CHAPTER 13

MORTALITY OF METAL MINERS—A RETROSPECTIVE COHORT AND CASE CONTROL STUDY

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INTRODUCTION

This mortality and case control study of metal miners is an outgrowth of a silicosis study carried out jointly by the U.S. Public Health Service (USPHS) and the U.S. Bureau of Mines (BOM) between 1958 and 1961 [1]. Prior studies of these two agencies relating to dust diseases had been conducted from 1913 to 1940 [1]. It is hoped that this current study will provide a baseline for other metal mine studies in progress.

SUBJECTS AND METHODS

Mortality Study

The present mortality study is a followup of 13,007 non-uranium miners originally examined in the 1958–1961 silicosis study [1]. These men were followed from 1958 through 1975 to determine the effects of ore mined, smoking status, airways obstruction and other variables on mortality. Table I shows the construction of the final cohort.

The final group available for followup consisted of 12,258 white men, of whom 1,987 were deceased. (Please note that Spanish-Americans are considered to be white for purposes of mortality calculations as per

Table I. Construction of Final Cohort

Source	Number of Men
Base Group	13,007
Lost to Followup	– 23
Incomplete Medical Records	– 666
Experimental Group	12,318
Nonwhite Members	– 60
Final Cohort	12,258

instructions from the National Center for Health Statistics.) This cohort contains metal miners from 16 states who were mining 11 categories of metals in 50 different mines.

Standardized Mortality Ratios (SMR) were calculated by means of a modified life table procedure. The standard population chosen for this cohort was an average for the years 1968, 1969 and 1970 and consisted of all white males in each of the 16 states in which the 50 mines were located. Death certificates were coded for cause of death by a qualified nosologist using the *Eighth Revision, International Classification of Diseases Adapted for Use in the United States* [2].

Case Control Study

To narrow the causative factors in cases in which statistically significant increases in SMRs were seen in the mortality study, it was decided to apply case control techniques in a limited number of causes of deaths related to respiratory diseases. In particular, 163 cases of cancer of the trachea, bronchus and lungs (SMR = 126.6; $p < 0.01$), hereafter referred to as lung cancer, were matched with controls on the basis of age, length of time underground and specific occupation. Case control matching was done on both a one-for-one and a two-for-one basis. Control cases for both sets of matches came from workers dying from all causes of death except cancer of the trachea, bronchus and lungs (and from accidents).

Potential causative factors examined included ore mined, radon daughter exposure, radiographic evidence of silicosis, presence of airways obstruction, diesel exposure and smoking habits.

Airways obstruction is defined as having a forced expiratory volume in one second to forced vital capacity ratio (FEV_1/FVC) of $\leqslant 0.69$, as specified in the standards published by the Intermountain Thoracic Society [3]. As these men were working at the time of examination and had an age range of 31 to 64, we feel that this is a reasonable standard.

Relative risk for the one-for-one matches were estimated ($\hat{p}$) by the method described by Miettinen [4] for matched pairs. The 95% confidence intervals for each of the relative risk values were computed using formulae described in the above reference. In the two-for-one matching, the relative risk was estimated ($\hat{p}'$) using the Mantel-Haenszel (1959) procedure of obtaining a point estimate of relative risk, again described by Miettinen [4]. As computation of confidence intervals is complex in two-for-one matching and requires special computer software, the values for the two-for-one match were not computed.

In some cases involving the FEV_1/FVC ratio, values are missing. The assumption is that certain workers were unable to complete the spirometry because of physical limitations of one kind or another, could not produce reproducible results, or that the spirometry equipment failed and workers did not repeat the test after repair of the equipment. In the estimation of relative risk, we deleted sets with missing data and calculated on a reduced number of sets.

RESULTS

Mortality Study

Of the 12,318 people in the final group, 10,798 were white, 1469 were Spanish-American and the balance were of various races. Table II shows the distribution of workers by race composition. As stated in the Methods section, whites and Spanish-Americans were combined into a single white race group for computation purposes. Other races were not analyzed.

Table III shows the distribution of combined white male deaths and mines by type of ore mined. This table is in rank order by numbers of workers in each type of ore. Copper miners, lead zinc miners and iron miners accounted for 76.3% of the total cohort and 74.0% of the mines that were included in the study.

