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# Heavy Smokers with Low Mortality

## *A 14 $\frac{1}{4}$ -Year Test of the Cigarette Hypothesis Of Lung Cancer Causation*

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### *A 14 $\frac{1}{4}$ -Year Test of the Cigarette Hypothesis Of Lung Cancer Causation*

This paper extends mortality rates of cigarette division employees of The American Tobacco Company to cover the period 1957-1960. Previous mortality studies of the same population were made by Dorn and Baum of the National Institutes of Health, embracing October, 1946, through 1952,<sup>1</sup> and by Haag and Hanmer, for the years 1953 through 1956.<sup>2</sup> An intensive investigation of this population's smoking habits was made in 1956 by Finkner et al.<sup>3</sup> of the Institute of Statistics of the University of North Carolina.

The 1957-1960 data confirm the findings of Dorn-Baum and Haag-Hanmer that the age-, color-, and sex-adjusted mortality rate for all causes, for cancer, for respiratory cancer, and for cardiovascular disease in this population are average or lower than average when compared with the general population rates.

The significance of this finding relates to the determinations of Finkner et al.<sup>3</sup> who found that the population under study had a markedly higher percentage of regular cigarette smokers than the general U. S. population. Finkner's study also indicated that the percentage of these factory employees consuming upwards of 20 cigarettes daily was twice that in the general population.

This series of studies thus establishes a distinctly heavier-than-average smoking population which has, over a period of 14 $\frac{1}{4}$  years, manifested fewer deaths of all kinds, and fewer deaths from cancer, lung cancer, and heart disease, than the expectancy for an average population of its age, sex, and racial composition. These results are

in direct opposition to the hypothesis that cigarette smoking per se causes higher mortality rates generally and for lung cancer and/or heart disease.

The three consecutive longevity investigations covered 70,532, 45,455 and 41,967 person-years respectively, for a total of 157,954. The average size of the population during the 171 months under study was slightly over 11,000.

#### Mortality Rates for 1957 through 1960

Table I compares the observed deaths in the population studied with the expected number based on age-sex-color-specific death rates for the general U. S. population. This table and the method of its calculation are patterned after those published by Dorn-Baum and Haag-Hanmer.

TABLE I.  
OBSERVED AND EXPECTED NUMBER OF DEATHS FROM  
SPECIFIED CAUSES AMONG FULL-TIME AND RETIRED  
EMPLOYEES OF CIGARETTE PLANTS AND STEMMERIES  
OF THE AMERICAN TOBACCO COMPANY  
JANUARY 1957 — DECEMBER 1960

Cause	Expected No. of Deaths	Observed No. of Deaths	Observed to Expected
All causes	425	325	76%
Cancer — all forms (140-205)	75	47	63%
Cancer — respiratory system (160-164)	14	6	43%
Cancer of bronchus and trachea, and of lung specified as primary (162)	2	0	0
Cardiovascular (400-458)	180	154	86%
Coronary disease (420)	116	100	86%

NOTE: Numbers in parentheses are cause-of-death categories of Seventh Revision of The International List, as used in Vital Statistics of The U. S.

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Table I indicates that the observed number of deaths during the 1957-1960 period was 76% of the number that would be expected to occur in an average U. S. population similarly stratified as to age, sex, and color. The number of cancer deaths was 63% of the expectancy. Respiratory cancer deaths were 43% of the expectancy, cardiovascular deaths 86% of the expectancy, and coronary deaths 86% of the expectancy. No deaths from primary lung cancer occurred during this period, although an expectancy of seven such deaths was derived from vital statistics for the U. S. as a whole.

#### Previous Mortality Rates for the Same Population

Similar percentages of observed-to-expected deaths in the several classifications were observed by Dorn-Baum for the period October 1946-1952 and by Haag-Hanmer for 1953-1956. Percentages of observed-to-expected deaths covering the results of all three studies as well as the complete time span of 14¼ years are arrayed in Table II. Allowing for the random fluctuation in the number of particular causes of death that is observed in most population subgroups, and especially for those causes from which the number of deaths is small (e.g., respiratory cancer), the results of the three investigations show internal consistency. Except for the aforementioned cause involving few deaths, the percentages from one study to the next show no radical variation. The over-all percentages in Column 4, Table II, characterizing the observed-to-expected ratio for the several cause categories during the entire 14¼ year period, fall within a range of nine percentage points. Observed deaths ranged from 70% to 79% of the expectancy for all causes, for cancer, for respiratory cancer, for cardiovascular and for coronary disease.

