BIOLOGICAL EFFECTS OF LOW LEVEL EXPOSURES: DOSE-RESPONSE RELATIONSHIPS

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CHAPTER 11

Positive Health Effects of Low Level Radiation in Human Populations

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Increased longevity and decreased cancer death rates have been observed in populations exposed to high natural background radiation and reported for several decades.[1-3] These observations contradict the radiation paradigm that all radiation, including that of natural background, is harmful in linear proportion to low level dose. Such observations have been considered by recognized radiation scientists to be spurious or inconclusive because of unreliable public health data or undetermined confounding factors such as pollution of air, water and food, smoking, income, education, medical care, population density, and other socioeconomic variables. Attempts to establish a threshold level below which radiation is not harmful have been negated by the great difficulty of obtaining accurate data on large human populations required to demonstrate the absence of very low risks of low-level radiation predicted by linear extrapolation of high-level radiation health effects. During the past four years, however, several epidemiologic studies have demonstrated that exposure to low or intermediate levels of radiation have apparently resulted in positive health effects.

Low Level Radiation of Nuclear Shipyard Workers

A ten-year study by the Johns Hopkins Department of Epidemiology, School of Public Health and Hygiene, of nuclear shipyard workers was concluded recently.[4] The Technical Advisory Panel (TAP), chaired by Arthur C. Upton, advised on the research and reviewed results. John Cameron, a member of the TAP, summarized the study and stated, "This study is probably the best evidence that low levels of ionizing radiation are without health hazard."

The results contradict the conclusions of the BEIR V report that small amounts of radiation have risk – the linear risk hypothesis.[5] The database

of almost 700,000 shipyard workers included almost 108,000 nuclear workers with exposures beginning in the 1960s until the end of 1981. Three study groups were selected: 33,352 non-nuclear workers (NNW), 10,462 nuclear workers with a working lifetime dose equivalent (DE) of less than 5mSv ($NW_{<5}$), and 28,542 nuclear workers with a DE greater than or equal to 5mSv ($NW_{>5}$). Five mSv (0.5rem) is approximately equal to the sea-level background radiation (340 mr/yr) one would receive in 1½ years. Deaths in each group were classified as due to: all causes, leukemia, lymphatic and hematopoietic cancers (LHC), mesothelioma, and lung cancer. The only cancer that showed a significantly increased incidence in the exposed groups as well as the NNW was the rare malignancy mesothelioma (36 deaths), a marker for asbestos exposure that is also associated with lung cancer. The data are summarized in Table 11.1.

The nuclear worker groups had a lower death rate from all causes, leukemia, and LHC than the non-nuclear workers. These apparently beneficial effects of low dose irradiation are consistent with the increased longevity and 15% lower mortality and cancer death rates seen in the seven western states with high natural background radiation averaging about 1mGy per year above that of the other states.[1-17]

The non-nuclear workers' death rates exactly matched those of the external non-shipyard matched control population. This demonstrates absence of the external healthy worker effect ascribed to adequate income, better health care, and the presence of health sufficient to allow maintenance of a reliable work schedule. There remains the question of an internal healthy worker effect resulting from the possible selection of more active individuals to be nuclear workers. The $NW_{>5}$ group with the greater exposure had a death rate from all causes of 0.76 the standardized mortality rate (SMR),

Table 11.1. Health Effects of Low Level Radiation in Shipyard Workers

Cause of Death	$NW_{>5}$	$NW_{<5}$	NNW
All Causes	2,787	1,166	4,483
SMR	0.76	0.81	1.00
(95% C.I.)	(0.73, 0.79)	(0.76, 0.86)	(0.97, 1.03)
Leukemia	21	4	29
SMR	0.91	0.42	0.97
(95% C.I.)	(0.56, 1.39)	(0.11, 1.07)	(0.65, 1.39)
LHC[a]	50	13	84
SMR	0.82	0.53	1.1
(95% C.I.)	(0.61, 1.08)	(0.28, 0.91)	(0.88, 1.37)
Mesothelioma	18	8	10
SMR	5.49	6.14	2.34
(95% C.I.)	(3.03, 8.08)	(2.48, 11.33)	(1.16, 4.43)
Lung Cancer	237	98	308
SMR	1.07	1.11	1.13
(95% C.I.)	(0.94, 1.21)	(0.90, 1.36)	(1.02, 1.29)

