Screening for Breast Cancer in Younger Women:
Life Expectancy Gains and Losses
An Analysis According to Risk Indicator Groups

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Only three decades ago, uterine cancer was the leading cancer killer of women in the United States. Since then, death rates from cancer of the uterus have plunged downward, the most convincing demonstration of the importance of early detection for the control of cancer.\(^1\) The position of principal cancer killer in women was then assumed by cancer of the breast, a position it has held without challenge to this day.\(^2\) Massive efforts to promote early diagnosis through educational programs on breast self-examination and through emphasis on periodic physical examinations made little dent in the breast cancer death rate, which continued on its inexorable course, unchanging year after year. For too many women, it became evident that even though a lesion in the breast did not appear threatening at diagnosis, the insidious disease had already spread throughout the body. Perhaps without such cancer control efforts the death rate would actually have increased as a result of a presumed increase in breast cancer incidence, but this is small consolation.

The advent of mammography in the 1960s provided a firm basis for the hope that breast cancer in large numbers of women might be detected at an early enough stage to appreciably alter the natural history of the disease. That screening with mammography and clinical examination could lead to a substantial reduction in the breast cancer death rate was then documented in the classic Health Insurance Plan (HIP) clinical trial.\(^3\) I believe that mammography was

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the key to this unprecedented success in breast cancer control. It could hardly have been fortuitous that the death rate was decreased in women over 50 years old, for whom mammography of the 1960s was most effective, and not decreased in women under 50, for whom mammography was much less effective in detecting breast cancer.

It is against this background of decades of helplessness in reducing the tragic toll of breast cancer and the new vistas of hope offered by mammography, that the National Cancer Institute and the American Cancer Society joined forces to sponsor the 27 Breast Cancer Detection Demonstration Projects (BCDDP). The program was designed to screen 280,000 women, ages 35-74 years, annually for five times, using mammography, physical examination, patient history and thermography (the latter was not to be used as a basis for further action, except for scheduling early recall visits). Its purpose was to show that the general public and the medical profession would cooperate to realize the life-saving potential of these procedures in large groups of women.

When these programs were first being planned, there was concern about the possible hazard of radiation exposure from mammography. It was judged that the potential benefits far outweighed the risks and the programs proceeded as planned, starting in 1973. More recently, the question of risk versus benefit has been raised anew. While it is generally agreed that there is surely net benefit for women over the age of 50, the situation for younger women is less clearcut.

Younger women comprise a fair-sized proportion of the breast cancer problem, and lives saved in this group would yield more years of life saved than for corresponding numbers of older breast cancer patients. While the rate of clinical surfacing of breast cancer is much lower in younger women, the key question is how many breast cancers might be detected well in advance of the usual surfacing.

On the other hand, the HIP study showed no reduction in breast cancer death rates for younger women. It was thought that benefits would be evident as a result of improvements in mammographic technology, but documentation was not available. In addition, the frequency of breast cancer pickup is likely to be lower in younger women so that the pickup per unit dose of radiation would also be lower. Furthermore, younger women have a longer future lifetime for exposure to the adverse effects of radiation and, from the fragmentary data at hand, they are, if anything, more sensitive to these adverse effects than their older counterparts.

Consequently, pending further study, the BCDDP adopted some interim guidelines for women 35 to 50 years of age. For women at high risk because of family history, reproductive history, prior breast cancer or tumor, etc., the benefits as well as the possible risks of X-ray mammography were to be fully explained to the woman concerned and the final decision made between her and the physician. The routine use of mammography was not recommended for screening asymptomatic women but was not to be withheld if she and the physician agreed that it was in her best immediate interest.

There has been a dearth of solid basic data about breast cancer risk indicators. One aim of this paper is to present new information that will substantially expand our knowledge of the frequency of breast cancer in the various risk indicator groups. However, the principal purpose is to use these and related data to study the risk:benefit ratio of screening in younger women. To do this, I have first constructed a picture of what the breast cancer incidence and life expectancy for the BCDDP women would have been under the conditions prevail-
Table 1
Estimated Breast Cancer Incidence Rates
For Risk Indicator Groups
By Age

