

EXHIBIT
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EPIDEMIOLOGICAL STUDY OF
LUNG CANCER
IN ASBESTOS MINERS



For

QUEBEC ASBESTOS MINING ASSOCIATION

Quebec, Canada

July, 1956 to July, 1957

By

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September, 1957

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FOREWORD

The success of a study of the type herein reported depends very greatly upon the availability of data from many sources, and the assistance and cooperation of those in possession of these data. Industrial Hygiene Foundation was fortunate in having the wholehearted cooperation of the asbestos-producing companies, and particularly of their medical and nursing personnel who have the responsibility for maintaining the medical records of the workers. In this connection, we are especially indebted to Dr. Paul Cartier and his staff at the Thetford Industrial Clinic, and to Dr. T. R. Grainger and the nurses at Asbestos. All records in these two medical centers were put completely at our disposal, and the care and completeness with which they are maintained assisted considerably in the preparation of the material relative to the worker population.

Data on population figures and on the causes of death in the Province of Quebec were obtained with the utmost assistance and cooperation from Dr. Paul Parrot, Head of the Department of Demography in the Ministry of Health. Not only were all vital statistics and reports made readily available to us, but Dr. Parrot and his entire staff rendered valuable assistance in many ways, including the location and interpretation of death certificates. Especially helpful in this part of the work was Miss Gauthier of Dr. Parrot's staff. The same helpful

cooperation was rendered by Messrs. Hardy and Hopkins of the Sun Life Assurance Company of Canada in Montreal, who made available their records of the death claims paid under the group policy covering the workers at Asbestos.

Valuable suggestions for the conduct of the study were made by Dr. J. A. Vidal, Chairman of the Silicosis Board, and Dr. Guy, Pathologist for the Board, as well as Dr. Gregoire, Deputy Minister of Health for the Province of Quebec, and Drs. Simard, Dufresne, and Groulx, in Montreal.

Statistics for the mortality rates for the Dominion of Canada were obtained through the kindness of Dr. Dean F. Davies, Administrator for Research on Lung Cancer for the American Cancer Society, and those for the United States were graciously furnished by Miss Guralnick in the National Office of Vital Statistics, Department of Health, Education, and Welfare of the United States Government. Finally, the very great assistance rendered by Dr. Kenneth W. Smith, Medical Director of Johns-Manville Corporation, and Mr. Ivan Sabourin, General Counsel for the Association, in making the necessary contacts, in travel arrangements, and in so many other ways, is gratefully acknowledged.

The methodology of this research is believed to be unique among the reported studies of lung cancer as related to asbestosis and exposure to asbestos. Assistance in planning the study in such a way as

to assure a proper epidemiological approach, and all biostatistical applications of the findings were provided by Mr. T. David Truan, formerly of the Graduate School of Public Health, University of Pittsburgh, and the staff of the Industrial Hygiene Foundation.

The report is believed to present the findings in an objective manner and is respectfully submitted for the consideration of the Association.

GLOSSARY

For the purpose of clarity and uniformity, the terms used in this report are herewith defined according to the manner of their use.

- Asbestos workers:** Workers exposed to asbestos dust in other than mining operations.
- Asbestos miners:** Workers engaged in the mining and preparation of asbestos in the areas under study.
- Asbestosis:** A generalized fibrosis of the lungs diagnosable by x-ray, or by microscopic examination of the lung tissue, but not necessarily accompanied by symptoms or by disability.
- Cohort:** A segment of the population, defined according to certain criteria, and representative of the whole population. Specifically in this study, a group of asbestos miners having at least five years of exposure in the industry and who were in the industry during 1950.
- Lung cancer, cancer of the lung:** A neoplasm of the lung or bronchus, wherever situated, and including adenocarcinoma, squamous cell, and undifferentiated, round, or "oat cell" histological types. Primary cancer of the lung means such a neoplasm originating in the lung, and not secondarily in the lung as the result of a metastasis from another primary location in the body.
- Smoker:** As used in this presentation, the term smoker refers to a cigarette smoker, habitually smoking more than five cigarettes per day. Persons who smoke pipes or cigars exclusively were not considered to be smokers for the purpose of this study.

I. INTRODUCTION

Ever since the pronounced increase in the incidence of lung cancer among males became apparent, there have been attempts to associate it with one or another of the various elements in the environment of man. The approach used by some workers has been to suspect one or several substances and then set about in an intensive search for lung cancer among persons who have had any exposure to those compounds. In this connection, Smith ⁽¹⁸²⁾ writes: "The tendency of authors reporting the coincidental occurrence of primary lung cancer with silicosis or with any other theoretical etiologic conditions, has been to emphasize the percentage relationship in extremely small series of cases, with control cases which are not in any way comparable."

