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UPDATE ON MORTALITY RESEARCH

Moderator: EDWARD A. LEW. Panelists: ROBERT J. JOHANSEN, MAX H. MYERS, WILLIAM H. WETTERSTRAND, JOHN C. WILKIN*

1. Long Term Conditional Survival of Cancer Patients

2. Exposure Draft - Derivation of the 1983 Table a for Individual Annuity Valuation**

3. Recent Trends in the Mortality of the Aged**

4. Parametric Models for Life Insurance Mortality Data: Gompertz's Law Over Time**

MR. EDWARD A. LEW: I propose to comment first on the circumstances affecting recent research on mortality.

There was a time, as for instance in the 1930's and 1940's, when actuaries were in the forefront of research on mortality. The information then available about death rates was considerably less than we have today, and much of it derived from studies of insured lives. Little work was being done in the way of mortality investigations by the Federal Government or at medical research centers and universities. After World War II, there was a great increase in research on mortality, and this activity shifted sharply away from actuaries to statisticians, demographers and medical scientists in the Federal Government and the universities. As a result, today, when we address ourselves to questions about mortality levels and trends in different populations, we need to consult the large volume of data that does not derive from studies of insured lives.

In recent years, Bob Johansen launched a program to acquaint actuaries with some of the work being done by statisticians both in government and medical research agencies.

*Dr. Meyers, not a member of the Society, is Chief of Biometric Research and Analytic Studies in the Biometry Branch of the National Cancer Institute.

**These papers and the discussions of these papers appear in the Transactions.

As a prime example of mortality investigations undertaken in government medical research agencies, we now turn to Dr. Max Myers, Chief of Biometric Research and Analytic Studies in the Biometry Branch of the National Cancer Institute. His paper on Long Term Conditional Survival on Cancer Patients presents a review of the latest findings of the National Cancer Institute's End Results Study. Earlier findings were made available to actuaries by Dr. Myers and his predecessors and were incorporated in the book "Medical Risks: Patterns of Mortality and Survival" published in 1976 by the Society of Actuaries and the Association of Life Insurance Medical Directors.

MR. MAX H. MYERS: Thank you. I am pleased to represent the American Statistical Association on your program today.

Diagnosis of cancer is viewed by many individuals as very serious and perhaps indicative of a progression of steps leading to an early death. Alternatively, many physicians who treat cancer patients are optimistic that a large fraction of patients will be cured with the armament of therapeutic strategies now available, especially for those whose cancer is diagnosed prior to metastatic spread or extension to neighboring organs. In fact, cancer is not a uniformly fatal disease, nor can all patients be cured with currently available treatments. Even patients with lung cancer, considered to be one of the more serious of cancers, have some chance of surviving 5, 10, 15 or even 20 years or longer.

The question of cure for cancer patients has been explored in several ways by scientists from different disciplines. Clinical oncologists tend to examine survival "free of disease" and frequently equate survival for 5 years "free of disease" with "cure." Statisticians have examined data for cohorts of cancer patients via mathematical models to estimate the fraction of cured patients (1, 2, 3) while others have examined survival characteristics for groups of patients over extended periods of follow-up (4, 5).

Simply surviving 5 years should not be equated with cure, nor is surviving 5 years free of disease necessarily indicative of cure. Figure 1 indicates, however, that 5-year survival is highly correlated with long-term survival as measured by 20-year survival rates. If 5-year survival isn't synonymous with cure, is there a length of survival beyond which patients may be considered cured? What factors determine the rate of approach to normal survival expectation?

In this report we present results of an analysis of long-term survival for patients with cancers of the breast, uterine cervix, uterine corpus, lung, colon and prostate. The results indicate the patterns of approach to normal survival expectation as a function of cancer site, age and extent of disease at diagnosis.

MATERIALS AND METHODS

The data used in this study were collected as part of the National Cancer Institute's End Results Program (6) from four Cancer Registries: California, Connecticut, University of Iowa, and Charity Hospital in New Orleans. Patients included in the analysis had cancer of the breast, cervix, corpus, colon, prostate, or lung and were diagnosed during 1950-59.

These sites were chosen primarily because of large numbers of patients; a requirement for the type of analysis that was done. Survival was calculated from date of diagnosis of the first registered tumor for each patient through the end of the 25th year after diagnosis. In an attempt to minimize the effects of possibly unreliable expected rates for ages 85 and older, patients 65 and older at diagnosis were excluded.

The results of the analysis are presented in a series of graphs depicting conditional 5-year relative survival rates as a function of the number of years after diagnosis. Conditional relative survival rates are calculated in exactly the same manner as relative survival rates as described by Ederer, Axtell and Cutler (7). Conventional relative survival rates are calculated according to length of time since cancer diagnosis whereas conditional rates are based on cohorts patients who have already survived a given number of years. Since relative survival is the ratio of observed survival in a patient group to expected survival from general population estimates, it is possible to observe the approach to "normal" by examining the subsequent experience of patients who are eligible for further follow-up after having survived successive lengths of time.

Figure 2 illustrates schematically the concept of conditional survival rates as a re-positioning of the vertical axis (survival percent) with successive quinquennia after diagnosis. The results shown in figures 3 through 18 are actually based upon conditional 5-year relative rates for each successive year after diagnosis.

Patients were classified by extent of disease and age. Rates (x100) having a standard error of 7.5 or greater are not shown in the graphs to be discussed for each site. The statistical significance of various comparisons is not assessed, however, the large numbers of patients in the various groups should result in obvious differences in patterns being statistically significant. The extent of disease classification was localized, regional and distant. Localized meant confined to the site of origin regardless of size; regional meant cancer which had passed the bounds of the site of origin but whose furthest spread was thought to be limited to neighboring organs or tissues, or to regional lymph nodes; distant or remote spread was cancer involving organs or tissues beyond those immediately draining or neighboring the site of origin. Of primary interest were those patients whose disease was classified as localized or regional since they had the potential to be clinically free of disease after treatment.

RESULTS

Breast Cancer - Figures 3, 4 and 5 present conditional 5-year relative survival rate patterns for breast cancer by stage and age. The horizontal axis indicates the cohorts of patients for whom 5-year relative survival rates were calculated, i.e., the rate associated with year 0 is the 5-year relative survival rate for the total patient cohort, the rate associated with year 1 is the 5-year relative survival rate for those patients who survived through the end of the first year, etc. For patients with localized breast cancer $<$ 35 years old the conditional rates start out lower than those for the older age groups but by 5 to 6 years after diagnosis the conditional rates for the 3 age groups are similar.

