Cancer Epidemiology: Shortcomings and Possibilities
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The development of the concepts of initiators and promotors in carcinogenesis necessitates deliberations of evidence from human cancer epidemiology.

Recent arguments in favor of mortality data as a more reliable indicator of trends in cancer incidence than morbidity data collected from cancer registries are disputed. Inconsistency in the use of data is pointed out. Comparisons of data from cancer registration in Denmark with those from Connecticut and upstate New York show such congruity that it is impossible to accept suggestions of systematic bias of significance without direct evidence to that effect.

Since accurate information on periods of exposure and on the onset of disease is fundamental to considerations of initiators and promotors the following proposals are made. Payrolls or similar data should be kept safe for 40 years for occupations where exposure to carcinogens may be suspected. Experience on latent periods from the last 100 years should be systematically reassured. Death certificates showing a diagnosis of malignant neoplasia should always state the histological diagnosis if any.

Modernization of international cancer epidemiology dates from 1946, when an international symposium held in Copenhagen recommended to the Interim Commission for a World Health Organization that each country should have a cancer registry (1, 2). By a series of subsequent symposia held in Oxford (1950), Louvain (1952), Kampala and Leopoldville (1956), Copenhagen (1958), London (1958), Tokyo (1960) and Cairo (1961), sponsored by the International Union against Cancer, we succeeded in turning attention to the advantages of cancer registration in epidemiology.

Today some 60 cancer registries function all over the world and as a result of the collection of accurate data, cancer epidemiology has changed its "Cinderella" existence in the backrooms of Public Health offices into a university life, indulging in discussions of its subdivisions, aims and philosophy. Cancer registries have contributed both to prevention studies and to carcinogenesis research (3), and although only a few of them cover sufficient years to verify trends in cancer morbidity, the time will soon come for many more.

Now the inspiring discussion around initiation and promotion of carcinogenesis is presenting its demands to epidemiology, and since recent reviews by Maclure and MacMahon (4) and by Doll and Peto (5) have confirmed that epidemiology at present is in no position to meet such demands, it will be our task to examine the reasons why, and point to ways to improve the instruments of cancer epidemiology.

In the first part of a voluminous report to the U.S. Congress (5) Doll and Peto have attempted to estimate the avoidable amount of cancer by comparing morbidity rates from cancer registries all over the world for those 50% of cancer patients aged between 34 and 64 years. Rates appear as taken by their face values from low-risk and high-risk areas, but without documentation of the quality of diagnoses in various places. In the last part of the review, however, the authors prefer mortality data as more reliable than morbidity data for verifying trends in cancer morbidity.

Accepting mortality data a priori as the more reliable source of information, they interprete deviations from the rates from the oldest registries in the United States—those for Connecticut and for the State of New York less New York City—in favor of the registries, and of incidence data in general.

Epidemiology Trends

Before evaluating this discrepancy, however, it is only fair to point out that according to the two re-
views mentioned, cancer epidemiology at present tends to follow different lines, sometimes intertwined in the same publication. The line favored by the reviews is colloquially termed "black box epidemiology"—not any macabre allusion to those mortality data which appear its favorite basis, but indicating some trend to containment of information on the mechanism of carcinogenesis, which some find of less immediate interest to epidemiology as they see it.

In contrast we find the authors referring to the epidemiology of "pure scientists," but since the whole discipline after all is medical, and thus applied science, it may be more adequate to distinguish between administration epidemiology (or perhaps PR Epidemiology) and research epidemiology or "scientific" or "critical" epidemiology (Table 1).

The first, orginal line of epidemiology is largely represented today by discussions of administrative or slightly political character, often addressing administrators or the lay public through mass media. Such reviews usually have to avoid complicated scientific problems or details. In their context, "cancer" often figures as a single disease entity, and a percent of the cancer total will often suffice, often covering the two sexes together, for an entire country. Here the number of persons "killed by cancer" will be of more immediate interest than the number of patients, and consequently the significant difference between morbidity and mortality data may be disregarded when convenient.

