionnaires once every two years giving an account of their illnesses during the intervening periods.

The enrollment of subjects was carried on between October 1, 1959, and February 15, 1960, by 68,116 volunteer workers of the American Cancer Society in 1,121 counties in 25 states.* The volunteer workers were so selected as to include all segments of the popu-

* Arizona, California, Florida, Georgia, Illinois, Indiana, Iowa, Kansas, Kentucky, Louisiana, Maryland, Massachusetts, Michigan, Minnesota, Mississippi, Missouri, New York State, North Carolina, Ohio, Oregon, Pennsylvania, South Carolina, Tennessee, Texas, Virginia.

**Table 2—Number and Per cent of Subjects by Education, Sex, and Age**

| Age Group | Total Persons | | Grammar School or Less | | Some High School | | High School Graduate | | Some College | | College Graduate | | Education Not Stated | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | No. | % | No. | % | No. | % | No. | % | No. | % | No. | % | No. | % |
| | | | | | | Men | | | | | | | | |
| <30 | 2,295 | 100.0 | 167 | 7.3 | 380 | 16.6 | 651 | 28.4 | 517 | 22.5 | 548 | 23.9 | 32 | 1.4 |
| 30-34 | 10,743 | 100.0 | 715 | 6.7 | 1,820 | 16.9 | 2,954 | 27.5 | 2,145 | 20.0 | 3,039 | 28.3 | 70 | 0.7 |
| 35-39 | 18,518 | 100.0 | 1,419 | 7.7 | 3,014 | 16.3 | 5,534 | 29.9 | 3,888 | 21.0 | 4,566 | 24.7 | 97 | 0.5 |
| 40-44 | 32,452 | 100.0 | 3,251 | 10.0 | 5,837 | 18.0 | 9,776 | 30.1 | 6,439 | 19.8 | 6,998 | 21.6 | 151 | 0.5 |
| 45-49 | 97,482 | 100.0 | 13,120 | 13.5 | 18,721 | 19.2 | 24,054 | 24.7 | 19,508 | 20.0 | 21,596 | 22.2 | 483 | 0.5 |
| 50-54 | 96,412 | 100.0 | 18,031 | 18.7 | 20,677 | 21.4 | 17,961 | 18.6 | 18,503 | 19.2 | 20,665 | 21.4 | 575 | 0.6 |
| 55-59 | 74,114 | 100.0 | 20,471 | 27.6 | 16,807 | 22.7 | 9,797 | 13.2 | 12,451 | 16.8 | 13,871 | 18.7 | 717 | 1.0 |
| 60-64 | 54,009 | 100.0 | 18,085 | 33.5 | 12,059 | 22.3 | 6,017 | 11.1 | 8,896 | 16.5 | 8,191 | 15.2 | 761 | 1.4 |
| 65-69 | 37,643 | 100.0 | 15,226 | 40.4 | 7,805 | 20.7 | 3,411 | 9.1 | 5,466 | 14.5 | 5,018 | 13.3 | 717 | 1.9 |
| 70-74 | 21,522 | 100.0 | 9,776 | 45.4 | 3,984 | 18.5 | 1,578 | 7.3 | 2,862 | 13.3 | 2,703 | 12.6 | 619 | 2.9 |
| 75-79 | 10,294 | 100.0 | 5,093 | 49.5 | 1,751 | 17.0 | 673 | 6.5 | 1,179 | 11.5 | 1,197 | 11.6 | 401 | 3.9 |
| 80-84 | 4,014 | 100.0 | 2,104 | 52.4 | 633 | 15.8 | 245 | 6.1 | 413 | 10.3 | 437 | 10.9 | 182 | 4.5 |
| 85+ | 1,942 | 100.0 | 1,129 | 58.1 | 228 | 11.7 | 97 | 5.0 | 185 | 9.5 | 185 | 9.5 | 118 | 6.1 |
| Total | 461,440 | 100.0 | 108,587 | 23.5 | 93,716 | 20.3 | 82,748 | 17.9 | 82,452 | 17.9 | 89,014 | 19.3 | 4,923 | 1.1 |
| | | | | | | Women | | | | | | | | |
| <30 | 4,311 | 100.0 | 160 | 3.7 | 726 | 16.8 | 1,737 | 40.3 | 960 | 22.3 | 681 | 15.8 | 47 | 1.1 |
| 30-34 | 19,061 | 100.0 | 775 | 4.1 | 2,913 | 15.3 | 8,032 | 42.1 | 4,186 | 22.0 | 3,066 | 16.1 | 89 | 0.5 |
| 35-39 | 36,901 | 100.0 | 2,050 | 5.6 | 5,390 | 14.6 | 15,320 | 41.5 | 8,928 | 24.2 | 5,070 | 13.7 | 143 | 0.4 |
| 40-44 | 75,057 | 100.0 | 5,622 | 7.5 | 12,540 | 16.7 | 29,392 | 39.2 | 16,531 | 22.0 | 10,648 | 14.2 | 324 | 0.4 |
| 45-49 | 118,464 | 100.0 | 11,948 | 10.1 | 21,923 | 18.5 | 37,566 | 31.7 | 27,599 | 23.3 | 18,859 | 15.9 | 569 | 0.5 |
| 50-54 | 107,310 | 100.0 | 14,557 | 13.6 | 21,681 | 20.2 | 26,012 | 24.2 | 25,623 | 23.9 | 18,755 | 17.5 | 682 | 0.6 |
| 55-59 | 82,942 | 100.0 | 17,239 | 20.8 | 18,492 | 22.3 | 15,778 | 19.0 | 18,555 | 22.4 | 12,118 | 14.6 | 760 | 0.9 |
| 60-64 | 61,504 | 100.0 | 16,777 | 27.3 | 13,872 | 22.6 | 10,349 | 16.8 | 12,162 | 19.8 | 7,517 | 12.2 | 827 | 1.3 |
| 65-69 | 44,885 | 100.0 | 14,522 | 32.4 | 10,473 | 23.3 | 6,131 | 13.7 | 8,118 | 18.1 | 4,693 | 10.5 | 948 | 2.1 |
| 70-74 | 27,369 | 100.0 | 10,185 | 37.2 | 6,074 | 22.2 | 3,393 | 12.4 | 4,541 | 16.6 | 2,363 | 8.6 | 813 | 3.0 |
| 75-79 | 14,415 | 100.0 | 6,191 | 42.9 | 3,136 | 21.8 | 1,717 | 11.9 | 1,933 | 13.4 | 941 | 6.5 | 497 | 3.4 |
| 80-84 | 6,739 | 100.0 | 3,245 | 48.2 | 1,286 | 19.1 | 764 | 11.3 | 795 | 11.8 | 395 | 5.9 | 254 | 3.8 |
| 85+ | 3,606 | 100.0 | 1,951 | 54.1 | 622 | 17.2 | 343 | 9.5 | 360 | 10.0 | 181 | 5.0 | 149 | 4.1 |
| Total | 602,564 | 100.0 | 105,222 | 17.5 | 119,128 | 19.8 | 156,534 | 26.0 | 130,291 | 21.6 | 85,287 | 14.1 | 6,102 | 1.0 |