Since Dorn-Baum did not compute a separate expectancy category for primary lung cancer as distinct from the general category of respiratory cancer both primary and secondary, this category does not appear in Table II. In the two

latter studies covering eight years, four deaths from this cause were recorded, representing 36% of the normal expectancy of 11.

#### Smoking Habits of the Population under Study

As previously reported by Finkner et al., the proportion of regular cigarette smokers among the tobacco employees studied was much greater than that in the general U. S. population. Among white males, 77.2% of the tobacco employees were regular cigarette smokers, compared with 49.9% for the general U. S. population; for nonwhite males, 84.1% compared with 48.4%; for white females, 44.4% compared with 23.6%; and for nonwhite females, 61.7% compared with 22.9%.

The tobacco employee population also included a considerably higher percentage of smokers consuming more than 20 cigarettes daily than the general U. S. population. Among white males, 32.8% of the tobacco employees smoked more than 20 cigarettes a day as against 13.3% for the general U. S. population. Nonwhite males among the tobacco employees included 16.5% smoking more than 20 cigarettes a day as against 6.9% in the general U. S. population. For white females the proportion was 6.9% among tobacco employees as against 2.4% in the general population, and for nonwhite females 4.0% as against 1.7%. In each category, the proportion of tobacco workers smoking more than 20 cigarettes a day is of the order of two and a half times that of the comparable segment of the U. S. population.

#### Methodology

In all three mortality studies, observed deaths were tabulated from reports of the Metropolitan Life Insurance Company, which underwrites insurance policies on all employees of the group studied, including those on leave, those retired for disability, and those retired for age. Death rates for the general U. S. population were computed by dividing total deaths, as reported in *Vital Statistics of the U. S., Volume II*,<sup>4</sup> by the population estimates issued by the Bureau of the Census for July 1 of each year (Series P-25).<sup>5</sup>

For the 1957-1960 period, rates for the year 1958 were used to compute expectancies for 1957 and 1958, and rates for the year 1959 were used to compute expectancies for 1959 and 1960. Rates were computed separately for male white, male nonwhite, female white, and female nonwhite, and for all the age groups 15-24, 25-34, 35-44, 45-54, 55-64, 65-74, 75 and over. These rates were applied to the number of person-years of exposure in each age, color, and sex category of the population under study. The roster of employees (including retired employees and those

TABLE II.  
PERCENTAGE OF OBSERVED TO EXPECTED DEATHS IN  
THREE SUCCESSIVE STUDIES OF FULL-TIME AND  
RETIRED EMPLOYEES OF CIGARETTE PLANTS  
AND STEMMERIES OF THE AMERICAN  
TOBACCO COMPANY

	Dorn- Baum (Oct. 1946- 1952)	Haag- Hanmer (1953- 1956)	(1957- 1960)	Total Period (Oct. 1946- 1960)
All causes	68%	69%	76%	71%
Cancer - all forms	73%	77%	63%	70%
Cancer - respiratory system	86%	100%	43%	71%
Cardiovascular	67%	76%	86%	76%
Coronary disease	80%	68%	86%	79%

on leave) was taken as of July 1 in each year. Expectancies throughout were calculated for each single year and summed for the period studied.

Measurement of the subject population's smoking habits by Finkner et al. was methodologically similar. Independent investigators recorded individual smoking histories and classified them by age, sex, color, and rate of cigarette consumption. These were ranged against the corresponding findings for the general population of the U. S. by subgroup, as reported by Haenszel, Shimkin, and Miller of the U. S. Department of Health, Education and Welfare,<sup>6</sup> based on a Census Bureau study.

The above procedure follows that of Haag and Hanmer, who compared employee smoking habits with those of the U. S. population, and employee mortality rates with those of the U. S. population, both stratified by age, sex, and color.

No sampling or estimating was involved in any of these studies. Smoking habits were measured by applying pretested procedures individually to virtually every member of the population under study (98.1%). Data on age, color, sex, and mortality were available for each individual member of the population and were summed as above described.

#### Characteristics of the Population

The population under study was that defined by Dorn and Baum of the National Institutes of Health. It consists of full-time employees in factories and leaf departments of The American Tobacco Company in Virginia, North Carolina, and Kentucky. Turnover in this employee group is negligible. On July 1, 1960, approximately 66% of the population had service records of ten years or more, and 20% had service records of 25 years or more. On August 1, 1953, 48% had been employed ten or more years, and 10%, 25 or more years.

As reported by Dorn and Baum, employees who are unable to work eventually are carried on the payroll as on leave without pay but remain covered by insurance so that they remain part of the population for purposes of these studies. Retired employees retain insurance coverage and also are included.