Table II. Race Composition

Race	Number	
White	10,789	12,258
Spanish-American	1,469	
Black	11	60
Indian	36	
Other	13	

Table III. Distribution of White Miners, Deaths and Mines by Type of Ore Mined

Rank	Ore Mined	No. of White Miners	No. Deceased	No. of Mines
1	Copper	3,853	694	12
2	Lead Zinc	3,402	642	15
3	Iron	2,097	232	10
4	Molybdenum	963	72	1
5	Gold and Gold Silver	906	129	2
6	Lead Zinc and Lead Silver	426	97	2
7	Mercury	274	71	4
8	Tungsten	173	20	1
9	Chromium	132	19	1
10	Silver and Copper	19	5	1
11	Lead Silver	13	6	1
		12,258	1,987	50

Table IV lists the SMRs of eight selected causes of death, including ICD numbers, causes of death, observed number dying, expected number dying and the SMR for each cause. Statistically significant increases of SMRs occur for all causes combined, respiratory cancer (including cancer of the trachea), bronchus and lungs, and diseases of the respiratory system (including pneumoconiosis and accidents). Statistically significant decreases of SMRs occur for digestive cancer and for hypertensive heart disease.

Table V is a summary of statistically significant SMRs by type of ore mined. SMRs that are circled are computed from less than five observations. Copper miners had the greatest number of significant increases, followed by mercury miners, lead zinc miners, gold and gold silver miners, and so forth.

Table IV. Standardized Mortality Ratios

ICD No.	Cause of Death	Observed	Expected	SMR
001-999	All causes	1987	1876.76	105.9[a]
150-159	Digestive cancer	72	98.19	73.3[a]
160-163	Respiratory cancer	169	136.34	124.0[a]
162	Cancer of trachea, bronchus and lungs	163	128.78	126.6[a]
400-402	Hypertensive heart disease	4	11.22	35.7[b]
460-519	Diseases of respiratory system	140	116.21	120.5[b]
515	Pneumoconiosis	27	7.86	343.6[a]
800-949	Accidents	244	130.24	187.3[a]

[a]Significant at 1% level.
[b]Significant at 5% level.

Table V. Summary of Statistically Significant SMRs by Ore Mined

	Copper	Lead Zinc	Iron	Molybdenum	Gold and Gold Silver	Lead Zinc and Lead Silver	Mercury	Chrome	Silver and Copper	Lead Silver
All Causes	112.4		88.4			136.1	144.9			
Respiratory Cancer							335.1	327.3		
Cancer of Trachea, Bronchus and Lung		130.0					354.6	346.5		
Stomach Cancer										2,344.0
All Malignant Neoplasms							185.9			
Respiratory System Disease	143.1		31.8	271.0						
Influenza				865.6						
Pneumoconiosis	268.3	245.9		2,152.5	1,291.3					
Tuberculosis	291.2					841.7				
Cirrhosis of Liver		18.2	9.5							
Nephritis and Nephrosis		283.5			394.7					
Cholelithiasis					694.8					
Ill Defined	197.8									
Other Arterial					345.4					
Accidents	195.5	184.4				548.1		269.0	1,436.4	
Suicides							478.8			
Homicides								722.7		

Iron miners had the greatest number of statistically significant decreases. These included decreases for all causes, diseases of the respiratory system and cirrhosis of the liver.

From a cause standpoint, accidental deaths were significantly increased in miners of five different ores: copper, lead zinc, combination of lead zinc and lead silver, chrome, and silver with copper. Pneumoconiosis deaths were increased in copper miners, lead zinc miners, molybdenum miners, and gold and gold silver miners. However, the sizes of both observed and expected deaths in the molybdenum miners and the gold and gold silver miners were too small to attach much weight to these two SMRs. Deaths caused by cancer of the trachea, bronchus and lungs were significantly increased in lead zinc miners, mercury miners and chrome miners. The category "All Causes" showed increases in copper miners, lead zinc and lead silver miners, and mercury miners. Cirrhosis of the liver showed a significant decrease in lead zinc miners and iron miners, but there were fewer than five observed deaths in both cases. In all, based on ore mined, 35 SMRs were statistically significant, none of which were elevated and some of which were reduced.

