



UNITED STATES
NUCLEAR REGULATORY COMMISSION
WASHINGTON, D. C. 20555

JUL 17 1985

Mr. Robert Alvarez
Environmental Policy Institute
218 D Street, S.E.
Washington, DC 20003

Dear Mr. Alvarez:

Enclosed is a copy of the long-sought final report by Kinetic Research Inc. entitled, "Health Effects of Low-Level Ionizing Radiation". We finally located a copy after an extensive search of both retired files from our warehouse and individual personal files. These searches were carried out due to our inability to otherwise locate a copy in response to your earlier informal requests and your recent Freedom-of-Information Act request.

There were three contracts that NRC sponsored to review the Hanford data: the Kinetic Research Inc. study, one by George Washington University and the other by the Mount Sinai School of Medicine. Copies of the other two reports are also enclosed as I thought that they might be of interest to you.

One of the conclusions of the Kinetic Research report seems to be that the data set they examined is clearly not identical to the data set used by Mancuso, Stewart and Kneale in their final progress report or their November 1977 paper in Health Physics. This is entirely understandable considering that the data set changes with time as deaths occur and that Dr. Mancuso has been very reluctant to provide us with a copy of the data set he analyzed, even after repeated requests for a copy. In fact, the possibility that the data set we could provide to these contractors might differ from that analyzed by Mancuso, Stewart and Kneale was recognized by NRC staff prior to initiating the contracts.

Let me know if you have any questions on these reports (427-4353). Although I was not directly involved with these studies, I'll try to track down the answers.

Sincerely,

Original Signed by

Harold T. Peterson, Jr.,
Senior Health Physicist
Health Effects Branch
Office of Nuclear Regulatory Research

Enclosures:

1. Kinetic Research Report
2. GWU Report
3. Mount Sinai Report

cc 7/16/85

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PDR CONTR
NRC-01-78-011 PDR

This letter is routine correspondence unrelated to any on-going regulatory action. Even though the requested documents are over 5 years old, this recent interest in them may be shared by others. If the PDR has general files on "Radiation and Health" or "Correspondence" this package may be appropriately filed in such files.

Howard Peterson
74353

7-14-78
J. H. Smith

FINAL REPORT

"HEALTH EFFECTS OF LOW LEVEL
IONIZING RADIATION"

CONTRACT NRC-01-73-011

KINETIC RESEARCH, INC.

~~79-11260024~~
151 pp.

NOTICE

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16. Abstract <p>This paper reports the results of an analysis of a data tape provided by the Nuclear Regulatory Commission purported to contain selected information including mortality, exposure, and work history data for workers employed at the Hanford Atomic Facility who were deceased by the end of 1972.</p> <p>The intent of the study was to analyze this data for dependencies of death due to cancer on exposure to low level ionizing radiation with proper control for other variables provided. If possible, dose response relationships were to be derived. The analysis methods used included descriptive univariate analysis, discriminant analysis, categorical analysis, and linear logistic regression.</p> <p>Unfortunately, examination of the data and investigation of background material discovered during the project concerning this data and its sources has lead to the conclusion that the data provided is not a consistent, reliable, and authentic representation of the <u>true facts</u> concerning the exposure experience of Hanford workers. In particular, the data provided has certain characteristics which are not consistent with the data as it is reported to be at its most reliable source. Therefore, while analysis of the data is presented, one should not presume that the results of this analysis accurately reflect relationships which exist in the real world.</p>			
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1. INTRODUCTION

In recent years a considerable amount of attention has come to focus on the biological effects of low levels of ionizing radiation as a possible occupational hazard for workers in the atomic industry. Historically, radiation protection criteria have attempted to provide conservative guidelines for avoidance of harm consistent with reasonable practicability in the workplace. In current recommendations permissible levels have been set based in part on data gathered at dose levels and in circumstances quite different from those prevalent in occupational situations (e.g. Japanese atomic bomb victims, radiotherapy patients, and the like). Until recently there have not been extensive and reliable analyses of the effects of chronic, low dose exposures to ionizing radiation in a large human population.

In 1964 a large scale epidemiological study of employees in AEC contractor facilities was undertaken in a project funded by AEC and directed by Dr. Thomas F. Mancuso of the University of Pittsburgh. This project, "Study of the Lifetime Health and Mortality Experience of Employees of ERDA (earlier AEC) Contractors" culminated in the publication of a paper by Mancuso, Alice Stewart, and George Kneale in Health Physics (Ref. 1) wherein definite statistical associations were reported between the incidence of various types of cancer and exposure to radiation for workers at the Hanford (Washington) Atomic Facility. The analysis also produced estimates of doubling doses for certain cancers which were much lower than had generally been estimated previously.

Mancuso's findings have resulted in considerable discussion and have motivated further analyses and re-analyses of exposure and mortality data from Hanford. The work presented in this paper is an analysis of certain data provided by the Nuclear Regulatory Commission purported to contain causes of death, exposure records, and other pertinent information for workers once employed at Hanford and now deceased. This data was to be analyzed for the possible dependence of death due to cancer on* exposure to ionizing radiation including derivation of dose response relationships where appropriate.

The statistical methodologies selected were descriptive univariate examinations of the data, discriminant analysis, categorical methods using chi-square and analysis of trend tests, and linear logistic regression. Results of these analysis are presented.

Unfortunately the data provided by NRC was very poorly documented and could not be meaningfully analyzed without further information concerning definitions of terms and units of quantities. In the process of investigating these matters and in attempting to answer other questions which were of concern to us we have discovered a number of problems with the data which cast into doubt any conclusions that might be drawn from the statistical analysis.

Consequently, a large part of the material presented in this report has to do with examination of the data with regard to its consistency, authenticity, reliability, and usefulness for purposes of analysis. It is our conclusion based on the information which we currently have in hand that the data presented to us cannot be

regarded as a usable representation of the actual experience of workers at Hanford. In particular, the data does not represent the reported state of the data maintained at its most reliable source. While analysis of the data can be and is presented, one should not and we do not presume that the results of this analysis accurately reflect relationships which exist in the real world.

2.0 THE DATA

In any statistical analysis it is important to understand the background to the data for two reasons: a) to avoid pitfalls such as confounding effects not represented in the variables under consideration; and, b) to develop meaningful interpretations for the results identified. For these reasons we conducted a background review of the data and have presented the results for the reader in sections 2.1 through 2.5 of this report. More specifically, section 2.1 includes a brief summary of primary conclusions; followed by section 2.2, a discussion of the historical origins of the data; section 2.3, a general characterization of the data; section 2.4, issues relating to the dose variables; and finally, section 2.5 includes issues relating to cause of death and other factors not contained in the data subset.

2.1 Summary of Primary Conclusions From the Background Review

Two primary conclusions have been developed from our background review of the data. The first is that neither all of the available data elements (variables) nor all the available cases have been provided to us for a thorough and complete analysis. This conclusion, in and of itself, is obviously of particular concern since the detail and accuracy with which any analyses can be conducted and subsequent interpretations developed is impeded.

The second primary conclusion is that the authenticity and reliability of the data provided to us for analysis has not been adequately established. Clearly, this conclusion presents problems in making statements about the true "state of nature" based on observations obtained from the data.

It cannot be overemphasized that the above conclusions can significantly influence the understanding and interpretation of the analyses presented in the following sections.

2.2 Historical Background

It has become apparent during the project that the exact background details of the data are not fully known by the Nuclear Regulatory Commission (NRC). The written documentation provided to us at the beginning of the project, shown in its entirety in Figure 1, was inadequate for a thorough understanding of the data and would have provided a serious problem in the interpretation of any analyses conducted. As a result, we have made an effort to identify some of the historical and technical aspects of the data. A brief review of the historical aspects of the data will be provided here.

The study was motivated, at least in part, by a series of events. An understanding of the project can be facilitated by a brief chronological presentation of the events preceding it. Our understanding of this sequence of events is presented below.

In 1964 the Atomic Energy Commission initiated and funded a program entitled, "The study of the lifetime health effects and mortality experience of employees of AEC contractors" under the direction of Dr. Thomas Mancuso at the University of Pittsburgh's School of Public Health. This program AT(30-1)-3394 was continued under contracts CHAT(11-1)-3428 and E(11-1)-3428 when the Energy Research and Development Administration (ERDA) was established incorporating the AEC. The stated purpose of the study is given in the following quote from the abstract of an early progress report:

"The objective of this study is to follow cohort employee populations of selected AEC Contractor installations, to test the feasibility of using personnel, employment, medical and radiation records in establishing the relationships, if any, between mortality

patterns and levels of radiation exposure. The reason for the study is the absence of empirically tested information pertaining to human populations exposed to recorded low levels of radiation over long periods of time. The procedure devised for the test runs is: to establish a series of cohorts of populations at each facility, those continuously employed as well as those separated, for each year, by tracing these individuals and sibling controls through Social Security records to determine those who have died and their place and date of death; to obtain death certificates to establish age-sex specific death rates; and to analyze causes of death for those with radiation exposure and work-connected health hazards in comparison to appropriate non-exposed controls. The following AEC Contractor facilities have been selected for the test runs: Oak Ridge X10, Oak Ridge Y12, Oak Ridge K25, Hanford and several small feed materials plants. These facilities provide large populations with long intervals of operation. Pilot studies of radiation exposure records of persons exposed in atomic energy facilities will be carried out to determine the average occupational exposure of these populations and appropriate confidence limits in exposure estimates for individuals and various sub-populations."

Format of Tape

<u>Cols.</u>	<u>Content</u>
1-4	age at death (to nearest tenth)
5-6	year of initial employment
7-8	final year of employment
9-11	total years of employment (to nearest tenth)
12-14	cause of death (primary cause) ICD 8th revision
15	race 0 = non-white, 1 = white
16	sex 0 = female, 1 = male
17	exposure code 0 = non-exp, 1 = exp.
18-23	cumulative lifetime dose
24-29	cumulative dose 3 years before death
30-35	" " 5
36-41	" " 10
42-47	" " 15
48-53	" " 20
54-59	" " 25
60-61	year of death

Figure 1. Copy of the documentation provided with the data by NRC.

One of the facilities considered by the Mancuso study was the Hanford Atomic Facility in Richland, Washington. Around 1974 Dr. Milham of the Department of Public Health for the State of Washington reported (Ref.2) that his analysis showed an increased incidence of cancer in persons who had worked at Hanford and died in Washington, relative to other persons in the State of Washington. This report spurred analysis of the data which was being collected by Mancuso's study group. Eventually Mancuso, et. al., prepared a paper (Ref.1) which reported a relationship between cancer and low level ionizing radiation. At the same time his contract was terminated by ERDA. In the ensuing furor other persons analyzed the same or similar data including S. Marks of the Battelle Northwest Laboratories (Ref.3) and C. Land of the National Cancer Institute (Ref.4). In addition, Congressional hearings were held (Ref.5). Apparently the NRC was not in a position to address the issue at the hearings and this subsequently led to the current program.

In this program NRC decided to use the data employed by Land, rather than study the Hanford data stored at Hanford. Thus, a brief review of the origin of Land's data is in order.

Land had originally requested data from the Oak Ridge Data Processing Facility. Oak Ridge had some version of the data collected in the Mancuso study for the Hanford employees. It is not known to us how or when the data given to Land got from Hanford to Oak Ridge. Land requested, apparently in late 1976, a set of variables for analysis. The rationale for the variables selected is not known to us.

It has been reported to us that the data used by Land is identical with the data used by us. The reported course of events is that a copy of Land's tape was made at Geomet Corporation, a computing services contractor, and was submitted to NRC. NRC then utilized the facilities of Harry Diamond Laboratories to prepare copies of that tape for use by the three contractors on this project. One of those tapes was provided to us. As a consequence of the numerous data handling efforts from Hanford to Hanford Environmental Health Foundation, to Oak Ridge, it is extremely difficult to determine precisely what the available data represents. In an effort to alleviate this problem we requested additional information regarding the data, as well as additional data elements. Our request was not implemented. As an alternative course of action, we took some characteristics of Land's data reported in his study and compared them with the data we received. We did the same with Mancuso's study. The key findings of these comparisons are presented below. A more detailed presentation of these results appears in Section 2.6.

The frequency of each cause of death in our file matches Land's data (Ref. 4), except for two cases in our file which have no cause of death. Our cumulative doses can be shown to be significantly different from Mancuso's reported in Ref. 1. Unfortunately, we were unable to compare cumulative dose frequencies with those in Land's data.

With respect to sample size, we have more cases than Mancuso (Ref. 1), the same number of cases as Land (Ref. 4), and fewer than reported by Mancuso in later reports (Ref. 6 and 7). Perhaps most importantly, we have shown that the

data we have received has doses in time intervals which are not possible in the data collection scheme purported to have been followed in the Hanford study (Ref 8, 9, 10). Specifically there are 138 cases which have reported dose subsequent to the final year of employment. The details and ramifications of this finding are discussed more fully in Section 2.4.3.

It should be noted that our impression, based on among other things, conversations with Howard Fore at Oak Ridge, is that Dr. Mancuso never requested nor was ever sent a data set identical with that used here and by Land. Whether the problems that exist in this data would be present in data used by Mancuso is open to question. In any case, it is certain that the actual data analyzed in the Mancuso paper (Ref. 1) is not the same as that used by Land and by us.

2.3 General Characteristics of the Data

As discussed in section 2.2 the data is an extracted subset, characterised as Hanford employees who have died, of the larger set which includes employees both living and dead. It does not represent a large number of maintenance workers (≈ 6500) employed by Jones Maintenance Contractors, who are reported to have received higher doses than the average Hanford worker (Ref. 11); nor does it include AEC employees who worked at Hanford.

The data consists of 3992 cases which primarily represent white males as shown in Table 1.

TABLE 1
Number of Deaths by Sex and Race

		SEX	
		Male	Female
RACE	White	3585	379
	Other	25	3

Of the 3585 white male cases, 62.1 percent were characterized as exposed as shown in Table 2.

TABLE 2
Number and Percentage of Cases
Characterized as Being Exposed.

		SEX	
		Male	Female
RACE	White	2226/62.1%	116/30.6%
	Other	12/48.0%	0/0%

It should be noted that the use of the term "exposed" may be somewhat misleading, since those employees who

are classified as non-exposed may be the result of them not being monitored for radiation rather than not being exposed to radiation. This issue is discussed more fully in section 2.5.

Histograms of each variable have been made and are contained in Appendix A to facilitate the readers understanding of at least some of the more general features of the data. The histogram presented for each variable is a frequency distribution over the values taken on by the particular variable.

The "cause of death" frequency distribution is included in Appendix B. However, two data omissions in the file must be noted. First, 5 cases had an invalid initial year of employment and the same 5 cases had invalid total years of employment. Secondly, two cases had no cause of death.

For the purposes of relating cancer to radiation various groupings of ICD (revision 8) codes were used. These are indicated below together with the total number of cases and the number of exposed cases for each group.

TABLE 3
Cancer Groupings Used for the Purpose of Analysis

<u>General Description</u>	<u>ICD CODE</u>	<u>Total Exposed</u>	
		<u>White Male Cases</u>	<u>Total Cases</u>
lip, mouth, pharynx	140-149	14	14
esophagus and stomach	150-151	35	57
small intestine	152	1	2
* large intestine and rectum	153-154	66	102
liver and bile	155-156	10	20
pancreas	157	32	53

TABLE 3 (Cont.)
Cancer Groupings Used for the Purpose of Analysis

<u>General Description</u>	<u>ICD CODE</u>	<u>Total Exposed White Male Cases</u>	<u>Total Cases</u>
	158	1	3
	159	1	1
	160	2	2
lung	161-163	136	213
bone	170	1	1
	171	3	6
skin	172-173	10	16
breast	174	--	31
	180	--	7
	181	--	---
	182-183-184	--	62
prostate	185	21	43
	186	3	4
	187	7	11
	188	--	---
urinary organs	189	15	25
eye, brain nerves	190-192	18	29
thyroid	193	1	2
	194	--	1
	195	2	5
	196	--	1
secondary lung	197	8	13
	198	2	2
unspecified secondary	199	13	30
	200-202,204	30	44
multiple myeloma	203	8	11
	205-206	7	14
	207-209	2	7

2.4 Issues Relating to Radiation Dose

An adequate identification of background information for the dose variables contained in the data extract file was not provided. This lack of information was perhaps due in part to the background of the data discussed in section 2.2. In any case thorough documentation of the dosimetry and data collection practices relevant to the dose variables was not provided during the program. In our own review of the Mancuso Study progress reports, it became clear that there were many potential pitfalls which could exist in the data we had received, depending on when, where and how the data extract file was created. In attempting to answer the questions which arose about what the dose data actually represented, it was the case that we time and time again identified inconsistencies between one information source and another (e.g. various persons and written reports) and between information sources and the actual data extract file. It is the prevalence of this inconsistency which perhaps is most troubling in trying to assess just exactly what the data extract file represents. Consequently, we have been able to establish what the data file at Hanford is supposed to represent; we have not been able to determine whether in fact the data we have is representative of that data.

There are at least three areas of uncertainty with respect to the dose variables in the data extract file and one general area relating to the exclusion of data believed to be relevant to a thorough analysis. These are discussed below.

2.4.1 Penetrating Dose

The dose variable we are supposed to have received is classified by NRC as the "penetrating radiation dose" received by a Hanford employee. Clearly, numerous questions arise as to the definitions and dosimetry used to calculate penetrating dose. These questions are aside from the question of when the dose was received.

It has been reported to us (ref.12) that the penetrating dose variable consists of a summation of various dose sources. Specifically, it is the summation of the gamma, neutron, and Tritium doses plus .35 of the x-ray dose.

It is generally accepted that as a minimum quality factors are necessary in the combination of exposures from various dose sources if such combinations are to be done at all. It has been reported to us that the penetrating dose we have is a simple summation (as described above) of whatever was recorded for each dose source. The next question, then, is what was recorded for each source? To this question we have received two conflicting answers. The first is that quality factors have been applied to the data using 1.0 for gamma rays 10 for fast neutrons, 3 for slow neutrons, 1.0 for x-rays and 1.7 for Tritium, although the value 1.0 may have been used at times for Tritium. To some radio-biologists these quality factors may inadequately reflect the relative efficiencies of each source when interacting with human cells. The other explanation to us was that the data was simply a direct report of various badge readings. It may of course, be the case that both of these reports are correct, but apply to different forms of the Hanford data files. As was stated in section 2.2, which form of the file we have is questionable.

An issue related to quality factors is the combination of the exposure and dose units, namely Roentgens and rads. This concern is applicable to the understanding of what manipulations were applied to data from pocket ionization chambers.

Further, the use of Tritium is particularly puzzling since Tritium becomes involved with the body through inhalation or other means and represents a contribution to the body burden as opposed to a "penetrating dose". At the same time other internal sources have not been included with the penetrating dose. The issue of whether internal burden should be combined with penetrating dose is open to considerable debate.

2.4.2 Dosimetry Aspects

How the reported doses were obtained in the first place is an important issue quite independent of the possible manipulations discussed in the previous section. Most notably the general pattern for the dosimetry is that procedures changed over time, as might be expected. For some procedure changes the consequences may be significant or at best not be clear; in others it is not clear as to whether certain procedures have actually been implemented in the data set we were provided with. Some of the more notable areas of concern are discussed below.

One notable change through time appears to have been improvements in badge quality. These improvements have come both in the expansion of dose sources considered (e.g. neutrons, various X-ray sources, etc.) as well as improvements in the badge sensitivity to low level exposures. In particular there were at least three different badge types used successively prior to 1964 (ref. 8), each representing an improvement to the previous version. In particular, the ability to accurately assess neutron dose may have been totally inadequate prior to 1950. Further, there have been reports that some doses for workers may have been estimated from work area measurements rather than from actual employee badge readings.

Interpretation of any analysis results would require full consideration of the effects induced by changes in both the sensitivity and quality of the dose data if these effects exist in our data extract file.

To further complicate matters, procedures in recording the badge data have changed over time. Two changes are notable here. First, the frequency of badge readings has changed dramatically over the years. In the early years badges were read weekly, followed by a change to bi-weekly readings. Subsequently the badges were read monthly and most recently badge readings were taken yearly. Keep in mind that up until approximately 1963 or 1964, the badge threshold was approximately 30 mr and that the reporting procedure for the data collection process may have been to record zero dose if the threshold was not exceeded. When there was no badge reading threshold a zero may still have been recorded if the dose were below 20 mr.

The consequence of the procedure used to record the doses in the data collection procedure in conjunction with changes in the badge reading frequencies may be severe. One might expect that for monitored workers the average yearly dose recorded would be lower in the early years and higher in later years, since in the early years it would be hard for the dose to accumulate over the threshold due to frequent badge readings. This could be the case even though the true average dose might be approximately constant over time. One further complicating feature when the badge threshold was not exceeded may be that for the very early data the threshold value may have been reported as the dose and then at a later time a zero may have been reported. If this were the case we would see somewhat higher yearly doses in the early years, a subsequent reduction when zeros were reported, and finally an increase as badge readings intervals were increased. In any case, this type of variation may have severe consequences on the interpretation of the analysis results and a full

explanation of the procedures used in the data collection process must be available for responsible conclusions to be produced.

Another aspect of the data collection process of concern is the years for which doses from various sources were incorporated into the data. We have conflicting information with regard to this point which may or may not be related to differing forms of the data file. Hanford personnel indicate that the data for each source is complete, back to the initiation of operations. A report in Mancuso's progress reports, at a time when worker exposure records were reported to have been complete, indicates that data for each source is complete back to varying times, at least for the file at Oak Ridge as shown in Figure 2. A preliminary sample output (Figure 3) contained in the same report shows no radiation records for each source prior to the year in which the relevant data is reported on tape in Figure 2.

Certainly things may have changed subsequent to the time of the report but we were unable to locate any mention of these changes in subsequent progress reports. This does not mean changes did not occur, however, because others working on the project began submitting their own progress reports at about this time. However, if the doses at the Oak Ridge Facility were not updated to include doses received prior to those reported in Figure 2, one might expect to see an increase in the average yearly dose over time. Again the consequences of this would be important in the development of conclusions.

Sources of Exposure Data

<u>Year</u>	<u>Beta-Gamma</u>	<u>X-Ray</u>	<u>Neutron</u>	<u>Tritium</u>	<u>Extremity</u>
1944	Tape				Photometry Records
1945	"				"
1946	"				"
1947	"				"
1948	"				"
1949	"			Bioassay Result Cards	"
1950	"		Hist. File	"	"
1951	"		"	"	"
1952	"		"	"	"
1953	"		"	"	"
1954	"		"	"	"
1955	"		"		"
1956	"		"		"
1957	"	Tape	"		"
1958	"	"	"		"
1959	"	"	Tape		"
1960	"	"	"		"
1961	"	"	"	Front of 1962 Year End Report	"
1962	"	"	"	Tape	Tape
1963	"	"	"	"	"
1964	"	"	"	"	"

Table 13 - Summary of Sources of Exposure Data at Hanford

Figure 2. Reported Source Summary of Exposure Data at Hanford from Ref. 13.

DATE	06/26/69	OCCUPATIONAL RADIATION FILE				PAGE	33				
SOCIAL SECURITY NUMBER	PAYROLL NUMBERS	FAST NAME	INITIALS								
YEAR	SITE CODE	RETA	GAMMA	X-RAY	NEUTRON	TRITIUM	RINGS	PERFORATING	SKIN	EXTREMITY	
44	-	.00	.00	.00	.00	.00	.00	.00	.00	.00	
45	-	.00	.00	.00	.00	.00	.00	.00	.00	.00	
SOCIAL SECURITY NUMBER	PAYROLL NUMBERS	FAST NAME	INITIALS								
YEAR	SITE CODE	RETA	GAMMA	X-RAY	NEUTRON	TRITIUM	RINGS	PERFORATING	SKIN	EXTREMITY	
48	-	.12	.03	.00	.00	.00	.00	.03	.15	.15	
49	-	.14	.03	.00	.00	.00	.00	.02	.12	.12	
SOCIAL SECURITY NUMBER	PAYROLL NUMBERS	FAST NAME	INITIALS								
YEAR	SITE CODE	RETA	GAMMA	X-RAY	NEUTRON	TRITIUM	RINGS	PERFORATING	SKIN	EXTREMITY	
46	-	.04	.04	.00	.00	.00	.00	.04	.08	.08	
47	-	.31	.15	.00	.00	.00	.00	.15	.46	.46	
48	-	.03	.00	.00	.00	.00	.00	.00	.03	.03	
49	-	.36	.00	.00	.00	.00	.00	.00	.45	.45	
50	-	.00	.14	.00	.00	.00	.00	.14	1.24	1.24	
52	-	.00	.00	.00	.00	.00	.00	.00	.00	.00	
53	-	.27	.36	.00	.00	.00	.00	.36	.63	.63	
54	-	1.22	1.15	.00	.00	.00	.00	1.15	2.37	2.37	
55	-	1.39	1.11	.00	.00	.00	.00	1.11	2.50	2.50	
56	-	.72	.68	.00	.00	.00	.00	.68	1.40	1.40	
57	-	.15	.04	.00	.00	.00	.00	.04	.19	.19	
58	-	.00	.70	.12	.00	.00	.00	.74	.82	.82	
59	-	.00	.24	.10	.00	.00	.00	.28	.34	.34	
60	-	.00	.32	.04	.00	.00	.00	.33	.36	.36	
61	-	.00	1.14	.35	.00	.00	.00	1.26	1.49	1.49	
62	-	.03	.65	.10	1.86	.00	.10	2.55	2.64	2.64	
63	-	.20	.18	.01	.38	.00	.00	.56	.77	.77	
64	-	.02	.41	.05	.28	.00	1.20	.71	.76	1.96	
SOCIAL SECURITY NUMBER	PAYROLL NUMBERS	FAST NAME	INITIALS								
YEAR	SITE CODE	RETA	GAMMA	X-RAY	NEUTRON	TRITIUM	RINGS	PERFORATING	SKIN	EXTREMITY	

Table 16 - Print out Showing Content of the Occupational Radiation File, Hanford

Figure 3. Reported Preliminary Sample Record From Oak Ridge
For Hanford Data as Reported in Ref. 13.

There is yet another conflicting report with regard to the exact nature of the dose data collection procedure. The data for x-rays prior to 1957 may have been combined with the Beta and Gamma doses (Ref.12). The consequences of this effect would depend on exactly how the doses were combined to form the penetrating dose. However, one might suspect that the x-ray data before 1957 (if it's contained in the Beta-Gamma dose) would have a different factor applied (1.0) than the x-ray data after 1957 (.35).

One might expect that the effect of this error if it exists in the data we have, would be to cause a decrease as a function of calendar years in the average yearly doses received by exposed workers while working, assuming a constant true x-ray exposure. The decrease would be caused by an inclusion at full dose in early years up to 1957, but a consideration of only .35 of the full dose after 1957.

In an attempt to resolve the above concerns we attempted within the constraints of the variables presented to assess just what the average yearly dose was for those Hanford deaths who are classified as "exposed" in the data extract file. This plot is shown in Figure 4.

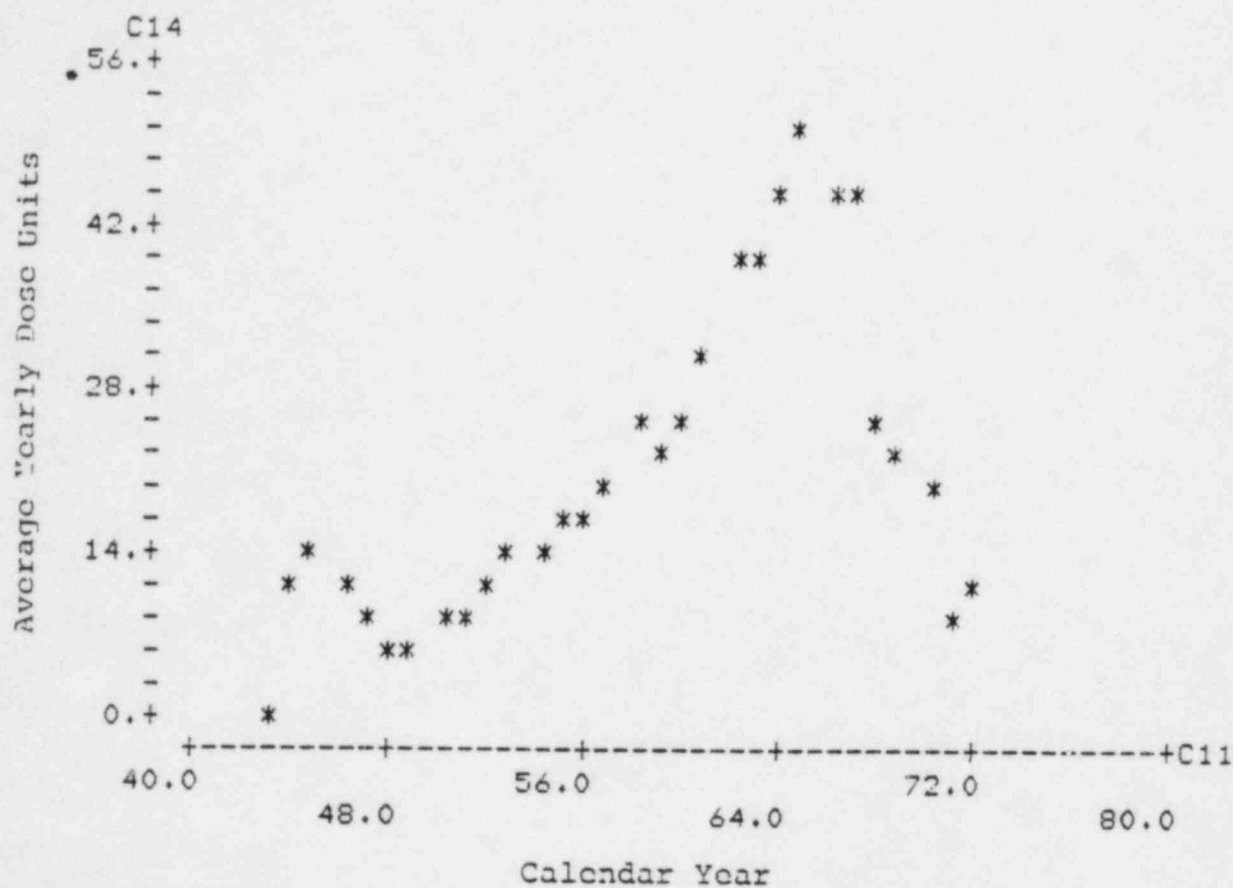


Figure 4. Average Yearly Dose Received by Exposed Workers While Employed Based on Semi-time Averaged Doses.

The exact causes for the shape of the curve (Figure 4) may be related to a combination of one or more of the possible effects which may be present in the data as discussed above or perhaps others which will be discussed in the following section. It should also be

recalled that the data provided to us in regard to dose-time histories was in reasonably broad time increments and as such the above plot will reflect a semi-time averaged view of the true average yearly dose which would be present if we had more detailed data.

Nevertheless, the implications of the graph are that serious time related effects are present in the data. It emphasizes the need for a detailed description of the exact background for this particular data extract file. Further, the plot suggests that extreme care be used in the interpretation of any analysis results using this data until a full and satisfactory explanation and understanding of this plot is available.

2.4.3 Pre- and Post- Employment Doses

According to several sources (ref. 8, 9, 10), the pre-employment doses for workers at Hanford were obtained by first asking the new employee whether there had been any previous employment where exposure might have been experienced. If the answer was affirmative the health records from previous facilities were requested. When and if they were received, they were apparently installed in an off-site radiation record, although the date assigned to the radiation was apparently the date of the receipt of the material at Hanford rather than the time period over which the dose was received. It is not known to us whether these pre-employment off-site radiation exposures have been included in the data we have, since we have seen conflicting reports with regard to its presence or absence from various data sets. If the data extract file did include this pre-employment exposure recorded on the dates received this might contribute in conjunction with other factors to the explanation of the early peak seen in Figure 4. However, it has been pointed out to us that the safety procedures at Hanford may have been very poor in the early years which in conjunction with the badge reading effects discussed earlier may be sufficient to explain this early peak.

With regard to post-employment exposures, it has been consistently reported that these doses were not collected and cannot be present in the data. This facet of the reported data collection procedure has been the most consistently reported feature of the data. We can definitely show that this feature (i.e. the

non-existence of dose after the final year of employment) is not displayed in the data extract file we have. It is perhaps this contradiction which more strongly than anything else suggests that extreme caution be exercised in any consideration of the analysis results.

We have examined our data file and have found that there are 138 cases for which post-employment doses exist in the dose history. Of these, 130 are white males representing approximately 5.8% of the total 2226 exposed white males in the file. An examination of these cases shows that generally the doses recorded after the final year of employment are likely to be two to three times the total dose recorded during the reported initial and final years of employment at Hanford. The computer program to assess whether post-employment doses exist in the data is contained in Appendix C in conjunction with its output.

The effects of such data problems are, of course, considerable. If the data indicating that doses are received after the end of employment are simply erroneous, then it reflects on the quality of the remaining data. If the data is correct, but was inadvertently included for some cases in the file, then it implies that doses received after employment at Hanford are not negligible, thus affecting quantitative values of possible dose relationships to cancer. Thus, in either case the effect of this finding is to cast serious concern on the reliability of any results based on this data extract file.

We pointed out this significant finding to the CTM and requested new data. The request for new data was denied, although the CTM did request verification of

the findings from other research groups working with this data. We see no reason, however, that these findings would not be substantiated by others.

2.5 Other Concerns

There are many other concerns with regard to data we did not receive, in addition to the concern for the meaning of the data which we did receive. These additional concerns will be discussed briefly below.

2.5.1 Other Exposures

We have not received data which is available with regard to other exposures. Other exposure information which does exist includes internal and accidental depositions. The lack of information with regard to the several hundred accidental depositions known to exist, not to mention the large amount of internal dose information available, is a serious constraint on the development of a responsible analysis.

If the pre-employment exposures are not included in the data they certainly are available and should be considered, although they should be provided as a separate data element.

Medical x-rays were shown in Mancuso's study to be on the average a significant fraction of the radiation received by a worker. Individual records for various procedures show that some workers could easily have received very large exposure from medical x-rays. This data is available for all workers, and the results of the medical x-ray study seem to point out that this is a source not to be neglected if possible.

Other occupational exposures to such things as carcinogenic materials like asbestos through involvement with specific industries at times other than when at Hanford are not included. They may, however, be available since work histories maintained by the Social Security Administration were used in the data collection effort. The inclusion of this information would be a desirable addition.

2.5.2 Cause of Death

The fact that a worker had died was established using the Social Security Administration (SSA) data file in conjunction with the worker's Social Security number, using the information provided by the SSA death certificates were obtained. The causes of death on the death certificate were recoded by a trained nosologist (ref. 8). The accuracy to which these assessments were made, not to mention potential errors on the death certificates which may be present due to lack of recognition of certain types of cancer in earlier years, is unaddressed. It is the case that up to 6 causes of death were recorded in an order reported to be primary, secondary, and tertiary. The consideration of only the primary cause of death raises serious questions in the sense of the actual cause of death (e.g. heart failure) which may have been brought on by stresses induced by cancer or treatment for cancer. The extent to which this phenomena may be present in the data cannot be assessed since only the primary cause of death is provided.

2.5.3 Initial and Final Year of Employment and Total Years of Employment

When considered in conjunction with the other data elements provided to us it is important to at least be aware that these variables do not allow recognition of the situation in which a worker leaves Hanford to work elsewhere and then returns to Hanford after some time interval. A check of all the cases in our data file shows that the variable total years of employment is (to within ± 1 year) simply the difference between initial and final years of employment. (The discrepancy

of ± 1 year comes about because total years of employment is recorded to one-tenth year while initial and final years are recorded to one year.) Thus we do not know what the true employment time periods were in this data set.

2.5.4 Monitored versus Exposed

Unfortunately the data we have indicates whether a worker was exposed or not exposed at some time during employment at Hanford. An exposed worker is one for which a dose was recorded. There is another variable available which we did not receive indicating whether the subject was monitored for radiation. One can see that if a worker was not monitored there could be no dose recorded. Thus a "non-exposed" worker did not necessarily receive zero dose. Further, the fact that a worker was monitored would not imply that they were monitored continuously at Hanford nor would an "exposed" worker have been monitored for the entire work period at Hanford. These effects might at least have been addressed if the yearly dose readings and the "monitored" variable had been provided to us.

2.6 Comparison to Data of T. Mancuso

Since the data analyzed in this report is from the same source as that analyzed by Mancuso, Stewart, and Kneale in 1977 (Ref. 1) it seems appropriate to compare the data provided to us with that used in the above paper. Table 4 is a comparison of our data to the data appearing in Table 3 of the Mancuso paper while Table 5 is a similar comparison with Table 11 in that same paper. Both tables are for male workers only.

It can be seen that the actual numbers of cases differ slightly between the two data sets. There are more total cases in our data but there are some causes of death where we have fewer cases either totally or for exposed workers only.

There are also differences in the mean doses which in some cases are not insignificant, most notably for lung and brain cancers. It can also be seen from the mean doses for non-cancers, RES neoplasms, and solid tumors that if there is an effect arising from these differences it is in the direction of reducing the doses received by persons dying of cancer and to increase those received by persons dying of causes other than cancer.

It is curious to note in Table 4 that of five diseases (multiple myeloma, pancreas, brain, lung, and kidney) which in our findings might be suspected to show dependencies of cancer incidence on dose received, three (brain, lung, kidney) show significant reductions in the mean dose relative to Mancuso's data while two (multiple myeloma and pancreas) show no significant

change. These last two are the same ones for which other researchers (notably Land) have also found significant relationships to radiation. One of these, pancreas, is a disease whose dose distribution is severely affected by increments of data after the final year of employment (see section 2.4.3). Multiple myeloma is characterized in this data by having only 8 exposed cases of which 3 are at anomalously high dose levels. The additional case (the sixth) in which we found suggestions of dose dependence was unspecified secondaries (ICD 199) which is not represented separately in Table 4.

Table 11 in the Mancuso paper is an examination of the trend in proportions of death by cancer as a function of dose controlled for age at death in 10 year intervals. Table 5 compares the proportions found by Mancuso, et. al., with similar proportions derived from the present data. It will be noticed that again the data is generally similar but that there is a tendency for the proportion of cancers at high doses to be reduced and those at low doses to be increased. In fact, if one ranks the differences in order by algebraic magnitude from most positive to most negative, one arrives at the rankings given in Table 3 to which can be applied a Spearman Rank Correlation Test. The rank correlation coefficients are shown in the last column of Table 3. For 5 pairs significance at the .10 level is reached when ρ exceeds .7 and significance at the .05 level is reached when ρ exceeds .8. In three age categories the coefficient of rank correlation is .7 or more and it is negative in only one of the five categories.

Mancuso, et. al., use a test of the same type to examine their data for a correlation of increase in proportion of death by cancer with increasing dose. They find coefficients of rank correlation of 0.1, 0.0, 0.3, 0.5, and 0.9 respectively for the various age groups. The significance of these correlations is tested by comparing the average value of these coefficients to the mean of 0.0 expected from a set of random rankings. In their case, the average is 0.46, which is different from the test mean of 0.0 by more than two standard deviations. We notice that in our data the results are almost the same except in the age group 60-69 where the rankings are changed and the coefficient is reduced from 0.5 to -0.1 thus reducing the average to 0.34 which is not more than two standard deviations away from the null result of 0.0.

The point of examining the comparison between the present data and the Mancuso data is not to suggest that results derived by Mancuso, et. al., would no longer be substantiated by the new data because the new data is different but rather to see whether or not the two sets of data should be considered to be compatible. While it seems that there are systematic differences between the two sets of data, it is more noteworthy that the differences are in fact quite small in magnitude. It is true that the outcome of one certain test cited in the Mancuso paper is altered, but one should recognize that this is more a consequence of the marginal nature of this test than of drastic changes in the data.

What is more bothersome is to understand why two separate extractions from the same data should produce different information, given that the difference is not

merely the consequence of the accumulations of additional cases as time has gone on.

In a normal sequence of events one would want to investigate the procedures used to prepare both sets of data in order to discover any sources of discrepancy. Since this alternative is not open, one can only note the difference and recognize that there are some uncertainties in the accumulation of the data which may have to be recognized in any evaluation of the results.

TABLE 4

MEAN DOSES BY CAUSE OF DEATH
 Column A - Results of Mancuso, et. al.¹
 Column B - Results of Current Analysis

Cause of Death by ICD Codes	Total Cases		Cases Exposed		Mean Dose-Total		Mean Dose-Exposed	
	A	B	A	B	A	B	A	B
Non-Cancers								
0-136 Infective	29	32 ²	16	18 ²	43	50	79	90
210-239 Benign Neoplasms	10	10	4	4	15	15	39	39
244-289 Endocr.	54	65	34	40	96	150	153	243
290-389 CNS	36	37	20	21	94	92	169	162
390-458 CVS	1837	1885	1149	1184	105	106	167	168
460-519 Respiratory	194	194	108	107	74	74	133	134
520-577 Digestive	139	140	83	86	114	136	190	221
800-999 Accidents	450	459	271	274	94	98	156	164
580-796 Residue	101	100	57	55	85	43	151	79
RES Neoplasms								
200-202 Lymphomas	34	35	28	28	119	117	145	146
203 Myelomas	11	11	8	8	775	775	1066	1066
204 Lymphatic Leukemia	3	3	2	2	19	19	29	28
205 Myeloid Leukemia	11	12	6	6	122	111	223	223
206-209 Residue	5	5	3	3	12	12	19	19
Solid Tumors								
140-149 Mouth & Pharynx	24	23	14	14	89	79	152	129
151 Stomach	38	38	26	26	60	58	86	85
153 Large Intestine	61	63	48	50	135	133	171	167
154 Rectum	19	19	16	16	99	99	118	118
150,152 Other Intestinal	18	20	10	10	32	28	58	57
155-156 Liver, Gall Bladder	18	19	10	10	31	29	56	56
157 Pancreas	49	51	31	32	253	253	399	404
162-163 Lung	192	195	130	129	169	142	249	214
185 Prostate	43	43	21	21	42	42	87	87
189 Kidney	21	23	14	15	187	171	281	263
186-188 Other G.U.	15	15	10	10	82	82	123	122
191 Brain	18	21	11	14	220	194	361	291
Residue	90	92	54	55	81	76	135	127
Totals:								
Non-Cancers	2850	2922	1742	1789	99	102	162	166
RES Neoplasms	64	66	47	47	219	213	299	299
Solid Tumors	606	622	395	402	130	119	199	184
TOTAL	3520	3610	2184	2238	107	107	172	172

¹ Mancuso, T. F., Alice Stewart, and George Kneale, Radiation Exposures of Hanford Workers Dying from Cancer and Other Causes, Health Physics, Vol. 33 (November 1977) p. 376.

² Including 2 with no cause of death (1 exposed).

TABLE 5

Proportion of Deaths Due to Cancer by Age and Dose for Male Workers
Comparison Between Results of Mancuso, et. al.¹, and Results of Current Analysis

DOSE

Age	0	1-19	20-99	100-499	500 +	Total	p
≤ 39.9	11.5/ 113	13.1/ 61	10.2/ 59	8.0/ 25	20.0/ 10	11.6/ 268	.9
	9.3/ 108	10.9/ 55	8.6/ 58	8.3/ 24	22.2/ 9	9.8/ 254	or
	2.2/1 or 2	2.2/2 or 1	1.6/3	-.3/4	-2.2/5	1.8	1.0
40.0-49.9	11.3/ 203	18.3/ 82	21.9/146	22.8/ 79	9.5/ 21	17.0/ 531	
	13.0/ 185	15.9/ 82	21.9/137	23.0/ 74	11.8/ 17	17.3/ 495	.4
	-1.7/4	2.4/1	.0/2	-.2/3	-2.3/5	-.3	
50.0-59.9	20.9/ 340	14.2/155	23.6/199	20.9/158	26.8/ 56	20.7/ 908	
	19.3/ 331	16.1/137	24.5/200	21.9/155	31.0/ 58	21.2/ 881	.
	1.6/1	-1.9/4	-.9/2	-1.0/3	-4.2/5	-.5	
60.0-69.9	22.9/ 375	23.2/164	26.2/260	24.1/191	21.7/ 60	23.9/1050	.8
	22.2/ 360	21.6/162	26.6/248	25.0/184	22.6/ 53	23.7/1007	or
	.7/2	1.6/1	-.4/3	-.9/4 or 5	-.9/4 or 5	.2	.9
≥ 70.0	13.5/ 341	10.4/183	18.3/246	18.3/ 71	41.7/ 12	15.0/ 853	
	13.6/ 352	11.6/189	17.5/251	18.9/ 74	29.4/ 17	15.1/ 883	-.5
	-.1/3	-1.2/5	.8/2	-.6/4	12.3/1	-.1	
Total	17.4/1372	15.8/645	21.8/910	21.4/524	23.3/159	19.1/3610	.9
	16.9/1336	15.7/625	21.7/894	22.0/511	25.3/154	19.0/3520	or
	.5/1	.1/2 or 3	.1/2 or 3	-.6/4	-2.0/5	.1	1.0
p	.4	.45	.15	.5	-.6	.2	

¹ Mancuso, T.F., Alice Stewart, and George Kneale, Radiation Exposures of Hanford Workers Dying from Cancer and Other Causes, Health Physics, Vol. 33 (November 1977) p. 376.

KEY: % cancer deaths/total cases - Current Results
% cancer deaths/total cases - Mancuso Results
Difference in percents/rank

3.0 DATA ANALYSIS

The general data analysis methodology employed together with a summary of the data survey analyses are contained in Section 3.1. The discussion is, however, limited to a brief overview. A more detailed analysis of respiratory cancers is contained in Section 3.2.

3.1 Methodology and Data Survey Results

The analysis methodology employed was comprehensive in that it applied a number of differing analytical tools to the data. The approach relied, however, not only on the use of differing statistical procedures but also on the consideration of a wide variety of subject groupings.

The data were first reviewed to identify the univariate distributions present in the data. An example of this procedure for the whole data set is contained in Appendix A. Similar distributions were developed for various case subgroups. These subgroups included cases accepted when filtering for various race-sex groupings, followed by subsequent filters on exposure and various causes of death. At the completion of this procedure it was apparent that if race and sex were to be considered as relevant factors, then only the white male group had an adequate number of cases for the analysis approach anticipated. All remaining statistical analyses considered only cases which were white males.

Following the univariate review various bivariate relationships were examined for the white male subgroup. Cumulative dose comparisons with various causes of death were examined for various groups.

In general, chi-square and t-test analyses were used to evaluate whether notable effects were being observed. An example of such an analysis is shown in Table 6 where the expected and observed dose frequencies for various causes of death are compared using the chi-square method.

EXPECTED FREQUENCIES ARE PRINTED BELOW OBSERVED FREQUENCIES

CAUSE OF DEATH

DOSE VARIABLE	CAUSE OF DEATH												TOTALS
	CAUSE OF DEATH												
	0-139	1240-409	1412-799	1410-411	1800-999	1157	1161-163	1200-202	1140-209				
	1	9	418	355	148	14	55	17	123				
	1-50	8.81	399.51	369.01	138.51	16.51	70.31	15.51	120.91				
	2	4	208	208	63	8	48	7	63				
	51-150	4.71	213.61	197.31	74.11	8.81	37.61	8.31	64.71				
	3	2	77	68	26	3	11	2	30				
	151-300	1.71	76.81	70.91	26.61	3.21	13.51	3.01	23.31				
	4	2	70	83	31	7	22	4	18				
301+	1.81	83.11	76.81	28.91	3.41	14.61	3.21	25.21					
TOTALS	17	773	714	268	32	136	30	234					

TOTAL CHI SQUARE =

.01 + .86 + .53 + .65 + .39 + 3.72 + .14 + .04 +
 .10 + .15 + .58 + 1.65 + .08 + 2.89 + .20 + .04 +
 .06 + .00 + .12 + .01 + .01 + .47 + .32 + 1.96 +
 .02 + 2.07 + .50 + .17 + 3.68 + 3.72 + .19 + 2.04 +

= 26.97

*Excluding ICD 170, 174, 193, 205, 206, 203, 210-239

Table 6. An example of a Chi-square Analysis of Dose Versus Cause of Death.

In addition, rank tests were used in an attempt to approximate results previously obtained by others. These are reported in section 2.6.

Due to the uncertainty in the validity of cases characterized as unexposed, as discussed in section 2.5.4, it was decided at this point that further survey analysis would consider two general groups. The first group would include both the exposed and unexposed white male (EUWM) workers. The second group would contain simply the exposed white male (EWM) workers.

The varying radio-sensitivity of cancers depending on the particular cells affected was recognized and considered important enough to call for separation of primary causes of death into consistent cancer groups. The ICDA codes used to group various cancers is shown in Table 3 contained in section 2.3. Only those cancer groups which had more than eight cases were considered in subsequent analyses.

In general, subsequent analyses considered the response as the probability of a particular cancer and no-cancer. The cancer group would include those cases which fell within a particular group specified by Table 3. The no-cancer group would contain cases with a primary cause of death which was not considered to be a cancer. However, we could clearly see the effects accidents had on the percent of cases which died of cancer as a function of ages, as shown in Figure 5. We recognized that accidental deaths from external causes are not diseases and may be considered to be a competing risk which might mask the effects of radiation due to the strong dependence of accidental death on age. As a result, our subsequent survey analyses considered two

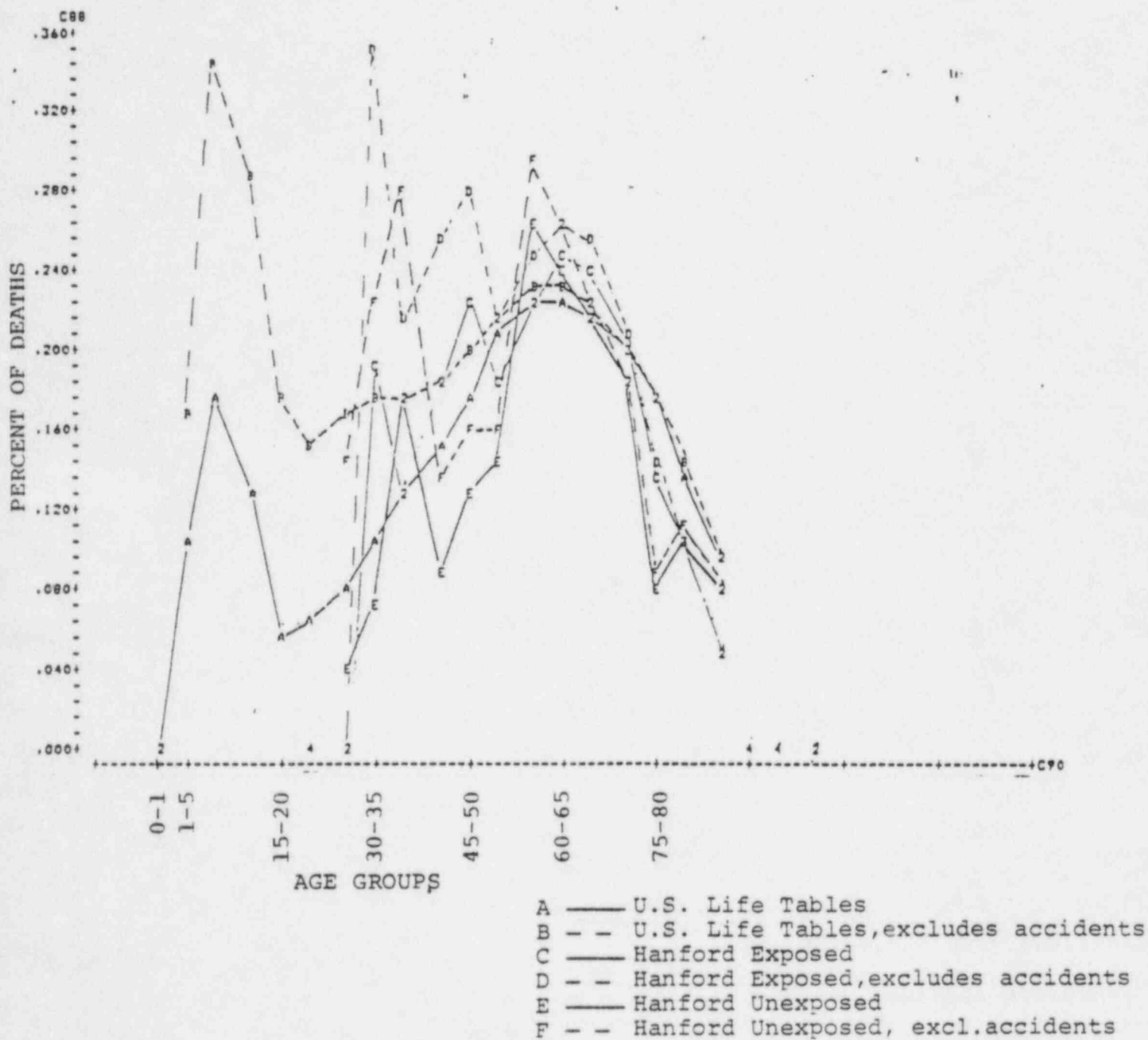


Figure 5. Percent of Deaths Due to Cancer As a Function of Age for White Males in Various Populations

additional subgroups of the EUWM and EWM groups mentioned previously. These additional subgroups were characterized by the non-cancer group containing either all non-cancers or all non-accident non-cancers, and denoted by the letters ALL or NA respectively. Thus, actually four general groups were evaluated for each cancer group of interest. These were 1) The exposed and unexposed white male workers with all non-cancers (EUWM-ALL); 2) The exposed and unexposed white male workers with accidental deaths excluded from the non-cancer group (EUWM-NA); 3) The exposed white males with all non-cancers (EWM-ALL); and 4) The exposed white males with no accidental deaths included in the non-cancer group (EWM-NA). The number of cases available in each group is shown below:

	EUWM-ALL	EUWM-NA	EWM-ALL	EWM-NA
Non-Cancers	2895	2446	1776	1508
All Cancers	684	684	449	449
Total	3579	3130	2225	1957

Table 7 Breakdown of Cases for Various Subgroups Considered in the Analysis.