In the long term the rates for the youngest age group reached 100 for the 58 patients still alive at the end of 20 years, whereas the rates for the older age groups remained somewhat constant but less than 100. Figure 3 suggests that the youngest age group contained a larger number of patients having relatively more aggressive tumors (which resulted in early death) as compared to the older age groups.

In figure 4 for patients with regional disease, it can be seen that again for the youngest patients the rates were poorer for about 5 years after diagnosis. The rates for all age groups gradually increase for at least 10 years after diagnosis after which time there was a general tendency to level off at a point indicating roughly a 15% excess 5-year mortality.

In figure 5 for patients with distant involvement, it can be seen that there was no age effect in the rate patterns. However, of particular interest is the increase of the conditional rates and the level they reach, e.g., those patients still alive 5 years after diagnosis had approximately a 60 percent chance of not dying of causes related to their cancer for 5 more years. This is certainly substantially higher than the 5-year relative survival of 21 percent at diagnosis.

In figure 6, conditional rates are given by stage (extent of disease) at diagnosis. There is little difference in age distributions for patients with localized and regional disease (table 1), therefore, differences in the curves for these patients are not due to age differences. It is interesting that the pattern of rates for those patients with distant involvement approached that for patients having regional involvement approximately 14-15 years after diagnosis. The patients having localized cancer appeared distinct from the other 2 groups in that their conditional rates increase slightly over the first 10 years subsequent to diagnosis and remain reasonably constant from that point with the rates for the other 2 groups never approaching those for patients with localized disease.

Cervical Cancer - Figure 7 presents conditional 5-year relative survival rates by age for cervical cancer patients with localized disease. There is a relatively small age difference between the youngest and the oldest patients which seems to prevail during the entire period of follow-up with the rates for the 35-49 age group more like those for the youngest age group. Also, there was apparently a small subgroup of patients with more aggressive tumors who died by the third or fourth year after diagnosis with the remainder of the patients experiencing relatively constant excess 5-year mortality related to age at diagnosis and ranging from 5 percent for the youngest age group to 10 percent for the oldest.

Figure 8 shows the conditional rate patterns for patients with regional cancer. By about 5 years after diagnosis the conditional rates are stable for all age groups except possibly the youngest with a constant excess 5-year mortality of 10% in the 35-49 age group and 20% in the 50-64 age group. By the end of 14 years after diagnosis, the rate for the 55 remaining patients in the youngest age group was 100 percent. This suggests that there was a small subgroup of patients who experienced normal mortality after diagnosis and treatment of their cancer.

Figure 9 presents conditional rate patterns by extent of disease for cervical cancer patients diagnosed during 1950-59. It can be seen that the point of leveling off appears related to extent of disease as it occurred earlier for patients with localized tumors and progressively later with more advanced disease. The differences seen here may be due in part to the effects of differences in age distribution by stage (table 1), however, the conditional rates by age for patients with localized disease (figure 7) are generally better than the corresponding rates by age for patients with regional disease (figure 8). After 4 to 5 years the remaining constant excess 5-year mortality appears to be related to extent of disease ranging from roughly 5 percent for the localized group to more than 20 percent for the distant group.

Corpus Cancer - Figure 10 presents conditional rate patterns for patients with localized disease by age. There is a small reasonably constant excess mortality for nearly 20 years after diagnosis with an indication of a very small age difference. The excess for such a long time is somewhat surprising since the 5-year relative survival rate at diagnosis is greater than 90 percent for those patients < 50 years old at diagnosis.

For patients with regional disease (figure 11), the behavior of the rates is somewhat erratic, but the rates steadily increase reaching 100 for those 86 patients alive at the end of the 10th year after diagnosis in the 50-64 age group.

There were not enough patients with distant disease to look for an age effect, but there were enough to compare the overall conditional rate patterns by stage (figure 12). The patterns are remarkably similar to those for cervical cancer with the rates for each stage increasing subsequent to diagnosis and stabilizing at a level related to stage of disease at diagnosis. The exception to this is the patients with regional disease who survived through the end of the 10th year after diagnosis. Their conditional rates subsequently approach 100 percent and then decrease. This latter behavior is likely due to the small numbers of patients at risk of dying.

Lung Cancer - Only data for male lung cancer patients were analyzed because of the paucity of female patients. The combination of high early mortality and available numbers of patients by stage confined our look for age effects by stage to those patients with localized disease (figure 13). It can be seen that there is substantial difference in the conditional rate patterns for the 2 age groups. Examination of figure 14 indicates rather interesting differences in the conditional rate patterns by stage. It is surprising that the conditional rates for patients with regional disease should be better than for those with localized disease after the 4th year subsequent to diagnosis. To gain some insight into this observation, the data were further examined by stage and histologic type. There were only 2 histologic types with enough patients to permit examination of conditional survival rate patterns by stage, i.e., carcinoma NOS and squamous cell carcinoma.

The better conditional survival of patients with regional disease was found to be due to the survival of patients with squamous cell carcinoma and regional involvement having better conditional survival than the corresponding patients with localized disease beginning with the cohort of patients alive 4 years after diagnosis. The other patients with regional disease had the expected poor survival leaving those patients with squamous cell carcinoma as the primary contributors to the conditional survival after 4 years subsequent to diagnosis. It is of course recognized that there are limitations in histology data that have not been reviewed. There was also a concern about age effects as there were relatively more young patients with regional involvement than with localized disease (table 1). However, the pattern of rates for those patients with regional involvement (figure 14) is more favorable beginning with the 6th year after diagnosis than either age group for those patients with localized disease (figure 13).

Colon Cancer - Conditional rate patterns were examined separately for males and females. The patterns for both sexes were quite similar; therefore, we have chosen to show only the patterns for females. The patterns by age are given in figure 15 for patients with localized disease and in figure 16 for patients with regional disease. There is no apparent age effect for patients with localized disease while for patients with regional disease the patterns are somewhat more difficult to assess. It does appear that the younger patients enjoyed roughly a 10 percent advantage in the conditional rates for the 4th through the 8th year with no apparent differences beyond the 8th year. Also, the 137 patients in the 50-64 age group alive at the end of 15 years had a 5-year relative survival rate of 100. There were not enough patients with distant disease to look for age differences in the conditional rate patterns.

Subsequent to 7 years after diagnosis, there is no difference in the conditional rate patterns by stage (figure 17). It is of interest to note that patients with localized disease had a 5-year excess mortality rate of roughly 5 percent from the 6th through the 20th year after diagnosis.