In contrast, the critical, scientific approach will have to base its analyses on data as accurate as possible, specified by race, sex, age and site and verified by histology from biopsy or autopsy. Therefore, its workers often may have to refer to original publications more detailed than the useful review tables such as in "Cancer in Five Continents" (6-8).

Also the use of scattergrams is characteristic of the two lines: (1) simple scattergrams plotting cancer incidence or mortality rates for various countries against national consumption of some or other factor suspected of carcinogenicity, and (2) a similar plotting allowing for some latent period and showing the correlation to be closer after specification of the suspect factor like substituting tobacco with cigarettes.

It seems obvious which method will be preferable to "those whose scholarly austerity is unbending," and which will appeal to public press, and politicians, less favorable to doubts and to qualifications of attitudes to carcinogens. However our present question is how to make any progress with the black box, if Doll and Peto are correct that mortality data are more reliable than morbidity rates.

### Mortality and Morbidity Data

In comparing mortality and morbidity data it is fundamental that mortality is a function of morbidity and therapy. Equally fundamental is that mortality and morbidity as given for the same year refer to cases originating in different years. A neoplasm of decreasing morbidity may therefore show more persons dying in one year than developed the disease, particularly if the average survival time is long.

Doll and Peto (5) have listed biases, or rather possible biases, in mortality and morbidity data (Table 2). While realizing that various diagnostic inaccuracies and errors may affect both sets of data, they have overlooked that mortality data may be influenced by overdiagnosis of cancer, and furthermore, that the consequences of changes in definitions and in the interest of physicians will not be restricted to morbidity rates.

Mortality rates will tend to be reduced by successful therapy, and morbidity data must be checked for redundant reports of the same case, which is not too difficult, but both systems will have to live with the effects of the inclusion of early and less malignant cases. For a cancer registry it is not too difficult to evaluate the impact of a screening program on morbidity data, and subsequently on survival, but the effect on mortality numbers from

| Table 1. Comparison of features in "administration epidemiology" and "research epidemiology." |
|-----------------------------------------------|
| **Administration epidemiology**               | **Research epidemiology**                     |
| (black-box epidemiology, PR epidemiology, suggestive epidemiology) | (epidemiology, documenting epidemiology) |
| **Staffing**                                  | **Sources**                                   |
| Committees                                   | Reviews                                       |
| **Data**                                      | **Mortality (percent, both sexes)**           |
| Mortality registration, specific by sex, age, site, histology | Scattergrams, simple |
| Scattergrams, simple                         | Scattergrams (correlation increased with specification) |
| Terms "Good" evidence, carcinogenic           | Terms Suggestive evidence, conclusive evidence, carcinopoteney specified by species, mutagenic |
| Opinions, hypotheses, suggestions, recommendations, reviews | Results Specified data, exclusions, conclusions, statements |
the elimination of an early carcinoma in situ may not appear till ten or more years later. Hence the apparent stability of mortality rates, which may convey a false impression of reliability.

We shall therefore never be able to interpret mortality rates without the assistance of cancer registration, which has been organized for such purposes. If the use of death certificates for cancer research should be taken seriously, no doubt the International Agency for Research in Cancer (IARC) would have used its affiliation with WHO to have histological diagnoses introduced on the certificates when available. Perhaps we may hope for an initiative with the U.S. Congress supported by the authority of Doll and Peto.

The need for improvements of some kind appears from the recent analysis by Percy et al. (9), who give the topmost deficit in cases reported on U.S. death certificates at 43.8% for rectum cancer.

Although from personal experience I would hesitate to share the confidence in cancer morbidity rates from all kinds of medical systems appearing from the first part of Doll and Peto’s review, I would still be more disinclined to subscribe to their depreciation in the last part of morbidity data from Connecticut and for upstate New York in favor of the mortality rates for the United States with a view to the evaluation of present-day epidemiology I shall, therefore, show a comparison of rates from the two old American registries with those from the Danish, (Table 3), which dates from 1942 and is about the same age (6-8, 10-12).