A very important factor in any health-oriented study is that of cigarette smoking. According to *Smoking and Health, a Report of the Surgeon General* [5], smoking is an important factor in many diseases, some of which may terminate in death; for example, lung cancer, heart attacks and strokes.

To try to assess the importance of smoking in this metal mining cohort, smoking histories were examined and SMRs were calculated controlling for smoking habits and years smoking. Table VI categorizes numbers and percentages of workers in each of five categories: nonsmokers, exsmokers, smokers (cigarette), pipe and cigar smokers, and unknowns. It can be seen that people who have smoked sometime during their lifetime account for 85.1% of the 12,258 white miners. This figure is quite high for this kind of a cohort [6,7].

Table VI. Numbers and Percentages of 12,258 Miners by Categories of Smoking (as of 1958–1961)[a]

Smoking Category	Number	Percentage
Nonsmokers	1,781	14.5
Exsmokers	1,330	10.9
Cigarette Smokers	8,642	70.5
Pipe and Cigar Smokers	450	3.7
Unknown	55	0.4
	12,258	100.0

[a]Exsmokers + cigarette smokers + pipe and cigar smokers = total

$$\underset{10.9}{\downarrow} + \underset{70.5}{\downarrow} + \underset{3.7}{\downarrow} = \underset{85.1\%}{\downarrow}$$

Table VII is a summary of statistically significant SMRs calculated on the basis of smoking category. In the case of nonsmokers, all statistically significant SMRs, with the exception of one for accidents, showed significant decreases. On the other hand, in the Cigarette Smoking category, all statistically significant SMRs showed increases, with the exception of cirrhosis of the liver. Accidents were a significant cause of death in all smoking categories except for pipe and cigar smokers. Even in this category, the SMR, while not statistically significant, had a value of 164.4. Respiratory cancer showed significant decreases in nonsmokers and exsmokers and a significant increase in cigarette smokers. Again, in pipe and cigar smokers there was a trend toward a decreased SMR for respiratory cancer. Diseases of the circulatory system showed significant decreased SMRs for nonsmokers and pipe and cigar smokers. Thus, except for accidents, only the smokers showed significant excess deaths.

During the 1958–1961 study, spirometry was done on each of the men. Therefore, we are able to look at mortality patterns based on the results

Table VII. Summary of Statistically Significant SMRs by Smoking Category

Category	Cause of Death	Observed	Expected	SMR
Nonsmokers	All causes	197	278.33	70.8[a]
	All malignant neoplasms	23	55.80	41.2[a]
	Digestive cancer	5	14.78	33.8[b]
	Respiratory cancer	7	20.11	34.8[a]
	Trachea, bronchus and lung	7	19.00	36.8[a]
	Diseases of circulatory system	90	138.99	64.8[a]
	Ischemic heart disease	66	105.35	62.7[a]
	Accidents	36	19.40	185.5[a]
Exsmokers	Respiratory cancer	12	21.18	56.7[b]
	Cirrhosis of liver	1	9.40	10.6[a]
	Accidents	22	14.51	151.7[b]
Smokers	All causes	1,451	1,208.43	120.0[a]
	All malignant neoplasms	284	238.42	119.1[a]
	Respiratory cancer	148	87.34	169.4[a]
	Trachea, bronchus and lung	142	82.48	172.2[a]
	Diseases of respiratory system	108	71.82	150.4[a]
	Pneumoconiosis	19	4.69	404.8[a]
	Cirrhosis of liver	28	47.73	58.7[a]
	Accidents	177	90.89	194.7[a]
Pipe and Cigar	All causes	73	97.22	75.1[a]
	Diseases of circulatory system	31	49.48	62.7[a]
	Ischemic heart disease	21	37.26	56.4[a]
	Pneumoconiosis	2	0.48	418.6[b]

[a]Significant at 1% level.
[b]Significant at 5% level.