Prostate Cancer - There were not enough prostate cancer patients under age 65 to look for age differences in the conditional rate patterns; therefore, only differences in the rate patterns by stage were considered (figure 18). For patients with localized disease, the conditional rates increased from 70 percent at diagnosis to only 75 percent by 13 years after diagnosis. The conditional rates for patients with regional and distant disease increased but remained substantially lower than the rates for patients with localized disease. Variation by stage is likely not due to age differences since 97.4 percent of patients with localized disease and 92.9 percent of patients with regional involvement were in the 50-64 year age group at diagnosis (table 1).

DISCUSSION

This analysis has shown that, for some forms of cancer, normal survival expectation is virtually achieved for some subgroups of patients. The rate of approach to normal expectation was rapid for patients with cancers of the uterine cervix, uterine corpus or colon. For breast cancer, a much more gradual increase was observed. Furthermore, even after 20 years, breast-cancer patients with localized disease seemed to only achieve 90 percent of expected survival. For lung and prostate patients, the maximum levels seemed to be of the order of 80 and 75 percents respectively of normal.

Thus, the chronic nature of cancer has been again observed, and it is clear that there is no single number of years survived that can be referred to as the break point for "cure." The maximum level and rate of approach to normal survival expectation is a function of cancer site, age, stage at diagnosis and perhaps other factors.

For reference, table 2 gives conditional 5-year relative survival rates by site, stage, and age for patients surviving through the end of 3, 5, and 10 years subsequent to diagnosis of their cancer. Some rates are given for completeness even though not included in the graphs because of their large standard errors.

It is of interest to compare the long-term survival patterns for the various sites in a general way. Certainly the patterns for cervix and corpus are somewhat similar. Breast, corpus, cervix, and prostate all display long-term conditional rate patterns which indicate a long-term excess mortality related to stage of disease at diagnosis. This does not appear to be true for colon where the effects of stage disappear at about 7 years after diagnosis and the same may also be true for lung at 3 to 4 years after diagnosis. Also, there seemed to be a very distinct age effect by stage for cervix and breast, and possibly lung (for patients with localized disease) but little indication of an age effect for colon and corpus.

An observation of some interest regarding biological behavior was that, of the 4 patient groups in which normal mortality eventually occurred (Breast, Localized, < 35; Cervix, Regional, < 35; Corpus, Regional, 50-64; and Colon, Regional, 50-64), three were groups with regional disease. Certainly it would have been anticipated that normal mortality, if observed, would have occurred primarily in patients with localized disease.

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6. Cutler, S.J. and Latourette, H.B.: A national cooperative program for the evaluation of end results in cancer. J Natl Cancer Inst 22: 633-646, 1959.