It would seem inevitable that asbestos should come under scrutiny in this manner, because prolonged exposure to this material is known to cause a specific type of pneumoconiosis, and because persons who show this form of pneumoconiosis often come to autopsy and provide a ready source of material for study. It was in this way that reports of the simultaneous occurrence of lung cancer and asbestosis began to accumulate after the report of a case by Lynch and Smith ⁽¹³⁹⁾ in 1935. Within the next ten years, about 15 additional cases were reported, and in 1946 Merewether ⁽¹⁵⁵⁾ reviewed all deaths from asbestosis recorded in England since March, 1924. Lung cancer occurred, according

to Merewether, in 13.2% of these cases. Continuing this study to include December, 1954, Merewether counted 55 cases of cancer of the lung among 344 cases of asbestosis, raising the incidence to 16%. Gloyne,⁽⁹²⁾ whose work is also frequently referred to as establishing a connection between asbestosis and cancer of the lung, reported in 1951 the results of his findings on 1205 autopsied cases. This series included 132 asbestos workers, of whom 121 showed asbestosis. Cancer of the lung was present in 14.1% of these asbestosis cases. In 1941, Nordmann and Sorge⁽¹⁶¹⁾ claimed to have produced lung cancer in mice which they exposed to asbestos dust.

Since 1951, additional cases of cancer of the lung coexisting with asbestosis have been reported, and, according to Hueper⁽¹²²⁾ about 100 such cases had been reported up to 1955. As a result, an association between the two diseases appears to have been accepted by many authors and several writers were using the term "asbestosis cancer" of the lung. Werber⁽²⁰⁵⁾ in 1952, stated categorically that in 7% to 17% of cases of asbestosis, after a latent period of about 1 1/2 to 20 years, carcinoma becomes established in the lung.

On the other hand, not all authors accepted the alleged association without reservation. Saupe⁽¹⁷⁷⁾ in 1939 had reported that he had discovered no cases of lung cancer among 620 cases of asbestosis which he had examined; and in 1942, Holleb and Angrist⁽¹⁰⁴⁾ expressed the opinion that the number of cases of asbestosis with lung cancer was too

small for statistical evaluation. In 1947, Wegelius⁽²⁰⁰⁾ reported 126 radiologically diagnosed cases of asbestosis among 476 workers in Finland, and found no cases of lung cancer in this group. Goldblatt and Goldblatt in their section of Merewether's latest book, ⁽⁹⁵⁾ state:

"But at no stage in all these impressive researches was any clue obtained which might have offered any support to the possibility that asbestos could act as a carcinogen. There is no reliable criterion by which one can anticipate carcinogenicity and, as is well known, relatively minute changes in the structure of a chemical carcinogen are sufficient to diminish or eliminate carcinogenic action.

If asbestos is indeed to be regarded as a carcinogen, the need is felt to demonstrate some property which can be regarded as something more than inertness."

These authors advance the theory that, until some more experimental evidence of direct carcinogenesis by asbestos or a decomposition product of it can be obtained, asbestos might be considered as a "co-carcinogen" which only induces a further development of a pre-neoplastic condition brought about by something independent of the asbestos, such as an endogenous factor.

Thus the literature, while tending to support the thesis that asbestosis is in some way related to the development of lung cancer, is by no means unanimous. Altogether, it is perhaps more confusing than enlightening.

Meanwhile, the Canadian Johns-Manville Company in Asbestos has been alert to the whole problem, and at the Thetford Industrial Clinic, Dr. Paul Cartier was studying the situation among a working population of about 6000, and made notable contributions to the literature just cited⁽⁴²⁻⁴⁴⁾. Between these two areas, a number of cases had been recognized and tabulated by the spring of 1956. At this time, at the suggestion of Dr. Kenneth W. Smith, Medical Director of the Johns-Manville Corporation, and Dr. Cartier, the Quebec Asbestos Mining Association approached Industrial Hygiene Foundation to determine whether it would be feasible to conduct an epidemiological study in order to discover whether the incidence of lung cancer was, in fact, greater among asbestos miners than among the general population, and whether there was a correlation between lung cancer and the disease asbestosis. The Foundation submitted, in March, 1956, a proposal for such a study based upon a preliminary survey of the type and accessibility of data which might be available. This proposal was accepted by the Association through its Secretary, Mr. W. H. Soutar, and its General Counsel, Mr. Ivan Sabourin, Esq.

II. CRITICAL REVIEW OF LITERATURE

A careful review of the published material on this subject shows that the majority of the reports are clinical and not epidemiological. They lack many elements necessary for the application of epidemiological techniques to their content and most of the authors do not make claim to having done so. What has happened is that succeeding authors have drawn conclusions and generalized beyond the scope of the works which they quote. Nowhere, for example, have we found references to a population of asbestos workers, although several authors who have quoted the observed incidence of lung cancer in autopsies of persons who also had asbestosis imply that this incidence applies to asbestos workers. We have likewise been unable to find any study which actually calculated the incidence of lung cancer among a population of persons who had asbestosis, and not just those who came to autopsy. With the exception of a paper by Doll ⁽⁶³⁾, none of those reviewed gave any data on exposure and dust concentrations, and even Doll's paper merely mentions "scheduled" areas, by which is meant, "those areas where processes are carried on which were scheduled under the Asbestos Industry Regulations of 1931 as being dusty."