Thus the population is a coherent group for purposes of mortality investigation. The degree of this coherence is indicated by its average age, which increased almost precisely three years between July 1, 1957, and July 1, 1960 — from 42.8 years to 45.7 years, respectively.

White males accounted for 43% to 46% of the population during this period, these percentages being minimum and maximum. Males white and nonwhite accounted for 57% to 61% of the sub-

ject population. Men over 45 accounted for 31% of the employee group on July 1, 1960.

#### Comment

The health history of this population of heavy-smoking tobacco company employees tends to disprove the hypothesis that cigarette smoking causes higher mortality from all causes, from cancer, from lung cancer, or from heart disease. This interpretation is strengthened by the following data of observation:

1. The substantial degree to which the studied population's cigarette consumption exceeds the national average: In the percentage smoking more than 20 cigarettes daily, the Finkner study group recorded the ratio as 2:1 or more in every subgroup and in virtually every age group. In view of the population's vocational interest in the product it manufactures, and the provision of a free package of cigarettes each working day, this characteristic of the group studied is not astonishing.

2. The unusually stable nature of this employee group, as indicated under "Characteristics of the Population" above: Stability of the population for purposes of these studies is also insured by the fact that employees on leave, retired for disability, or retired for age, continue to be covered under the group insurance plan. These employees or former employees were included on the July 1 rosters used to compute expected deaths; and actual deaths among them were reported by the Metropolitan Life Insurance Company.

3. The extended nature of the mortality research, covering a continuous time span of 14¼ years.

4. The consistently lower-than-average mortality of the studied population for each of the three mortality studies (Table II).

5. The consistency of the degree to which this mortality for the entire 14¼ year period is lower than the national rate, as between the various causes of deaths (Table II, Column 4).

#### Other Statistical Studies

A number of studies, of which those of Doll-Hill<sup>7</sup> and Hammond-Horn<sup>8</sup> are representative, have yielded a statistical association in individuals between cigarette smoking and higher mortality rates. Other studies, including Eastcott, Dean, and the present study, have shown no such association. A number of distinctions may be noted in connection with the diametric opposition between the results of the two groups of studies.

Statistical association studies of the Ham-

mond-Horn, Doll-Hill type compute expected deaths on the basis of mortality rates shown by professed nonsmokers. The professed nonsmoker is taken as the norm or "average" against which various types of smokers are compared. This raises two questions: (1) whether those smokers who manifest higher mortality rates do so as a direct result of the effects of smoking, or whether the smoking habits of some of these higher-mortality smokers are diagnostic of other factors that predispose to shorter life, and (2) whether the professed nonsmoker with his low mortality rate can be taken as a norm.

The former question cannot be answered from the statistics themselves, since this would require that all relevant or predisposing factors other than smoking be held constant. No attempt was made in the Doll-Hill, Hammond-Horn, or their counterpart studies to do this, since all relevant factors affecting mortality and/or cancer mortality are not known, and since some of the suspected factors — previous medical history, genotypic differences, constitutional predisposition, exposure to various environmental agents, "rate of living," the "stress" factor, etc. — are difficult if not impossible to reduce to mathematical terms, even if they could be gathered for populations large enough for statistical study.

Touching on the latter question, Berkson<sup>9</sup> has noted that

... persons who are nonsmokers, or relatively light smokers, are of a constitutional type that is biologically disposed to self-protective habits. . . . It is not implausible that they should be, on the average, relatively longevous, and this implies that the death rates generally in this segment of the population will be relatively low.

The extent of this difference between death rates of professed nonsmokers and average U. S. citizens was indicated by Hammond-Horn, who computed mortality rates of 777, 1,253, 1,781, and 3,280 per 100,000 for nonsmoking white males in their 50-54, 55-59, 60-64 and 65-69 age groups, compared with rates of 1,439, 2,210, 3,402, and 4,895 per 100,000 for white males of the same age groups in the general population. These mortality differences between the professed nonsmoker and the "average" white male reported by Hammond-Horn were great — 85%, 76%, 91%, and 49%. Should Berkson's characterization of nonsmokers be correct even for a number of persons in that category, the Hammond-Horn interpretation that cigarette smokers incur "excess" mortality rates becomes meaningless. That is, the association their data showed reflects only the choice of an abnormally longevous group as a criterion of what is "normal." The

same would be true of a number of other statistical association studies patterned on the Doll-Hill model.