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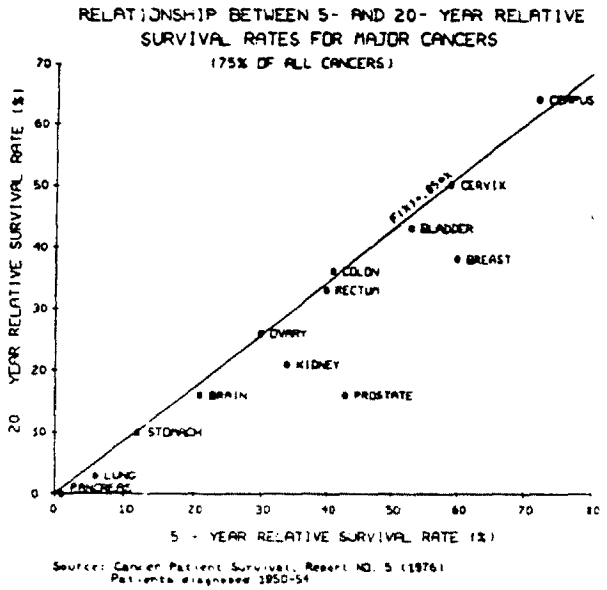
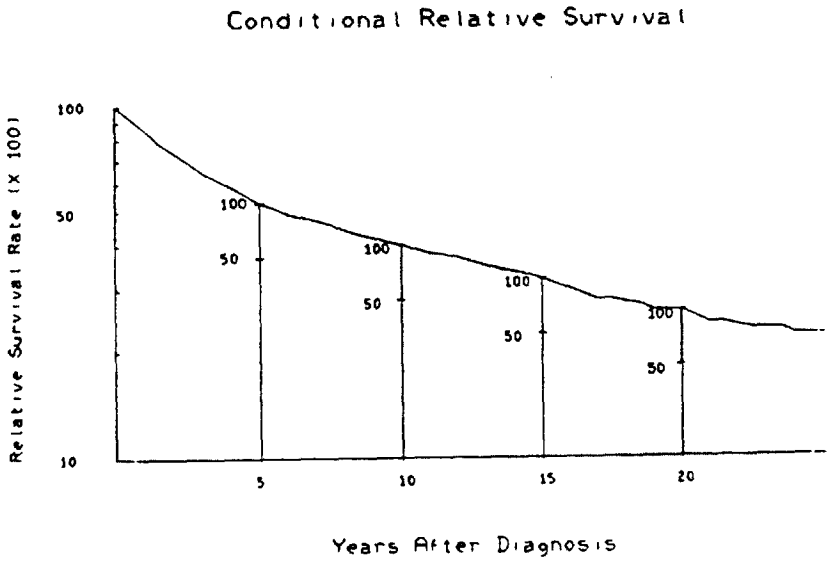
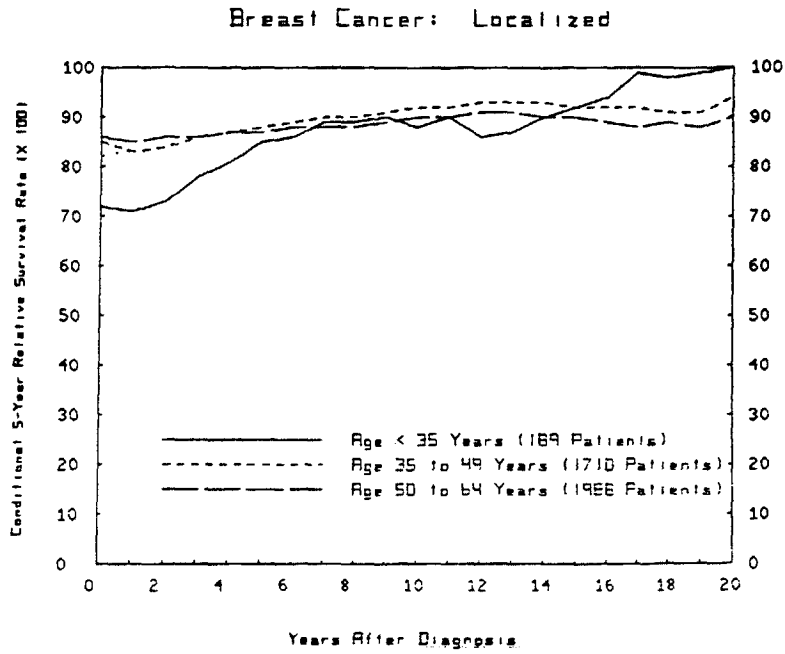
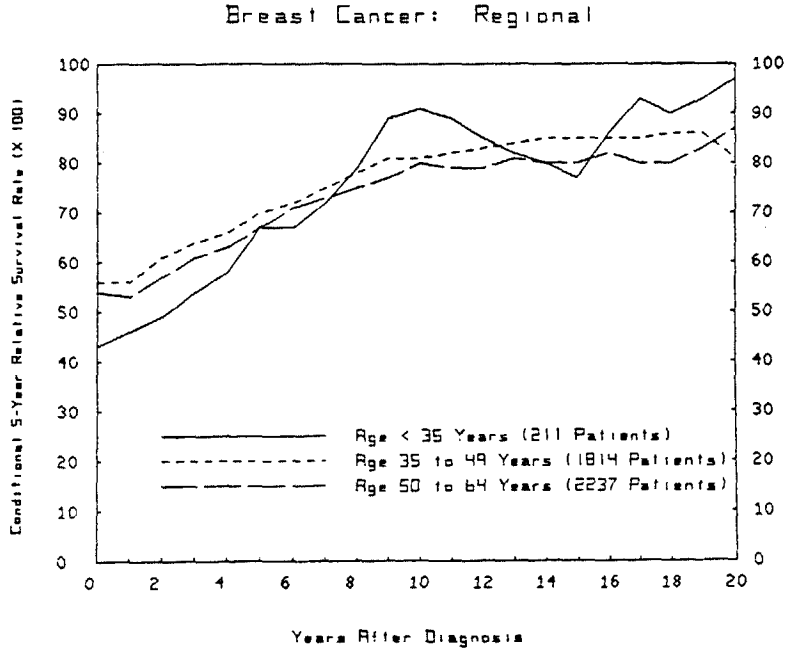
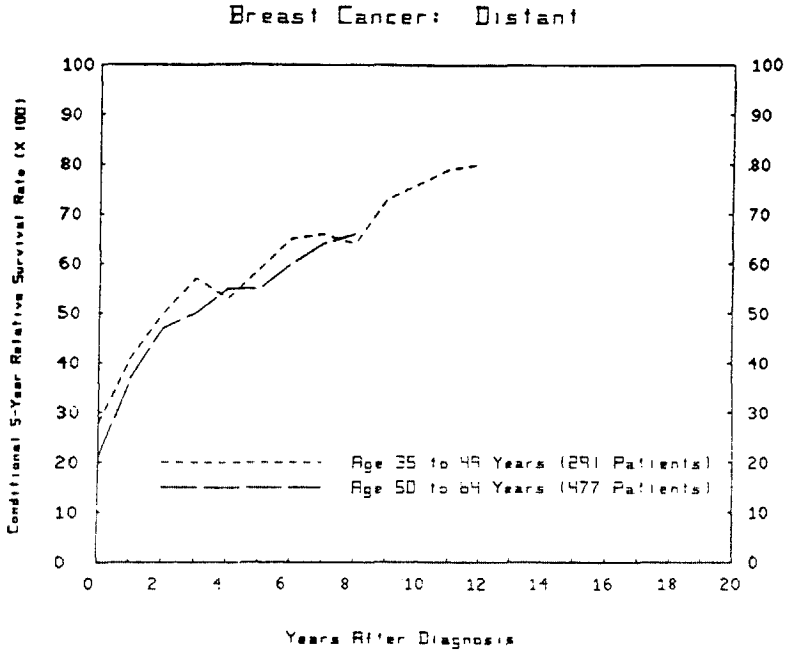
Figures

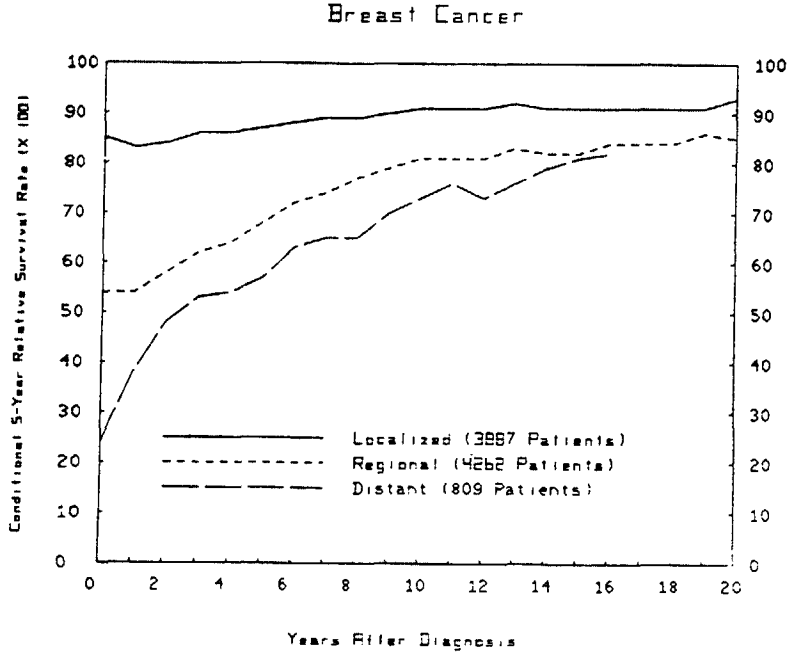

RELATIONSHIP BETWEEN 5- AND 20- YEAR RELATIVE SURVIVAL RATES FOR MAJOR CANCERS
(75% OF ALL CANCERS)
20 YEAR RELATIVE SURVIVAL RATE (%)
5 - YEAR RELATIVE SURVIVAL RATE (%)
0
10
20
30
40
50
60
70
80
CORPUS
CERVIX
BLADDER
BREAST
COLON
RECTUM
OVARY
KIDNEY
BRAIN
PROSTATE
STOMACH
LUNG
PANCREAS
Source: Cancer Patient Survival, Report NO. 5 (1976)
Patients diagnosed 1950-54