There is, furthermore, a complete lack of definition of terms as used in the published literature. For example, the term

"asbestosis", as used, may refer to changes observable only by microscopic examination of the lung tissue, or it may mean a radiologically detectable condition.

Most of the published reports obviously included women among their cases, but some of them do not give the number or proportion of women involved in the study.

There is also a lack of uniformity as to what type of exposure most studies have dealt with. Of 99 cases enumerated by Hueper (122) in 1955, only ten appear to have originated in the United States, and seven in Canada. Some of the earlier reports apparently included asbestos miners, but it can be assumed, since 82 of the 99 cases had originated in England, and since no asbestos mining operations are carried on in that country, that most of the reported cases have involved workers in the textile or fabricating industries.

Such factors as smoking habits, family history of cancer, length of time in the industry, and age of the individual case are also notably absent in the majority of these reports.

With this understanding of the limitations of the existing literature with respect to epidemiological generalization, it may be of value to consider in somewhat more detail some representative earlier publications, a few of which were referred to briefly in the previous section.

One of the most detailed studies and one which deserves the most serious consideration is that reported by Doll ⁽⁶³⁾ in 1955.

This study reviews causes of death among asbestos workers based on coroners' records. It also attempts to estimate the risk by studying records of men who worked for at least 20 years in exposed situations. Doll concluded that lung cancer was a specific industrial hazard of certain asbestos workers and that, after 20 years of exposure, the risk is ten times as great as for the general population.

This article is important for several reasons, in addition to the definite conclusions at which it arrives. For example, it begins by stating that "in view of the infrequency of asbestosis, this large number of cases (61 cases of lung cancer) suggests—but does not prove—that lung cancer is an occupational hazard of asbestos workers."

Neither this article or any previous one which we have examined presents any figures to prove that asbestosis is an infrequent occurrence. Estimates of the number of persons potentially exposed to asbestos dust in the United States alone vary from 10,000 to 35,000 and the incidence of asbestosis of any degree might be higher than Doll imagines.

This study, like so many others, involves autopsy records. The number of persons involved in the statistical analysis is only 113 representing only 1,042.25 man years of life. It is also true that in selecting men who had been employed for at least 20 years, the study automatically excluded those who died from other causes after shorter employment.

It also seems that this review does not add any new cases to the literature, although Hueper in enumerating 99 cases reported prior to 1955, lists 11 discussed in it. Clearly, also, the paper is not dealing with asbestos miners.

Another reason why this publication is of importance is a statement which it contains to the effect that "the strongest evidence that it (lung cancer) may be a hazard (in asbestos workers) has been produced by Merewether and by Gloyne." An examination of these references leaves at least some question as to the strength of the evidence produced.

In 1951 Gloyne ⁽⁹²⁾ presented a review of 1205 autopsies on persons who had worked in various dusty occupations. This number included 132 asbestos workers, of whom 121 showed "pneumoconiosis" —presumably asbestosis. Primary cancer of the lung occurred 17 times in this group, an incidence rate of 14.1% for lung cancer among autopsied asbestosis cases. There were in his series 796 cases with silicosis, and 6.9% of these also showed primary cancer of the lung. The incidence of lung cancer in other forms of pneumoconiosis was 6.7%, and in 169 cases which proved not to have any type of pneumoconiosis it was 8.3%. Gloyne considered "the mortality of the asbestos workers" to be "disturbing". First of all, it is obvious that the paper does not deal with the "mortality of asbestos workers", and secondly, it must be borne in mind that all of Dr. Gloyne's cases were submitted to him

for study because the findings were unusual for uncomplicated pneumoconiosis. Presumably, all cases, including those of asbestosis, in which the findings were not considered unusual were never brought to Dr. Gloyne's attention. As a matter of fact, in the same paragraph in which he expresses concern over the incidence rate in asbestosis, Dr. Gloyne himself points out that the rate for lung cancer based on necropsies at the London Chest Hospital was 21.3% while the figures of the Registrar-General showed only 2.4%. He thus recognized that autopsies on a certain selected group of cases were not representative of the general population. It would seem, then, that notwithstanding the value of Dr. Gloyne's work, its importance as an index of the prevalence of lung cancer in asbestotics has been misinterpreted by those who have quoted him. All that it really shows is the fact that in a group of 121 cases, selected for special study primarily because they seemed abnormal by preliminary examination, 17, or 14.1% had lung cancer.

Merewether (155) in 1947, in the report of the Chief Inspector of Factories, reviewed all cases reported between 1924 and 1946 in which asbestosis was the cause of death or a coexisting condition. This work was later extended to include all such cases reported up to December, 1954, by which time there were 344 deaths including 205 males and 139 females. Among them were 55 cases (16%) of cancer of the lung, 41 in males and 14 in females. It is quite possible that a large number of asbestotics who did not die of their asbestosis, or in

whose death certificate it was not mentioned, may have been missed.