[a]Lymphatic and Hematopoietic Cancers

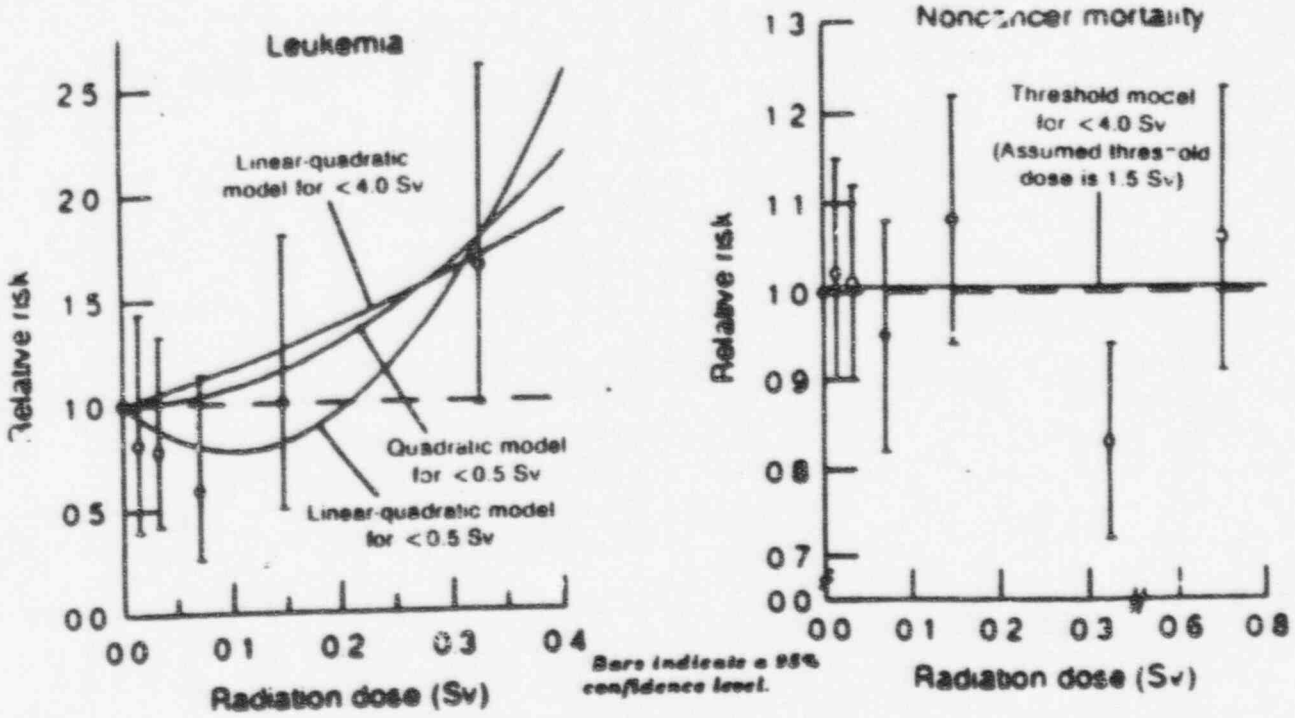
16 standard deviations below that of the non-nuclear worker group (NNW). The $NW_{<5}$ with lesser exposure had 0.81 SMR, about 8SD below the NNW. While a possible internal healthy worker effect could contribute to the lowered SMR of nuclear workers, comparison of the $NW_{>5}$ group with the $NW_{<5}$ group demonstrates that the group with the greater dose had the lower SMR with even greater statistical power. This provides very strong evidence that low levels of ionizing radiation are without health hazard.

Leukemia and Mortality of Atomic Bomb Survivors Exposed to Low Level Radiation

A recent article by Shimizu, et al.[10] concerning the effects of low level radiation in atomic bomb survivors concluded that analysis of dose response "in the less-than-0.5Sv region fails to indicate the presence of hormesis." They did not observe any significant decrease in the relative risks (RR) of (a) leukemia, (b) all cancers except leukemia, (c) lung cancer, (d) thyroid cancer, or (e) noncancer mortality. This conclusion is in agreement with the data shown for the three cancer groups (b,c,d), but appears inconsistent with the data presented for the RR of the leukemia and noncancer mortality groups.

The upper half of Figure 11.1 shows the data for these two groups as analyzed by the authors with a variety of models. The discussion of leukemia states that though the RR is less than 1 for the three groups with doses less than 0.1Sv, since all had $p > 0.10$ they did not differ statistically from unity and thus, were within the range of random variation. In clear contradiction to least square fits, the quadratic model for <0.5Sv was considered to better fit the data than the linear-quadratic model for <0.5Sv that demonstrated a RR of 0.78 at 0.11Sv. The lower half of Figure 11.1 shows analysis of the data with models that provide a better fit. The five data points for leukemia are fitted by an empirical polynomial function. The RR for the 0.010 to 0.019, 0.020 to 0.049, and 0.050 to 0.099 Sv dose categories appear consistently related to one another, not varying randomly. The RR of 0.6 plotted at 0.075Sv is 1.5SD less than 1 ($p < 0.15$). This study of atomic bomb survivors is in agreement with the decreased leukemia mortality seen in the nuclear shipyard worker study. In both studies the very low incidence of leukemia makes it difficult to obtain sufficient numbers for high statistical power.

Desired statistical power is present, however, for mortality rates. In the upper half of Figure 11.1 the RR data for noncancer mortality after low-level radiation are ignored and fitted with a threshold model derived from a prior study of survivors in the <4.0Sv high-level dose range, assuming the threshold dose is 1.5. Though the mortality RR of 0.83 in the 0.200 to 0.499 Sv dose category is 3.2 SD below 1 ($p = 0.001$) and is the most statistically significant data point of the entire study, nevertheless, this highly significant decreased RR is rejected with the statement, "The RRs for the sub-