It should be noted that the data provided in the above table excludes some cases in the data set which contained invalid codes for one or more variables.

3.1.1 Discriminant Analyses

Having identified the general groups of data to be considered it was desired to scan the data on a detailed basis to identify those variables which exhibited a relationship to the incidence of particular cancers for each data group. An automated procedure to select relevant variables was desirable since an additional 15 variables (shown in Appendix D) had been created from the original data elements given to us. Stepwise discriminant analysis was particularly suited to this task, since the response groups could characterize a particular cancer (e.g. pancreas) and no-cancer.

Program used to do the discriminant analyses was BMD-7M. The procedure is based on the assumption of equal population covariances for the groups (as well as multivariate normality of the discriminating variables, but this normality assumption is usually not critical). The sample variances of many of the discriminating variables are different enough between the groups that one could question the assumption of equal population covariances. However, since the goal in using discriminant analysis was simply to pick out those variables which bear a strong relationship to the incidence of cancer, it was felt that the above objection would present no serious problem. The cure for unequal population covariances is to use quadratic discrimination, but it was felt that this procedure would not produce a set of discriminating variables different from that obtained from linear discriminant analysis. Furthermore, quadratic discriminant analysis is sensitive to departures from normality. (See Lachenbruch, pg. 20.) At the conclusion of the analysis it did, however, appear that in some cases the analysis did suffer from lack of homogeneity of variance.

At each step of the discriminant analysis the BMDP program computes an F-statistic for each variable to enter which measures the amount of discriminating power which that variable has. As new variables are entered, the F-statistic for variables previously entered can decrease to the point where the old variable is no longer providing significant discrimination. In such a case, the old variable may be removed at some step. This removal did not occur in our discriminant analyses. For the set of discriminating variables determined at each step of the stepwise procedure, the BMDP program computes the probability of membership for each case in each group and uses this probability to classify each case into the group for which it has the highest probability of membership. The probability is a posterior probability based on a prior probability distribution of group membership specified by the user. In our discriminant runs we always specified equal priors since we were interested solely in the relationship between the incidence of cancer and the variables characterizing the workers history, and we did not want to make use of information about the relative frequency of occurrence of various causes of death. In our runs the probability of overall correct classification varied roughly from 50% to 90%. When using two groups, the probability of correct classification of a particular cancer occasionally dropped below 50%. A more complete description of the computational aspects of discriminant analysis appears in Ref. 14.

Table 8 summarizes the discriminant analysis results obtained for each specific cancer considered. The specific cancer groups considered are shown along the top edge of the table. Under each cancer label are four columns.

VARIABLE	RESPIRATORY 161-163				RECTAL 153-154				ESOPHAGEAL & STOMACH 150-151			
	1 EWM- ALL	2 EWM- NA	3 EWM- ALL	4 EWM- NA	1 EWM- ALL	2 EWM- NA	3 EWM- ALL	4 EWM- NA	1 EWM- ALL	2 EWM- NA	3 EWM- ALL	4 EWM- NA
1 DEATHAGE		3				2		*				
2 INITLYR		*	2	2								
3 FINALYR												
4 TOTALYR					*		*					
5 EXPOSURE	C	C			1	1						
6 CUMDOSE												
7 CDOS 3+									**			
8 CDOS 5+												
9 CDOS 10+									*	**		
10 CDOS 15+												
11 CDOS 20+												
12 CDOS 25+												
13 YRDEATH	2	2								*	1	1
14 DT1	3Δ											
15 DT2								**				
16 DT3												
17 DOS0-3												
18 DOS 4-5	*		*	*								
19 DOS6-10												
20 DOS11-15												
21 DOS16-20	4	**	3	3								
22 DOS21-25												
23 DOS25+												
24 MAXDOS	**		**	**								
25 TMAXDOS												
26 AGE SQ	1	1	1	1	**				1	1	2	*
27 CAUSE												
No. Cancers	202	202	136	136	82	82	66	66	56	56	35	35
No. Non-cancers	2895	2446	1776	1508	2895	2446	1776	1508	2895	2446	1776	1508
% c.c. cancer	67.3	64.9	58.8	51.5	80.5	73.2			73.2		57.1	54.3
% c.c. non-cancer	57.0	54.1	56.3	63.5	38.7	47.8			40.8		60.8	60.7

TABLE 8 Summary of stepwise discriminant analyses, showing the order in which the variables were chosen for inclusion in the model.

VARIABLE	PANCREAS 157				LYMPHOCYTIC LEUKEMIA 200-204, 204				PROSTATE 185			
	1 EUWM- ALL	2 EUWM- NA	3 EWM- ALL	4 EWM- NA	1 EUWM- ALL	2 EUWM- NA	3 EWM- ALL	4 EWM- NA	1 EUWM- ALL	2 EUWM- NA	3 EWM- ALL	4 EWM- NA
1 DEATHAGE					1	1	1	1	1	1	1	1
2 INTLYR	**											
3 FINALYR												
4 TOTALYR								*				
5 EXPOSURE					C	C			C	C		
6 CUMDOSE												
7 CDOS 3+												
8 CDOS 5+												
9 CDOS 10+												
10 CDOS 15+												
11 CDOS 20+												
12 CDOS 25+												
13 YRDEATH												
14 DT1			**			**						
15 DT2							**	**				
16 DT3			*									
17 DOS0-3					*							
18 DOS 4-5	1	1	1	1								
19 DOS6-10						*						
20 DOS11-15												
21 DOS16-20												
22 DOS21-25												
23 DOS25+	*		***	*	**		***					
24 MAXDOS												
25 TMAXDOS					2	2	*		2	2	*	*
26 AGE SQ	2	*										
27 CAUSE												
No. Cancers	51	51	32	32	38	38	30	30	43	43	21	21
No. Non-cancers	2895	2446	1776	1508	2895	2446	1776	1508	2895	2446	1776	1508
% c.c. cancer	21.6	13.7	21.9	21.9	68.4	73.7	63.3	66.7	62.8	62.8	66.7	57.1
% c.c. non-cancer	88.1	91.7	90.4	90.8	63.7	66.9	58.7	61.8	61.6	61.7	57.5	56.2

TABLE 8 Summary of Discriminant Analyses (cont.)

VARIABLE	BRAIN 190-192				KIDNEY 189				MOUTH PHARYNX 140-149			
	1 EWM- ALL	2 EWM- NA	3 EWM- ALL	4 EWM- NA	1 EWM- ALL	2 EWM- NA	3 EWM- ALL	4 EWM- NA	1 EWM- ALL	2 EWM- NA	3 EWM- ALL	4 EWM- NA
1 DEATHAGE	2	1	2	1								
2 INITLYR												*
3 FINALYR												
4 TOTALYR												
5 EXPOSURE												
6 CUMDOSE												
7 CDOS 3+												
8 CDOS 5+												
9 CDOS 10+												
10 CDOS 15+												
11 CDOS 20+												
12 CDOS 25+												
13 YRDEATH					**	2	1					
14 DT1	3	2	3	2								
15 DT2												
16 DT3							*	1				
17 DOS0-3	**	*	**		1	1	2					
18 DOS 4-5												
19 DOS6-10												
20 DOS11-15												
21 DOS16-20			*	**								
22 DOS21-25												
23 DOS25+	1	3	1	*	*							
24 MAXDOS												
25 TMAXDOS												**
26 AGE SQ	*						**		1	1	*	***
27 CAUSE												
No. Cancers	27	27	18	18	22	22	15	15	23	23	14	14
No. Non-cancers	2895	2446	1776	1508	2895	2446	1776	1508	2895	2446	1776	1508
% c.c. cancer	59.3	66.7	72.2	77.8	22.7	45.5	53.3	80.0	78.3	78.3		
% c.c. non-cancer	69.4	69.5	72.4	68.2	91.2	73.2	72.2	61.5	41.6	41.1		

TABLE 8 Summary of Discriminant Analyses (cont.)

VARIABLE	UNSPECIFIED SECONDARY 199				LIVER 155-156				SKIN CANCER 172-173			
	1 EUMM- ALL	2 EUMM- NA	3 EWM- ALL	4 EWM- NA	1 EUMM- ALL	2 EUMM- NA	3 EWM- ALL	4 EWM- NA	1 EUMM- ALL	2 EUMM- NA	3 EWM- ALL	4 EWM- NA
1 DEATHAGE							1	*	*	1	1	1
2 INIT'LYR				*							**	**
3 FINALYR			2	***						*	*	*
4 TOTALYR	*	**										
5 EXPOSURE					**							
6 CUMDOSE												
7 CDOS 3+												
8 CDOS 5+												
9 CDOS 10+												
10 CDOS 15+												
11 CDOS 20+												
12 CDOS 25+												
13 YRDEATH									**			
14 DT1				**								
15 DT2												
16 DT3												
17 DOS0-3					*							
18 DOS 4-5												
19 DOS6-10												
20 DOS11-15												
21 DOS16-20												
22 DOS21-25	1	*	1	1								
23 DOS25+	**											
24 MAXDOS												
25 TMAXDOS												
26 AGE SQ					1	*		**				***
27 CAUSE												
No. Cancers	27	27	13	13	19	19	10	10	13	13	10	10
No. Non-cancers	2895	2446	1776	1508	2895	2446	1776	1508	2446	2446	1776	1508
% c.c. cancer	11.1		53.8	23.1	73.7		70.0			53.8	60.0	60.0
% c.c. non-cancer	94.2		74.7	91.9	41.6		57.8			62.5	63.7	65.5

TABLE 8 Summary of Discriminant Analyses (cont.)

VARIABLE	SECONDARY LUNG CANCER 197				MULTIPLE MYELOMA 203			
	1 EWM- ALL	2 EWM- NA	3 EWM- ALL	4 EWM- NA	1 EWM- ALL	2 EWM- NA	3 EWM- ALL	4 EWM- NA
1 DEATHAGE								
2 INITLYR			*	*				
3 FINALYR								
4 TOTALYR								
5 EXPOSURE								
6 CUMDOSE								
7 CDOS 3+								
8 CDOS 5+								
9 CDOS 10+								
10 CDOS 15+								
11 CDOS 20+								
12 CDOS 25+								
13 YRDEATH	1	1						
14 DT1								
15 DT2								
16 DT3								
17 DOS0-3								
18 DOS 4-5								
19 DOS6-10							*	*
20 DOS11-15					2	2	2	2
21 DOS16-20					1	1	1	1
22 DOS21-25								
23 DOS25+								
24 MAXDOS					3	3	3	3
25 TMAXDOS							**	**
26 AGE SQ	*	*						
27 CAUSE								
No. Cancers	16	16	8	8	11	11	8	8
No. Non-cancers	2895	2446	1776	1508	2895	2446	1776	1508
% c.c. cancer	43.8	63.8			27.3	27.3	37.5	37.5
% c.c. non-cancer	62.6	65.6			97.3	97.3	97.2	97.9

TABLE 8 Summary of Discriminant Analyses (cont.)

These columns correspond to the four groups which were to be considered as mentioned previously. Specifically, the first column corresponds to the EUWM-ALL group, the second the EUWM-NA group. Column 3 contains the results of the analysis using the EWM-ALL group and column 4 the results of the analysis of the EWM-NA group for the particular cancer group of interest. The rows correspond to the variables considered for selection during the discriminant analysis. The numbers which appear in the columns correspond to the order in which each variable was selected for inclusion in the classification function. Up to five variables were allowed to be selected by the discriminant analysis as long as the F-statistic exceeded 3.0. The maximum number ever selected was 4. At the bottom of each column is presented a number of cases in each of the response groups and the correct classification percentage which resulted from the final classification function. Stars in the table indicate variables which would have been selected after the last variable selected if the F to enter had been set lower.

The letter C by the variable "exposure" indicates that this variable had an F-statistic of more than 2 on the initial step. For the EWM-ALL and EWM-NA "exposure" of course was not considered since all cases in these groups were exposed by definition.

To illustrate the interpretation of the table, consider the respiratory cancer analyses. The first of the four columns under this heading is a summary of the results found when the exposed and unexposed white males were considered. The response groups were, on the one hand, those cases with a cause of death described as respiratory cancer in Table 3, and on the other, those

cases with a non-cancer cause of death including accidental causes of death. We can see at the bottom of the column that there were 2895 non-cancer cases considered which were compared with 202 respiratory cancer cases. The first variable selected was AGESQ, measuring age squared as defined in Appendix D. Note that before any variables had entered the model, the exposure variable was found to be mildly significant as indicated by the C next to exposure. At the second step of the analysis, the variable YRDEATH entered. YRDEATH represents the calendar year of death. The third variable which entered the model was DT1 which is the time interval between the initial year of employment and the year of death. The fourth variable to enter was the dose which was recorded as being received in the time interval 16 to 20 years prior to death. We can also see that other dose variables might have entered the model had the F-to-enter been set low enough, as indicated by the stars. One star means it had the highest F-statistic at that point, two stars the second highest, etc.

We can also see that the correct classification function was 67.3% for the respiratory cancers and 57.0% for the no-cancer group. Thus from this column we have an indication of those variables which are likely to provide the best predicative capability for the incidence of respiratory cancer from those variables considered for the EUWM-ALL group.

A number of features present in Table 8 are perhaps worth noting. As a general rule, AGE or AGESQ appear as important factors in modeling the incidence of cancer

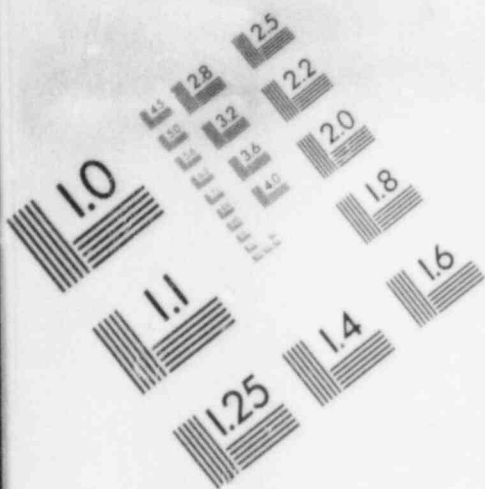
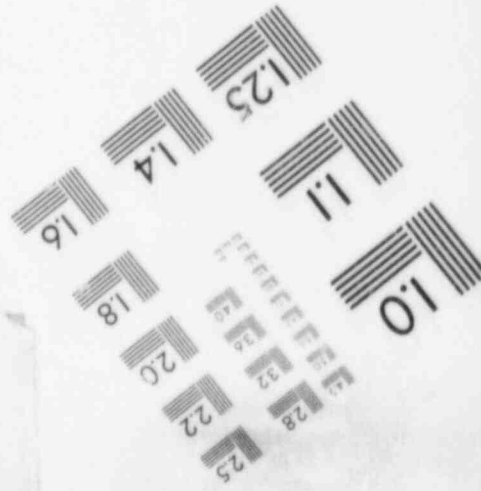
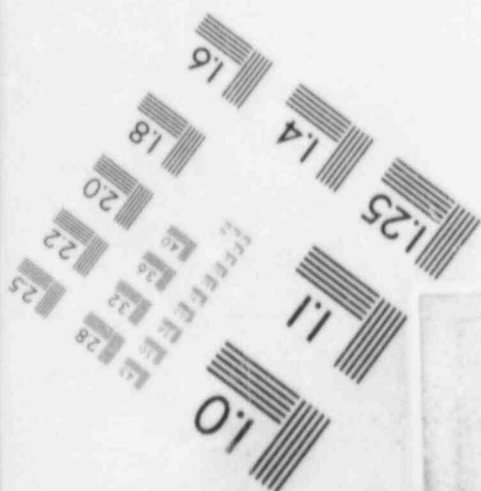
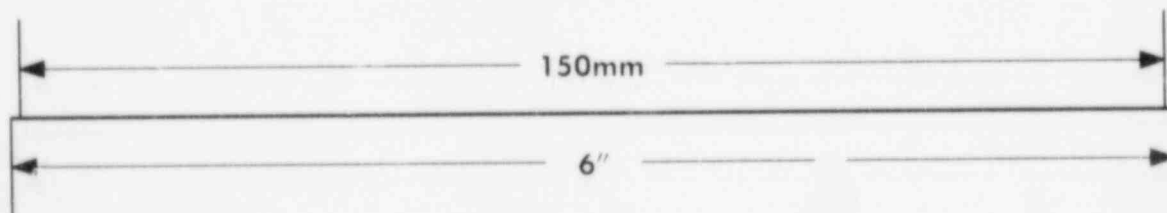
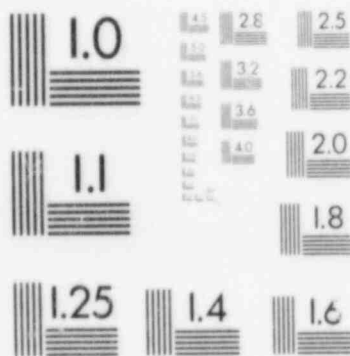
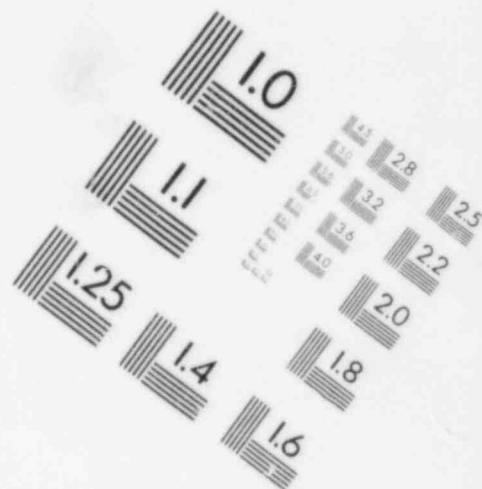


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for most cancer groups. Pancreas (157) cancer for the EWM-ALL and EWM-NA groups are notable exceptions, as are kidney cancers (189), unspecified secondary cancers (199), and multiple myeloma (203). Various calendar year effects such as the year of death (YRDEATH), initial year (INITLYR), and various length of time indicators such as total years of employment (TOTALYR), time from maximum dose (TMAXDOS) and DT1, DT2 and DT3 all appear as variables of interest for one cancer group or another. However, their significance may be classified in a general way as very marginal except in a few cases.

A very notable feature in the table is that the cumulative dose (CUMDOSE) was never selected as a variable to enter any model. The fact that the doses received in specific time intervals (e.g. DOS 4-5: dose received in the time interval four to five years prior to death) were selected on numerous occasions, explains the fact that the total cumulative dose was not selected. This fact may simply reflect the concept that there is a latency period between dose and cancer incidence, although the time intervals available to us and the manner in which the time intervals are modeled, are likely to be only a simple minded version of the true relationships. Notable by the inclusion of dose variables in their classification functions are: Respiratory Cancer (161-163), Pancreas (157), Brain (190-192), Kidney (189), Unspecified Secondary cancers (199), and Multiple Myeloma (203). In addition, dose variables were remotely sensitive although not selected in a number of other cancer groups.

The interpretation of the inclusion of the dose variables in the classification functions are of course subject to the concerns identified in section 2.

3.1.2 Logistic Regression Models

In the case of a model with two possible responses, e.g., death from cancer and death from cause other than cancer, the logistic regression model expresses the probability of one response as $p = e^Y / (1 + e^Y)$, or equivalently, as $\log [p / (1 - p)] = y$ where $y = \alpha + \sum \beta_j x_j$ is a linear combination of the covariates x_j with unknown parameters α and β_j which are to be estimated. The probability of the other response is then $1 - p$. The parameters α and β_j are estimated by the method of maximum likelihood. The logistic regression model has several features which make it more appealing than a model in which the data is categorized. First, the logistic regression model can handle continuous covariates as continuous variables. There is no need to categorize these variables; and since the choice of cutpoints is somewhat arbitrary and subjective, one would like to avoid splitting a variable into categories, if possible. Also, in the logistic regression model the probability comes out as a continuous function of a continuous covariate such as dose. There are no jumps in probability as one crosses a boundary. A second consideration which favors the logistic regression model over a categorical model is that when one is dealing with a number of categorical variables the number of cells increases rapidly and the number of observations per cell goes down rapidly. The categorical analysis does not behave well with small cell counts. Finally, the logistic regression model usually results in a simpler model since it contains only one parameter for each independent variable in the model. A possible objection to the logistic model is that it postulates a very specific form for the response probability, i. e., that $\log [p / (1 - p)]$ be a linear function of the independent

variables. However, if this relationship is not linear, one can add square terms, etc. to the model to achieve the desired linearity.

The stepwise discriminant analyses have identified a number of specific cancers in which some dose variable was selected. The next step in our approach at this point is to model the probability of death from cancer as a function of the variables suggested by the discriminant analyses. However, in view of the serious questions raised in section 2 concerning the data, most notably, 1) The marked increase in average dose over the years which the workers received, 2) The failure to distinguish between monitored and not-monitored cases, 3) The failure to distinguish internal depositions, and 4) The occurrence of 138 cases which have relatively large doses recorded after the final year of employment, we feel that no reliable interpretation can be placed on such models. Nevertheless, if one is willing to accept the data at face value, such models may be of interest. We have presented selected models for respiratory cancer, cancer of the pancreas and cancer of the brain in Appendix E. Also, the modeling of respiratory cancer, using exposed workers only, is subjected to a detailed analysis in section 3.2.

In Appendix E for each model the coefficients α and β_j are given, the chi-square value for testing statistical significance of the β_j . (This chi-square value has 1 degree of freedom), the value of $-2 \cdot \log L$, and finally, the decrease in $-2 \cdot \log L$ for the given model relative to the model with a constant alone. The size of $-2 \cdot \log L$ for a given model as compared to that for the constant model may be used as a measure of goodness of fit of the model to the data.

For the logistic modeling four subsets of the file of exposed white males were used, 1) all cases, 2) all cases less accidents, 3) exposed cases only, and 4) exposed cases less accidents. The main features of these models are the following. For respiratory cancer, statistical significance of the dose variables is borderline, at best. There seems to be a definite relation between cancer of the pancreas and dose. However, this conclusion is based on approximately 30 pancreas cases, of which 5 had relatively large post-employment doses (generally twice as large as the dose received during employment) recorded in the data file. Because of the uncertainty of the meaning of these doses, we would be hesitant to draw any conclusions until this question is cleared up. For cancer of the brain, the dose received 25 or more years before death is selected by discriminant analysis as being important. When this variable is put in the logistic model it also tests highly significant. However, when age at death and time from initial employment to death are controlled for, the dose variable becomes totally non-significant. We believe that further modeling work is desirable, but must wait until more basic questions concerning the data are answered.

3.2 Further Detailed Analysis of Respiratory Cancer

This group was chosen for further analysis because it had a large number of cases of cancer and because of the relationship of cancer to dose suggested by the discriminant analysis. Since the argument can be made that workers who have zero cumulative lifetime dose are in essentially different occupations from those who have dose, we have chosen here to work with "exposed" workers only, i.e., those whose cumulative lifetime dose is positive. There were a total of 2225 such cases in the file. When the non-respiratory cancers were removed we were left with 1912 cases, of which 136 or 7.1% were deaths from respiratory cancer. A stepwise discriminant analysis was done on this data using two groups, those dying from respiratory cancer (ICD 161-163) and those dying from causes other than cancer (ICD 1-139, 210-999). Twenty-six variables were used, 13 of the variables appearing in the data set originally sent to us, and 13 variables calculated from those, such variables as time from initial employment to death (DT1), dose received 0-3 years before death, etc. The complete list is described in Appendix D. The means of each of these variables are given in Table 9 and their standard deviations in Table 10. The F-ratios for four steps of the discriminant analysis are given in Tables 11 thru 14. For step 0 (Table 11) it can be seen that the most important variable is AGESQ which is defined as $[(\text{DEATHAGE}-60)/5]^2$. This expression defines AGESQ as a parabola with its vertex at age 60. This particular functional form was suggested by a plot of the percent of cancer deaths vs. categories of age as seen in Figure 6. The data for this plot is in Table 15 below.

MEANS				
	GROUP =	RESPCANC	NOCANCER	ALL GPS.
VARIABLE				
1	DEATHAGE	61.08750	60.05327	60.12683
2	INITLYR	46.97794	46.50507	46.53870
3	FINALYR	58.47059	54.65541	54.72452
4	TOTALYR	9.41618	8.07838	8.17354
5	EXPOSURE	1.00000	1.00000	1.00000
6	CUMDOSE	209.45588	166.43581	169.53138
7	CDOS 3+	190.44853	147.55630	150.60722
8	CDOS 5+	167.57353	128.12331	130.92939
9	CDOS 10+	106.43382	72.17342	74.81036
10	CDOS 15+	53.72059	38.81363	39.87395
11	CDOS 20+	16.56618	15.40428	15.48692
12	CDOS 25+	4.10294	4.22128	4.21287
13	YRDEATH	65.30147	63.97917	64.07322
14	DT1	18.32353	17.47410	17.53452
15	DT2	8.83088	9.52376	9.28870
16	DT3	13.57721	13.39893	13.41161
17	DOS0-3	19.50735	18.87950	18.92416
18	DOS4-5	22.87500	19.43300	19.67782
19	DOS6-10	61.13971	55.94989	56.31904
20	DOS11-15	52.71323	33.35980	34.73640
21	DOS16-20	37.15441	23.43933	24.36703
22	DOS21-25	12.46324	11.18300	11.27406
23	DOS25+	4.10294	4.22128	4.21287
24	MAXDOS	102.31615	89.53209	90.44142
25	TMAXDOS	13.19853	13.53435	13.51046
26	AGE SQ	3.58075	6.94376	6.70455
27	CAUSE	.00000	1.00000	.92887
COUNTS		136.	1776.	1912.

Table 9. Means of variables used in discriminant analysis of respiratory cancers; No cancer group includes all non-cancer deaths.

STANDARD DEVIATIONS

VARIABLE	GROUP. =	RESPCANC	NOCANCER	ALL GPS.
1 DEATHAGE		9.43349	13.17908	12.94996
2 INITLYR		4.10684	3.88611	3.90212
3 FINALYR		8.55651	7.67790	7.74328
4 TOTALYR		7.79186	7.12960	7.17841
5 EXPOSURE		.00000	.00000	.00000
6 CUMDOSE		491.47090	431.82021	436.30421
7 CDOS 3+		444.26281	390.03605	394.11383
8 CDOS 5+		389.94979	344.84724	348.22697
9 CDOS 10+		244.23652	189.08908	194.10213
10 CDOS 15+		117.93373	89.10683	91.44326
11 CDOS 20+		34.23485	41.18084	40.72861
12 CDOS 25+		15.46143	19.36115	19.11166
13 YRDEATH		5.83136	6.31983	6.26655
14 DT1		6.37690	6.84206	6.81022
15 DT2		8.15003	8.24547	8.23876
16 DT3		6.20271	6.69390	6.66037
17 DOS0-3		63.54560	71.92290	71.36308
18 DOS4-5		67.58867	69.79293	69.63940
19 DOS6-10		163.99697	186.39070	184.89697
20 DOS11-15		148.52942	121.30639	123.42787
21 DOS16-20		100.46173	88.58640	89.52489
22 DOS21-25		29.73684	32.80420	32.59687
23 DOS25+		15.46143	19.36115	19.11166
24 MAXDOS		177.85926	195.58638	194.38833
25 TMAXDOS		7.29441	7.69571	7.66803
26 AGE SQ		4.90601	9.34438	9.10203
27 CAUSE		.00000	.00000	.00000

Table 10. Standard deviation of variables used in discriminant analysis of respiratory cancers; no cancer group includes all non-cancer deaths.

TABLE	F TO FORCE	*	VARIABLE	F TO FORCE	TOLERANCE
	REMOVE LEVEL	*		ENTER LEVEL	
	DF= 1 1911	*		DF= 1 1910	
		*	1 DEATHAGE	.806 1	1.000000
		*	2 INITLYR	1.855 1	1.000000
		*	3 FINALYR	6.942 1	1.000000
		*	4 TOTALYR	4.387 1	1.000000
		*	5 EXPOSURE	.000 1	.000000
		*	6 CUMDOSE	1.257 1	1.000000
		*	7 CDOS 3+	1.496 1	1.000000
		*	8 CDOS 5+	1.621 1	1.000000
		*	9 CDOS 10+	3.936 1	1.000000
		*	10 CDOS 15+	3.357 1	1.000000
		*	11 CDOS 20+	.103 1	1.000000
		*	12 CDOS 25+	.005 1	1.000000
		*	13 YRDEATH	5.589 1	1.000000
		*	14 DT1	1.965 1	1.000000
		*	15 DT2	.452 1	1.000000
		*	16 DT3	.090 1	1.000000
		*	17 DOS0-3	.010 1	1.000000
		*	18 DOS4-5	.309 1	1.000000
		*	19 DOS6-10	.100 1	1.000000
		*	20 DOS11-15	3.106 1	1.000000
		*	21 DOS16-20	4.937 1	1.000000
		*	22 DOS21-25	.195 1	1.000000
		*	23 DOS25+	.005 1	1.000000
		*	24 MAXDOS	.546 1	1.000000
		*	25 TMAXDOS	.242 1	1.000000
		*	26 AGE SG	17.245 1	1.000000

Table 11. F-ratios at initial step of discriminant analysis on exposed white males using two groups: death from respiratory cancer and death from non-cancer.

— VARIABLE ENTERED 26 AGE SQ —

VARIABLE	F TO FORCE REMOVE LEVEL
26 AGE SQ	17.245
	1
	DF= 1 1910

VARIABLE	F TO FORCE ENTER LEVEL	TOLERANCE
	DF= 1 1909	
1 DEATHAGE	.006	.943687
2 INITLYR	4.909	.960984
3 FINALYR	4.477	.983959
4 TOTALYR	1.236	.940090
5 EXPOSURE	.000	.000000
6 CUMDOSE	.572	.992312
7 CDOS 5+	.697	.991272
8 CDOS 5+	.777	.991112
9 CDOS 10+	2.531	.991066
10 CDOS 15+	2.269	.993940
11 CDOS 20+	.019	.998037
12 CDOS 25+	.025	.999529
13 TRDEATH	3.556	.986519
14 DT1	.247	.951442
15 DT2	.296	.999073
16 DT3	.006	.991196
17 DOS0-3	.000	.999595
18 DOS4-5	.100	.996717
19 DOS6-10	.000	.995855
20 DOS11-15	1.915	.991724
21 DOS16-20	3.614	.994158
22 DOS21-25	.069	.998163
23 DOS25+	.025	.999529
24 MAXDOS	.233	.996231
25 TMAXDOS	.446	.998154

CLASSIFICATION FUNCTIONS

GROUP	RESPCANC	NOCANCER
VARIABLE		
26 AGE SQ	.04322	.08381
CONSTANT	-.77053	-.98414

CLASSIFICATION MATRIX

GROUP	PERCENT CORRECT	NUMBER OF CASES CLASSIFIED INTO GROUP -	
		RESPCANC	NOCANCER
RESPCANC	76.5	104	32
NOCANCER	40.4	1058	718
TOTAL	43.0	1162	750

Table 12. F-ratios, classification functions and classification matrix at first step of discriminant analysis on exposed white males using two groups: death from respiratory cancer and death from non-cancer.

STEP NUMBER 2			
VARIABLE ENTERED 2 INITLYR			
VARIABLE	F TO FORCE	REMOVE LEVEL	
DF= 1 1909			
2 INITLYR	4.909	1	
26 AGE SQ	20.316	1	

VARIABLE	F TO FORCE	TOLERANCE
ENTER LEVEL		
DF= 1 1908		
1 DEATHAGE	.466	.840417
3 FINALYR	1.627	.796628
4 TOTALYR	1.576	.936767
5 EXPOSURE	.000	.000000
6 CUMDOSE	.202	.972815
7 CDOS 3+	.321	.976362
8 CDOS 5+	.435	.980933
9 CDOS 10+	2.536	.991062
10 CDOS 15+	3.088	.981992
11 CDOS 20+	.308	.983806
12 CDOS 25+	.014	.984102
13 YRDEATH	2.168	.947557
14 DT1	2.168	.807435
15 DT2	.001	.933560
16 DT3	.551	.867066
17 DOS0-3	.150	.967433
18 DOS4-5	.010	.961899
19 DOS6-10	.197	.957014
20 DOS11-15	1.469	.985635
21 DOS16-20	3.912	.992906
22 DOS21-25	.386	.973108
23 DOS25+	.014	.984102
24 MAXDOS	.008	.964233
25 TMAXDOS	.012	.876700

CLASSIFICATION FUNCTIONS			
VARIABLE	GROUP =	RESPCANC	NOCANCER
2 INITLYR		3.18978	3.13801
26 AGE SQ		-.22689	-.18191
CONSTANT		-75.21168	-73.02815

CLASSIFICATION MATRIX			
GROUP	PERCENT CORRECT	NUMBER OF CASES CLASSIFIED INTO GROUP -	
		RESPCANC	NOCANCER
RESPCANC	73.5	100	36
NOCANCER	48.0	949	827
TOTAL	48.5	1049	863

Table 13. F-ratios, classification functions and classification matrix at second step of discriminant analysis on exposed white males using two groups: death from respiratory cancer and death from non-cancer.

STEP NUMBER 3
VARIABLE ENTERED 21 DOS16-20

VARIABLE	F TO REMOVE	FORCE LEVEL
2 INITLYR	5.206	1
21 DOS16-20	3.912	1
25 AGE SQ	15.961	1

* VARIABLE	F TO ENTER	FORCE LEVEL	TOLERANCE
1 DEATHAGE	.355	1	.838792
3 FINALYR	.766	1	.761025
4 TOTALYR	.736	1	.894653
5 EXPOSURE	.000	1	.000000
6 CUMDOSE	1.473	1	.524902
7 CDOS 3+	1.456	1	.478205
8 CDOS 5+	1.548	1	.429224
9 CDOS 10+	.070	1	.239191
10 CDOS 15+	.009	1	.170724
11 CDOS 20+	.009	1	.860583
12 CDOS 25+	.002	1	.978012
13 YRDEATH	1.146	1	.903645
14 DT1	1.146	1	.770016
15 DT2	.004	1	.933236
16 DT3	.311	1	.859355
17 DOS0-3	.628	1	.929846
18 DOS4-5	.479	1	.883384
19 DOS6-10	2.725	1	.718253
20 DOS11-15	.060	1	.500792
22 DOS21-25	.010	1	.846596
23 DOS25+	.002	1	.978012
24 MAXDOS	2.110	1	.592837
25 TMAXDOS	.004	1	.876199

CLASSIFICATION FUNCTIONS

GROUP =	RESPCANC	NOCANCER
VARIABLE		
2 INITLYR	3.19907	3.14564
21 DOS16-20	.01443	.01187
25 AGE SQ	-.21925	-.17563
CONSTANT	-75.71145	-73.36654

CLASSIFICATION MATRIX

GROUP	PERCENT CORRECT	NUMBER OF CASES CLASSIFIED INTO GROUP	
		RESPCANC	NOCANCER
RESPCANC	58.6	80	50
NOCANCER	56.5	773	1003
TOTAL	56.6	853	1053

Table 14. F-ratios, classification functions and classification matrix at third step of discriminant analysis on exposed white males using two groups: death from respiratory cancer and death from non-cancer.

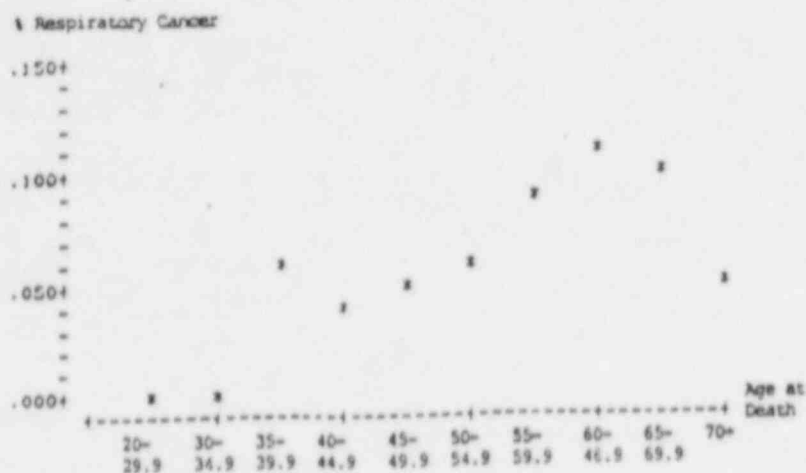


Figure 6 Percent of deaths from respiratory cancer for exposed white males as a function of age at death.

	20- 29.9	30- 34.9	35- 39.9	40- 44.9	45- 49.9	50- 54.9	55- 59.9	60- 64.9	65- 69.9	70+	Total
No. Cancers	0	0	4	5	8	13	24	32	28	22	136
Total	37	29	71	114	156	226	260	289	279	451	1912
% Cancer	0.0	0.0	5.6	4.4	5.1	5.8	9.2	11.1	10.0	4.9	7.1

Table 15 Numbers of and percent of Respiratory Cancers as a function of age for exposed white males.

The left portion of this graph for ages less than 50 departs from a parabolic shape, but this part involves only 407 cases out of a total of 1912 cases. Thus, nearly 80% of the cases are in the age group from 50-70 and the quadratic form which we used ought to provide a good fit. In fitting a logistic model one fits $\log [p/(1-p)]$ to the independent variables, where p is the probability of death from cancer. A plot of this expression vs. age is shown in Figure 7, where the percents in Figure 6 were used for p . Again the

parabolic shape stands out in the range 50-70 years where the largest portion of the data is located.

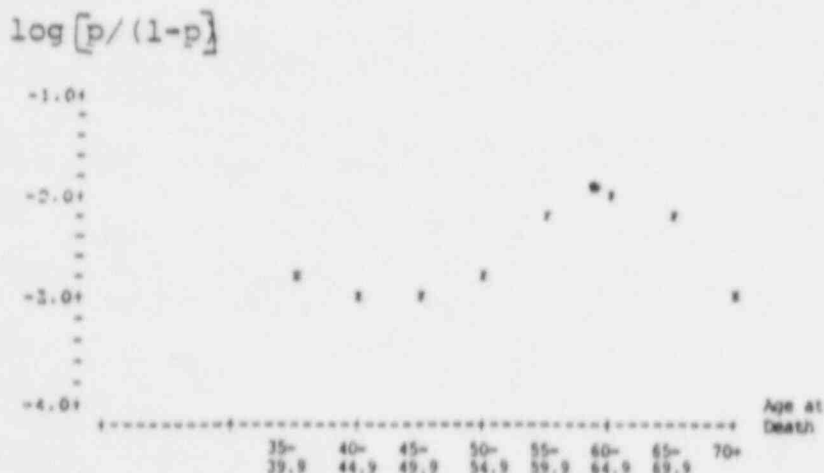


Figure 7 $\log [p/(1-p)]$ for exposed white males as a function of age at death, where p is the percent of deaths from respiratory cancer vs. non-cancer.

As seen in Table 11, other important variables at the initial step of the discriminant analysis are final year of employment (FINALYR), year of death (YRDEATH), total years of employment (TOTAL YR), dose received 16 to 20 years before death (DOS16-20) and dose received 11 to 15 years before death (DOS11-15).

After the variable AGESQ is entered in the first step of the discriminant analysis, a curious thing happens. The variable initial year of employment (INITLYR) becomes the next candidate to enter with an F-ratio of 4.9. Other variables that are close are FINALYR, YRDEATH, and DOS16-20. We are at a loss to explain the meaning of this. The coefficients on INITLYR in the classifications functions

are such that the larger the value of INITLYR, the greater the chance of death from respiratory cancer. One might argue that INITLYR is acting as a surrogate for dose, particularly in view of Figure 4 which shows that the average dose which Hanford workers have been receiving has been going up over the years. However, if this is the case, one would expect the dose variables to show up with F-ratios comparable to that of INITLYR, but aside from DOS16-20, they don't. Furthermore, after INITLYR is entered, the F-ratio for DOS16-20 increases a little. If INITLYR were acting as a surrogate for DOS16-20, this F-ratio should decrease considerably. Thus it seems that INITLYR is not acting as a surrogate for any of the dose variables. This question is considered later in more detail and this conclusion is contradicted. One might feel that INITLYR is acting as a surrogate for YRDEATH and that since the incidence of respiratory cancer has been increasing over the years, this produces a positive relation between death from respiratory cancer and INITLYR. Perhaps this is so, but then one would expect the F-ratio for YRDEATH at step 1 of the discriminant analysis to be somewhat higher than that of INITLYR, and this is not the case.

After AGESQ and INITLYR are entered in the stepwise discriminant procedure, DOS16-20 is chosen next with an F-ratio of 3.9 ($\alpha = .048$). The coefficients on DOS 16-20 in the classification functions are such that higher dose gives higher chance of cancer.

The stepwise discriminant analysis procedure was used to suggest a set of variables to be used in developing a model to give the probability of death from respiratory cancer. The variables chosen were:

AGESQ, INITLYR, YRDEATH, DOS6-10 and DOS16-20.

At all of the steps of the discriminant analysis, correct classification was not impressive, being typically around 50%. One interesting fact which stands out is that cumulative lifetime dose (CUMDOS) does not show up at all (F-ratios all less than 1.5). The stepwise discriminant analysis was also run on the above data set, leaving out accidental deaths, and the results were essentially the same. Finally, the analysis was done including cases with zero cumulative lifetime dose. The biggest difference here was that YRDEATH showed up quite a bit more significant than INITLYR.

A logistic regression model was developed for exposed white males. Two response categories were used: respiratory cancer death (136 cases) and non-cancer deaths (1776 cases). The form of the model is:

$$\log [P/(1-p)] = \alpha + \sum_{j=1}^k \beta_j x_j$$

where p is the probability of respiratory cancer being the cause of death, as opposed to a non-cancer cause of death, x_j is the value of the j -th predictor variable in the model and α and β_j are coefficients to be estimated from the data. Table 16 summarizes the results of 8 different logistic regression models which were fit to the data. First, based on the discriminant analysis results, we would certainly want to include AGESQ in the model. Then discriminant analysis would suggest that INITLYR be included, while the fact that the incidence of respiratory cancer is increasing over time would say that YRDEATH should be in the model. Each of these variables was tried separately (with AGESQ, of course) and together. See models 3, 4 and 5 of Table 16. With both INITLYR and YRDEATH in the model the chi-square values for these variables are about 3.0 ($\alpha=.09$),

Model	Constant	AGESQ	INITLYR	YRDEATH	DOS16-20	-2*log L
1	-2.57					981.1
2	-2.21	-.291 (16.6)				956.4
3	-4.37	-.301 (18.0)	.047 (4.7)			952.1
4	-4.35	-.290 (16.2)		.033 (4.4)		951.7
5	-5.78	-.298 (17.3)	.038 (2.96)	.028 (3.02)		949.0
6	-4.51	-.296 (17.4)	.048 (4.99)		.0018 (3.5)	949.2
7	-4.13	-.286 (15.7)		.029 (3.3)	.0012 (1.6)	950.3
8	-5.64	-.294 (16.9)	.041 (3.4)	.023 (1.9)	.0014 (2.0)	947.2

Table 16. Results of fitting eight logistic regression models using respiratory cancer and no cancer as the two response categories. Only exposed white males are included in the model. Variables which have no entry for a particular model were not used in that model. For each model, the first value under the variable is the coefficient of that variable in the logistic regression model, while the second value (below in parentheses) is the chi-square value for a test of statistical significance of that variable. All chi-square values have one degree of freedom.

but either one alone has a chi-square of 4.7 or 4.4. This suggests that either one, but not both, of these variables belongs in the model. Since YRDEATH has an obvious interpretation while INITLYR does not, it would seem that a reasonable model at this point would consist of AGESQ and YRDEATH. Next, DOS16-20 was added to some of the above models. See models 6, 7 and 8 of Table 16 for the results. When DOS16-20 is added to the model consisting of AGESQ and INITLYR, it has a chi-square value of 3.497 with 1 degree of freedom ($\alpha=.06$). When DOS16-20 is added to the model consisting of AGESQ and YRDEATH, it has a chi-square value of only 1.6. Also, the chi-square value of YRDEATH drops from 4.4 to 3.3. Finally, when DOS16-20 is added to the model consisting of AGESQ, INITLYR and YRDEATH, both YRDEATH and DOS16-20 drop in significance. This suggests that YRDEATH and DOS16-20 are correlated. This is substantiated further on. This shows that YRDEATH contains information about DOS16-20 and vice-versa; and that we cannot separate the effects of each (except, for example, by having an independent estimate of the effect of YRDEATH on respiratory cancer deaths among Hanford workers). In any case, from the point of view of statistical significance, DOS16-20 is border line at best ($\alpha=.06$ when we include in DOS16-20 any effect of YRDEATH). The coefficients on AGESQ in all of the models are nearly the same (all between $-.301$ and $-.286$) which is reassuring. The coefficients on DOS16-20, on the other hand, vary between $.0012$ and $.0018$; which is not a very large magnitude, but percentagewise the change is 33% or 50% depending on one's point of view. This is quite large and can have a considerable effect if one attempts to estimate the effect of dose on the probability of death from respiratory cancer. In view of the relation between YRDEATH and DOS16-20 in the data file, we are reluctant to attempt such an estimate.

Another curious point about the logistic modeling is the fact that when INITLYR is added to the model consisting of AGESQ, YRDEATH and DOS16-20, it is on the border line of testing significant (chi-square = 3.366 with 1 d.f., $\alpha = .07$). As stated before, we are unable to find an interpretation for this.

Based on the above discussion, it is difficult to recommend a single model. Our inability to find an interpretation for INITLYR makes us want to leave it out of the model. On the other hand, the statistical analysis is hinting (mildly, at least) that it belongs in the model. Also, the statistical analysis is hinting that YRDEATH and DOS16-20 belong in the model. However, these variables are correlated, so that when both are put in the model their significance drops, as do the values of their coefficients. Thus it is not possible to estimate the effect of each variable separately on the response.

An attempt to get at the meaning of INITLYR in the model and to see the relation between YRDEATH and dose prompted a more detailed look at the data. Scatterplots were made of three dose variables, DOS6-10, DOS11-15 and DOS16-20 against both INITLYR and YRDEATH. In these plots the extremely low doses were omitted. The plots are shown in Figures 8 thru 13 on the following pages. A number, such as 3, indicates 3 or more points on top of one another on the graph while a plus sign indicates 10 or more points on top of one another. The scatterplots show little or no relationship between INITLYR and the dose variables. However, YRDEATH bears a definite positive relationship with each of the dose variables.

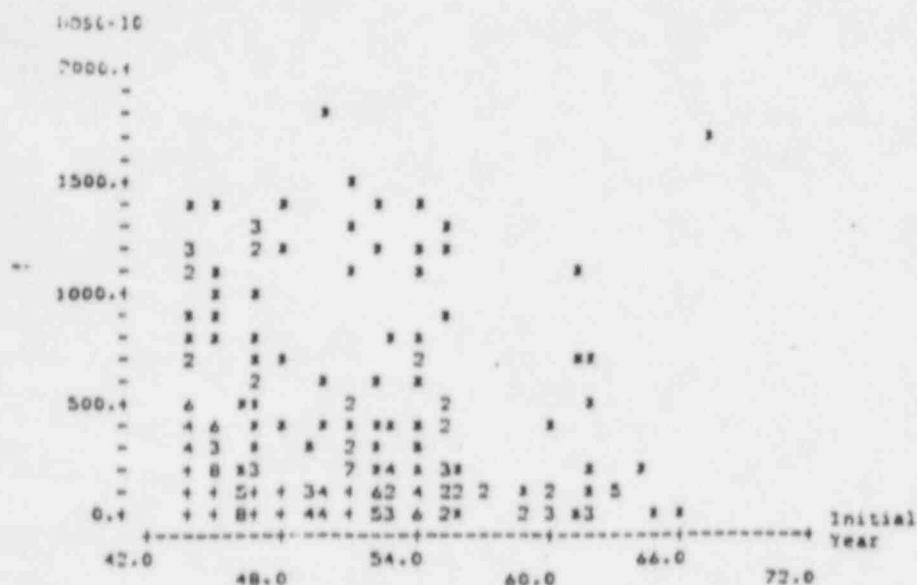


Figure 8. Scatterplot of DOS6-10 vs. Initial Year of Employment for Exposed White Males With Respiratory Cancer or no Cancer as Cause of Death. Cases with DOS 6-10 Less or Equal to 15 have not been plotted.

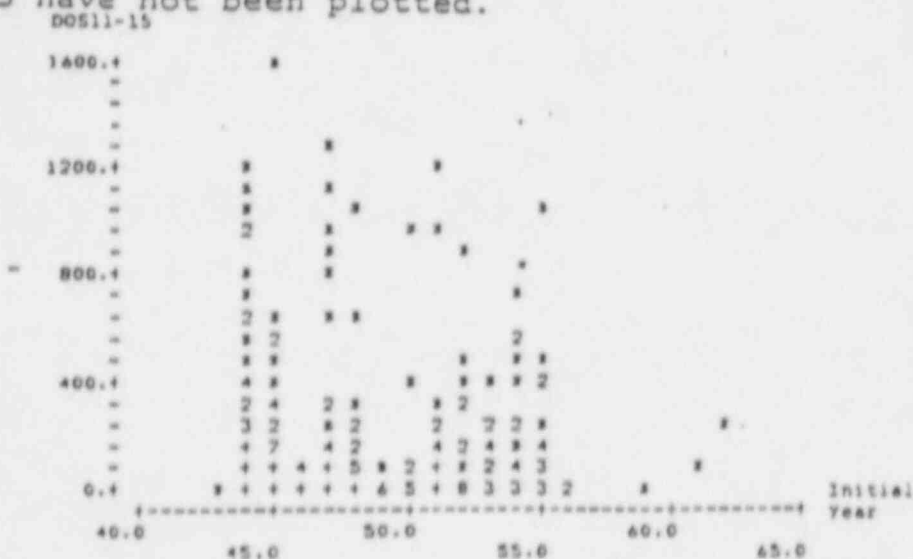


Figure 9. Scatterplot of DOS11-15 vs. Initial Year of Employment for Exposed White Males With Respiratory Cancer or no Cancer as Cause of Death. Cases with Dose Less or Equal to 10 have not been plotted.

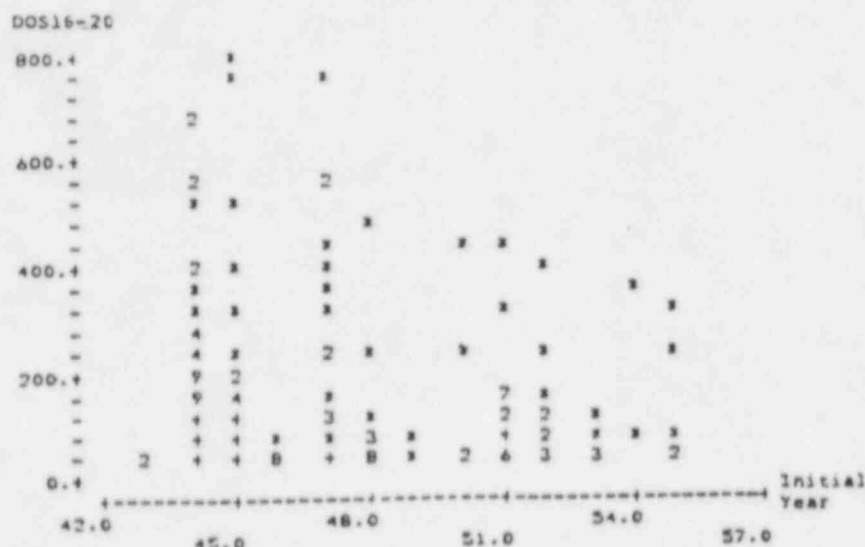


Figure 10. Scatterplot of DOS16-20 vs. Initial Years of Employment for Exposed White Males with Respiratory Cancer or no Cancer as Cause of Death. Cases with Dose Less or Equal to 25 have not been plotted.