The import of this 16% is enhanced by the simultaneous statement that the incidence of lung cancer in autopsies of the general population is only 1%. The danger of attempting to compare a rate found in 344 cases with the rate for the general population without respect to age, occupation, and many other variables, such as smoking habits, is obvious.

Lynch,⁽¹⁴²⁾ who with Smith⁽¹³⁹⁾ had reported the first case in 1935, reported four cases of carcinoma of the lung in a series of 49 autopsies on workers in an asbestos manufacturing plant who were shown to have "demonstrable deposits of asbestos in the lungs." This, of course, is not necessarily identical with the disease asbestosis. Lynch, himself, points out that, although this is an incidence of 8.2%, "both figures are too small for very serious statistical types of calculation." Nevertheless, later writers have used this paper to strengthen the case for an association of carcinoma of the lung with asbestosis. It is of interest to note that Klotz⁽¹³²⁾ found only four instances of lung cancer in 478 cases of asbestosis, a series 11 times as large.

Behrens, as quoted in Merewether⁽¹⁵⁶⁾, estimated that, of 309 cases of asbestosis in the literature, 44 showed associated cancer of the lung—giving an incidence of 14.2%. This is another case of generalizing an incidence obtained in a group of cases which were

undoubtedly reported only because some of them showed lung cancer, to possibly hundreds of asbestotics whose cases were never reported. The same applies to the conclusion of Teleky ⁽¹⁹²⁾ who appears to have reviewed reports of 39 autopsies on persons with asbestosis among which six cases of lung cancer occurred. Information from those sources does not justify generalizations with regard to mortality rates.

Werber ⁽²⁰⁵⁾ who made the unequivocal statement that lung cancer would result in from 7% to 17% of cases of asbestosis, allowed himself considerable latitude by qualifying it, as regards time, to an interval of 1 1/2 to 20 years. Finally, mention should be made of some entirely unsupported statements which tend to build up a mistaken viewpoint through mere repetition. One example is a sentence in "Nontuberculous Diseases of the Chest" ⁽⁷⁶⁾ where the authors say simply, "an excessive incidence of pulmonary cancer has occurred among workers in other occupations, such as asbestos industries, nickel-copper refineries, stokers in generator plants, etc." without substantiating reference.

As an illustration of the ease with which a few reports which merely suggest a certain conclusion can, through the lack of a sufficiently critical attitude, be summarized to produce the conclusion in a definite form, an editorial ⁽⁶⁹⁾ in the Journal of the American Medical Association mentions the work of Wedler and the report of Merewether and then establishes the causal relation between asbestosis and cancer of the lung as settled. As a final convincing argument, it refers to "recent experimental

proceeds by first carefully and accurately describing characteristics of the disease in different population groups and its essential objective is the formulation, testing, and verification of generalizations concerning the disease in question.

In order to apply this method of investigation to the problem under discussion, the Foundation was of the opinion that a study should be planned so as to provide:

1. A well defined population group.
2. Available data for all members of this population, including the healthy as well as the ill.
3. A sample which is truly representative of the population.
4. Reliable and valid observations relating to the problem of the study.

A serious defect, common to most of the studies which have been reported, is that little or no information concerning the healthy people in the group seems to have been available to the author. Therefore, results of these studies cannot properly be generalized to include such people.

In order to draw a generalization regarding all asbestos workers, it is necessary for a study to include living persons as well as the dead. Limiting the investigation to autopsied cases, as has been frequently done in earlier studies, still further restricts its use

in generalization. The problem with which the Quebec Asbestos Mining Association is concerned is whether asbestos miners experience more lung cancer than does the general population. The answer necessitates the collection of reliable information on asbestos miners as a group, as well as on the general population.

It seems advisable to discuss the differences between the epidemiological approach and that used in the studies which have been reported to date. A very important consideration is the fact that lung cancer, in spite of its increasing numbers, is still a disease of low incidence; that is, in a given population not many persons will contract this particular disease. This fact requires that large samples or groups must be studied to provide meaningful results.

Recognizing the difficulty of obtaining such large samples, most earlier writers deviated from the epidemiological method and sought to circumvent the requirement of observing well persons by:

1. Comparing the relative frequency of cancer in various sites.
2. Comparing the relative frequency of cancer in a group of hospitalized patients.
3. Comparing the relative frequency of cancer in a group of cases coming to autopsy.

The frequency of cancer of the lung relative to the total of all types of cancer may be increased merely by reason of a decrease

in the incidence of cancer of other sites. This could be true even though the incidence of lung cancer remained constant, or if it decreased less rapidly than that of the other types.

Attempting to compare two population groups, looking only at the relative frequency of cancer in various body sites, may result in finding a higher percentage (relative frequency) in one of the groups, when, in fact, the mortality rate of cancer of a particular organ is exactly the same in both groups. This is because the relative frequency of cancer in other organs may be lower in the second group. The mortality rate from a particular cause is the true measure of comparison.