of these tests. We will look at the results based on the concept of airways obstruction. For purposes of this study, airways obstruction will be defined as having an FEV_1/FVC ratio equal to, or less than, 0.69. FEV_1 and FVC are values obtained in the spirometry test. Table VIII gives SMRs on the basis of airways obstruction or no obstruction. With miners experiencing airways obstruction, $FEV_1/FVC \leq 0.69$ we see significant increases in all causes, all malignant neoplasms including respiratory cancer, diseases of the respiratory system including emphysema and pneumoconiosis, accidents and ill-defined causes. The increase in pneumoconiosis is six times normal. Cirrhosis of the liver shows a substantial decrease from normal. In the case of miners having no obstruction, $FEV_1/FVC \geq 0.70$, we see the reverse of the above with the exception of accidents, which show a significant increase. All malignant neoplasms, diseases of the circulatory system, diseases of the respiratory system including emphysema, and cirrhosis of the liver show significant decreases.

It is instructive to note the similarities between the SMRs for ventilatory obstructed workers and smokers on one hand and those for ventilatory nonobstructed workers and nonsmokers on the other hand.

Miners were categorized into one of seven occupational categories based on a scheme used by the Division of Respiratory Disease Studies (DRDS) of the National Institute of Occupational Safety and Health (NIOSH) in other

Table VIII. SMRs by Airways Obstruction (summary table)

FEV_1/FVC Ratio	Cause of Death	Observed	Expected	SMR
$\leq$0.69 Obstructed	All causes	884	757.98	116.8[a]
	All malignant neoplasms	187	154.29	121.2[a]
	Respiratory cancer	91	56.47	161.1[a]
	Trachea, bronchus and lung	88	53.36	164.9[a]
	Diseases of respiratory system	100	50.41	198.4[a]
	Emphysema	29	18.15	159.8[b]
	Pneumoconiosis	22	3.62	607.9[a]
	Cirrhosis of the liver	13	25.50	51.0[b]
	Accidents	69	39.93	172.8[a]
	Ill defined	18	10.13	177.6[b]
$\geq$0.70 Not Obstructed	All malignant neoplasms	143	179.36	79.7[a]
	Diseases of circulatory system	391	431.38	90.6[b]
	Cerebrovascular disease	32	46.84	68.3[b]
	Diseases of respiratory system	25	53.00	47.2[a]
	Emphysema	4	17.84	22.4[a]
	Cirrhosis of the liver	13	37.71	34.5[a]
	Accidents	152	78.35	194.0[a]

[a]Significant at 1% level.
[b]Significant at 5% level.

mining studies. These categories are: underground face, underground transportation, underground maintenance, underground miscellaneous, surface, open pit and unknown. In general, underground face workers seem to experience the most significant increases of SMRs, followed by underground transportation workers. Included in the face workers group are increases in both malignant and nonmalignant respiratory diseases. Increased deaths from pneumoconiosis are present in all groups except open pit workers and underground maintenance and construction workers, where there were no deaths recorded that could be charged to pneumoconiosis. Increased accidental deaths were common in all groups, with the exception of open pit workers. Significantly increased accidental deaths occurred in underground face workers, underground transportation workers and unknown job status workers. Cirrhosis of the liver showed statistically significant reductions of SMRs in underground face workers and surface workers and showed reduced SMRs in the other occupational groups.

Case Control Study

Estimations of relative risks for deaths caused by lung cancer based on the type of ore mined are shown in Table IX. This table gives the 95% confidence intervals for the one-for-one match. Miners working with chrome ore, gold and gold silver ore, lead zinc ore, and mercury ore showed elevated relative risks for lung cancer in the one-for-one match. Risks for miners in these four ores ranged from a low of 1.6 in the mercury ore, with a confidence interval of 0.9 to 2.9, to a high in gold and gold silver ore miners of 9.0, with a confidence interval of 1.3 to 332.3. Miners in mercury and chrome ore were the only ones who showed elevated relative risks in the two-for-one match.

The next factor to be considered was presence of airways obstruction,

Table IX. Type of Ore–Relative Risk–Lung Cancer

Ore	One-for-One Relative Risk	95% Cancer Incidence (CI)	Two-for-One Relative Risk
Gold and Gold Silver	9.0	1.3–332.3	0.6
Chrome	5.0	0.6–249.0	10.0
Mercury	2.5	0.7–10.9	3.5
Lead-Zinc	1.6	0.9–2.9	1.2
Iron	0.8	0.4–1.6	0.8
Copper	0.5	0.3–0.9	0.9
Molybdenum			0.2

defined by the Intermountain Thoracic Society [3] as a FEV_1/FVC ratio equal to, or less than, 0.69. Table X indicates the increased relative risks for this factor from a low of 1.3 in the one-for-one comparison to a high of 1.5 in the two-for-one comparison. The 95% confidence interval is 0.7 to 2.2.