## Comparison of American and Danish Registration Data

As an introduction of this hobby of mine, besides clinical and pathology work, I show the percent of cases admitted to a hospital and histologically examined for some neoplasms (Table 3) studied particularly by Doll and Peto, and in the following.

It appears that since 1950, more than 90% of patients have been admitted to a hospital, so that the data are as good as from any other registry. The same applies to histological verification.

## Upstate New York

As the first bias of registration data, Doll and Peto mention the difficulties involved in delimitation of the population at risk. This might be expected to be particularly pronounced for a registry serving the State of New York less New York City, and to be nonexistent in Denmark. So, when we found the absence in upstate New York of the increase in testis cancer found in Denmark and in Connecticut (13), this was our immediate explanation, but we cannot be certain. There may be a real difference in risk as between Denmark and Finland, or between Quebec and Manitoba, since we have not found other evidence of such differences due to bias.

In fact, comparison of morbidity-age curves for Copenhagen and upstate New York for 1950 (1) and for 1970 (21) show practically identical age-curves for Hodgkin’s disease (Fig. 1). What is more the same applies to leukemia, for which correspondence extends to data specially collected from Brooklyn by MacMahon and Clarke (14) as well as to multiple myeloma (1). It does seem difficult from these obser-

### Table 2. Alleged biases in cancer registration and their exclusion.

| Bias                                | Exclusion                      |
|-------------------------------------|--------------------------------|
| Difficulties to population estimate | Census                         |
| Multiple recording of cases         | Linkage (number, name, etc.)   |
| Improvements in diagnostic standards| Contact with clinicians        |
| Improvements in physicians’ interest| Contact with clinicians        |
| Changes in diagnostic definitions   | Definitions watched            |
| Search for “lumps” (of low malignancy) | Analysis of search results and of survival. |

| Biases in mortality data            |                                |
|-------------------------------------|--------------------------------|
| Cases not recognized                |                                |
| Primary site unknown                |                                |
| Primary site misdiagnosed           |                                |
| Primary site miscertified           |                                |
| Cases cured                         |                                |
| Cases misdiagnosed as cancer        |                                |

### Table 3. Cases in Copenhagen admitted to hospital and histologically verified cases (Danish Cancer Registry).

|          | Hosp. | Hist. | Hosp. | Hist. | Hosp. | Hist. | Hosp. | Hist. | Hosp. | Hist. | Hosp. | Hist. | Hosp. | Hist. | Hosp. | Hist. | Hosp. | Hist. | Hosp. | Hist. | Hosp. | Hist. | Hosp. | Hist. | Hosp. | Hist. |
|----------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| Stomach (m) | 86%   | 46%   | 89%   | 59%   | 91%   | 65%   | 80%   | 79%   | 94%   | 75%   | 95%   | 69%   | 93%   | 88%   | 95%   | 83%   | 97%   | 82%   | 96%   | 78%   | 97%   | 89%   | 95%   | 91%   | 93%   | 92%   |
| Colon (m)    | 89    | 64    | 90    | 70    | 92    | 83    | 96    | 83    | 98    | 87    | 95    | 72    | 96    | 88    | 95    | 84    | 97    | 82    | 96    | 78    | 97    | 89    | 95    | 91    | 93    | 92    |
| Sigmoid (m)  | 94    | 79    | 90    | 82    | 98    | 85    | 98    | 90    | 98    | 89    | 93    | 83    | 95    | 76    | 98    | 91    | 95    | 82    | 96    | 78    | 97    | 96    | 95    | 91    | 93    | 92    |
| Rectum (m)   | 93    | 81    | 95    | 85    | 98    | 80    | 96    | 91    | 96    | 86    | 95    | 76    | 98    | 91    | 95    | 82    | 96    | 78    | 97    | 96    | 95    | 91    | 93    | 92    | 92    | 92    |
| Bladder (m)  | 95    | 84    | 95    | 86    | 99    | 94    | 98    | 93    | 99    | 91    | 96    | 82    | 98    | 92    | 95    | 83    | 97    | 84    | 96    | 79    | 97    | 89    | 95    | 92    | 93    | 92    |
| Prostate (m) | 97    | 90    | 99    | 89    | 100   | 93    | 99    | 93    | 99    | 95    | 96    | 86    | 98    | 92    | 97    | 89    | 95    | 88    | 96    | 88    | 97    | 95    | 91    | 93    | 92    | 92    |
| Breast (f)   |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |       |
vations to accept a theory of a systematic bias on population at risk.