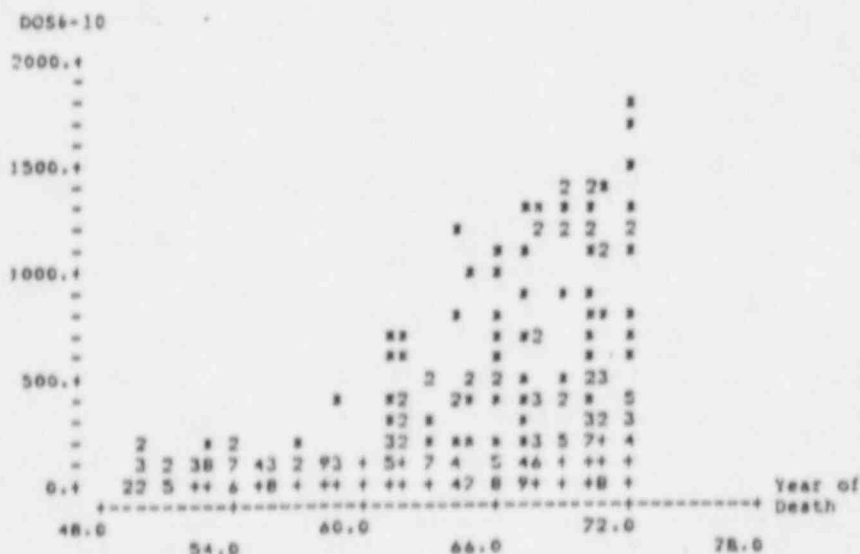


Figure 11. Scatterplot of DOS6-10 vs. Year of Death for Exposed White Males with Respiratory Cancer or no Cancer as Cause of Death. Cases with DOS6-10 Less or Equal to 15 have not been plotted.

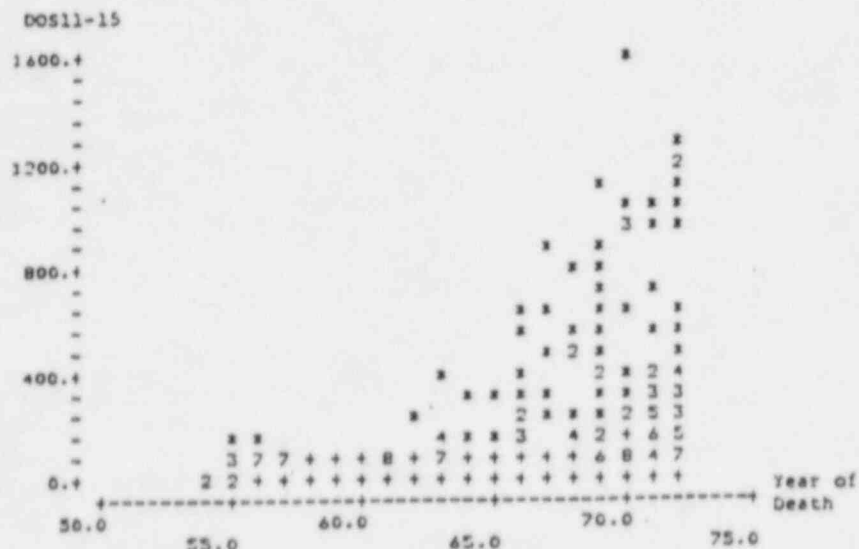


Figure 12. Scatterplot of DOS11-15 vs. Year of Death for Exposed White Males with Respiratory Cancer or no Cancer as Cause of Death. Cases with Dose Less or Equal to 10 have not been plotted.

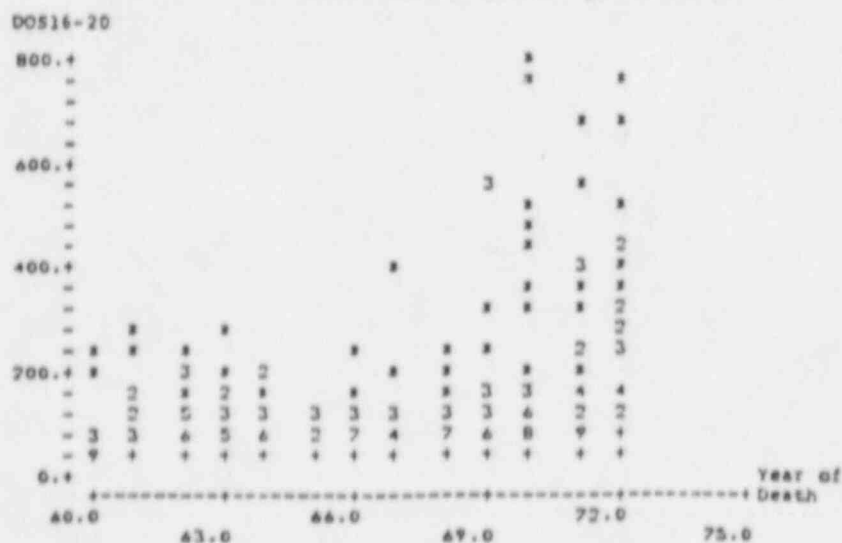


Figure 13. Scatterplot of DOS16-20 vs. Year of Death for Exposed White Males with Respiratory Cancer or no Cancer as Cause of Death. Cases with Dose Less or Equal to 25 have not been plotted.

A close look at the scatterplot of DOS6-10 vs. YRDEATH in Figure 11 shows that the envelope of the dose levels is flat up to about '57 where it begins to rise linearly. The doses plotted for '57 were received 6-10 years earlier, i.e., in '47 to '51. This suggests that the doses (recorded in our file) which Hanford workers received began to rise sometime between 1947 and 1951. Similar considerations for DOS11-15 in Figure 12 would put the beginning of the rise between 1946 and 1950, while consideration of DOS16-20 in Figure 13 would put it between 1945 and 1949. These observations are consistent with Figure 4 which shows that the average dose which Hanford workers received increased over time and that the increase began around 1949. Furthermore, the flat parts of the envelopes of the dose levels in Figures 11, 12, and 13 suggest that the dose which Hanford workers received decrease linearly from 1944 to around 1948 or so; a look at the graph in Figure 4 shows that this is approximately true. Thus, we have established a very definite positive relationship between the dose variables and year of death in our data file.

Next, for each of the dose variables, the average dose was determined for each initial year and each year of death. Plots of these averages appear in Figures 14 thru 19. The plot of average DOS6-10 vs. INITLYR in Figure 14 shows a linear rise up to '55 after which the plot becomes erratic. We don't have an explanation for this erratic behavior. However, the vast majority of cases, 1857 out of 1910 (two cases with initial year of '72 are not included), are on or before '55, so this plot would suggest a positive relationship between DOS6-10 and INITLYR. Such a relationship didn't show up in Figure 8, but a look at the vertical scales of the two graphs shows that the rise detected in Figure 14 is

Average DOS6-10

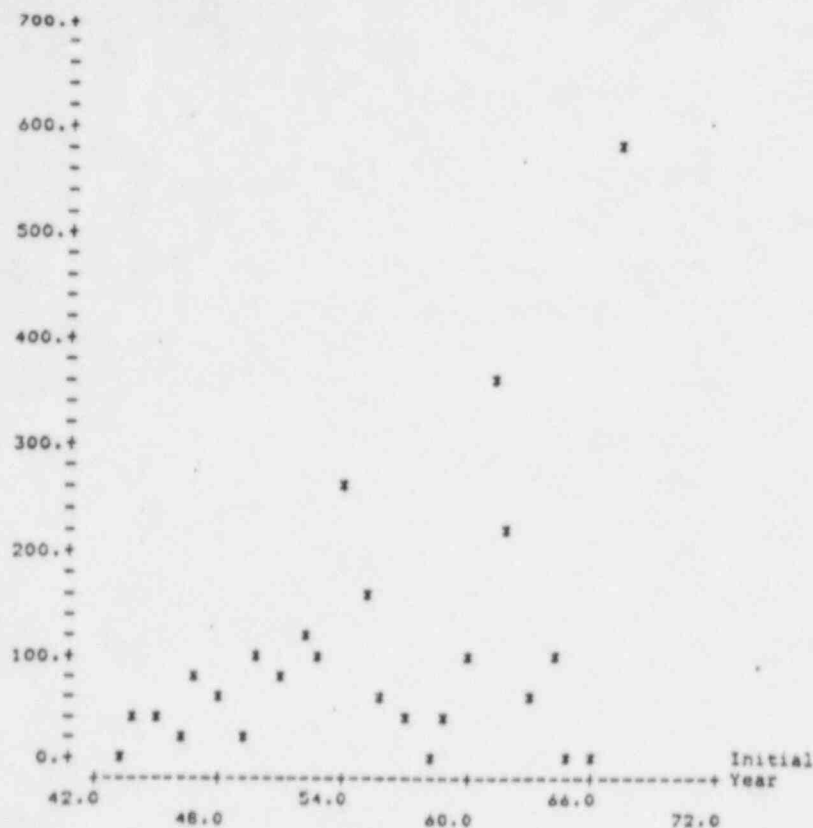


Figure 14. Plot of average DOS6-10 for workers with the specified initial year of employment. Only exposed white males with respiratory cancer or no cancer as cause of death are used.

Average DOS11-15

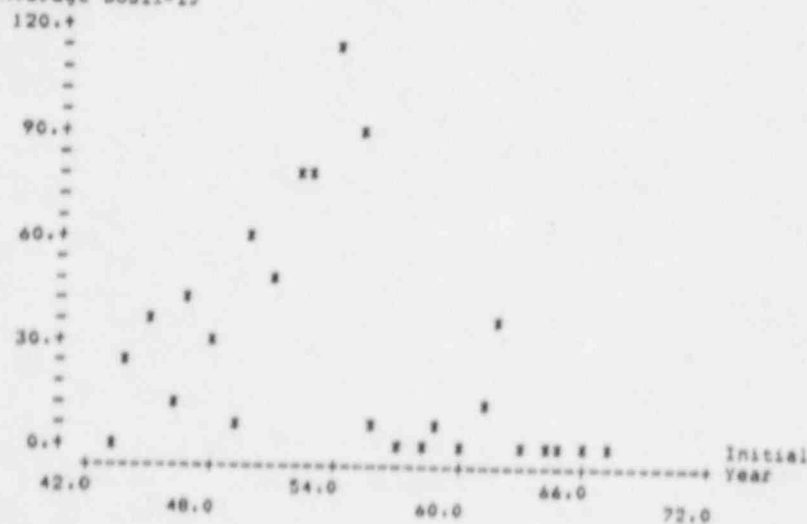


Figure 15. Plot of average DOS11-15 for workers with the specified initial year of employment. Only exposed white males with respiratory cancer or no cancer as cause of death are used.

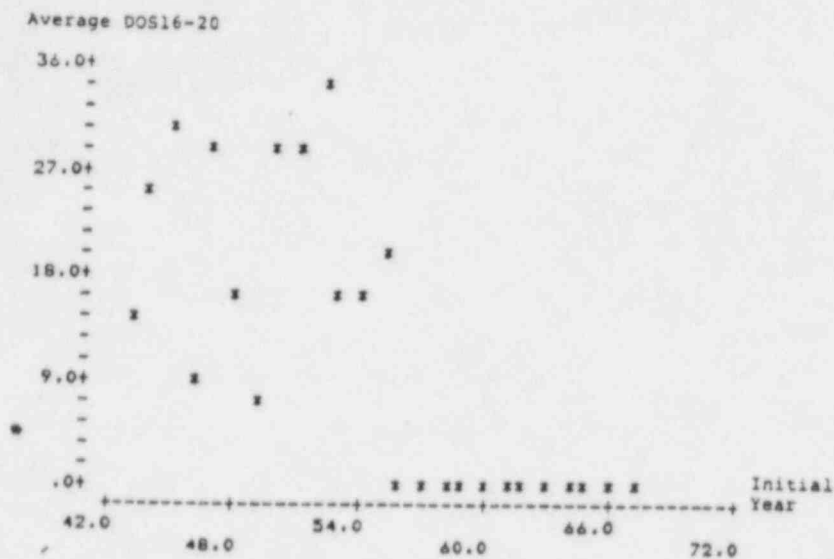


Figure 16. Plot of average DOS16-20 for workers with the specified initial year of employment. Only exposed white males with respiratory cancer or no cancer as cause of death are used.

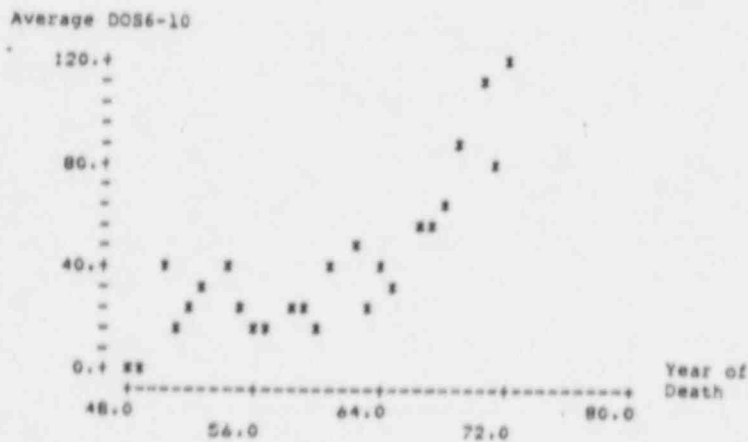


Figure 17. Plot of average DOS6-10 for workers with the specified year of death. Only exposed white males with respiratory cancer or no cancer as cause of death are used.

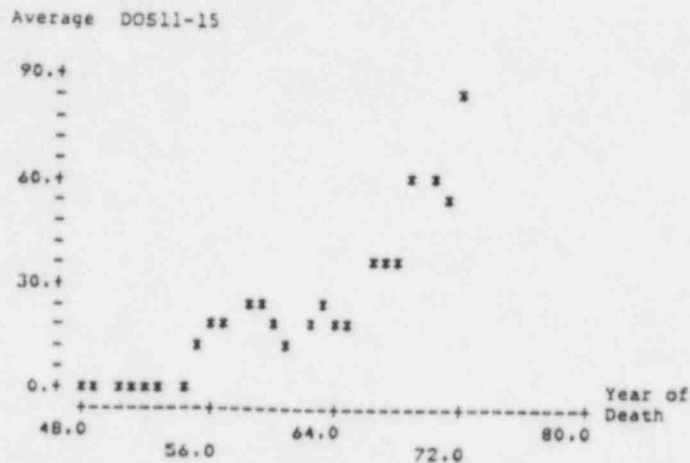


Figure 18. Plot of average DOS11-15 for workers with the specified year of death. Only exposed white males with respiratory cancer or no cancer as cause of death are used.

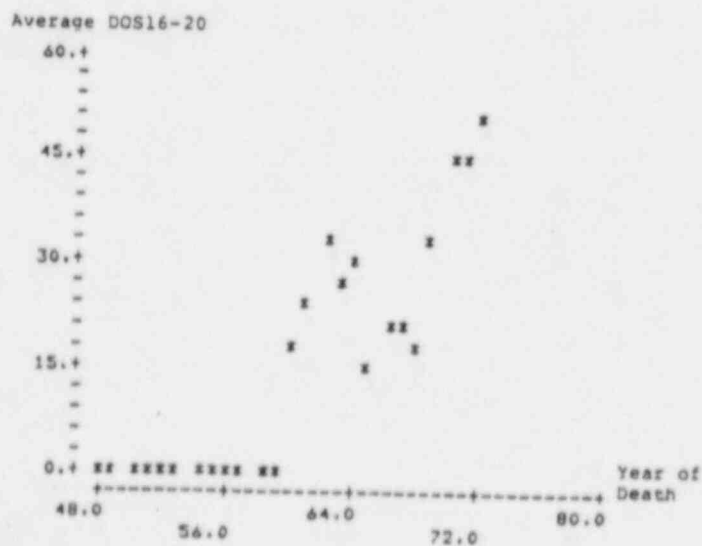


Figure 19. Plot of average DOS16-20 for workers with the specified year of death. Only exposed white males with respiratory cancer or no cancer as cause of death are used.

rather slight compared to the vertical scale of Figure 8 so one would not expect to see that rise in Figure 8 . Similar comments apply to Figure 15. The doses from '63 up must be zero in this figure, since all of the cases are deaths that occurred on or before '72. There is no relation between DOS16-20 and INITLYR other than the logical requirement that average DOS16-20 be zero from '57 up. Thus there is some indication of a positive relationship between dose and initial year of employment. With regard to year of death, Figures 17, 18, and 19 show a very definite positive relationship between the dose variables and year of death, reinforcing that observed in Figures 11, 12, and 13. The implications of these relationships in the logistic modelling have been discussed above.

4.0 PRINCIPAL CONCLUSIONS

A number of conclusions have been reached pertaining to the quality of the data analyzed in this project and the results that can be obtained. These may be listed as follows:

1. We are not convinced that the data is in fact the same data as that collected for Hanford workers and maintained by Battelle Pacific Northwest Laboratories. This concern is due in part to inconsistencies among various sources concerning the data and in part to lack of clear documentation of the chain of events leading to the preparation of the data.
2. The data is not consistent with the purported data collection procedures as evidenced for example by the existence of reported doses after the final year of employment.
3. The data does not correspond with that presented in the Mancuso paper.
4. The data contains a systematic trend of increasing average yearly dose over calendar years, which suggests a possible bias in the data collection procedure applicable to the file from which the current data was extracted.
5. We have not been able to receive or discover an authoritative definition of the meaning of the dose variables, including the units, types of radiation included, and quality factors.
6. The absence of data pertaining to other information that is available but which was not provided was a hindrance to a proper completion of analysis. This includes among other items, data on radiation

- (Cont.) 6. monitoring, secondary causes of death, internal exposures, accidental deposition, yearly dose records broken down by radiation sources, and inclusion of additional fatalities occurring after 1972.
7. The lack of adequate documentation from NRC forced us to spend considerable time and effort identifying and researching the supporting material required for the preparation of a responsible analysis.
8. In view of the above conclusions concerning the data, it does not seem appropriate to attempt to draw conclusions from the statistical analysis.
9. It is a useful corollary of the evidence presented in this paper that future efforts must carefully consider the reliability of the data studied. This would include careful documentation of the sources of the data and of the procedures used in compiling it.
10. It is our recommendation that this contract should be modified in such a way that the work can be repeated with data which is adequate for the purpose intended.

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APPENDIX A

Univariate Distributions of All Variables
Except Race, Sex, and Exposed-Unexposed
For All Cases and For Exposed White Males

21.5 TO	22.5-	11***
22.5 TO	23.5-	5*
23.5 TO	24.5-	4*
24.5 TO	25.5-	10***
25.5 TO	26.5-	11***
26.5 TO	27.5-	7**
27.5 TO	28.5-	15*****
28.5 TO	29.5-	9***
29.5 TO	30.5-	11***
30.5 TO	31.5-	22*****
31.5 TO	32.5-	15*****
32.5 TO	33.5-	20*****
33.5 TO	34.5-	16*****
34.5 TO	35.5-	19*****
35.5 TO	36.5-	23*****
36.5 TO	37.5-	31*****
37.5 TO	38.5-	37*****
38.5 TO	39.5-	46*****
39.5 TO	40.5-	32*****
40.5 TO	41.5-	40*****
41.5 TO	42.5-	44*****
42.5 TO	43.5-	51*****
43.5 TO	44.5-	65*****
44.5 TO	45.5-	68*****
45.5 TO	46.5-	63*****
46.5 TO	47.5-	71*****
47.5 TO	48.5-	71*****
48.5 TO	49.5-	81*****
49.5 TO	50.5-	83*****
50.5 TO	51.5-	83*****
51.5 TO	52.5-	86*****
52.5 TO	53.5-	105*****
53.5 TO	54.5-	111*****
54.5 TO	55.5-	87*****
55.5 TO	56.5-	112*****
56.5 TO	57.5-	119*****
57.5 TO	58.5-	99*****
58.5 TO	59.5-	103*****
59.5 TO	60.5-	108*****
60.5 TO	61.5-	106*****
61.5 TO	62.5-	123*****
62.5 TO	63.5-	119*****
63.5 TO	64.5-	120*****
64.5 TO	65.5-	126*****
65.5 TO	66.5-	115*****
66.5 TO	67.5-	123*****
67.5 TO	68.5-	99*****
68.5 TO	69.5-	92*****
69.5 TO	70.5-	97*****
70.5 TO	71.5-	83*****
71.5 TO	72.5-	114*****
72.5 TO	73.5-	88*****
73.5 TO	74.5-	83*****
74.5 TO	75.5-	70*****
75.5 TO	76.5-	76*****
76.5 TO	77.5-	62*****
77.5 TO	78.5-	48*****
78.5 TO	79.5-	44*****
79.5 TO	80.5-	33*****
80.5 TO	81.5-	41*****
81.5 TO	82.5-	20*****
82.5 TO	83.5-	33*****
83.5 TO	84.5-	27*****
84.5 TO	85.5-	21*****
85.5 TO	86.5-	10***
86.5 TO	87.5-	6**
87.5 TO	88.5-	5*
88.5 TO	89.5-	4*
89.5 TO	90.5-	3
90.5 TO	91.5-	2
91.5 TO	92.5-	0
92.5 TO	93.5-	0
93.5 TO	94.5-	0
94.5 TO	95.5-	1
95.5 TO	96.5-	1
96.5 TO	97.5-	0-
97.5 TO	98.5-	0
98.5 TO	99.5-	0
99.5 TO	100.5-	1
100.5 TO	101.5	1

All Cases Age at Death

42.5 TO 43.5-	9
43.5 TO 44.5-	1866*****
44.5 TO 45.5-	574*****
45.5 TO 46.5-	107**
46.5 TO 47.5-	441*****
47.5 TO 48.5-	330*****
48.5 TO 49.5-	58*
49.5 TO 50.5-	66**
50.5 TO 51.5-	217*****
51.5 TO 52.5-	75**
52.5 TO 53.5-	44*
53.5 TO 54.5-	43*
54.5 TO 55.5-	62**
55.5 TO 56.5-	16
56.5 TO 57.5-	7
57.5 TO 58.5-	4
58.5 TO 59.5-	7
59.5 TO 60.5-	8
60.5 TO 61.5-	6
61.5 TO 62.5-	8
62.5 TO 63.5-	10
63.5 TO 64.5-	3
64.5 TO 65.5-	2
65.5 TO 66.5-	12
66.5 TO 67.5-	7
67.5 TO 68.5-	0
68.5 TO 69.5-	1
69.5 TO 70.5-	4

THIS HISTOGRAM DOES NOT INCLUDE 5.00 OBS .LT. 40.5 AND .000 OBS .GE. 79.5

All Cases Initial Year of Employment

43.5 TO 44.5-	364
44.5 TO 45.5-	790
45.5 TO 46.5-	212
46.5 TO 47.5-	116
47.5 TO 48.5-	227
48.5 TO 49.5-	250
49.5 TO 50.5-	136
50.5 TO 51.5-	195
51.5 TO 52.5-	194
52.5 TO 53.5-	136
53.5 TO 54.5-	102
54.5 TO 55.5-	110
55.5 TO 56.5-	104
56.5 TO 57.5-	120
57.5 TO 58.5-	102
58.5 TO 59.5-	107
59.5 TO 60.5-	74
60.5 TO 61.5-	92
61.5 TO 62.5-	83
62.5 TO 63.5-	77
63.5 TO 64.5-	75
64.5 TO 65.5-	88
65.5 TO 66.5-	32
66.5 TO 67.5-	25
67.5 TO 68.5-	24
68.5 TO 69.5-	39
69.5 TO 70.5-	41
70.5 TO 71.5-	34
71.5 TO 72.5-	43

All Cases Final Year of Employment

-.5 TO .5-	1012
.5 TO 1.5-	765
1.5 TO 2.5-	295
2.5 TO 3.5-	172
3.5 TO 4.5-	163
4.5 TO 5.5-	130
5.5 TO 6.5-	140
6.5 TO 7.5-	116
7.5 TO 8.5-	115
8.5 TO 9.5-	110
9.5 TO 10.5-	96
10.5 TO 11.5-	98
11.5 TO 12.5-	82
12.5 TO 13.5-	69
13.5 TO 14.5-	93
14.5 TO 15.5-	77
15.5 TO 16.5-	59
16.5 TO 17.5-	80
17.5 TO 18.5-	56
18.5 TO 19.5-	52
19.5 TO 20.5-	52
20.5 TO 21.5-	39
21.5 TO 22.5-	20
22.5 TO 23.5-	12
23.5 TO 24.5-	17
24.5 TO 25.5-	26
25.5 TO 26.5-	13
26.5 TO 27.5-	14
27.5 TO 28.5-	14

THIS HISTOGRAM DOES NOT INCLUDE .000 OBS .LT. -.500 AND 5.00 OBS .GE. 29.5

All Cases Total Years Employed

8	1
9	4
11	13
23	1
38	2
39	1
40	2
41	1
43	2
46	1
52	1
70	2
93	1
95	1
112	1
136	1
140	1
141	6
142	3
144	2
145	3
146	3
147	1
148	2
149	2
150	18
151	39**
152	2
153	79*****
154	23*
155	9
156	11
157	53****
158	3
159	1
160	2
161	10
162	202*****
163	1
170	1
171	6
172	13
173	3
174	31*
180	7
182	6
183	13
185	43***
186	4
188	11
189	25*
190	1
191	23*
192	5
193	2
194	1
195	5
196	1
197	13
198	2
199	30*
200	22
201	14
202	3
203	11
204	5
205	13
206	1
207	5
208	1
209	1
211	2
218	2
225	1
228	1
231	1
238	5
244	1
250	48***
253	1
255	4
258	1

n.b. Two cases with no cause of death are excluded.

All Cases Cause of Death (ICD Codes)

269	3
272	4
276	1
277	3
279	3
284	4
289	2
291	2
299	1
303	11
309	3
320	2
322	1
323	2
330	1
331	1
340	2
342	7
345	2
347	3
348	6
355	1
393	1
394	14
395	15
396	9
397	4
398	11
400	8
401	4
402	15
403	7
404	8
410	1109-----
411	19
412	340*****
413	1
421	2
422	3
423	1
424	1
425	2
426	3
427	29*
428	15
429	20
430	31*
431	75*****
432	8
433	58****
434	1
436	61*****
437	19

All Cases Cause of Death

470	6
471	23*
472	55*****
473	3
474	4
475	4
476	3
477	2
480	13
481	2
482	1
483	2
484	2
485	1
486	1
487	5
488	3
489	16
490	2
491	26*
492	19
493	1
494	16
495	81*****
496	9
513	1
514	2
515	1
517	9
518	5
519	9
530	2
531	7
532	18
533	8
534	1
535	1
537	1
540	4
551	2
552	1
553	2
560	3
561	1
562	5
563	4
565	1
569	5
570	1
571	75*****
573	5
574	3
575	1
576	3
577	10
581	4
582	16
583	1
584	1
590	12
592	2
593	4
596	1
599	3
600	1

All Cases Cause of Death

601	1
602	3
694	1
695	1
712	1
716	1
717	1
720	1
729	1
733	2
734	4
746	1
747	5
748	1
751	1
753	2
780	1
782	9
786	1
792	1
794	2
795	1
796	25*
805	2
807	1
810	9
812	44***
813	3
814	15
815	1
816	36***
818	6
819	57*****
821	1
830	11
832	4
840	3
841	17
853	1
854	4
873	1
874	2
880	5
881	3
882	2
883	1
884	3
885	2
887	13
890	10
891	3
894	1
895	1
898	3
899	2
910	16
911	7
913	2
916	7
918	1
921	1
922	11
923	3
924	3
925	6
926	1
927	3
928	3
929	4
930	6
940	1
942	1
943	1
950	17
952	24*
953	11
954	4
955	80*****
958	2
963	1
965	8
968	3
980	3
981	1
982	1
984	3
985	4
986	2
988	2
994	3
995	3

All Cases Cause of Death

49.5 TO	49.5-	2851
49.5 TO	99.5-	439
99.5 TO	149.5-	226
149.5 TO	199.5-	120
199.5 TO	249.5-	63
249.5 TO	299.5-	45
299.5 TO	349.5-	30
349.5 TO	399.5-	20
399.5 TO	449.5-	20
449.5 TO	499.5-	13
499.5 TO	549.5-	10
549.5 TO	599.5-	16
599.5 TO	649.5-	19
649.5 TO	699.5-	9
699.5 TO	749.5-	5
749.5 TO	799.5-	7
799.5 TO	849.5-	5
849.5 TO	899.5-	0
899.5 TO	949.5-	8
949.5 TO	999.5-	3
999.5 TO	1049.5-	5
1049.5 TO	1099.5-	1
1099.5 TO	1149.5-	3
1149.5 TO	1199.5-	2
1199.5 TO	1249.5-	3
1249.5 TO	1299.5-	2
1299.5 TO	1349.5-	1
1349.5 TO	1399.5-	2
1399.5 TO	1449.5-	2
1449.5 TO	1499.5-	2
1499.5 TO	1549.5-	4
1549.5 TO	1599.5-	2
1599.5 TO	1649.5-	1
1649.5 TO	1699.5-	6
1699.5 TO	1749.5-	4
1749.5 TO	1799.5-	1
1799.5 TO	1849.5-	1
1849.5 TO	1899.5-	0
1899.5 TO	1949.5-	0
1949.5 TO	1999.5-	2
1999.5 TO	2049.5-	3
2049.5 TO	2099.5-	1
2099.5 TO	2149.5-	1
2149.5 TO	2199.5-	2
2199.5 TO	2249.5-	0
2249.5 TO	2299.5-	0
2299.5 TO	2349.5-	1
2349.5 TO	2399.5-	1
2399.5 TO	2449.5-	0
2449.5 TO	2499.5-	0
2499.5 TO	2549.5-	1
2549.5 TO	2599.5-	5
2599.5 TO	2649.5-	0
2649.5 TO	2699.5-	1
2699.5 TO	2749.5-	2
2749.5 TO	2799.5-	1
2799.5 TO	2849.5-	0
2849.5 TO	2899.5-	2
2899.5 TO	2949.5-	1
2949.5 TO	2999.5-	0
2999.5 TO	3049.5-	0
3049.5 TO	3099.5-	1
3099.5 TO	3149.5-	3
3149.5 TO	3199.5-	1
3199.5 TO	3249.5-	0
3249.5 TO	3299.5-	1
3299.5 TO	3349.5-	0
3349.5 TO	3399.5-	0
3399.5 TO	3449.5-	6
3449.5 TO	3499.5-	0
3499.5 TO	3549.5-	0
3549.5 TO	3599.5-	0
3599.5 TO	3649.5-	1
3649.5 TO	3699.5-	0
3699.5 TO	3749.5-	0
3749.5 TO	3799.5-	0
3799.5 TO	3849.5-	1
3849.5 TO	3899.5-	0
3899.5 TO	3949.5-	0
3949.5 TO	3999.5-	0
3999.5 TO	4049.5-	1
4049.5 TO	4099.5-	0
4099.5 TO	4149.5-	0
4149.5 TO	4199.5-	0
4199.5 TO	4249.5-	0
4249.5 TO	4299.5-	0
4299.5 TO	4349.5-	1
4349.5 TO	4399.5-	0
4399.5 TO	4449.5-	1

All Cases Cumulative Lifetime Dose

.5 TO	49.5-	2920
49.5 TO	99.5-	4548
99.5 TO	149.5-	1788
149.5 TO	199.5-	1208
199.5 TO	249.5-	59
249.5 TO	299.5-	36
299.5 TO	349.5-	29
349.5 TO	399.5-	16
399.5 TO	449.5-	21
449.5 TO	499.5-	11
499.5 TO	549.5-	8
549.5 TO	599.5-	20
599.5 TO	649.5-	12
649.5 TO	699.5-	5
699.5 TO	749.5-	2
749.5 TO	799.5-	9
799.5 TO	849.5-	4
849.5 TO	899.5-	1
899.5 TO	949.5-	7
949.5 TO	999.5-	3
999.5 TO	1049.5-	3
1049.5 TO	1099.5-	3
1099.5 TO	1149.5-	5
1149.5 TO	1199.5-	2
1199.5 TO	1249.5-	2
1249.5 TO	1299.5-	2
1299.5 TO	1349.5-	2
1349.5 TO	1399.5-	2
1399.5 TO	1449.5-	2
1449.5 TO	1499.5-	3
1499.5 TO	1549.5-	5
1549.5 TO	1599.5-	1
1599.5 TO	1649.5-	1
1649.5 TO	1699.5-	3
1699.5 TO	1749.5-	3
1749.5 TO	1799.5-	0
1799.5 TO	1849.5-	0
1849.5 TO	1899.5-	0
1899.5 TO	1949.5-	0
1949.5 TO	1999.5-	1
1999.5 TO	2049.5-	3
2049.5 TO	2099.5-	0
2099.5 TO	2149.5-	4
2149.5 TO	2199.5-	1
2199.5 TO	2249.5-	0
2249.5 TO	2299.5-	1
2299.5 TO	2349.5-	1
2349.5 TO	2399.5-	0
2399.5 TO	2449.5-	1
2449.5 TO	2499.5-	1
2499.5 TO	2549.5-	0
2549.5 TO	2599.5-	3
2599.5 TO	2649.5-	1
2649.5 TO	2699.5-	2
2699.5 TO	2749.5-	2
2749.5 TO	2799.5-	0
2799.5 TO	2849.5-	3
2849.5 TO	2899.5-	0
2899.5 TO	2949.5-	1
2949.5 TO	2999.5-	0
2999.5 TO	3049.5-	0
3049.5 TO	3099.5-	1
3099.5 TO	3149.5-	2
3149.5 TO	3199.5-	1
3199.5 TO	3249.5-	0
3249.5 TO	3299.5-	0
3299.5 TO	3349.5-	0
3349.5 TO	3399.5-	0
3399.5 TO	3449.5-	3
3449.5 TO	3499.5-	0
3499.5 TO	3549.5-	0
3549.5 TO	3599.5-	2
3599.5 TO	3649.5-	0
3649.5 TO	3699.5-	0
3699.5 TO	3749.5-	0
3749.5 TO	3799.5-	0
3799.5 TO	3849.5-	0
3849.5 TO	3899.5-	0
3899.5 TO	3949.5-	1
3949.5 TO	3999.5-	0
3999.5 TO	4049.5-	1

All Cases Cumulative Dose
3 Years Before Death

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- .5 TO 49.5- 3005*****
49.5 TO 99.5- 433*****
99.5 TO 149.5- 188*****
149.5 TO 199.5- 87#
199.5 TO 249.5- 58
249.5 TO 299.5- 32
299.5 TO 349.5- 21
349.5 TO 399.5- 13
399.5 TO 449.5- 12
449.5 TO 499.5- 16
499.5 TO 549.5- 9
549.5 TO 599.5- 14
599.5 TO 649.5- 9
649.5 TO 699.5- 5
699.5 TO 749.5- 7
749.5 TO 799.5- 8
799.5 TO 849.5- 2
849.5 TO 899.5- 1
899.5 TO 949.5- 8
949.5 TO 999.5- 4
999.5 TO 1049.5- 4
1049.5 TO 1099.5- 1
1099.5 TO 1149.5- 2
1149.5 TO 1199.5- 2
1199.5 TO 1249.5- 3
1249.5 TO 1299.5- 1
1299.5 TO 1349.5- 4
1349.5 TO 1399.5- 1
1399.5 TO 1449.5- 1
1449.5 TO 1499.5- 0
1499.5 TO 1549.5- 2
1549.5 TO 1599.5- 1
1599.5 TO 1649.5- 0
1649.5 TO 1699.5- 2
1699.5 TO 1749.5- 2
1749.5 TO 1799.5- 1
1799.5 TO 1849.5- 1
1849.5 TO 1899.5- 2
1899.5 TO 1949.5- 1
1949.5 TO 1999.5- 2
1999.5 TO 2049.5- 3
2049.5 TO 2099.5- 0
2099.5 TO 2149.5- 0
2149.5 TO 2199.5- 1
2199.5 TO 2249.5- 2
2249.5 TO 2299.5- 2
2299.5 TO 2349.5- 1
2349.5 TO 2399.5- 1
2399.5 TO 2449.5- 1
2449.5 TO 2499.5- 2
2499.5 TO 2549.5- 0
2549.5 TO 2599.5- 2
2599.5 TO 2649.5- 0
2649.5 TO 2699.5- 2
2699.5 TO 2749.5- 2
2749.5 TO 2799.5- 0
2799.5 TO 2849.5- 0
2849.5 TO 2899.5- 0
2899.5 TO 2949.5- 1
2949.5 TO 2999.5- 1
2999.5 TO 3049.5- 1
3049.5 TO 3099.5- 0
3099.5 TO 3149.5- 1
3149.5 TO 3199.5- 0
3199.5 TO 3249.5- 0
3249.5 TO 3299.5- 0
3299.5 TO 3349.5- 0
3349.5 TO 3399.5- 0
3399.5 TO 3449.5- 2
3449.5 TO 3499.5- 1
3499.5 TO 3549.5- 0
3549.5 TO 3599.5- 0
3599.5 TO 3649.5- 0
3649.5 TO 3699.5- 0
3699.5 TO 3749.5- 0
3749.5 TO 3799.5- 0
3799.5 TO 3849.5- 1

```

All Cases Cumulative Dose
5 Years Before Death

-.5 TO	49.5-	3264
49.5 TO	99.5-	3648
99.5 TO	149.5-	1268
149.5 TO	199.5-	55
199.5 TO	249.5-	44
249.5 TO	299.5-	24
299.5 TO	349.5-	21
349.5 TO	399.5-	6
399.5 TO	449.5-	13
449.5 TO	499.5-	10
499.5 TO	549.5-	6
549.5 TO	599.5-	10
599.5 TO	649.5-	6
649.5 TO	699.5-	4
699.5 TO	749.5-	3
749.5 TO	799.5-	1
799.5 TO	849.5-	3
849.5 TO	899.5-	2
899.5 TO	949.5-	1
949.5 TO	999.5-	0
999.5 TO	1049.5-	1
1049.5 TO	1099.5-	3
1099.5 TO	1149.5-	0
1149.5 TO	1199.5-	0
1199.5 TO	1249.5-	3
1249.5 TO	1299.5-	2
1299.5 TO	1349.5-	3
1349.5 TO	1399.5-	3
1399.5 TO	1449.5-	1
1449.5 TO	1499.5-	2
1499.5 TO	1549.5-	1
1549.5 TO	1599.5-	2
1599.5 TO	1649.5-	2
1649.5 TO	1699.5-	1
1699.5 TO	1749.5-	1
1749.5 TO	1799.5-	0
1799.5 TO	1849.5-	0
1849.5 TO	1899.5-	0
1899.5 TO	1949.5-	0
1949.5 TO	1999.5-	0
1999.5 TO	2049.5-	0
2049.5 TO	2099.5-	0
2099.5 TO	2149.5-	0
2149.5 TO	2199.5-	0
2199.5 TO	2249.5-	0
2249.5 TO	2299.5-	1
2299.5 TO	2349.5-	1
2349.5 TO	2399.5-	0
2399.5 TO	2449.5-	1
2449.5 TO	2499.5-	0
2499.5 TO	2549.5-	1

All Cases Cumulative Dose
10 Years Before Death

-.5 TO	49.5-	3506
49.5 TO	99.5-	2428
99.5 TO	149.5-	998
149.5 TO	199.5-	42
199.5 TO	249.5-	35
249.5 TO	299.5-	17
299.5 TO	349.5-	16
349.5 TO	399.5-	2
399.5 TO	449.5-	7
449.5 TO	499.5-	5
499.5 TO	549.5-	3
549.5 TO	599.5-	4
599.5 TO	649.5-	4
649.5 TO	699.5-	2
699.5 TO	749.5-	1
749.5 TO	799.5-	1
799.5 TO	849.5-	0
849.5 TO	899.5-	1
899.5 TO	949.5-	2
949.5 TO	999.5-	1
999.5 TO	1049.5-	0
1049.5 TO	1099.5-	0
1099.5 TO	1149.5-	1
1149.5 TO	1199.5-	0
1199.5 TO	1249.5-	1

All Cases Cumulative Dose
15 Years Before Death

0.5 TO	49.5-	3742
49.5 TO	99.5-	1382
99.5 TO	149.5-	45	
149.5 TO	199.5-	27	
199.5 TO	249.5-	9	
249.5 TO	299.5-	5	
299.5 TO	349.5-	3	
349.5 TO	399.5-	1	
399.5 TO	449.5-	0	
449.5 TO	499.5-	2	

All Cases Cumulative Dose
20 Years Before Death

0.5 TO	49.5-	3923
49.5 TO	99.5-	47	
99.5 TO	149.5-	13	
149.5 TO	199.5-	5	
199.5 TO	249.5-	3	
249.5 TO	299.5-	1	

All Cases Cumulative Dose
25 Years Before Death

43.5 TO	44.5-	72	
44.5 TO	45.5-	1522	
45.5 TO	46.5-	26222222	
46.5 TO	47.5-	25222222	
47.5 TO	48.5-	3522222222	
48.5 TO	49.5-	6522222222222222	
49.5 TO	50.5-	5322222222222222	
50.5 TO	51.5-	6922222222222222	
51.5 TO	52.5-	81222222222222222222	
52.5 TO	53.5-	91222222222222222222	
53.5 TO	54.5-	80222222222222222222	
54.5 TO	55.5-	84222222222222222222	
55.5 TO	56.5-	99222222222222222222	
56.5 TO	57.5-	1242222222222222222222	
57.5 TO	58.5-	1182222222222222222222	
58.5 TO	59.5-	1392222222222222222222	
59.5 TO	60.5-	1642222222222222222222	
60.5 TO	61.5-	1762222222222222222222	
61.5 TO	62.5-	2002222222222222222222	
62.5 TO	63.5-	1792222222222222222222	
63.5 TO	64.5-	1942222222222222222222	
64.5 TO	65.5-	2012222222222222222222	
65.5 TO	66.5-	2082222222222222222222	
66.5 TO	67.5-	2212222222222222222222	
67.5 TO	68.5-	2552222222222222222222	
68.5 TO	69.5-	2542222222222222222222	
69.5 TO	70.5-	2852222222222222222222	
70.5 TO	71.5-	2482222222222222222222	
71.5 TO	72.5-	2762222222222222222222	

All Cases Year of Death

Exposed White Males Age At Death

21.5	TO	22.5	4444
22.5	TO	23.5	4444
23.5	TO	24.5	3333
24.5	TO	25.5	666666
25.5	TO	26.5	4444
26.5	TO	27.5	22
27.5	TO	28.5	88888888
28.5	TO	29.5	0
29.5	TO	30.5	88888888
30.5	TO	31.5	666666
31.5	TO	32.5	88888888
32.5	TO	33.5	1111111111
33.5	TO	34.5	666666
34.5	TO	35.5	1111111111
35.5	TO	36.5	1388888888
36.5	TO	37.5	1388888888
37.5	TO	38.5	1988888888
38.5	TO	39.5	22888888888888
39.5	TO	40.5	148888888888
40.5	TO	41.5	22888888888888
41.5	TO	42.5	27888888888888
42.5	TO	43.5	30888888888888
43.5	TO	44.5	36888888888888
44.5	TO	45.5	36888888888888
45.5	TO	46.5	37888888888888
46.5	TO	47.5	37888888888888
47.5	TO	48.5	37888888888888
48.5	TO	49.5	42888888888888
49.5	TO	50.5	42888888888888
50.5	TO	51.5	42888888888888
51.5	TO	52.5	49888888888888
52.5	TO	53.5	52888888888888
53.5	TO	54.5	52888888888888
54.5	TO	55.5	54888888888888
55.5	TO	56.5	65888888888888
56.5	TO	57.5	74888888888888
57.5	TO	58.5	52888888888888
58.5	TO	59.5	54888888888888
59.5	TO	60.5	59888888888888
60.5	TO	61.5	68888888888888
61.5	TO	62.5	73888888888888
62.5	TO	63.5	67888888888888
63.5	TO	64.5	67888888888888
64.5	TO	65.5	65888888888888
65.5	TO	66.5	78888888888888
66.5	TO	67.5	62888888888888
67.5	TO	68.5	72888888888888
68.5	TO	69.5	70888888888888
69.5	TO	70.5	54888888888888
70.5	TO	71.5	39888888888888
71.5	TO	72.5	70888888888888
72.5	TO	73.5	51888888888888
73.5	TO	74.5	46888888888888
74.5	TO	75.5	37888888888888
75.5	TO	76.5	45888888888888
76.5	TO	77.5	37888888888888
77.5	TO	78.5	24888888888888
78.5	TO	79.5	27888888888888
79.5	TO	80.5	138888888888
80.5	TO	81.5	24888888888888
81.5	TO	82.5	118888888888
82.5	TO	83.5	18888888888888
83.5	TO	84.5	14888888888888
84.5	TO	85.5	12888888888888
85.5	TO	86.5	58888888
86.5	TO	87.5	58888888
87.5	TO	88.5	58888888
88.5	TO	89.5	28
89.5	TO	90.5	1
90.5	TO	91.5	1
91.5	TO	92.5	0
92.5	TO	93.5	0
93.5	TO	94.5	0
94.5	TO	95.5	0
95.5	TO	96.5	0
96.5	TO	97.5	0
97.5	TO	98.5	0
98.5	TO	99.5	0
99.5	TO	100.5	0
100.5	TO	101.5	1

42.5 TO 43.5-	0
43.5 TO 44.5-	1008*****
44.5 TO 45.5-	352*****
45.5 TO 46.5-	74*****
46.5 TO 47.5-	242*****
47.5 TO 48.5-	132*****
48.5 TO 49.5-	33**
49.5 TO 50.5-	33**
50.5 TO 51.5-	132*****
51.5 TO 52.5-	45***
52.5 TO 53.5-	30*
53.5 TO 54.5-	35**
54.5 TO 55.5-	41***
55.5 TO 56.5-	7
56.5 TO 57.5-	4
57.5 TO 58.5-	4
58.5 TO 59.5-	4
59.5 TO 60.5-	7
60.5 TO 61.5-	6
61.5 TO 62.5-	7
62.5 TO 63.5-	6
63.5 TO 64.5-	2
64.5 TO 65.5-	2
65.5 TO 66.5-	6
66.5 TO 67.5-	4
67.5 TO 68.5-	0
68.5 TO 69.5-	0
69.5 TO 70.5-	2

Exposed White Males Initial Year of Employment

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43.5 TO 44.5- 19####
44.5 TO 45.5- 340#####
45.5 TO 46.5- 119#####
46.5 TO 47.5- 46#####
47.5 TO 48.5- 69#####
48.5 TO 49.5- 112#####
49.5 TO 50.5- 78#####
50.5 TO 51.5- 123#####
51.5 TO 52.5- 98#####
52.5 TO 53.5- 91#####
53.5 TO 54.5- 67#####
54.5 TO 55.5- 88#####
55.5 TO 56.5- 75#####
56.5 TO 57.5- 94#####
57.5 TO 58.5- 88#####
58.5 TO 59.5- 84#####
59.5 TO 60.5- 66#####
60.5 TO 61.5- 74#####
61.5 TO 62.5- 76#####
62.5 TO 63.5- 67#####
63.5 TO 64.5- 64#####
64.5 TO 65.5- 77#####
65.5 TO 66.5- 31#####
66.5 TO 67.5- 19#####
67.5 TO 68.5- 24#####
68.5 TO 69.5- 34#####
69.5 TO 70.5- 38#####
70.5 TO 71.5- 30#####
71.5 TO 72.5- 36#####

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2.5 TO 1.5- 177#####
.5 TO 1.5- 362#####
1.5 TO 2.5- 159#####
2.5 TO 3.5- 119#####
3.5 TO 4.5- 105#####
4.5 TO 5.5- 92#####
5.5 TO 6.5- 93#####
6.5 TO 7.5- 90#####
7.5 TO 8.5- 92#####
8.5 TO 9.5- 82#####
9.5 TO 10.5- 78#####
10.5 TO 11.5- 86#####
11.5 TO 12.5- 71#####
12.5 TO 13.5- 61#####
13.5 TO 14.5- 79#####
14.5 TO 15.5- 67#####
15.5 TO 16.5- 51#####
16.5 TO 17.5- 68#####
17.5 TO 18.5- 50#####
18.5 TO 19.5- 49#####
19.5 TO 20.5- 47#####
20.5 TO 21.5- 36#####
21.5 TO 22.5- 19###
22.5 TO 23.5- 12#
23.5 TO 24.5- 16##
24.5 TO 25.5- 24####
25.5 TO 26.5- 13#
26.5 TO 27.5- 14#
27.5 TO 28.5- 14#

```

9	1
11	5
38	1
40	1
43	2
52	1
70	2
93	1
95	1
112	1
136	1
141	3
142	2
144	2
145	3
146	1
147	1
148	1
149	1
150	9
151	26**
152	1
153	50*****
154	16*
155	7
156	3
157	32***
158	1
159	1
160	2
161	7
162	128*****
163	1
170	1
171	3
172	9
173	1
185	21*
186	3
188	7
189	15
190	1
191	14
192	3
193	1
195	2
197	8
198	2
199	13
200	16*
201	10
202	2
203	8
204	2
205	6
206	1
207	1
209	1
211	2
225	1
238	1
244	1
250	26**

n.b. One case with no cause
of death is excluded.