The influence of this choice of criterion on their final calculations is evident from Hammond-Horn's own comparison of death rates among their "heavy cigarette smokers" with death rates among U. S. white males generally. In a 20-month period these rates were 1,222; 2,140; 2,707; and 3,856 per 100,000 for "heavy cigarette smokers" against 1,288; 2,006; 2,991; and 4,354 per 100,000 for U. S. white males in the four age groups. These rates hardly differ. In a subsequent 24-month period the "heavy cigarette smokers" showed slightly higher death rates than the U. S. average.

Apart from the question whether nonsmokers constitute a valid criterion of "normal" mortality — and Hammond-Horn's figures strikingly suggest they do not — a basic difference exists between the two types of studies mentioned. Those patterned after the Doll-Hill model (including Hammond-Horn) attempt a correlation between mortality rates and smoking habits in individuals. This requires the assumption that no unmeasured other factors exist that might account for or explain any correlation that is found. The number of such factors investigated, alone or in conjunction with smoking habits, is thus far small — the so-called "urban factor" (assumed by some to be air pollution), certain special occupational exposures, and alcohol consumption.

By contrast, studies of population subgroups including this series, those by Eastcott,<sup>10</sup> and that by Dean,<sup>11</sup> deal with mortality rates and smoking habits of groups. Dean compared native white male South Africans with British male immigrants to South Africa 45-64 years of age. Between 1947 and 1956 the death rate from lung cancer among the former was 50 per 100,000, and among the latter, 112. At the same time, white South Africans are among the world's heaviest cigarette consumers, with a per capita usage reported 68% above that in the United Kingdom in 1950 and 40% higher than the U. K. figure in 1955. Dean found urban residence to correlate with lung cancer incidence among South African whites, and concluded that "bronchial carcinoma must result from the total effect of genetic and environmental factors."<sup>12</sup>

<sup>9</sup>Dean later gathered smoking habit data for about half the lung cancer deaths in his study. Using these and a set of matched "controls" — deaths from other causes — he estimated mortality rates by age groups, by country of origin, by rural-urban residence, by occupational air pollution, and by rate of smoking.

The greatest relative association with lung cancer in these estimates involved country of origin (U.K. vs. Union of South Africa), but urban residence also showed consistent association. Occupation showed no association. As to smoking, rural South

Eastcott found a parallel difference in lung cancer mortality between immigrants from Great Britain to New Zealand and native-born New Zealanders; at the same time tobacco consumption for the two groups was observed to be comparable. Eastcott concluded that "Differences in habits of tobacco-smoking are unlikely to contribute to this picture," and "The environmental factors concerned are unlikely too to be of a personal kind related to the way of life of the immigrant." In 1960, his data were extended to cover ten years' comparison of the mortality experience of 250,000 immigrants from the U. K. against that of 2,800,000 native-born New Zealanders.

Neither Dean nor Eastcott nor the present study offers a correlation between a single factor and mortality rates. They merely indicate that the higher mortality, whether from lung cancer alone or from this and other causes, does not associate with higher tobacco consumption. Rigorous interpretation of these findings as opposing the tobacco theory does not require the assumption that other factors remained constant. Actually, the results indicated that other factors did not remain constant, since important death rate differences were recorded despite similar or contrahypothetical rates of smoking, although the precise identification of these other factors is not germane to this inquiry.

Bearing on both types of study is the observed tendency of many selected population subgroups to manifest lower mortality rates than the population as a whole. Hammond-Horn, for example, estimated that "the death rate of our study population would stabilize at about 81% to 85% of the rate for white males in the general United States population," attributing this favorable comparison to selection of subjects from counties with lower death rates and to "a slight degree of socioeconomic selection."

Employee populations, such as the one studied by Dorn-Baum, Haag-Hanmer and the writers, also represent a degree of selection resulting from the initial medical "screening" of applicants for employment. This effect, according to Hammond-Horn, "diminishes rapidly with time, is relatively slight after the third year, and for

all practical purposes wears off within five years." Although the exact duration of this screening effect would not be important in a study extending 14½ years, the significance of the present study does not lie in the fact that the tobacco employee population (like other selected groups) shows lower-than-average mortality. Rather, it lies in the fact that this lower-than-average mortality exists concurrent with a pattern of distinctly heavy smoking and in the fact that respiratory cancer mortality — alleged to be specifically and causally linked to cigarette consumption — is as much below average in this heavy-smoking population as is mortality from other causes or from all causes.

It has been pointed out that employee groups enjoy better-than-average medical care and for this reason are likely to manifest lower-than-average mortality rates. In the first mortality study in this series, Dorn-Baum noted the findings "are not surprising in view of the medical care program provided by the company for its employees." To the extent that medical care favorably affects the mortality rates of the employee population, the postulate is denied that cigarette smoking in and of itself is a major cause of respiratory cancer, or heart disease, or decreased longevity.