Eleven of the 50 mines used diesel equipment of some type at the time of examination. The diesel equipment in use ranged from a single diesel truck or haulageway locomotive up to several pieces of equipment. Table XI shows the relative risk calculations for diesel exposure. For deaths due to lung cancer, the one-for-one comparison showed an elevated mortality relative risk for diesel exposure of 1.5, with a 95% confidence interval of 0.8 to 2.8. In the two-for-one comparison there was no elevation, with the relative risk equal to 1.1.

The final factor considered is that of smoking. Of the mortality study cohort [1], a total of 74.2%, or 9092 miners, were current smokers. As smoking is a known factor in lung cancer [5], it was of paramount importance to see what effect, if any, smoking played in those metal miners who died of lung cancer. Table XII(a) gives a breakdown by case and controls as to numbers of current smokers versus exsmokers and nonsmokers. The numbers of smokers were significantly greater in the case group, $\chi^2 = 11.35$, $p < 0.01$. Table XII(b) gives the results of the case control analysis between current smokers and exsmokers and nonsmokers. In the case of the one-for-one match, we see a relative risk of 2.7, with a 95% confidence interval of 1.4 to 5.2. In the two-for-one match, the relative risk is 2.2. Of 162 lung cancer deaths, 142 occurred in miners who were current smokers at the time of examination.

Table X. Airways Obstruction ($FEV_1/FVC \leq 0.69$)–Relative Risk

Cause of Death	Comparison	n (pairs)	Relative Risk	95% CI
Cancer of Trachea, Bronchus and Lung	1-for-1	121	1.3	0.7–2.2
	2-for-1	115	1.5	

Table XI. Diesel Exhaust Exposure–Relative Risk

Cause of Death	Comparison	n (pairs)	Relative Risk	95% CI
Cancer of Trachea, Bronchus and Lung	1-for-1	163	1.5	0.8–2.8
	2-for-1	163	1.1	

Table XII(a). Current Smokers Versus Ex- and Nonsmokers—Number Comparison[a]

	Case	Control
Smokers	143	118
Ex- and Nonsmokers	19	44

[a] $\chi^2 = 11.35$, $p < 0.01$.

Table XII(b). Current Smokers Versus Ex- and Nonsmokers—Relative Risk

Cause of Death	Comparison	n (pairs)	Relative Risk	95% CI
Cancer of Trachea,	1-for-1	162	2.7	1.4–5.2
Bronchus and Lung	2-for-1	161	2.2	

Other factors that were considered included radon daughter exposure and radiographic evidence of silicosis. These factors did not result in increased relative risk in this study.

CONCLUSIONS

SMRs were calculated for a cohort of 12,258 metal miners who were originally examined by the U.S. Public Health Service in 1958–1961 as part of a study of silicosis. In addition, case control studies were done on 163 metal miners of this cohort who died from cancer of the trachea, bronchus and lungs. The conclusions from these studies are as follows:

1. The metal miners cohort showed statistically significant increases in SMRs for all causes, respiratory cancer, nonmalignant diseases of the respiratory system (including pneumoconiosis) and accidents, and statistically significant decreases in digestive cancer and hypertensive heart disease.
2. In terms of ore mining environment, there were differences between the ores mined and significant causes of death, with copper miners having the greatest number of significant increases of SMRs and iron miners having the greatest significant decreases.
3. Lead zinc miners, mercury miners and chrome miners showed significant increases in SMRs for lung cancer. The case control study confirmed this, showing increased relative risk for these miners plus gold and gold silver miners.
4. Smokers showed significant increases of SMRs for all causes, all malignant neoplasms, diseases of the respiratory system and accidents. They show an increase in the case control study of relative risk of 2.7 in the one-for-one

match and 2.2 in the two-for-one match for lung cancer. Nonsmokers show significant decreases in SMRs for all causes, all malignant neoplasms and diseases of the circulatory system.