Connecticut

In Connecticut fresh data on morbidity have been collected since 1941, and in order to test the effect of inclusion of premalignant cases on numbers, we may turn to a comparison of data for the uterine cancers with those from Copenhagen. It may be recalled that at a time when English mortality data had shown a social gradient for uterine cancer deaths unfavorable to the poor, the highly specified morbidity data for Copenhagen made it possible to refer the gradient to differences in morbidity—not to the effect of therapy—limited to cervical uterine cancer (1). Nonspecified uterine cancers in Copenhagen (1943-47) amounted only to 3.8% against 25.8% for Connecticut, which only 25 years later attained a corresponding coverage of specification.

Nevertheless, histology in Connecticut proved the more efficient (Table 4). Cases of carcinoma in situ of the cervix were collected in large numbers, which resulted in continuous decrease in morbidity from cervix carcinoma. In Copenhagen screening began only 20 years later, which allowed a rise in rates, until screening turned it into a decrease (12).

Besides showing how prevention of cancer may spoil good statistics this combination of registration...
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Data reflects a complex situation in a way mortality data could never do.

Cancer of the Bladder

Cancer of the urinary bladder has been suspected of bias by the inclusion during later years of cases previously taken as papillomas. Such cases, when untreated, invariably end as malignant and have therefore always been included in Danish data, which, without bias, offer a good opportunity to check for its possible effects (Fig. 2).

The first increase in morbidity from bladder cancer was in fact, observed from Danish morbidity data, and an immediate analysis of an interview study by Lockwood (15) revealed an association with smoking, although less than that found for lung cancer in most places. The influence of non-tobacco factors must vary considerably, since the ratio of lung cancer to bladder tumors remains at ca. 2.8 in Denmark, Norway and Sweden, while English registries reporting morbidity rates for lung about the same as Copenhagen's show only half its rates for bladder, (2). A rough estimate of a ratio for the U.S. calculated from mortality rates (16) was similar to Norway's but varied considerably among the states (17).

Logically, an absence of an increase in bladder cancer rates for the United States would, if real, be significant as a clue to tobacco carcinogenesis of the bladder. In fact Doll and Peto, and before them DeVesa and Silverman (18) referred to decreasing mortality rates, despite a rise reported for morbidity. Also in this case Doll and Peto accept mortality rates as the more reliable indicator and ascribe the discrepancy partly to inclusion in the data of an increasing number of "papillomas." Nevertheless, in Denmark where this does not apply, crude five-year survival rates have risen from 23% about 1945 to ca. 40% twenty years later with general survival unchanged (12).

A comparison of the pattern of increase in bladder cancer morbidity for Copenhagen (Denmark), and Connecticut shows approximately the same pattern as a similar one in upstate New York (Fig. 3). Once more, it is difficult to find place for a bias, and an estimate of the avoidable amount of the bladder cancer is difficult.

Also the numerical values of morbidity rates for the three registries seem quite comparable (Table

![Figure 2](image-url)  
**Figure 2.** Bladder tumors (including papillomas). Incidence rates at various ages for birth group cohorts born around year indicated, for males in all of Denmark and in Denmark's capital.
5). It may be noted that age adjustment to the European Standard tends to increase American rates more than it does the Danish.

For further evaluation of mortality versus morbidity data, Doll and Peto have chosen cancers of the female breast, the intestine and the prostate.

**Breast Cancer**

Breast cancer is increasing according to Devesa and Silverman (18), and also in this case Connecticut seems ahead of Copenhagen, while upstate New York shows rates between those for the Danish capital and all of Denmark (Table 6, Fig. 4). Here again an increase is ascribed to the inclusion of biologically less malignant "lumps" discovered by the screening.