It is apparent that selected groups such as hospitalized patients or autopsy cases may not be representative in any way of a larger group, and that in dealing with such samples, the observer may easily find more cases of any kind than would be found in a group of the same size, but representative of the general population. It is true that investigation of cases from such a sample can furnish information valuable for research, but the use of this information in drawing generalizations is necessarily restricted. It is the obligation of both the investigator and of those who read his report to make proper comparisons and to draw only those conclusions which are valid and justified. A good statistical study of cases of cancer of the lung occurring in a group of autopsies can lead to a proper inference concerning the frequency of lung cancer among cases coming to autopsy, but only to such cases. For

information from such a study to be projected to some larger group, it is necessary that the autopsies represent a good sample of that larger group. To assume that such is the case in any particular series is dangerous and likely to be false.

There is some danger that the figures reported by some authors may be misconstrued as applying to asbestos workers or even asbestos miners, when, in fact, the authors in question do not make this generalization, nor can the generalization be made for the reasons stated. Close study of the reports reveals that the percentages quoted relate only to the group of autopsies covered by the particular investigation.

The present study, in contrast to the earlier works, has been planned to utilize the epidemiological method. A well-defined group of asbestos miners has been established in such a way that it constitutes a good sample of the whole population of asbestos miners in Quebec. Data for all members of this group have been collected and analyzed. Those concerning lung cancer have received most careful consideration. Details of the methods employed will be set forth in a later section, but the type of approach is considered to permit of fair comparisons and valid generalizations.

IV. COLLECTION AND ANALYSIS OF DATA

A preliminary survey of potential sources of information in February of 1956 involved discussions with the physicians in charge of the asbestos companies' programs and with clinicians, pathologists, representatives of City and Provincial health departments and of the Canadian Cancer Society, and other interested persons. It was found that morbidity data, although somewhat limited, were available from such sources as the hospitals in Montreal and Quebec City, and the 13 Cancer Detection Centers in the Province. However, because of the high mortality in lung cancer, it seemed advisable to depend upon data relating to deaths. These we found to be obtainable at the vital statistics department of the Ministry of Health in Quebec City. From the preliminary survey, it was apparent that extensive and detailed information could be gathered with respect to both the persons employed in the asbestos mining industry and mortality figures for the general population.

Following this exploratory survey, the initial effort was directed to the collection of data relating to all workers who had been processed through the clinic at Thetford Mines since its inception in 1947. Similar information was obtained regarding all workers at the Canadian Johns-Manville Company in Asbestos. Data from the clinical records included the age, family and personal medical histories, smoking habits, number of years of exposure, an estimate of weighted exposure,

TABLE 22

Comparison of the Actual and Expected Number of
Lung Cancer Deaths by Age Among Asbestos Miners

Age Group	Province	No. of Miners	Expected ⁺ No. of Deaths	Observed No. of Deaths	
	Total Specified Primary Rate per 100,000			Proved	Total
20-44	1.8	3901	0*	1	1
45-54	24.5	1124	2	1	3
55-64	67.6	615	2	3	3
65 +	89.3	315	2	4	5
Unknown	--	3	--	0	0

* Actually .4

+ The expected number is based on the average of the 1954 and 1955 age-specific rates for the Province of Quebec.

Table 22 also answers a question previously raised. It shows that the members of these cohorts have not died from lung cancer at an age earlier than the general population, and that such an explanation cannot be offered for the absence of lung cancer in 240 men with more than 40 years of employment referred to on page 37.

A comparison between the asbestos miners and the population of the Dominion as a whole was made, using statistical material from several sources. In one source, Phillips ⁽¹⁷¹⁾ gave age- and sex-specific rates for Canada for three periods between 1931 and 1952.

The rates for males are given in Table 23.

TABLE 23

Annual Death Rates per 100,000
for Cancer of the Lung in Canada*

Age Groups	Groups of Years		
	1931-1933	1941-1943	1950-1952
Under 30	0.2	0.3	1.0
30-34	0.9	0.9	0.8
35-39	2.0	3.2	3.0
40-44	3.0	5.4	6.5
45-49	5.2	12.5	16.7
50-54	8.2	18.9	37.2
55-59	12.7	27.0	59.7
60-64	12.5	33.7	77.8
65-69	15.1	34.5	102.9
70-74	10.7	30.6	86.3
75-79	15.8	30.0	83.9
80-84	8.2	27.9	59.7
85 +	11.4	14.3	71.0
All Ages	2.8	7.1	15.8

* "Mortality from Lung Cancer in Canada", 1931 to 1952.

These figures show strikingly the increase in rates between 1931 and 1952, and this increase is particularly marked after age 50, confirming an observation previously made, to the effect that lung cancer has probably been under-diagnosed in the older age groups in the general population.