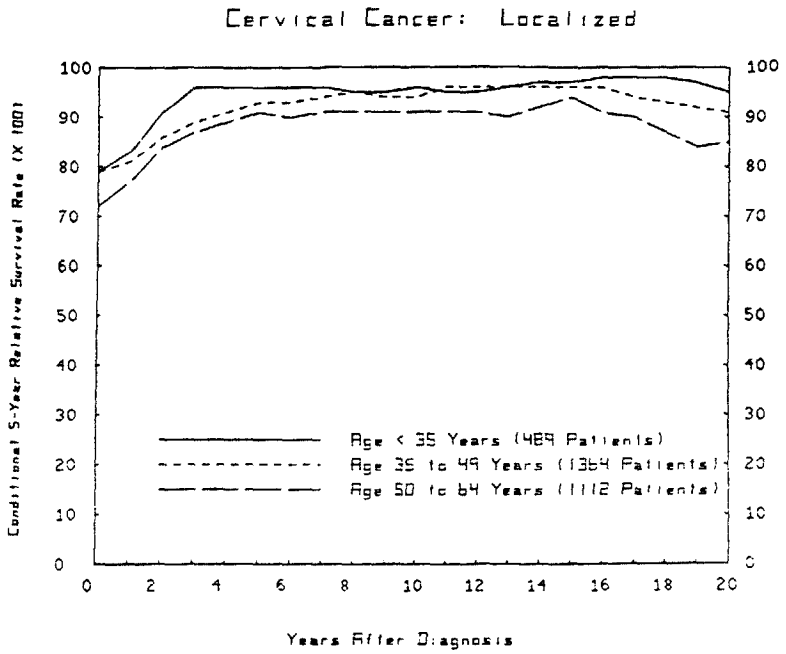

Conditional Relative Survival
Relative Survival Rate (X 100)
100
50
10
100
50
100
50
100
50
100
50
5
10
15
20
Years After Diagnosis

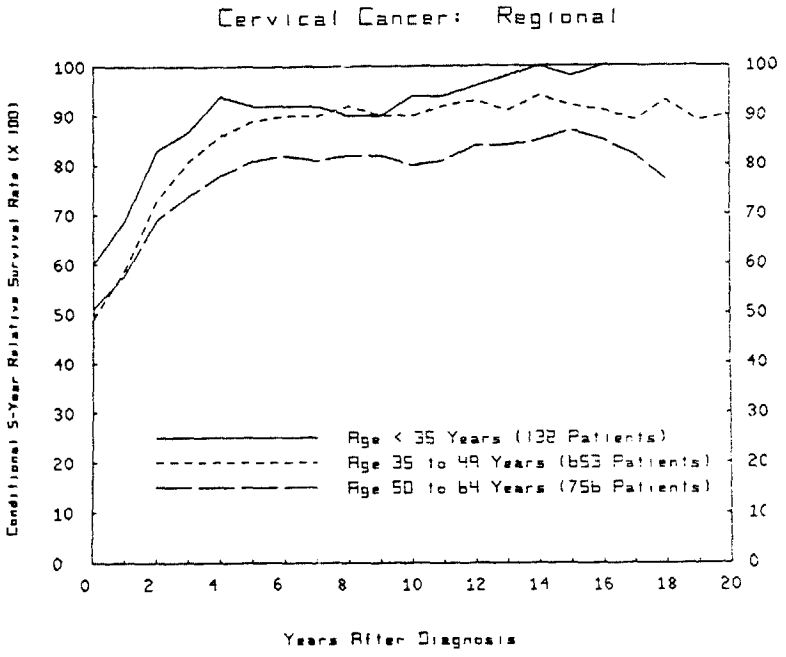

Breast Cancer: Localized
Conditional 5-Year Relative Survival Rate (X 100)
Age < 35 Years (189 Patients)
Age 35 to 49 Years (1710 Patients)
Age 50 to 64 Years (1988 Patients)
Years After Diagnosis

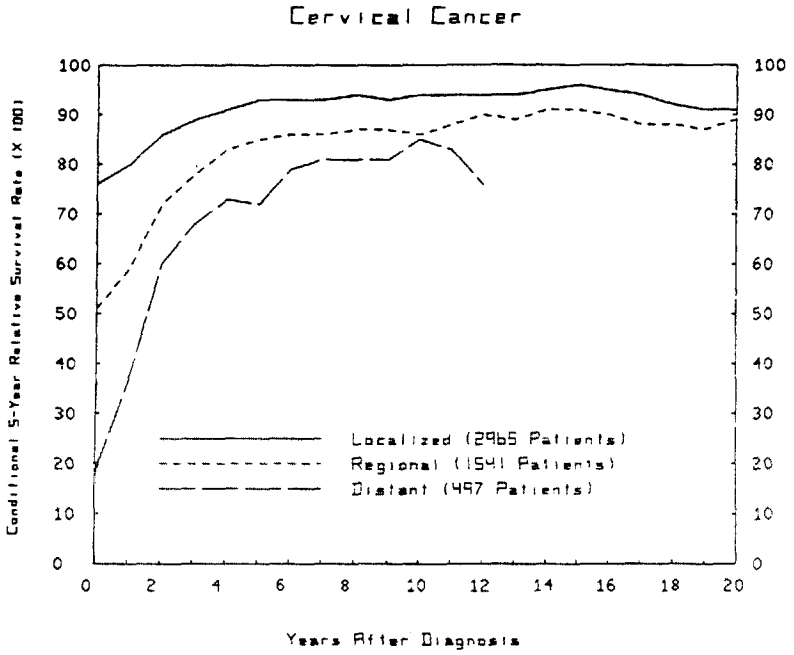

Breast Cancer: Regional
Conditional 5-Year Relative Survival Rate (X 100)
Age < 35 Years (211 Patients)
Age 35 to 49 Years (1814 Patients)
Age 50 to 64 Years (2237 Patients)
Years After Diagnosis