Exposed White Males Cause of Death (ICD codes)

255	3
258	1
269	1
272	3
276	1
277	1
279	2
284	1
303	8
309	1
320	2
323	2
340	1
342	2
347	1
348	5
355	1
394	6
395	11
396	3
397	2
398	3
400	7
401	2
402	7
403	4
404	3
410	703
411	11
412	180
421	1
422	1
425	2
427	18*
428	3
429	11
430	14
431	34****
432	5
433	35****
434	1
436	36****
437	15
438	2
440	13
441	33***
442	2
444	1
445	2
446	2
450	4
451	1
452	1
453	1
458	1
470	2
480	2
481	5
485	9
486	10
490	1
491	11
492	46*****
493	5

Exposed White Males Cause of Death (ICD codes)

513	1
514	1
517	4
518	3
519	6
530	1
531	4
532	8
533	6
534	1
537	1
540	3
551	2
552	1
560	2
561	1
562	4
569	2
570	1
571	35****
573	3
574	2
575	1
576	2
577	5
581	1
582	8
584	1
590	6
592	1
593	2
599	1
601	1
602	2
695	1
716	1
729	1
733	2
734	2
747	2
748	1
753	2
782	5
786	1
792	1
795	1
796	11
805	1
810	5
812	28****
813	3
814	5
816	16*
818	4
819	29****
830	8
832	2
840	3
841	12
873	1
874	2
880	1
881	2
882	2
884	3
885	2
887	7
890	2
891	1
895	1
898	1
899	1
910	8
911	4
913	1
916	2
918	1
922	10
923	3
924	1
925	4
926	1
927	1
928	2
929	1
930	3
943	1
950	3
952	13
953	6
955	53*****
958	1
980	2
985	2
986	1
988	1
994	1

49.5 TO 49.5-	1141	*****
49.5 TO 99.5-	406	*****
99.5 TO 149.5-	218	*****
149.5 TO 199.5-	116	*****
199.5 TO 249.5-	60	***
249.5 TO 299.5-	44	***
299.5 TO 349.5-	30	***
349.5 TO 399.5-	19	
399.5 TO 449.5-	20	
449.5 TO 499.5-	13	
499.5 TO 549.5-	9	
549.5 TO 599.5-	14	
599.5 TO 649.5-	17	
649.5 TO 699.5-	9	
699.5 TO 749.5-	5	
749.5 TO 799.5-	7	
799.5 TO 849.5-	5	
849.5 TO 899.5-	0	
899.5 TO 949.5-	8	
949.5 TO 999.5-	3	
999.5 TO 1049.5-	5	
1049.5 TO 1099.5-	1	
1099.5 TO 1149.5-	3	
1149.5 TO 1199.5-	2	
1199.5 TO 1249.5-	3	
1249.5 TO 1299.5-	2	
1299.5 TO 1349.5-	1	
1349.5 TO 1399.5-	2	
1399.5 TO 1449.5-	1	
1449.5 TO 1499.5-	2	
1499.5 TO 1549.5-	4	
1549.5 TO 1599.5-	2	
1599.5 TO 1649.5-	1	
1649.5 TO 1699.5-	6	
1699.5 TO 1749.5-	4	
1749.5 TO 1799.5-	1	
1799.5 TO 1849.5-	1	
1849.5 TO 1899.5-	0	
1899.5 TO 1949.5-	0	
1949.5 TO 1999.5-	2	
1999.5 TO 2049.5-	3	
2049.5 TO 2099.5-	1	
2099.5 TO 2149.5-	1	
2149.5 TO 2199.5-	2	
2199.5 TO 2249.5-	0	
2249.5 TO 2299.5-	0	
2299.5 TO 2349.5-	1	
2349.5 TO 2399.5-	1	
2399.5 TO 2449.5-	0	
2449.5 TO 2499.5-	0	
2499.5 TO 2549.5-	1	
2549.5 TO 2599.5-	5	
2599.5 TO 2649.5-	0	
2649.5 TO 2699.5-	1	
2699.5 TO 2749.5-	2	
2749.5 TO 2799.5-	1	
2799.5 TO 2849.5-	0	
2849.5 TO 2899.5-	2	
2899.5 TO 2949.5-	1	
2949.5 TO 2999.5-	0	
2999.5 TO 3049.5-	0	
3049.5 TO 3099.5-	1	
3099.5 TO 3149.5-	3	
3149.5 TO 3199.5-	1	
3199.5 TO 3249.5-	0	
3249.5 TO 3299.5-	1	
3299.5 TO 3349.5-	0	
3349.5 TO 3399.5-	0	
3399.5 TO 3449.5-	6	
3449.5 TO 3499.5-	0	
3499.5 TO 3549.5-	0	
3549.5 TO 3599.5-	0	
3599.5 TO 3649.5-	1	
3649.5 TO 3699.5-	0	
3699.5 TO 3749.5-	0	
3749.5 TO 3799.5-	0	
3799.5 TO 3849.5-	1	
3849.5 TO 3899.5-	0	
3899.5 TO 3949.5-	0	
3949.5 TO 3999.5-	0	
3999.5 TO 4049.5-	1	
4049.5 TO 4099.5-	0	
4099.5 TO 4149.5-	0	
4149.5 TO 4199.5-	0	
4199.5 TO 4249.5-	0	
4249.5 TO 4299.5-	0	
4299.5 TO 4349.5-	1	
4349.5 TO 4399.5-	0	
4399.5 TO 4449.5-	1	

Exposed White Males Cumulative Lifetime Dose

49.5 TO	49.5-	1206
49.5 TO	99.5-	421
99.5 TO	149.5-	174
149.5 TO	199.5-	117
199.5 TO	249.5-	56
249.5 TO	299.5-	35
299.5 TO	349.5-	29
349.5 TO	399.5-	16
399.5 TO	449.5-	21
449.5 TO	499.5-	10
499.5 TO	549.5-	7
549.5 TO	599.5-	18
599.5 TO	649.5-	11
649.5 TO	699.5-	5
699.5 TO	749.5-	2
749.5 TO	799.5-	9
799.5 TO	849.5-	4
849.5 TO	899.5-	1
899.5 TO	949.5-	7
949.5 TO	999.5-	3
999.5 TO	1049.5-	3
1049.5 TO	1099.5-	3
1099.5 TO	1149.5-	5
1149.5 TO	1199.5-	2
1199.5 TO	1249.5-	2
1249.5 TO	1299.5-	2
1299.5 TO	1349.5-	2
1349.5 TO	1399.5-	2
1399.5 TO	1449.5-	1
1449.5 TO	1499.5-	3
1499.5 TO	1549.5-	5
1549.5 TO	1599.5-	1
1599.5 TO	1649.5-	1
1649.5 TO	1699.5-	3
1699.5 TO	1749.5-	3
1749.5 TO	1799.5-	0
1799.5 TO	1849.5-	0
1849.5 TO	1899.5-	0
1899.5 TO	1949.5-	0
1949.5 TO	1999.5-	1
1999.5 TO	2049.5-	3
2049.5 TO	2099.5-	0
2099.5 TO	2149.5-	4
2149.5 TO	2199.5-	1
2199.5 TO	2249.5-	0
2249.5 TO	2299.5-	1
2299.5 TO	2349.5-	1
2349.5 TO	2399.5-	0
2399.5 TO	2449.5-	1
2449.5 TO	2499.5-	1
2499.5 TO	2549.5-	0
2549.5 TO	2599.5-	3
2599.5 TO	2649.5-	1
2649.5 TO	2699.5-	2
2699.5 TO	2749.5-	2
2749.5 TO	2799.5-	0
2799.5 TO	2849.5-	3
2849.5 TO	2899.5-	0
2899.5 TO	2949.5-	1
2949.5 TO	2999.5-	0
2999.5 TO	3049.5-	0
3049.5 TO	3099.5-	1
3099.5 TO	3149.5-	2
3149.5 TO	3199.5-	1
3199.5 TO	3249.5-	0
3249.5 TO	3299.5-	0
3299.5 TO	3349.5-	0
3349.5 TO	3399.5-	0
3399.5 TO	3449.5-	3
3449.5 TO	3499.5-	0
3499.5 TO	3549.5-	0
3549.5 TO	3599.5-	2
3599.5 TO	3649.5-	0
3649.5 TO	3699.5-	0
3699.5 TO	3749.5-	0
3749.5 TO	3799.5-	0
3799.5 TO	3849.5-	0
3849.5 TO	3899.5-	0
3899.5 TO	3949.5-	1
3949.5 TO	3999.5-	0
3999.5 TO	4049.5-	1

Exposed White Males
Cumulative Dose 3 Years Before Death

- .5 TO	49.5-	1281	*****
49.5 TO	99.5-	407	*****
99.5 TO	149.5-	182	*****
149.5 TO	199.5-	86	*****
199.5 TO	249.5-	55	*****
249.5 TO	299.5-	32	*
299.5 TO	349.5-	21	
349.5 TO	399.5-	13	
399.5 TO	449.5-	10	
449.5 TO	499.5-	16	
499.5 TO	549.5-	8	
549.5 TO	599.5-	13	
599.5 TO	649.5-	8	
649.5 TO	699.5-	5	
699.5 TO	749.5-	7	
749.5 TO	799.5-	8	
799.5 TO	849.5-	2	
849.5 TO	899.5-	1	
899.5 TO	949.5-	6	
949.5 TO	999.5-	4	
999.5 TO	1049.5-	4	
1049.5 TO	1099.5-	1	
1099.5 TO	1149.5-	2	
1149.5 TO	1199.5-	2	
1199.5 TO	1249.5-	3	
1249.5 TO	1299.5-	1	
1299.5 TO	1349.5-	3	
1349.5 TO	1399.5-	1	
1399.5 TO	1449.5-	1	
1449.5 TO	1499.5-	0	
1499.5 TO	1549.5-	2	
1549.5 TO	1599.5-	1	
1599.5 TO	1649.5-	0	
1649.5 TO	1699.5-	2	
1699.5 TO	1749.5-	2	
1749.5 TO	1799.5-	1	
1799.5 TO	1849.5-	1	
1849.5 TO	1899.5-	2	
1899.5 TO	1949.5-	1	
1949.5 TO	1999.5-	2	
1999.5 TO	2049.5-	3	
2049.5 TO	2099.5-	0	
2099.5 TO	2149.5-	0	
2149.5 TO	2199.5-	1	
2199.5 TO	2249.5-	2	
2249.5 TO	2299.5-	2	
2299.5 TO	2349.5-	1	
2349.5 TO	2399.5-	1	
2399.5 TO	2449.5-	1	
2449.5 TO	2499.5-	2	
2499.5 TO	2549.5-	0	
2549.5 TO	2599.5-	2	
2599.5 TO	2649.5-	0	
2649.5 TO	2699.5-	2	
2699.5 TO	2749.5-	2	
2749.5 TO	2799.5-	0	
2799.5 TO	2849.5-	0	
2849.5 TO	2899.5-	0	
2899.5 TO	2949.5-	1	
2949.5 TO	2999.5-	1	
2999.5 TO	3049.5-	1	
3049.5 TO	3099.5-	0	
3099.5 TO	3149.5-	1	
3149.5 TO	3199.5-	0	
3199.5 TO	3249.5-	0	
3249.5 TO	3299.5-	0	
3299.5 TO	3349.5-	0	
3349.5 TO	3399.5-	0	
3399.5 TO	3449.5-	2	
3449.5 TO	3499.5-	1	
3499.5 TO	3549.5-	0	
3549.5 TO	3599.5-	0	
3599.5 TO	3649.5-	0	
3649.5 TO	3699.5-	0	
3699.5 TO	3749.5-	0	
3749.5 TO	3799.5-	0	
3799.5 TO	3849.5-	1	

Exposed White Males
Cumulative Dose 5 Years Before Death

- .5 TO	49.5-	1526
49.5 TO	99.5-	345
99.5 TO	149.5-	125
149.5 TO	199.5-	55
199.5 TO	249.5-	42
249.5 TO	299.5-	32
299.5 TO	349.5-	19
349.5 TO	399.5-	6
399.5 TO	449.5-	12
449.5 TO	499.5-	10
499.5 TO	549.5-	6
549.5 TO	599.5-	10
599.5 TO	649.5-	5
649.5 TO	699.5-	4
699.5 TO	749.5-	3
749.5 TO	799.5-	1
799.5 TO	849.5-	3
849.5 TO	899.5-	2
899.5 TO	949.5-	1
949.5 TO	999.5-	0
999.5 TO	1049.5-	1
1049.5 TO	1099.5-	3
1099.5 TO	1149.5-	0
1149.5 TO	1199.5-	0
1199.5 TO	1249.5-	3
1249.5 TO	1299.5-	2
1299.5 TO	1349.5-	3
1349.5 TO	1399.5-	3
1399.5 TO	1449.5-	1
1449.5 TO	1499.5-	2
1499.5 TO	1549.5-	1
1549.5 TO	1599.5-	2
1599.5 TO	1649.5-	2
1649.5 TO	1699.5-	1
1699.5 TO	1749.5-	1
1749.5 TO	1799.5-	0
1799.5 TO	1849.5-	0
1849.5 TO	1899.5-	0
1899.5 TO	1949.5-	0
1949.5 TO	1999.5-	0
1999.5 TO	2049.5-	0
2049.5 TO	2099.5-	0
2099.5 TO	2149.5-	0
2149.5 TO	2199.5-	0
2199.5 TO	2249.5-	0
2249.5 TO	2299.5-	1
2299.5 TO	2349.5-	1
2349.5 TO	2399.5-	0
2399.5 TO	2449.5-	1
2449.5 TO	2499.5-	0
2499.5 TO	2549.5-	1

Exposed White Males
Cumulative Dose 10 Years Before Death

- .5 TO	49.5-	1758
49.5 TO	99.5-	220
99.5 TO	149.5-	97
149.5 TO	199.5-	41
199.5 TO	249.5-	34
249.5 TO	299.5-	17
299.5 TO	349.5-	16
349.5 TO	399.5-	2
399.5 TO	449.5-	7
449.5 TO	499.5-	5
499.5 TO	549.5-	3
549.5 TO	599.5-	4
599.5 TO	649.5-	4
649.5 TO	699.5-	2
699.5 TO	749.5-	1
749.5 TO	799.5-	1
799.5 TO	849.5-	0
849.5 TO	899.5-	1
899.5 TO	949.5-	2
949.5 TO	999.5-	1
999.5 TO	1049.5-	0
1049.5 TO	1099.5-	0
1099.5 TO	1149.5-	1
1149.5 TO	1199.5-	0
1199.5 TO	1249.5-	1

Exposed White Males
Cumulative Dose 15 Years Before Death

- .5 TO	49.5-	2004	*****
49.5 TO	99.5-	131	****
99.5 TO	149.5-	45	
149.5 TO	199.5-	26	
199.5 TO	249.5-	9	
249.5 TO	299.5-	5	
299.5 TO	349.5-	3	
349.5 TO	399.5-	1	
399.5 TO	449.5-	0	
449.5 TO	499.5-	2	

Exposed White Males
Cumulative Dose 20 Years Before Death

- .5 TO	49.5-	2159	*****
49.5 TO	99.5-	46	
99.5 TO	149.5-	13	
149.5 TO	199.5-	4	
199.5 TO	249.5-	3	
249.5 TO	299.5-	1	

Exposed White Males
Cumulative Dose 25 Years Before Death

43.5 TO	44.5-	1	
44.5 TO	45.5-	5*	
45.5 TO	46.5-	7**	
46.5 TO	47.5-	8***	
47.5 TO	48.5-	6**	
48.5 TO	49.5-	23*****	
49.5 TO	50.5-	21*****	
50.5 TO	51.5-	30*****	
51.5 TO	52.5-	38*****	
52.5 TO	53.5-	47*****	
53.5 TO	54.5-	37*****	
54.5 TO	55.5-	39*****	
55.5 TO	56.5-	52*****	
56.5 TO	57.5-	59*****	
57.5 TO	58.5-	72*****	
58.5 TO	59.5-	80*****	
59.5 TO	60.5-	85*****	
60.5 TO	61.5-	96*****	
61.5 TO	62.5-	102*****	
62.5 TO	63.5-	105*****	
63.5 TO	64.5-	111*****	
64.5 TO	65.5-	105*****	
65.5 TO	66.5-	132*****	
66.5 TO	67.5-	124*****	
67.5 TO	68.5-	146*****	
68.5 TO	69.5-	159*****	
69.5 TO	70.5-	183*****	
70.5 TO	71.5-	170*****	
71.5 TO	72.5-	183*****	

Exposed White Males Year of Death

APPENDIX B

CAUSE OF DEATH DISTRIBUTION

<u>NO. OF CASES</u>	<u>CODE</u>	<u>DESCRIPTION</u>
1	8	Enteritis due to other specified organism
4	9	Diarrhoeal disease
13	11	Pulmonary tuberculosis
1	23	Brucellosis
2	38	Septicaemia
1	39	Other bacterial diseases
2	40	Acute paralytic poliomyelitis specified as bulbar
1	41	Acute poliomyelitis with other paralysis
2	43	Acute poliomyelitis, unspecified
1	46	Other enterovirus diseases of central nervous system
1	52	Chickenpox
2	70	Infectious hepatitis
1	93	Cardiovascular syphilis
1	95	Other forms of late syphilis, with symptoms
1	112	Moniliasis
1	136	Other and unspecified infective and parasitic diseases
1	140	Malignant neoplasm of lip
6	141	Malignant neoplasm of tongue
3	142	Malignant neoplasm of salivary gland
2	144	Malignant neoplasm of floor of mouth
3	145	Malignant neoplasm of other and unspecified parts of mouth
3	146	Malignant neoplasm of oropharynx
1	147	Malignant neoplasm of nasopharynx

<u>NO. OF CASES</u>	<u>CODE</u>	<u>DESCRIPTION</u>
2	148	Malignant neoplasm of hypopharynx
2	149	Malignant neoplasm of pharynx, unspecified
18	150	Malignant neoplasm of oesophagus
39	151	Malignant neoplasm of stomach
2	152	Malignant neoplasm of small intestine, including duodenum
79	153	Malignant neoplasm of large intestine, except rectum
23*	154	Malignant neoplasm of rectum and rectosigmoid junction
9	155	Malignant neoplasm of liver and intrahepatic bile ducts, specified as primary
11	156	Malignant neoplasm of gallbladder and bile ducts
53	157	Malignant neoplasm of pancreas
3	158	Malignant neoplasm of peritoneum and retroperitoneal tissue
1	159	Malignant neoplasm of unspecified digestive organs
2	160	Malignant neoplasm of nose, nasal cavities, middle ear and accessory sinuses
10	161	Malignant neoplasm of larynx
202	162	Malignant neoplasm of trachea, bronchus and lung
1	163	Malignant neoplasm of other and unspecified respiratory organs
1	170	Malignant neoplasm of bone
6	171	Malignant neoplasm of connective and other soft tissue
13	172	Malignant melanoma of skin
3	173	Other malignant neoplasm of skin

<u>NO. OF CASES</u>	<u>CODE</u>	<u>DESCRIPTION</u>
31	174	Malignant neoplasm of breast
7	180	Malignant neoplasm of cervix uteri
6	182	Other malignant neoplasm of uterus
13	183	Malignant neoplasm of ovary, fallopian tube and broad ligament
43	185	Malignant neoplasm of prostate
4	186	Malignant neoplasm of testis
11	188	Malignant neoplasm of bladder
25	189	Malignant neoplasm of other and unspecified urinary organs
1	190	Malignant neoplasm of eye
23	191	Malignant neoplasm of brain
5	192	Malignant neoplasm of other parts of nervous system
2	193	Malignant neoplasm of thyroid gland
1	194	Malignant neoplasm of other endocrine glands
5	195	Malignant neoplasm of ill-defined sites
1	196	Secondary and unspecified malignant neoplasm of lymph nodes
18	197	Secondary malignant neoplasm of respiratory and digestive systems
2	198	Other secondary malignant neoplasm
30	199	Malignant neoplasm without specification of site
22	200	Lymphosarcoma and reticulum-cell sarcoma
14	201	Hodgkin's disease
3	202	Other neoplasms of lymphoid tissue
11	203	Multiple myeloma
5	204	Lymphatic leukaemia

<u>NO. OF CASES</u>	<u>CODE</u>	<u>DESCRIPTION</u>
13	205	Myeloid leukaemia
1	206	Monocytic leukaemia
5	207	Other and unspecified leukaemia
1	208	Polycythaemia vera
1	209	Myelofibrosis
2	211	Benign neoplasm of other parts of digestive system
2	218	Uterine fibroma
1	225	Benign neoplasm of brain and other parts of nervous system
1	228	Benign neoplasm of other and unspecified organs and tissues
1	231	Neoplasm of unspecified nature of respiratory organs
5	238	Neoplasm of unspecified nature of eye, brain and other parts of nervous system
1	244	Myxoedema
48	250	Diabetes mellitus
1	253	Diseases of pituitary gland
4	255	Diseases of adrenal glands
1	258	Polyglandular dysfunction and other diseases of endocrine glands
3	269	Other nutritional deficiency
4	272	Congenital disorders of lipid metabolism
1	276	Amyloidosis
3	277	Obesity not specified as of endocrine origin
3	279	Other and unspecified metabolic diseases
4	284	Aplastic anaemia
2	289	Other diseases of blood and blood-forming organs

<u>NO. OF CASES</u>	<u>CODE</u>	<u>DESCRIPTION</u>
2	291	Alcoholic psychosis
1	299	Unspecified psychosis
11	303	Alcoholism
3	309	Mental disorders not specified as psychotic associated with physical conditions
2	320	Meningitis
1	322	Intracranial and intraspinal abscess
2	323	Encephalitis, myelitis, and encephalomyelitis
1	330	Hereditary neuromuscular disorders
1	331	Hereditary diseases of the striato-pallidal system
2	340	Multiple sclerosis
7	342	Paralysis agitans
2	345	Epilepsy
3	347	Other diseases of brain
6	348	Motor neurone disease
1	355	Other and unspecified forms of neuralgia and neuritis
1	393	Disease of pericardium
14	394	Disease of mitral valve
15	395	Diseases of aortic valve
9	396	Diseases of mitral and aortic valves
4	397	Diseases of other endocardial structures
11	398	Other heart disease, specified as rheumatic
8	400	Malignant hypertension
4	401	Essential benign hypertension
15	402	Hypertensive heart disease

<u>NO. OF CASES</u>	<u>CODE</u>	<u>DESCRIPTION</u>
7	403	Hypertensive renal disease
8	404	Hypertensive heart and renal disease
1109	410	Acute myocardial infarction
19	411	Other acute and subacute forms of ischaemic heart disease
348	412	Chronic ischaemic heart disease
1	413	Angina pectoris
2	421	Acute and sub-acute endocarditis
3	422	Acute myocarditis
1	423	Chronic disease of pericardium, non-rheumatic
1	424	Chronic disease of endocardium
2	425	Cardiomyopathy
3	426	Pulmonary heart disease
29	427	Symptomatic heart disease
15	428	Other myocardial insufficiency
20	429	Ill-defined heart disease
31	430	Subarachnoid haemorrhage
75	431	Cerebral haemorrhage
8	432	Occlusion of pre-cerebral arteries
58	433	Cerebral thrombosis
1	434	Cerebral embolism
61	436	Acute but ill-defined cerebrovascular disease
19	437	Generalized ischaemic cerebrovascular disease
6	438	Other and ill-defined cerebrovascular disease

<u>NO. OF CASES</u>	<u>CODE</u>	<u>DESCRIPTION</u>
23	440	Arteriosclerosis
55	441	Aortic aneurysm (non-syphilitic)
3	442	Other aneurysm
4	444	Arterial embolism and thrombosis
4	445	Gangrene
3	446	Polyarteritis nodosa and allied conditions
2	447	Other diseases of arteries and arterioles
13	450	Pulmonary embolism and infarction
2	451	Phlebitis and thrombophlebitis
1	452	Portal vein thrombosis
2	453	Other venous embolism and thrombosis
2	458	Other diseases of circulatory system
1	463	Acute tonsillitis
1	466	Acute bronchitis and bronchiolitis
5	470	Influenza unqualified
3	480	Viral pneumonia
16	481	Pneumococcal pneumonia
2	482	Other bacterial pneumonia
26	485	Bronchopneumonia, unspecified
19	486	Pneumonia, unspecified
1	490	Bronchitis, unqualified
16	491	Chronic bronchitis
81	492	Emphysema
9	493	Asthma
1	513	Abscess of lung
2	514	Pulmonary congestion and hypostasis

<u>NO. OF CASES</u>	<u>CODE</u>	<u>DESCRIPTION</u>
1	515	Pneumoconiosis due to silica and silicates
9	517	Other chronic interstitial pneumonia
5	518	Bronchiectasis
9	519	Other diseases of respiratory system
2	530	Diseases of oesophagus
7	531	Ulcer of stomach
18	532	Ulcer of duodenum
8	533	Peptic ulcer, site unspecified
1	534	Gastrojejunal ulcer
1	535	Gastritis and duodenitis
1	537	Other diseases of stomach and duodenum
4	540	Acute appendicitis
2	551	Other hernia of abdominal cavity without mention of obstruction
1	552	Inguinal hernia with obstruction
2	553	Other hernia of abdominal cavity with obstruction
3	560	Intestinal obstruction without mention of hernia
1	561	Gastro-enteritis and colitis, except ulcerative, of non-infectious origin
5	562	Diverticula of intestine
4	563	Chronic enteritis and ulcerative colitis
1	565	Anal fissure and fistula
5	569	Other diseases of intestines and peritoneum
1	570	Acute and subacute necrosis of liver
75	571	Cirrhosis of liver

<u>NO. OF CASES</u>	<u>CODE</u>	<u>DESCRIPTION</u>
5	573	Other diseases of liver
3	574	Choletithiasis
1	575	Cholecystitis and cholangitis, without mention of calculus
3	576	Other diseases of gallbladder and biliary ducts
10	577	Diseases of pancreas
4	581	Nephrotic syndrome
16	582	Chronic nephritis
1	583	Nephritis unqualified
1	584	Renal sclerosis unqualified
12	590	Infections of kidney
2	592	Calculus of kidney and ureter
4	593	Other diseases of kidney and ureter
1	596	Other diseases of bladder
3	599	Other diseases of urinary tract
1	600	Hyperplasia of prostate
1	601	Prostatitis
3	602	Other diseases of prostate
1	694	Pemphigus
1	695	Erythematous conditions
1	712	Rheumatoid arthritis and allied conditions
1	716	Polymyositis and dermatomyositis
1	717	Other non-articular rheumatism
1	720	Osteomyelitis and periostitis

<u>NO. OF CASES</u>	<u>CODE</u>	<u>DESCRIPTION</u>
1	729	Other diseases of joint
2	733	Other diseases of muscle, tendon, and fascia
4	734	Diffuse diseases of connective tissue
1	746	Congenital anomalies of heart
5	747	Other congenital anomalies of circulatory system
1	748	Congenital anomalies of respiratory system
1	751	Other congenital anomalies of digestive system
2	753	Congenital anomalies of urinary system
1	780	Certain symptoms referable to nervous system and special senses
9	782	Symptoms referable to cardiovascular and lymphatic system
1	786	Symptoms referable to genito-urinary system
1	792	Uraemia
2	794	Senility without mention of psychosis
1	795	Sudden death (cause unknown)
25	796	Other ill-defined and unknown causes of morbidity and mortality
2	E805	Hit by rolling stock
1	E807	Railway accident of unspecified nature
9	E810	Motor vehicle traffic accident involving collision with train
44	E812	Motor vehicle traffic accident involving collision with another motor vehicle
3	E813	Motor vehicle traffic accident involving collision with other vehicle
15	E814	Motor vehicle traffic accident involving collision with pedestrian

<u>NO. OF CASES</u>	<u>CODE</u>	<u>DESCRIPTION</u>
1	E815	Other motor vehicle traffic accident involving collision
36	E816	Non-collision motor vehicle traffic accident due to loss of control
6	E818	Other non-collision motor vehicle traffic accident
57	E819	Motor vehicle traffic accident of unspecified nature
1	E821	Motor vehicle non-traffic accident involving collision with stationary object
11	E830	Accident to watercraft causing submersion
4	E832	Other accidental submersion or drowning in water transport
3	E840	Accident to powered aircraft take-off or landing
17	E841	Accident to powered aircraft, other and unspecified
1	E853	Accidental poisoning by analgesics and antipyretics
4	E854	Accidental poisoning by other sedatives and hypnotics
1	E873	Accidental poisoning by motor vehicle exhaust gas
2	E874	Accidental poisoning by carbon monoxide from incomplete combustion of domestic fuels
5	E880	Fall on or from stairs or steps
3	E881	Fall on or from ladders or scaffolding
2	E882	Fall from or out of building or other structure
1	E883	Fall into hole or other opening in surface
3	E884	Other fall from one level to another
2	E885	Fall on same level from slipping, tripping or stumbling

<u>NO. OF CASES</u>	<u>CODE</u>	<u>DESCRIPTION</u>
13	E887	Other and unspecified fall
10	E890	Accident caused by conflagration in private dwelling
3	E891	Accident caused by conflagration in other building or structure
1	E894	Accident caused by ignition of highly inflammable material
1	E895	Accident caused by controlled fire in private dwelling
3	E898	Accident caused by other specified fires or flames
2	E899	Accident caused by unspecified fire
16	E910	Accidental drowning and submersion
7	E911	Inhalation and ingestion of food causing obstruction or suffocation
2	E913	Accidental mechanical suffocation
7	E916	Struck accidentally by falling object
1	E918	Caught accidentally in or between objects
1	E921	Accident caused by explosion of pressure vessel
11	E922	Accident caused by firearm missiles
3	E923	Accident caused by explosive material
3	E924	Accident caused by hot substance, corrosive liquid, and steam
6	E925	Accident caused by electric current
1	E926	Accident caused by radiation
3	E927	Vehicle accidents not elsewhere classifiable
3	E928	Machinery accidents not elsewhere classifiable
4	E929	Other and unspecified accidents
6	E930	Complications and misadventures in operative therapeutic procedures

<u>NO. OF CASES</u>	<u>CODE</u>	<u>DESCRIPTION</u>
1	E940	Late effect of motor vehicle accident
1	E942	Late effect of accidental poisoning
1	E943	Late effect of accidental fall
17	E950	Suicide and self-inflicted poisoning by solid or liquid substances
24	E952	Suicide and self-inflicted poisoning by other gases
11	E953	Suicide and self-inflicted injury by hanging, strangulation and suffocation
4	E954	Suicide and self-inflicted injury by submersion (drowning)
80	E955	Suicide and self-inflicted injury by firearms and explosives
2	E958	Suicide and self-inflicted injury by other and unspecified means
1	E963	Assault by hanging and strangulation
8	E965	Assault by firearms and explosives
3	E968	Assault by other and unspecified means
3	E980	Poisoning by solid or liquid substances, undetermined whether accidentally or purposely inflicted
1	E981	Poisoning by gases in domestic use, undetermined whether accidentally or purposely inflicted
1	E982	Poisoning by other gases, undetermined whether accidentally or purposely inflicted
3	E984	Submersion (drowning), undetermined whether accidentally or purposely inflicted
4	E985	Injury by firearms and explosives, undetermined whether accidentally or purposely inflicted
2	E986	Injury by cutting and piercing instruments, undetermined whether accidentally or purposely inflicted
2	E988	Injury by other and unspecified means, undetermined whether accidentally or purposely inflicted

<u>NO. OF CASES</u>	<u>CODE</u>	<u>DESCRIPTION</u>
2	E994	Injury due to war operations by destruction of aircraft
3	E995	Injury due to war operations by other and unspecified forms of conventional warfare

APPENDIX C

Program and Output Which Reviews Dose Time Histories and
Generates Average Yearly Dose of Workers

FURFUR=HACC 4.14 RL1834 12/17-07:52:03
2873400908*REGRESS(1),IRUN(3)

```

1  @RUN X,13015,2873400908,*50.00,1000
2  @ASQ,AX,OUTFILE.
3  @BKRPT PRINT$/OUTFILE
4  @PRT,S,REGRESS,IRUN
5  @PRT,S,REGRESS,1
6  @ASQ,AX,DATA.
7  @USE 20.,DATA.
8  @ASQ,T,TEMP2.
9  @USE 21.,TEMP2.
10 @FOR,IXC
11 @ADD REGRESS,1
12 @EOF
13 @XDT
14 @COST,A
15 @BKRPT PRINT$
16 @FIN

```

@PRT,S,REGRESS,1

2873400908*REGRESS(1),1(1)

```

11  DIMENSION A(18),YC(100),YI(100),YIC(100),ITABLE(100),DOS(7)
12  DATA ITABLE/481,1,182,543,544,545,546,748//
13  ICOUNT = 0
14  ICONT = 0
5110 READ,20:100:END*300) (A(110):110=1:16)
61  ICONT = ICONT + 1
71  I1 = A(18) = A(3) + 1
81  I2 = A(18) = A(2) + 1
91  ITOP = ITABLE(I1)
101 IBOT = ITABLE(I2)
111 IFLAG = 0
121 DO 700 I = 1,7
131 DOS(I) = A(8+I) = A(9+I)
141 IF(I.EQ.7) DOS(I) = A(15)
151 IF((I.LT.ITOP).OR.(I.GT.IBOT)) GO TO 701
161 GO TO 700
171701 IF((DOS(I).GT.0.).AND.(IFLAG.EQ.0))WRITE(=,*) (A(I7),I7=1:16)
181 IF(DOS(I).EQ.0.) GO TO 700
191 IF(IFLAG.EQ.0) ICOUNT = ICOUNT + 1
201 IFLAG = 1
211700 CONTINUE
221100 FORMAT(F4.0,2F2.0,2F3.0,3F1.0,7F6.0,F2.0)
231 I4 = A(18)
241 DO 200 I = 1,35
251 IX1 = IX = I + 1
261 IF(A(3))
271 IF(IX1.GT.IF) GO TO 200
281 IH = A(2)
291 IF(IX1.LT.IH) GO TO 200
301 IF (I.GT.3) GO TO 190
311 IFIN = A(3)
321 INIT = A(2)
331 IU = A(18) = I. + 1.
341 IL = A(18) = 3. + 1.
351 IF(IFIN.LT.IU) IU = IFIN
361 IF(INIT.GT.IL) IL = INIT
371 XINT = IU = IL + 1.
381 YI(IX1) = (A(7) = A(10))/XINT
391 YIC(IX1) = YIC(IX1) + YI(IX1)
401 YC(IX1) = YC(IX1) + 1.
411 GO TO 200
421190 IF(I.GT.5) GO TO 192
431 IFIN = A(3)
441 INIT = A(2)
451 IU = A(18) = 4. + 1.
461 IL = A(18) = 5. + 1.
471 IF(IFIN.LT.IU) IU = IFIN
481 IF(INIT.GT.IL) IL = INIT
491 XINT = IU = IL + 1.
501 YI(IX1) = (A(10) = A(11))/XINT

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511 VIC(I,1) = VIC(I,1) + Y1(I,1)
521 YC(I,1) = YC(I,1) + 1.
531 GO TO 200
541 IF (I.GT.15) GO TO 194
551 IFIN = A(1)
561 INIT = A(2)
571 IU = A(16) = 9. + 1.
581 IL = A(16) = 10. + 1.
591 IF (IFIN.LT.IU) IU = IFIN
601 IF (INIT.GT.IL) IL = INIT
611 XINT = IU - IL + 1.
621 Y1(I,1) = (A(11) - A(12))/XINT
631 VIC(I,1) = VIC(I,1) + Y1(I,1)
641 YC(I,1) = YC(I,1) + 1.
651 GO TO 200
661 194 IF (I.GT.15) GO TO 196
671 IFIN = A(3)
681 INIT = A(2)
691 IU = A(16) = 11. + 1.
701 IL = A(16) = 15. + 1.
711 IF (IFIN.LT.IU) IU = IFIN
721 IF (INIT.GT.IL) IL = INIT
731 XINT = IU - IL + 1.
741 Y1(I,1) = (A(12) - A(13))/XINT
751 VIC(I,1) = VIC(I,1) + Y1(I,1)
761 YC(I,1) = YC(I,1) + 1.
771 GO TO 200
781 196 IF (I.GT.20) GO TO 198
791 IFIN = A(3)
801 INIT = A(2)
811 IU = A(16) = 16. + 1.
821 IL = A(16) = 20. + 1.
831 IF (IFIN.LT.IU) IU = IFIN
841 IF (INIT.GT.IL) IL = INIT
851 XINT = IU - IL + 1.
861 Y1(I,1) = (A(13) - A(14))/XINT
871 VIC(I,1) = VIC(I,1) + Y1(I,1)
881 YC(I,1) = YC(I,1) + 1.
891 GO TO 200
901 198 IF (I.GT.25) GO TO 199
911 IFIN = A(3)
921 INIT = A(2)
931 IU = A(16) = 21. + 1.
941 IL = A(16) = 25. + 1.
951 IF (IFIN.LT.IU) IU = IFIN
961 IF (INIT.GT.IL) IL = INIT
971 XINT = IU - IL + 1.
981 Y1(I,1) = (A(14) - A(15))/XINT
991 VIC(I,1) = VIC(I,1) + Y1(I,1)
1001 YC(I,1) = YC(I,1) + 1.
1011 GO TO 200
1021 199 CONTINUE
1031 D = A(15) - A(2)
1041 IF (D.LE.25.) GO TO 200
1051 IFIN = A(3)
1061 INIT = A(2)
1071 IU = A(16) = 26. + 1.
1081 IL = A(16) = 30. + 1.
1091 IF (IFIN.LT.IU) IU = IFIN
1101 IF (INIT.GT.IL) IL = INIT
1111 XINT = IU - IL + 1.
1121 Y1(I,1) = (A(15))/XINT

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113:      YIC(IK1) = YIC(IK1) + YI(IK1)
114:      YC(IK1) = YC(IK1) + 1.
115:200  CONTINUE
116:      GO TO 10
117:300  CONTINUE
118:      WRITE(1,1) ICNT1
119:      WRITE(1,1) ICOUNT
120:      WRITE(1,201)
121:201  FORMAT(10X,'YR',10X,'TOTAL DOSE',10X,'COUNTS',10X,'AVERAGE DOSE')
122:      DO 500 IJK = 1,100
123:      AS = 0.
124:      IF (YC(IJK).EQ.0.) GO TO 37
125:      AS = YIC(IJK)/YC(IJK)
126:37  CONTINUE
127:      WRITE(1,500) IJK,YIC(IJK),YC(IJK),AS
128:      WRITE(1,500) IJK,YIC(IJK),YC(IJK),AS
129:500  CONTINUE
130:500  FORMAT(10X,I3,10X,F7.1,10X,F7.1,10X,F7.1)
131:      STOP
132:      END

```

RASG:AX DATA.

RUSE 20.:DATA.

RASG:T TEMP2.

RUSE 21.:TEMP2.

RFOR:IXC

FORTRAN-MACC 1.175-12/19/78-09:52:09

NAME\$

END OF COMPILATION:

NO DIAGNOSTICS.

EXOT

MAP28-2 RL1935 12/19-09:52:15

ADDRESS LIMITS

001000 012622

5011 IBANK WORDS DECIMAL

RDI

040000 045207

2696 DBANK WORDS DECIMAL

000004

STARTING ADDRESS 011452

SEGMENT MAIN\$

001000 012622

040000 045207

ERUS

NTAB\$/FORIO

NFTCH\$/FORIO

FORIO\$2/FORIO

NFFT1\$/FORIO

FORIO\$3/FORIO

NQSYN\$/FORIO

NFFT0\$/FORIO

FORIO\$4/FORIO

FORIO\$1/FORIO

NAME\$

SY\$*RLIB\$. LEVEL 41

END MAP

480.0000	53.0000	55.0000	14.0000	284.0000	1.0000	0.0	1.0000
17.0000	17.0000	17.0000	0.0	0.0	0.0	0.0	70.0000
415.0000	44.0000	54.0000	100.0000	142.0000	1.0000	1.0000	1.0000
222.0000	213.0000	126.0000	88.0000	56.0000	17.0000	0.0	48.0000
418.0000	63.0000	66.0000	31.0000	142.0000	1.0000	1.0000	1.0000
97.0000	71.0000	63.0000	0.0	0.0	0.0	0.0	72.0000
513.0000	48.0000	49.0000	2.0000	250.0000	1.0000	1.0000	1.0000
74.0000	29.0000	9.0000	4.0000	0.0	0.0	0.0	66.0000
493.0000	44.0000	62.0000	181.0000	185.0000	1.0000	1.0000	1.0000
253.0000	253.0000	233.0000	117.0000	100.0000	77.0000	33.0000	72.0000
637.0000	45.0000	56.0000	115.0000	197.0000	1.0000	1.0000	1.0000
228.0000	210.0000	162.0000	117.0000	111.0000	49.0000	0.0	69.0000
631.0000	48.0000	51.0000	34.0000	410.0000	1.0000	1.0000	1.0000
224.0000	183.0000	100.0000	23.0000	14.0000	8.0000	0.0	72.0000
514.0000	55.0000	59.0000	43.0000	930.0000	1.0000	1.0000	1.0000
147.0000	16.0000	0.0	0.0	0.0	0.0	0.0	65.0000
647.0000	48.0000	48.0000	1.0000	412.0000	1.0000	1.0000	1.0000
9.0000	9.0000	9.0000	6.0000	0.0	0.0	0.0	58.0000
177.0000	55.0000	57.0000	18.0000	110.0000	1.0000	1.0000	1.0000

2562.0000	2562.0000	2562.0000	1369.0000	338.0000	0.0	0.0	72.0000
645.0000	48.0000	49.0000	6.0000	410.0000	1.0000	1.0000	1.0000
368.0000	368.0000	356.0000	239.0000	103.0000	39.0000	0.0	72.0000
365.0000	45.0000	56.0000	117.0000	410.0000	1.0000	1.0000	1.0000
353.0000	335.0000	282.0000	171.0000	103.0000	21.0000	0.0	48.0000
619.0000	46.0000	52.0000	56.0000	153.0000	1.0000	1.0000	1.0000
67.0000	16.0000	0.0	0.0	0.0	0.0	0.0	67.0000
456.0000	44.0000	54.0000	100.0000	410.0000	1.0000	1.0000	1.0000
292.0000	292.0000	288.0000	170.0000	145.0000	91.0000	44.0000	71.0000
616.0000	48.0000	48.0000	2.0000	202.0000	1.0000	1.0000	1.0000
7.0000	7.0000	7.0000	7.0000	7.0000	4.0000	0.0	68.0000
584.0000	47.0000	53.0000	58.0000	410.0000	1.0000	1.0000	1.0000
3113.0000	3113.0000	2729.0000	1393.0000	444.0000	22.0000	0.0	72.0000
610.0000	44.0000	46.0000	16.0000	410.0000	1.0000	1.0000	1.0000
646.0000	444.0000	485.0000	321.0000	217.0000	146.0000	28.0000	69.0000
501.0000	47.0000	49.0000	15.0000	562.0000	1.0000	1.0000	1.0000
201.0000	201.0000	133.0000	13.0000	0.0	0.0	0.0	70.0000
537.0000	44.0000	57.0000	129.0000	410.0000	1.0000	1.0000	1.0000
3447.0000	3104.0000	2727.0000	1570.0000	621.0000	100.0000	0.0	70.0000
567.0000	44.0000	45.0000	6.0000	95.0000	1.0000	1.0000	1.0000
173.0000	173.0000	154.0000	0.0	0.0	0.0	0.0	50.0000
633.0000	49.0000	51.0000	15.0000	492.0000	1.0000	1.0000	1.0000
156.0000	156.0000	136.0000	59.0000	43.0000	11.0000	0.0	72.0000
598.0000	46.0000	51.0000	49.0000	429.0000	1.0000	1.0000	1.0000
958.0000	773.0000	651.0000	162.0000	88.0000	69.0000	0.0	69.0000
380.0000	64.0000	65.0000	13.0000	963.0000	0.0	1.0000	1.0000
207.0000	190.0000	144.0000	0.0	0.0	0.0	0.0	71.0000
495.0000	51.0000	51.0000	1.0000	812.0000	1.0000	1.0000	1.0000
134.0000	59.0000	47.0000	47.0000	0.0	0.0	0.0	65.0000
633.0000	45.0000	58.0000	134.0000	410.0000	1.0000	1.0000	1.0000
198.0000	198.0000	198.0000	42.0000	14.0000	14.0000	14.0000	71.0000
587.0000	49.0000	65.0000	159.0000	432.0000	1.0000	1.0000	1.0000
111.0000	72.0000	29.0000	15.0000	91.0000	0.0	0.0	68.0000
555.0000	44.0000	44.0000	1.0000	532.0000	1.0000	1.0000	1.0000
24.0000	24.0000	24.0000	24.0000	23.0000	0.0	0.0	60.0000
624.0000	59.0000	63.0000	38.0000	410.0000	1.0000	1.0000	1.0000
58.0000	58.0000	48.0000	0.0	0.0	0.0	0.0	69.0000
635.0000	45.0000	51.0000	68.0000	571.0000	1.0000	1.0000	1.0000
132.0000	113.0000	83.0000	61.0000	50.0000	29.0000	0.0	69.0000
636.0000	44.0000	50.0000	58.0000	162.0000	1.0000	1.0000	1.0000
17.0000	17.0000	14.0000	0.0	0.0	0.0	0.0	55.0000
666.0000	44.0000	55.0000	108.0000	412.0000	1.0000	1.0000	1.0000
313.0000	313.0000	295.0000	196.0000	176.0000	101.0000	64.0000	72.0000
493.0000	48.0000	55.0000	70.0000	410.0000	1.0000	1.0000	1.0000
161.0000	134.0000	130.0000	12.0000	0.0	0.0	0.0	72.0000
586.0000	44.0000	47.0000	24.0000	410.0000	1.0000	1.0000	1.0000
3183.0000	3066.0000	2913.0000	1747.0000	599.0000	23.0000	0.0	69.0000
448.0000	48.0000	51.0000	23.0000	183.0000	1.0000	0.0	1.0000
96.0000	45.0000	38.0000	38.0000	10.0000	0.0	0.0	65.0000
567.0000	45.0000	48.0000	34.0000	812.0000	1.0000	1.0000	1.0000
1469.0000	1379.0000	1151.0000	382.0000	215.0000	68.0000	0.0	70.0000
510.0000	51.0000	65.0000	135.0000	832.0000	1.0000	0.0	1.0000
169.0000	153.0000	123.0000	39.0000	39.0000	0.0	0.0	70.0000
361.0000	56.0000	56.0000	4.0000	238.0000	1.0000	1.0000	1.0000
101.0000	64.0000	53.0000	5.0000	0.0	0.0	0.0	66.0000
387.0000	52.0000	54.0000	17.0000	433.0000	1.0000	1.0000	1.0000
384.0000	103.0000	78.0000	24.0000	0.0	0.0	0.0	63.0000
572.0000	48.0000	56.0000	83.0000	188.0000	1.0000	1.0000	1.0000
210.0000	194.0000	164.0000	50.0000	35.0000	20.0000	0.0	72.0000
459.0000	44.0000	48.0000	43.0000	428.0000	1.0000	1.0000	1.0000
324.0000	324.0000	324.0000	314.0000	281.0000	0.0	0.0	61.0000
656.0000	51.0000	59.0000	81.0000	532.0000	1.0000	1.0000	1.0000
54.0000	54.0000	54.0000	48.0000	36.0000	0.0	0.0	69.0000
578.0000	44.0000	61.0000	169.0000	174.0000	1.0000	0.0	1.0000
1439.0000	1439.0000	1316.0000	441.0000	218.0000	170.0000	152.0000	71.0000
477.0000	54.0000	87.0000	78.0000	470.0000	1.0000	1.0000	1.0000

1781.0000	1566.0000	1253.0000	408.0000	21.0000	0.0	0.0	71.0000
577.0000	56.0000	64.0000	79.0000	348.0000	1.0000	1.0000	1.0000
115.0000	115.0000	97.0000	13.0000	0.0	0.0	0.0	71.0000
609.0000	54.0000	57.0000	32.0000	441.0000	1.0000	1.0000	1.0000
2875.0000	2456.0000	2000.0000	591.0000	14.0000	0.0	0.0	69.0000
689.0000	48.0000	48.0000	8.0000	428.0000	1.0000	1.0000	1.0000
74.0000	24.0000	24.0000	3.0000	0.0	0.0	0.0	59.0000
384.0000	51.0000	57.0000	58.0000	955.0000	1.0000	1.0000	1.0000
385.0000	330.0000	194.0000	65.0000	0.0	0.0	0.0	68.0000
552.0000	45.0000	55.0000	106.0000	395.0000	1.0000	1.0000	1.0000
1691.0000	1152.0000	770.0000	407.0000	71.0000	27.0000	0.0	67.0000
625.0000	45.0000	48.0000	34.0000	446.0000	1.0000	1.0000	1.0000
701.0000	192.0000	175.0000	120.0000	117.0000	95.0000	72.0000	71.0000
570.0000	51.0000	58.0000	65.0000	985.0000	1.0000	1.0000	1.0000
3629.0000	3578.0000	3111.0000	1625.0000	463.0000	8.0000	0.0	72.0000
591.0000	45.0000	50.0000	55.0000	410.0000	1.0000	1.0000	1.0000
328.0000	276.0000	271.0000	268.0000	254.0000	199.0000	0.0	66.0000
631.0000	44.0000	65.0000	206.0000	441.0000	1.0000	1.0000	1.0000
185.0000	164.0000	145.0000	78.0000	73.0000	34.0000	3.0000	70.0000
453.0000	45.0000	45.0000	7.0000	157.0000	1.0000	1.0000	1.0000
149.0000	141.0000	84.0000	59.0000	55.0000	37.0000	0.0	69.0000
670.0000	44.0000	56.0000	120.0000	412.0000	1.0000	1.0000	1.0000
66.0000	66.0000	62.0000	51.0000	32.0000	0.0	0.0	62.0000
532.0000	48.0000	49.0000	10.0000	410.0000	1.0000	1.0000	1.0000
198.0000	172.0000	141.0000	52.0000	32.0000	3.0000	0.0	71.0000
462.0000	54.0000	64.0000	96.0000	410.0000	1.0000	0.0	1.0000
84.0000	84.0000	62.0000	8.0000	0.0	0.0	0.0	69.0000
673.0000	44.0000	47.0000	30.0000	276.0000	1.0000	1.0000	1.0000
3443.0000	3443.0000	3015.0000	1662.0000	713.0000	154.0000	0.0	71.0000
569.0000	55.0000	58.0000	28.0000	410.0000	1.0000	1.0000	1.0000
625.0000	580.0000	556.0000	59.0000	0.0	0.0	0.0	65.0000
500.0000	47.0000	53.0000	59.0000	162.0000	1.0000	1.0000	1.0000
275.0000	275.0000	275.0000	275.0000	247.0000	133.0000	0.0	71.0000
541.0000	52.0000	54.0000	19.0000	412.0000	1.0000	1.0000	1.0000
228.0000	228.0000	226.0000	165.0000	144.0000	30.0000	0.0	72.0000
651.0000	44.0000	46.0000	26.0000	151.0000	1.0000	1.0000	1.0000
23.0000	20.0000	0.0	0.0	0.0	0.0	0.0	49.0000
580.0000	47.0000	56.0000	94.0000	412.0000	1.0000	1.0000	1.0000
241.0000	214.0000	188.0000	120.0000	29.0000	29.0000	8.0000	72.0000
538.0000	48.0000	52.0000	41.0000	410.0000	1.0000	1.0000	1.0000
104.0000	14.0000	8.0000	8.0000	0.0	0.0	0.0	67.0000
538.0000	45.0000	60.0000	148.0000	191.0000	1.0000	1.0000	1.0000
266.0000	240.0000	183.0000	89.0000	80.0000	28.0000	0.0	70.0000
631.0000	44.0000	56.0000	120.0000	410.0000	1.0000	1.0000	1.0000
166.0000	166.0000	131.0000	71.0000	49.0000	30.0000	10.0000	72.0000
536.0000	44.0000	60.0000	159.0000	395.0000	1.0000	1.0000	1.0000
398.0000	351.0000	320.0000	236.0000	219.0000	150.0000	117.0000	72.0000
504.0000	47.0000	61.0000	138.0000	571.0000	1.0000	1.0000	1.0000
62.0000	25.0000	5.0000	4.0000	0.0	0.0	0.0	65.0000
721.0000	47.0000	49.0000	15.0000	162.0000	1.0000	1.0000	1.0000
754.0000	754.0000	754.0000	664.0000	608.0000	30.0000	0.0	69.0000
491.0000	50.0000	62.0000	116.0000	412.0000	1.0000	1.0000	1.0000
180.0000	167.0000	139.0000	80.0000	68.0000	10.0000	0.0	71.0000
619.0000	44.0000	53.0000	80.0000	185.0000	1.0000	1.0000	1.0000
128.0000	110.0000	70.0000	29.0000	25.0000	19.0000	0.0	69.0000
615.0000	44.0000	52.0000	79.0000	410.0000	1.0000	0.0	1.0000
69.0000	69.0000	67.0000	20.0000	19.0000	0.0	0.0	71.0000
648.0000	52.0000	52.0000	3.0000	792.0000	1.0000	1.0000	1.0000
110.0000	110.0000	48.0000	10.0000	0.0	0.0	0.0	68.0000
652.0000	51.0000	59.0000	76.0000	410.0000	1.0000	1.0000	1.0000
116.0000	96.0000	72.0000	26.0000	20.0000	0.0	0.0	69.0000
651.0000	55.0000	65.0000	100.0000	410.0000	1.0000	1.0000	1.0000
1626.0000	1544.0000	1365.0000	420.0000	0.0	0.0	0.0	70.0000
666.0000	45.0000	58.0000	130.0000	162.0000	1.0000	1.0000	1.0000
696.0000	696.0000	675.0000	477.0000	207.0000	142.0000	122.0000	71.0000
696.0000	696.0000	696.0000	696.0000	696.0000	696.0000	696.0000	696.0000

74.0000	69.0000	40.0000	0.0	0.0	0.0	0.0	68.0000
610.0000	44.0000	46.0000	20.0000	412.0000	1.0000	1.0000	1.0000
3.0000	3.0000	3.0000	3.0000	3.0000	0.0	0.0	70.0000
424.0000	50.0000	52.0000	18.0000	812.0000	1.0000	1.0000	1.0000
2176.0000	2113.0000	1953.0000	1398.0000	447.0000	9.0000	0.0	70.0000
681.0000	51.0000	59.0000	76.0000	153.0000	1.0000	1.0000	1.0000
235.0000	235.0000	202.0000	80.0000	55.0000	0.0	0.0	71.0000
410.0000	54.0000	58.0000	33.0000	531.0000	1.0000	1.0000	1.0000
1375.0000	1039.0000	907.0000	243.0000	0.0	0.0	0.0	67.0000
613.0000	45.0000	48.0000	34.0000	410.0000	1.0000	1.0000	1.0000
177.0000	169.0000	143.0000	75.0000	70.0000	11.0000	3.0000	70.0000
535.0000	44.0000	55.0000	104.0000	410.0000	1.0000	1.0000	1.0000
173.0000	137.0000	123.0000	103.0000	89.0000	32.0000	0.0	69.0000
537.0000	44.0000	56.0000	124.0000	157.0000	1.0000	1.0000	1.0000
168.0000	168.0000	124.0000	52.0000	49.0000	45.0000	7.0000	70.0000
535.0000	45.0000	62.0000	171.0000	410.0000	1.0000	1.0000	1.0000
2882.0000	2326.0000	1861.0000	752.0000	175.0000	9.0000	0.0	66.0000
545.0000	44.0000	48.0000	38.0000	154.0000	1.0000	1.0000	1.0000
142.0000	96.0000	77.0000	53.0000	17.0000	6.0000	0.0	67.0000
572.0000	47.0000	55.0000	78.0000	157.0000	1.0000	1.0000	1.0000
2198.0000	1685.0000	1170.0000	282.0000	0.0	0.0	0.0	66.0000
705.0000	44.0000	46.0000	20.0000	410.0000	1.0000	1.0000	1.0000
67.0000	52.0000	52.0000	52.0000	52.0000	52.0000	52.0000	71.0000
483.0000	45.0000	49.0000	39.0000	173.0000	1.0000	1.0000	1.0000
1552.0000	1517.0000	1349.0000	722.0000	293.0000	92.0000	2.0000	70.0000
641.0000	51.0000	54.0000	29.0000	348.0000	1.0000	1.0000	1.0000
141.0000	135.0000	120.0000	33.0000	8.0000	4.0000	0.0	72.0000
652.0000	44.0000	51.0000	64.0000	162.0000	1.0000	1.0000	1.0000
100.0000	97.0000	46.0000	10.0000	7.0000	0.0	0.0	69.0000
495.0000	56.0000	56.0000	2.0000	480.0000	1.0000	1.0000	1.0000
75.0000	75.0000	75.0000	20.0000	0.0	0.0	0.0	72.0000
476.0000	51.0000	54.0000	23.0000	433.0000	1.0000	1.0000	1.0000
1746.0000	1225.0000	781.0000	272.0000	0.0	0.0	0.0	66.0000
436.0000	50.0000	63.0000	127.0000	810.0000	1.0000	1.0000	1.0000
186.0000	139.0000	90.0000	15.0000	15.0000	0.0	0.0	71.0000
599.0000	45.0000	53.0000	83.0000	431.0000	1.0000	1.0000	1.0000
1102.0000	1062.0000	977.0000	577.0000	247.0000	88.0000	43.0000	72.0000
557.0000	54.0000	56.0000	21.0000	410.0000	1.0000	1.0000	1.0000
2374.0000	2122.0000	1659.0000	473.0000	0.0	0.0	0.0	68.0000
538.0000	44.0000	56.0000	120.0000	922.0000	1.0000	1.0000	1.0000
166.0000	166.0000	159.0000	68.0000	57.0000	39.0000	0.0	70.0000
550.0000	46.0000	53.0000	62.0000	432.0000	1.0000	1.0000	1.0000
68.0000	66.0000	23.0000	4.0000	0.0	0.0	0.0	69.0000
511.0000	51.0000	56.0000	55.0000	410.0000	1.0000	1.0000	1.0000
154.0000	154.0000	114.0000	52.0000	37.0000	18.0000	0.0	72.0000
656.0000	53.0000	58.0000	54.0000	410.0000	1.0000	1.0000	1.0000
143.0000	104.0000	79.0000	55.0000	0.0	0.0	0.0	67.0000
384.0000	60.0000	61.0000	2.0000	400.0000	1.0000	1.0000	1.0000
168.0000	154.0000	119.0000	0.0	0.0	0.0	0.0	70.0000
296.0000	60.0000	65.0000	43.0000	450.0000	1.0000	1.0000	1.0000
839.0000	611.0000	368.0000	0.0	0.0	0.0	0.0	68.0000
532.0000	45.0000	46.0000	11.0000	410.0000	1.0000	1.0000	1.0000
222.0000	222.0000	196.0000	143.0000	118.0000	0.0	0.0	67.0000
516.0000	48.0000	49.0000	4.0000	410.0000	1.0000	1.0000	1.0000
46.0000	30.0000	15.0000	7.0000	3.0000	3.0000	0.0	69.0000
639.0000	48.0000	49.0000	7.0000	410.0000	1.0000	1.0000	1.0000
288.0000	96.0000	65.0000	49.0000	18.0000	0.0	0.0	66.0000
322.0000	63.0000	65.0000	16.0000	812.0000	1.0000	1.0000	1.0000
325.0000	302.0000	81.0000	0.0	0.0	0.0	0.0	69.0000
560.0000	51.0000	52.0000	12.0000	425.0000	1.0000	1.0000	1.0000
614.0000	523.0000	448.0000	290.0000	160.0000	3.0000	0.0	71.0000
555.0000	47.0000	59.0000	119.0000	199.0000	1.0000	1.0000	1.0000
218.0000	151.0000	120.0000	99.0000	11.0000	0.0	0.0	67.0000
373.0000	55.0000	55.0000	5.0000	410.0000	1.0000	1.0000	1.0000
59.0000	11.0000	11.0000	11.0000	0.0	0.0	0.0	68.0000
481.0000	48.0000	50.0000	18.0000	185.0000	1.0000	1.0000	1.0000