To use these figures for purposes of comparison, it is necessary to combine the rates for certain age groups in order to conform to the age distributions used in this study. Since the exact populations in each age group for the years indicated is not known,

this must be an approximation. However, the rates would be somewhat as follows:

<u>Age Group</u>	<u>Rate</u>
20-44	5
45-54	27
55-64	69
65 +	90-95

These rates are, in general, lower than those developed for the total (proved and suspected) cases of lung cancer among the asbestos miners. The only large difference, however, is in the age group of 65 years and over, and it is quite possible that the rate for this group may have increased for Canada between 1952 and 1954 as it did for the Province of Quebec. (See Table 21)

A further comparison has been made with an over-all rate obtained from the American Cancer Society for respiratory cancer deaths in Canada in 1953. This rate, for males, is 20.8 per 100,000, an increase of 5 per 100,000 over Phillips' 1950-1952 rate, and compares with 25.5 per 100,000 for proved cases and 34.0 per 100,000 for total cases among the asbestos miners in this study. It is therefore obvious that there are no important differences between the rates for asbestos miners and those for the general population of Quebec and the Dominion of Canada.

Since it is probable that figures for the United States are more complete and, therefore, possibly more comparable to the data for the miners, age-specific rates were computed from "Vital Statistics of the United States", Volumes I and II, for 1952. These rates have been tabulated in Table 24.

TABLE 24

Number of Deaths and Death Rates per 100,000
by Age Groups for the Adult Male Population of
the United States—Data From
"Vital Statistics of the United States", Volumes I and II, 1952

<u>Age Group</u>	<u>Population</u>	<u>Cases</u>	<u>Rate per 100,000</u>
20-44	24,544,000	883	3.6
45-54	8,065,000	2979	36.9
55-64	6,340,000	6254	98.6
65 +	5,670,000	6483	114.3
Total	44,619,000	16,599	37.2

It is apparent that these rates compare favorably with those for the asbestos miners as shown in Table 6. Still other rates for the United States were obtained from the American Cancer Society, and for males, these were 25.3 per 100,000 in 1953, and 28.0 per 100,000 in 1955. They are not identical with the rate calculated from the figures of the office of Vital Statistics, but this is possibly because the American Cancer Society rates are for males of all ages. Nevertheless, they, too, compare favorably with the rates of 25 (or 34 for total cases) obtaining among the asbestos miners.

Returning to a comparison between the asbestos n
and persons who are exposed to asbestos in one form or another
distinguished from the general population groups just discussed.
have no exposure) an interesting observation can be developed by
duction. Hueper (122) has stated that there are about 35,000 pers
exposed in the United States, and we have found that the Canadian
mines employ about 8,000. Elsewhere, it has been estimated that t
workers in England who have exposure total between 3,000 and 5,000
With workers in Africa, Denmark, Norway, and other countries, at
least 50,000 persons must be exposed throughout the world, and it can
be assumed that this number has been fairly constant in the 20 years
since 1935 when the first case of asbestosis with lung cancer was re-
ported. At least a million man-years of exposure has thus been accumu-
lated, and this figure can be divided by the approximately 150 cases of
lung cancer with asbestosis reported during the 20-year period. This
gives a rate of 15 per 100,000 which is at least indicative that any lung
cancer rate which can be calculated for workers exposed to asbestos
dust is not much greater than that for the unexposed persons.

Comparison Between Eight Counties And
Asbestos-Producing Areas and Eight Selected

To compare lung cancer mortality rates surrounding the asbestos-producing areas with rates of counties in which no asbestos miners are likely to be found, mortality rates were computed on the basis of figures for the years 1950 through 1955. The eight counties selected for comparison are Argenteuil, Chateaugay, Montmagny, Portneuf, Richlieu, St. Hyacinthe, and Terrebonne, mainly because they present a wide geographic distribution throughout the Province. The eight counties selected because of their proximity to the asbestos-producing areas include Arthabaska, Beauce, Drummond, Frontenac, Megantic, Richmond, Sherbrooke, and Wolfe. Table 25 shows the number of lung cancer deaths for the years 1950 through 1955 for each of the eight counties, and a mortality rate, based on the adult male population in 1952. To emphasize the comparison Megantic County has been shown separately, as has the Province of Quebec and also the Province with the eight "asbestos-producing" counties subtracted. Because of its unique lung cancer death rate, Montreal et Isle de Jesus has also been listed in order to provide further comparison.

TABLE 25
Number of Lung Cancer Deaths and Rate per 100,000 Man-Years

Counties	Adult Male Population 1952	Male Lung Cancer Deaths*							Rate per 100,000
		1950	1951	1952	1953	1954	1955	Total	
Megantic County	13,100	3	1	3	3	1	4	15	18.9
Eight "Adjacent" Counties	97,600	6	3	9	16	4	16	54	9.4
Eight Selected Counties	83,000	2	10	5	18	5	9	49	9.8
Province of Quebec	1,198,000	196	220	245	303	303	357	1624	22.6
Province of Quebec less Eight "Adjacent" Counties	1,100,000	190	217	236	287	299	341	1570	23.8
Montreal et Isle de Jesus	394,000	3	7	158	192	185	225	770	32.3

* It is assumed that all male lung cancer deaths occurred after age 20

It is apparent from the table that the lung cancer death rate for the eight counties immediately surrounding the asbestos-producing areas is practically identical with that of eight counties selected for comparison. While Megantic County has a rate nearly twice that of the combined eight selected counties, it is lower than the rate for the Province, and considerably lower than the rate for Montreal. The figure for Montreal would certainly be higher except for the very low numbers of deaths reported for 1950 and 1951, and it would appear that some error in reporting has undoubtedly been made. On the basis of the other years, 1950 and 1951 deaths would be expected to be about 200 greater, and this would result in a rate of 40 per 100,000.