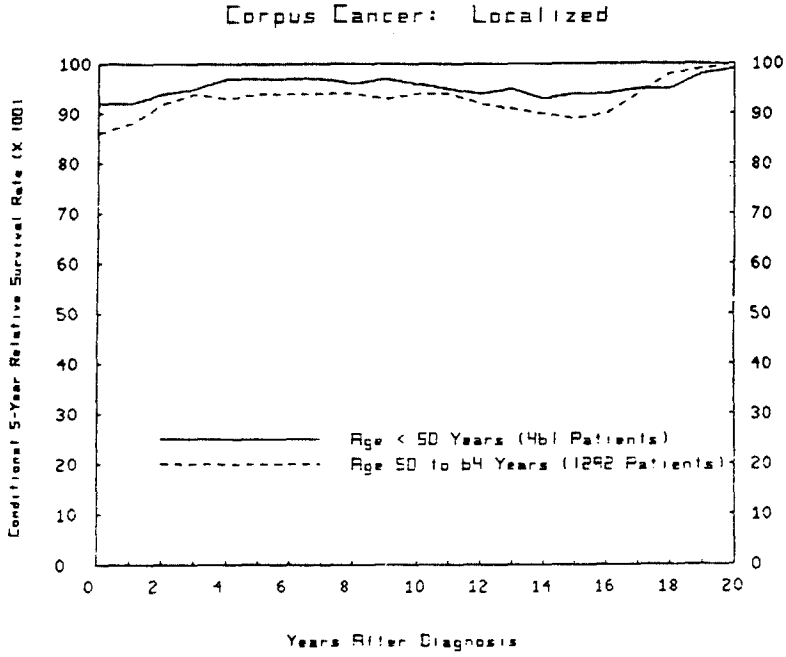

Breast Cancer: Distant
Conditional 5-Year Relative Survival Rate (X 100)
Age 35 to 49 Years (291 Patients)
Age 50 to 64 Years (477 Patients)
Years After Diagnosis

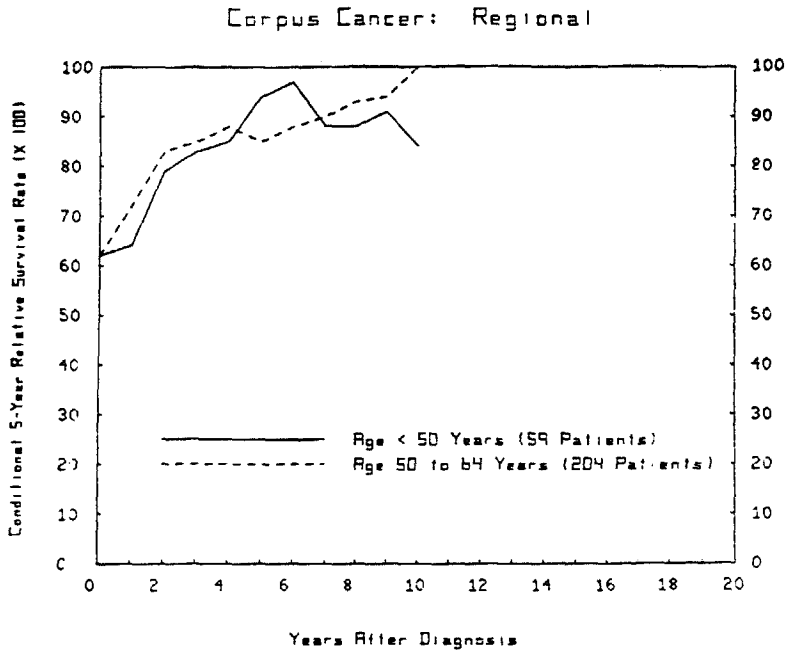

Breast Cancer
Conditional 5-Year Relative Survival Rate (X 100)
Localized (3887 Patients)
Regional (4262 Patients)
Distant (809 Patients)
Years After Diagnosis

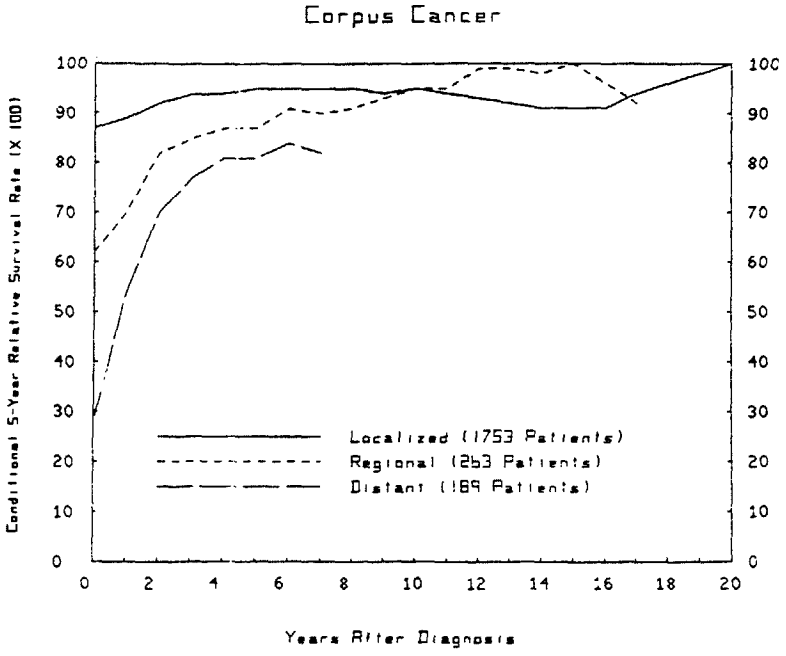

Cervical Cancer: Localized
Conditional 5-Year Relative Survival Rate (X 100)
Age < 35 Years (489 Patients)
Age 35 to 49 Years (1364 Patients)
Age 50 to 64 Years (1112 Patients)
Years After Diagnosis