Leukemia
Relative risk
2.5
2.0
1.5
1.0
0.5
0.0
Linear-quadratic model for < 4.0 Sv
Quadratic model for < 0.5 Sv
Linear-quadratic model for < 0.5 Sv
0.0
0.1
0.2
0.3
0.4
Radiation dose (Sv)
Bars indicate a 95% confidence level.
Noncancer mortality
Relative risk
1.3
1.2
1.1
1.0
0.9
0.8
0.7
0.0
Threshold mocel for < 4.0 Sv (Assumed thres-old dose is 1.5 Sv)
0.0
0.1
0.2
0.3
0.6
0.8
Radiation dose (Sv)

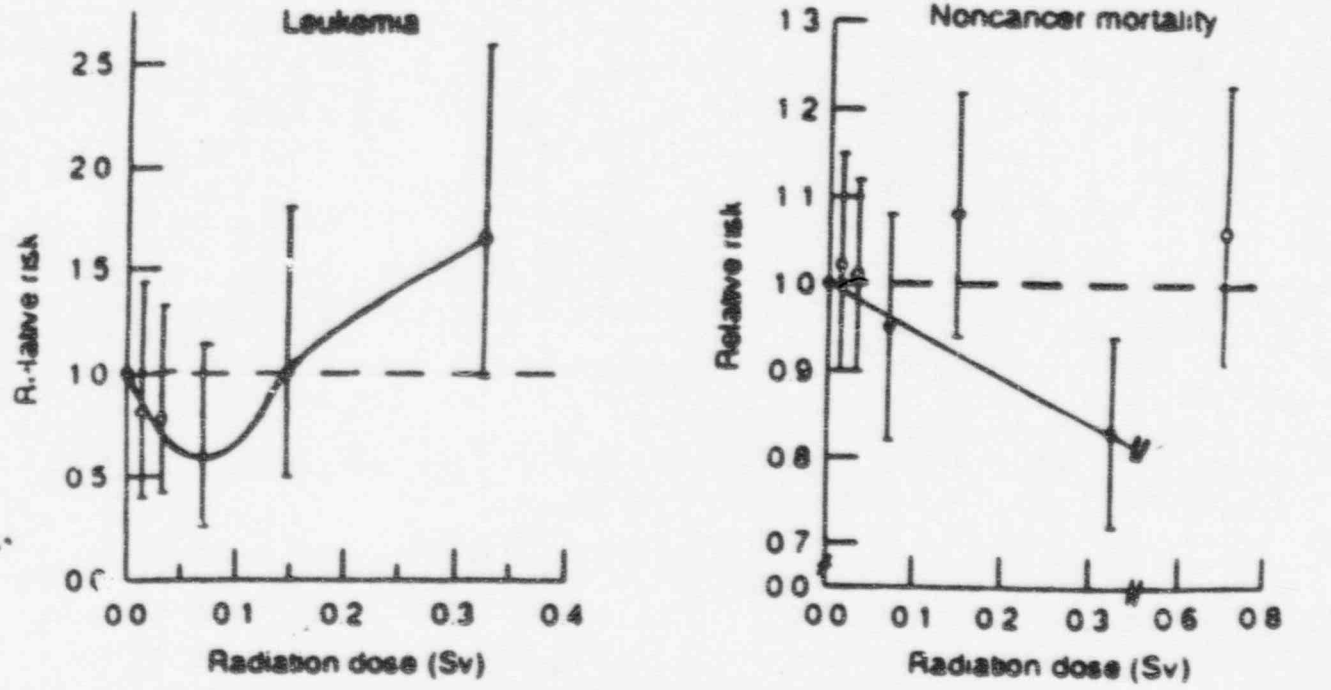


Figure 11.1. Dose-response analysis of atomic bomb survivors exposed to low-level radiation. The upper pair of relative risks of leukemia and noncancer mortality show the best fit models of the authors to their data. The lower pair of relative risks show the best fit models of the author of this review to their data.

groups within the low dose group (<0.5Sv) when compared with the 0 Sv group did not differ and were close to unity." If the only mathematical models used for analysis are those that a priori exclude a U-shaped dose-response relationship, it is not surprising that such analysis "fails to indicate the presence of hormesis." The lower half of Figure 11.1 fits a linear model down to, but no farther than, the noncancer mortality RR of 0.83. This decreased mortality risk associated with acute low-level radiation is consistent with the highly significant (-16SD and -8SD) decreased standardized mortality rates observed in prolonged very low level exposures of the nuclear groups of shipyard workers.[8]

Effect on Lifespan of Low-Intermediate Doses of Atomic Bomb Radiation

The above-mentioned decreased mortality risk reported by the US-Japan Radiation Effects Research Foundation (RERF) study of Hiroshima and Nagasaki is also consistent with the recent article on Nagasaki survivors from Nagasaki University and the Atomic Energy Research Institute, Kinki University, Japan. Mine et al. report upon the "apparently beneficial effect of low to intermediate doses of A-bomb radiation on human lifespan."[11] The decreased RR of noncancer male deaths to 0.65 ($p<0.05$) in the 0.50–0.99Gy dose range was to a large extent offset by the RR increase to 1.56 in cancer deaths (Table 11.2B). The male RR for total deaths in this dose range was 0.88 (Table 11.2A), with low statistical power ($p=0.34$). Fitting of a U-shaped dose-response relationship confirmed the significantly lower male RR for noncancerous diseases with maximum reduction to 0.76 ($p<0.02$) in the 1.00 to 1.49, average 1.08,Gy dose range (Table 11.2C). Female survivors, on the other hand, showed no significant change in RR of death from all causes until the 2.00 to 5.99Gy dose range was reached, in which there was a rise of the RR of both cancer deaths ($p<0.01$) and total deaths.