In Denmark a campaign for breast self-examination was begun in 1951, much on the American pattern, planned and followed in collaboration with the cancer registry. Numbers of fresh cases rose from 1082 in 1950 to 1407 in 1952, but dropped somewhat again when the campaign ended, having brought survival rate up to the U.S. level, where it remained despite later attempts to improve it (1). It is interesting that the 7-year survival rate for women under 44 years of age improved, so that for the first time the New York rate for women 35 to 44 in 1950-1955 was 11.4%.

| Period     | Connecticut | Upstate NY | Denmark | Copenhagen |
|------------|-------------|------------|---------|------------|
| 1940-1944  | 11.4        | —          | —       | —          |
| 1941-1943  | —           | 10.6       | —       | —          |
| 1943-1945  | —           | —          | 8.7, 6.4| 13.8       |
| 1944-1945  | 15.5        | —          | —       | —          |
| 1949-1951  | —           | 11.9       | —       | —          |
| 1948-1952  | —           | —          | 11.9, 9.3| 20.8       |
| 1950-1954  | 17.2        | —          | —       | —          |
| 1953-1957  | —           | —          | 16.2, 13.3| 26.7       |
| 1955-1959  | 20.3        | —          | —       | —          |
| 1956-1960  | —           | 16.1, 20.3 | —       | —          |
| 1960-1962  | 19.8, 25.3  | —          | —       | —          |
| 1958-1962  | —           | —          | 18.7, 16.4| 28.3       |
| 1963-1965  | 29.9        | —          | —       | —          |
| 1963-1967  | —           | —          | 24.1, 22.2| 37.5       |
| 1968-1972  | 31.7        | —          | 29.7, 28.7| 43.8       |
| 1969-1971  | —           | 25.1       | —       | —          |

*aAge-adjusted European standard.

Figure 3. Bladder cancer. Morbidity rates at various ages for birth cohorts for Connecticut and for upstate New York.
time it exceeded the rate for older women, and it remained in that position. The overall increase in morbidity continued, however, and, therefore, cannot be explained by discovery of benign lumps.

It should be noted that peaks on morbidity rate curves, as seen for Connecticut, cannot be expected to show in mortality data, until after average survival has expired, and then the spread of survival time will tend to even them out.

For comparison, morbidity rates for smaller communities are preferable to mortality data covering populations of scores of millions with widely different lifestyle.

Devesa and Silverman found that while gastric cancer decreased in the U.S., morbidity of intestinal cancer increased, while rectum cancer decreased in morbidity (Table 7); this is exactly what happened in Denmark. Also Connecticut and upstate New York showed increases for intestinal cancer, but no clear decrease for sigmoid and rectum cancer is visible in Table 7, possibly due to the effect of the age adjustment. Here again, the shortcomings of mortality data are evident, since they vary considerably in coverage for the various sites (9).

**Prostate Cancer**

Since 1935, prostatic cancer has been known to be histologically demonstrable in many men without symptoms, such as 14% between ages 41 and 50 years. It is particularly frequently reported among the very old, and therefore the apparent increase in morbidity has been followed with some reservation, awaiting diagnoses of more clinical relevance.

Data for Connecticut and upstate New York show a considerable effect from age adjustment to a European Standard, and naturally Copenhagen less so, and the difference between Connecticut and Copenhagen rates seems to be increasing (Table 8). However, it is difficult to see how mortality data could provide better information, or how it should be possible to estimate the avoidable amount of cancer.