| Summary Risk Indicator Group | Age at Entry (And Number of Women in Cohort) | 35–39 (36,452 Women) | 40–44 (73,976 Women) |
|-----------------------------|---------------------------------------------|-----------------------|-----------------------|
|                             | Percent of Total Women in Cohort             | Percent of Total Women in Cohort |
|                             | Incidence Rate/1,000 Women-Years             | Incidence Rate/1,000 Women-Years |
|                             | Ratio to Rate of "None" Category             | Ratio to Rate of "None" Category |
| Total women                 | 100.0                                       | 100.0                 |
| None                        | 58.2                                        | 56.8                  |
|                             | 0.53                                        | 0.87                  | 1.00                  |
| Lump or thickening of breast| 3.8                                         | 3.8                   |
| Only                        | 0.82                                        | 1.14                  | 2.46                  |
|                             | 2.1                                         | 0.81                  | 1.75                  | 2.08                  |
|                             | 1.7                                         | 0.84                  | 1.82                  | 2.96                  |
| Discharge from breast       | 0.8                                         | 0.6                   |
| Only                        | 1.29                                        | 1.22                  |
|                             | 0.3                                         | 0.31                  | 1.57                  | 1.52                  |
|                             | 1.74                                        | 0.76                  | 3.76                  | 3.46                  |
| History of breast operation | 1.6                                         | 2.0                   |
| Only                        | 0.63                                        | 0.60                  |
|                             | 1.04                                        | 2.23                  |
|                             | 0.29                                        | 0.62                  | 1.66                  | 1.89                  |
| History of breast cancer in mother or sister | 2.6                            | 2.3                   |
| Only                        | 1.23                                        | 1.09                  |
|                             | 1.4                                         | 1.68                  | 1.19                  | 3.22                  |
|                             | 2.14                                        | 4.62                  | 4.26                  | 3.89                  |
| No live child prior to age 30 | 24.1                                        | 26.1                  |
| Only                        | 0.54                                        | 1.15                  | 1.32                  |
|                             | 1.02                                        | 1.66                  | 2.19                  |
|                             | 5.7                                         | 1.52                  | 1.91                  | 1.79                  |
| Less than age 12 at menarche| 16.7                                        | 16.2                  |
| Only                        | 0.69                                        | 1.23                  |
|                             | 1.46                                        | 1.42                  |
|                             | 0.72                                        | 1.55                  | 1.78                  | 2.04                  |

ing in the 1960s (pre-general use of mammography). Comparison is then made with the life expectancy likely to occur among the BCDDP women actually found to have breast cancer at the initial and second annual screenings (1973–March, 1976). Further comparison is made with the life expectancy lost as a consequence of a presumed radiation hazard per unit of radiation.

**Material and Methods**

The breast cancer picture of the 1960s was developed by using unique data on approximately 560,000 women over 30 years of age. These women were enrolled in a prospective study from October, 1959 through February, 1960 by 68,000 volunteers of the American Cancer Society under the leadership of Dr. E. Cuyler Hammond.11 Thanks to Dr. Hammond’s vision and genius, among the items asked of women at enrollment were questions on current presence of lump or thickening of the breast, current discharge from the breast, his-
### Age at Entry (And Number of Women in Cohort)

| Percent of Total Women in Cohort | Incidence Rate/1,000 Women-Years | Ratio to Rate of "None" Category | Percent of Total Women in Cohort | Incidence Rate/1,000 Women-Years | Ratio to Rate of "None" Category | Percent of Total Women in Cohort | Incidence Rate/1,000 Women-Years | Ratio to Rate of "None" Category |
|----------------------------------|----------------------------------|----------------------------------|----------------------------------|----------------------------------|----------------------------------|----------------------------------|----------------------------------|----------------------------------|
| 1.01                             | 1.56                             | 1.23                             | 100.0                            | 1.68                             | 1.23                             | 100.0                            | 1.88                             | 1.22                             |
| 51.4                             | 1.29                             | 1.00                             | 49.0                             | 1.37                             | 1.00                             | 52.5                             | 1.54                             | 1.00                             |
| 3.7                              | 3.54                             | 2.78                             | 2.5                              | 4.93                             | 3.60                             | 1.7                              | 7.45                             | 4.86                             |
| 1.6                              | 2.98                             | 2.34                             | 1.0                              | 4.59                             | 3.34                             | 0.7                              | 7.14                             | 4.84                             |
| 3.7                              | 4.01                             | 3.15                             | 1.5                              | 5.21                             | 3.79                             | 1.0                              | 7.66                             | 4.98                             |
| 0.4                              | 2.84                             | 2.24                             | 0.3                              | 3.88                             | 2.82                             | 0.2                              | 6.88                             | 4.28                             |
| 0.1                              | 1.28                             | 1.00                             | 0.1                              | 1.63                             | 1.19                             | 0.1                              | 8.88                             | 3.17                             |
| 0.3                              | 3.74                             | 2.94                             | 0.2                              | 5.07                             | 3.70                             | 0.1                              | 7.55                             | 4.91                             |
| 1.4                              | 3.64                             | 2.86                             | 1.0                              | 2.60                             | 1.90                             | 0.9                              | 2.07                             | 1.34                             |
| 1.4                              | 3.84                             | 2.86                             | 1.4                              | 4.75                             | 3.46                             | 1.2                              | 6.27                             | 4.08                             |

*Based on data from the first five years of the ACS prospective study exclusive of women with a history of breast cancer at entry.*

Tory of breast operations, history of breast cancer in the subject or her mother or sisters, age at menarche and age at birth of first live child, if any. Subsequent follow-up established which of these women died during the ensuing 12 years, as well as the date and causes of death. In addition, the surviving women completed short questionnaires in 1961, 1963, 1965 and 1972 detailing, among other things, if they had had an operation for breast cancer and the date.