**Table 3—Number of Subjects by Place of Residence**

| Type of Area | No. of Subjects | | |
|---|---|---|---|
| | Male | Female | Total |
| Metropolitan Areas: | | | |
| 2 million + | 93,529 | 122,387 | 215,916 |
| 1–2 million | 49,316 | 64,560 | 113,876 |
| ½ to 1 million | 49,499 | 65,867 | 115,366 |
| 50,000 to ½ million | 90,797 | 121,538 | 212,335 |
| Nonmetropolitan Areas: | | | |
| 10,000 to 50,000 | 45,016 | 61,099 | 106,115 |
| 2,500 to 10,000 | 36,698 | 48,775 | 85,473 |
| Rural | 94,492 | 115,727 | 210,219 |
| Not Classified: | 2,093 | 2,611 | 4,704 |
| Total | 461,440 | 602,564 | 1,064,004 |

lation except illiterates and migrant workers. Each worker was instructed to enroll about ten families in which there was at least one person over the age of 45, and then request all members of these families over the age of 30 to fill out a confidential questionnaire.

A total of 1,078,894 subjects filled out questionnaires, but 14,890 of the questionnaires lacked information on age or were otherwise seriously inadequate. Thus 1,064,004 subjects were effectively enrolled. Their age and sex distribution is shown in Table 1. As shown in Table 2, we succeeded in enrolling subjects of all educational levels, although the percentage of college graduates was somewhat higher than in the general population. A particular effort was made to enroll an adequate number of subjects from rural areas and small towns as well as metropolitan areas of all sizes (Table 3).

The first follow-up started on October 1, 1960, and was highly successful. The second follow-up started on October 1, 1961, and was also highly successful, but it was not completed in time to include all the data in this report.

The volunteer workers are organized in 1,370 units, there being one or more units in each of the 1,121 counties. This report is based upon records from 1,116 units which had largely completed their work by August 15, 1962. These units enrolled 904,408 subjects over the age of 30 and succeeded in tracing 890,394 (98.5 per cent) of them through October 1, 1961 (Table 4). A total of 16,722 deaths was reported among these subjects from the start of the study up to October 1, 1961, and, up to the cut-off date for this analysis, we had obtained death certificates on 14,681 (87.8 per cent) of them. Since it took some time to code the follow-up information and put it on magnetic tape, we have only had time to prepare a few preliminary tables. We have not yet completed coding the repeat questionnaires which were filled out during the second follow-up period.

## Present Physical Complaints

The second page of the original questionnaire contained questions on "present" physical complaints, there being 24 listed for men and 26 listed for women. Those who said that they had a complaint were asked whether it was "slight," "moderate," or "severe." These questions were answered by 877,645 of the subjects (16,458 of whom later died)

but were skipped by the remaining 12,749 subjects.

Table 5 shows the percentage of men who reported various complaints. Some complaints such as headache and cough are very common, but often are present to only a slight degree. For example, 34.2 per cent of the men said that they had a cough, but only 1.8 per cent said that they had a "severe" cough. Table 6 shows the percentage of women who reported various complaints.