I am in full sympathy with the effort by Doll and Peto to correct exaggerations of the increase in morbidity from most cancers (cf. Fig. 5) by claims of a cancer “epidemic.” However, I should appeal to their understanding of the views of the late William Cramer (19, 20), whose advice I had the privilege of taking in the late 1930s as a guest at the Imperial Cancer Research Fund. With some pangs of conscience I realize, that like Doll and Peto I have used the term “theory” of Cramer’s rule that the number of persons susceptible to cancer seemed the same everywhere. It seems to me somewhat overinterpreted to read it that Cramer failed to realize that the coefficient of variation of total cancer must of

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**Table 6. Breast cancer (females), morbidity per 100,000, 1940-1972.**

| Period    | Connecticut | Upstate NY | Denmark | Copenhagen |
|-----------|-------------|------------|---------|------------|
| 1940-1944 | 55.3        | —          | —       | —          |
| 1941-1943 | —           | 56.4       | —       | —          |
| 1943-1947 | —           | —          | 59.4<sup>a</sup> | 71.8<sup>a</sup> |
| 1945-1949 | 59.7        | —          | —       | —          |
| 1949-1951 | —           | 55.0       | —       | —          |
| 1948-1952 | —           | —          | 61.2<sup>a</sup> | 73.3<sup>a</sup> |
| 1950-1954 | 64.7        | —          | —       | —          |
| 1953-1957 | —           | —          | 61.4<sup>a</sup> | 71.1<sup>a</sup> |
| 1955-1959 | 64.0        | —          | —       | —          |
| 1958-1960 | —           | 55.9, 67.9<sup>a</sup> | —       | —          |
| 1960-1962 | 66.2, 81.9<sup>a</sup> | —          | —       | —          |
| 1958-1962 | —           | 63.6<sup>a</sup> | —       | 73.5<sup>a</sup> |
| 1963-1965 | 85.3<sup>a</sup> | —          | —       | —          |
| 1963-1967 | —           | 68.9<sup>a</sup> | —       | 79.5<sup>a</sup> |
| 1968-1972 | 97.7<sup>a</sup> | —          | 74.7<sup>a</sup> | 83.3<sup>a</sup> |
| 1969-1971 | —           | 78.7<sup>a</sup> | —       | —          |

<sup>a</sup>Age-adjusted European standard.
necessity be less than that of individual cancer rates. However, I find consolation in the fact that the same could be said of their comparison of cancer morbidity rates for single states and mortality rates for the U.S. population of some 200 million.

**Future Requirements to Cancer Epidemiology**

Analysis of human data with regard to effects from initiators and promoters will increase the demands for accuracy of the time factors involved in carcinogenesis.

Accurate information on periods of suspected exposure should be made available as much as possible. Safekeeping of payrolls or similar information should be provided for by chemical and related industries over four decades.

The demand for accuracy also applies to data for the development of neoplasms, which means that we need more accurate data on the duration of la-