Utilizing this information, the frequencies of breast cancer in the various risk indicator groups were first computed directly and then calculated at the level of the 1969-1971 Third National Cancer Survey (TNCS) incidence rates as follows:

- For five-year age-group cohorts (30-34 years, 35-39 years, etc.) in each risk indicator group note was made of the instances of breast cancer specified for the first five years after enrollment, either on the follow-up questionnaires or as underlying, second or third cause of
| Summary Risk Indicator Group | 35-39 (36,452 Women) | 40-44 (73,976 Women) |
|-----------------------------|----------------------|----------------------|
|                             | Percent of Total Women in Cohort | Incidence Rate/1,000 Women-Years | Ratio to Rate of "None" Category | Percent of Total Women in Cohort | Incidence Rate/1,000 Women-Years | Ratio to Rate of "None" Category |
| Total women                 | 100.0 | 0.53 | 1.15 | 100.0 | 1.03 | 1.18 |
| None                        | 58.2  | 0.46 | 1.00 | 56.8  | 0.87 | 1.00 |
| Minors only                 |        |      |      |        |      |      |
| One minor only              | 33.8  | 0.56 | 1.20 | 34.6  | 0.99 | 1.14 |
| Two minors only             | 7.7   | 0.58 | 1.25 | 7.9   | 0.94 | 1.08 |
| None plus minors only       | 92.0  | 0.50 | 1.09 | 91.4  | 0.92 | 1.06 |
| One major, total            |        |      |      |        |      |      |
| One major only              | 7.3   | 0.87 | 1.89 | 7.8   | 2.09 | 2.39 |
| One major plus minors       | 4.6   | 0.75 | 1.63 | 4.8   | 1.90 | 2.17 |
| Two or more majors, total   | 0.7   | 1.41 | 3.04 | 0.8   | 3.84 | 4.40 |
| Majors, total               | 8.0   | 0.92 | 1.99 | 8.6   | 2.25 | 2.58 |

death listed on reports from attending physicians verifying information on death certificates.

Women with a history of breast cancer at enrollment have been excluded from consideration. These women are known to be at very high risk of a second cancer and there is no good way of distinguishing whether a report of breast cancer during the five-year follow-up period was for a new cancer or was further information on an old one.

The number of women with breast cancer was then related to the number of years lived by the cohort during the five-year period after enrollment. On the average, a given cohort was two and a half years older during the five-year period than at the start. Therefore, the rates for a given cohort were averaged with the preceding one to see how the absolute rates would compare with the incidence rates from the TNCS. The rates per 100,000 women-years turned out to be 61, 109, 144, 151 and 153 for total women 35-39 years, 40-44 years, 45-49 years, 50-54 years and 55-59 years, respectively. Corresponding rates for the TNCS were 53, 103, 156, 168 and 188. The age-specific rates for women in the various ACS study risk indicator groups were then raised or lowered proportionately so that the rates for total women would be equal to the TNCS rates.

The women who agreed to participate in the long-range ACS Prospective
Study were not necessarily representative of the general population. However, they do provide a reasonably good approximation of the population of stable women who would be able to commit themselves to five annual screenings. As such, they are an appropriate group to relate to BCDDP women. Also, in both the ACS study and the BCDDP programs, the women’s own statements were the basis for establishing risk indicator groups.

BCDDP was formulated as a service demonstration project, not as a research undertaking. Despite the self-selected nature of the women who chose to participate and the problems of achieving some semblance of uniformity among 27 disparate and independent programs, it became apparent that there was a potential for much useful information ancillary to the service aspect.

The evolution of this information gathering poses some difficulties in distinguishing risk indicator groups. The earliest patient history form, completed for about six percent of the BCDDP women, was very cumbersome and consistency with later forms cannot be achieved. Its successor, completed for about 29 percent of the BCDDP women, was still unwieldy but did provide full information on risk indicators. The last patient history form, completed for about 65 percent of the BCDDP women, was a streamlined version, so stream-
lined that it omitted information on menarche and childbearing and, in the section on family history of breast cancer, did not specify the particular relatives affected but was limited to the total number of relatives involved.

Because of the enormous volume of data accumulated, some shortcuts have been employed in storing the patient history information on tape. The total form was initially key punched for a sample 10 percent of the women and only the “first” page was key punched for all women. The total form is punched subsequently for any woman recommended for biopsy or found to have breast cancer, etc. This undoubtedly leads to some inconsistencies.

There also are time-lags between the recommendations of actions based on findings at screenings, the accomplishment of these actions, the reports of these actions to the 27 program offices, the transmittal of these reports to the central repository (the Data Management Center, supported by the National Cancer Institute) and the storage of these records on tape. As an aftermath of the July 19, 1976 discussions of the pros and cons of mammography screening, I wanted to make a critical examination of what the BCDDP results might indicate with respect to the risks versus the benefits of screening. To do this, a great deal of information as yet unreported to DMC was necessary. Thus, I requested

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Table 3.
BCDDP Results of Initial and Second Annual Screenings
For Summary Risk Indicator Groups
By Age at Entry*
that details be obtained from the project offices for all breast cancers detected through June, 1976 as a result of screenings through March, 1976. It was important for me to know whether the cancer was in situ or invasive, the number of axillary nodes examined pathologically and the number found to be positive, the size of the principal mass and the type of treatment. The cooperation of the Project Coordinators was superb. Breast cancer was reported for 1,776 women in the initial screening, the interval to second annual screening, the second annual screening and the interval to the third annual screening. Pathologic reports were available for verifying details for 967 patients; in 809 patients we relied fully on reports from the Project Coordinators. A second breast cancer was specified for 50 women. However, in this paper, only the first cancer detected has been considered or, if two were found concurrently, the one with the poorer prognosis. In addition, women with a prior history of breast cancer at initial examination have been omitted.