The only possible conclusion from this comparison is that there is no evidence that the persons who live in the counties surrounding and adjacent to the asbestos-producing areas have any greater incidence of lung cancer than those who live elsewhere in the Province.

Discussion of All Recorded Lung Cancer Cases,
Living and Dead, at Asbestos and Thetford Mines

Although a simple enumeration of all the known or suspected cases of cancer of the lung in these areas has no particular value from a statistical point of view, it is of interest to summarize

such cases for the record. There were nine deaths prior to the beginning of the time period covered by the study, including one in which the diagnosis was mediastinal lymphosarcoma. All of these nine cases occurred at Thetford Mines. It is somewhat surprising that there is no record of any lung cancer deaths among the Asbestos group in the interval preceding the beginning of the study and equally so that no cases have been reported in 1956 and 1957. During the period covered by this investigation, there were six proved cases and three suspected cases at Thetford Mines, as well as three proved cases at Asbestos. Through 1956 and to date in 1957, there were eight deaths at Thetford Mines, six of which were merely suspected and included such diagnoses as mediastinal lymphosarcoma, mesothelioma, cancer of the leg with metastases to lung, abscess of lung, and cancer of the pancreas. One other was diagnosed on the basis of x-ray only. In addition, there are now living four cases in which the diagnostic evidence is strongly suggestive of lung cancer. This is a total of 33 cases of all types, including ten "suspected" but unproved cases, and four that are still living. The remaining 19 constitute the total of proved cases of cancer of the lung in both areas since 1940. Sixteen of these have been at Thetford Mines and only three at Asbestos, all of which occurred during the period of the study.

The proved cases averaged 59 years of age at death, and varied between 37 years and 68 years. Their working span covered

periods varying between a minimum of 14 years and maximum of 37 years. Only three men had less than 25 years of employment in the industry. Seven among those on whom such information is available had a weighted exposure placing them in category III, and six worked in an exposure represented by category I.

Although they were subjected to post-mortem examination, there were three among these proved lung cancer cases in which we do not have information regarding the presence of asbestosis. Of the remaining 17, asbestosis was present in nine, although it was minimal in two, and two pathologists disagreed regarding its presence in one. Eight of the proved lung cancers, therefore, were not accompanied by asbestosis.

VI. SUMMARY AND CONCLUSIONS

Interest in the question of whether there may be an association between lung cancer and asbestosis or exposure to asbestos has been evident since the report in 1935 by Lynch and Smith of a case in which lung cancer and asbestosis were both present. As additional cases in which the two diseases coexisted were reported, a causal association appears to have been gradually accepted by many authors, although a few workers considered the correlation to be inconclusive. Cases of lung cancer which had occurred among the asbestos miners in Quebec had been carefully recorded over the years, and the present study was commissioned in an effort to determine whether a causal relationship did, in fact, exist between exposure to asbestos and cancer of the lung.

Reference to the literature shows a remarkable uniformity both of method and of conclusions. In general, the method has been to study a circumscribed series of cases of asbestosis and to enumerate those in which lung cancer occurred. The series may consist of cases coming to autopsy or of death certificates mentioning asbestosis, and the total number has served as the denominator by which the number of lung cancer cases is divided to produce a certain "incidence rate". This rate, as reported by various authors has been consistently high, and its uniformity is indicated by the following tabulation.

<u>Author</u>	<u>Asbestosis Deaths</u>	<u>Cancer of Lung</u>	<u>Percentage Incidence</u>
Merewether	344	55	16.0
Wedler	92	15	16.3
Wyers	115	17	14.8
Lynch & Cannon	40	3	7.5
Gloyne	<u>121</u>	<u>17</u>	<u>14.1</u>
Totals	712	107	15.0

The notable characteristic of all previous publications is the adherence to the development of a percentage relationship in a relatively small and very selected group of cases. Only Doll,⁽⁶³⁾ among all of these authors, has described a representative population group and studied it for the mortality rate from lung cancer and compared this rate with that for a control group. His investigation dealt with only 113 men in the study population.

Since most earlier studies had been limited to enumerating the lung cancers found in certain selected samples, such as cases coming to autopsy or death certificates in which asbestosis was mentioned, it was apparent that they could not fulfill the requirements of an epidemiological and statistical approach to the problem. The present study was, therefore, designed to meet the requirements of this method.