| Period   | Site      | Morbidity per 100,000 |
|----------|-----------|-----------------------|
|          | Connecticut | Upstate NY | Denmark | Copenhagen |
| 1940-1944| Colon     | 22.6       | —        | —          | —          |
|          | Sig-Rect  | 17.6       | —        | —          | —          |
|          | Total     | 40.2       | —        | —          | —          |
| 1941-1943| Colon     | —          | 16.6     | —          | —          |
|          | Sig-Rect  | —          | 13.8     | —          | —          |
|          | Total     | —          | 30.4     | —          | —          |
| 1943-1947| Colon     | —          | —        | 13.7³     | 17.2⁴     |
|          | Sig-Rect  | —          | —        | 38.0³     | 47.9⁴     |
|          | Total     | —          | —        | 51.7³     | 65.1⁴     |
| 1945-1949| Colon     | 24.7       | —        | —          | —          |
|          | Sig-Rect  | 20.1       | —        | —          | —          |
|          | Total     | 44.7       | —        | —          | —          |
| 1949-1951| Colon     | —          | 19.7     | —          | —          |
|          | Sig-Rect  | —          | 15.5     | —          | —          |
|          | Total     | —          | 35.2     | —          | —          |
| 1948-1952| Colon     | —          | —        | 13.3³     | 17.0³     |
|          | Sig-Rect  | —          | —        | 36.6³     | 45.8³     |
|          | Total     | —          | —        | 49.9³     | 62.8³     |
| 1950-1954| Colon     | 27.0       | —        | —          | —          |
|          | Sig-Rect  | 20.7       | —        | —          | —          |
|          | Total     | 47.7       | —        | —          | —          |
| 1953-1957| Colon     | —          | —        | 12.8³     | 19.9³     |
|          | Sig-Rect  | —          | —        | 33.5³     | 41.6³     |
|          | Total     | —          | —        | 46.3³     | 61.5³     |
| 1955-1959| Colon     | 30.2       | —        | —          | —          |
|          | Sig-Rect  | 19.3       | —        | —          | —          |
|          | Total     | 49.5       | —        | —          | —          |
| 1958-1960| Colon     | —          | 22.7     | —          | —          |
|          | Sig-Rect  | —          | 15.3     | —          | —          |
|          | Total     | —          | 38.1     | —          | —          |
| 1960-1962| Colon     | 29.2, 38.8³| —        | —          | —          |
|          | Sig-Rect  | 17.1, 22.7³| —        | —          | —          |
|          | Total     | 46.3, 61.5³| —        | —          | —          |
| 1958-1962| Colon     | —          | —        | 13.6³     | 18.3³     |
|          | Sig-Rect  | —          | —        | 30.8³     | 45.1³     |
|          | Total     | —          | —        | 50.4³     | 63.4³     |
| 1963-1965| Colon     | 40.5³     | —        | —          | —          |
|          | Sig-Rect  | 15.8³     | —        | —          | —          |
|          | Total     | 57.3³     | —        | —          | —          |
| 1963-1967| Colon     | —          | —        | 14.6³     | 19.1³     |
|          | Sig-Rect  | —          | —        | 36.3³     | 44.8³     |
|          | Total     | —          | —        | 50.9³     | 63.9³     |
| 1968-1972| Colon     | 46.2³     | —        | —          | —          |
|          | Sig-Rect  | 27.2³     | —        | —          | —          |
|          | Total     | 73.4³     | —        | —          | —          |
| 1969-1971| Colon     | —          | 37.7³    | —          | —          |
|          | Sig-Rect  | —          | 20.5³    | —          | —          |
|          | Total     | —          | 58.2³    | —          | —          |

³Age-adjusted European standard.
tent periods for human tumors, and on the spread of these values.

The definition of latent period varies from experiments to human data, but for human data so many factors may have played a part in their estimate in the past, that the time has come for a critical reassessment of data from the last 100 years, which easily could be done by three scientists and a secretary. Death certificates mentioning cancer should always state the histological diagnosis, if any.

With the necessary information (Fig. 6) we may have to discard much old material, but we will be able to plan the collection of the relevant data for the estimate of the influence of initiators and promoters.

Table 8. Prostatic carcinoma, morbidity per 100,000, 1940-1972.

| Period      | Connecticut | Upstate NY | Denmark | Copenhagen |
|-------------|-------------|------------|---------|------------|
| 1940-1944   | 26.7        | -          | -       | -          |
| 1941-1943   | -           | 21.4       | -       | -          |
| 1943-1947   | -           | -          | 18.2a   | 24.0a      |
| 1945-1949   | 29.0        | -          | -       | -          |
| 1949-1951   | -           | 24.9       | -       | -          |
| 1948-1952   | -           | -          | 23.7a   | 31.5a      |
| 1950-1954   | 34.8        | -          | -       | -          |
| 1953-1957   | -           | -          | 29.5a   | 37.3a      |
| 1955-1959   | 37.5        | -          | -       | -          |
| 1958-1960   | -           | 24.9, 39.1a| -       | -          |
| 1960-1962   | 39.3, 55.2a | -          | -       | -          |
| 1958-1962   | -           | -          | 32.6a   | 37.5a      |
| 1963-1965   | 54.0a       | -          | -       | -          |
| 1963-1967   | -           | -          | 36.4a   | 41.5a      |
| 1964-1972   | 41.4a       | -          | 37.2a   | 43.0a      |
| 1968-1971   | -           | 48.3a      | -       | -          |
| 1969-1971   | -           | -          | -       | -          |

*Age-adjusted European standard.

Figure 5. Age-adjusted incidence for cancer of various sites in males for Denmark, 1943-76.

Figure 6. Various concepts of latent periods in cancer.
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