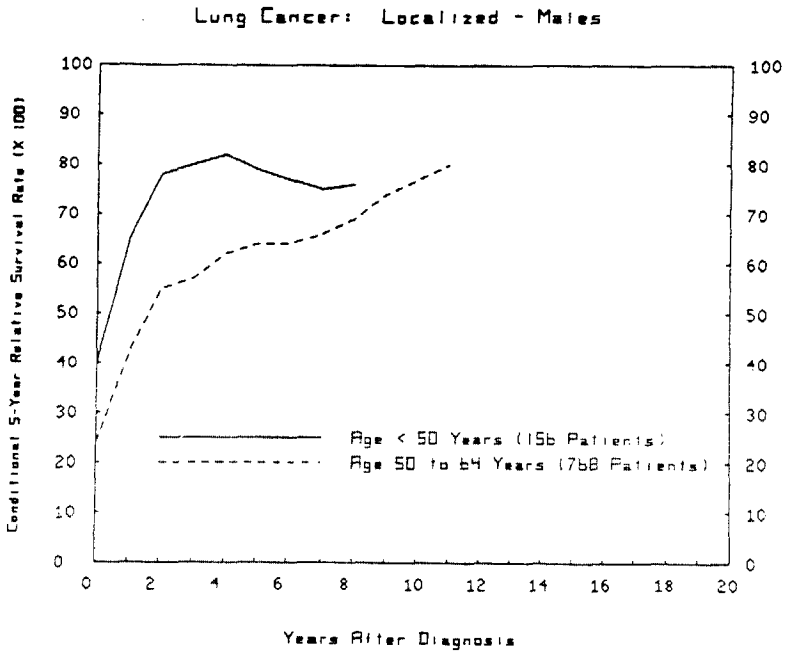

Cervical Cancer: Regional
Conditional 5-Year Relative Survival Rate (X 100)
Age < 35 Years (132 Patients)
Age 35 to 49 Years (653 Patients)
Age 50 to 64 Years (756 Patients)
Years After Diagnosis

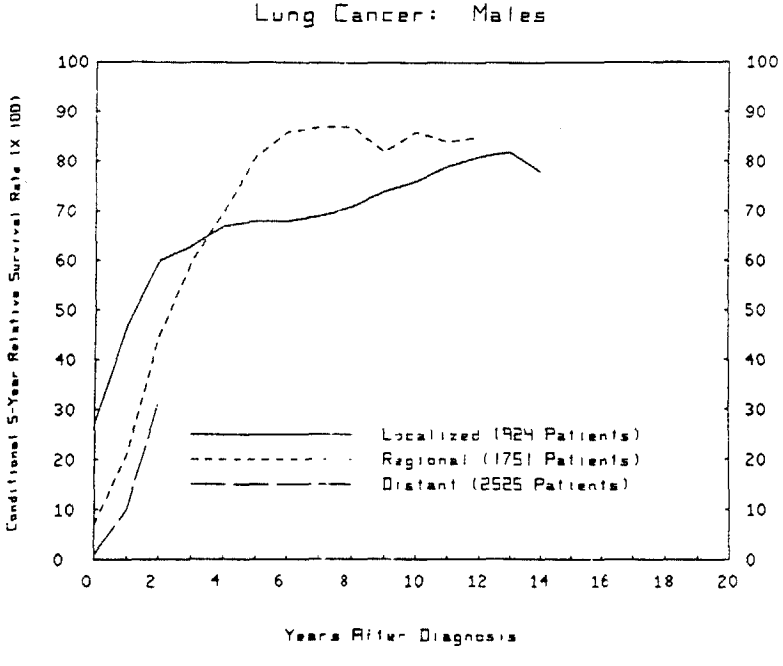

Cervical Cancer
Conditional 5-Year Relative Survival Rate (X 100)
Localized (2965 Patients)
Regional (1541 Patients)
Distant (497 Patients)
Years After Diagnosis

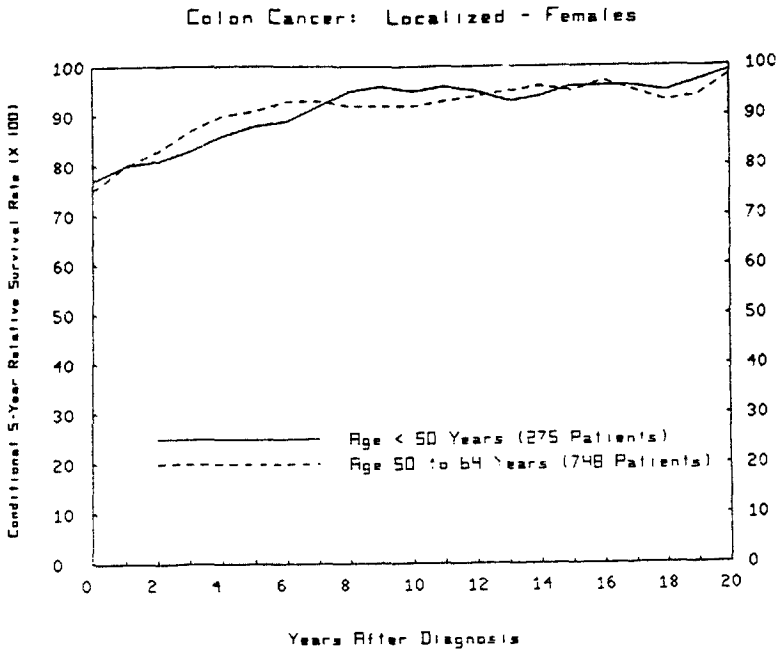

Corpus Cancer: Localized
Conditional 5-Year Relative Survival Rate (X 100)
Age < 50 Years (461 Patients)
Age 50 to 64 Years (1292 Patients)
Years After Diagnosis

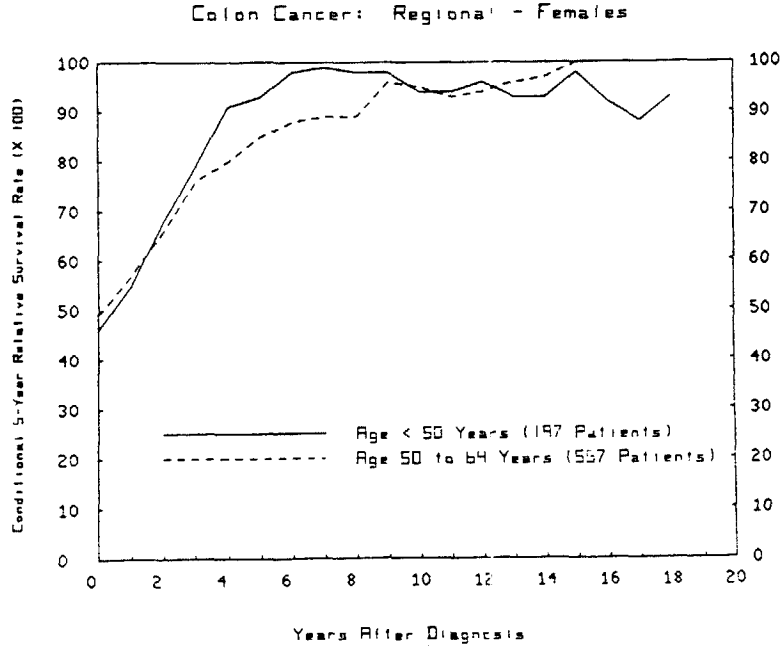

Corpus Cancer: Regional
Conditional 5-Year Relative Survival Rate (X 100)
100
90
80
70
60
50
40
30
20
10
0
0 2 4 6 8 10 12 14 16 18 20
Age < 50 Years (59 Patients)
Age 50 to 64 Years (204 Patients)
Years After Diagnosis