237.0000	237.0000	225.0000	138.0000	127.0000	82.0000	0.0	72.0000
401.0000	51.0000	58.0000	68.0000	205.0000	1.0000	1.0000	1.0000
119.0000	104.0000	72.0000	43.0000	34.0000	0.0	0.0	69.0000
565.0000	45.0000	60.0000	149.0000	200.0000	1.0000	1.0000	1.0000
50.0000	50.0000	38.0000	38.0000	38.0000	1.0000	0.0	67.0000
447.0000	51.0000	57.0000	61.0000	955.0000	1.0000	1.0000	1.0000
520.0000	358.0000	290.0000	179.0000	99.0000	0.0	0.0	67.0000
778.0000	47.0000	49.0000	13.0000	552.0000	1.0000	1.0000	1.0000
26.0000	26.0000	26.0000	26.0000	10.0000	0.0	0.0	69.0000
467.0000	54.0000	65.0000	104.0000	162.0000	1.0000	1.0000	1.0000
142.0000	133.0000	113.0000	26.0000	6.0000	0.0	0.0	72.0000
580.0000	47.0000	52.0000	47.0000	412.0000	1.0000	1.0000	1.0000
3267.0000	2817.0000	2297.0000	1077.0000	260.0000	30.0000	0.0	68.0000
539.0000	54.0000	58.0000	39.0000	410.0000	1.0000	1.0000	1.0000
78.0000	62.0000	18.0000	0.0	0.0	0.0	0.0	69.0000
543.0000	46.0000	54.0000	74.0000	157.0000	1.0000	1.0000	1.0000
177.0000	165.0000	156.0000	76.0000	65.0000	40.0000	2.0000	71.0000
393.0000	53.0000	63.0000	104.0000	410.0000	1.0000	1.0000	1.0000
99.0000	60.0000	27.0000	15.0000	0.0	0.0	0.0	68.0000
387.0000	51.0000	55.0000	31.0000	812.0000	1.0000	1.0000	1.0000
112.0000	82.0000	30.0000	16.0000	6.0000	0.0	0.0	68.0000
526.0000	51.0000	64.0000	132.0000	540.0000	1.0000	1.0000	1.0000
198.0000	181.0000	164.0000	89.0000	79.0000	31.0000	0.0	72.0000
593.0000	44.0000	63.0000	183.0000	410.0000	1.0000	1.0000	1.0000
224.0000	208.0000	176.0000	77.0000	65.0000	33.0000	0.0	70.0000
509.0000	62.0000	65.0000	35.0000	410.0000	1.0000	1.0000	1.0000
636.0000	596.0000	524.0000	0.0	0.0	0.0	0.0	71.0000
392.0000	47.0000	50.0000	29.0000	410.0000	1.0000	1.0000	1.0000
109.0000	39.0000	27.0000	20.0000	2.0000	0.0	0.0	65.0000
515.0000	44.0000	45.0000	13.0000	410.0000	1.0000	1.0000	1.0000
35.0000	35.0000	35.0000	32.0000	8.0000	0.0	0.0	59.0000
595.0000	55.0000	58.0000	24.0000	410.0000	1.0000	1.0000	1.0000
986.0000	969.0000	773.0000	377.0000	0.0	0.0	0.0	61.0000
525.0000	51.0000	52.0000	8.0000	410.0000	1.0000	1.0000	1.0000
16.0000	16.0000	16.0000	16.0000	16.0000	0.0	0.0	72.0000
592.0000	53.0000	54.0000	15.0000	441.0000	1.0000	1.0000	1.0000
12.0000	7.0000	0.0	0.0	0.0	0.0	0.0	70.0000
619.0000	53.0000	58.0000	46.0000	830.0000	1.0000	1.0000	1.0000
637.0000	595.0000	473.0000	227.0000	10.0000	0.0	0.0	71.0000
427.0000	48.0000	58.0000	101.0000	157.0000	1.0000	1.0000	1.0000
458.0000	332.0000	233.0000	205.0000	58.0000	0.0	0.0	65.0000
462.0000	47.0000	48.0000	10.0000	601.0000	1.0000	1.0000	1.0000
149.0000	149.0000	30.0000	0.0	0.0	0.0	0.0	69.0000
383.0000	47.0000	51.0000	40.0000	753.0000	1.0000	1.0000	1.0000
948.0000	948.0000	711.0000	324.0000	21.0000	0.0	0.0	66.0000
519.0000	44.0000	56.0000	118.0000	410.0000	1.0000	1.0000	1.0000
273.0000	100.0000	76.0000	52.0000	20.0000	3.0000	0.0	66.0000
603.0000	44.0000	65.0000	206.0000	436.0000	1.0000	1.0000	1.0000
555.0000	503.0000	358.0000	142.0000	115.0000	44.0000	0.0	69.0000
810.0000	44.0000	49.0000	53.0000	412.0000	1.0000	1.0000	1.0000
33.0000	33.0000	33.0000	33.0000	33.0000	25.0000	12.0000	72.0000
592.0000	47.0000	58.0000	104.0000	162.0000	1.0000	1.0000	1.0000
4421.0000	4036.0000	3472.0000	2253.0000	970.0000	194.0000	3.0000	72.0000
696.0000	47.0000	56.0000	87.0000	151.0000	1.0000	1.0000	1.0000
248.0000	248.0000	248.0000	85.0000	3.0000	0.0	0.0	71.0000
630.0000	45.0000	54.0000	95.0000	450.0000	1.0000	0.0	1.0000
146.0000	40.0000	28.0000	12.0000	0.0	0.0	0.0	67.0000
644.0000	55.0000	58.0000	27.0000	410.0000	1.0000	1.0000	1.0000
2568.0000	2173.0000	1776.0000	491.0000	0.0	0.0	0.0	68.0000

3992
138
YR
1
2
3
4

TOTAL DOSE

COUNTS

AVERAGE DOSE

4	.0	.0	.0
5	.0	.0	.0
6	.0	.0	.0
7	.0	.0	.0
8	.0	.0	.0
9	.0	.0	.0
10	.0	.0	.0
11	.0	.0	.0
12	.0	.0	.0
13	.0	1.0	.0
14	.0	1.0	.0
15	.0	3.0	.0
16	.0	3.0	.0
17	.0	3.0	.0
18	.0	3.0	.0
19	.0	4.0	.0
20	.0	4.0	.0
21	.0	4.0	.0
22	.0	4.0	.0
23	.0	4.0	.0
24	.0	4.0	.0
25	.0	4.0	.0
26	.0	4.0	.0
27	.0	4.0	.0
28	.0	4.0	.0
29	.0	4.0	.0
30	.0	4.0	.0
31	.0	5.0	.0
32	.0	5.0	.0
33	.0	5.0	.0
34	.0	5.0	.0
35	.0	5.0	.0
36	.0	5.0	.0
37	.0	5.0	.0
38	.0	5.0	.0
39	.0	5.0	.0
40	.0	5.0	.0
41	.0	5.0	.0
42	.0	5.0	.0
43	6.8	14.0	.5
44	10865.4	1774.0	6.1
45	19167.9	2044.0	9.4
46	11406.0	1399.0	8.2
47	8935.3	1397.0	5.6
48	9030.2	1850.0	4.9
49	8814.0	1681.0	5.2
50	8647.8	1497.0	5.8
51	10568.3	1578.0	6.7
52	12672.0	1458.0	8.8
53	14945.0	1308.0	11.4
54	14426.7	1215.0	11.9
55	16010.0	1175.0	13.6
56	16225.0	1081.0	15.0
57	16607.3	984.0	16.9
58	19187.3	868.0	22.1
59	15085.0	773.0	19.5
60	14913.2	674.0	22.1
61	17473.8	606.0	28.8
62	18290.2	522.0	35.0
63	16424.5	449.0	36.6
64	15515.7	375.0	41.4
65	14353.9	302.0	47.5
66	9359.6	226.0	41.4
67	8079.9	201.0	40.2
68	4229.5	176.0	24.0
69	3270.8	153.0	21.4
70	1887.7	118.0	11.8

71	632.8	77.0	8.2
72	432.3	43.0	10.1
73	.0	.0	.0
74	.0	.0	.0
75	.0	.0	.0
76	.0	.0	.0
77	.0	.0	.0
78	.0	.0	.0
79	.0	.0	.0
80	.0	.0	.0
81	.0	.0	.0
82	.0	.0	.0
83	.0	.0	.0
84	.0	.0	.0
85	.0	.0	.0
86	.0	.0	.0
87	.0	.0	.0
88	.0	.0	.0
89	.0	.0	.0
90	.0	.0	.0
91	.0	.0	.0
92	.0	.0	.0
93	.0	.0	.0
94	.0	.0	.0
95	.0	.0	.0
96	.0	.0	.0
97	.0	.0	.0
98	.0	.0	.0
99	.0	.0	.0
100	.0	.0	.0

APPENDIX D

DEFINITION OF VARIABLE NAMES

<u>VARIABLE NAME</u>	<u>DEFINITION</u>
DEATHAGE	Age at death to nearest tenth.
INITLYR	Initial year of employment.
FINALYR	Final year of employment
TOTALYR	Total years of employment to nearest tenth.
EXPOSURE	0=zero lifetime dose recorded. 1=positive lifetime dose recorded.
CUMDOSE	Cumulative lifetime dose.
CDOS 3+	Cumulative lifetime dose 3 years before death.
CDOS 5+	Cumulative lifetime dose 5 years before death.
CDOS 10+	Cumulative lifetime dose 10 years before death.
CDOS 15+	Cumulative lifetime dose 15 years before death.
CDOS 20+	Cumulative lifetime dose 20 years before death.
CDOS 25+	Cumulative lifetime dose 25 years before death.
YRDEATH	Year of death.
DT1	Represents the difference between year of death and the initial year of employment.
DT2	Represents the difference between the year of death and the final year of employment.
DT3	Represents the differences between the year of death and the year at the middle of employment.
DOS0-3	Represents the differences between cumulative dose and cumulative dose three years before death.

<u>VARIABLE NAME</u>	<u>DEFINITION</u>
DOS4-5	Represents the difference between cumulative dose 3 years before death and cumulative dose 5 years before death.
DOS6-10	Represents the difference between cumulative dose 5 years before death and 10 years before death.
DOS11-15	Represents the difference between cumulative dose 10 years before death and 15 years before death.
DOS16-20	Represents the difference between cumulative dose 15 years before death and cumulative dose 20 years before death.
DOS21-25	Represents the difference between cumulative dose 20 years prior to death and cumulative dose 25 years prior to death.
DOS25+	Represents the cumulative dose 25 years prior to death.
MAXDOS	Represents the maximum value of DOS0-3, DOS4-5, DOS6-10, DOS11-15, DOS16-30, DOS21-25, and DOS25+
TMAXDOS	Represents the time from the center of the interval in which the maximum dose is found.
AGESQ	Represents the age at death minus 60 all divided by 5 and then squared.

```

1      C 100,NEWVARFOR,FINA,(0)
2      DIMENSION XID(100),XTAB(799),DOS(10),DT(10),XDATE(10),XWIDTH(10),
3      IXINT(50),XREC(10)
4      DATA XWIDTH/3.,2.,5.,5.,5.,5.,4.,3.,3.,
5      DATA XTAB/13*1.,17*13.,5.,3*13.,3*6.,6*13.,7.,
6      13*13.,8.,16*13.,9.,6*13.,3*10.,10.,10.,11.,11.,
7      13*13.,30*14.,170*2.,2*3.,388*2.,200*4./
8      DATA XDATE/1.5,4.0,7.3,13.0,18.5,24.0,27.75,3*0./
9      READ(20,50,END=300) (XID(J),J=1,16)
10     C 50
11     C 50
12     C 50
13     C 50
14     C 50
15     C 50
16     C 50
17     C 50
18     C 50
19     C 50
20     C 50
21     C 50
22     C 50
23     C 50
24     C 50
25     C 50
26     C 50
27     C 50
28     C 50
29     C 50
30     C 50
31     C 50
32     C 50
33     C 50
34     C 50
35     C 50
36     C 50
37     C 50
38     C 50
39     C 50
40     C 50
41     C 50
42     C 50
43     C 50
44     C 50
45     C 50
46     C 50
47     C 50
48     C 50
49     C 50
50     C 50
51     C 50
52     C 50
53     C 50
54     C 50
55     C 50
56     C 50
57     C 50
58     C 50
59     C 50
60     C 50
61     C 50
62     C 50
63     C 50
64     C 50

```

1 = ICDA FROM 1 TO 139
 2 = ICDA FROM 140 TO 409 AND 410 TO 799
 3 = ICDA 410 AND 411
 4 = ICDA FROM 800 TO 999
 5 = ICDA 1157... PANCREAS CANCER
 6 = ICDA 161 TO 63 ... RESPIRATORY CANCER
 7 = ICDA 170 ... BONE CANCER
 8 = ICDA 174 ... BREAST CANCER
 9 = ICDA 173... THYROID CANCER
 10 = ICDA 200 TO 202 AND 204... LYMPHOID CANCER
 11 = ICDA 205 AND 206 ... MYELOID LEUK
 12 = ICDA 203 ... MULT. MYELOMA
 13 = ICDA 207 TO 209 (EXCLUDING THOSE CODES 5 THROUGH 12 ABOVE)
 14 = ICDA 210 TO 239 OTHER CANCER TYPES (BENIGN OR UNSPECIFIED)
 K = XID(5)
 XREC(1) = XTAB(K)
 RECODE CAUSE OF DEATH INTO THREE GROUPS
 BLOOD CANCER = 0
 NON CANCER = 1
 SOLID TUMORS = 2
 XREC(2) = 9
 IF((XID(5).LT.40.) .OR. (XID(5).GT.49.)) XREC(2) = 1
 IF((XID(5).GE.40.) .AND. (XID(5).LE.49.)) XREC(2) = 2
 IF((XID(5).GE.200.) .AND. (XID(5).LE.209.)) XREC(2) = 0
 GET THE DELTA T FROM VARIOUS POINTS IN EMPLOYMENT AND DEATH
 DT(1) IS TIME FROM INITIAL EMPLOY. TO DEATH
 DT(2) IS TIME FROM END OF EMPLOYMENT TO DEATH
 DT(3) IS THE TIME FROM THE MIDDLE OF EMPLOY. TO DEATH
 DT(1) = XID(16) - XID(1)
 DT(2) = XID(16) - XID(3)
 DT(3) = XID(16) - (((XID(3)-XID(2))/2.)*XID(2))
 DOSES RECEIVED IN VARIOUS DELTA T INTERVALS
 DETERMINE THE DOSES AT VARIOUS TIMES TIL DEATH
 VARIABLE TIME INTERVAL
 DOS(1) 0 TO 3
 DOS(2) 4 TO 5
 DOS(3) 6 TO 10
 DOS(4) 11 TO 15
 DOS(5) 16 TO 20
 DOS(6) 21 TO 25
 DOS(7) MORE THAN 25
 DOS(1) = XID(9) - XID(10)
 DOS(2) = XID(10) - XID(11)
 DOS(3) = XID(11) - XID(12)
 DOS(4) = XID(12) - XID(13)
 DOS(5) = XID(13) - XID(14)
 DOS(6) = XID(14) - XID(15)
 DOS(7) = XID(15)

Program used to generate variables DT1, DT2, DT3, DOS0-3,
 DOS4-5, DOS6-10, DOS11-15, DOS16-20, DOS21-25, DOS25+,
 MAXDOS and TMAXDOS. (Continued on next page)

```

65 C FIND THE MAXIMUM DOSE RECEIVED IN ANY GIVEN TIME INTERVAL
66 C NOTE THAT THE TIME INTERVALS ARE OF DIFFERENT LENGTH
67 C AND THAT THIS PUTS SOME TIME INTERVALS AT A DISADVANTAGE SINCE
68 C THEY HAVE FEWER YEARS TO ACCUMULATE DOSE...HOWEVER
69 C AT THIS POINT WE'LL SEE WHAT THIS DOES AND IF IT LOOKS AT
70 C ALL PROMISING WE CAN TAKE THIS EFFECT INTO ACCOUNT
71 XMAXD = AMAX1(DOS(1),DOS(2),DOS(3),DOS(4),DOS(5),DOS(6),DOS(7))
72 N = 0
73 DO 125 I = 1,7
74 IF(XMAXD.EQ.DOS(I)) N = I
75 IF(XMAXD.EQ.DOS(I)) GO TO 126
76 125 CONTINUE
77 IF(N.EQ.0) WRITE(---) N,N,N,(XID(L5),L5=1,16)
78 126 CONTINUE
79 XDATE(7) = ((XID(16) - XID(2) - 25.)/2.)+25.
80 IF((XDATE(7).LT.25.).AND.(N.EQ.7)) WRITE(---) (XID(L),L=1,16)
81 C FIND THE TIME FROM THE MAXIMUM DOSE
82 DT(4) = XDATE(N)
83 X.NT(2) = XID(1)**2.
84 WRITE(21,70) (XID(L6),L6=1,16),
85 IXREC(1),XREC(2),DT(1),DT(2),DT(3),(DOS(I),I=1,7),XMAXD,DT(4),
86 IXINT(2)
87 70 FORMAT(16F8.1,15F8.1)
88 GO TO 1
89 998 ICNT = ICNT + 1
90 GO TO 1
91 997 ICNT1 = ICNT1 + 1
92 GO TO 1
93 996 ICNT2 = ICNT2 + 1
94 GO TO 1
95 995 ICNT3 = ICNT3 + 1
96 GO TO 1
97 994 CONTINUE
98 ICNT4 = ICNT4 + 1
99 GO TO 1
100 300 CONTINUE
101 WRITE(---) ICNT,ICNT1,ICNT2,ICNT3,ICNT4
102 STOP
103 END

```

Program used to generate variables DT1, DT2, DT3, DOS0-3, DOS4-5, DOS6-10, DOS11-15, DOS16-20, DOS21-25, DOS25+, MAKDOS and TMAXDOS. (Continued from previous page)

APPENDIX E
SUMMARY OF LOGISTIC MODELING

APPENDIX E

KEY

EUWM-ALL	Exposed and Unexposed White Males - All cases included.
EUWM-NA	Exposed and Unexposed White Males - No accident cases included.
EWM-ALL	Exposed White Males - All cases included.
EWM-NA	Exposed White Males - No accident cases included.
-2LOG(L)	Log of the likelihood ratio
Δ	Decrease in -2LOG(L) from the constant model to the specific model.

The tables below contain models which specify

$$\log \left[\bar{P} / (1-P) \right]$$

where P is the probability that death was due to the specific cancer.

n.b. Definitions of variables are contained in Appendix D. In particular, note the specific form of AGESQ.

RESPIRATORY MODELS*

<u>Model</u>	RESP-ALL EUWM-ALL	
	<u>-2LOG(L)</u>	<u>Δ</u>
-2.6625	1493.4	
-2.2484-.3440 (AGESQ) 30.1	1445.9	47.7
-5.0539-.3470 (AGESQ)+.0439 (YRDEATH) 29.8 13.0	1431.9	61.5
-4.9076-.3438 (AGESQ)+.0412 (YRDEATH)+.0012 (DOS16-20) 29.3 11.1 1.5	1430.6	62.8
	<u>-2LOG(L)</u>	<u>Δ</u>
-6.18-.346 (AGESQ)+.037 (YRDEATH)+.033 (INITYR)+ 30.2 8.6 2.9 .0013 (DOS16-20) 1.8	1427.9	65.5
-6.43-.353 (AGESQ)+.041 (YRDEATH)+.0337 (INITYR) 30.9 10.9 2.92 -.0003 (DOS6-10) .44	1428.9	64.5
-6.49-.356 (AGESQ)+.0375 (YRDEATH)+.0397 (INITYR) 31.1 8.7 4.0 +.0026 (DOS16-20)-.001 (DOS6-10) 4.7 2.6	1424.8	68.6
	RESP ALL-ACC EUWM-NA	
	<u>-2LOG(L)</u>	<u>Δ</u>
-2.4939	1427.8	
-2.1417-.3139 (AGESQ) 23.7	1394.6	33.2
-4.6868-.3240 (AGESQ)+.0399 (YRDEATH) 24.9 10.4	1383.5	44.3
-4.1035-.3017 (AGESQ)+.0464 (YRDEATH)-.0167 (AGE) 22.0 13.3 4.0	1379.6	48.2

*NOTE: Numbers below the variable names represent chi square values for the variable after all other terms are entered.

EWM-ALL

Model	Constant	AGESQ	INITLYR	YRDEATH	DOS16-20	-2 log L
1	-2.57					981.1
2	-2.21	-.291 (16.6)				956.4
3	-4.37	-.301 (18.0)	.047 (4.7)			952.1
4	-4.35	-.290 (16.2)		.033 (4.4)		951.7
5	-5.78	-.298 (17.3)	.038 (2.96)	.028 (3.02)		949.0
6	-4.51	-.296 (17.4)	.048 (4.99)		.0013 (3.5)	949.2
7	-4.13	-.286 (15.7)		.029 (3.3)	.0012 (1.6)	950.3
8	-5.64	-.294 (16.9)	.041 (3.4)	.023 (1.9)	.0014 (2.0)	947.2

Results of fitting eight logistic regression models using respiratory cancer and no cancer as the two response categories. Only exposed white males are included in the model. Variables which have no entry for a particular model were not used in that model. For each model, the first value under the variable is the coefficient of that variable in the logistic regression model, while the second value (below in parentheses) is the chi-square value for a test of statistical significance of that variable. All chi-square values have one degree of freedom.

	EWM-NA	
	<u>-2LOG(L)</u>	<u>Δ</u>
-2.406	938.3	
-2.109-.259 (AGESQ) 12.4	921.9	16.4
-5.0770-.2563 (AGESQ)+.0626 (INITYR)+.0017 (DOS16-20) 12.3 7.9 3.3	912.5	25.8
-5.4571-.2718 (AGESQ)+.0715 (INITYR)-.0010 (DOS6-10) 13.2 9.9 2.5 +.0030 (DOS16-20) 6.3	909.6	28.7

PANCREAS MODELS

	PANCREAS	
	EUWM-ALL	
-4.0389	514.9	
-3.7519-.2093 (AGESQ) 4.6	508.5	6.4
-3.8432-.1951 (AGESQ)+.0033 (DOS4-5) 4.1 7.3	503.5	11.4
	EUWM-NA	
-3.8704	497.8	
-3.9494+.0037 (DOS4-5) 9.1	491.7	6.1
-3.6534-.1708 (AGESQ) 2.8	494.4	3.4
	EWM-ALL	
-4.0164	321.6	
-4.1436+.0036 (DOS4-5) 8.5	315.9	5.7
-3.977+.0035 (DOS4-5) -.1107 (AGESQ) 7.7 1.2	314.5	7.1

	EWM-NA	
	<u>-2LOG (L)</u>	<u>Δ</u>
-3.8528	311.3	
-3.9827+.0038 (DOS4-5)	305.1	6.2
9.0		
-3.9051+.0037 (DOS4-5) -.0550 (AGESQ)	304.8	6.5
8.4 .25		

BRAIN MODELS

	BRAIN	
	EUWM-ALL	
-4.6749	306.7	
-4.7401+.0121 (DOS25+)	303.2	3.5
5.8		
-3.2417+.0132 (DOS25+) -.0260 (AGE)	299.9	6.8
7.1 3.4		
-3.2660+.0085 (DOS25+) -.0541 (AGE) +.0937 (DT1)	292.7	14.0
2.4 8.6 6.6		
-3.3680+.1054 (DT1) -.0551 (AGE)	294.4	12.3
8.7 9.1		

	EUWM-NA	
-4.506	297.6	
-2.0058-.0424 (AGE)	290.1	7.5
7.6		
-1.9059-.0453 (AGE) +.0125 (DOS25+)	286.3	11.3
8.4 6.4		
-2.1103-.0713 (AGE) +.0993 (DT1)	281.5	16.1
13.9 7.8		
-1.9985-.0704 (AGE) +.0877 (DT1) +.0080 (DOS25+)	279.97	17.63
13.4 5.8 2.1		

	EWM-ALL	
-4.5917	201.5	
-4.6909+.0118 (DOS25+)	198.2	3.3
5.3		
-3.4725-.0907 (AGE) +.2089 (DT1)	181.1	19.4
11.4 14.5		
-2.9896+.0130 (DOS25+) -.0296 (AGE)	195.5	6.0
6.6 2.8		
-3.3311+.0047 (DOS25+) -.0896 (AGE) +.1965 (DT1)	180.5	21.0
.6 11.1 12.0		

	EWM-NA	
	<u>-2LOG(L)</u>	<u>Δ</u>
-4.4282	195.6	
-1.8145-.0444 (AGE) 5.4	190.3	5.3
-2.3346-.1041 (AGE)+.2006 (DT1) 14.4 13.2	173.4	22.2
-1.6547-.0490 (AGE)+.0124 (DOS25+) 6.2 6.0	186.6	9.0
-2.1928-.1031 (AGE)+.1887 (DT1)+.0042 (DOS25+) 14.0 10.8 .46	173.0	22.6

A CRITICAL EVALUATION OF THE MANCUSO, STEWART, AND
KNEALE REPORT AND A RE-ANALYSIS OF THEIR DATA

Final Report
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ABSTRACT

This report presents both a general and detailed critical analysis of the paper entitled Radiation Exposures of Hanford Workers Dying from Cancer and Other Causes, by T.F. Mancuso, A. Stewart, and G. Kneale.

We have concluded that the investigation was not conducted in a sufficiently rigorous manner to allow for any firm or defensible conclusions regarding the relationship between exposure to low level ionizing radiation and mortality from cancer. In addition, our re-analysis of these data did not reveal any convincing associations, although we recommend that the question of possible associations be resolved by a well designed and executed epidemiologic study.

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XV	Cases = All Lung Cancers
XVI	Cases = Kidney Cancer (ICD 189)
XVII	Cases = Brain Cancers (ICD 191)

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A CRITICAL EVALUATION OF THE MANCUSO, STEWART, AND
KNEALE REPORT AND A RE-ANALYSIS OF THEIR DATA

GENERAL COMMENTS

We will begin with a general presentation of our reactions to the study under review¹ and will follow this by a detailed examination of the paper itself. The reader should be aware of the fact that the specific justifications for the comments in this first section will appear with the detailed comments in the second section, to which reference should be made for more complete understanding of the foundations for our conclusions.

The major limitations of the paper can be summarized as follows: absence of a clear statement of design and rationale for analysis; lack of sensitivity for the limitations of a numerator data analysis; almost complete absence of control for potential confounders; use of means as the major measure of effects when odds ratios would be far more appropriate; and very selective and incomplete use of statistical tests of significance, especially when small observed differences may have been due to chance or confounding.

The most striking feature of the report is the general absence of a clear statement of the intent and design of the investigation, the neglect to state the specific hypotheses, if any, under scrutiny and the reasons for studying these hypotheses, and the failure to present the findings in a

¹Mancuso, TF, Stewart, A., Kneale, G.: Radiation exposures of Hanford workers dying from cancer and other causes. Health Physics 33:369-385, 1977.

clear and orderly fashion which would enable the reader to assimilate the information offered. Simply reading the paper was a terribly difficult chore, while understanding it was often impossible. The direction (or general scheme) of the investigation and analysis were not evident, and the reader could rarely anticipate the next step nor integrate the bits of data presented into some meaningful whole. This general absence of organization made the task of reviewing the paper most unpleasant and may have occasionally resulted in the adoption of an overly critical attitude by the reviewers.

Regarding the absence of a statement of the specific hypotheses under investigation, we must say that it is never clearly stated whether this study is of the hypothesis testing or generating type. If it is the former, we are not advised of the questions under investigation; if it is the latter, it appears as if any and all associations encountered in the analysis are offered as hypotheses, or even firm conclusions, with little or no biomedical interpretation or explanation of these relationships. For instance, numerous cancers are cited as being associated with higher mean cumulative radiation doses, but no evidence from other research is presented concerning the similarity between doses and latency periods observed in these data and those found by other investigators for the suspect sites.

In addition, we were very troubled by the avoidance of a discussion of possible alternate explanations of the findings, such as the strong probability that smoking habits

may explain the observed excess proportion of lung cancer. One must also be concerned with the absence of any discussion of the possible impact of earlier (non-Hanford) occupational exposures, especially in view of the fact that the mean age at hire for this group of employees was approximately 40. This leaves unexplained the 20 years of earlier employment at younger ages (20-40), when sensitivity to cancer induction is thought to be greatest. It is the failure to engage in discussions of this nature which we find very disturbing.

Of special concern to us was the inadequate expression of appreciation, or perhaps even awareness, of the severe limitations of a 'numerator' type study which is based entirely on an analysis of deaths only, from a cohort of workers (both living and dead) about whom very little is known. This limitation brings into serious question the validity of extending the findings (or making inferences) to the general population and will be further discussed below.

If one wishes to make statements, say, about the effects of smoking on the incidence of lung cancer in the general population, one would ideally conduct a cohort study, drawing from the entire Population at Risk (PAR) an appropriate (random or representative) sample of non-smokers and smokers. These groups would then be followed for an extended period of time (whence is derived the term 'prospective study'), and the occurrence of lung cancer would

be carefully noted.

After completion of this type of investigation, it would be appropriate to make inferences back to the PAR (all smokers and non-smokers) concerning the impact of smoking on the risk of developing lung cancer. Case-control (or retrospective) studies present greater problems for inference making. In the first place, the disease has already occurred, and the exposure must be determined retrospectively (usually by history). Secondly, we are not at all assured of having in our study a 'representative' sample of cases or controls.

Many of these problems are overcome in retrospective occupational studies by the identification of a cohort of workers - for instance, all men ever employed at Hanford, whether presently living or dead - from which all cases of the disease under study are drawn, and whose exposures are compared with an appropriately selected control group. The criteria for selection of this group is of paramount importance, since it is this group which will serve as the 'standard' from which 'expected' exposure levels will be derived. Everyone in the cohort should therefore be eligible for selection as a control, and control selection should not be limited only to those members of the cohort who are deceased, since this latter group may not be representative of the entire cohort.

If controls are selected properly, it would be reasonable to extend the findings back to the entire cohort from which cases and controls were drawn, and if this cohort is similar

to other cohorts or to the general population it would be reasonable to make inferences, with due caution, back to these other groups as well.

The present investigation is termed a 'numerator type' analysis since, from the original cohort, only the experiences of the deceased are utilized. Rates of specific diseases (which would require in the denominator the inclusion of all cohort members whether living or dead) are never presented, unfortunately, and the comparison group used throughout the study (the non-cancers) are drawn entirely from the deceased members of the cohort.

In view of the above discussion concerning the drawing of inferences from case-control studies, and in view of the method utilized in this investigation for 'control' selection, one must question the validity of even extending the findings back to the original cohort, and we must certainly object to the extension of the findings to the general population, as is strongly implied in the entire discussion of the 'doubling doses.' These objections seem reasonable even in the absence of effects of possible confounders; when we realize that the effects of confounders may have seriously distorted the observed associations, extension of the findings becomes completely unjustified.

A confounder can be simply described as a predictor (or alternate cause) of the disease under study, independent of exposure. In a study of the association between smoking and lung cancer, for instance, residence in a dirty urban

environment can be anticipated to be a confounder since residents in these areas will experience higher rates of lung cancer than those who live in clean environments, irrespective (independent) of their smoking habits.

If residence is distributed differently in the case and control groups (e.g., a higher proportion of controls reside in urban areas with much pollution), confounding in the estimate of effect can be expected. If the effects of residence (the confounder) are not controlled for either in the design of the investigation or during the analytic phase, the estimate of the effect of smoking on lung cancer will be distorted by (or confounded with) residence.

Therefore the presence of confounding within ones data, which is considered to be the central methodologic issue in the conduct of epidemiologic investigations, may entirely invalidate all estimates of effect. It is this possibility for distortion which leads experienced practitioners of epidemiology to treat these potential confounders with proper respect, and even reverence.

Throughout the entire paper, very little, or insufficient, attention has been directed at the possible effects of confounding factors, such as age at and year of hire, duration of employment, intensity of exposure, and the sex and race of the workers, among others. In every comparison of 'cases' and 'controls', for instance, a presentation of the distribution of these factors, which would be helpful in dispelling our fears, is omitted.

Our next major area of concern relates to the general failure to use appropriate measures of effect and to determine the statistical significance of the observed differences between the compared groups.

The comparison of mean cumulative doses forms the foundation for the entire analysis, and we must question the reliance on this parameter for testing the associations between exposure and cause of death. A mean value is simply not an ideal measure of effect, especially because the mean may not be a good descriptor of the underlying distribution and also because it is really not a measure of effect. An examination of the medians for cumulative radiation dose, for instance, indicates that the means are being very heavily weighted by a few outlying doses, which leads to the conclusion that the mean is not an accurate summary statistic for the characterization of the exposures. Even if it were, however, one would still prefer true measures of effect, such as odds ratios or relative risks, which more directly express the relationship between exposure and the risk of developing the disease. Unfortunately, not a single odds ratio is presented in the paper.

Notwithstanding the possibility for distortion which is introduced by reliance on averages, we must further object to the arbitrariness in the use of statistical tests of significance as well. We are often presented with very small differences in means which are deemed to be of causal

importance without the performance of appropriate statistical tests which would clearly establish the significance of the difference, while we also frequently encounter the use of tests of significance which are inadequately or not at all described. Even when measures other than means are used, significance testing is also arbitrary. For instance, the authors conclude that there is an excess of brain cancers, based on a ratio of observed: expected cases of 1.04, or a 4 percent excess; unfortunately, this conclusion is not based on a test of the significance of this difference. The instances of this type of neglect are simply too numerous for citation in this discussion.

There is, in addition to these problems, a pervasive use of terminology which either remains undefined or is used in a manner different from conventional use. Terms such as cohort, cohort resemblances, case-control contrast, high risk years, pre-death years, employment years, controlled analyses, and standard, among many others, cause continual problems for the reader in following the reasoning of the investigators and their presentation of findings. The latter is especially confusing in many ways, among which one can include the following: table titles are often misleading, the use of percentages is often inappropriate, denominators are generally not specified, and the totals presented are frequently entirely meaningless and only obfuscate the issue at hand.

Despite the enumerated limitations, and others which have not been here discussed, the investigators do not hesitate to make very strong conclusions and broad extrapolations of their findings to the population-at-large. In the absence of a clear description of the characteristics of the true cohort of all Hanford workers, and the failure to establish the existence, in acceptably rigorous fashion, of a real excess in disease occurrence, there is nevertheless no reluctance in making inferences back to this undefined cohort, and in then boldly extending the data to all those in the universe who receive low-level ionizing radiation, even so far as to derive from these data estimates of the dose needed to double the incidence of cancer at many sites. Even if the biostatistical procedures are appropriate, one must seriously question the legitimacy of this type of extension of findings because of the inadequacy of the epidemiologic design - namely, the numerator nature of the analysis already discussed.

SUMMARY

The paper by Mancuso, et al. demonstrates inappropriate use of limited data to support what seem to be a priori conclusions rather than hypotheses. Review of the report presented enormous difficulties caused by the failure of the authors to provide the following:

1. A clear statement of the intent and design of the study; the hypotheses under investigation and their rationale.
2. A logical sequence and clear presentation of findings.
3. Adequate expression of appreciation for the limitations of numerator data (i.e., without reference to a base population); the potential impact of unknown confounding factors such as age, sex, personal habits and co-morbidity; estimates of completeness of ascertainment of mortality; methodologic justification for shifting denominators; and biologic justification for aggregating cancer of multiple sites.
4. Clear partition of age/radiation dose categories and the application of age-adjustment to summary data.

Even if the deficiencies cited above were not present, the nature of the information cited by the authors would not support a statement of risk. Such a statement would require

estimates of incidence of cancer of specific sites, related to radiation, among categories of exposed persons in whom the prevalence of confounding factors such as cigarette smoking would be known.

The reported levels of exposure cited in the paper are several orders less than the estimate of carcinogenic effect in other human experience. The need to document human effects of chronic exposure to low level radiation, however urgent, is incompletely served by the Mancuso report.

SPECIFIC COMMENTS

This section will include specific comments on the paper, arranged by page and line number. While the preliminary discussion summarized our general impressions of the research and the possible limitations in interpretation, this section will elucidate, in detail, the reasons for our concern.

Page 370 - Preliminary Findings

The expression 'certified deaths' is not self-explanatory. Does this refer to deaths for which a death certificate was found, or does it refer to nosologized death certificates? At any rate, 190 of 3710 deaths, which is more than 5 percent, are not included in the present analysis for reasons not clearly stated. While on this topic, it should also be noted that throughout the entire analysis, only the underlying (presumably) cause of death is used, and its method of derivation is not specified.

C.L.-P.2*

The argument here is a bit circuitous but seems to be as follows: The greatest number of deaths occurred among those who were members of the earlier cohorts (mostly 1944), at which time there was both a high proportion of unexposed workers, while those who were exposed were likely to have low level exposures prior

*This notation should be interpreted as follows:

C.L. - the left column; C.R. - the right column;

P.2 - the second paragraph which begins in the left column.

to 1954. Does it then follow from this argument that there were changes in the plant which explain the higher exposures beyond 1954? If so, there is no discussion of what these changes might have been and what possible impact they may have on deaths after 1973. The statement is also made that among both the cancer and non-cancer group, the proportions of those hired in 1944 and after 1948 are similar. What is the implication of this statement? Does this finding fit in with the above argument? How? Might not one argue that if radiation is predictive of cause of death, perhaps we would have expected a lower proportion of those who eventually died of cancer to have been hired during the low dose-low proportion of exposed worker period. One should not get too involved in these arguments, however, because they are based exclusively on year of hire, which is of major importance in an occupational study only if there were changes in some aspect of production, with concomitant differences in exposure following these changes.

While on this topic, it should be noted that Table 1, as are many of the other tables in this report, is presented in an awkward fashion which makes interpretation difficult. It would be of interest to examine each cohort (here defined as the group of workers hired during the specified year) separately and then to compare their characteristics with those of other cohorts. To accomplish this, the data should have been percentaged across, not down. In other words, we would like to

know, say for the 1944 cohort, what proportion of the 5,256 members of this cohort survived, died of cancers and non-cancers, etc. We could then compare this with the 1949-1971 cohort, for instance, and compare the proportions in a manner

which would permit us to determine whether the cohorts truly resemble one another. As the data are presented, however, we are informed that, of the 21,206 survivors, for instance, 16.4 percent come from the 1944 cohort and 2.3 percent were in the 1946 cohort. What is the significance of this? By percentaging down instead of across, the characteristics of individual cohorts are obscured rather than clarified. It is only in the very last line that the across percentages are offered in summary, which again does not permit comparison of individual cohorts.

C.L.-P.3

This paragraph opens with a statement about 'cohort resemblances' where the meaning of the term cohort is suddenly changed from members of the group of workers hired during a specified year, to members of the group of cancer and non-cancer deaths. This inconsistency in the definition of terms is misleading, and the conclusion that the cohorts are 'similar' does not necessarily follow from the single piece of information offered in the paragraph above.

The reader is also referred to Table 2, from which it is deduced in the text that "men who eventually developed fatal cancers had been more often and more intensively exposed to external radiation than men with other causes of death."

Table 2 does not provide evidence for either of these two conclusions. There are no data whatsoever concerning how 'often' members of the two groups had been exposed, nor is there any information presented concerning the 'intensity' of exposure, which simply cannot be equated with mean cumulative radiation dose without examining and including in the calculations the duration of employment.

One possible way to define intensity would be mean annual exposure, and while we have objected to the over reliance on means earlier in our discussion and will not here repeat our arguments, in the context of the manner in which the data are presented, mean annual exposure would at least incorporate duration of employment, a factor of utmost importance which has received very little attention throughout the entire publication. From the data presented in Table 2, however, no conclusions can be drawn concerning how often or intense the exposure has been, although it is reasonable to conclude that a higher proportion of those who developed cancer had been exposed at some time; in view of the rather small observed difference in the proportion exposed (66 vs 61 percent), one wonders, however, why no test of the significance of this difference was performed.

While we have already pointed out the central importance of the possible impact of confounding in epidemiologic investigations, it is well to remember, and it will not be continually repeated, that in none of the analyses presented

was there appropriate control for the possible effects of the numerous suspect confounders, such as age at and year of hire, duration of employment, etc.

C.R.-P.1

The statement is here made, based on the data in Table 3, that for no specific non-cancer was the mean radiation dose higher than the average for all cancers combined. Clearly, the all cancer average is being fairly heavily weighted by a few sites with high mean doses (lymphatic leukemia, pancreatic and brain malignancies) and, in fact, the all cancer mean doses are not even presented, but instead the doses for RES neoplasms and solid tumors are presented separately.

A careful examination of the contents of the table reveals that the mean dose for many of the specific non-cancers exceeds the mean for many of the specific cancers, and while we once again mention the limitations of working with means, we must strongly object to the comparison of means (or overall means for a large group of all cancers) with the means for much smaller groups of specific non-cancers. One must also wonder, again, why tests of significance (such as T-Tests for the comparison of means) were not performed on these findings, although it would have been far more preferable to calculate the odds ratios, which is a commonly used

epidemiologic measure of effect, for the relationship between exposure and disease. Indeed, examination of the percent of exposed workers in each disease category intimates that most odds ratios would be close to unity.

In general, it should be stated here that even among those who developed cancer, approximately 40 percent were never exposed to any radiation at all, and one must wonder why they are left in the analysis, especially since their cancers cannot be attributed to the exposure under investigation. Indeed, the text often cites the Mean Cumulative Exposure for all workers, including those unexposed, as evidence of the effects of radiation, rather than consistently citing the mean dose for exposed workers only.

Page 371
C.L.-P.1

One generally, in the conduct of an epidemiologic investigation, would establish the existence of an excess in certain diseases within an employed cohort, and after the excess (along with its statistical significance) has been established, look for the possible effects of occupational exposures. More will be said shortly on the methods used to establish the existence of an excess, but it should first be pointed out that the data were apparently first examined for associations between cause of death and exposure, and this was followed, instead of being preceded, by identification of those deaths occurring in excess. In addition, the relationship between

excess deaths and higher than expected radiation doses is inconsistent and not sufficiently, if at all, discussed.

For instance, from Table 4 we see that there was a 44 percent excess of neoplasms of the liver and gall-bladder, while the mean radiation dose, from Table 3, was exceptionally low, lower indeed than 8 of the 9 categories of non-cancer. On the other hand, a case is made for a possible causal association between neoplasms of the brain and large intestine, which appear at a 4 percent excess and a 3 percent deficit, respectively, or essentially which appear at the expected frequency. The method used for establishing the existence of an excess, aside from the conceptual problems summarized above, are not at all clear and may actually invalidate any conclusions regarding the excess. The statement is made that Table 4 presents the "expected number which shows how the same diseases were distributed among the 1960 cancer deaths of U.S. white males." It seems, therefore, that a proportional mortality analysis (PMR) of some sort was performed, although it seems reasonable to conclude that the PMR was not only not standardized for age or race, but that indeed while the expected numbers are based on the experience of U.S. white males, the observed numbers may include blacks as well, a problem which did not prevent the authors from generating observed:expected ratios.

We have here, therefore, a situation where the procedure used to establish the occurrence of an excess (the proportional mortality approach) is of dubious epidemiologic validity even in the best of circumstances; that the procedure did not even standardize for the common confounders only furthers the difficulty in interpreting the findings.

One must seriously wonder why SMRs (Standardized Mortality Ratios) were not used, especially since from Table 1 one may surmise that the appropriate denominators necessary for the calculation of SMRs were indeed somewhere available.

Even despite these serious limitations, one must further wonder why tests of significance were not performed on these ratios, especially since not a single ratio reached a value of 2 - that is, none of the diseases occurred at twice the expected proportion. In view of these non-impressive excesses, some statistical test is clearly indicated but none is offered. Instead, the Table draws the readers' attention to the mean cumulative dose and how it compares with the mean for all non-cancers - a comparison which has already been discussed and which is replete with serious limitations.

C.L.-P.2

Despite the problems thus far enumerated, the authors conclude that the "preliminary findings are compatible with a causal association." The stated conclusion is clearly unwarranted, although one might suggest at this point that

further analyses are appropriate in view of possible associations. This section then continues with a description of what are called 'controlled analyses,' a term which is entirely misleading. Presumably, this section addresses the question of the effects of confounders, although this is done either incompletely or inappropriately, if at all. In fact, controlled analyses - properly defined as an analytic procedure which describes the relationship between exposure and disease after the effects of the confounder(s) have been removed - were never at all performed. Instead, each of the 5 listed "possible sources of false impressions" - i.e., confounders - is described separately, and while differences between cases and controls are observed and noted, analytic techniques capable of controlling for these differences are not used, or at least not presented.

C.R.-P.1

We will not repeat our objection, in examining the statements made about the five possible confounders, that "controlled analyses" were never actually performed, but will instead examine whether the statements made about the data presented are appropriate. The statement is made concerning "calendar years," which is never clearly defined, that "only during the high dose period [second half of study period] were differences between cancers and non-cancers at all pronounced." What does "differences" mean? Examination of Figure 1 reveals that "differences" between the two groups

were never pronounced. Examination of Table 5, about which more will be said shortly, reveals that "differences" (either radiation dose or high risk year) were rarely pronounced. While much is made of the "high risk year" concept, the actual differences in radiation dose between the cancer and non-cancer groups are miniscule. For instance, the period 1958-1959 credits the cancer group with two high risk years, while the difference in mean dose (53.6 vs. 51.7) was 1.9 centirads. How significant, both biologically and statistically, is this difference, and does it warrant calling the entire period a high risk period for the cancer group? In fact, the entire Table 5 is presented in an awkward manner. The column "Exposed Workers" is misleading, for instance, because the 333 exposed cancer workers in 1946-47, for instance, may and probably does include the 237 from 1944-45. The totals of 3005 and 10,385 presented at the bottom of the columns therefore have no interpretation by themselves. Also, why are the 'calendar years' presented two at a time, while the 'high risk years' column separates the two years. Clearly, the authors had and used more data than they presented.

One must also question the pooling of these two-year periods - from Figure 1 we see that in 1944 approximately 18 percent of cancers were exposed, while in 1945 it rises to over 30 percent. Should these two years be pooled? Are the data being obscured by this procedure? Further comparison of Figure 1 with Table 5 causes even more problems. For instance,

from the Table we see that during 1946-47, 333 of the 670 cancers, or about half were exposed. The figure, on the other hand, indicates an exposure rate for cancers which is less than 40 percent!

While this may be explained by the use of a denominator other than the 670 total cases of cancer, the reader is not informed of the nature of the denominator; the most appropriate one would be the number of workers employed at that time (i.e., the total number eligible for inclusion in the numerator). The central questions pertaining to this "controlled analysis" and the others which follow are: do the "analyses" really "control" for the confounders or do they merely describe them; are the proper "differences" being examined - i.e., what is the rationale for choosing these and not others, and indeed, are the data presented internally consistent.

Page 372
C.L.-P.I

The section on "employment years" suffers from the same general problems as those encountered in the calendar year analysis already described, although one major additional comment must here be made concerning this and the following ("pre-death years") analysis: the two terms are simply not clearly defined, making interpretation of the presented data extremely difficult. In the introduction to the controlled analyses, the first factor is referred to as "employment year of exposure" while in Table 6 it is referred to as "employed years," and in the text there is

a statement about the "progressive lengthening of the interval between hire and exposure." So the meaning of this term is ambiguous. Figure 2 reveals that the abscissa, which is employment year, takes on values from 0 to 29, which implies that Year 0 = 1943, or the first year of operation of the Hanford Works, while Year 29 is the last year included in this study, namely 1972. If this is true, then Figures 1 and 2, as well as Tables 4 and 5, should be exactly the same, and they are not, which still leaves open the definition and intended use of the term.

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C.L.-P.1

The same general objections can be made regarding the term "pre-death year," although a definition is offered in the footnote to Table 7: pre-death year = interval between exposure [presumably first exposure] and death. Apparently this is therefore synonymous with latency period, where this period is calculated from the first year of any exposure.

In this discussion, and in the discussion of the other four possible confounders, any and all observed differences are presented without any attempt to amplify on their meaning. For instance, what is the validity of pooling all cancers (both those occurring in excess and those not) and then presenting data on their latency period in the aggregate? In this section, for instance, we read that "when the interval...was less

than 8 or more than 20 years...there were over twice as many high risk years for non-cancers." What is the import and significance of this finding? How does it fit with the other conclusions? Is there duplication of these findings by other investigators?

In addition, there again appears to be an inconsistency between the data presented in Figure 3 and Table 7, unless we are interpreting the data improperly, which is possible. From the Table, for pre-death years 24-25, we see that 111 (of the 670) cancers, or approximately 15 percent, were exposed. Examination of the Figure for the same period suggests that the exposure rate for cancers was over 40 percent. Where does the error lie? Is it again due to undefined denominators?

C.R.-P.2

The data for exposure age, which is presumably age at hire, may have been improperly interpreted - the statement is made, for instance, based on Figure 4, that "the proportion of exposed workers was virtually independent of age." Examination of the Figure in question reveals quite a different picture. Among the cancer group, a considerably higher proportion of those who enter before the age of 35 are exposed. One can hardly conclude from these data that the proportion exposed is independent of age at hire, unless one pools the data for the cancer and non-cancer groups and obscures the true differences.

But aside from these problems in interpretation, what does this analysis tell us? It says, in essence, that the greatest danger for cancer induction, if there is indeed any danger at all, is found among those who were first exposed at the older ages, while biologic theory generally postulates that exposures among the young usually carry the heaviest ultimate penalties. Perhaps some valid underlying relationship with age at first exposure is being obscured here because of the pooling of all cancers - which includes many sites which were not in excess among Hanford workers and others with radically different estimated latency periods.

Page 375
C.L.-P.2

The first statistical test of significance is reserved for the analysis which presumably controls for age at death. Now age at death is clearly related to cause, even in the absence of any occupational exposures. For instance, we would expect that men dying of accidents will die at younger ages than those whose cause of death is lung cancer, independent of occupational exposures. What is the purpose, then, of this analysis? Why control for age at death itself, unless one demonstrates that this variable is related to another, say duration of employment, which can affect cumulative radiation dose. Questions are therefore immediately being raised concerning the very propriety of this analysis.