The term “screening” as used in this article includes the whole series of visits referable to that screening, as well as early recall visits. The large majority of breast cancers found were pathologically confirmed shortly after the first visit of a series. It sometimes took several months for confirmation, especially if recall visits were involved.
Table 4.
Estimated Lead Times for Breast Cancers
Detected at Initial and Second Annual Screenings
For Summary Risk Indicator Groups
By Age at Entry

| Summary Risk Indicator Group and Screening Series | Age at Entry |          |          |          |
|--------------------------------------------------|-------------|----------|----------|----------|
|                                                  | 35-39       | 40-44    |          |          |
|                                                  | Years with | Mean no. | Years with | Mean no. |
|                                                  | Respect to | of Entry  | Respect to | of Entry  |
| Rate per | Sufficient | Lead     | Rate per | Sufficient | Lead     |
| 1,000    | Incidence  | Time     | 1,000    | Incidence  | Time     |
| Total    | Initial screening | 1.00  | 0.267  | 1.33* | 2.21  | 0.225  | 1.12  |
|          | Second screening | 0.50  | 2.87-3.33 | 2.00* | 1.92  | 2.25-3.48 | 1.86  |
| None plus minors only                          | Initial screening | 0.80  | 0.284  | 1.42* | 1.78  | 0.346  | 1.73  |
|          | Second screening | 0.61  | 2.84-4.14 | 2.49* | 1.21  | 3.46-4.98 | 3.22  |
| One major, total                               | Initial screening | 1.05  | 0.234  | 1.17  | 2.54  | 0.158  | 0.79  |
|          | Second screening | 0.15  | 2.34-2.50 | 1.42  | 2.73  | 1.58-2.82 | 1.20  |
| Two or more majors, total                      | Initial screening | 3.25  | 0.306  | 1.53  | 5.59  | 0.170  | 0.85  |
|          | Second screening | 1.18  | 3.06-3.58 | 2.32  | 3.84  | 1.70-2.55 | 1.13  |

Cancers arose either as newly emergent cancers or as false-negative cancers not detected at screening. There was difficulty in applying consistent rules for classifying the latter cancers. A pending review to achieve uniformity will result in the reclassification of some of these screening-detected cancers.

These data were the best available at the time (July, 1976). New information is continually accumulating that will change some details both quantitatively and qualitatively, but the updatings are unlikely to seriously affect the overall patterns of our findings.

For the breast cancers detected at BCDDP screenings in the various risk indicator groups, we have estimated the "lead time," that is, the time prior to usual clinical pickup gained by screening detection. This was accomplished by starting with the rates for breast cancer found at the screenings. It was then determined, using very simple assumptions, how far into the future one would have to project to yield these rates if the usual cancer surfacing rates were at the level indicated for that group of women by the ACS Prospective Study, allowing for the aging of the women and the rates of finding interval cancers.

Life expectancy calculations were based on the 1969-1971 United States life tables for women. The age-specific probabilities of breast cancer patients surviving for successive five-year
| Age at Entry | 45-49 | 50-54 | 55-59 |
|---|---|---|---|
| Years with Respect to Entry which would Yield Sufficient Years of Entry (per 1,000 Incidence Time) | Rate | Mean no. | Years with Respect to Entry which would Yield Sufficient Years of Entry (per 1,000 Incidence Time) | Rate | Mean no. | Years with Respect to Entry which would Yield Sufficient Years of Entry (per 1,000 Incidence Time) | Rate | Mean no. |
| 4.43 | 0.27 | 1.50* | 5.06 | 2.08 | 1.45* | 6.52 | 3.19 | 1.59* |
| 3.88 | 3.00-4.15 | 2.58* | 4.15 | 1.83 | 1.90* | 5.23 | 2.68 | 2.21* |
| 1.85 | 3.85-5.63 | 3.74* | 5.73 | 2.08 | 1.17 | 8.11 | 4.01 | 1.30 |
| 5.21 | 2.42 | 1.21 | 2.42 | 2.35-3.09 | 1.72 | 12.43 | 4.22 | 2.28-2.86 | 1.56 |
| 2.72 | 0.271 | 1.35 | 4.50 | 2.71-3.43 | 2.07 |

*Estimated from age and risk indicator group specific incidence rates weighted by the distribution of BCDDP women and allowing for the reallocation of women with a family history of breast cancer aside from mother or sister.

Note: Based on screenings through March 1976 exclusive of women with a history of breast cancer at initial screening.

Intervals after diagnosis were computed as ratios of general population survival. Survival data for the usual clinical breast cancer patient for the first 20 years after diagnosis were very kindly prepared for us by the End Results Group based on cases diagnosed from 1950 to 1969. At the end of 20 years (the fourth five-year interval), survivors among patients 35-59 years at diagnosis had attained about 91 percent of the general population survival. The future survival of the cancer patients was extrapolated by assuming convergence to general population survival in another 20 years and normal survival thereafter.