Table 7 shows the observed vs. the expected number of deaths during the entire study period for men who reported various physical complaints. In each instance, the expected number is based upon the age-specific death rates of men who said that they did not have the complaint. Six complaints showed mortality ratios of 1.84 or greater, these being loss of weight, loss of appetite, shortness of breath, pain or discomfort in chest, fatigue easily, and blood in urine. Such high mortality ratios indicate that these complaints must be either indicative of a multiplicity of different diseases or highly indicative of one or

**Table 4—Subjects Included in Present Analysis**

| Age Group | No. of Subjects | No. of Deaths | | |
|---|---|---|---|---|
| | | Total | 1st Period Prior to 10/1/60 | 2nd Period 10/1/60 to 9/30/61 |
| | | Men | | |
| 30-34 | 8,694 | 28 | 13 | 15 |
| 35-39 | 15,234 | 62 | 25 | 37 |
| 40-44 | 27,139 | 181 | 82 | 99 |
| 45-49 | 82,374 | 743 | 335 | 408 |
| 50-54 | 81,879 | 1,146 | 493 | 653 |
| 55-59 | 63,023 | 1,412 | 648 | 764 |
| 60-64 | 45,890 | 1,607 | 670 | 937 |
| 65-69 | 31,599 | 1,611 | 744 | 867 |
| 70-74 | 18,019 | 1,371 | 601 | 770 |
| 75-79 | 8,597 | 935 | 431 | 504 |
| 80-85 | 3,337 | 564 | 232 | 332 |
| 85+ | 1,642 | 422 | 194 | 228 |
| Total men | 387,427 | 10,082 | 4,468 | 5,614 |
| | | Women | | |
| 30-34 | 15,319 | 24 | 13 | 11 |
| 35-39 | 30,401 | 68 | 27 | 41 |
| 40-44 | 63,034 | 191 | 78 | 113 |
| 45-49 | 100,337 | 438 | 171 | 267 |
| 50-54 | 90,670 | 581 | 240 | 341 |
| 55-59 | 70,083 | 675 | 295 | 380 |
| 60-64 | 51,803 | 714 | 302 | 412 |
| 65-69 | 37,544 | 873 | 375 | 498 |
| 70-74 | 22,958 | 898 | 366 | 532 |
| 75-79 | 12,139 | 836 | 360 | 476 |
| 80-85 | 5,671 | 700 | 300 | 400 |
| 85+ | 3,008 | 642 | 274 | 368 |
| Total women | 502,967 | 6,640 | 2,801 | 3,839 |
| Total, both sexes | 890,394 | 16,722 | 7,269 | 9,453 |

**Table 5—Percentage of Men Reporting Specific Complaints by Age Group**

| Complaint | Total | 30-34 | 35-39 | 40-44 | 45-49 | 50-54 | 55-59 | 60-64 | 65-69 | 70-74 | 75-79 | 80-84 | 85+ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Headaches | 38.7 | 45.6 | 46.7 | 46.0 | 43.8 | 40.9 | 37.8 | 33.5 | 30.1 | 26.3 | 23.6 | 23.9 | 21.4 |
| Cough | 34.2 | 30.5 | 32.0 | 32.5 | 33.5 | 34.6 | 35.0 | 35.4 | 34.9 | 34.8 | 34.6 | 37.3 | 34.0 |
| Fatigue easily | 33.0 | 19.0 | 21.5 | 24.5 | 28.6 | 32.2 | 35.1 | 38.5 | 40.5 | 42.2 | 44.1 | 48.8 | 54.7 |
| Indigestion | 26.2 | 24.3 | 26.8 | 26.5 | 26.7 | 25.9 | 25.8 | 25.9 | 26.5 | 26.7 | 26.9 | 28.6 | 27.1 |
| Shortness of breath | 25.3 | 16.2 | 17.6 | 19.4 | 22.5 | 24.8 | 26.7 | 29.4 | 31.0 | 31.2 | 30.6 | 33.1 | 34.8 |
| Constipation | 18.5 | 12.5 | 12.8 | 13.6 | 14.5 | 15.9 | 17.8 | 21.3 | 25.2 | 31.1 | 36.4 | 44.0 | 54.7 |
| Dizziness | 16.4 | 10.8 | 11.3 | 12.3 | 13.5 | 14.8 | 16.3 | 19.0 | 21.7 | 24.2 | 28.0 | 34.0 | 37.7 |
| Pain or discomfort in chest | 15.1 | 15.1 | 15.5 | 14.9 | 14.7 | 14.3 | 14.4 | 16.0 | 16.4 | 16.3 | 16.4 | 18.0 | 14.2 |
| Sore throat | 14.6 | 16.6 | 16.0 | 14.5 | 13.7 | 13.9 | 14.1 | 15.3 | 15.8 | 16.8 | 16.5 | 16.9 | 13.7 |
| Pain in stomach | 13.6 | 13.2 | 14.1 | 13.9 | 13.8 | 13.5 | 13.1 | 13.5 | 13.8 | 14.2 | 15.0 | 15.2 | 14.8 |
| Too frequent urination | 13.0 | 5.4 | 6.1 | 7.1 | 8.5 | 10.3 | 12.9 | 17.3 | 21.8 | 25.2 | 28.2 | 32.4 | 31.4 |
| Insomnia | 13.0 | 7.9 | 8.9 | 10.9 | 12.8 | 13.6 | 13.6 | 13.7 | 13.7 | 13.4 | 13.5 | 16.9 | 16.1 |
| Pain in lower abdomen | 11.8 | 10.1 | 10.9 | 10.8 | 11.2 | 11.5 | 11.7 | 12.3 | 13.1 | 13.7 | 14.5 | 15.8 | 14.1 |
| Hoarseness | 11.2 | 9.0 | 9.4 | 9.6 | 9.8 | 10.6 | 11.0 | 12.4 | 13.6 | 15.2 | 15.6 | 17.8 | 15.0 |
| Loss of weight* | 7.7 | 6.7 | 6.7 | 6.7 | 6.9 | 7.4 | 7.7 | 8.6 | 9.0 | 8.7 | 9.6 | 9.3 | 8.5 |
| Difficulty in urinating | 7.1 | 1.5 | 1.9 | 2.3 | 3.4 | 5.0 | 7.4 | 10.9 | 14.1 | 15.8 | 18.0 | 19.7 | 22.1 |
| Diarrhea | 6.0 | 5.9 | 6.7 | 6.5 | 6.2 | 5.9 | 5.5 | 5.7 | 5.8 | 6.2 | 7.4 | 8.0 | 8.7 |
| Blood in stool | 5.8 | 6.0 | 6.7 | 6.5 | 6.6 | 6.0 | 5.3 | 5.1 | 4.7 | 4.4 | 4.7 | 5.2 | 5.5 |
| Gain of weight* | 5.3 | 7.7 | 6.6 | 6.2 | 5.8 | 5.4 | 5.2 | 4.8 | 4.5 | 3.6 | 3.0 | 2.4 | 2.9 |
| Nausea or vomiting | 5.1 | 5.0 | 5.5 | 5.5 | 5.1 | 4.9 | 4.9 | 5.0 | 5.0 | 5.5 | 6.0 | 6.5 | 5.9 |
| Loss of appetite | 4.9 | 4.3 | 4.0 | 3.9 | 3.9 | 4.2 | 4.7 | 5.6 | 6.4 | 8.0 | 9.5 | 12.3 | 14.8 |
| Recent change in bowel habits | 4.5 | 4.0 | 4.3 | 4.1 | 3.9 | 3.8 | 4.1 | 4.7 | 5.8 | 7.3 | 9.1 | 10.6 | 8.2 |
| Difficulty in swallowing | 3.3 | 2.8 | 3.2 | 2.9 | 2.8 | 2.9 | 3.0 | 3.6 | 4.2 | 4.8 | 6.0 | 7.3 | 9.7 |
| Blood in urine | 1.3 | 0.7 | 0.9 | 0.9 | 1.0 | 1.0 | 1.2 | 1.5 | 2.0 | 2.3 | 3.2 | 3.8 | 4.3 |