This significant difference in gender response to low and intermediate acute doses of radiation parallels the observations of Lorenz et al.[12] and Congdon[13] regarding comparison of the survival of male and female mice exposed to 0.0011Gy delivered in 8 hours daily from age 2 months to death. The longevity of irradiated male mice was significantly increased to 115% of irradiated controls (783 days vs 683 days). However, the longevity of female mice did not increase significantly above their control level of 803 days that was nearly matched by the extended lifespan of the irradiated male mice. Human populations also demonstrate that female longevity is greater than that of the male. These results suggest that low level irradiation of men and mice may stimulate a physiologic process in the male, relatively unenhanced in the female, that enables male longevity to approximate that of the female.

Table 11.2. Total Deaths and Relative Risks of Male and Female A-Bomb Survivors in Nagasaki During 1970–1985 Classified by T65 Dose

A. Initial numbers of subjects (1970), observed (*O*) and expected (*E*) numbers of total deaths and relative risk in 1970–1985 in Nagasaki among A-bomb survivors classified by T65D dose and sex.

T65D Dose (cGy)	Initial No. of Subjects		Total Deaths				Relative Risk (*O*:*E*)	
			Observed		Expected		All Causes	
	M	F	M	F	M	F	M	F
1–49	582	936	162	202	106·7	209	1·01	0·97
50–99	182	166	56	39	63·3	34·7	0·88	1·12
100–149	108	158	36	39	39·7	34·7	0·91	1·12
150–199	196	267	56	46	56·7	46	1·01	1·00
200–589	440	437	172	79	149·7	59·3	1·15	1·33

B. Observed (*O*) and expected (*E*) deaths in 1970–1985 in Nagasaki among A-bomb survivors classified by natural causes of death, sex and T65D dose.

Dose (cGy)	Number of Deaths from:			
	Non-Cancerous Diseases		Cancer	
	O	*O*:*E*	*O*	*O*:*E*
Males				
1–49	126	1·09	35	0·84
50–99	30	0·65	26	1·58
100–149	23	0·77	13	1·34
150–199	38	0·84	21	1·58
200–589	113	1·07	54	1·32
Females				
1–49	144	0·89	58	1·24
50–99	70	1·11	8	1·10
100–149	26	0·96	13	1·66
150–199	31	0·91	16	1·60
200–589	50	1·11	29	2·11

C. Calculated (μ_i) values by the logistic function $p = 1/[1 + \exp\{-a - b_1(D - \langle D \rangle) - b_2(D - \langle D \rangle)^2 - cA\}]$ and observed (*O*) values for deaths from non-cancerous diseases in males in Nagasaki classified by T65D dose.

Dose (D_i) (cGy)	Number of Non-Cancer Deaths			
	Observed (*O*)	Corrected *O*:*E*	Calculated (μ_i)	Corrected μ_i:*E*
27 (1–49)	126	1·07	123	1·05
79 (50–99)	30	0·88	35·3	0·80
108 (100–149)	23	0·80	21·9	0·76
167 (150–199)	38	0·88	35·3	0·82
286 (200–589)	113	1·11	113·1	1·11

$\langle D \rangle$ = 130; a = −6.14 ($p < 0.01$); b_1 = 0·29 × 10^{-3} (p NS); b_2 = 0·213 × 10^{-4} ($p < 0·02$); c = 0·115 ($p < 0·01$).

NS = not significant.

Correlation of Lung Cancer Risk with Radon in Homes

The BEIR IV report [14] based upon a linear-no threshold extrapolation of the incidence of lung cancer in uranium mine workers exposed to high radon concentrations, predicts that the lifetime mortality risk of lung cancer is increased linearly by 10.8% per $pCiL^{-1}$. One $pCiL^{-1}$ approximates the world average[15] and is equivalent to 0.2 working-level-month (WLM).[16] The American Cancer Society projects for the United States 170,000 new cases of lung cancer in 1993.[17] Accordingly, prior continued home exposure of the population to one additional $pCiL^{-1}$ of radon would have produced 18,000 additional new cases of lung cancer in 1993. Five-year survival of treated lung cancer is only slightly more than 10%.[17] Relying upon the BEIR IV theoretical prediction, the Environmental Protection Agency (EPA) considers radon in the home to be the nation's leading health hazard.

However, there is no epidemiologic evidence to support the risks predicted by BEIR IV. To the contrary, epidemiologic studies in the United States,[18-20] Sweden,[21] Finland,[22] and China,[23] with increased radon concentrations up to 12 $pCiL^{-1}$, as well as in these areas below the average radon concentration of $1 pCiL^{-1}$,[24-26] have all demonstrated a negative correlation of lung cancer with radon concentration. For a variety of reasons, these studies which contradict the linear-no threshold theory have been considered invalid by the National Academy of Sciences Committee on Biological Effects of Ionizing Radiation, National Council on Radiation Protection and Measurements, and the International Commission on Radiologic Protection. Criticisms have included poor statistical power, inadequate controls, and inadequate determination of the degree to which data have been altered by smoking and confounding factors such as numerous socioeconomic variables, geography, altitude, and climate. An extensive University of Pittsburgh National Survey of radon in homes was completed in 1992 that addresses these criticisms with excellent statistical power.