In order to estimate the number of years of life expectancy for the BCDDP breast cancer patients, six categories have been defined on the basis of invasiveness, tumor size and extent of lymph node involvement. These six categories are:

1. **In situ**;
2. Invasive or unknown invasiveness, no positive axillary nodes and size < 1 cm. in diameter;
3. Invasive, no positive axillary nodes, size one or two cm. in diameter; or one + or unknown positive axillary nodes, size < one cm. in diameter;
4. Invasive, no positive axillary nodes and size three + or unknown cm. in diameter; or one
to three or unknown positive axillary nodes and size one or two cm. in diameter;

V. Invasive or unknown invasiveness, one to three or unknown positive axillary nodes and size three + or unknown cm. in diameter; or four + positive axillary nodes and size one or two cm. in diameter;

VI. Invasive, four + positive axillary nodes and size three + or unknown cm. in diameter.

*Includes unknown status of axillary lymph nodes and less than radical mastectomy.

Categories III, IV, V and VI closely follow the groupings of the Surgical Adjuvant Breast Study (SABS)\(^7\) employed by Shwartz as his Prognostic Classes I, II, III and IV.\(^{18}\) However, while Shwartz uses 93 percent, 81 percent, 67 percent and 25 percent for these classes directly as the ratios to general population survival for the first five years, these figures were adjusted so that their average, weighted by the SABS distribution of cases, equals the age-specific ratios for total invasive cancer in the End Results Group data. For age-groups 35-39 years through 55-59 years, these average out to 85 percent, 73 percent, 61 percent and 23 percent, respectively. The ratios for Categories III-VI for time intervals subsequent to the first five years were then calculated assuming convergence to general population survival proportionate to that for usual clinical breast cancer.

Categories I and II were regarded as cancers that would only rarely have been encountered in the 1960s. The survival ratios for Category II were arbitrarily assumed to be halfway between 100 percent and the ratios for Category III. The ratios for Category I were assumed to be

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Table 5.
Mean Ratios of Age-Specific Survival Probabilities After Diagnosis of Cancer to Corresponding Survival in General Population of U.S. Women

| Category of Breast Cancer                                                                 | Periods of Years after Diagnosis |
|------------------------------------------------------------------------------------------|---------------------------------|
| Total invasive, usual case finding                                                        | 0-5                             |
| Cat. I. In situ                                                                           | 0.63                            |
| Cat. II. Invasive or unknown invasiveness, no* positive axillary nodes and size < 1 cm. diameter | 0.96                            |
| Cat. III. Invasive, no* positive axillary nodes and size 1 or 2 cm. diameter; or 1+ or unknown positive axillary nodes and size < 1 cm. diameter | 0.82                            |
| Cat. IV. Invasive, no* positive axillary nodes and size 3+ or unknown cm. diameter; or 1-3 or unknown positive axillary nodes and size 1 or 2 cm. diameter | 0.73                            |
| Cat. V. Invasive or unknown invasiveness, 1-3 or unknown positive axillary nodes and size 3+ or unknown cm. diameter; or 4+ positive axillary nodes and size 1 or 2 cm. diameter | 0.61                            |
| Cat. VI. Invasive, 4+ positive axillary nodes and size 3+ or unknown cm. diameter          | 0.23                            |

*Mean ratios for age-group 35-39 through 55-59 at diagnosis, by category of cancer.

*Includes unknown status of axillary nodes and less than radical mastectomy.

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halfway between 100 percent and the ratios for Category II. The ratios for Category I are lower than the virtually 100 percent customary for in situ cancer. They were set this way to compensate for the fact that women with breast cancer are at high risk of a second breast cancer, which may be aggressive. Also, with further investigation, some cancers are established to be invasive, though initially found to be non-invasive. Finally, in some instances, there may be uncertainty about the very classification as cancer and about whether the in situ cancer would ever progress to invasion, if untreated.

The loss of life expectancy as a result of the breast cancers presumably induced by the radiation of mammography has been estimated by first accepting for purposes of calculation, the BEIR report estimates of six breast cancers induced per million women per year per rad to the breast after a latent period of 10 years. These figures were then applied to the number of women-years the BCDDP women would be expected to live throughout their lifetime in each five-year period following the latent period. This gave the number of induced breast cancers to be anticipated. Next, these numbers were multiplied by the number of years of life lost per breast cancer, computed as the difference between general population life expectancy and that for the usual clinical invasive breast cancer patient, age being taken into account.

### Results

Table 1 presents the breast cancer incidence rates for the various risk indicator groups as delineated by the ACS Prospective Study. A small proportion of the population falls into definitely high-risk indicator groups, that is those with well over twice the rates of the "none" group in most ages. These groups include women who at entry into the study had a lump or thickening of the breast, discharge from the breast, a history of breast operation or a history of breast cancer in mother or sister. I have termed these major risk indicators.

More women fall into groups with incidence rates somewhat higher than...
those of the "none" group, but not twice as high, such as those with menarche at early age or women who prior to age 30 had not given birth to a live child. These are termed minor risk indicator groups. Subgroups of the minor risk indicator groups, for instance women who first gave birth after age 35, have higher rates than those of their total group, but these rates don't approach twice as high as the rates of the "none" group.