* Change in weight in past two years.

**Table 6—Percentage of Women Reporting Specific Complaints by Age Group**

| Complaint | Total | 30-34 | 35-39 | 40-44 | 45-49 | 50-54 | 55-59 | 60-64 | 65-69 | 70-74 | 75-79 | 80-84 | 85+ |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Headaches | 56.2 | 61.6 | 62.8 | 62.8 | 61.8 | 58.9 | 54.3 | 50.5 | 45.8 | 42.4 | 39.4 | 36.1 | 32.5 |
| Fatigue easily | 45.7 | 42.1 | 43.5 | 44.7 | 45.8 | 45.7 | 44.6 | 44.9 | 45.1 | 48.4 | 53.7 | 59.5 | 63.5 |
| Constipation | 33.7 | 27.9 | 27.3 | 27.8 | 30.3 | 34.1 | 35.4 | 36.2 | 38.6 | 42.1 | 47.3 | 52.2 | 54.5 |
| Dizziness | 29.1 | 23.3 | 24.2 | 26.0 | 27.3 | 28.0 | 28.6 | 31.1 | 33.4 | 37.7 | 42.2 | 46.0 | 47.5 |
| Indigestion | 28.6 | 22.2 | 23.6 | 25.1 | 26.5 | 28.2 | 30.3 | 32.0 | 32.9 | 34.9 | 34.7 | 34.4 | 32.8 |
| Insomnia | 26.4 | 13.9 | 15.9 | 19.8 | 23.8 | 29.0 | 31.1 | 31.5 | 31.0 | 31.4 | 30.2 | 30.8 | 30.6 |
| Shortness of breath | 22.5 | 19.4 | 20.7 | 21.9 | 22.0 | 21.4 | 21.6 | 22.9 | 23.7 | 26.3 | 30.0 | 33.8 | 34.3 |
| Cough | 21.2 | 24.1 | 22.4 | 22.1 | 21.4 | 20.0 | 19.5 | 20.1 | 21.6 | 22.6 | 25.2 | 25.7 | 28.3 |
| Pain in lower abdomen | 17.8 | 23.6 | 22.6 | 21.8 | 19.6 | 16.7 | 15.1 | 14.6 | 14.7 | 15.4 | 15.6 | 16.7 | 16.0 |
| Sore throat | 17.3 | 20.0 | 17.6 | 16.5 | 15.9 | 16.1 | 17.2 | 18.0 | 19.6 | 20.4 | 20.0 | 18.0 | 15.4 |
| Hoarseness | 14.8 | 13.4 | 12.9 | 12.5 | 13.4 | 14.7 | 15.3 | 16.3 | 17.6 | 18.5 | 19.9 | 18.7 | 16.2 |
| Pain or discomfort in chest | 13.3 | 13.8 | 13.7 | 13.8 | 13.4 | 13.1 | 12.8 | 12.8 | 12.7 | 13.8 | 14.4 | 15.1 | 15.0 |
| Pain in stomach | 13.2 | 13.5 | 13.6 | 13.7 | 13.4 | 12.9 | 12.5 | 12.8 | 12.8 | 13.6 | 14.9 | 15.1 | 15.4 |
| Loss of weight* | 10.4 | 12.0 | 11.1 | 10.0 | 9.8 | 10.2 | 10.4 | 10.4 | 10.8 | 11.4 | 12.1 | 12.7 | 10.8 |
| Nausea or vomiting | 10.3 | 10.9 | 10.4 | 10.5 | 10.2 | 10.3 | 10.1 | 9.8 | 9.8 | 10.4 | 11.3 | 11.8 | 12.0 |
| Gain of weight* | 8.1 | 10.1 | 9.9 | 10.0 | 9.9 | 9.1 | 7.2 | 6.2 | 5.0 | 3.8 | 3.3 | 2.1 | 1.8 |
| Recent change in bowel habits | 6.3 | 5.9 | 5.5 | 5.8 | 6.2 | 6.4 | 6.1 | 6.2 | 6.7 | 7.3 | 8.5 | 9.3 | 8.9 |
| Diarrhea | 6.0 | 5.4 | 5.8 | 5.9 | 6.0 | 5.8 | 5.7 | 6.3 | 6.3 | 6.9 | 7.0 | 8.2 | 8.9 |
| Difficulty in swallowing | 4.9 | 4.9 | 4.9 | 4.6 | 4.6 | 4.8 | 4.7 | 4.7 | 4.9 | 5.8 | 7.3 | 8.6 | 11.2 |