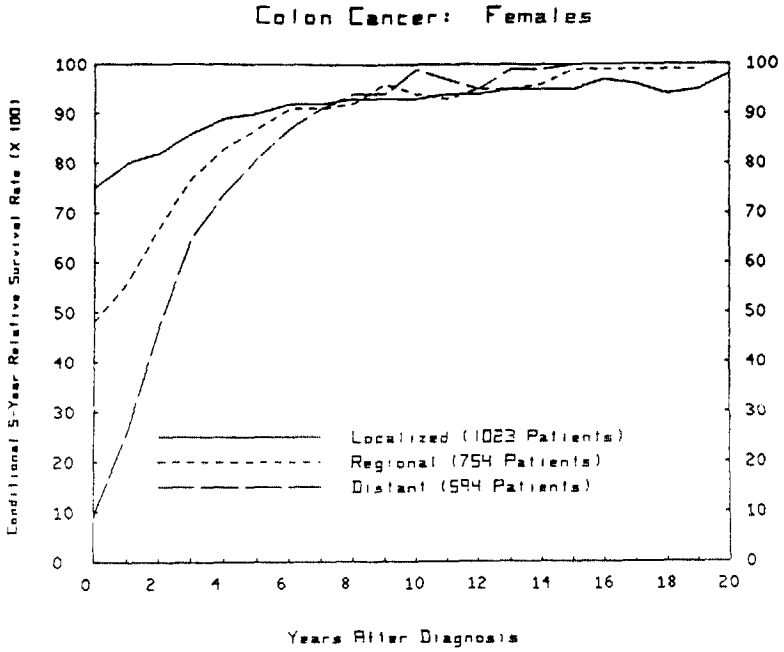

Corpus Cancer
Conditional 5-Year Relative Survival Rate (X 100)
100
90
80
70
60
50
40
30
20
10
0
0 2 4 6 8 10 12 14 16 18 20
Localized (1753 Patients)
Regional (263 Patients)
Distant (189 Patients)
Years After Diagnosis

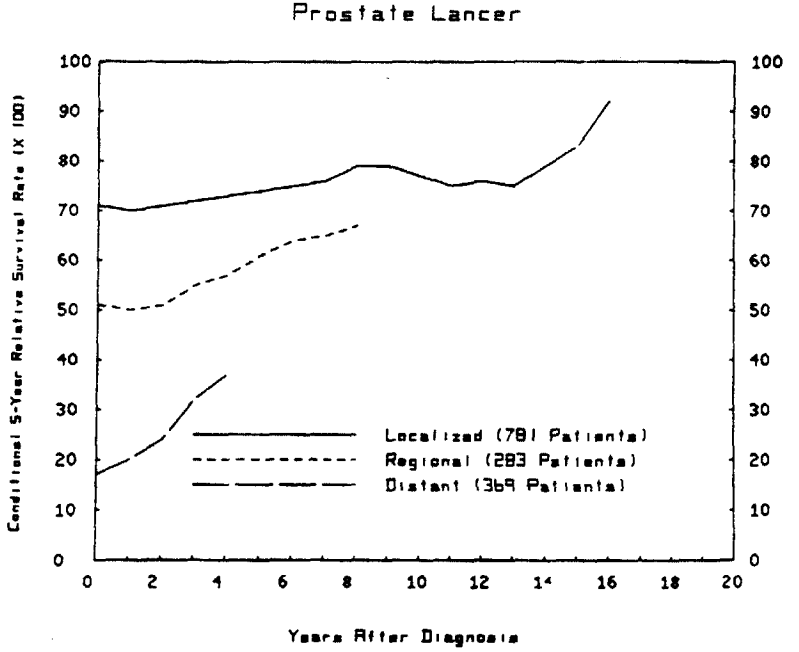

Lung Cancer: Localized - Males
Conditional 5-Year Relative Survival Rate (X 100)
Age < 50 Years (156 Patients)
Age 50 to 64 Years (768 Patients)
Years After Diagnosis


Lung Cancer: Males
Conditional 5-Year Relative Survival Rate (X 100)
Localized (924 Patients)
Regional (1751 Patients)
Distant (2525 Patients)
Years After Diagnosis


Colon Cancer: Localized - Females
Conditional 5-Year Relative Survival Rate (X 100)
Age < 50 Years (275 Patients)
Age 50 to 64 Years (748 Patients)
Years After Diagnosis


Colon Cancer: Regional - Females
Conditional 5-Year Relative Survival Rate (X 100)
Age < 50 Years (197 Patients)
Age 50 to 64 Years (557 Patients)
Years After Diagnosis


Colon Cancer: Females
Conditional 5-Year Relative Survival Rate (X 100)
Years After Diagnosis
Localized (1023 Patients)
Regional (754 Patients)
Distant (594 Patients)


Prostate Cancer
Conditional 5-Year Relative Survival Rate (X 100)
Years After Diagnosis
Localized (781 Patients)
Regional (283 Patients)
Distant (369 Patients)

MR. LEW: Thank you for the valuable information and analysis you have given us. One can think of this analysis in terms of conditional death rates rather than in terms of conditional survival rates, and actuaries will probably feel more at home with the former. Corresponding to each conditional survival rate, there is a specific conditional death rate over the period of years considered. If one plots the conditional death rates, one will be in a position to decide at what point in time after treatment for cancer persons with a history of cancer may be insured. This kind of information has been so used in the past.

I would add that the life insurance business can now handle computer tapes such as those given us by the National Cancer Institute for the End Results Study through the facilities at the Center for Medico-Actuarial Statistics in the Medical Information Bureau in Boston. This Center has the equipment and the personnel to tabulate material from various kinds of mortality investigations and adapt it for use in the life insurance business. We have with us today Mr. John R. Avery, Director of the Center for Medico-Actuarial Statistics and Mr. Frank Kouble, Vice President of the Medical Information Bureau. Actuaries can turn to these two gentlemen for assistance in research on mortality, whether based on the experience among insured lives or on the experience drawn from government, medical research centers or other sources.