The University of Pittsburgh nationwide study based upon 272,000 measurements in the homes of 1217 counties was completed in 1992. This study and nine individual state studies were normalized to the EPA National Residential Radon Survey. The combined data set compiled from Pittsburgh, states, and EPA studies includes 1729 counties containing nearly 90% of the U.S. population. After deleting Arizona, California, and Florida, states with high retirement migration, and counties with incomplete data, 1601 counties remain included.[27] Figure 11.2 shows plots of mean age-adjusted lung cancer mortality rates (m) for white males (Figure 11.2a) and females (Figure 11.2c) vs mean radon levels (r) in homes of all counties within various ranges of r, along with the standard deviation of the mean, first and third quartiles, and the best linear fit to the data for individual counties, $m = 1a(1 + br)$. These mortality rates are corrected for smoking by use of Bureau of Census Population Surveys of smoking prevalence and BEIR IV risk estimates for smokers and nonsmokers, and are shown

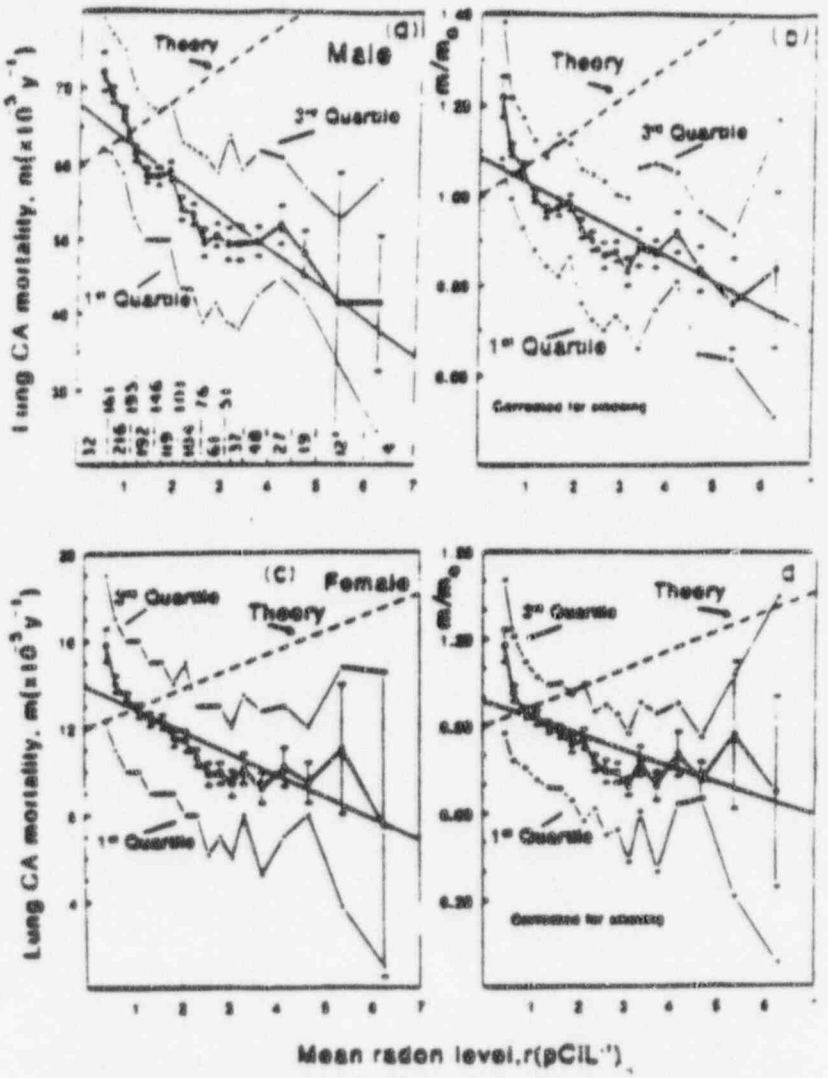


Figure 11.2. Lung cancer mortality rates in male (11.2a) and female (11.2c) residents vs mean radon level for 1601 counties. Data points shown are average of ordinates for all counties within the range of r-values shown on the baseline of Figure 11.2a, the number of counties within that range is also shown there. Error bars are standard deviation of the mean, and the first and third quartiles of the distribution are also shown. Figure 11.1b, 1d are m/m_o vs r which incorporate the effects of smoking prevalence. Theory lines are arbitrarily normalized lines increasing at a rate of $7.3\%/r_o$.

together with the best linear fit, $M = m/m_o = A + Br$ in Figures 11.2(b) and 11.2(d). BEIR IV theory lines are normalized lines with slope B increasing mortality at a rate of 7.3%/pCiL^{-1}. After correction for variations in smoking frequency, there is a very strong tendency for lung cancer mortality to decrease with increasing mean radon level in homes, in sharp contrast to the increased mortality expected from the linear-no threshold theory. The discrepancy between theoretical and measured slopes is by 20 standard deviations. An earlier study based upon data for 965 counties furnished additional details of methodology and somewhat less steep negative slopes of m/m_o vs r, with the discrepancy between theoretical and measured slopes by 7 standard deviations.[28]