| Loss of appetite | 4.7 | 5.4 | 4.5 | 4.1 | 3.9 | 3.7 | 3.8 | 4.4 | 5.5 | 7.7 | 11.2 | 14.4 | 18.3 |
| Blood in stool | 4.6 | 5.0 | 5.0 | 5.2 | 5.1 | 4.7 | 4.3 | 4.1 | 3.7 | 3.7 | 3.9 | 3.8 | 4.1 |
| Unusual discharge from vagina | 3.8 | 10.1 | 7.8 | 5.9 | 4.6 | 3.3 | 2.3 | 1.8 | 1.5 | 1.5 | 1.5 | 1.6 | 1.8 |
| Lump in breast | 2.7 | 3.9 | 3.9 | 3.9 | 3.8 | 2.7 | 1.9 | 1.4 | 1.4 | 1.3 | 1.3 | 1.5 | 1.4 |
| Unusual bleeding from vagina | 1.8 | 3.2 | 2.9 | 3.1 | 2.7 | 1.6 | 0.9 | 0.8 | 0.8 | 0.8 | 0.9 | 1.0 | 1.1 |
| Blood in urine | 1.5 | 1.3 | 1.4 | 1.5 | 1.5 | 1.5 | 1.6 | 1.6 | 1.5 | 1.7 | 1.8 | 1.9 | 2.4 |
| Unusual discharge from breast | 0.4 | 0.8 | 0.8 | 0.6 | 0.4 | 0.3 | 0.2 | 0.2 | 0.2 | 0.2 | 0.3 | 0.2 | 0.4 |

* Change in weight in last two years.

**Table 7—Observed vs. Expected Deaths for Each Specific Complaint (Men—All Deaths Prior to October 1, 1962)**

| Complaint | Observed Deaths | Expected Deaths | Mortality Ratio |
|---|---|---|---|
| Loss of weight* | 2,301 | 1,029.3 | 2.24 |
| Loss of appetite | 1,301 | 608.6 | 2.14 |
| Shortness of breath | 4,575 | 2,204.7 | 2.08 |
| Pain or discomfort in chest | 2,678 | 1,365.9 | 1.96 |
| Fatigue easily | 5,404 | 2,838.8 | 1.90 |
| Blood in urine | 304 | 184.7 | 1.84 |
| Difficulty in swallowing | 678 | 408.1 | 1.66 |
| Nausea or vomiting | 809 | 502.3 | 1.61 |
| Recent change in bowel habits | 888 | 585.9 | 1.52 |
| Cough | 4,288 | 3,099.5 | 1.36 |
| Dizziness | 2,573 | 1,943.2 | 1.32 |
| Insomnia | 1,715 | 1,303.1 | 1.32 |
| Blood in stool | 657 | 507.8 | 1.29 |
| Too frequent urination | 2,228 | 1,807.6 | 1.23 |
| Constipation | 2,894 | 2,381.5 | 1.22 |
| Pain in stomach | 1,614 | 1,333.6 | 1.21 |
| Difficulty in urinating | 1,369 | 1,128.8 | 1.21 |
| Pain in lower abdomen | 1,458 | 1,245.3 | 1.17 |
| Diarrhea | 705 | 615.4 | 1.15 |
| Hoarseness | 1,390 | 1,282.6 | 1.08 |
| Indigestion | 2,758 | 2,578.7 | 1.07 |
| Gain of weight* | 695 | 694.7 | 1.00 |
| Sore throat | 1,511 | 1,530.8 | 0.99 |
| Headaches | 3,042 | 3,354.0 | 0.91 |

* Change of weight in last two years.

two very common causes of death. A number of other complaints, which showed lower mortality ratios, are presumably not related to disease in general but may be highly related to certain specific diseases.