In addition to our fundamental concern for the rationale of this analysis, we were also puzzled by the statistical techniques chosen by the authors. All three variables involved in this analysis - cumulative radiation dose, proportion dying from cancer, and age at death - are continuous variables, for which there exist numerous statistical techniques which utilize fully the available interval data. Why these continuous variates should be rank-ordered, with the accompanying significant loss of information, before statistical tests are applied is difficult to understand.

Aside from these fundamental biologic and statistical objections, however, we find it difficult to understand the meaning of the conclusions presented in the context of the present investigation. For instance, we read the following:

"although accidents were often causes of early death, men who eventually developed malignant diseases did not have appreciably longer life spans [i.e., lived slightly longer] than men with other causes of death."

How does this fit in with the hypotheses and relationships under investigation? Is this expected or unexpected, important or unimportant, etc.? In fact, we are being told that those who die of cancer live longer than those who die of other causes. Perhaps, then, radiation exposure is beneficial and ought to be encouraged; on the other hand, perhaps it is a function of the first objection concerning age at death analysis discussed above. We are further informed that

"between two thirds and three quarters of all the deaths occurred between 50 and 80 years of age." This sounds entirely reasonable, and in the absence of any comparison with other groups, contributes nothing to our understanding of the relationship between radiation exposure and cancer deaths.

Examination of Tables 9-12 reveals some very interesting things which are not all discussed. From Table 9 (which should have been percentaged across also) we see that 53.2 percent ($26.9 + 20.1 + 6.2$) of all the non-cancer group live to be 60 or older, while the corresponding figure for the cancer group is 55.5 percent ($35.7 + 17.3 + 2.5$). That is, a higher proportion of those who died of cancer, which is presumably associated with radiation exposures, are living until the age of 60, than are those who died of non-radiation-related conditions. Table 10 reveals that those with the highest cancer: non-cancer radiation dose ratio lived much longer (until the age range 70-79) than those with the lower ratios. What is the meaning of these and similar conclusions which can be extracted from the presented data?

Page 376
C.L.-P.I

The interpretation of the findings in Table 11 is difficult indeed. It should be recalled that our major objection concerned the transformation of continuous data into an ordinal scale, which is then subjected, after considerable loss of information, to a

statistical test of significance whose results (p-values) are not consistently presented. That is, a rho was calculated for the rankings in each of the five age groups, while the p-value for these rhos are not presented. Apparently, only the correlation coefficient (rho) for age at death among those 70 and older is significant, and indeed that only among those who die at the oldest ages is cancer a significant cause of death among the highest exposure group - but one should not lose sight of the fact that those in this group, who had the highest exposure and highest cancer proportion, are living the longest.

The mean for each exposure category is then calculated, and a rho is calculated for the ranking of these means, which is a statistical manipulation of dubious validity; it is only for this procedure that a statement is made concerning the significance of the derived correlation coefficient. Based entirely on the result of these questionable analytic procedures (the actual p-value is not even presented), the authors conclude that there was a "firm rejection of the null hypothesis by the statistical test," a statement which hardly seems warranted, or which at least requires further justification.

Page 376 - Special Tests of Radiation Associations

Reference is again made to 'controlled analyses' which, as mentioned earlier, have for the most part not really been conducted. At this stage of the analysis, nevertheless, the authors

feel confident in attempting to describe the nature of a relationship whose very existence has not yet been firmly established. This section, along with the appendix in which many of the ideas are expanded, is quite biostatistical in nature, and since we are not biostatisticians, we will not offer a detailed reaction to the procedures used, although a few general comments are in order.

Once again we must state our objection to the over-reliance on arithmetic means as the central measure of effect. In addition, we must point out that N , which is defined as the size of the whole population, in the text, refers only to the population of certified deaths and not to the true cohort of all workers at Hanford. This is an extremely important point, because it is very possible, and indeed probable, that the cumulative radiation doses experienced by many of the survivors far exceeds those of the deceased members of the cohort, as the authors themselves state on the second page of the publication. How this can be ignored when making inferences about the potential effects on the general population (e.g., doubling dose) is most difficult to comprehend. As pointed out in the introduction, from a numerator type analysis one should be reluctant to extend the findings back to even the original cohort from which the deaths were drawn; extending the results to the general population should be tempered by even greater discretion. While we are not competent to evaluate the validity of the biostatistical modeling, and are willing to assume that it is appropriate, we nevertheless

feel that the use of an inappropriate N (all deaths and not all members of the cohort) raises serious doubts about the epidemiologic validity of the conclusions, especially when from these data inferences are drawn concerning the anticipated effects of exposure among the general population.

Page 377
C.L.-P.5

The statement is made that "there are strong grounds for believing that tissue specific cancers have characteristic, albeit long, intervals between initiation and death." How does this statement agree with the earlier finding that the "high risk years" for cancers occurred later (or closer to the year of death) than those for non-cancers, and the findings reported here where we see that for all sites examined, the only statistically significant differences in exposure occurred rather shortly, and not a long time, before death? In not a single site was there significant excess exposure earlier than 18 years before death, which is certainly not a "long" interval, and the intervals for all sites, in general, fell between 18 and 0 years prior to death, which hardly demonstrates that each site has a "characteristic" interval. We should also mention at this point that there is no description of the specific statistical tests used for determining which exposures were significantly different from the experience of the non-cancer group, although p-values are presented.

The statement is also made that "sensitivity to the cancer induction effects of any mutagen is strongly age-dependent," although this idea is not further clarified. Are we speaking of age at first exposure or age at which the greatest exposure occurred, among other possibilities? Which, in fact, are the most sensitive ages? How does this age-dependence statement fit with the earlier observation (p. 375) that the "proportion of exposed workers was virtually independent of age." If workers are sensitive at a young age, for instance, then we would expect that a higher proportion of those destined to get cancer would have been exposed at younger ages - yet this proportion is declared to be independent of age on the basis of the data utilized in this study.

A further problem with the "age analysis" is that, although referred to, it was never really done. The reader is referred to Table 16, which again presents data relating to "pre-death periods," meaning latency period or years prior to death. This absolutely cannot be equated with age - for a man who died at 80, an exposure which occurred 20 years prior to death occurred when he was 60, while for the worker who died at 60 the exposure occurred when he was aged 40. Analysis based on "pre-death years" therefore say nothing about the actual age at which the exposure occurred unless age at death is statistically controlled in the analysis, which was not done for Tables 12-16, from which one therefore cannot make any deductions concerning sensitive ages for cancer induction.

It should also be noted, when discussing the data in these tables, that the cumulative radiation doses for other sites reported to be in excess in Table 4 (mouth and pharynx, liver and gallbladder) are not presented. In view of the fact that cancers at all sites did not occur in excess, and that not all sites showed significant excess cumulative exposure when compared with on-cancers, one must wonder why the investigators continued to pool all cancers and make inferences about this large aggregate.

C.B.-P.1

The discussion here attempts to enumerate additional characteristics of those cancers with "definite radiation associations," but as we have been indicating, we cannot agree that definite associations have indeed been established, which throws the appropriateness of all succeeding analyses into considerable doubt.

Page 378
C.R.-P.2

The investigators state here that the "critical interval between exposure and death" for all cancers was 12 years, while they further report "critical intervals" of 14, 11, and 9 years for lung cancers, RES neoplasms, and bone marrow cancers. Once again we must note that this is not in agreement with the earlier statement (p. 377) concerning the long and characteristic intervals between initiation and death for tissue-specific

cancers - the intervals presented here seem to be short and similar to one another. While on this topic, we must also be concerned with biomedical plausibility of such short latency periods - for instance, 14 years is a rather short interval for lung cancer compared with the intervals estimated from studies based on smoking histories, and how does a latency estimate of less than one year for pancreatic tumors agree with the findings of other investigators?

It is also difficult to understand how the investigators can conclude that lung cancer is one with definite radiation associations without even a passing reference to the complete absence of any information on the cigarette smoking characteristics of this group of workers. Despite these and other objections already described, the authors remain quite "certain" of the reported radiation associations since, in reference to other sites, they refer to "less certain evidence of a causal association." Among these latter sites is cancers of the large intestine which, it should be recalled from Table 4, appeared in less than expected numbers among this group of workers.

Page 379
C.L.-P.I

This section on "doubling doses" is disturbing for numerous reasons already discussed, but mainly because the estimates are based on the experience of deceased workers only (the N cited in the Appendix) and not on the entire cohort of all workers employed at the plant, which is the true cohort under scrutiny. Even aside

from this major difficulty, one must further wonder how the category "all cancers" can be causally associated with radiation exposures in view of the preceding discussion concerning the biomedical validity of pooling so many different sites.

In anticipation of possible objections to such low estimates of doubling doses (0.8-12.2 rads) the authors cite Table 16 and state that from the observed and expected proportions of different cancers, Standardized Mortality Ratios (SMRs) were obtained. SMRs are based on a comparison of rates derived from the true cohort of all workers, whether living or dead, while the proportions presented in Tables 16 and 4 refer to proportions based only on the distribution of deaths. How one derives SMRs from a proportional mortality analysis, and obtains these estimates "in the usual way" is baffling. In addition, we are not told for which factors (age, race, sex) the SMRs were standardized. Indeed, if SMRs were available, they should have been presented as the very first piece of evidence concerning the existence of an excess and should have formed the foundation for all further analyses. While Table 17 presents "SMRs," the reader is referred back to Table 16 for an explanation of the manner in which they were derived and this Table, as already indicated, deals with proportions and not rates. Without further clarification, the interpretation of these calculations is impossible.

Page 380
C.R.-P.2

Since our data set did not include any information on internal radiation, we will not comment on this section and will instead resume our discussion with the section on age and sensitivity.

We must frankly admit that we do not understand the discussion and the data (Tables 21 and 22) on which it is based. Nevertheless, the statement is made that these data are "strongly suggestive of an exponential increase in cancer sensitivity with advancing age." Once again we must remind the reader that the entire analysis is based on numerators (deaths) only, from which it simply cannot be concluded that sensitivity (presumably among all workers) increases with age. Even if the data presented are accurate, from the fact that cases of cancer at age 45 had 15 percent higher than expected doses, while at age 50 there was a 50 percent higher cumulative exposure, one simply cannot conclude that the "risk of" (sensitivity to) cancer is increasing - after all, everyone in this group has already developed and died of the disease.

While this may be conceptually similar to the use of an Odds Ratio as an estimate of Relative Risk, this transformation is based on rigorous epidemiologic and biostatistical foundations which have been continuously re-examined, modified, and strengthened by countless investigators over a period of 20 years, and we cannot assume that the procedure used here is as defensible. We must therefore state our substantial concern with this entire section and the inferences drawn from the available data.

Page 381
C.R.-P.2

The approach used for the analysis of the female experience is similar to that used for the male analyses and we will not further discuss the issues already raised, although a few comments are in order.

Presumably, females were not included in the earlier analysis, although this is the first indication of this analytic decision. We must wonder what the rationale is for this separation. It is also not clear whether there were 126 or 127 deaths from cancer among females (perhaps this is a typo), or how the 285 deaths from causes other than cancer among the 412 women gives a percentage of 30. Despite the statement that the "proportion of these workers with records of external radiation was small" Table 23 ranks all females for radiation exposure, which would be impossible if data were not available for all of them. If the '0' in this table refers to those for whom records were not available, and not the truly unexposed, the statistical test becomes inappropriate and the results misleading.

Page 382
C.L.-P.2

The procedure used to arrive at these estimates of attributable risk are not at all clear to us. We must say, however, that attributable risks are best derived from prospective (or cohort) studies. While they are occasionally derived from case-control studies, there are numerous methodologic

problems associated with this derivation, and the assumption is generally made that all members of the cohort were eligible for selection as controls. Since this present investigation was based on numerator data only, this assumption cannot have been met.

Page 383
Discussion

Based on the critique presented thus far, the four enumerated conclusions in the first paragraph are simply unwarranted. While the authors, in the following paragraph, finally acknowledge the possible impact of confounders, and indicate that the next stage of the analysis will include standardization for these factors, they do not hesitate to conclude, prior to the execution of these analyses, that there is a "now remote possibility that the positive findings were merely the result of the radiation exposures having associations with other cancer-related factors." One need only be reminded of the overwhelming impact of smoking on the incidence of lung cancer, for instance, as evidence for the inappropriateness, at least for now, of the stated conclusions.

ANALYSIS

General Comments

This analysis is being undertaken in an attempt to replicate, in a manner of speaking, the efforts of Mancuso, et al. We state again very emphatically however, as we indicated in our examination of the paper, that the design was inappropriate for a determination of the relationship between radiation exposure and disease.

It should also be recalled that we were not in possession of denominators, which made it impossible to rigorously establish the existence of an excess number of deaths from any of the causes. We therefore relied entirely on the data set as received from NCR, which contained the following variables: age at death, years of hire and departure, duration of employment, cause of death, race, sex, exposure code, cumulative lifetime external radiation dose, cumulative dose at 3, 5, 10, 15, 20 and 25 years prior to death, and year of death. From these given variables we determined year of birth, from which we further calculated age at hire and age at departure; one must wonder why these three variables were not originally provided.

While we mentioned above that we will attempt to 'replicate' the work of the investigators as presented in the paper under examination, it should be pointed out here that the data we received are not parallel to those used in the paper, and we must wonder why. For instance, much is made of

the calendar year analysis, although we did not get doses for specified calendar years; instead, we received cumulative doses for specified (3-25) years prior to death, and 3 years prior to death, for instance, represents different calendar years for people who died in different years.

In addition, there are fully four tables in the paper which utilize this 'years prior to death' analysis, and 15 categories of this variable are used in each of the tables. We received values of this variable for 6 categories. It is surprising that, of the 15 they used and the 6 we received, only one coincides, which makes a replication of their analysis impossible without extrapolating from the data at hand, which is never as precise as the real thing. One must wonder why the data have been presented to us in a non-replicable manner.

Our reluctance to perform the analysis is thus far based on both the inadequacy of the epidemiologic design and the differences between the data received and those actually used in the paper. In addition to these two factors, we performed a rather cursory editing (internal consistency) check and found, to our dismay, numerous definite and possible errors which cast reasonable doubt on the accuracy of the information and therefore on the question of whether the data merit analysis.

Listed below are the inconsistencies and curiosities encountered, although it should be reiterated that we did not perform an extensive search for errors since we were laboring under the assumption that the data received were accurate, especially since we have no means for checking their accuracy. The list is therefore only partial and is limited to inconsistencies and illogicalities:

1. There were five individuals whose age at hire, according to our calculations as described above, was less than 17. The actual values were: -15, -11, -1, 2, and 3 years of age.
2. According to our calculations, there were 49 individuals whose age at hire was between 65 and 79 years, which seems highly unlikely, unless the retirement age was waived for those individuals because of the wartime manpower problems. Even allowing for a one year error in our calculations, there would still be a total of 32 people hired after the age of 65.
3. Along the same lines, we calculate that for 533 individuals, the age at departure was between 65 and 83; allowing for a one year error, the total would still be 370. While wartime expediency may explain some of these occurrences, it should be noted that, for instance, not all those whose age at hire was over 65 were hired during wartime years, and

also that working into one's mid-80's must be highly unusual under any circumstances.

4. Five individuals had 1900 listed as their year of hire; perhaps these are the same individuals whose age at hire was incorrect. In addition, there were 5 individuals with durations of employment exceeding 45 years, no doubt a function of the incorrect year of hire.
5. The most perplexing problem is the difference in the total number of workers on the file we received; our total was 3992 while Mancuso, et al. had 3520. While these investigators had 412 certified deaths among females, we had only 382. Adding both sexes would give a total of 3902, which means that an additional 90 deaths have appeared on our files. This cannot be explained even if blacks, who numbered 28, were handled separately by the original investigators.

From this superficial examination of the data, therefore, enough has been seen to at least provide grounds for questioning the accuracy of the data. Coupled with the concerns voiced earlier regarding the design and absence of denominators, the following analysis is being presented with serious reservations. In essence, we simply asked what a more appropriate analysis, given the data at hand, would reveal, although not much significance should be attached to the findings.

DATA ANALYSIS

Demographic Factors

Tables I-VI present the distributions for numerous variables of interest, from which the following points should be noted:

1. Almost 70 percent of the workers included in this study were hired between ages 30 and 60. One must therefore be very concerned about the occupational histories of these individuals prior to employment at the Hanford Works, during which time other significant work exposures, in other industries, are likely to have occurred. The nature of these exposures is entirely unknown, at least to us, and the possible impact of these exposures on the health outcomes under investigation are not at all discussed in the paper under examination. In addition, over 61 percent of workers included in this study were hired between 1943-1945, which of course were the war years, and given the added fact that approximately 15 percent of the workers were hired between the ages of 17 and 29, one must wonder whether these men were not drafted into the combat forces because of some health factor. If this occurred, we would have a sizeable proportion of workers who were 'unhealthy' in some rather serious way, a fact which may well have affected their causes

of death. We have therefore, if this reasoning is correct, a workforce which is less healthy, rather than being healthier, than the general population; this, of course, would be contrary to the general situation encountered in an occupational study, where workers, as a group, are healthier than the general population of comparable age.

2. Over 50 percent of the workers had a duration of employment which was less than two years. One must wonder whether this length of time, given the generally low doses to which they were exposed, is sufficient to justify their inclusion in the analysis. This is naturally related to cumulative dose, and over 80 percent of workers had lifetime doses under 100 centirads; the same question regarding inclusion of these workers in the study can be raised, especially since a one rad exposure is not uncommonly encountered in the use of diagnostic X-rays.
3. The table summarizing causes of death is an exact duplicate of the one presented in the paper, and the very same terminology was used for comparative purposes. It should be recalled that our total number of deaths did not match that of Mancuso, et al. and also that we did not separate the experiences of

males and females since there was no ready biological justification for doing so. It will be especially difficult for the reader to compare this table with the one presented in the paper where the numbers of deaths for the different causes were not presented for females. In addition, one must wonder why the authors did not report on mortality for breast cancer, which the literature suggests may well be associated with radiation exposure.

Radiation Associations

Table VII presents, in summary fashion, the characteristics of workers dying from those causes for which Mancuso, et al. claimed significant radiation associations: cancers of the lymphatic and hematopoietic tissues, and cancers of the large intestine, pancreas, lung, kidney, and brain. Examination of the first and last rows of this table, which compare all non-neoplasms with all malignant neoplasms, immediately reveals that the characteristics of individuals in the two groups are remarkably similar. Those dying of malignant neoplasms, however, had a slightly longer duration of employment which no doubt was at least partly, and probably entirely, responsible for the difference in lifetime dose.

The point should be made here, and this point is as important as any made in this paper, that a comparison of the means and medians for duration of employment, cumulative

lifetime dose, and intensity of exposure immediately reveals, because of the substantial difference in the two, that the mean is not a good measure of central tendency on account of the skewness of the distribution. This then provides additional support for the contention that means should not have been used as the main measure of effect - in the best of circumstances, they are simply not a measure of effect, while in this instance they are quite misleading as well because of the presence of a few outliers which heavily weight the mean, and because of the high proportion of unexposed individuals in every group.

Further perusal of Table VII reveals that the characteristics of workers dying from select cancers are rather similar to those of workers dying from non-malignancies, with some differences in duration of employment and hence lifetime dose. It should be noted here that the numbers of people dying from select cancers ranged from 24 to 203, while the non-neoplasm and total malignant neoplasm groups numbered 3177 and 803, respectively, resulting in much more stable estimates for the latter groups. This is a constant problem in these comparisons, and while a statistical test for differences in means would incorporate sample size in its assignment of a p-value, we are clearly against the use of means as a measure of effect.

While we do not wish to spend too much time on this table, it would be profitable to examine closely the characteristics of the 24 individuals who died from multiple myeloma and

myeloid leukemia (ICD 203,205). While the means for duration of employment, lifetime dose, and intensity of exposure all appear to be high, the medians reveal quite a different story - the medians for each of these three variables were the lowest of all causes, including non-malignancies, presented in the table.

Table VII presented the data from the perspective of the outcome (cause of death), while Table VIII examines the data from the exposure perspective. The characteristics of four categories (unexposed, low, moderate, and high exposure) are presented. Once again, we are struck with the similarities in the values of the parameters, except of course for duration and cumulative dose, which are a direct function of the definition of the four categories. Perhaps the most interesting comparison is presented at the bottom of the table, where the proportions dying from all cancers and from lymphatic and hematopoietic cancers in each of the four groups are compared. Again, these proportions are strikingly similar. The chi-square test was performed on these proportions, and the results, as presented in Table IX, indicate that there is no significant association between dose and cause of death.

We will make a general comment here, which would be obvious from a careful examination of the tables, that we have consistently eliminated from the non-cancer group those individuals whose cause of death was listed as a benign neoplasm (ICD 210-239), and for this reason, the totals often fall 11 short of 3992, and these deaths have been effectively eliminated from most of the analyses.

Finally, for each of the cancers which Mancuso, et al. claimed were associated with radiation exposure, we calculated odds ratios and confidence intervals for different definitions of exposure and non-exposure; that is, different definitions for non-exposure were tried, ranging from zero to anything less than 1000 centirads. The totals for each stratum within any table are therefore constant. By altering the definition of non-exposure (and hence exposure) we were, in essence, giving those with high exposures a chance to have an impact on the odds ratios, but examination of the findings in Tables X - XVII consistently reveals non-significantly elevated odds ratios for these different sites and definitions of exposure.

It should be noted here that we have used the 95 percent test-based confidence interval, defined as the $OR(1 \pm \frac{z}{x})$, where $z = 1.96$. While many of the point estimates of the odds ratios are slightly elevated, one concludes that the OR is not significantly high if the confidence interval includes unity(1), which it does in almost every instance.

Indeed, only for lung cancer were some of the odds ratios significantly elevated, but of all sites examined, we can put least faith in a possible association between radiation and lung cancer in the absence of availability of smoking histories, because smoking prevalence is generally higher among blue collar workers and approximately 80 percent of all lung cancers are attributable to prior smoking histories.

In summary then, analysis of the data as received does not indicate any association between cause of death and radiation exposure. To fully resolve this issue, however, a rigorously designed and executed epidemiologic investigation is necessary.

Table I
Distribution for Age at Hire

<u>Age at Hire</u>	<u>Number</u>	<u>Percent</u>
<17*	5	0.1
17-19	43	1.1
20-29	526	13.2
30-39	973	24.4
40-49	1211	30.3
50-59	999	25.0
60-64	184	4.6
65+	51	1.3
<u>TOTAL</u>	<u>3992</u>	<u>100.0</u>

*According to our calculations (Age at Hire=(Year of Hire + 1900)
- Year of Birth, where Year of Hire on the file is the last two
digits only.

Table II
Distribution of Age at Death

<u>Age</u>	<u>Number</u>	<u>Percent</u>
< 40	311	7.8
40-49	587	14.7
50-59	990	24.8
60-69	1130	28.3
70-79	766	19.2
80+	208	5.2
<u>TOTAL</u>	<u>3992</u>	<u>100.0</u>

Table III
Distribution of Duration of Employment

<u>Duration (in years)</u>	<u>Number</u>	<u>Percent</u>
< 1	1012	25.4
1-2	1060	26.5
3-7	723	18.1
8-11	419	10.5
12+	778	19.5
<u>TOTAL</u>	<u>3992</u>	<u>100.0</u>

Table IV
Race and Sex Characteristics

<u>Race</u>	<u>Number</u>	<u>Percent</u>
White	3964	99.3
Black	28	0.7
TOTAL	3992	100.0

<u>Sex</u>	<u>Number</u>	<u>Percent</u>
Male	3610	90.4
Female	382	9.6
TOTAL	3992	100.0

Table V
Causes of Death

<u>Cause</u> <u>(with ICD 8th Rev.)</u>	<u>Number</u>	<u>Percent</u>
1. NON-CANCERS		
Infective (000-136)	37	0.9
Benign Neoplasms (210-239)	12	0.3
Endocrine & Blood (240-289)	75	1.9
CNS (290-389)	45	1.1
CVS (390-458)	2022	50.6
Respiratory (460-519)	207	5.2
Digestive (520-577)	164	4.1
Accidents (800-999)	515	12.9
Residue	<u>112</u>	<u>2.8</u>
SUBTOTAL	3189	79.9
2. RES Neoplasms		
Lymphomas (200-202)	39	1.0
Lymphatic Leukemia (204)	5	0.1
Myelomas (203)	11	0.2
Myeloid Leukemia (205)	13	0.3
Residue (206-209)	<u>8</u>	<u>0.2</u>
SUBTOTAL	76	1.9
3. SOLID TUMORS		
Mouth & Pharyngeal (140-149)	23	0.6
Stomach (151)	39	1.0
Large Intestine (153)	79	2.0
Rectum (154)	23	0.6
Other Intestinal (150,152)	20	0.5
Liver & Gallbladder (155-156)	20	0.5
Pancreas (157)	53	1.3
Lung (162-163)	203	5.1
Prostate (185)	43	1.1
Kidney (189)	25	6.3
Other GU (186-188)	15	0.4
Brain (191)	23	0.6
Residue	<u>161</u>	<u>4.0</u>
SUBTOTAL	727	18.2
<u>TOTAL</u>	<u>3992</u>	<u>100.0</u>

Table VI

Percentages for Cumulative External
Lifetime Radiation Dose

<u>Dose*</u>	<u>Percentage</u>
0	41.0
1-22	19.0
23-84	20.0
85-174	10.0
175-385	5.0
386-807	2.5
808-1781	1.5
1782-4421	1.0

*in centirads

Table VII

Summary Table of the Characteristics of Workers with Select Causes of Death

Cause of Death	N	Age at Death		Age at Hire		Duration of Employment		Percent Unexposed
		Mean	Median	Mean	Median	Mean	Median	
All Non-Neoplasms (ICD # 140-239)	3177	60	61	43	44	5.5	1.9	41
Lym. + Hemat Neos (ICD 200-209)	76	55	56	38	37	5.5	1.9	37
Mult Myel + My. Leuk (ICD 203, 205)	24	53	51	38	37	6.7	1.5	42
Neos Lg Int (ICD 153)	79	58	59	41	42	7.3	5.6	32
Neos of Pancreas (ICD 157)	53	60	60	43	45	6.1	2.0	38
Neos of Lung (ICD 162, 163)	203	61	61	42	42	6.7	3.3	35
Neos of Kidney (ICD 189)	24	59	59	43	43	6.2	2.3	30
Neos of Brain (ICD 191)	23	54	55	35	33	8.7	5.1	35
ALL MALIG NEOS (ICD 140-209)	803	59	60	42	42	6.1	2.8	40

continued...

Table VII (contd.)

Summary Table of the Characteristics of Workers with Select Causes of Death

Cause of Death	N	Year of Hire		Lifetime Dose		Intensity of Exposure*	
		Mean	Median	Mean	Median	Mean	Median
All Non-Neoplasms (ICD \neq 140-239)	3177	1946	1945	95	7.2	20.8	2.5
Lym. + Hemat Neos (ICD 200-209)	76	1947	1945	186	15.5	22.5	2.5
Mult Myel + My. Leuk (ICD 203, 205)	24	1946	1945	411	3.5	26.1	1.6
Neos Lg Int (ICD 153)	79	1946	1945	115	25.0	13.4	3.5
Neos of Pancreas (ICD 157)	53	1946	1944	244	12.0	27.1	3.3
Neos of Lung (ICD 162, 163)	203	1947	1945	135	24.0	20.2	3.6
Neos of Kidney (ICD 189)	24	1946	1945	168	11.5	17.9	3.9
Neos of Brain (ICD 191)	23	1946	1945	179	36.0	22.3	3.3
ALL MALIG NEOS (ICD 140-209)	803	1946	1945	115	11.9	17.0	2.9

*Intensity = Mean per annum exposure (Lifetime Dose \div Duration of Employment)

Table VIII

Characteristics of Four Groups with Different Cumulative External Radiation Doses

	Cumulative Lifetime External Radiation Dose (in centirads)							
	0 (N=1638)		1-24 (N=775)		25-84 (N=778)		85+ (N=801)	
	Mean	Median	Mean	Median	Mean	Median	Mean	Median
Age at Hire	43	45	44	45	43	45	40	40
Year of Hire	1946	1944	1947	1945	1946	1944	1947	1945
Year of Departure	1948	1946	1951	1950	1954	1953	1960	1961
Duration of Employment	1.9	0.4	3.9	2.4	7.5	6.9	12.9	13.3
Cumulative Dose	0	0	9.8	8.7	49	46	435	177
Year of Death	1962	1963	1963	1964	1963	1964	1966	1968
Age at Death	59	60	60	61	61	62	59	60
Year of Birth	1902	1902	1903	1901	1902	1901	1907	1907

Cumulative Dose

Proportions Dying From All Cancers (ICD 140-209) and From Lymph. and Hemat. Cancers (ICD 200-209)															
0		1-24		25-84		85+									
ICD 140-209		ICD 200-209		ICD 140-209		ICD 200-209		ICD 140-209		ICD 200-209		ICD 140-209		ICD 200-209	
N	Percent	N	Percent	N	Percent	N	Percent	N	Percent	N	Percent	N	Percent	N	Percent
327	20.0	28	1.7	138	17.8	15	1.9	169	21.7	16	2.0	180	22.5	17	2.1

Table IX

Chi-Square Tests for Association between Select Causes of Death
and Cumulative Lifetime External Radiation Doses

1. Cause = all Cancers (ICD 140-209) vs. Non-Cancers (ICD# 140-239)

	D O S E				
	0	1-24	25-84	85+	Total
Cancer	320	135	169	179	803
Non-Cancer	1311	637	609	621	3178
TOTAL	1631	772	778	800	3981

$\chi^2 = 7.32$ - there is therefore no significant
association between Dose and Cause of Death ($\chi^2_{3, .05} = 7.81$)

2. Cause = Neoplasms of Lymph and Hemato Sys (ICD 200-209) vs
Non-Cancers (ICD# 140-239)

	D O S E				
	0	1-24	25-84	85+	Total
Cancer	28	15	16	17	76
Non-Cancer	1311	637	609	621	3178
TOTAL	1339	652	625	638	3254

$\chi^2 = 0.795$ - there is therefore no significant
association between Dose and Cause of Death ($\chi^2_{3, .05} = 7.81$)

Table X

Odds Ratios (OR) and Tests of Significance for the Relationship
between Varying Levels of Exposure and Disease:

Cases = All Cancers (ICD=140-209) and

Controls = All Causes other than
Benign or Malignant Neoplasms
(ICD#140-239)

1. Exposure \geq 1 centirad

	EXP	$\overline{\text{EXP}}$	OR	χ^2	CONF INT
CASES	483	320			
			1.06	0.53	0.91-1.23
CONTROLS	1866	1311			

2. Exposure \geq 100 centirads; all others unexposed

	EXP	$\overline{\text{EXP}}$	OR	χ^2	CONF INT
CASES	158	645			
			1.19	2.95	0.97-1.27
CONTROLS	543	2634			

3. Exposure \geq 500 centirads; all others unexposed

	EXP	$\overline{\text{EXP}}$	OR	χ^2	CONF INT
CASES	41	762			
			1.32	2.33	0.92-1.89
CONTROLS	124	3053			

4. Exposure \geq 1000 centirads; all others unexposed

	EXP	$\overline{\text{EXP}}$	OR	χ^2	CONF INT
CASES	21	782			
			1.31	1.10	0.79-2.17
CONTROLS	64	3113			

Table XI

Odds Ratios (OR) and Tests of Significance for the Relationship
between Varying Levels of Exposure and Disease:

Cases = Neoplasms of Lymphatic and Hematopoietic Tissue (ICD=200-209) and
Controls = All Causes other than Benign or Malignant Neoplasms (ICD#140-239)

1. Exposure > 1 centirad

	EXP	$\overline{\text{EXP}}$	OR	χ^2	CONF INT
CASES	48	28	1.20	0.60	0.76-1.90
CONTROLS	1866	1311			

2. Exposure \geq 100 centirads; all others unexposed

	EXP	$\overline{\text{EXP}}$	OR	χ^2	CONF INT
CASES	16	60	1.30	0.82	0.74-2.28
CONTROLS	543	2634			

3. Exposure \geq 500 centirads; all others unexposed

	EXP	$\overline{\text{EXP}}$	OR	χ^2	CONF INT
CASES	6	70	2.11	3.08	0.92-4.86
CONTROLS	124	3053			

4. Exposure \geq 1000 centirads; all others unexposed

	EXP	$\overline{\text{EXP}}$	OR	χ^2	CONF INT
CASES	4	72	2.70	3.82	0.39-18.7
CONTROLS	64	3113			

Table XII

Odds Ratios (OR) and Tests of Significance for the Relationship
between Varying Levels of Exposure and Disease:

Cases = Multiple Myeloma and Myeloid Leukemia (ICD=203,205) and

Controls = All Causes other than Benign or Malignant Neoplasms (ICD#140-239)

1. Exposure \geq 1 centirad

	EXP	$\overline{\text{EXP}}$	OR	χ^2	CONF INT
CASES	14	10			
			0.98	<0.001	upper bound <1
CONTROLS	1866	1311			

2. Exposure \geq 120 centirads; all others unexposed

	EXP	$\overline{\text{EXP}}$	OR	χ^2	CONF INT
CASES	4	20			
			1.19	0.10	0.40-3.57
CONTROLS	457	2720			

3. No further calculations since numbers are too small

Table XIII

Odds Ratios (OR) and Tests of Significance for the Relationship
between Varying Levels of Exposure and Disease:
Cases = Cancer of Large Intestine (ICD 153) and
Controls = All Causes other than Benign or
Malignant Neoplasms (ICD#140-239)

1. Exposure \geq 1 centirad

	EXP	<u>EXP</u>	OR	χ^2	CONF INT
CASES	54	25			
			1.51	2.94	0.94-2.41
CONTROLS	1866	1311			

2. Exposure \geq 100 centirads; all others unexposed

	EXP	<u>EXP</u>	OR	χ^2	CONF INT
CASES	17	62			
			1.33	1.06	0.77-2.28
CONTROLS	543	2634			

3. No further calculations since numbers are too small

Table XIV

Odds Ratios (OR) and Tests of Significance for the Relationship
between Varying Levels of Exposure and Disease:
Cases = Pancreatic Cancer (ICD 157) and
Controls = All Causes other than Benign or
Malignant Neoplasms (ICD#140-239)

1. Exposure \geq 1 centirad

	EXP	$\overline{\text{EXP}}$	OR	χ^2	CONF INT
CASES	33	20			
			1.15	0.27	0.68-1.94
CONTROLS	1866	1311			

2. Exposure \geq 100 centirads; all others unexposed

	EXP	$\overline{\text{EXP}}$	OR	χ^2	CONF INT
CASES	13	40			
			1.58	2.02	0.84-2.97
CONTROLS	543	2634			

3. No further calculations since numbers are too small

Table XV

Odds Ratios (OR) and Tests of Significance for the Relationship
between Varying Levels of Exposure and Disease:
Cases = All Lung Cancers (ICD=162,163) and
Controls = All Causes other than Benign or
Malignant Neoplasms (ICD#140-239)

1. Exposure \geq 1 centirad

	EXP	$\overline{\text{EXP}}$	OR	χ^2	CONF INT
CASES	132	71			
			1.31	3.28	0.91-1.23
CONTROLS	1866	1311			

2. Exposure \geq 100 centirads; all others unexposed

	EXP	$\overline{\text{EXP}}$	OR	χ^2	CONF INT
CASES	51	152			
			1.63	8.49	1.17-2.26
CONTROLS	543	2634			

3. Exposure \geq 500 centirads; all others unexposed

	EXP	$\overline{\text{EXP}}$	OR	χ^2	CONF INT
CASES	15	188			
			1.96	5.88	1.13-3.38
CONTROLS	124	3053			

4. Exposure \geq 1000 centirads; all others unexposed

	EXP	$\overline{\text{EXP}}$	OR	χ^2	CONF INT
CASES	5	198			
			1.23	0.44	0.48-3.09
CONTROLS	64	3113			

Table XVI

Odds Ratios (OR) and Tests of Significance for the Relationship
between Varying Levels of Exposure and Disease:
Cases = Kidney Cancer (ICD 189) and
Controls = All Causes other than Benign or
Malignant Neoplasms (ICD#140-239)

1. Exposure > 1 centirad

	EXP	<u>EXP</u>	OR	χ^2	CONF INT
CASES	17	7			
			1.71	1.44	0.71-4.10
CONTROLS	1866	1311			

2. Exposure > 100 centirads; all others unexposed

	EXP	<u>EXP</u>	OR	χ^2	CONF INT
CASES	4	20			
			0.97	0.003	0.35-2.62
CONTROLS	543	2634			

3. No further calculations since numbers are too small

Table XVII

Odds Ratio (OR) and Tests of Significance for the Relationship
between Varying Levels of Exposure and Disease:
Cases = Brain Cancers (ICD 191) and
Controls = All Causes other than Benign or Malignant
Neoplasms (ICD#140-239)

1. Exposure \geq 1 centirad

	EXP	$\overline{\text{EXP}}$	OR	χ^2	CONF INT
CASES	15	8			
			1.32	0.40	0.56-3.13
CONTROLS	1866	1311			

2. Exposure \geq 100 centirads; all others unexposed

	EXP	$\overline{\text{EXP}}$	OR	χ^2	CONF INT
CASES	7	16			
			2.12	2.86	0.89-5.07
CONTROLS	543	2634			

3. No further calculations since numbers are too small

APPENDIX

Report being Evaluated

(copy follows)

RADIATION EXPOSURES OF HANFORD WORKERS DYING FROM CANCER AND OTHER CAUSES*

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(Received 24 February 1977)

Abstract—Data from the Hanford study have shown that sensitivity to the cancer-induction effects of radiation is at a low ebb between 25 and 45 yr of age. Nevertheless, at younger and older ages there is probably a cancer hazard associated with low level radiation which affects bone marrow cancers more than other neoplasms and cancers of the pancreas and lung more than other solid tumors.

INTRODUCTION

HANFORD Works in Richland, Washington is one of the largest atomic plants in the United States, and most of the staff are in some way concerned with the manufacture of radioactive substances. For these workers, who are predominantly white males, there is systematic recording of data under the following headings as part of a study of the lifetime health and mortality experience of employees of ERDA contractors (Ma71):

- (1) Sex, date of birth, date of hire and social security number.
- (2) Dates of entering and leaving specified occupations.
- (3) External and internal radiation.
- (4) Date and cause of death.

The wearing of radiation badges in all workshops and laboratories is obligatory, and the badges are read at frequent intervals to ensure that no worker ever receives more than the maximal permissible dose of 5 rems/yr (BRPC71). In several high risk occupations the workers are also examined at regular intervals and following accidents or radiation "leaks" for internal depositions of radioactive substances. Therefore, there are both records of the total amount of external penetrating radiation received by each worker by the end of each calendar year (annual

doses in centirads) and similar records relating to intakes of radioactive materials (positive urine analyses or internal radiation).

Deaths of Hanford employees are identified through death benefit claims by a nationwide system of social security numbers. These numbers probably provide better identification of males than females but the method of death identification has two major advantages: intervals between discharge and death may be of long duration and there is coverage of all deaths in any U.S. state or territory. Finally, certified causes of death are taken direct from death certificates, copies of which are obtained from official sources and filed with the other records.

Radiation monitoring has been in operation since 1943 and sufficient time has now elapsed for most of the non-survivors to be men who died 10 or more years after leaving the industry. Therefore, from the records of men with certified causes of death we should be able to discover whether NCRP recommendations for protection of radiation workers (BRPC71)—which are strictly enforced by all ERDA contractors—have succeeded in eliminating the cancer hazard or, failing that, are keeping the risk within reasonable bounds. As a first approach to this problem we have examined the records of workers who died within 29 yr of Hanford Works going into full production (1944).

*Under Contract No. E(11-1)-3428.

PRELIMINARY FINDINGS

Death benefit claims on behalf of men who died before 1973 totaled 3710 and included 3520 certified deaths for the period 1944-1972 (Table 1). Compared with the much larger number of survivors from the same work force, these deaths were strongly biased in favor of the first and largest work cohort. Among the men who were hired during 1944 were some workers who, strictly speaking, were not members of the monitored population (e.g. construction workers). Nevertheless, these men have always been so regarded (Ma74), since, in the early records, there is difficulty in distinguishing between workers in monitored occupations who never received any radiation (non-exposed workers) and workers who were not obliged to wear radiation badges (non-monitored occupations).

The high proportion of non-exposed workers in the 1944 cohort and the relatively low doses recorded before 1954 and by men with short periods of employment (Tables 5 and 6), are reasons why we would expect non-survivors to have lower radiation doses than survivors. This has been a constant feature of earlier analyses of Hanford data (Ma74) and will be mentioned again after we have completed the analysis of certified deaths (see discussion). Meanwhile, it should be noted that division of the certified deaths into cancers (670 cases) and non-cancers (2850 cases) left both groups with the same proportions of men hired in 1944 (48%) and men hired later than 1948 (16%).

In spite of their cohort resemblances the two groups of certified deaths had dissimilar radiation records, also ones which showed

that men who eventually developed fatal cancers had been more often and more intensively exposed to external radiation than men with other causes of death (Table 2). Thus the proportion of exposed workers for men who had one or more positive badge readings) was 66% for cancers and 61% for non-cancers, and for these workers the mean cumulative radiation dose was higher for the cancers (210 centirads) than for the non-cancers (162). Therefore, the "all-worker dose" was appreciably higher for cancers (138) than non-cancers (99).

A classification of the deaths by ICD Nos. showed that for none of the Main Orders of non-malignant diseases was the level of radiation dose higher than the level for all cancers (Table 3). But within the group of malignant diseases there was wide variation in the dose level, also higher doses for RES neoplasms (ICD Nos. 200-209) than solid tumors (ICD Nos. 149-199), and exceptionally high doses for a small group of bone marrow cancers (ICD Nos. 203 and 205). For example, the "all-worker" dose averaged 94 for accidents, 105 for cardiovascular diseases, 114 for digestive diseases, 130 for solid tumors, 219 for RES neoplasms and 449 for bone marrow cancers. Other malignant dis-

Table 2. External radiation records for two groups of non-survivors: cancers and non-cancers.

	Cases (Nos.)	Exposed* workers (Nos.)	Cumulative radiation dose (centirads)	Exposed* workers %	Mean radiation dose (centirads)
Cancers	670	442	12547	66.0	210
Non-cancers	2850	1742	282961	61.1	162
All certified deaths	3520	2184	275618	62.0	172

*Men with one or more positive badge readings.

†A = Mean cumulative radiation dose for exposed workers.

B = Mean cumulative radiation dose for all workers.

Table 1. Hanford workers: survivors and non-survivors from 1944 to 1972 work cohorts.

Cohort*	% Survivors*	% Non-survivors*		Totals	
		Uncertified deaths	Cancers	Non-cancers	Early discharges*
1944	16.4	41.3	46.7	47.8	1256
1945	4.7	14.7	12.5	14.5	42.7
1946	2.2	2.0	2.1	3.1	197
1947	10.3	11.3	12.5	11.0	2815
1948	7.8	10.7	8.2	7.5	927
1949-71	58.3	20.0	16.0	16.1	13,620
Total Nos.	21,206	213	670	2850	24,939
Total %	33.0	0.9	3.7	11.4	100.0

*Cohort = year of hire.

Survivors = alive in 1973.

Non-survivors = pre-1973 deaths.

Early discharges = men discharged during the calendar year of hire or the following year.

RADIATION EXPOSURES OF HANFORD WORKERS DYING FROM CANCER 371

Table 3. External radiation records for stated causes of certified deaths

Certified causes of death (ICD Nos.)	Totals (Nos.)	Exposed workers* (Nos.)	Cumulative radiation dose (centurads)	Exposed workers* (%)	Mean R dose (centurads)*	
					(A)	(B)
Non-cancers:						
Infective (000-136)	29	16	1258	55.2	79	43
Benign neoplasms (210-219)	10	4	155	40.0	39	13
Endocr. & blood (240-299)	54	34	5199	51.0	153	96
C.N.S. (290-389)**	56	20	1389	55.6	169	94
C.V.S. (390-458)**	1837	1149	191,987	62.3	167	105
Respiratory (460-519)	194	108	14,330	55.7	137	74
Digestive (520-577)	139	53	15,807	59.7	190	114
Accidents (800-999)	450	271	42,244	60.2	156	94
Residue (580-799)	101	57	5592	56.4	151	85
RES neoplasms:						
Lymphomas (200-2)	34	28	4049	82.4	145	119
Lymphatic Lk (204)	1	2	57	56.7	29	19
Myelomas (203)	11	8	8510	72.7	1066	775
Myeloid leukemias (205)	11	6	1337	54.5	223	122
Residue (206-9)	5	3	58	60.0	19	12
Solid tumors:						
Mouth & pharynx (140-9)	24	14	2134	58.3	152	89
Stomach (151)	38	26	2227	58.4	56	60
Large intestine (153)	61	46	8222	75.7	171	122
Rectum (154)	19	16	1887	84.2	118	99
Other intestinal (150; 152)	18	10	581	55.6	58	32
Liver & gall bl. (155-6)	18	10	157	55.6	56	31
Pancreas (157)	49	31	12,377	63.3	199	253
Lung (162-3)	192	130	52,384	67.7	249	169
Prostate (185)	41	21	817	48.8	47	42
Kidney (189)	21	14	1915	56.7	281	187
Other G.U. (180-4)	15	10	122	66.7	123	82
Brain (191)	18	11	1467	61.1	161	220
Residue	90	54	7313	60.0	135	81
Totals:						
Non-cancers	2850	1742	2829,61	61.1	162	98
RES neoplasms	64	47	140,11	71.4	299	219
Solid tumors	606	395	786,26	65.2	99	150

*See footnotes to Table 2.

**C.N.S. = Neurological diseases.

C.V.S. = Cardiovascular diseases.

eases with high radiation doses were cancers of the pancreas (253), brain (220), kidney (187), lung (169) and large intestine (135).

In Table 4, the various neoplasms are listed in accordance with the all-worker dose and the number of cases in each diagnostic category is compared with an expected number which shows how the same diseases were distributed among the 1960 cancer deaths of U.S. white males (Bu71). For 8 neoplasms, the radiation dose was higher than the level for all certified deaths (107 centirads) and for 9 the dose was below this level. For the group with above average doses, the observed and expected numbers were 397 and 318 (ratio 1.25), and for the other group they were 273 and 352 (ratio 0.78).

Controlled analyses

The preliminary findings were compatible with a causal association between the radiation exposures and some of the cancer deaths. Therefore comparisons between the

two main groups of certified deaths (cancers and non-cancers) were continued in analyses which controlled separately for five possible sources of false impressions, namely:

- (1) Calendar year of the exposures.
- (2) Employment year of the exposures.
- (3) Pre-death year of the exposures.
- (4) Exposure age or age at the end of each badge-reading year.
- (5) Death age.

Calendar years (Table 5 and Fig. 1)

The calendar year classification showed that: (i) the proportion of exposed workers was higher during the first half of the study period than the second half, but the opposite was true of the annual radiation doses of exposed workers (AREW doses in centirads) and (ii) only during the high dose period were differences between cancers and non-cancers at all pronounced.

Each year the proportion of exposed workers remained a fraction higher for cancers than non-cancers (Fig. 1). However, from

Table 4. Observed and expected numbers of specific neoplasms listed according to mean cumulative dose of external radiation.

No. Neoplasms*	Mean cumulative radiation dose (centirads)	No. of deaths†		Ratio (Obs-Exp)
		Observed	Expected	
1. Myelomas	77.1	11	7.6	1.45
2. Pancreas	15.1	29	17.3	1.31
3. Brain	220.1	18	17.3	1.04
4. Kidney	187.2	21	15.0	1.40
5. Lung	169.6	192	144.4	1.33
6. Large intestine	11.1	51	61.1	0.87
7. Myeloid leukemia	122.2	11	8.8	1.25
8. Lymphomas	119.2	34	27.7	1.23
9. Rectum	9.9	19	29.6	0.64
10. Mouth & pharynx	4.9	24	21.9	1.10
11. Other genito-urinary	8.2	15	19.4	0.77
12. Stomach	4.9	18	18.7	0.96
13. Prostate	4.2	43	67.5	0.64
14. Other intestinal	1.2	18	18.0	1.00
15. Liver & gall bladder	3.1	18	12.5	1.44
16. Lymphatic leukemia	1.9	3	9.4	0.32
17. Other RES neoplasms	1.2	5	20.3	0.25
18. Other solid	8.1	90	83.0	0.59
No. 1-8	188.8	297	118.2	1.25
9-18	6.5	273	151.8	0.78
All cancers	188.8	670	670.0	1.00

*See Table 3.

†Observed see Table 3; expected see 1960 cancer deaths of white U.S. males in NCI Monograph 11.

1 = Above the mean value for all certified deaths (1971), see Table 2.

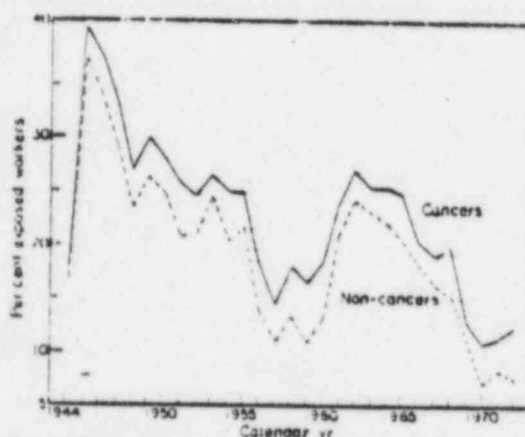


FIG. 1. Per cent of exposed workers by calendar years cancer and non-cancer deaths of males.

1944 to 1957 (when AREW doses averaged 14.9 for cancers and 18.7 for non-cancers), there were equal numbers of years with above average doses for the two causes of death (high risk years); and from 1958 to 1972 (when AREW doses averaged 51.3 for cancers and 47.7 for non-cancers), there were more high risk years for cancers (11) than non-cancers (4) (Table 5).

Employment years (Table 6 and Fig. 2)

The employment year classification showed that: (i) the proportion of exposed workers

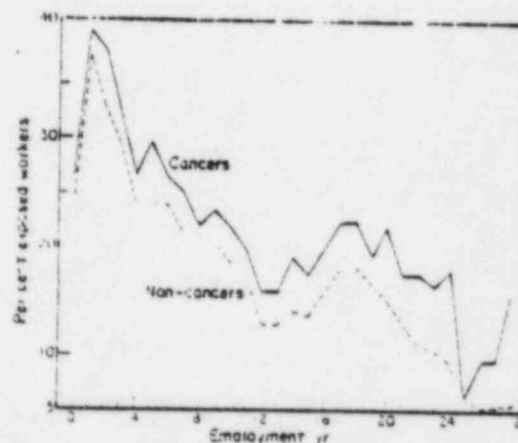


FIG. 2. Per cent of exposed workers by employment years cancer and non-cancer deaths of males.

decreased with progressive lengthening of the interval between hire and exposure but the trend for AREW doses was in the opposite direction, and (ii) only during the high dose period were differences between cancers and non-cancers at all pronounced.

Each year the proportion of exposed workers remained a fraction higher for cancers than non-cancers (Fig. 2). However, when intervals from hire to exposure were shorter than 10 yr (and AREW doses averaged 21.5 for cancers and 21.1 for non-cancers), there

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Table 5. Mean annual radiation doses for exposed workers (cancer and non-cancer) (calendar years)

Calendar years	Exposed workers*		Radiation doses*		High risk years†	
	Cancers	Non-cancers	Cancers	Non-cancers	Cancers	Non-cancers
1944-45	237	901	26.5	26.0	2	—
1946-47	333	1258	11.9	13.2	—	—
1948-49	325	1169	12.5	8.4	1	1
1950-51	311	1101	12.4	12.8	—	2
1952-53	302	1119	—	20.2	—	—
1954-55	288	1007	23.4	21.1	—	—
1956-57	185	748	40.8	41.6	—	2
1958-59	183	724	53.6	51.7	—	—
1960-61	203	661	53.0	47.8	—	—
1962-63	227	799	47.4	43.2	—	—
1964-65	184	799	63.1	59.6	1	1
1966-67	120	799	44.1	46.6	1	1
1968-69	75	213	39.0	43.1	1	1
1970-72	72	76	42.8	19.4	2	1
Total	3094	10,384	30.6	27.8	18	11
Under 10 yr	1981	7133	19.9	18.7	7	7
Over 10 yr	1024	3252	51.3	47.7	11	4

*Number of workers with positive badge readings in each year.

†Mean annual radiation doses of exposed workers in centirads (AREW doses).

‡Number of years with higher doses for cancers than non-cancers or vice versa.

Note: There are small differences in the totals for Tables 3-4 which are due to the time units being measured to the nearest whole year.