Correction for the effects of smoking was made using the separate risk estimates for smokers and nonsmokers given by BEIR IV theory and estimations of the fraction(s) of the adult populations that smoke cigarettes in each county derived from Bureau of Census Surveys, with a correction factor for the fraction of the county population that lives in an urban area. The resultant slopes (B) in units of % per pCiL^{-1} are -7.3 ± 0.6 SD males and -8.3 ± 0.8 females, discrepant by 20 SD with the slope expected from BEIR IV theory, $B = +7.3$. Many other factors in addition to smoking are carefully analyzed to see whether any can explain this discrepancy. Pittsburgh radon measurements are consistent with EPA and state measurements. Potential problems concerning outliers and sampling issues are demonstrated to be absent. Uncertainties in lung cancer mortality rates (m) and smoking prevalence(S) are given elaborate consideration and shown to be unimportant causes of the discrepancy between theoretical and measured slopes.

A careful investigation was made of the possibility that one or more socioeconomic confounding factors other than smoking could correlate strongly and with opposite signs with both m and r. Those would introduce a strong negative correlation between m and r which would not be due to a direct causal relationship. The 54 socioeconomic variables (SEV) which are analyzed singly and in combination are listed in Table 11.3. The 54 values of B free of confounding by each SEV vary for males from -5.6 to -7.7, mean -6.9 ± 0.5, and for females from -5.4 to -9.1, mean -7.7 ± 0.8, and are quite close to values for the entire data set -7.3 and -8.3, respectively. Extensive statistical analysis of the possibility that some combination of SEV may act cooperatively to confound the m-r relationship concluded that the actual effect of confounding by combinations of SEV is to reduce the discrepancy between slopes by no more than 10%. Confounding by geography was also analyzed by considering the 34 states with at least 20 counties having known radon levels. The average of B-values is -6.1 for males and -7.2 for females; reductions in the discrepancy by 8.2% and 7.1%, respectively.

In addition to the 54 SEV and geography, also considered are the possible confounding physical features of altitude, average winter and summer temperatures, inches of precipitation, number of days per year with more than

Table 11.3. Socioeconomic Variables Used in the Analysis for Radon Radiation Lung Carcinogenesis in the Low Dose, Low Dose Rate Region

Population Characteristics	
PT-	total population
PD-	population/square mile
PI-	% pop. increase 1980–86
PU-	% in urban areas
PW-	% white
PS-	males/100 females
PE-	% age > 64y
PO-	% age > 74Y
PY-	% 5–17 years old
PN-	% born in state
PH-	persons/household
Vital and Health Statistics	
VS-	births/1000 pop.
VC-	% births to mothers < 20y
VD-	deaths/1000 pop.
VI-	infant deaths/1000 births
VM-	marriages/1000 pop.
VS-	divorces/1000 pop.
VP-	physicians/100,000 pop.
VH-	hospital beds/100,000 pop.
Social	
SS-	social sec. benefit/1000 pop.
SC-	crimes/100,000 pop.
SH-	% high school grad.
SU-	% college grad.
SE-	$/cap for education
Housing	
HO-	% owner occupied
HA-	% with > 1 automobile
HV-	median value ($)
HN-	% < 5 years old
Economics	
EI-	$ per capita income
EH-	median household inc., $
EJ-	% persons below poverty level
EV-	% fam below poverty level
EU-	% unemployment
EW-	average salary, wage
EP-	$ per cap personal income
EM-	% earnings from manufact.
ER-	% earnings from retail trade
ES-	% earnings from services
EG-	% earnings from government
EF-	% earnings from farming
EA-	av. acres per farm
EL-	% mfg. firms > 100 employs.
ED-	$/cap. sales–food stores
EC-	$/cap. sales–clothing
EX-	$/cap. sales–eating, drink
Government	
GF-	federal govt., $/cap
GL-	local govt., $/cap
GE-	% loc govt. expend.–educ.
GH-	% loc govt. expend.–health
GP-	% loc govt. expend.–police
GW-	% loc govt. expend.–welf
GR-	% loc govt. expend.–roads
GJ-	loc govt. employs/10,000 Pop.
GV-	% vote for lead party, 1984

0.01 inch precipitation, average wind speed, and percent of time with sunshine as compared with the maximum possible. Studies of these physical features concluded that none is an important confounding factor. The strong decrease in lung cancer mortality rates corrected for smoking frequency with increasing radon exposure is found in only the low altitude states or only the high altitude states; in only the warmest or only the coldest; in only the wettest or only the driest; etc. It is also found in only the states selected where the physical features are close to average. The BEIR IV theoretical prediction of lung cancer mortality from radon exposure corrected for smoking, $M = m/m_o = A + Br$, does not take into account two recognized r-S correlations: (1) urban houses have 25% lower radon levels than rural houses and urban people smoke more frequently, and (2) houses of smokers have 10% lower radon levels than houses of nonsmokers. An extensive statistical study of the effects of these r-S correlations leads to the

conclusion that the BEIR IV prediction of B is reduced from +7.3 to +6.9, which contributes very little to decreasing the discrepancy with the large negative values of B, -7.3 and -8.3 obtained from the actual measured and reported data.