5. Underground face workers had the greatest number of increased SMRs, followed by underground transportation workers, maintenance workers, miscellaneous workers and surface workers. Both face workers and transportation workers show significant increases for pneumoconiosis.
6. Workers exhibiting airways obstruction have excess deaths in the following cause of death categories: all causes, all malignant neoplasms including respiratory cancer, diseases of the respiratory system including emphysema and pneumoconiosis, accidents and ill-defined causes. Airways obstruction as a causative factor in lung cancer showed a range of increased relative risk of 1.3 to 1.4.
7. Some effect of diesel exposure was seen in the case control study on lung cancer. There was an increased relative risk of 1.5 in the one-for-one match, which was not confirmed in the two-for-one match.

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DISCUSSION

Question: Did the smoking history include questions as to the number of cigarettes smoked and the age that smoking began?

Response: I am well aware that this study lacks pack-years, and this is a result of the way in which the data were collected. Data fell into arbitrary groups, e.g., less than two packs a day or less than three packs a day. We could not find a good way to sort out that information.

Question: The study had a relatively low percentage of nonsmokers and exsmokers compared to national averages. Were you able, using American Cancer Society statistics from their prospective study, to estimate what the difference in the smoking pattern would have contributed? As I recall, Vic Archer, in one of the studies of uranium miners, calculated or estimated that the smoking patterns of uranium miners might account for perhaps a 40% increase in their lung cancer rate, which, of course, did not explain the seven- or eight-fold increase that they were finding.

Response: To this point, we have not estimated what the difference in smoking pattern has contributed, but this will be done.

Question: Were you able to identify those people in whom diagnoses of silicosis were made or who were working in high-risk mines to test the hypothesis that there may be some effect of silica as a lung carcinogen?

Response: As part of the case control study, we looked at silica and silicosis. We decided, however, that to keep the study presented within manageable levels, we would leave those data out and publish them at a later time.

Question: I noticed some data in your presentation that I think may be relevant to the Lawler paper. The overall Standardized Mortality Ratio was less than 100 for digestive cancers, whereas in the iron ore paper it was considerably above 100. However, when you broke the data apart by smoking status, you found a fairly dramatic significant increase in stomach cancer in the smokers and the obstructed group. I think that, in a way, this supports the recent work done by Ames in a test of the Meyer hypothesis. Meyer claimed that miners who smoke bring up phlegm containing dust, which is then swallowed, becoming one of the agents that produce stomach cancer. Ames did not actually confirm the Meyer hypothesis. He found that only heavy smoking in combination with heavy dust exposure resulted in high risk factors in stomach cancer.

Response: I'd like to make one comment. The iron ore workers in this study were from eastern Pennsylvania, primarily in the Allentown/Bethlehem/Reading area. That area is very heavily Mennonite and, when we reviewed the data and found a reduced SMR for iron workers and knew that the Scandinavian literature showed increased ones, we started looking for answers. I looked at the smoking of the iron miners versus the smoking of the other miners and found that religion did not explain the difference.

Question: I was interested in the results with reference to the diesel exposure. Did you look at the power of the study to detect the effect, giving the small relative risk that was suggested, and did you look at smoking distribution within that component of the study?

Response: The problem that we saw with the diesel exposure was that we really had very few data. We knew if the mines had or didn't have diesels. We knew roughly how many pieces of diesel equipment were onsite; however, there really weren't enough data to make any broad conclusions.

Question: I think I heard you say that lung cancer might have been caused by airway obstruction, and I think it might be more correct to say there is an association. I would like to know if it was possible for you to look for some potential confounds, such as differences in the amount of radiation in these mines, as most of these underground mines do have relatively high levels, and the degree of ventilation in the mines, as those mines with a high ventilation would have less radiation and diesel fumes, etc.

Response: That is something that could be done. We have not done it. I did not mean to imply that lung cancer is caused by airway obstruction.

Question: In Table VII I did not see the relationship between nonsmokers and pneumoconiosis. It is shown for smokers.

Response: This presentation is a summary, and I only took significant values.

HEALTH ISSUES RELATED TO METAL AND NONMETALLIC MINING

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