Table 2 shows the breast cancer incidence rate patterns for various combinations of major and minor risk indicator groups in the ACS Prospective Study. In the younger age-groups, the women were predominantly premenopausal and in the older, predominantly postmenopausal. It is well known that there are breast cancer differences according to menopausal status. This makes even more noteworthy the remarkable consistency throughout the various agegroups of progressions of breast cancer incidence rates from low to high, comparing "none," to "minors only," to "one major only," to "one major plus minors," to "two or more majors."

In the absence of a major risk indicator, the minor risk indicator group does not show much elevation in breast cancer incidence rates over the "none" group. Adding another "minor only" to a lone "minor only" shows inconsistent differences in incidence rates as compared with the single "minor only." Many of the history forms of the BCDDP women do not contain data concerning the minor risk indicators. Since there is so little difference in the breast cancer incidence rates, the composite group of "none plus minors only" is a feasible group to study.

Table 3 indicates that the rate of breast cancer detected in the initial screening series of BCDDP women ranged from 1.0 per 1,000 women in the 35-39 agegroup to 6.5 for those 55-59 years old. This posed no surprising departure from the usual breast cancer clinical surfacing pattern. For each age-group, rates were lowest in the "none plus minors only" risk indicator group and several times higher in the "two or more majors" group. Again we see no surprising departure from clinical surfacing figures. The progression in the rates are actually sharper than those shown in Table 3 because there is a little overstatement of the rates for the "none plus minors only" group, and a little understatement for the "majors" categories. This is due to the fact that all of the required recoding of the short patient history forms to long forms, has not yet been accomplished.

The pool of breast cancers detectable (and confirmable) at initial screening by the technology and medical procedures employed includes the lifetime accumulation of such cancers, minus those that have already surfaced clinically, and minus preclinical cancers that have already been found through some other special examination. The pool of detectable breast cancers at the second annual screening are those missed at initial screening, plus those that became detectable during the year, minus cancers that showed up as interval cancers during the year (and, at least theoretically, minus those that regressed).

A priori, it may be unclear as to how the detection rates for the two screening series will compare. In Table 3 it may be seen that actually the rates for the second annual screening series were generally about 25 or 75 percent those of the initial series. Except for women 35-39 years, rates were lowest in the "none plus minors only" group and several times higher in the "two or more majors" group in the second screening series as well.

There is a discrepancy between the BCDDP and ACS risk-groups in the assignment of those women with a family history of breast cancer aside from mother or sister. Examination of the re-
BCDDPs were heavily overweighted with women at higher risk of breast cancer, about 30 percent falling into the “one major” group and six percent into the “two or more majors” risk indicator categories. This connotes that for ages 35-59, the breast cancer frequency for BCDDP women is about one-quarter higher than for women in general, even aside from a possible tendency for further high-risk breast cancer self-selection within risk indicator groups.

It is also evident in Table 3 that there was an even greater representation of
higher-risk women among those who returned for the second annual screening. In part, this is attributable to the fact that these women were the early entrants into the BCDDP programs where overweighting with higher-risk women was more pronounced (at least one major risk indicator for 43 percent of the 1973 and 1974 entrants, compared with 31 percent of the 1975 and 1976 entrants). Also, the higher-risk women tended to return for the second annual screening more than the lower-risk ones. Thus, among 1973 and 1974 entrants, the return rates were 82 percent, 87 percent and 88 percent for the “none plus minors only,” “one major” and “two or more majors” groups.

Using the data of Table 3 in conjunction with those of Table 2, and the revised incidence rates for the “none plus minors only” group, we have estimated the mean lead time for the breast cancers detected by screening to be about 1.4
years for the initial screening series and over two years for the second annual screenings. Further details may be seen in Table 4.

Table 5 presents the mean ratios of the various age-groups to general population survival probabilities, which enabled us to obtain the survival probabilities for breast cancer patients. Using these probabilities, the years of life expectancy were calculated for the various cancer categories shown in Table 6. These expectancies show a loss ranging from about 21 years for the usual invasive breast cancer patient at age 35-39 years, to roughly half that for a woman age 55-59 years. Category I-IV cancers show less of a loss, while Category V and VI cancers show more. (Table 6.)

Table 7 indicates the categories of breast cancer detected by screening. A large number of cancers were found in favorable life expectancy categories. This is a requisite condition if screening
is to show any benefit. It is also essential that there not be a compensating concentration of lethal cancers among those not detected by screening. Scrutiny of the interval cancers (details not shown here) reveals that these cancers tend to be in favorable categories, not in unfavorable ones.

As evident in Table 7, the advantageous distribution of the breast cancers by categories was, in general, only slightly less for those found in the second screening as compared with the initial. This implies that "length bias," the bias of detecting a disproportionate number of the slower-growing cancers that take longer to surface, was not of any great import here.

The life expectancies in Table 6 were next multiplied by the number of breast cancers in the appropriate category in Table 7 to obtain the number of years of life expectancy for the breast cancers detected by screening. (Table 8A.) The number of years of life expectancy for the usual cancer case finding in Table 8A was calculated by adding the mean lead times from Table 4 to the life expectancies for usual cancer case finding commencing at the ages implied by adding the mean lead times to the ages at screening. The gain by screening detection of breast cancers is then the difference between the number of years of life expectancy for screening detection and for the usual case finding, allowing for lead time.