Table 6. Mean annual radiation doses for exposed workers (cancer and non-cancer) (employment years)

Employed years	Exposed workers*		Radiation doses*		High risk years†	
	Cancers	Non-cancers	Cancers	Non-cancers	Cancers	Non-cancers
0-1	461	1756	21.8	23.1	—	—
2-3	424	1747	15.6	16.8	—	—
4-5	368	1294	18.3	17.2	—	—
6-7	371	1162	24.9	22.7	1	1
8-9	273	985	34.4	28.1	—	—
10-11	232	811	41.9	33.1	—	—
12-13	166	528	47.5	33.1	1	1
14-15	171	521	54.4	44.4	2	—
16-17	171	541	47.2	45.6	2	—
18-19	144	461	46.5	41.1	1	1
20-21	103	394	53.3	42.4	1	1
22-23	73	160	40.3	32.0	1	—
24-25	35	74	37.0	31.7	—	—
26-29	14	—	44.4	26.1	—	—
Total	3087	10,386	30.1	27.8	18	11
Under 10 yr	1970	6974	21.5	21.1	1	2
Over 10 yr	1107	3412	48.1	41.7	17	9

*See footnotes to Table 5.

were equal numbers of high risk years for the two causes of death. When intervals from hire to exposure were longer than 10 yr (and AREW doses averaged 46.3 for cancers and 41.7 for non-cancers), there were twice as many high risk years for cancers (13) as non-cancers (6).

Pre-death years (Table 7 and Fig. 3)

The pre-death year classification showed that: (i) the proportion of exposed workers decreased with progressive shortening of the pre-death period, but the trend for AREW doses was in the opposite direction and (ii) in the middle of the time scale, the radiation doses were consistently higher for cancers than non-cancers but towards the beginning and end of the range, the radiation doses

were frequently lower for cancers than non-cancers.

Each year the proportion of exposed workers remained a fraction higher for cancers than non-cancers (Fig. 3). However, when the interval between exposure and death was less than 8 or more than 20 yr (and AREW doses averaged 30.1 for cancers and 30.6 for non-cancers), there were over twice as many high risk years for non-cancers (12) as cancers (5). Between these extremes (when AREW doses averaged 31.0 for cancers and 25.1 for non-cancers), there was an unbroken series of high risk years for cancers (Table 7).

Exposure age (Table 8 and Fig. 4)

The exposure age analysis, which was restricted to men between 20 and 65 yr and to

Table 7. Mean annual radiation doses for exposed workers (cancers and non-cancers).

Pre-death years†	Exposed workers*		Radiation doses*		High risk years*	
	Cancers	Non-cancers	Cancers	Non-cancers	Cancers	Non-cancers
0-1	156	675	29.6	28.8	1	1
2-3	241	954	41.8	19.4	2	—
4-5	271	974	39.8	42.4	1	1
6-7	305	1015	17.1	39.1	—	2
8-9	110	1022	36.8	12.7	—	—
10-11	281	911	13.4	28.2	—	—
12-13	242	868	18.1	18.4	—	—
14-15	247	663	39.0	—	—	—
16-17	239	861	27.1	21.3	—	—
18-19	210	724	21.4	18.2	—	—
20-21	186	592	12.9	14.2	—	—
22-23	143	481	14.9	15.4	—	—
24-25	111	353	18.2	16.9	1	1
26-28	56	172	15.7	23.5	—	3
Total	3012	10,388	30.6	27.8	17	12
5-19 yr	1541	5271	31.0	24.1	12	—
Other yr	1471	5117	30.1	30.6	5	12

*See footnotes to Table 5.

†Interval between exposure and death (in yr).

Table 8. Mean annual radiation doses for exposed workers (cancers and non-cancers).

Exposure age in years†	Exposed workers*		Radiation doses*		High risk years*	
	Cancers	Non-cancers	Cancers	Non-cancers	Cancers	Non-cancers
20-22	11	22	25.2	13.8	2	1
23-25	21	99	11.4	21.4	1	—
26-28	55	172	25.9	25.9	1	—
29-31	93	272	22.3	10.0	—	1
32-34	111	419	14.4	10.9	—	1
35-37	150	556	19.7	23.8	1	2
38-40	160	609	20.9	21.3	2	1
41-43	224	665	25.8	24.9	2	1
44-46	233	748	28.9	26.4	2	1
47-49	253	777	37.6	11.9	3	—
50-52	281	876	33.7	30.7	3	—
53-55	265	950	34.3	26.0	3	—
56-58	235	863	30.7	25.3	2	1
59-61	196	708	28.4	24.5	3	—
62-64	160	527	34.5	24.2	3	—
Total	2448	8219	28.9	25.5	28	17
Under 35 yr	291	964	18.4	28.4	4	11
35-55 yr	1566	5137	30.0	25.8	16	4
Over 55 yr	191	2098	31.0	24.1	4	1

*See footnotes to Table 5.

†Excluding exposures before 20 yr of age, or after 65 yr, or within 5 yr of death.

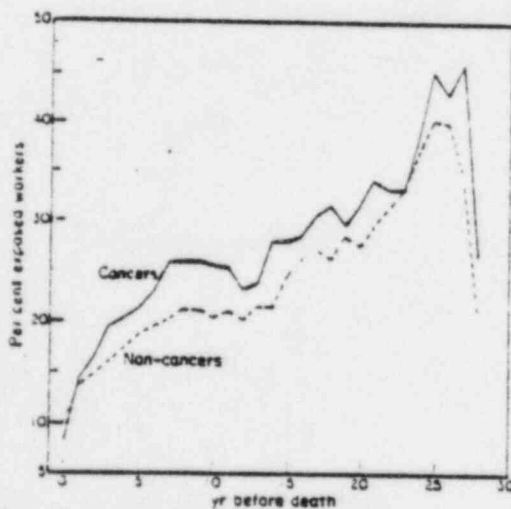


FIG. 3. Per cent of exposed workers by years before death cancer and non-cancers deaths of males.

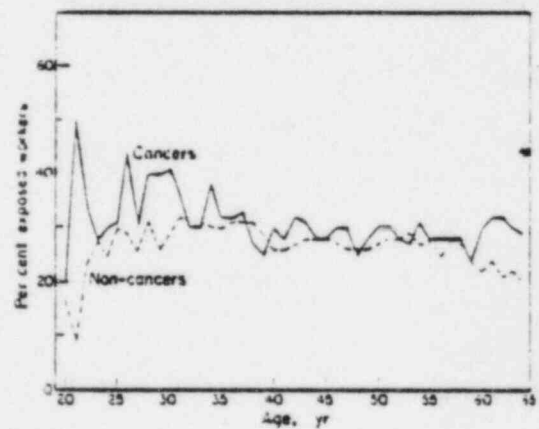


FIG. 4. Per cent of exposed workers by exposure age (excluding exposures within 5 yr of death).

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exposures more than 5 yr before death, showed that: (i) the proportion of exposed workers was virtually independent of age (Fig. 4) and (ii) only after 40 yr were the radiation doses noticeably higher for cancers than non-cancers.

From 20 to 35 yr of age, there were more than twice as many high risk years for non-cancers (11) as cancers (4) and AREW doses were also higher for non-cancers (23.4) than cancers (18.4). However, for the group with initially high radiation doses there was a decrease with age (non-cancers) and for the group with initially low doses there was an increase with age (cancers). Therefore, by 40 yr the men who eventually developed fatal cancers were recording higher doses than the men with other causes of death. Thus, from 35 to 55 yr there were 16 high risk years for cancers and 5 for non-cancers, and from 56 to 65 yr the corresponding numbers were 3 and 1. In the younger of these two age groups the AREW doses were 30.0 for cancers and 26.8 for non-cancers, and in the older age group they were 31.0 and 24.3.

Age at death

With recurrent events as controlling factors (e.g. exposure years and exposure ages), there was no way whereby men who re-

mained in the monitored population for short periods of time could contribute as much to the final results as men who remained for long periods and no way whereby the findings for each subgroup could be totally independent. However, with age at death as the controlling factor, there was no difficulty in obtaining strictly independent findings for any number of subgroups. Therefore, the analysis proceeded along new lines and was directed towards obtaining a stringent test of the null hypothesis of no correlation between the radiation dose and the proportion of cancer deaths after controlling for age at death (see Spearman's rank correlation coefficients in Table 11).

The basic data for this test were: (i) age at death for subgroups defined by cause of death (Table 9); (ii) radiation doses for subgroups defined by age and cause of death (Table 10); and (iii) cancers as a proportion of all certified deaths in groups defined by age at death and radiation dose (Table 11). Thus Table 9 shows that: (i) although accidents were often causes of early death, men who eventually developed malignant diseases did not have appreciably longer life spans than men with other causes of death and (ii) between two thirds and three quarters of all the deaths occurred between 50 and 80 yr of age.

Table 9. Age distributions of cancer and non-cancer deaths: stated causes of death (and I.C.D. Nos.)

Age at death in years	Cardiovascular (390-415)	Respiratory: digestive (460-577)	Accidents (800-999)	Other non-malignant	All non-cancers	Cancers (140-239)	All causes
	%	%	%	%	%	%	%
Under 40	2.6	5.1	20.0	12.5	4.0	1.7	7.2
40-49	11.9	12.3	27.3	11.7	14.4	12.8	14.1
50-59	25.3	20.7	21.6	27.0	24.4	27.9	25.0
60-69	29.0	32.5	16.2	25.0	26.9	35.7	28.6
70-79	23.4	24.9	4.2	19.9	22.1	17.3	19.6
80+	7.8	4.5	0.7		6.2	2.5	5.3
Totals:							
Nos.	1837	133			2890	670	3520
%	52.2	9.5			81.0	19.0	100.0

Table 10. Mean cumulative radiation doses for stated causes of death and stated age at death

Age at death in years	Mean cumulative doses (R) in centirads						Radiation dose Ratios*		
	Cardiovascular (390-415)	Accidents (800-999)	Other non-cancers	Solid tumors (140-239)	RES neoplasms (200-239)	All cancers (140-239)	All non-cancers (1001-136; 210-999)	All deaths (1001-999)	C: Non-Ca RES: Solid
Under 40	59	47	76	55	40	52	76	55	0.91
40-49	94	114	104	100	67	93	102	100	0.91
50-59	157	133	64	187	129	201	136	150	1.48
60-69	172	116	125	145	62	140	129	132	1.09
70-79	46	24	72	60	787	101	11	60	7.92
80+	39	6	13	17	97	22	34	33	0.63
All ages	105	94	58	130	219	138	99	107	1.39

*C: Cancers; Non-Ca: Non-cancers; RES: RES Neoplasms; Solid: Solid tumors.

Table 11. Test for correlation between the percentage of cancer deaths and the cumulative radiation dose after standardization for age at death.

Mean cumulative radiation dose for all workers (in centirads)												
Age at death in years	Zero		1-19		20-99		100-499		500+		Total	
	Nos.	% Cancers	Nos.	% Cancers	Nos.	% Cancers	Nos.	% Cancers	Nos.	% Cancers	Nos.	% Cancers
Under 40	106	9.1	54	10.9	58	8.6	24	8.1	9	22.2	254	9.8
40-49	185	11.0	82	14.9	117	21.9	74	21.0	17	11.8	495	17.1
50-59	311	19.1	137	16.1	200	24.5	155	21.9	58	11.0	861	21.2
60-69	160	22.2	162	21.6	248	26.6	184	24.0	51	22.6	1005	21.7
70+	152	11.6	189	11.6	241	17.5	74	18.9	17	29.4	583	15.1
Total	1316	16.9	625	14.7	894	21.7	511	22.0	154	21.1	1920	19.0

Ranking Nos. for cancer proportions						Value of t (two)
Under 40	3	4	2	1	5	0.1
40-49	2	3	4	5	1	0.0
50-59	1	1	4	3	5	0.8
60-69	2	1	5	4	3	0.5
70+	2	1	3	4	5	0.9
Means	2.2	2.0	3.6	2.4	3.8	$0.46 \pm 0.22^*$

*This value is statistically significant at the 1% level.

†Value of Spearman's rank correlation coefficient between the percentage of cancer deaths and the radiation dose level.

Table 10 shows that division of men who lived for more than 50 and less than 80 yr into three age groups still left each subgroup of cancers with a higher radiation dose than the corresponding group of non-cancers and still left each subgroup of RES neoplasms with a higher dose than the corresponding group of solid tumors.

Finally, Table 11 includes the results of the correlation test and shows that division of the certified deaths into 5 age groups and 5 dose levels still left the highest radiation dose groups (over 500 centirads) with the highest proportion of cancer deaths. As a result of this consistent trend, there was a firm rejection of the null hypothesis by the statistical test. Thus in three age groups Spearman's rank correlation coefficient (between the proportion of cancer deaths and the radiation dose level) had a value equal to or greater than 0.5 and the mean coefficient over age had a value of 0.46 ± 0.22 . This is a statistically significant result since the coefficient for (n) observations has a variance of $(1/n - 1)$. Therefore, for a mean coefficient from 5 age groups, each with 5 dose levels, the variance is $(1/20)$ implying a standard error of 0.22.

SPECIAL TESTS OF THE RADIATION ASSOCIATIONS

The impression of a causal association between the exposures to external radiation and the cancer deaths was strengthened rather than weakened by the controlled analyses. Therefore it only remained to test the safety

threshold hypothesis (i.e. the theory that below the maximal permissible dose radiation has no carcinogenic properties) against the only logical alternative, namely, that with any exposure to ionizing radiation there is a cancer hazard which is proportional to the dose.

The choice of statistical test was influenced by the following assumptions: first, the most plausible alternative to the safety threshold hypothesis is a dose-response relationship that is either linear or at least monotonically increasing. Secondly, in Hanford data the stimulus or radiation dose, is continuously variable and the response or development of a fatal cancer, is a binary one (or an all-or-nothing response). Therefore, the most appropriate statistical model was the logistic or log-linear one which states that the logarithm of the odds-ratio of a response is linearly related to the stimulus over a suitable range of intensity (Co70).

Under the assumptions of this model the most powerful test of the null hypothesis was the permutation test of the difference between the mean cumulative radiation dose for men developing fatal cancers and the mean for all certified deaths. Therefore the test could be carried out in three stages:

(1) Test for cancers with definite radiation associations

Let N = size of whole population;

n = size of subpopulation of cancer deaths;

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R = average value of radiation dose for the whole population;

r = average value of radiation dose for the subpopulation cancer deaths;

S = average value of the squared dose for the whole population.

Then, the estimate of variance in whole population (V) = $(N/(N-1))(S - R^2)$ and $t = [(r - R)/\sqrt{V[(1/n) - (1/N)]}]$ where this statistic is approximately distributed as a t statistic with $(N-1)$ degrees of freedom for testing the null hypothesis (see Appendix).

(2) Quantitative estimates of radiation sensitivity (doubling dose)

Should the null hypothesis of no associations between the radiation doses and the cancer deaths be rejected by the first test (as a result of t exceeding a critical value of approx +2.0), a quantitative estimate of radiation sensitivity would be required and could be obtained in the following way:

Let D = the radiation dose which is just sufficient to double the normal risk of a cancer death (doubling dose). Then r will have an expected value of $(R + S/D)/(1 + R/D)$ (see Appendix).

Therefore, by solving this equation with observed values of r , one could obtain for any cancer with definite radiation associations an estimate of the doubling dose (D).

(3) Quantitative estimates of radiosensitivity in relation to pre-death years and ages

There is no reason why the above formulas should not be used in relation to radiation doses for stated time periods or ages; and there are strong grounds for believing that: (i) tissue specific cancers have characteristic, albeit long, intervals between initiation and death, and (ii) sensitivity to the cancer-induction effects of any mutagen is strongly age dependent. Therefore, in Hanford data, the search for radiosensitive cancers can be directed towards discovering which of several pre-death years or ages (in relation to tissue specific cancers) are associated with statistically significant differences between observed and expected radiation doses (or t values equal to or greater than 2.0).

By taking this approach the identification of cancers with definite radiation associations (radiosensitive cancers) can be combined with estimates of: (i) the relative sensitivity of different tissues (as measured by doubling doses for the relevant cancers); (ii) characteristic intervals between initiation dates and death (or the pre-death years showing the maximum contrast between observed and expected radiation doses); and (iii) the ages of maximal and minimal sensitivity to the cancer-induction effects of ionizing radiation (or the ages showing maximum and minimum differences between observed and expected doses). Therefore, the search for radiosensitive cancers (and other diseases with radiation associations) was pursued, first in relation to pre-death periods (Tables 12-15), then in relation to age (Table 16).

Table 12. Cumulative radiation doses for stated pre-death periods

Pre-death years*	Non-cancers			
	All non-cancer deaths	Cardiovascular diseases	Accidents	Other non-cancers
28	1.2	1.4	0.0	1.2
26	15.8	15.3	7.1	19.2
24	19.4	17.4	10.9	28.2
22	22.4	20.6	18.3	29.4
20	24.1	22.7	20.0	30.7
18	29.0	27.9	23.5	35.1
16	35.2	24.8	32.3	38.1
14	41.3	41.3	37.1	43.2
12	48.2	48.9	44.7	47.9
10	56.6	57.2	54.8	55.5
8	67.7	68.0	66.4	66.6
6	80.0	81.6	76.4	76.7
4	92.6	94.6	91.0	86.6
2	100.9	104.0	100.5	93.7
0	106.0	110.9	101.4	91.2
Number of deaths	2850	1817	250	561

*See footnote to Table 7.

†Standard values, see later tables.

Table 13. Cumulative radiation doses for stated pre-death periods

Pre-death years†	Cancers		
	All cancers	RES neoplasms	Solid tumors
28	1.9	0.7	2.2
26	12.5	24.6	11.5
24	18.9	14.3	19.3
22	22.2	23.1	22.7
20	25.2	23.0	24.5
18	24.0	25.2	32.3
16	44.3	83.0†	40.6
14	54.3*	105.2*	49.1
12	65.0*	126.0†	58.8
10	76.7*	154.0*	69.1
8	90.4*	175.4†	81.7
6	104.2	194.5*	95.0
4	116.6	200.9*	107.7
2	129.0	216.2*	119.6
0	134.4	223.1*	125.0
Number of deaths	670	54	406

Figures in italics significantly differ from the standard values in Table 12.

Levels of significance:

* $P < 0.05$.

† $P < 0.01$.

‡ $P < 0.001$.

§See footnote to Table 7.

Table 14. Cumulative radiation doses for stated pre-death periods

Pre-death years*	Mean cumulative radiative radiation doses in centirads†	
	Bone marrow (203, 205)	Other sites (200-2, 204, 206-9)
28	1.0	0.0
26	1.0	17.0
24	4.2	26.4
22	19.0	26.7
20	37.6	29.1
18	53.1	31.1
16	121.64	30.5
14	190.52	34.0
12	221.12	40.7
10	170.27	63.4
8	401.42	62.3
6	166.92	65.0
4	138.51	72.9
2	466.12	90.3
0	466.22	100.1
Number of deaths	22	42

*See footnote to Table 7.

†See footnotes to Tables 12 and 13.

‡See significance levels in Table 13.

Table 15. Cumulative radiation doses for stated pre-death periods

Pre-death years*	Mean cumulative radiation doses in centirads†				
	Large intestine (153)	Pancreas (157)	Lung (162)	Kidney (189)	Other solid tumors (191)
28	0.0	12.0	4.0	1.0	0.0
26	8.7	12.0	15.0	2.0	40.0
24	19.1	25.6	18.4	1.3	39.2
22	27.9	33.6	23.3	2.6	36.5
20	27.7	35.9	25.0	3.0	46.9
18	45.2	35.9	35.3	13.7	59.3
16	54.7	48.2	49.7	24.9	70.7
14	63.1	65.5	61.82	35.9	70.8
12	74.3	90.1	72.12	74.8	93.7
10	92.3	119.92	86.9	88.9	96.1
8	106.5	142.72	103.4	96.1	124.8
6	125.1	173.92	117.1	123.6	158.4
4	129.6	214.52	132.6	159.9	193.9
2	137.0	247.02	147.5	172.7	226.8
0	141.8	289.02	153.4	171.3	233.4
Number of deaths	91	49	192	21	18

*See footnote to Table 7.

†See footnotes to Tables 12 and 13.

‡See significance levels in Table 13.

radiation was 48.2 centirads for all non-cancer deaths (standard or control group). For cardiovascular deaths, the corresponding dose was 48.9 (case: control ratio 1.01), for fatal accidents 44.3 (ratio 0.92) and other non-cancer deaths 47.9 (ratio 0.99). There were, however, positive findings for all cancers and for some of the neoplasms with exceptionally high radiation doses.

Thus for all cancers (ICD Nos. 140-209), there were positive findings (i.e. significant differences between observed and expected doses of external radiation) over a period of nearly 10 yr, namely, 7-15 yr before death; and for RES neoplasms there were positive findings over a period of nearly 20 yr, namely, from 0 to 18 yr before death (Table 13). For bone marrow cancers there were exceptionally strongly positive findings for the period 0-17 yr before death (Table 14), and for 2 of the 5 solid tumors with high radiation doses some of the differences between observed and expected doses were statistically significant. Thus, for pancreatic tumors, there were positive findings for the period 0-11 yr before death, and for lung cancers there were similar findings for the period 11-14 yr before death (Table 15).

For all cancers the critical interval between exposure and death—or the period of maximum case:control contrast as indicated by the *t* value—was 12 yr (case:control ratio 1.35 and *t* = 2.4). For RES neoplasms the

Table 16. Estimated doubling doses for critical pre-death years*

Radio-sensitive cancers	Critical pre-death periods		Proportion of all deaths	
	Years before death	Estimated doubling dose in rads	Observed %	Expected† %
Bone marrow	9	0.8	0.62	0.30
Pancreas	0	7.4	1.39	0.85
Lung	14	6.1	5.45	3.26
All RES neoplasms	11	2.1	1.82	1.15
All cancers	13	12.2	19.02	15.15

*The years before death which showed the maximum contrast compared with the standard group of all non-cancer deaths (see Tables 13-15).

†See U.S. Vital Statistics for deaths of white males (1960).

RADIOSENSITIVITY AND CRITICAL PRE-DEATH PERIODS

Division of the non-cancer deaths into several subgroups failed to produce any evidence of radiation associations in either the pre-death period or the age analysis (Table 12). For example, 12 yr before death the mean cumulative radiation dose for external

corresponding period was 11 yr (ratio 2.71 and *t* = 3.7), and for bone marrow cancers 9 yr (ratio 5.86 and *t* = 6.1). For lung cancers the critical interval was 14 yr (case: control ratio 1.50 and *t* = 2.0), and for pancreatic tumors under 1 yr (ratio 1.50 and *t* = 3.0).

For other cancers with high radiation doses, there was less certain evidence of a

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causal association. However, for brain tumors there was a period of 3 yr when observed doses were twice as high as expected doses and t values were greater than +1.5 (i.e. 17–19 yr before death), and for cancers of the large intestine the observed dose 18 yr before death was 58% above the expected dose ($t = 1.3$). Finally, there were two findings which suggested that, given a longer period of records, there might have been a wider range of radiosensitive cancers. As a result of the study being restricted to men who died before 1973, there were very few records of radiation exposures 26 yr before the final (death) year. However, in this rare group 3 cases of brain tumors recorded a radiation dose which was almost 3 times as high as the expected dose ($t = 1.3$), and 2 cases of lymphosarcomas recorded a radiation dose nearly 4 times as high as the expected dose ($t = 1.8$).

DOUBLING DOSES FOR RADIOSENSITIVE CANCERS

From the records for critical pre-death periods, estimates were made of the amount of radiation which would be needed to double the normal risk of developing any of the cancers with definite radiation associations (see doubling doses in Table 16). According to these estimates, 12.2 rads would be needed to double the normal risk of dying from any form of cancer. For cancers of pancreas or lung, the doses would be somewhat lower (7.4 or 6.1 rads) and for RES neoplasms or bone marrow cancers, they would be even lower (2.5 or 0.8 rads).

These suggested doses are so much lower than the estimates based on atom bomb survivors (Co70) that they are unlikely to go unchallenged. Therefore, we have included in Table 16 the proportions of certified deaths caused by the cancers with definite radiation associations, and the proportions of these cancers expected on the basis of all certified deaths of U.S. white males in 1960 (VSUS60). From these observed and expected proportions, standardized mortality ratios (SMRs) were obtained in the usual way and compared with the results of solving the following equation with observed values of D and R :

$$EMR = 100 \times \left(1 + \frac{R}{D}\right)$$

where EMR = excess mortality from a radiosensitive cancer relative to a standard risk of 100 for all certified deaths.

According to the SMRs, the risks for Hanford workers were increased by 26% for all cancers, by 58% for RES neoplasms, and by 107% for bone marrow cancers (Table 17) and, according to the EMRs, the risks were increased by 4% for all cancers, by 21% for RES neoplasms, and by 79% for bone marrow cancers. Since the more conservative estimates were based on the doubling doses in Table 16, we are faced with two alternatives: either the actual doubling doses were even smaller than the estimates in this table; or, more likely, external radiation was not the only source of trouble for Hanford workers. In other words our analysis of the records relating to external radiation has shown the need for a similar analysis of the records relating to internal radiation.

Table 17. Excess cancer mortality of Hanford workers: Comparisons between conventional SMRs and estimates based on radiation doubling doses (EMRs)

Cancers with definite Radiation Associations	SMRs*	EMRs†
Bone marrow	207	179
Pancreas	163	114
Lung	167	107
All RES neoplasms	158	121
All cancers	126	104

*See Table 16. (Standard = 100)

†See text

INTERNAL RADIATION

The data relating to depositions of radioactive substances are not yet in a form suitable for testing the null hypothesis of no trouble from this potential source of radiation-induced cancers. It is, however, possible to distinguish between Hanford workers with and without positive urine analyses and thus discover whether the positive findings in Tables 13–15 were due solely to workers in high risk or doubly monitored occupations or partly to men in low risk occupations or ones which were only monitored for external radiation.

Division of the certified deaths into two

groups (with and without records of internal radiation) showed that: (i) the proportion of cancer deaths was higher in the positive group (22%) than in the negative group (18%) (Table 18) and (ii) the all-worker dose for external radiation was much higher in the positive group (357 centirads) than in the negative group (23). However, even in the low dose group the external radiation dose was higher for cancers (29) than non-cancers (21), and in both groups a pre-death period analysis produced positive findings in relation to RES neoplasms (Tables 18 and 19).

In the high dose group there were 17 RES neoplasms and 7 bone marrow cancers, and in the low dose group there were 47 RES neoplasms and 15 bone marrow cancers. In the first of these two groups there were positive findings in relation to these neoplasms for 8 of the 29 pre-death years (Table 18), and in the second group there were positive findings for 5 of these years (Table 19). Also,

Table 18. External radiation doses of workers with positive and negative records of internal radiation.

Internal radiation*	Diagnostic categories	Cases		External radiation in centirads	
		Nos.	%	Total	Mezz
Positive	Cancers	194	21.9	79,004	477
	Non-cancers	691	78.1	256,940	143
	Total	885	100.0	335,944	157
Negative	Cancers	476	18.1	13,653	29
	Non-cancers	2159	81.9	46,021	21
	Total	2635	100.0	59,674	23
Both	Cancers	670	19.0	92,657	138
	Non-cancers	2850	81.0	282,961	159
	Total	3520	100.0	375,618	197

*One or more depositions of radioactive substances.

Table 19. Cumulative doses of external radiation for stated pre-death years.

Pre-death years	Men with positive urine analyses			
	Non-cancers	RES neoplasms	Lung and pancreas	Other solid tumors
28	13.7	—	27.6	4.9
26	21.1	17.0	15.5	11.8
24	28.4	26.2	29.2	26.2
22	36.7	33.2	49.1	31.5
20	47.2	49.2	49.9	37.0
18	59.4	102.1*	78.6	52.3
16	76.1	201.2*	114.4	73.7
14	99.9	241.3*	130.2	92.1
12	127.6	257.1*	172.3	135.0
10	158.4	309.1	224.8	174.4
8	196.2	312.5	259.3	212.1
6	245.2	376.8	323.8	260.7
4	292.1	396.2	379.1	307.5
2	324.6	407.6	409.5	335.9
0	380.5	418.7	460.4	351.1
Number of deaths	691	17	56	91

*See significance levels in Table 13.

Table 20. Cumulative doses of external radiation for stated pre-death years.

Pre-death years	Men with no record of internal radiation			
	Non-cancers	RES neoplasms	Lung and pancreas	Other solid tumors
28	8	0.5	20.5	24.5
26	12.3	1.7	14.5	19.8
24	14.1	1.4	19.0	19.5
22	16.0	12.3	16.4	18.2
20	16.0	15.1	15.4	18.6
18	17.5	24.7	18.0	20.6
16	18.6	—	17.3	22.1
14	19.1	29.8	19.7	23.5
12	19.9	36.0*	—	25.2
10	22.0	42.0*	24.5	25.5
8	24.5	46.6*	29.2	27.2
6	27.1	46.3	30.9	28.2
4	29.5	46.4	34.6	30.1
2	31.8	49.9	34.7	32.5
0	40.1	51.7	36.2	39.7
Number of deaths	2159	47	155	274

*See significance levels in Table 13.

for the period associated with positive findings in both high and low dose groups (i.e. 12 yr before death), the estimated doubling doses were not significantly different for the two occupational groups.

AGE AND SENSITIVITY TO THE CANCER-INDUCTION EFFECTS OF RADIATION

The search for sensitive age groups utilized a single set of controls (all non-cancer deaths) and two sets of cases, viz RES neoplasms and solid tumors with high radiation doses (see pancreas, lung, brain, kidney and large intestine in Table 3).

Towards the beginning and end of the age range of external radiation records (which covered the period between 21 and 78 yr), there was virtually no data for the smaller case group (RES neoplasms), but between 30 and 70 yr of age the records for this group were strongly suggestive of an exponential increase in cancer sensitivity with advancing age. Thus, between 30 and 40 yr of age the observed doses were consistently lower than the expected doses. However, by 45 yr the observed doses were 15% higher than the standard dose; and by 50 yr they were 50% higher. These differences were not statistically significant, but by 55 yr there was a threefold difference between the observed and expected doses ($t = 2.5$), and by 70 yr a 14-fold difference ($t = 9.2$).

For the larger case group, there were positive findings at both ends of the age scale and a full period between 25 and 40 yr. Thus, in

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Table 21. Mean cumulative doses of external radiation by stated ages: Non-cancers, RES neoplasms and other selected cancers*

Age in years	Non-cancers		RES neoplasms		Other cancers*		No. of observations		
	R†	t‡	R	t	R	t	Non-cancers	RES Neoplasms	Other cancers
21	8	—	—	—	10	2.2	43	1	4
22	7	—	—	—	10	1.1	47	2	7
23	9	—	—	—	47	1.2	118	3	—
24	13	—	11	—	40	2.1	145	5	9
25	19	—	11	—	14	—	179	3	12
30	18	—	37	—	40	—	143	13	43
35	51	—	39	—	42	—	623	22	81
40	56	—	15	—	48	—	470	10	126
45	59	—	58	—	56	—	1093	14	175
50	73	—	116	—	105	2.0	1302	13	205
55	83	—	220	2.5	154	3.2	1397	10	213
60	80	—	211	2.0	130	2.1	1326	28	169
65	76	—	448	5.7	132	2.0	1072	19	112
70	48	—	701	9.2	90	—	716	8	59
72	41	—	731	9.9	89	—	665	8	42
73	41	—	14	—	98	1.7	587	5	40
74	18	—	14	—	100	1.5	521	5	29
75	37	—	35	—	48	1.1	454	4	24
76	36	—	45	—	48	2.8	386	3	28
77	35	—	45	—	115	1.3	338	3	16
78	35	—	45	—	112	1.0	275	3	15
79	37	—	58	—	119	2.5	221	2	10

*Cancers of the pancreas, lung, brain, kidney, and large intestine (see Table 3).

†R = Mean cumulative dose of external radiation.

‡t-values greater than the critical value of 2.0.

the youngest age group (21 yr with 6 cases and 43 controls), the observed and expected radiation doses were 39 and 8 ($t + 2.3$). In the next three age groups (22–24 yr), differences between observed and expected doses remained statistically significant, but from 25 to 45 yr there was nothing to choose between the observed and expected doses. Thereafter there was a steady increase in the cancer: non-cancer contrasts and by 60 yr the observed dose was 63% higher than the expected dose ($t + 2.1$). Finally, by 72 yr there was a twofold difference between the ob-

served and expected doses ($t + 2.7$), and by 78 yr a threefold difference ($t + 2.5$).

These findings were suggestive of greater sensitivity to the cancer-induction effects of radiation in early and late adult life than during the intervening period and this impression was re-enforced by doubling dose estimates for various ages (Table 22). These estimates were also based on RES neoplasms and solid tumors with high radiation doses, and they showed that (i) for men between 25 and 40 yr of age the exposures to external radiation probably had no delayed effects; (ii) for older men the doubling doses decreased rapidly with age; and (iii) for younger men the trend was probably in the opposite direction.

Table 22. Estimated doubling dose for stated ages: RES neoplasms and other selected cancers*

Age in years	Estimated doubling doses in rads	
	RES neoplasms	Other selected cancers†
21	—	0.2
22	—	0.1
23	—	0.2
24	—	0.4
25	—	1.5
30	—	49.2
35	—	—
40	10.0	76.4
45	13.0	17.9
50	5.2	14.6
55	6.8	18.1
60	1.2	14.8
65	0.1	16.0
70	0.1	8.7
72	—	2.5
73	—	1.1
74	—	1.1
75	—	1.2
76	—	0.8
77	—	0.9
78	—	0.9

*See Table 21 for the number of cases for each estimate.

†Cancers of the pancreas, lung, brain, kidney, and large intestine.

Females

Certified deaths of female workers totalled 412 and included 126 or 31% of cancers. The proportion of these workers with records of external radiation was small compared with the men and equally small for 127 women whose deaths were ascribed to cancers and 285 women with other causes of death (30%). Nevertheless, within the group of exposed workers the mean cumulative radiation dose was twice as high for cancers (133) as non-cancers (68).

Division of the cancer and non-cancer deaths of females into 4 age groups (Table 23)

Table 23. Cancer and non-cancer deaths of females by age and radiation dose.

Age at death	Radiation dose levels (centirads)	No. of deaths		%*	Cancers Rank	Radiation doses in centirads			
		(N)	(C)			Totals (N)	(C)	Means for exposed workers (N)	(C)
20-49	0	71	35	13.0	(2)				
	1-	24	11	31.4	(1)				
	50-	4	3	42.9	(4)				
	100+	2	1	33.3	(3)				
	Σ	101	50	33.1		0.6	1071	564	33
50-59	0	31	30	49.2	(3)				
	1-	10	5	33.3	(2)				
	50-	6	2	25.0	(1)				
	100+	3	4	57.1	(4)				
	Σ	50	41	45.1		0.2	1190	2172	63
60-69	0	46	13	22.0	(2)				
	1-	9	1	10.0	(1)				
	50-	3	2	28.6	(3)				
	100+	6	3	33.3	(4)				
	Σ	66	19	22.4		0.8	2451	1372	123
70+	0	52	11	17.5	(2)				
	1-	11	—	3.0	(1)				
	50-	4	4	50.0	(3)				
	100+	1	—	—	(4)				
	Σ	68	17	20.0		0.8	1085	927	56
All ages	0	200	89	30.8	(2.25)				
	1-	54	17	23.9	(1.25)				
	50-	19	11	16.7	(2.75)				
	100+	12	10	45.3	(3.75)				
	Σ	285	127	30.8		0.608 0.29	5797	5035	46

*% of all certified deaths.

†See Table 11.

N = Non-cancers

C = Cancers

‡This is a significant finding at the 5% level.

showed that: (i) radiation dose levels were always higher for cancers than non-cancers; (ii) cancer: non-cancer contrasts were greater for deaths after 50 yr of age than for earlier deaths; and (iii) in three age groups the proportion of cancer deaths was highest for the top level of radiation dose (over 100 centirads).

Finally, despite the small numbers of female workers with records of external radiation, the null hypothesis of no correlation between the radiation dose and the proportion of cancer deaths after controlling for age was rejected by a correlation test. According to this test, 3 of 4 Spearman's rank correlation coefficients (between proportions of cancer deaths and radiation dose levels) were equal to or greater than 0.6 and the mean coefficient over age had a value of 0.60 ± 0.29 (which is significant at the 5% level).

Estimates of the number of cancer deaths attributable to external radiation

In the final stages of the analysis, the best estimates of risk were used to discover how many of the cancers with records of external

Table 24. Estimated frequency of radiation-induced cancers among certified deaths of Hanford workers*.

Certified causes of death	Exposed workers Nos.	Radiation-induced cancers	
		Nos.	%
Bone marrow	14	9.3	66.1
Pancreas	11	6.0	54.4
Lung	130	12.6	9.7
RES neoplasms	47	11.1	23.6
All cancers	442	25.8	5.8
All certified deaths	2184	25.8	1.2

*Provisional estimates for deaths during the period 1944-72.

radiation (442 cases) were attributable to these exposures (Table 24). For 14 bone marrow cancers, the estimated number of radiation-induced cases was 9.3, and for 161 cancers of the pancreas or lungs, the estimate was 18.6. The estimate for all cancers (25.8) was a fraction smaller than the sum of the estimates for the three cancers with definite radiation associations (27.9), and the estimate for all RES neoplasms (11.1) was a fraction larger than the estimate for bone marrow cancers (9.3). Therefore, the proportion of radiation-induced cancers among the exposed cases probably lay between 5 and 7%, and the corresponding proportion for all certified deaths probably lay between 1% and 2%.

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DISCUSSION

A preliminary analysis of the records relating to external radiation has shown that there is sufficient data in the Hanford study to: (i) identify some of the more radiosensitive cancers; (ii) quantify the radiosensitivity of these neoplasms; (iii) obtain estimates of characteristic intervals between initiation and death; and (iv) recognize the ages of maximum and minimum sensitivity to the cancer induction effects of radiation.

Further analyses will be needed to rule out the now remote possibility that the positive findings were merely the result of the radiation exposures having associations with other cancer-related factors. These analyses will proceed in two directions. First, there will be joint standardization for all the factors with known or suspected radiation or cancer associations (e.g. exposure age, interval between hire and exposure, intervals between exposure and death, and depositions of radioactive substances). Secondly, there will be an extension of these analyses from non-survivors with certified causes of death to other members of the monitored population, or workers who are still alive at the time of follow-up.

Meanwhile cursory inspection of the records relating to men who were still alive in 1973 (Table 1) has shown that one of the reasons why the doses of external radiation have always been higher for survivors than non-survivors (Ma74) is because the survivors include a disproportionately large number of men with positive urine analysis (Table 25). This bias is due to an association between high risk occupations and young recruits, which has caused the proportion of young recruits to be different for: (i) singly and doubly monitored occupations; (ii) men with positive and negative urine analyses and (iii) survivors and non-survivors.

Since workers with positive urine analyses were more often and more intensively exposed to external radiation than other workers (Table 18), it is essential, when comparing survivors with non-survivors, to include internal radiation among the con-

Table 25. Age distributions of men monitored for internal and external radiation

Age at hire in years	Doubly monitored*		Singly monitored*	Survivors†	Certified deaths
	(A) %	(B) %			
Under 30	54.8	49.1	41.1	55.8	13.1
30-39	28.1	26.4	28.4	28.6	24.5
40-49	3.2	12.4	17.7	11.7	31.0
50-59	3.7	10.8	10.2	3.6	25.4
60+	0.2	1.3	2.6	0.3	6.0
Σ Nos.	12,095	3716	9128	21,206	3520
%	48.5	14.9	36.6	85.0	14.1

*Doubly Monitored = Monitored for internal and external radiation.

A = Positive urine analyses.

B = Negative urine analyses.

†Singly monitored = Only monitored for external radiation.

*See Table 1.

Table 26. Standardized radiation doses of survivors and non-survivors in relation to certain controlling factors

Controlling factors	Standardized radiation doses*		
	(1)	(2)	(3)
Nil	56	63	81
Exposure year (E)	142	71	87
Cohort or year of hire (C)	138	72	90
E + C	127	79	94
E + C + internal radiation	101	64	112

*Standard (100) = External radiation doses recorded by the 1973 Survivors and certified deaths in Table 1.

(1) = 1973 Survivors.

(2) = Non-cancer deaths.

(3) = Cancer deaths.

trolling factors. This necessity is clearly seen in Table 26 where 5 sets of standardized radiation doses are shown for 3 groups in Table 1 (survivors, non-cancers and cancers). For instance even controlling for two factors simultaneously (i.e. exposure year and cohort), still left the survivors with a higher dose (127) than the non-cancers (79) or the cancers (94), but when internal radiation was added to the other controlling factors, the standardized dose was not only lower for non-cancers (84) than cancers (112) but also lower for the survivors (101) than cancers.

Nevertheless, the absolute doses were higher for the men who were still alive in 1973 than for the non-survivors included in the present investigation, and for Hanford workers as a whole, the trend of radiation doses (and proportions of exposed workers) is in an upward direction. Therefore we should be prepared for future analyses of Hanford data to show both a wider range of cancers with definite radiation associations (due to better representation of cancers with long latent periods) and a higher proportion of radiation-induced cancers among the exposed workers.

HEALTH EFFECTS OF LOW-LEVEL IONIZING RADIATION

Final Report

July 1979

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Prepared for the Nuclear Regulatory Commission

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ABSTRACT

The investigators analyzed mortality data provided by The Nuclear Regulatory Commission on almost four thousand former employees at the Hanford works, one of the largest nuclear processing plants in the United States.

Fifty-nine percent of these employees were exposed to low-level ionizing radiation during the course of their occupational activities: the other forty-one percent were not. The purpose of our analysis was to investigate any relationship between occupational exposure to low-level ionizing radiation and subsequent death by cancer.

The analysis revealed several important findings. The statistical procedures employed show:

- . No hazard for the aggregate male and female populations using basic bivariate procedures.
- . The Mantel-Haenzel procedure reveals significant heterogeneity across age groups for males with regard to the degree of association between simple exposure and subsequent cancer death.
- . In the 45-54 bracket for age at death, men who were not exposed died of cancer 11.8 percent of the time while exposed men died of cancer in 20.7 percent of cases.
- . An age stratified multivariate analysis shows significant association of radiological exposure variables and subsequent cancer death for both the 45-54 age bracket and the 75-84 age bracket for males.
- . Multivariate analysis shows a result of borderline significance for the women of the cohort. Further investigation as more data for women becomes available is recommended.

Background and Objective of the Study

There is an intense interest on the part of the general public as well as governmental agencies in the accurate determination of the long-term health effects from exposure to low level ionizing radiation.

Therefore, from the standpoint of the public health role of the NRC, it is important to analyze those data on human exposure to low level exposures to ionizing radiation which are available.

The NRC provided a tape which contains data on occupational radiation exposure and other relevant information. The objective of this study is the analysis of the data provided. More specifically, this report undertakes to:

- . Examine the relationship between exposure of individuals to low level ionizing radiation and subsequent death by cancer.
- . Describe the method employed to deal with the statistical variability of the data as it impacts the performance of the above two tasks.

The relationship between exposure and subsequent cancer death is discussed in the section entitled "Basic Statistical Tests". The relationship is further examined in the section entitled "Combined Impact," which deals with multivariate composites of both radiological and demographic variables as they apply to the prediction of death by cancer.

Specific Questions and Analysis Performed

The analysis of the Nuclear Regulatory Commission's Hanford mortality data is comprised of four major phases:

- . Univariate summary which allows for basic familiarization with the character of the data.
- . The search for covariates which will provide for the detection of variables impacting the dependent variable--namely, death by cancer--but which are unrelated to low level ionizing radiation.
- . Basic statistical analysis of the impact of independent variables which describe the low level ionizing radiation exposure of the study population on death by cancer. This will, of course, reflect important covariates uncovered by preliminary analysis.
- . Multivariate analysis to assess the combined impact of the "risk factors" of low level ionizing radiation on death by cancer. This will be done in a manner analogous to that first used in assessing risk factors in coronary heart disease in the Framingham Study.

This analysis was performed with two goals in mind. These were to:

- . Resolve, as best possible, the questions motivating the analysis which are set forth presently.
- . Provide a general reference document from which other investigators can answer related questions with a minimum of computer work.

We compiled a list of specific questions which could be reasonably investigated using conventional statistical techniques and the variables at hand. They are:

- . Is the probability of death by cancer significantly different for the population exposed to low level ionizing radiation from

Specific Questions and Analysis Performed

that for the unexposed population?

- . Is the rate of dosage per year related to the rate of death by cancer?
- . Is the total lifetime dose related to the probability of death by cancer?
- . What is the combined impact of the risk factors based on low-level ionizing radiation? That is to say, to what extent can we predict who will die of cancer knowing who was exposed and the characteristics of their exposure?
- . Does age at death differ from exposed versus non-exposed Hanford workers?

Cause of Death Classification

The major orders of the ICDA classification consist of:

1. Infective and Parasitic Diseases
2. Neoplasms
3. Endocrine, Nutritional and Metabolic Diseases
4. Diseases of the Blood and Blood-forming Organs
5. Mental Disorders
6. Diseases of the Nervous System and Sense Organs
7. Diseases of the Circulatory System
8. Diseases of the Respiratory System
9. Diseases of the Digestive System
10. Disease of the Genitourinary System
11. Complications of Pregnancy, Childbirth and the Puerperium
12. Diseases of the Skin and Subcutaneous Tissue
13. Diseases of the Musculoskeletal System and Connective Tissue
14. Congenital Anomalies
15. Certain causes of Perinatal Morbidity and Mortality
16. Accidents, Poisonings and Violence (Nature of Injury)
17. Accidents, Poisonings and Violence (External Cause)

Our analysis proceeded along the coarsest level of grouping possible, so as to leave no question remaining about the effect of low levels of ionizing radiation on the probability of death by cancer. Therefore, we grouped the data into two classes for cause of death. These were: neoplasms (noting that benign neoplasms rarely cause death and that general population data are available for the U.S. census on death by malignant neoplasms for purposes of comparison), and other. We realize that this is not the customary division. We point, however, to the success obtained by the method

Cause of Death Classification

in establishing the relationship of radiological exposure to subsequent death by cancer as its justification.

The Nuclear Regulatory Commission provided data on the cause of death for each individual in the cohort. The causes of death were classified according to the International Classification of Diseases (ICDA - adapted for use in the United States - 8th edition).

Univariate Summary

In order to familiarize ourselves and the reader with the data provided by The Nuclear Regulatory Commission, we performed basic tabulations of the important variables and computed the following statistics:

- . mean
- . variance
- . median
- . mode

The variables studied in the statistics listed above were:

- . age at death
- . total years of employment
- . primary cause of death examined in two ways:
 - by whether or not the person died of cancer
 - by the seventeen major categories of the International Classification of Diseases, adapted for use in the United States.
- . race
- . sex
- . exposure
- . cumulative lifetime dose
- . cumulative dose at 3, 525 years before death
- . year of death
- . maximum radiation dose in a given year
- . average radiation dose in a given year

Table 1

NRC HANFORD LOW LEVEL RADIATION DATA -- UNIVARIATE SUMMARY

-- Age at Death

<u>Age at Death</u>	<u>ABSOLUTE FREQ</u>	<u>RELATIVE FREQ (PCT)</u>	<u>CUM FREQ (PCT)</u>
20 - 24	11	0.3	0.3
25 - 29	37	0.9	1.2
30 - 34	73	1.8	3.0
35 - 39	109	2.7	5.8
40 - 44	199	5.0	10.7
45 - 49	318	8.0	18.7
50 - 54	404	10.1	28.8
55 - 57	534	13.4	42.2
60 - 64	539	13.5	55.7
65 - 69	603	15.1	70.8
70 - 74	485	12.1	83.0
75 - 79	379	9.5	92.5
80 - 84	186	4.7	97.1
85 - 89	97	2.4	99.5
90 - 94	14	0.4	99.9
95 - 97	2	0.1	99.9
100 - UP	2	0.1	100.0
TOTAL	3992	100.0	

Mean 59.5

Variance 176.1

Median 60.3

Mode 65

Table 2

NRC HANFORD LOW LEVEL RADIATION DATA — UNIVARIATE SUMMARY

-- NUMBER OF YEARS WORKED AT HANFORD

<u>NUMBER OF YEARS WORKED</u>	<u>ABSOLUTE FREQ</u>	<u>RELATIVE FREQ (PCT)</u>	<u>CUM FREQ (PCT)</u>
0 - 4	2072	51.9	51.9
5 - 9	721	18.1	70.0
10 - 14	501	12.6	82.5
15 - 19	378	9.5	92.0
20 - 24	219	5.5	97.5
25 - 29	82	2.1	99.5
30 - 34	14	0.4	99.9
TOTAL	3987	100.0	

Missing Cases 5

Mean 5.3

Median 2.3

Mode 0-4

Table 3

NRC HANFORD LOW LEVEL RADIATION DATA -- UNIVARIATE SUMMARY

- CANCER

	<u>PRESENCE OF CANCER</u>	<u>ABSOLUTE FREQ</u>	<u>RELATIVE FREQ (PCT)</u>	<u>ADJUSTED FREQ (PCT)</u>	<u>CUM FREQ (PCT)</u>
NOT CANCER	0	3177	79.6	79.6	79.6
CANCER	1	815	20.4	20.4	100.0
		<hr/>	<hr/>	<hr/>	
TOTAL		3992	100.0	100.0	

Table 4

NRC HANFORD LOW LEVEL RADIATION DATA --- UNIVARIATE SUMMARY

- ICD CODE FOR CAUSE OF DEATH

	<u>ICD</u>	<u>ABSOLUTE FREQ</u>	<u>RELATIVE FREQ (PCT)</u>	<u>CUM FREQ (PCT)</u>
INFECTIVE PARASITIC	1.	37	0.9	0.9
NEOPLASMS	2.	815	20.4	21.3
ENDO NUTRI METABOLIC	3.	69	1.7	23.1
BLOOD ORGANS	4.	6	0.2	23.2
MENTAL DISORDERS	5.	17	0.4	23.6
NERVOUS SENSE ORGANS	6.	28	0.7	24.3
CIRCULATORY	7.	2022	50.7	75.0
RESPIRATORY	8.	207	5.2	80.2
DIGESTIVE	9.	16	4.1	84.3
GENITOURINARY	10.	49	1.2	85.5
SKIN SUBCUTANEOUS	12.	2	0.1	85.6
MSKEL CONNECTIVE	13.	11	0.3	85.8
CONGENITAL ANOMALIES	14.	10	0.3	86.1
SYMPTOMS CONDITIONS	16.	40	1.0	87.1
ACCIDENT POISON VIOL	17.	515	12.9	100.0
TOTAL		3992	100.0	

Table 6

NRC HANFORD LOW LEVEL RADIATION DATA - UNIVARIATE SUMMARY

MALE OR FEMALE

	<u>Sex</u>	<u>Absolute Freq</u>	<u>Relative Freq (PCT)</u>	<u>Cum Freq (PCT)</u>
FEMALE	0.	382	9.6	9.6
MALE	1.	<u>3610</u>	<u>90.4</u>	100.0
TOTAL		3992	100.0	

Table 7

NRC HANFORD LOW LEVEL RADIATION DATA - UNIVARIATE SUMMARY

EXPOSED OR NOT EXPOSED

	<u>Exposure</u>	<u>Absolute Freq</u>	<u>Relative Freq (PCT)</u>	<u>Cum Freq (PCT)</u>
NOT EXPOSED	0.	1638	41.0	41.0
EXPOSED	1.	<u>2354</u>	<u>59.0</u>	100.0
TOTAL		3992	100.0	

Table 8

NRC HANFORD LOW LEVEL RADIATION DATA -- UNIVARIATE SUMMARY

- YEAR OF DEATH

<u>YEAR OF DEATH</u>	<u>ABSOLUTE FREQ</u>	<u>RELATIVE FREQ (PCT)</u>	<u>CUM FREQ (PCT)</u>
45 - 49	73	1.8	1.8
50 - 54	303	7.6	9.4
55 - 59	478	12.0	21.4
60 - 64	797	20.0	41.4
65 - 69	1003	25.1	66.5
70 - +	1338	33.5	100.0
	<hr/>	<hr/>	
TOTAL	3992	100.0	

Table 5

NRC HANFORD LOW LEVEL RADIATION DATA - UNIVARIATE SUMMARY

RACE CODE

	<u>Race</u>	<u>Absolute Freq</u>	<u>Relative Freq (PCT)</u>	<u>Cum Freq (PCT)</u>
NONWHITE	0.	28	0.7	0.7
WHITE	1.	<u>3964</u>	<u>99.3</u>	<u>100.0</u>
	TOTAL	3992	100.0	

Table 9

NRC HANFORD LOW LEVEL RADIATION DATA — UNIVARIATE SUMMARY

- LIFETIME RADIATION DOSE

<u>CODE</u>	<u>ABSOLUTE FREQ</u>	<u>RELATIVE FREQ (PCT)</u>	<u>CUM FREQ (PCT)</u>	
0 - 9	1867	46.8	46.8	
10 - 19	330	8.3	55.0	
20 - 29	216	5.4	60.4	
30 - 39	205	5.1	65.6	
40 - 49	164	4.1	69.7	
50 - 59	123	3.1	72.8	
60 - 69	108	2.7	75.5	
70 - 79	86	2.2	77.6	
80 - 89	92	2.3	79.9	
90 - 99	73	1.8	81.8	
100 - 199	252	6.3	88.1	
200 - 299	183	4.6	92.7	
300 - 399	75	1.9	94.5	
400 - 499	40	1.0	95.5	
500 - 599	23	0.6	96.1	
600 - 699	35	0.9	97.0	
700 - 799	14	0.4	97.3	
800 - 899	12	0.3	97.6	
900 - 999	8	0.2	97.8	
1000 - 1999	26	0.7	98.5	
2000 - 2999	30	0.8	99.2	Mean 93.5
3000 - 3999	25	0.6	99.9	Variance 119637.4
				Median 8.9
4000 TOTAL	5 3992	0.1 100.0	100.0	

Table 10

NRC HANFORD LOW LEVEL RADIATION DATA -- UNIVARIATE SUMMARY

- TOTAL DOSE 3 YEARS BEFORE DEATH

<u>CODE</u>	<u>ABSOLUTE FREQ</u>	<u>RELATIVE FREQ (PCT)</u>	<u>CUM FREQ (PCT)</u>		
0 - 9	1943	48.7	48.7		
10 - 19	324	8.1	56.8		
20 - 29	221	5.5	62.3		
30 - 39	206	5.2	67.5		
40 - 49	165	4.1	71.6		
50 - 59	121	3.0	74.6		
60 - 69	109	2.7	77.4		
70 - 79	89	2.2	79.6		
80 - 89	93	2.3	81.9		
90 - 99	75	1.9	83.8		
100 - 199	208	5.2	89.0		
200 - 299	179	4.5	93.5		
300 - 399	65	1.6	95.1		
400 - 499	37	0.9	96.1		
500 - 599	19	0.5	96.5		
600 - 699	32	0.8	97.3		
700 - 799	7	0.2	97.5		
800 - 899	13	0.3	97.8		
900 - 999	8	0.2	98.0		
1000 - 1999	29	0.7	98.8		
2000 - 2999	26	0.7	99.4		
3000 - 3999	19	0.5	99.9	Mean	87.5
4000 -	<u>4</u>	<u>0.1</u>	100.0	Variance	99174.6
Total	3992	100.0		Median	6.6

Table 11

TOTAL DOSE 5 YEARS BEFORE DEATH

<u>CODE</u>	<u>ABSOLUTE FREQ</u>	<u>RELATIVE FREQ (PCT)</u>	<u>CUM FREQ (PCT)</u>	
0 - 9	2011	50.4	50.4	
10 - 19	325	8.1	58.5	
20 - 29	233	5.8	64.4	
30 - 39	200	5.0	69.4	
40 - 49	167	4.2	73.5	
50 - 59	123	3.1	76.6	
60 - 69	108	2.7	79.3	
70 - 79	80	2.0	81.3	
80 - 89	90	2.3	83.6	
90 - 99	69	1.7	85.3	
100 - 199	220	5.5	90.8	
200 - 299	145	3.6	94.5	
300 - 399	53	1.3	95.8	
400 - 499	25	0.6	96.4	
500 - 599	25	0.6	97.0	
600 - 699	23	0.6	97.6	
700 - 799	12	0.3	97.9	
800 - 899	10	0.3	98.2	
900 - 999	9	0.2	98.4	
1000 - 1999	23	0.6	99.0	
2000 - 2999	27	0.7	99.6	
3000 - 3999	13	0.3	100.0	
4000 -	1	0.0	100.0	Mean 76.
TOTAL	<u>3992</u>	<u>100.0</u>		Variance 73949.
				Median 4.