Table 8 shows observed vs. expected number of deaths among women with physical complaints. Loss of appetite showed the highest mortality ratio. Lump in breast showed the second highest mortality ratio. We do not yet know whether this is entirely accounted for by the relationship of lump in breast to breast cancer. It is possible that women who are not feeling well have a greater than average tendency to examine their breasts, and this could partly account for the high mortality ratio.

Mortality ratios for specific complaints vary with age and with the severity of the complaint. Furthermore, in some instances, they vary with time. These details are shown in Table 9 for cough among men. The magnitude of the mortality ratio increased with severity of cough and decreased with age. The mortality ratios were lower in the second follow-up period (i.e., October 1, 1960, through September 30, 1961) than in the first follow-up period (i.e., from start of study through September 30, 1960).

The value of danger signals is that they serve as a warning to a person that he should see his doctor. Thus we are primarily interested in physical complaints among people who are unaware

that they are sick. The data shown in Table 10 are confined to men who at the time of enrollment said that they were "not sick at present" and had never had cancer, heart disease, stroke, or high blood pressure. In the second follow-up period, the death rate was twice as high among men who originally said that they had a severe cough than among men who said that they did not have a cough.

Since we have not yet received death certificates on all deaths reported, I can only give a few tentative and incomplete figures on specific causes of death.

Table 11, which shows mortality ratios for lung cancer, is confined to men who at the time of enrollment said that they had never had cancer. Actually, some of them may have had lung cancer at that time, but presumably it was not diagnosed. Up to October 1, 1962, 9,325 of these men had died and lung cancer was indicated on 283 of the death certificates so far received.

Cough is considered to be a danger signal for lung cancer. Mortality ratios from this disease were 2.44 for men with a slight cough, 4.06 for moderate cough, and 7.00 for severe cough. Shortness of breath and pain or discomfort in chest are not usually included in the list of cancer danger signals. Nevertheless, the

**Table 8—Observed vs. Expected Deaths for Each Specific Complaint (Women—All Deaths Prior to October 1, 1961)**

| Complaint | Observed Deaths | Expected Deaths | Mortality Ratio |
|---|---|---|---|
| Loss of appetite | 1,067 | 467.0 | 2.28 |
| Lump in breast | 226 | 114.1 | 1.98 |
| Loss of weight* | 1,751 | 891.2 | 1.96 |
| Unusual discharge from breast | 35 | 19.5 | 1.79 |
| Pain or discomfort in chest | 1,414 | 803.1 | 1.76 |
| Shortness of breath | 2,518 | 1,446.0 | 1.74 |
| Difficulty in swallowing | 631 | 385.2 | 1.64 |
| Fatigue easily | 3,991 | 2,521.9 | 1.58 |
| Recent change in bowel habits | 683 | 454.2 | 1.50 |
| Unusual bleeding from vagina | 111 | 75.7 | 1.47 |
| Blood in urine | 161 | 110.1 | 1.46 |
| Nausea or vomiting | 917 | 660.0 | 1.39 |
| Diarrhea | 569 | 432.2 | 1.32 |
| Cough | 1,816 | 1,413.4 | 1.28 |
| Unusual discharge from vagina | 194 | 151.6 | 1.28 |
| Blood in stool | 338 | 265.2 | 1.27 |
| Dizziness | 2,553 | 2,186.1 | 1.17 |
| Pain in lower abdomen | 1,190 | 1,019.4 | 1.17 |
| Pain in stomach | 1,015 | 880.5 | 1.15 |
| Constipation | 2,831 | 2,612.0 | 1.08 |
| Hoarseness | 1,141 | 1,098.5 | 1.04 |
| Gain of weight* | 589 | 565.1 | 1.04 |
| Insomnia | 1,896 | 1,925.5 | 0.98 |
| Sore throat | 1,139 | 1,192.8 | 0.95 |
| Indigestion | 1,974 | 2,142.7 | 0.92 |
| Headaches | 2,855 | 3,310.8 | 0.86 |

* Change of weight in last two years.

**Table 9—Mortality Ratios in Relation to Cough (All Men in Study)**

| Age | No Cough | Slight Cough | Moderate Cough | Severe Cough |
|---|---|---|---|---|
| First follow-up period* | | | | |
| <45 | 1.00 | 1.62 | 2.12 | 4.00 |
| 45-59 | 1.00 | 1.36 | 1.56 | 2.61 |
| 60-74 | 1.00 | 1.14 | 1.50 | 2.04 |
| 75+ | 1.00 | 1.04 | 1.52 | 1.41 |
| Second follow-up period† | | | | |
| <45 | 1.00 | 1.03 | 1.71 | 2.14 |
| 45-59 | 1.00 | 1.33 | 1.79 | 2.39 |
| 60-74 | 1.00 | 1.19 | 1.37 | 1.86 |
| 75+ | 1.00 | 0.96 | 1.19 | 1.35 |

* Start of study through September 30, 1960.
† October 1, 1960, through September 30, 1961.

lung cancer mortality ratio was 5.59 for men with severe shortness of breath and 3.20 for men with severe pain or discomfort in chest. Men who complained of loss of appetite (any degree) had a lung cancer mortality ratio of 2.47, and men who complained of "fatigue easily" to a severe degree had a lung cancer mortality ratio of 2.80 (Table 11).