The previous study in this series<sup>2</sup> was criticized on several grounds by Case<sup>12</sup> who, in turn, was quoted by Cornfield et al.<sup>13</sup> This criticism if valid, also would apply to the present report:

1. Case questions the comparability of the tobacco workers with the general population in regard to characteristics other than smoking (and age-sex-color, which is allowed for in the determination of expected rates). On grounds such as these all statistical studies in this area may be called into question, but the present study less than most, since it represents a cross-sectional population with regard to socioeconomic-occupational levels. Further, the basis of Case's argument, that mortality, particularly from primary lung cancer, is associated with other factors, calls into question the specificity of the tobacco hypothesis.

2. Case applies a Hammond-Horn factor for increased lung cancer mortality expectation (based on the tobacco workers' greater smoking rate) of 1.7 to the previous study and arrives at an expected number of lung cancer deaths of seven. He then demonstrates that the sampling error of this study is such that 0-8 such deaths could occur at the  $P = .05$  level, and that since this includes the adjusted frequency of seven, the results cannot refute the

African-born men smoking 1-20 cigarettes a day showed lower lung cancer mortality rates than nonsmokers in such U.K. locations as Liverpool, Lancashire, Denbigh S.E., Flint and Cheshire. Also, "In South African rural areas the lung cancer mortality rate for men aged 45 to 64 years was very low for both nonsmokers and moderate smokers, and increased only with heavy cigarette smoking," and "The highest lung cancer mortality rates were found where heavy smoking was combined with exposure to air pollution." (*Brit. Med. J.* 2:1593, 1961)

Dean's estimates suggest the possibility that excessive smoking may be diagnostic of other factors predisposing to higher mortality rates; this could account for the associations found by Doll-Hill and similar studies and would also be compatible with the finding of low mortality rates for large groups of smokers in Dean, Eastcott, and the present study.

Hammond-Horn tobacco hypothesis. Using exactly this reasoning on the cumulative 1953-1960 results, the expected frequency is 11 (four in 1953-1956 and seven in the current period), the .05 confidence interval is  $11 \pm 2\sqrt{11}$  which provides a range of 4.4 to 17.6. Applying the Hammond-Horn factor of 1.7 to the expected value of 11 results in a hypothetical expectancy of 18.7 lung cancer deaths, a value that falls outside and above range of the confidence interval. Although the writers have serious reservations about the procedure suggested by Case, its application to the extended series results in a rejection of the Hammond-Horn tobacco hypothesis.

3. The additional points made by Case are hypothetical ones regarding the possible unrepresentativeness of the population and shortness of the period studied. Data with regard to some of these issues were lacking in the Haag and Hanmer<sup>2</sup> report, but have been included above. They indicate that the representativeness of this population, and the length of time over which relevant data have now been gathered, cannot be called into serious question.

#### Summary

This study extends to 14¼ years mortality data of approximately 11,000 employees of cigarette factories and stemmeries in Richmond, Virginia; Durham and Reidsville, North Carolina; Louisville, Kentucky; and other locations. It confirms the findings of previous studies that this population shows lower mortality rates for all causes, for cancer, for respiratory cancer, for heart and coronary disease, than the expectancy for a population of its age, sex, and color composition based on mortality rates of the U. S. population in general. For the full period studied, the degree to which its mortality is lower than average is similar for all death causes mentioned. Independent measurement has indicated that the subject population includes more than twice as many more than 20-per-day cigarette smokers as the percentage in the general U. S. population. These findings, obtained without recourse to sampling or estimates, are contradictory to the hypothesis that cigarette smoking per se is causally related to increased mortality, from all causes, from respiratory tract cancer, or from heart disease.

The low turnover of this employee group, and the inclusion of retired and disabled personnel

on the insurance rosters make this a relatively stable population suitable for an extended mortality study. The margin by which its cigarette consumption exceeds the U. S. average makes it further suited to a test of the cigarette theory.

Analysis of statistical association studies on which the cigarette theory is largely based indicates certain assumptions and criteria as to "normal" death rates which influence the final calculations of these studies. The validity of these assumptions and criteria is called into question by the results of this and other studies that do not confirm the cigarette theory.

The negative findings of these data with respect to the cigarette theory parallel and confirm the negative findings of other extended tests of the same hypothesis: that of Eastcott, who studied cancer mortality of the entire census population of New Zealand and of immigrants of similar stock from the U. K. over a 10-year period; and that of Dean, who studied lung cancer mortality among male white native South Africans and male white immigrants from the U. K. to South Africa, also over a 10-year period.

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