Linear-no threshold theories other than BEIR IV are considered which involve different treatments of smoking. Also considered is the "intensity of smoking." Analytic statistical study of these considerations lead to the conclusion that other theoretical predictions of B could reduce the discrepancy between 3% and 8%. The possibility that an unrecognized confounding factor could explain the discrepancy is recognized. However, the following properties are required of an unrecognized confounder that could resolve the discrepancy: (1) It must have a very strong correlation with lung cancer, comparable to that of cigarette smoking, but still be unrecognized; (2) It must have a very strong correlation of opposite sign with radon levels; (3) It must *not* be strongly correlated with any of the 54 socioeconomic variables (SEV); (4) It must be applicable in a wide variety of geographic areas and independent of altitude and climate. The first property alone requires of the unrecognized confounder that it must have increased by orders of magnitude since the beginning of this century, and have been much more important in males in the first half of the century, with effects on females rapidly catching up in recent years. The remaining properties impose additional requirements that are also most difficult to meet singly, while to satisfy the four simultaneously becomes incredible. These multiple restrictions upon an unknown confounder make it extremely improbable that one exists that would resolve the discrepancy.

These tests of the linear-no threshold theoretical prediction of lung cancer mortality induced by radon exposure, with the slope of the line determined by high dose exposures, demonstrate that the theory fails badly by gross overestimation of mortality in low dose, low dose rate range of radiation. A likely explanation is that stimulated biological defense mechanisms more than compensate for the radiation "insult" and are protective against cancer in a low dose, low dose rate range.

Breast Cancer in Women Exposed to Low Level Radiation

The Canadian study of fluoroscoped women includes 31,710 patients admitted to national sanitoriums between 1930 and 1952 and alive on January 1, 1950.[8] The results relate deaths from breast cancer between 1950 and 1980 that occurred 10 or more years after first exposure to fluoroscopic radiation. Fluoroscopic examination in Nova Scotia was performed AP (anterior-posterior), with the patient facing the fluoroscope. This position increased the breast dose to 50mGy per exposure compared to 2mGy per exposure in all the other provinces in which the examination was performed PA (posterior-anterior), with the patient's back against the fluoroscope. The standardized mortality rates from breast cancer for various dose ranges

is shown in Table 11.4 with the high dose, high dose rate data of Nova Scotia separated from the low dose rate data of the other provinces.

Linear and linear-quadratic dose-response models were compared with respect to data fit. The authors concluded "that the most appropriate form of dose response relation is a simple linear one, with different slopes for Nova Scotia and the other provinces." On the basis of this linear model, Table 11.5 predicts the lifetime excess risk of death from breast cancer after a single exposure to 1cGy, an amount approximately three times the average annual background radiation.

The epidemiologic data listed in Table 11.4 and the associated fitted models were not presented graphically. The omitted graph is shown in Figure 11.3, together with an empirical polynomial function fitted to the data. The linear model for 2mGy exposures discards the data at 0.15Gy and

Table 11.4. Canadian Study of the Incidence of Breast Cancer Following Fluoroscopic Examinations

Dose Gy	Standardized Rate Per 10^6 Person Years		
	Nova Scotia	Other Provinces	All Provinces
0–0.09	486.6 (131)	566.8 (288)	578.6 (301)
0.10–0.19		369.0 (29)	421.8 (32)
0.20–0.29		497.8 (24)	580.7 (28)
0.30–0.39	1709 (11)	630.5 (17)	650.8 (18)
0.40–0.69		632.1 (19)	610.0 (19)
0.70–0.99			1382 (13)
1.00–2.99	2080 (14)		1392 (17)
3.00–5.99	2811 (13)	873.1 (14)	2334 (.4)
6.00–10.00	7582 (8)		8000 (9)
≥ 10.00	21.810 (12)		20.820 (13)

*The number of deaths is shown in parentheses. The calculations exclude the values for 10 years after the first exposure and have been standardized according to age at first exposure (10 to 14, 15 to 24, 25 to 34, and ≥ 35 years) and time since first exposure (10 to 14, 15 to 24, 25 to 34, and ≥ 35 years) to the distribution for the entire cohort.

Table 11.5. Predicted Lifetime Excess Risk of Death from Breast Cancer per Million Women after a Single Exposure to 1 cGy

Age at Exposure Yr.	Additive-Risk Model	Relative-Risk Model
10	125	108
20	95	89
30	67	56
40	42	27