A preliminary look at findings in respect to cancer of some other common sites may be briefly summarized as follows:

Loss of appetite and loss of weight show a fairly high degree of relationship to subsequent death from cancer of most of the common sites in both men and women. It remains to be seen whether these complaints become manifest before the disease has advanced to an incurable stage.

As would be expected, change in

**Table 10—Mortality Ratios in Relation to Cough—Men Who at Time of Enrollment Said That They Were "Not Sick at Present," and Had Never Had Cancer, Heart Disease, Stroke or High Blood Pressure**

| Age | No Cough | Slight Cough | Moderate Cough | Severe Cough |
|---|---|---|---|---|
| First follow-up period* | | | | |
| <45 | 1.00 | 1.04 | 1.28 | 10.00 |
| 45-59 | 1.00 | 1.49 | 1.50 | 2.21 |
| 60-74 | 1.00 | 1.19 | 1.50 | 0.99 |
| 75+ | 1.00 | 1.12 | 1.59 | 0.71 |
| Second follow-up period† | | | | |
| <45 | 1.00 | 0.88 | 1.25 | 3.33 |
| 45-59 | 1.00 | 1.28 | 1.75 | 2.78 |
| 60-74 | 1.00 | 1.27 | 1.40 | 1.70 |
| 75+ | 1.00 | 0.79 | 1.22 | 1.41 |

* Start of study through September 30, 1960.
† October 1, 1960, through September 30, 1961.

**Table 11—Lung Cancer Mortality Ratios, Men Who Had Not Had Cancer Up to Time of Enrollment**

| Complaint | Without Complaint | With Complaint | | | |
|---|---|---|---|---|---|
| | | Total | Slight | Moderate | Severe |
| Cough | 1.00 | 3.44 | 2.44 | 4.06 | 7.00 |
| Shortness of breath | 1.00 | 2.47 | 1.85 | 2.41 | 5.59 |
| Pain or discomfort in chest | 1.00 | 1.78 | 1.38 | 2.14 | 3.20 |
| Fatigue easily | 1.00 | 1.76 | 1.33 | 1.89 | 2.80 |
| Loss of appetite | 1.00 | 2.47 | — | — | — |

bowel habits and blood in stool show a very high degree of relationship with cancer of the rectum and colon, and pain in lower abdomen shows a substantial degree of association with this disease.

Also as would be expected, "lump in breast" is highly associated with the later discovery of breast cancer.

Both difficulty in urination and too frequent urination are highly related to cancer of the prostate; several other complaints including constipation, change in bowel habits, and pain in lower abdomen are also somewhat associated with this disease.

From this preliminary analysis, it appears that the "seven cancer danger signals" as now taught are indeed indicative of the presence of cancer in many instances. In addition, some of them are importantly related to diseases other than

**Table 12—Deaths* per 100 Men by Degree of Exercise (Selected Age Groups)**

| Age | No Exercise | Slight Exercise | Moderate Exercise | Heavy Exercise |
|---|---|---|---|---|
| First follow-up period | | | | |
| 45-49 | 1.06 | 0.56 | 0.38 | 0.23 |
| 50-54 | 2.08 | 0.80 | 0.55 | 0.33 |
| 55-59 | 3.60 | 1.58 | 0.86 | 0.59 |
| 60-64 | 4.90 | 2.32 | 1.19 | 0.92 |
| 65-69 | 10.33 | 3.85 | 1.74 | 1.38 |
| 70-74 | 11.02 | 4.92 | 2.60 | 1.56 |
| 75-79 | 16.05 | 6.55 | 3.46 | 1.96 |
| 80-84 | 16.43 | 8.49 | 3.96 | 4.49 |
| 85+ | 22.13 | 12.08 | 5.67 | 2.78 |
| Second follow-up period | | | | |
| 45-49 | 1.14 | 0.63 | 0.45 | 0.40 |
| 50-54 | 1.31 | 1.15 | 0.75 | 0.49 |
| 55-59 | 3.23 | 1.81 | 1.02 | 0.93 |
| 60-64 | 5.40 | 3.01 | 1.84 | 1.37 |
| 65-69 | 6.45 | 4.65 | 2.34 | 1.62 |
| 70-74 | 12.09 | 6.84 | 3.53 | 2.57 |
| 75-79 | 15.69 | 9.07 | 4.38 | 3.00 |
| 80-84 | 26.30 | 12.15 | 7.08 | 4.71 |
| 85+ | 24.46 | 18.70 | 9.73 | 2.86 |

* Deaths during period divided by number of men alive at beginning of period.

Table 13—Deaths* per 100 Men by Hours of Sleep (Selected Age Groups)