The gain in life expectancy in terms of the mean per breast cancer detected through screening is presented in Table 8B. There is no consistent trend according to risk indicator groups. Women under 50 years of age show greater gains than those in their 50's. At initial screening, the mean gain for those under 50 is about five to seven years, and for those in their 50's, about two to four years. Overall, these gains represent a reduction of roughly one-third in the loss of life expectancy of the usual clinical
breast cancer patient.

Table 9 shows the number of breast cancers presumably induced and the number of years of life expectancy lost thereby, per rad of radiation to the breast on the basis of the BEIR report figures. The median radiation-induced breast cancer would occur about 26 years after screening for women 35-39 years at screening, and about 19 years after screening for those 55-59 years at screening.

Table 10 brings together the gains in life expectancy through screening detection of breast cancer from Table 8 and the loss per rad of radiation to the breast from Table 9, and shows the results per 1,000 screenees.

The gains through screening detection of breast cancer per woman screened are modest. The highest gain in Table 10 is .08 years per screenee (78 years per 1,000 screenees). On the other hand, at the dosage level to the breast of one or two rads per screening and even doubling the loss to allow for the sampling variation of the BEIR report estimates, the loss per screenee would range from only .006 years at ages 35-39 (six years per 1,000 screenees) to .001 years at ages 55-59 (one year per 1,000 screenees). Except in the 35-39 age-group, the detection benefit is many times the radiation loss, at least for the initial screening. The 45-49 age-group shows gains paralleling and perhaps exceeding those of women in their 50's.

The expectation that the greater frequency of breast cancer in higher-risk women would yield an increased gain through screening is well borne out by the patterns of gain in Table 10.

**Discussion**

The definitive way to determine the degree of gain through screening detection of breast cancer in women under 50 years of age would be to conduct a clinical trial. This would involve many women for many years, especially to

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**Table 1**

| Age at Entry | 45-49 | 50-54 | 55-59 |
|-------------|------|------|------|
| Thousands of Women-Years | No. of Breast Cancers Induced | Days of Life Expectancy Lost | No. of Breast Cancers Induced | Days of Life Expectancy Lost | No. of Breast Cancers Induced | Days of Life Expectancy Lost |
| 1,024 | 6.1 | 36 | 365 | 2.2 | 10 | 197 | 1.2 |
| 666 | 4.0 | 23 | 514 | 3.1 | 15 | 284 | 1.7 |
| 285 | 1.7 | 10 | 221 | 1.3 | 6 | 115 | 0.7 |
| 301 | 1.8 | 11 | 223 | 1.3 | 6 | 135 | 0.8 |
| 165 | 1.0 | 6 | 117 | 0.7 | 3 | 68 | 0.4 |
| 57 | 0.3 | 2 | 43 | 0.3 | 1 | 21 | 0.1 |
| 41 | 0.2 | 1 | 27 | 0.2 | 1 | 14 | 0.1 |

*Per rad of radiation to the breast assuming six breast cancers per million women-years per rad subsequent to 10 years after screening for initial screening and second annual screening.

Note: Based on screenings through March 1976 exclusive of women with a history of breast cancer at initial screening.
evaluate different strategies, such as omitting mammography as part of the present procedure, or establishing the optimal periodicity of repeat screening. Difficult as the problems of ascertaining the dynamic biologic significance of minimal breast cancer may be, to directly ascertain any loss due to radiation exposure would be even more difficult, considering the low level of the dosage and the length of time it would take for an effect to be present, let alone detectable.

This means that alternative methods of assessment, however unsatisfying, are necessary. Several investigators have already constructed mathematical models to estimate the gains of screening. Their evaluations were based on previously available data. Current estimates presented in this article are based on new data, albeit imperfect, which were developed and applied in a direct, straightforward manner with as few and as simple assumptions as possible. I limited myself to these procedures because of the tentative nature of much of the data.

It may be anticipated that as further BCDDP data accumulate and as the mathematicians have an opportunity to work with the new data, firmer estimates will be made of the gains through screening.

Determining the loss through radiation is bound to remain a knotty problem, however. Putting aside all of the difficulties involved for the low radiation dosage level of mammography in approximating the frequency of breast cancers to be induced many years into the future, there remains the fact that this type of cancer has not been identified. What are its clinical characteristics and

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Table 10.
Gain Through Screening Detection of Breast Cancer Compared With Loss per Rad of Radiation of the Breast* For Initial and Second Annual Screenings By Risk Indicator Groups and Age at Entry

| Summary Risk Indicator Group And Screening Series | Age at Entry | 35-39 | 40-44 |
|--------------------------------------------------|--------------|-------|-------|
|                                                  | Number of Years of Life Expectancy per 1,000 Screenings | Gain Through Screening | Loss per Rad of Radiation |
|                                                  | Number of Years of Life Expectancy per 1,000 Screenings | Gain Through Screening | Loss per Rad of Radiation |
| Total                                            |              |       |       |
| Initial screening                                |              | 6.3   | 1.5   |
| Second screening                                 |              | 2.8   | 1.4   |
| None plus minors only                           |              | 5.2   | 1.5   |
| Initial screening                                |              | 3.2   | 1.4   |
| One major, total                                 |              | 9.4   | 1.5   |
| Initial screening                                |              | 2.4   | 1.4   |
| Second screening                                 |              | 0.9   | 1.5   |
| Two or more majors, total                        |              | 1.8   | 1.4   |