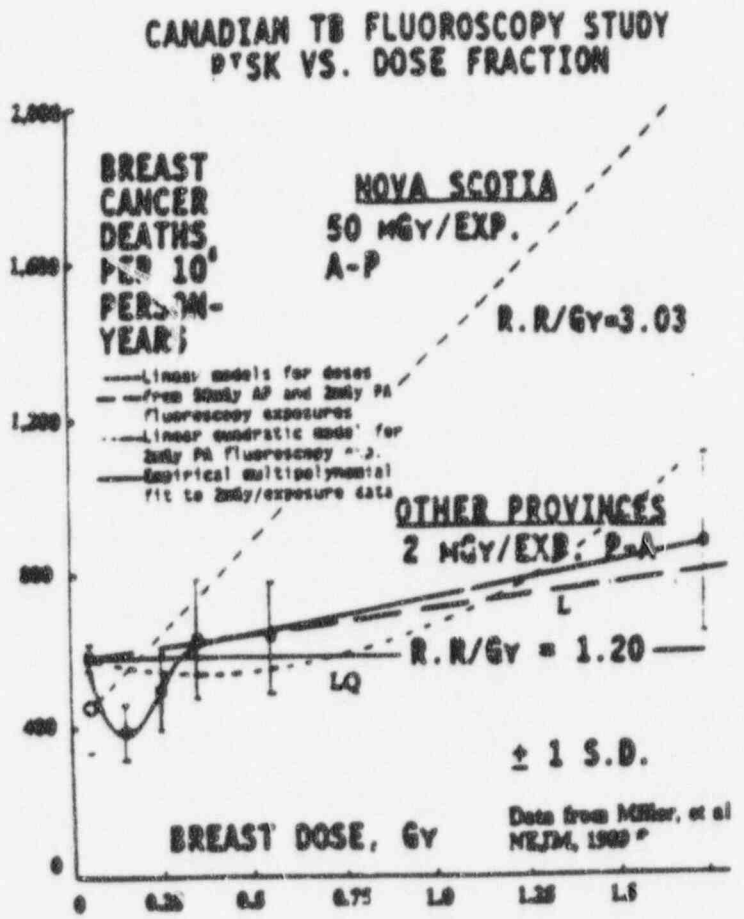


Figure 11.3. A graphic plot of the authors' data shown in Table 11.4. No graph was presented in their publication. The figure includes their "best fit" linear models, their linear quadratic model, and the best fit model of the author of this review to their data, an empirical polynomial function.

at 0.25Gy, the data with the best confidence limits. Compared to the controls receiving 0 to 0.09Gy, 0.15 Gy and 0.25 Gy demonstrate relative risks (RR) of 0.66 ($p < .01$) 0.85 ($p < .38$), respectively. While the RR of 0.85 is not statistically significant, it is consistent with the significant RR of 0.66 and the zero equivalent point of 0.31Gy indicated by the fitted polynomial function. For exposures above the zero equivalent point, the RR becomes positive after being negative in the range of 0 to 0.31 Gy. The decreased RR of breast cancer produced by low dose, low dose rate radiation were rejected a priori by the choice of mathematical models that extrapolate the

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dose-risk relation from high dose exposures to low dose exposures. The risks associated with low dose exposures cannot be measured, the authors state "because the expected small excess of breast cancers would be obscured by the much higher background rate of breast cancer." Consequently, the unexpected was rejected since the possibility of a measurable decreased risk associated with low exposures appeared to be inconceivable. The highly significant decreased RR of 0.66 at 0.15Gy and the RR of 0.85 at 0.25Gy, both with the highest confidence limits of the entire study, are not shown graphically, not even discussed. Instead, the linear model for 0.002Gy exposures is used in Table 11.5 to predict the lifetime excess risk of death from breast cancer to be approximately 60 per million women after a single exposure to 1cGy at the age of 36. Nine hundred excess deaths from breast cancer are predicted theoretically from the exposure of one million women to 0.15Gy. However, the quantified low dose data predicts with better than 99% confidence limits that instead of causing 900 deaths, a dose of 0.15Gy would prevent 10,000 deaths in these million women.

Significant positive health effects associated with low level radiation have been demonstrated in a review of five epidemiologic studies: decreased mortality of nuclear shipyard workers, decreased noncancer mortality of atomic bomb survivors in both Hiroshima and Nagasaki and Nagasaki alone, decreased lung cancer mortality associated with increased radon exposure of the U.S. population, and decreased breast cancer mortality of women in Canada after having received multiple fluoroscopic examinations. The tendency to neglect or reject data that contradicts the linear-no threshold theory of radiation carcinogenesis is supported by confidence that chromosome aberration and gene mutation can be produced by a single particle of ionizing radiation and so initiate a malignancy. The number of such interactions with cell nuclei is both logically and demonstrably proportional to the dose. However, no consideration is given to biological defense mechanisms that could be stimulated further by low level increments of radiation above the background level. Such stimulated defense mechanisms could also decrease carcinogenesis by chemical and other non-ionizing agents as well as high level ionizing radiation. Multiple defense mechanisms at molecular, cellular, organ, and systemic levels involving enzymatic, hormonal, immunologic, and stress protein interactions are currently being demonstrated and confirmed by numerous investigators.[10-12] Recently a human radiation repair gene has been cloned and transfected into a mutant Chinese hamster with sensitivity to both ionizing radiation and certain alkylating agents resulting from defective repair of DNA strand breaks. These transfected mutants demonstrate overexpression of the human DNA repair minigene with repair capacity increased above that of the wild-type Chinese hamsters.[13]

Mounting reproducible evidence of the operation of various defense mechanisms and their stimulation by low dose ionizing radiation will provide further details of how biological defense mechanisms, nonoperative at

high doses, are stimulated and enhanced by low level radiation damage so as to overcorrect and predominate. These investigations have clarified why the negative health effects observed at high levels of radiation that effectively overwhelm these defense mechanisms cannot be extrapolated to the low levels in which these stimulated defense mechanisms predominate with decreased cancer induction, decreased mortality, and other observed positive health effects.

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