Table 14

NRC HANFORD LOW LEVEL RADIATION DATA - UNIVARIATE SUMMARY

TOTAL DOSE 20 YEARS BEFORE DEATH

<u>CODE</u>	<u>ABSOLUTE FREQ</u>	<u>RELATIVE FREQ (PCT)</u>	<u>CUM FREQ (PCT)</u>
0 - 9	3274	82.0	82.0
10 - 19	196	4.9	86.9
20 - 29	114	2.9	89.8
30 - 39	88	2.2	92.0
40 - 49	61	1.5	93.5
50 - 59	43	1.1	94.6
60 - 69	34	0.9	95.4
70 - 79	25	0.6	96.1
80 - 89	32	0.8	96.9
90 - 99	24	0.6	97.5
100 - 199	54	1.4	98.8
200 - 299	36	0.9	99.7
300 - 399	3	0.2	99.9
400 - 499	1	0.0	99.9
500 - 599	<u>2</u>	<u>0.1</u>	100.0
TOTAL	3992	100.0	
MEAN	9.1		
VARIANCE	1007.7		
MEDIAN	1.1		

Table 12

NRC HANFORD LOW LEVEL RADIATION DATA — UNIVARIATE SUMMARY

- TOTAL DOSE 10 YEARS BEFORE DEATH

<u>CODE</u>	<u>ABSOLUTE FREQ</u>	<u>RELATIVE FREQ (PCT)</u>	<u>CUM FREQ (PCT)</u>		
0 - 9	2328	58.3	58.3		
10 - 19	305	7.6	66.0		
20 - 29	223	5.6	71.5		
30 - 39	189	4.7	76.3		
40 - 49	158	4.0	80.2		
50 - 59	114	2.9	83.1		
60 - 69	95	2.4	85.5		
70 - 79	66	1.7	87.1		
80 - 89	78	2.0	89.1		
90 - 99	53	1.3	90.4		
100 - 199	145	3.6	94.0		
200 - 299	99	2.5	96.5		
300 - 399	45	1.1	97.6		
400 - 499	19	0.5	98.1		
500 - 599	16	0.4	98.5		
600 - 699	16	0.4	98.9		
700 - 799	7	0.2	99.1		
800 - 899	4	0.1	99.2		
900 - 999	3	0.1	99.3		
1000 - 1999	18	0.5	99.7	Mean	42.9
2000 - 2999	10	0.3	100.0	Variance	23239.3
3000 - +	1	0.0	100.0	Median	3.57
TOTAL	3992	100.0			

Table 13

NRC HANFORD LOW LEVEL RADIATION DATA - UNIVARIATE SUMMARY

TOTAL DOSE 15 YEARS BEFORE DEATH

<u>CODE</u>	<u>ABSOLUTE FREQ</u>	<u>RELATIVE FREQ (PCT)</u>	<u>CUM FREQ (PCT)</u>
0 -9	2733	68.5	68.5
10 -19	266	6.7	75.1
20 -29	181	4.5	79.7
30 -39	163	4.1	83.7
40 -49	118	3.0	86.7
50 -59	72	1.8	88.5
60 -69	63	1.6	90.1
70 -79	46	1.2	91.2
80 -89	51	1.3	92.5
90 -99	38	1.0	93.5
100 -199	116	2.9	96.4
200 -299	77	1.9	98.3
300 -399	33	0.8	99.1
400 -499	9	0.2	99.3
500 -599	8	0.2	99.5
600 -699	8	0.2	99.7
700 -799	3	0.1	99.8
800 -899	1	0.0	99.8
900 -999	3	0.1	99.9
1000 -1999	<u>3</u>	<u>0.1</u>	100.0
TOTAL	3992	100.0	

MEAN 23.0
 VARIANCE 5175.6
 MEDIAN 2.3

Table 15

NRC HANFORD LOW LEVEL RADIATION DATA---UNIVARIATE SUMMARY

TOTAL DOSE 25 YEARS BEFORE DEATH

<u>CODE</u>	<u>ABSOLUTE FREQ</u>	<u>RELATIVE FREQ (PCT)</u>	<u>CUM FREQ (PCT)</u>
0 - 9	3750	93.9	93.9
10 - 19	87	2.2	96.1
20 - 29	36	0.9	97.0
30 - 39	25	0.6	97.6
40 - 49	20	0.5	98.1
50 - 59	10	0.3	98.4
60 - 69	8	0.2	98.6
70 - 79	9	0.2	98.8
80 - 89	11	0.3	99.1
90 - 99	9	0.2	99.3
100 - 199	18	0.5	99.8
200 - 299	8	0.2	100.0
300 - 399	1	0.0	100.0
TOTAL	3992	100.0	

MEAN 2.5

VARIANCE 221.2

MEDIAN 0.32

The Method of Proportional Mortality

The method of proportional mortality, a statistical technique, is used for a major portion of the analysis in this report. The method, while highly useful, must be applied carefully.

It is particularly useful in cases whose morbidity or mortality data is available but not data on the population at risk where the diseases or deaths occurred. This is the situation with the NRC data.

The analysis cannot, therefore, consider absolute rates of death from a particular cause. Instead, the relative death rates from a cause or group of causes can be shown.

In some cases, the method can artificially show a high death rate. For instance, where two populations have identical cancer death rates, and the first is fortunate in a particularly low rate of death from other causes. There, the first group would falsely appear to have a proportionally higher cancer death rate. In the Hanford data, such a death rate may appear proportionally higher in the exposed group than the non-exposed.

In spite of the drawbacks of the method, the nature of the data necessitated its use, and the results contained herein must be viewed with caution.

Mantel and others have pointed out that while the method is widely used it should only be taken to provide leads for rigorous research. In general, a single retrospective study should not be taken as conclusive.

Tests for Covariates

There are radiological and demographic variables in the data file provided by The Nuclear Regulatory Commission for this study. This section describes statistical tests which were performed in order to determine which of the demographic variables are related to death by cancer.

It is widely known that cancer death rates differ for various subgroups of the population of the United States. For example, the U.S. Decennial Life Tables for 1969-1971 show that the chance of eventually dying of a malignant neoplasm is:

- . 16.3 percent for the total population
- . 16.9 percent for white males
- . 15.9 percent for white females
- . 15.3 percent for non-white males
- . 13.5 percent for non-white females.

These variations indicate that sex and race should be taken into account in the analysis to follow.

Another important source of heterogeneity in cancer death rates is age. Death rates, generally, increase with age and, in particular, cancer death rates rise rapidly with age. The cancer death ratio (i.e., the fraction of total deaths which are cancer deaths) also varies with age.

The question which we address in this section is a simple one: what important intervening factors effect the probability of death by cancer? The primary statistical method which was employed to answer this question was that of simple cross tabulation. The cancer vs. not cancer cause of death indicator was cross tabulated by each of the covariates of interest. The results of these cross tabulations together with statistical tests of significance are presented below.

Tests for Covariates

A Chi square test of a four-fold table with not-cancer/cancer vs. male/female was performed:

Table 16

	female	male	
not cancer	265	2912	3177
cancer	117	698	815
	382	3610	3992

The results of the Chi square test of the hypothesis that sex and death by cancer are unrelated were:

- . Chi square = 26.4
- . df = 1
- . $p \text{ (Chi square} > 26.4) < .0001$

This indicates that sex is a significant covariate of death by cancer in the Hanford cohort. It is to be noted that the table contains thirty-nine more cases of death by cancer for women than would be expected if there were no relationship between cancer death and sex.

It is also of interest to note the cancer death rate for the women of the Hanford cohort is higher than thirty percent. This is substantially higher than the 15.9 percent for white females which was reported in the Decennial Life Table as mentioned earlier.

In order to determine if race is a significant covariate of cancer death, a Chi square test was performed on a four-fold table with not-cancer/cancer vs. race as non-white/white. The resulting table is shown below.

Tests for Covariates

Table 17

	non- white	white	
not-cancer	25	3152	3177
cancer	3	812	815
	28	3964	3992

A Chi square test of the hypothesis that race and cancer death are unrelated was performed. The results of that test were:

- . Chi square = 1.09
- . df = 1
- . $p(\text{Chi square} > 1.09) = .297$

This result must be regarded with caution for two reasons:

- . The lowest cell frequency is only 3, and the chi square test generally requires 5 or more in each cell to be accurate.
- . In general, there are very few non-whites in the cohort.

For practical purposes the race variable will be disregarded in subsequent analysis, but in no sense is this a generalizable conclusion.

Next, stratifying age into moderately broad intervals, the relationship between cancer death and age was investigated. Since sex was found to be an important covariate, this test was performed for each of the sexes.

The contingency tables for age at death vs. not-cancer/cancer are presented along with the Chi square test of the hypothesis that age at death is unrelated to the cancer death ratio (i.e. probability of death by cancer given death at age t). It is seen that, for both sexes, the cancer death ratio is strongly dependent on age at death. Therefore, all subsequent

Table 18

MALES

Age at Death

	25-34	35-34	45-54	55-64	65-74	75-84	85-94	95-104	105-115	
Not Cancer	66	169	439	717	797	564	154	5	1	2912
Cancer	2	31	92	191	253	113	16	0	0	698
	68	200	531	908	1050	677	170	5	1	3610

. Chi square = 47.12

. df = 8

. p (Chi square > 47.12) < .00009

Table 19

FÉMALES

Age at Death

	25-34	34-45	45-54	55-64	65-74	75-84	85-94	105-115	
Not Cancer	11	30	58	47	63	43	12	1	265
Cancer	2	18	29	40	16	12	0	0	117
	13	48	87	87	79	55	12	1	382

. Chi square = 24.18

. df = 7

. p (Chi square > 24.18) = .0011

Tests for Covariates

analysis shall statistically adjust for age at death.

To summarize the results of this section, the subsequent analysis will:

- . Control for sex-based differences in cancer death.
- . Control for age at death.
- . Disregard race since few non-whites are in the cohort.

Basic Statistical Tests

This section describes the application of various commonly used statistical tests to the Hanford data. Its primary purpose is to explore the relationship of certain of the independent variables which describe the character of exposure to low level ionizing radiation in the cohort to death by cancer. The analyses described in this section are primarily bivariate tests of one of the exposure variables at a time as it relates to death by cancer. These analyses are grouped under the specific questions which each is designed to investigate, and which were set forth in the section on the goals of the study and specific questions to be investigated.

One statistical procedure was also performed to assess the relationship between exposure and subsequent death by cancer as it is shown in a set of four-fold tables which result from the stratification of the cohort into several age brackets. This is the Mantel-Haenzel procedure. It is used to assess two factors of interest to this study. These are:

- . The average degree of association of exposure with death by cancer.
- . The degree of homogeneity across the age brackets into which the cohort was stratified.

The details of the Mantel-Haenzel procedure will be summarized in the text of the report. Further explanation can be found in Fleiss which is listed in the bibliography.

One of the simplest and most important questions under investigation in this study is: is the probability of death by cancer different for exposed versus unexposed populations in the Hanford cohort. First the relationship in the aggregate population was investigated.

Basic Statistical Tests

A Chi square test of a four-fold table having not-cancer versus cancer crossed with not-exposed versus exposed was performed. The table which resulted follows:

Table 20

	Exposed	Not-Exposed	
Not-Cancer	1311	1866	3177
Cancer	327	488	815
	1638	2354	3992

A Chi square test of the hypothesis that exposure and cancer death are unrelated in the total population under study was performed. The results of that test were:

- . Chi square = .304
- . df = 1
- . $p(\text{Chi square} > .304) = .58$

This can be interpreted to mean that simple occupational exposure is not significantly related to subsequent death by cancer or that any such relationship as exists is not clear until some of the covariates which effect cancer death rates are taken into account.

Next, the cohort was stratified by sex to clarify the nature of relationship between exposure and cancer death rates for each of the sexes.

The data provided on the Hanford cohort contains almost four thousand cases and over eight hundred deaths by cancer. This allows the question under investigation to be investigated using asymptotically normal procedures. That is to say, the difference in the mean rates of death by cancer for the exposed vs. the non-exposed populations is normally distributed. This

Basic Statistical Tests

difference can be normalized to unit variance and zero mean in the usual way. The statistical tests of hypothesis which is thus generated are equivalent to Chi square test of the corresponding four-fold tables. However, the rate tables given more easily lend themselves to interpretation. These rates are described in the following table:

Table 21

	\hat{p} (cancer)	σ	n
Not-exposed	.1996	.3998	1638
Exposed	.2073	.4055	2354
Total	.2042	.4031	3992

$d = \hat{P} \text{ not exposed} - \hat{P} \text{ exposed}$

The normalized difference observed for the two proportions and the test of the hypothesis that they are equal resulted in the following:

$$d/\sigma_d = -.5935$$

$$p(|d/\sigma_d| > .5935) = .55$$

This can be interpreted to indicate that cancer death rates were not significantly different for exposed versus non-exposed populations. As might be expected, this statistic is in nearly perfect agreement with the previous chi square test. However, sex was found to be a significant intervening variable with death by cancer. Therefore, the above test was repeated for males only, and females only, with the following results.

Basic Statistical Tests

Table 22

Males Only $d = \hat{P} \text{ not-exposed} - \hat{P} \text{ exposed}$

	\hat{p} (cancer)	σ	n
Not-exposed	.1786	.3831	1372
Exposed	.2024	.4019	2238
Total	.1934	.3950	3610

The normalized difference and the test of the hypothesis that the cancer rates are equal for the exposed and unexposed population resulted in:

- . $d/g = -1.75$
- . $p(|d/g| > 1.75) = .08$

This may be interpreted to indicate that there is a difference in the cancer rates, which is at most marginally significant, for exposed versus non-exposed males.

The classical values used to indicate significance are, of course, .05 and .01. This p-value is not as small as either of these. In cases where loss is very high (such as increased cancer deaths) such a result might at least prompt interest and further investigation even though risk seems low or uncertain.

The cancer rates in the females of the cohort were tested by identical means. The results of that test are presented below:

Basic Statistical Tests

Table 23

Females only $d = \hat{p} \text{ not-exposed} - \hat{p} \text{ exposed}$

	\hat{p} (cancer)	σ	n
Not-Exposed	.3083	.4626	266
Exposed	.3017	.4610	116
Total	.3063	.4622	382

The normalized difference and the test of the hypothesis of equality of cancer rates for exposed versus non-exposed women resulted in the following:

$$d/g = .13$$

$$p(|d/g| > .13) = .9$$

This indicates that females who are exposed to low level ionizing radiation die of cancer less frequently than those who are not. However, there is no reason to reject the null hypothesis of equality of the rates. Therefore, the observed difference is quite possibly accidental.

To summarize the above results: Simple occupational exposure to low-level ionizing radiation does not appear to be related to the chance of death by cancer.

The final analysis of this section which is addressed to the question of the relatedness of simple exposure to death by cancer employs the Mantel-Haenzel procedure. This will provide even further stratification of the cohort to remove the effects of the significant covariates discovered earlier. To this end a set of four-fold tables were generated. One of these for each of a set of moderately broad age strata, and of course, for each sex. The tables were then combined into the following layouts and the Mantel-Haenzel statistics computed. The Mantel-Haenzel (M-H) procedure addresses three questions:

Basic Statistical Tests

- . Is there evidence that the degree of association is consistent from one age group to another?
- . If the degree of association is consistent is it also statistically significant?
- . Assuming that the common degree of association is significant, what is the best estimate of its magnitude?

To answer these questions the M-H procedure involves the computation the three Chi square distributed statistics. These are:

$$. \chi^2_{\text{total}} = \sum_{i=1}^g W_i M_i^2 \text{ with } g \text{ degrees of freedom}$$

$$. \chi^2_{\text{assoc}} = \left(\sum_{i=1}^g W_i M_i \right)^2 / \left(\sum_{i=1}^g W_i \right) \text{ with one degree of freedom}$$

$$. \chi^2_{\text{homog}} = \chi^2_{\text{total}} - \chi^2_{\text{assoc}} \text{ with } g-1 \text{ degrees of freedom}$$

This becomes the M-H procedure with the definition of:

$$m_i = d_i = \frac{n_{i.}^{-1}}{n_{i.}} \frac{P_{i1} - P_{i2}}{\bar{P}_i - \bar{Q}_i}$$

and

$$w_i = \frac{\bar{P}_i \bar{Q}_i n_{i1} n_{i2}}{N_i - 1}$$

This requires the definition of:

$$\bar{P}_i = \frac{N_{i1}P_{i1} + N_{i2} P_{i2}}{N_i}$$

and

$$\bar{Q}_i = 1 - \bar{P}_i$$

Further in the i th group, n_{i1} is the number of people not exposed and P_{i1} is the proportion of the unexposed subjects with cancer as cause of death. The quantity n_{i2} is the number of subjects in the i th group who were exposed, and P_{i2} is the proportion of exposed subjects with cancer as cause of death. The total number of subjects in the i th group is given

Basic Statistical Tests

as $n_i = n_{i1} + n_{i2}$.

Proceeding now by sex we obtained the following results by the application of the M-H procedure:

Table 24

Males

Age Group	Not Exposed		Exposed				
	n_{i1}	P_{i1}	n_{i2}	P_{i2}	$n_{i.}$	d_i	w_i
25-34	29	.069	39	0	68	2.41	3.7
35-44	84	.143	116	.164	200	-.16	6.38
45-54	203	.118	328	.207	531	-.621	17.94
55-64	340	.215	568	.208	908	.042	35.28
65-74	375	.235	675	.244	1050	-.049	44.1
75-84	267	.146	410	.180	677	-.244	22.49
85-94	70	.1	100	.09	170	.177	3.51
95-104	4	0	1	0	5	0	0
105-114	0	0	1	0	1	0	0

From this we have (discarding ages 95 and above for insufficient data):

$$. \chi^2_{\text{total}} = \sum_{i=1}^7 w_i d_i^2 = 30.13$$

$$. \chi^2_{\text{assoc}} = \left(\sum_{i=1}^7 w_i d_i \right)^2 / \left(\sum_{i=1}^7 w_i \right) = 9^2 / 133.4 = .607$$

$$. \chi^2_{\text{homog}} = \chi^2_{\text{total}} - \chi^2_{\text{assoc}} = 30.13 - .607 = 29.52$$

Testing the hypothesis that the degree of association is homogenous from age bracket to age bracket we have:

$$. \text{Chi square} = 29.52$$

Basic Statistical Tests

$$. \quad df = 7-1 = 6$$

$$. \quad p \text{ (Chi square } > 29.52) < .001$$

This strongly indicates that the degree of association varies from age bracket to age bracket. Therefore, it is not possible to analyze the common degree of association. The degree of significance of association between exposure and subsequent cancer death must be examined for each individual age bracket. Since the actual four-fold tables can be reconstructed from the above layout only the Chi square statistics and the significance of each is shown below.

Table 25

Males

Age Group	Chi Square	Significance
25-34	.88	.347
35-44	.042	.837
45-54	6.34	.011
55-64	.027	.869
65-74	.078	.779
75-84	1.14	.285
85-94	.002	.962

From the above it can be seen that there is a statistically significant degree of association in only one age bracket: namely 45-54. The four-fold table for that age bracket is presented below.

Table 26

Males Age 45-54

	Not Cancer	Cancer	
Not Exposed	179	24	203
Exposed	260	68	328
	439	92	531

Basic Statistical Tests

As mentioned above:

- . Chi square 6.34
- . df = 1
- . p (Chi square > 6.34) = .011

The odds ratio for this age bracket is given as:

$$O = \frac{P_{i1}(1-P_{i2})}{P_{i2}(1-P_{i1})} = \frac{.118(1-.207)}{.207(1-.118)} = .51$$

This indicates that subjects who were not exposed in this age bracket died of cancer only fifty-one percent as often as those who were exposed. More directly: 11.8 percent of those who were not exposed died of cancer, while 20.7 percent of those exposed died of cancer. To summarize: given death between the ages of 45-54, simple occupational exposure is associated with a two-fold higher cancer death rate than the rate for unexposed men in the cohort.

Applying the M-H procedure to the age stratified women of the cohort, the following layout was obtained: (see next page).

Basic Statistical Tests

TABLE 27

Females

Age Group	not exposed		exposed		n_i	d_i	W_i
	n_{i1}	P_{i1}	n_{i2}	P_{i2}			
25-34	8	0	5	.4	13	-2.83	.434
35-44	40	.375	8	.375	48	0	1.596
45-54	54	.37	33	.273	87	.432	4.6
55-64	59	.475	28	.429	87	.185	4.77
65-74	53	.189	26	.231	79	-.26	2.86
75-84	41	.22	14	.214	55	.035	1.81
85-94	12	0	2	0	12	0	0
105-114	1	0	0	0	1	0	0

From this we have (discounting ages 85 and above for insufficient data):

$$x^2 \text{ total} = \sum_{i=1}^7 W_i d_i^2 = 4.69$$

$$x^2 \text{ assoc} = \left(\sum_{i=1}^7 W_i d_i \right)^2 / \left(\sum_{i=1}^7 W_i \right) = (.961)^2 / (16.07) = .057$$

$$x^2 \text{ homog} = x^2 \text{ total} - x^2 \text{ assoc} = 4.96 - .057 = 4.63$$

Testing the hypothesis that the degree of association is homogeneous from age bracket to age bracket we have:

$$\text{Chi square} = 4.63$$

$$df = 7 - 1 = 6$$

$$p(\text{chi square} > 4.63) \approx .59$$

Basic Statistical Tests

We find no reason to reject the hypothesis that the degree of association between exposure and subsequent cancer death is homogeneous from age bracket to age bracket.

The hypothesis that this average degree of association is zero resulted in the following:

$$\chi^2 = .057$$

$$df = 1$$

$$p(\chi^2 > .057) \approx .81$$

This does not indicate that, for the women of the cohort, simple occupational exposure is associated with subsequent cancer death.

Next, we shall describe the analysis done to investigate the question: Is the rate of dosage related to the incidence of death by cancer? The rate of dosage was derived from the data available on the cohort as follows:

$$\text{dose rate} = (\text{cumulative lifetime dose}) / (\text{total years of exposure})$$

It must be observed that this indicator is, at best, a crude estimate, and that the dosages involved were certainly not accumulated uniformly over the course of exposure. However, in the interest of such information as is contained in this index, we performed the following analysis. The difference in mean dosage rates per year for the cancer vs. the non-cancer groups was tested for statistical significance. We proceeded, as usual, with the total population first, then the male and female populations separately. The analysis and results follows:

Basic Statistical Tests

TABLE 28

Total Population

($d = \bar{R}$ not cancer $-\bar{R}$ cancer)

	mean rate	σ	n
not cancer	7.8	25.93	3177
cancer	8.2	24.93	815
all	7.8	25.73	3992

The test which was computed and the statistical significance of the observed difference between the mean rates for the cancer vs. the non-cancer groups were as follows:

$$d/\sigma_d = - .395$$

$$P(|d/\sigma_d| = .395) = .692$$

$$H_0: d = 0 \text{ vs. } H_1: d \neq 0$$

There is a slight difference in the mean rates of exposure for the cancer vs. the non-cancer groups. However, we would expect a result which was this different, or more so, seven times in ten by chance alone. This definitely gives no indication that H_0 should be rejected in favor of H_1 . Proceeding as above for males only we have:

TABLE 29

Males Only

(d = \bar{R} not cancer - \bar{R} cancer)

	mean rate	σ	n
not cancer	8.36	26.97	3177
cancer	9.15	26.61	815
all	8.51	26.9	3992

The test statistic and the results of the test of the hypothesis that the observed difference between the males who died of cancer vs. those who did not is due to chance alone are presented below:

$$d/\sigma_d = -.697$$

$$P(|d/\sigma_d| > .697) = .1038$$

$$H_0: d = 0 \text{ vs. } d \neq 0$$

This result indicates a marginal but not classical degree of significance between the cancer vs. the non-cancer groups. Again, if the risk is great, this degree of difference certainly prompts further research. Now, for the female groups in the cohort we obtain:

TABLE 30

Females Only

(d = \bar{R} not cancer - \bar{R} cancer)

	mean rate	σ	n
not cancer	1.82	5.35	3177
cancer	2.60	8.14	815
all	2.06	6.33	3992

Basic Statistical Tests

The test statistic and the results of the test of the hypothesis that the observed difference is due to chance factors alone for females who did not die of cancer vs. those who did are as follows:

- . $d/\sigma_d = -1.11$
- . $P(|d| > 1.11) = .2669$
- . $H_0: d = 0$ vs. $d \neq 0$

Another non-significant result. Therefore we cannot reject H_0 with any confidence.

To summarize the results of the above analysis: The average rate at which occupational exposure to low-level ionizing radiation was incurred does not appear to be significantly different for those who die of cancer vs. those who do not. It is to be remembered that the variable used above is only a crude estimator and that the dosages involved almost certainly did not occur uniformly across the interval of exposure.

Next, we shall describe the analysis which was performed to investigate the question: Is the total lifetime dose of radiation related to the probability of death by cancer?

Since it is difficult to compute the probability of death by cancer as a function of the independent variable at hand, we will again stratify the variable for those cases who died from cancer vs. those who did not. This means we will test the hypothesis that the mean life-time dose for the two groups is, in fact, equal. The difference of the mean lifetime exposure for cancer vs. not cancer population was tested:

Table 31

	Mean life dose	σ	n
Not cancer	95.0	333.3	3177
Cancer	113.7	382.8	815
All	98.8	344.1	3992

Basic Statistical Tests

The results were:

- . $d/\sigma_d = -1.38$
- . $P(|d/\sigma_d| > 1.38) = .1662$
- . $H_0 : d = 0 \text{ vs. } d \neq 0$

Which provides no evidence for the rejection of the null hypothesis that the group means are identical.

Proceeding as above for the male population in the cohort we found:

Table 32

Males Only

$d = \bar{D} \text{ not cancer} - \bar{D} \text{ Cancer}$

	Mean Life Dose	σ	n
Not Cancer	101.77	346.81	2912
Cancer	126.41	407.34	698
All	106.53	359.38	3610

The test statistic and the results of the test of the hypothesis that the observed difference in the mean lifetime dose differs for males who died vs. those who did not die of cancer resulted in the following:

- . $d/\sigma_d = -1.627$
- . $P(|d/\sigma_d| > 1.627) = .104$
- . $H_0 : d = 0 \text{ vs. } H_1 : d \neq 0$

We can interpret this to give us at best marginal reason to reject the hypothesis that the lifetime dose of radiation in males differs by cause of death.

Proceeding as above for females in the Hanford cohort we obtained:

Basic Statistical Tests

Table 33

Females Only

$$d = \bar{D} \text{ not cancer} - \bar{D} \text{ cancer}$$

	Mean Life Dose	σ	n
Not Cancer	20.85	70.08	265
Cancer	38.31	157.63	117
All	26.2	105.03	382

The test statistic and the results of the test of the hypothesis is that the mean dose for females who died of cancer is equal to the mean dose for those who did not die of cancer are below:

- . $d/\sigma_d = -1.497$
- . $P(|d/\sigma_d| > 1.497) = .1344$
- . $H_0 : d = 0 \text{ vs. } H_1 : d \neq 0$

Which again provides no definite evidence of a difference in the mean lifetime doses of the cancer vs. not cancer groups. However, it must be noted that the standard deviations in the lifetime dose for the cancer vs. the non-cancer groups are highly different (70.80 vs 157.63). The statistical test which was used above is quite sensitive to differences in the group standard deviations. The result which it gives cannot be accurately interpreted. Therefore, an additional test statistic was computed for this table. That statistic is the Welch-Alpin t-test. The statistic is computed as follows:

$$t = \frac{\bar{R}_n - \bar{R}_c}{\sqrt{\frac{\sigma_n^2}{R_n} + \frac{\sigma_c^2}{K_c}}}$$

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For the data in question this statistic evaluates :

$$t = \frac{20.85 - 38.31}{\sqrt{\frac{(70.08)^2}{265} + \frac{(157.63)^2}{117}}} = \frac{-17.46}{15.19} = -1.15$$

That statistic is distributed as Student's distribution for degrees of freedom which depend on the standard deviation of the two groups. However, even for infinite degrees of freedom the value -1.15 will not allow us to reject the hypothesis that the group means are equal with the same degree of confidence that the above procedure allowed. We find, therefore, no reason to reject the hypothesis of equality.

To summarize the results of the above analysis: The total lifetime dose incurred by the cancer vs. the non-cancer groups of the population are not statistically different and we see no reason to claim that the simple lifetime dose is related to death by cancer. This is, of course, not to claim that the same would be true for all lifetime doses at all non-lethal levels only that it is true for the occupational levels encountered by the Hanford cohort.

The final basic question with which this section shall deal is: Does age at death differ for exposed vs. non-exposed populations? We performed two basic types of analyses to investigate the question.

First the mean age at death was computed for the exposed vs. the non-exposed groups with the following results:

Basic Statistical Tests

Table 34

$$d = \bar{A} \text{ not exposed} - \bar{A} \text{ exposed}$$

	Mean Age At Death	σ	n
Not Exposed	59.17	13.66	2354
Exposed	59.72	12.87	1638
All	59.50	13.20	3992

The test statistic and the results of the test of the hypothesis that the observed difference in the mean age at death for exposed vs. non-exposed population are shown below:

$$\begin{aligned} \cdot d/\sigma_d &= -1.29 \\ \cdot P(|d/\sigma_d| > 1.295) &= .1953 \\ \cdot H_0 : d &= 0 \text{ vs. } H_1 : d \neq 0 \end{aligned}$$

Again we have no reason to reject the hypothesis that the age at death is, on average, equal.

In addition, we correlated age at death with lifetime dose with the following results:

Table 35

	r	r ²	P(r)	n
All	-.0104	.00011	.37	3992
Male	.00729	.00005	.41	3610
Female	.0822	.00675	.05	382

We note that over all and in the male sub-population that there is no significant correlation between life span and lifetime dose. However, there is a slight positive correlation in women at the .05 level of confidence. This indicates that longer life spans are weakly associated with

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higher lifetime dosages. The source of this relationship is unclear at present. As further data accumulate from other sites the issue will, presumably, be resolved.

With one noteworthy exception, the analysis described in this section can be characterized as uninformative with regard to who will die of cancer.

To summarize the analytical results of this section we found one significant result and many non-significant results:

- . Men who died at ages from 45-54 and were exposed died from cancer almost twice as often as similar men who were not exposed. There were 531 men in that age bracket and 20.7 percent of the exposed men died of cancer while 11.8 percent of the non-exposed men died of cancer.
- . No significant relationship between exposure and cancer death in any other age bracket for men.
- . No significant relationship between exposure and cancer death for women.
- . No difference in the rate of dosage for subjects who died of cancer versus subjects who did not die of cancer. With rate of dosage being computed as:
$$(\text{lifetime dose}) / (\text{years exposed}).$$
- . No difference in the average age at death for exposed versus non-exposed populations.
- . No correlation between lifetime dose and life span for males.
- . A slight positive correlation between life span and total lifetime dose for females. It is to be emphasized that this correlation is very weak and that it is certainly not clear that higher lifetime doses cause longer life.

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This section describes the application of multivariate discriminant analysis to the prediction of which subjects in the cohort died of cancer. It does not attempt to develop a dose response for the population because of the multivariate nature of the predictive model. The presence of non-radiological variables in the model also makes the interpretation of any dose response relationship difficult and error prone.

The primary purpose of the section is to explore the relationship of certain of the independent variables as they act in concert to predict who in the cohort died of cancer. As was shown in the section in basic statistical tests, these variables taken one at a time have little power to predict who died of cancer except in one age bracket for the men of the cohort. However, it is sometimes the case that the more complete description provided by several variables will allow good predictions to be made even when those same variables, individually, do not. There are a variety of variables in the Hanford data which may act--both simply and jointly--in explaining variations in the risk of cancer death observed in the cohort. Since there are several relevant variables and some of these are continuous in nature the method of multi-way contingency tables which is often employed for multi-variate analysis is not practical. In this case it would result in more cells in the multi-way cross classification than there are cases in the Hanford data. We will therefore employ a discriminant analysis which will develop a linear combination of variables which will maximally separate the cancer from the non-cancer groups. We will then use this linear combination to classify the cases as cancer vs. non-cancer as cause of death. Several analyses of this type were performed in the attempt to identify those variables in the data that have the best ability to separate the cancer from the non-cancer deaths. The set of variables with which we began our discriminant analysis is

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comprised of:

- . Total life time dose
- . The peak exposure rate
- . Years exposed
- . The cancer death ratio for women
- . The cancer death ratio for men
- . The year at death
- . Average rate of exposure.

Several of these variables were derived from the data provided by the commission. How each of these was derived is described below:

- . The peak exposure rate - The cumulative lifetime dose is available at death, three years prior, five years prior, ten years prior, fifteen years prior, twenty years prior and twenty-five years prior to death. The average dose rate for each of the intervals defined by these cumulative doses was computed as: $(\text{incremental exposure in interval})/(\text{years in interval})$. The maximum rate of the above set is taken as peak exposure rate.
- . Years exposed - Years exposed is found by examining each of cumulative lifetime exposures at the above described points. For example, if the dose twenty-five years before death is non-zero then the years exposed variable is nominally defined as 25. If the twenty-five years prior to death exposure is zero and the twenty years prior to death exposure is non-zero then the years exposed variable is defined as 20.

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- . The cancer death ratio for women - The cancer death ratio for women is computed as a function of age at death. For each of the age brackets:

- 25-34
- 35-44
- 45-54
- 55-64
- 65-74
- 75-84
- 85-94
- 95-104
- 105-114

The cancer death ratio (CDR) was computed as follows:

- . $CDR = (\# \text{ of female cancer deaths}) / (\# \text{ of female deaths})$
- . The cancer death ratio for men - The cancer death ratio for men was computed as above, except that male deaths were used.
- . The average rate of exposure - The average rate of exposure was computed as: $(\text{lifetime dose}) / (\text{years exposed})$.

Though this method is well established in the field of cardiovascular epidemiology, as can be found in the references, there are certain hazards which must be guarded against in its use.

One problem which may cause difficulty is the form of the cancer death ratio as a function of age at death. If this ratio is increasing with age at death, and the total lifetime dose is increasing with age at death, increasing risk of death by cancer may be falsely attributed to dose when the better

FIGURE 1

• CHANCE OF DEATH BY MALIGNANT NEOPLASM
FOR MALES GIVEN DEATH AT AGE x
SOURCE: U.S. DECENNIAL LIFE TABLES 1965-1971
* AS ABOVE FOR NONFORD MALES

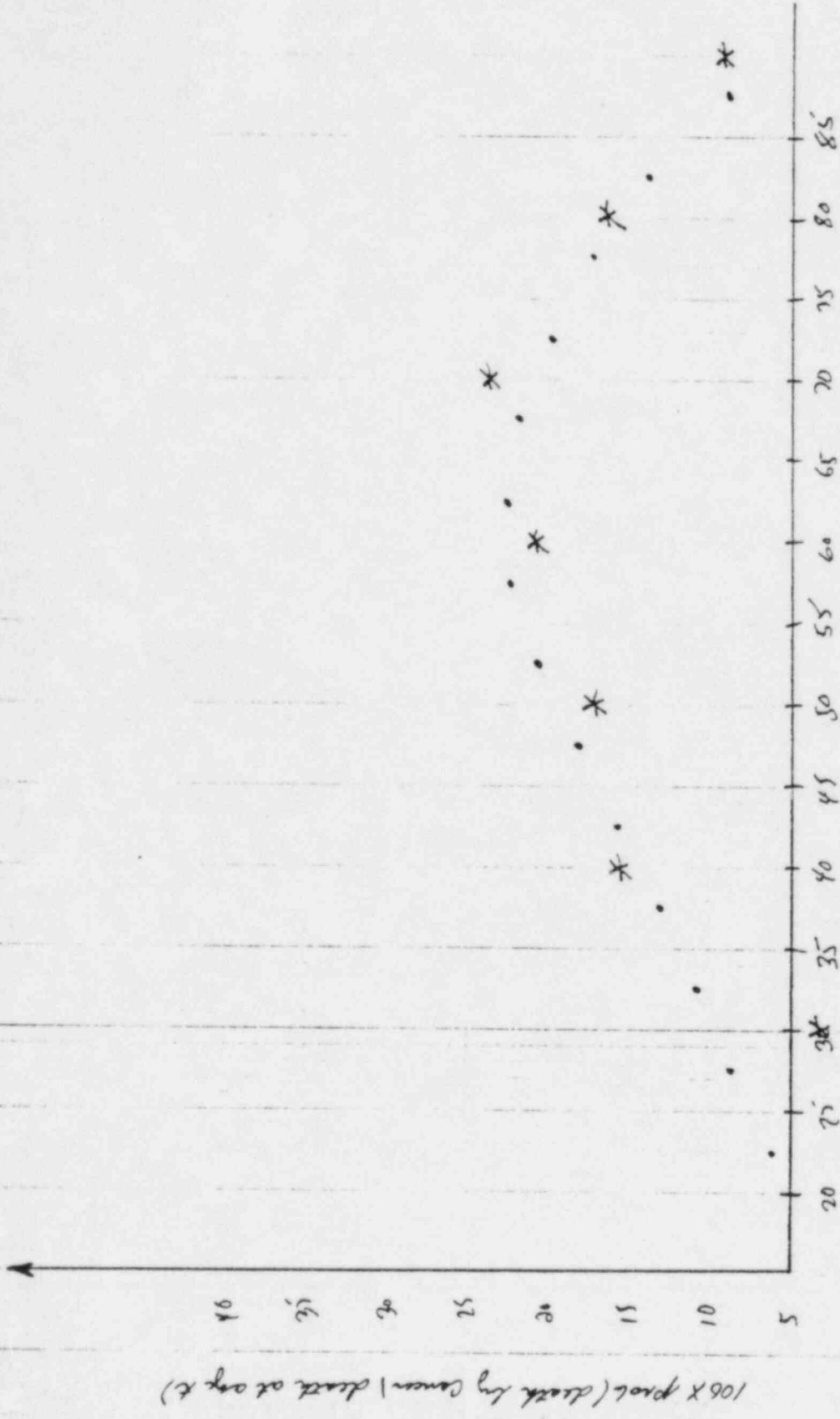
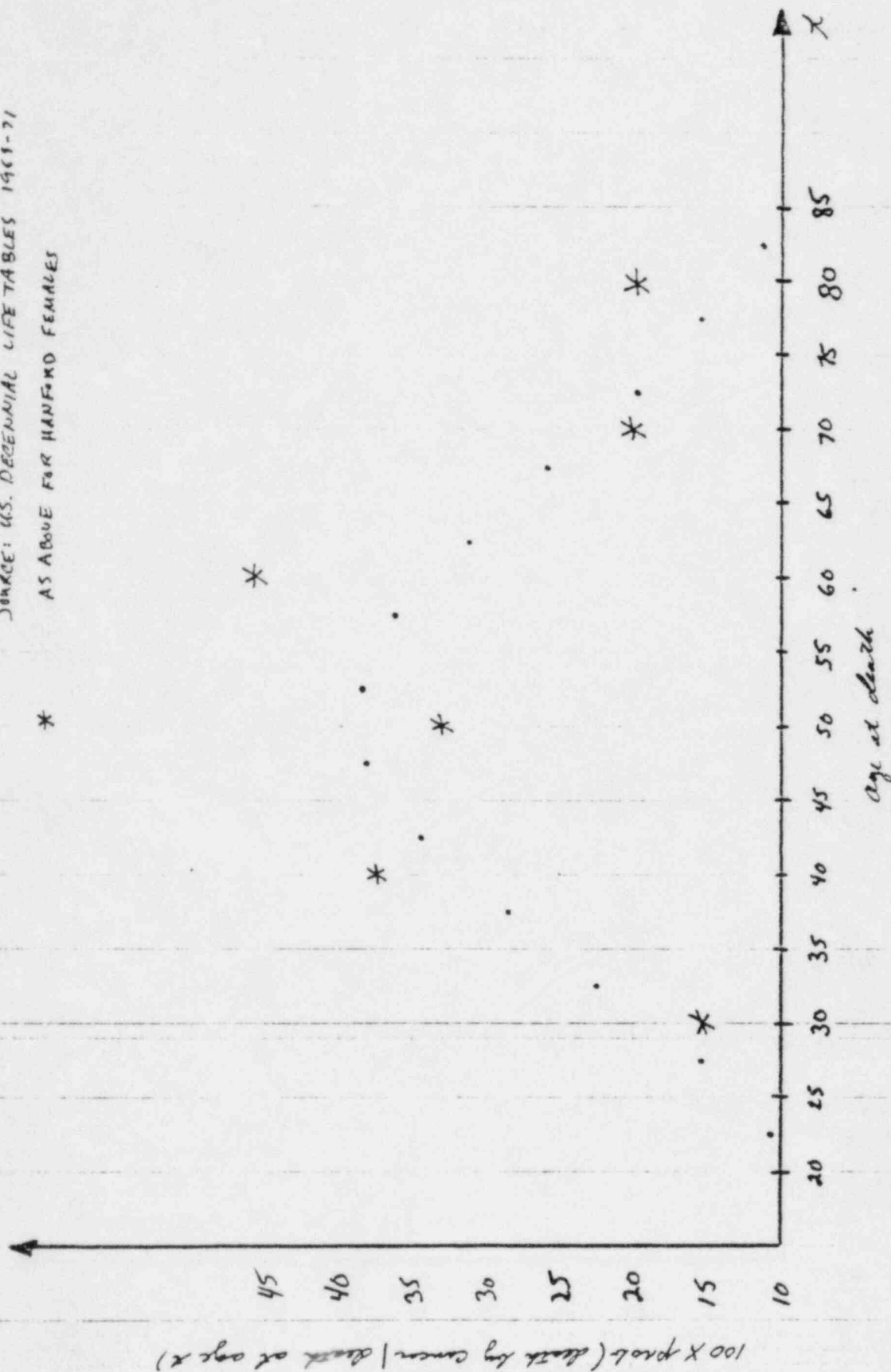


FIGURE 2

• CHANCE OF DEATH BY MALIGNANT NEOPLASMS
FOR MALES GIVEN DEATH AT AGE X
SOURCE: U.S. DECENNIAL LIFE TABLES 1969-71
* AS ABOVE FOR HANFORD FEMALES



explanation is age.

Another problem is that the individual variables may be highly inter-correlated leading to results which are difficult to interpret.

Regarding the first possible problem, the form of the cancer death ratio is of primary interest. The cancer death ratio for the male and female general populations of the United States was computed. The results are shown on the following pages. It is clearly observable that the cancer death ratio is not increasing with age at death after age 60 for men and after age 50 for women. The cancer death ratio which was derived for the men and women of the cohort is shown on the same axes. This implies that, even if lifetime dose and age at death are correlated, that confounding of the effects of increasing dosage and increasing age is not a problem of practical concern for this study.

To address the problem of the degree to which the independent variables in the discriminant model are correlated, a matrix of correlation coefficients was computed for the independent variables used in the discriminant models to be derived. The correlation matrix for males is given below.

TABLE 36

Correlation Matrix for Males*

	life dose	average rate	peak rate	years exposed	age at death	year of death
life dose	1	.854	.929	.257	-.034	.182
average rate		1	.907	.129	-.128	.082
peak rate			1	.239	-.076	.158
years exposed				1	.24	.494
age at death					1	.3827
year of death						1

*All correlation coefficients significant at .05

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Some important observations on this correlation matrix are:

- . Three of the radiological variables are strongly intercorrelated. These are lifetime dose and the two variables which were derived from it, so intercorrelation is not surprising.
- . Age at death shows slight negative correlations with lifetime dose, average rate, and peak rate. This again points up the fact that age and age correlated factors will not be confounded with these three radiological variables.
- . Age at death is correlated with years of exposure for the male subpopulation of the cohort.
- . Year at death and age at death are correlated.

-The correlation matrix for the independent variables used in predicting which females in the cohort died of cancer is shown on the accompanying Table 36. Some important observations about this correlation matrix are:

- . There is no significant correlation between age at death and lifetime dose, average rate of exposure, peak rate of exposure, and years exposed.
- . As with the males, the radiological variables are inter-correlated among one another.
- . Years exposed is correlated with age at death

These observations will be recalled in order to clarify the interpretation of the discriminant models which have been constructed for this study.

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TABLE 37

Correlation Matrix for Females

	life dose	average rate	peak rate	years exposed	age at death	year of death
life dose	1	.881*	.945*	.426*	.074	.09
average rate		1	.889*	.389*	.04	.039
peak rate			1	.423*	.064	.065
years exposed				1	.095	.221*
age at death					1	.095*
year of death						1

*Significant at the .05 level of confidence.

In many cases, such as the highly correlated radiological variables used here, the complete set of independent variables at hand contain redundant information about the difference between the two groups being investigated. In some cases the variables at hand may not be useful in discriminating the members of one group from the members of the other. Sequential selection procedures for variables to be used in discriminant models have been developed. In this analysis a generalized distance measure (V which was proposed by C.R. Rao) is used. The final discriminant model is constructed in a step-wise manner one variable at a time. First, the variable which produces the greatest distance between the groups is used to create a single variable prediction for group membership. Thereafter, the model is sequentially augmented by the variable from the full set which adds most to the distance between groups already attained with the previous

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variables. Often a reduced set of variables can be found which is almost as good, or even better than the full set. When no variable from the full set can be found which increases the distance of the two groups from one another, the analysis is terminated. The interested reader is referred to the references listed under statistical methods in the bibliography. The test of significance for each of the variates as they are added to the model can be found in Cooley and Lohnes (1971 page 175).

The first discriminant analysis which was conducted was based on the male population and the following set of variates:

- . Cancer death ratio for males (CDRM)
- . Peak exposure rate
- . Lifetime dose*
- . Average rate of exposure
- . Year at death
- . Years exposed

The actions taken in the step-wise procedure are summarized on Table 37. Of the six available variables, three entered the model.

*Coded as 0=0, 1-99=1, 99+=2. The raw lifetime dosages never entered into the models generated by step-wise methods. Raw dosages in fact decreased the distance between the cancer and not-cancer groups.

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TABLE 38

Step-wise Discriminant Analysis-Males

step	variable entered	Rao's V	ΔV	significance
1	CDRM	47.72	47.72	$p < .00009$
2	* year at death	51.53	3.81	.05
3	life dose*	52.79	1.26	.26

*Coded as 0=0, 1-99=1, 99+=2. The raw lifetime dosages never entered into the models generated by stepwise methods. Raw dosages in fact decreased the distance between the cancer and not-cancer groups.

For the male subpopulation, in the aggregate, only one radiological variable enters and it is not associated with subsequent death by cancer at an even marginal level of significance. However, since significant variability from age bracket to age bracket was observed for the association of simple exposure with cancer death using the Mantel-Haenzel procedure in the previous section an age stratified analysis was undertaken here as well. For each of the age brackets previously described, a step-wise discriminant analysis was performed. The findings for each age bracket were:

- . 25-34 - Only two cases of cancer caused death were found so no significant findings were possible.
- . 35-44 - No significant predictive variables were found.
- . 45-54 - Years exposed is correlated (canonically) at the .001 level of confidence with subsequent death by cancer. The average rate of exposure enters the model but is significant only at .09.

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- . 55-64 - No variables were significantly associated with subsequent cancer death.
- . 65-74 - No variables were significantly associated with subsequent cancer death.
- . 75-84 - The average rate of exposure was associated with subsequent cancer death with p-value .0001, 2nd year of death at .035.
- . 85-94 - No radiological variables were significantly associated with subsequent cancer death.

For each of the two age brackets in which significant findings were uncovered, the step-wise analysis is presented in a table. First, for the 45-54 age bracket we have:

TABLE 39

Step-wise Discriminant Analysis
Males ages 45-54 at death

step	variable entered	Rao's V	ΔV	significance
1	years exposed	10.55	10.55	.001
2	life dose	13.45	2.39	.089

Canonical Correlation: .157, significance: .001

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The power of this model to predict who in this age bracket died from cancer is shown in the following four-fold table:

<u>Actual</u>	<u>Predicted</u>	
	not-cancer	cancer
not-cancer	328	157
cancer	46	46

From which it can be seen that the model correctly predicts 328 of 531 or 61.77 percent of the cases.

As was noted earlier, the years exposed variable is correlated with age at death, but in a single age bracket this is of no great concern. It is to be noted that increasing periods of exposure point towards increasing risk of cancer death.

Turning now to the other age bracket in which significant results were focused we have the following:

TABLE 40

Step-wise Discriminant Analysis
Males ages 75-85 at death

step	variable entered	Rao's V	ΔV	significance
1	average rate	15.68	15.68	.0001
2	year of death	20.11	4.4	.0353

Canonical Correlation: .17, significance: .0001

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The predictive power of this model is expressed in the following table:

<u>Actual</u>	<u>Predicted</u>	
	not-cancer	cancer
not-cancer	404	160
cancer	68	45

From which it can be seen that the model correctly predicts 449 out of 677 or 66.3 percent of the cases correctly with high average rates pointing in the direction of increasing cancer risk.

The method of step-wise discriminant analysis was applied to the women of the cohort. The variables available for inclusion into the model are the same as were available for the males except for the cancer death ratio (CDRF), which was computed specifically for the female sub-sample. The lifetime dose was again coded as was that for the males. When the raw lifetime dose scores were made available to the step-wise discriminant procedure the variable was not included in the model because it decreased the inter-group separation rather than increasing it - even trivially. The table describing the course of the stepwise discriminant analysis for the female subpopulation is shown on the following page (Table 39). Two of the radiological variables are associated with subsequent cancer death at a p-value of .06. This is not quite significant to a classical degree of one chance in twenty. They are significant to one chance in 16.67. This is obviously a borderline value. It is to be observed, however, that this degree of association arises from

TABLE 41

Step-wise Discriminant Analysis-Females

step	variable entered	Rao's V	ΔV	significance
1	CDRF	25.68	25.68	$p < .00009$
2	peak rate	29.09	3.41	.06
3	years exposed	32.52	3.43	.06
4	average rate	33.86	1.34	.24
5	life dose	36.36	2.5	.11

Canonical Correlation: .295, significance: $p < .00009$

the rather small set of cases available in the cohort which were female. This result must be called ambiguous at this time. As more data become available the question should be reinvestigated. The addition of a few hundred cases may suffice to settle the issue.

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