| Age | <4 | 4 | 5 | 6 | 7 | 8 | 9 | 10+ |
|---|---|---|---|---|---|---|---|---|
| First follow-up period | | | | | | | | |
| 45-49 | — | 1.22 | 0.60 | 0.32 | 0.34 | 0.43 | 0.37 | 1.45 |
| 50-54 | 5.08 | 2.65 | 1.14 | 0.63 | 0.45 | 0.58 | 0.95 | 1.54 |
| 55-59 | 3.70 | 1.89 | 2.31 | 0.93 | 0.88 | 0.91 | 1.48 | 3.06 |
| 60-64 | 11.43 | 2.84 | 1.72 | 1.51 | 1.15 | 1.33 | 1.83 | 4.16 |
| 65-69 | 4.65 | 6.59 | 4.37 | 2.23 | 1.90 | 2.07 | 2.63 | 5.59 |
| 70-74 | 8.33 | 6.48 | 5.87 | 3.22 | 2.36 | 3.11 | 3.72 | 5.59 |
| 75-79 | 11.54 | 12.70 | 6.35 | 6.48 | 2.49 | 4.57 | 5.08 | 8.74 |
| 80-84 | 14.29 | 7.14 | 5.75 | 5.09 | 3.58 | 6.44 | 6.50 | 12.72 |
| 85+ | 50.00 | 15.00 | 8.33 | 11.93 | 7.22 | 8.03 | 10.33 | 20.18 |
| Second follow-up period | | | | | | | | |
| 45-49 | 1.96 | 1.23 | 0.45 | 0.49 | 0.42 | 0.53 | 0.63 | 0.90 |
| 50-54 | 5.36 | 1.17 | 0.69 | 0.77 | 0.66 | 0.85 | 1.15 | 1.28 |
| 55-59 | 3.85 | 1.92 | 2.26 | 1.20 | 1.03 | 1.26 | 1.22 | 2.39 |
| 60-64 | 12.90 | 2.93 | 2.42 | 2.12 | 1.73 | 2.03 | 2.40 | 4.70 |
| 65-69 | 2.44 | 7.05 | 3.84 | 3.16 | 2.46 | 2.56 | 3.29 | 4.18 |
| 70-74 | — | 6.93 | 5.04 | 5.19 | 3.98 | 3.96 | 5.02 | 6.76 |
| 75-79 | 13.04 | 7.27 | 7.34 | 4.72 | 4.56 | 5.93 | 7.04 | 10.36 |
| 80-84 | — | 23.08 | 7.32 | 9.58 | 13.40 | 8.33 | 12.11 | 14.29 |
| 85+ | — | 29.41 | 18.18 | 14.58 | 13.33 | 14.23 | 10.70 | 23.08 |

* Deaths during period divided by number of men alive at beginning of period.

cancer; some may be predictive of the later occurrence of cancer. If these preliminary findings are borne out, it may be that several general complaints such as loss of appetite, loss of weight, and fatigue easily are highly useful as danger signals which indicate the need for medical attention both for cancer and for diseases other than cancer.

## Exercise

Now let us consider a few factors other than physical complaints. Men enrolled in the study were asked: "How much exercise do you get (work or play)?" They were given the choice of checking "none," "slight," "moderate," or "heavy." Table 12 shows death rates* in relation to replies to this question. Death rates were far higher for men who checked "none" than for men who checked "slight," "moderate," or "heavy." This was found in both the first and the second period of the study. Among those who said that they get exercise, the death rates tended to decrease somewhat with increasing amount of exercise.

It is generally thought that exercise is good for health. Conversely, ill health may reduce the ability or the desire to indulge in exercise. Be that as it may, the answers to this question showed a considerable degree of relationship to death rates in subsequent months.

## Sleep

Nightly amount of sleep is another factor which may have an influence on health and may also be influenced by state of health. As shown in Table 13, men who said that they get about seven hours of sleep per night had lower death

* These rates are expressed in terms of $q_x$ (i.e., the number of men dying during a specified period divided by the number of men alive at the beginning of the period). The first period averaged 0.866 years and the second period was a full year.

**Table 14—Mortality Ratio of Subjects Who Took Certain Medicines**

| | All Subjects | | "Well" Subjects* | |
|---|---|---|---|---|
| | Men | Women | Men | Women |
| Antiacid medicine | 1.01 | 0.91 | 0.98 | 0.84 |
| Laxatives | 1.16 | 1.06 | 1.09 | 0.97 |
| Tranquilizers | 1.78 | 1.41 | 1.29 | 1.13 |

* Subjects who at time of enrollment said that they were "not sick at present" and had never had cancer, heart disease, stroke, or high blood pressure.

rates than those who get either more or less sleep than this. Those who get less than five hours of sleep per night had very high death rates, and those who get ten or more hours of sleep per night had higher-than-average death rates.

## Common Medicines

Since medicine is prescribed for the treatment of disease, the taking of medicine generally identifies people with illness or complaints of some sort. Unfortunately, many people treat themselves with various medicines without bothering to see their doctors. Therefore, it is of interest to examine death rates in relation to the taking of common medicines.

Table 14 shows mortality ratios in relation to the taking of "antiacid medicine," laxatives, and tranquilizers. In each instance, the mortality ratio was computed from the expected number of deaths based upon the age-specific death rates of people who said that they did not take the medicine.

The taking of antiacid medicine showed no relationship to later death rates, and the taking of laxatives showed very little relationship to later death rates. On the other hand, the death rates of subjects who said that they took tranquilizers were considerably higher than the death rates of subjects who said that they did not take tranquilizers. The relationship just mentioned is not so pronounced in an analysis confined to subjects who when enrolled said that they were "not sick at present" and had never had cancer, heart disease, stroke, or high blood pressure.

## Concluding Remarks

Since the second follow-up has only just been completed, and second questionnaire returns have not yet been put on tape, I could only prepare a few preliminary tabulations in time for this presentation. Obviously, a much more detailed analysis must be made before any definite conclusions can be drawn. However, these preliminary findings suggest that we will obtain a considerable amount of information of value in educational programs directed toward the early detection of cancer.

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