After a preliminary survey to explore the availability of reliable information, data were gathered on workers in the asbestos mines in Quebec, based on medical records at the two main locations

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of these operations. Cohorts were defined according to certain criteria and all workers who met these criteria were included in the study. Through their medical records, data relative to their characteristics were collected and their status at the end of a six-year period of observation was determined. In the case of those who had died, an exhaustive search of death certificates and insurance records was carried out in order to determine as nearly as possible the exact cause of death. Mortality rates from lung cancer for the general population of the Province of Quebec and its various counties and for the Dominion of Canada, as well as the United States were calculated from statistics collected in the appropriate places. Comparisons of the rates obtained for asbestos workers and for the other population groups were made according to accepted statistical methods which have been explained in some detail in section IV.

Records were obtained on 6091 persons who fulfilled the criteria of our cohorts. It was not possible to trace 133 of these for the whole period, but 5771 of the remaining 5958 were found to be still living in 1955 or later. Of the 187 known dead, cancer of the lung was considered to have been reasonably proved in nine and to be strongly suggested in three.

The members of the cohorts were studied with respect to age, length of employment, a weighted average of their exposure, and their smoking habits. Four thousand, six hundred and seventy-three

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were found to be smokers within the definition of that term as used in this study. Thirty-four percent of the cohort were more than 45 years of age, and 30% had been employed for longer than 20 years. Thirty percent had a weighted exposure which placed them in category III.

The mortality rates for lung cancer, as computed on the basis of six "proved" deaths among the Thetford Mines cohort and three "proved" deaths among the Asbestos cohort, were 27.6 per 100,000 for the Thetford Mines group, and 22.2 per 100,000 for the Asbestos group. When the three "suspected" cases were added, the "total" rate for the Thetford Mines cohort rose to 41.3. The rate for the combined cohort was 25.5 per 100,000 for "proved" cases, and 34 per 100,000 for "proved" and "suspected" cases. The importance of the suspected but unproved cases in determining these rates has been reiterated because it is likely that such cases would not be included in the statistics for the general population.

According to the findings in this study, the mortality rate from lung cancer does not appear to increase with length of exposure or with degree of exposure, a fact which presents strong evidence against the carcinogenicity of asbestos. On the other hand, the study indicates that cigarette smoking is a very important factor in the incidence of cancer of the lung.

A comparison of relative frequency of lung cancer and asbestosis is less reassuring, but we believe that this is because of an

under-reporting of asbestosis cases. The incidence of asbestosis indicated by the medical records is far below that which would be expected on the basis of all previously published figures. Naturally, when the cases of lung cancer are compared with an artificially low figure, its relative incidence will be higher than it should. However this may be, 12.5% of the recorded cases of asbestosis in this study developed lung cancer, a figure slightly lower than those quoted by authors who confined themselves to this type of comparison.

Comparison of the experience among the asbestos miners with that of various segments of the unexposed, comparable population shows that the observed number of deaths among the miners is not significantly greater. The rate for proved cases among the asbestos miners (25.5 per 100,000) compares well with the rate of 22.5 per 100,000 for the rest of the Province, and 20.8 per 100,000 for adult males throughout the Dominion of Canada. It also compares satisfactorily with rates of 37.2, 25.3, and 28.0 obtained from various sources for adult males in the United States. Finally, in this matter of comparison, it would appear that the world-wide experience of persons exposed to asbestos dust is not worse with respect to lung cancer than that of the unexposed population.

The counties surrounding the asbestos-producing areas, and in which it is presumed most of the asbestos miners live, have almost identical mortality rates with those of eight counties widely scattered

through the Province, and are lower than those for the remainder of the Province, and much lower than the rate for Montreal.

Since 1940, there have been 19 cases in which the diagnosis of primary cancer of the lung may be considered to have been proved. Approximately half of these cases were associated with asbestosis. All but one died in the recognized "cancer age" and at least one-third had only the lightest exposure (category I) to asbestos dust.

Conclusions

On the basis of a careful and detailed study of what are believed to be complete and reliable data, it seems fair to conclude that the asbestos miners at Thetford Mines and Asbestos in the Province of Quebec do not have a significantly higher death rate from lung cancer than do comparable segments of the general population. Despite this, the results suggest that a miner who develops the disease asbestosis does have a greater likelihood of developing cancer of the lung than a person without this disease. We suspect, however, that under-reporting of asbestosis cases had led to a fallacious finding in this connection.

The death rate from lung cancer in the areas contiguous to the asbestos operations is comparable to that in areas widely scattered throughout the Province of Quebec and is lower than in some urbanized areas within the Province.

The present study indicates that the effect of cigarette smoking is a much more important consideration in the production of lung cancer than is exposure to asbestos, and in this respect, it tends to confirm recent studies dealing with the effect of smoking.

The value of this investigation would be considerably enhanced by continuing the observation of the cohorts formulated herein on a year-by-year basis. It is strongly recommended that the chest x-rays of all workers be submitted to an independent reading for the diagnosis of asbestosis, since an inaccurately low incidence rate for this disease creates an artificially high relative incidence for lung cancer.

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