* For initial and second annual screenings.
prognosis? No one knows. In this paper, the life expectancy of a patient with the usual clinical invasive cancer was assigned to the radiation-induced breast cancers calculated by assuming the BEIR report estimates. Certainly one would hope that this is unduly conservative, and that 10, 20 or 30 years from now, much improved therapeutic measures would be available to such patients.

Another difficult problem is whether there is any special radiation effect in the various breast cancer risk groups. Though there is concern about possible synergism of radiation exposure with high-risk breast cancer factors, there is virtually no information. However, it is reassuring that what little information exists, the fragmentary indications from the atomic bomb studies concerning the risk factor of advancing age, does not suggest synergism.

**Summary**

- Using data from the ACS Prospective Study and excluding women with a history of breast cancer who are known to be at very high risk of a second breast cancer, breast cancer incidence rates are estimated for age-groups 35-39 through 55-59 years for various risk categories defined by the women’s own statements. The women with none of the risk indicators, the “none” group, comprised about 54 percent of the total women and showed breast cancer rates, which though the lowest of any risk indicator group, were still quite appreciable, being 80 percent of the rates for total women of their age group.
- Women with menarche prior to age 12 or who had not given birth to a live...
child before age 30 showed an excess of 15 percent to 50 percent over the breast cancer incidence rates of the "none" group. These risk indicators are termed "minor" (relatively). The "minors only" group comprised about 38 percent of total women and had breast cancer rates much the same as those of the total women of their age.

- Current breast lump or discharge, or a history of breast surgery or of breast cancer in mother or sister are termed "major" risk indicators. One such indicator was noted for about eight percent of total women and generally denoted breast cancer incidence rates somewhat over 100 percent in excess of the rates of the "none" group. Two or more "major" risk indicators, observed in less than one percent of the women, meant an excess of 200 percent to over 400 percent compared with the incidence rates of the "none" group.

- Using these data in conjunction with information from the initial screening series of the BCDDP women ages 35-59, and similarly excluding women with a history of breast cancer at initial screening, it is found that the BCDDP women are overweighted with high-risk women, having a breast cancer risk about one-quarter higher than the general population.

- The rate of breast cancer per 1,000 women detected in the initial screening series ranged from 1.0 for women 35-39 years to 6.5 for those 55-59 years. The detection rates at the second annual screenings were about 25-75 percent of those at initial screenings.

- It is estimated that the mean "lead time" was about 1.4 years for the breast cancers detected at initial screening and over two years for those detected at the second annual screening.

- Using survival probabilities for the general population from U.S. life tables, and data on the survival of various categories of breast cancer patients, estimates are made of the life expectancies following cancer detection for patients in various categories. As compared with normal expectancy, the usual clinical invasive breast cancer patient is subject to a loss of 21 years of life at ages 35-39 years and about half that at ages 55-59 years.

- Combining the estimates of life expectancy with the number of breast cancers detected in the various categories, data are developed showing the gain in life expectancy through screening. This is computed as the difference between years of life expectancy for the cancers detected by screening, and the years of life expectancy for the usual breast cancer case finding plus mean lead time. The mean gain per breast cancer detected at initial screening for those under 50 is about five to seven years, and for those in their 50’s, about two to four years. These gains represent a reduction of roughly one-third in the loss of life expectancy of the usual clinical breast cancer patient.

- Using the BEIR report estimates of six radiation-induced breast cancers per million women per year per rad of dosage to the breast after a 10-year latent period, calculations are made concerning the number of breast cancers presumably to be induced, and the loss in life expectancy thereby. The median cancer case would occur about 26 years after screening of the 35-39 year-old women, and 19 years after screening of those 55-59 years.

- The estimated gains in life expectancy per woman screened through screening detection of breast cancers are seen to be modest. For the initial or second annual screening series, the highest gain among the groups stud-
ied is .08 years per screenee (78 years per 1,000 screenees). For a given screening, the upper limit of the presumable loss due to radiation-induced breast cancers is perhaps .006 years per screenee at ages 35-39 (six years per 1,000 screenees) and .001 years per screenee at ages 55-59 (one year per 1,000 screenees).

Except in 35-39-year-old women, the estimated detection benefit is many times the presumed radiation loss at initial screening. The expectation that the greater frequency of breast cancer in higher-risk women would yield an increased gain through screening is validated by these data.

The "major" risk indicators delineate a small proportion of women who are at substantially higher risk of developing breast cancer and who show more gain from screening than the large majority of women of their age. However, even without such risk factors, women have an appreciable risk of developing breast cancer. This risk is of sufficient magnitude to alert all physicians to the possible presence of breast cancer at the time of clinical examination.

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