CHAPTER 6

All-Cancers-Combined, Males: Relation with Medical Radiation

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The term "All-Cancers" includes all malignancies, no matter how uncommon. After Chapters 6 and 7 on All-Cancers, we limit the cancer-chapters to malignancies (or to groups of malignancies) where the number of annual deaths per 100,000 population has been large enough to make the numbers relatively reliable. Even so, in some of our cancer-chapters, the "small numbers problem" is worrisome. The smaller the numbers per 100,000, the greater are the impacts of random fluctuations and of various types of reporting errors.

"All-Cancers, Males" and "All-Cancers, Females" include, of course, those malignancies which are subsequently examined in separate chapters, as well as all the malignancies (such as leukemia) which are NOT examined in separate chapters.

Hypothesis-1: All-Cancers (Combined) vs. Specific Cancers

Hypothesis-1 is that medical radiation is the principal cause of cancer-mortality in the United States during the Twentieth Century.

It deserves emphasis that Hypothesis-1 concerns cancer in the aggregate --- All-Cancers (combined). We explore subsets in this book in order to learn their roles in the overall result, but Hypothesis-1 does not demand that the impact of medical radiation be the same for every type of cancer, or for the two sexes. Indeed, because Hypothesis-1 leaves plenty of room for contributions by nonradiation carcinogens (Part 6 of this chapter), we expect to observe some biology-based differences (not just statistical noise) among the cancer subsets which we explore.

Chapter 6 as the General Model for Other Chapters

The "materials and methods" of our studies have been set forth in Chapters 3, 4, and 5. Chapter 6 demonstrates the first results. Chapter 6 also provides the general model for studies in the rest of this monograph. Chapter 6 explains the boxes, figures, and table which will be standard items in many subsequent chapters --- where these standard items will need no text. Chapter 6 includes various comments which apply also to later chapters, but which will seldom be repeated.

For everyone's convenience, Chapter 22, Box 1, tabulates the results from Chapters 6 through 21 --- for easy comparison with each other.

• Part 1. All-Cancer Mortality Rates, Males

At the end of this chapter are Tables 6-A and 6-B. Table 6-A provides the mortality rates by the Nine Census Divisions, 1940-1988, and Table 6-B provides the NATIONAL mortality-rates, 1940-1988. Although this chapter requires the rates only for 1940, the post-1940 rates will be used in Section Five of the book. The ICD numbers change with time (Chapter 4, Part 2d).

• Part 2. How the Dose-Response Develops, 1921-1940

In Part 2, we regress the 1940 MortRates (from Table 6-A) upon the non-interpolated sets of PhysPop values 1921-1940 (from the Universal PhysPop Table 3-A). The summary-results of all the regression analyses are presented in Box 1. The correlations in Box 1, between PhysPop and the 1940 All-Cancer MortRates, steadily improve --- and Chapter 22 (Part 2) discusses why.

In our dose-response studies, PhysPops for the Nine Census Divisions represent the relative radiation doses accumulated from medical procedures, so they are the x-values in our linear regression analyses. The corresponding MortRates for the Nine Census Divisions are the responses to be studied, so they are the matching y-values. Both the x and the y variables have the denominator "per 100,000 population." The 1940 MortRates are the y-input for all ten regression analyses in this chapter.

The strongest dose-response relationship (Part 2j) has an R-squared value of 0.951 and a ratio of 11.6 for the X-Coefficient over its Standard Error. The strength of the correlation is rather dazzling. What follows are the linear regression analyses from which Box 1's summary arises.

Readers need to avoid a pitfall, as they inspect these regressions. The pitfall would be to imagine that the regressions examine correlations between various PRE-1940 cancer MortRates and PhysPop. No. There is only one set of MortRates --- the 1940 set --- because complete nationwide cancer-MortRate data do not exist for 1930 or 1920 or earlier (Chapter 4, Part 1). Therefore, the regressions examine how the 1921 to 1940 PhysPops "line up with" (correlate with) a single "end-point": The 1940 cancer MortRates. We can not predict WHICH set of PhysPops will display the highest observed correlation with the 1940 MortRates. It is worth remembering that the 1940 cancer MortRates are influenced by medical radiation received BEFORE 1921, as well as after 1921 --- because latency periods can last 40 years or longer in irradiated populations of mixed ages (Chapter 2, Part 8a).

• - Part 2a.	x 1921 PhysPop	y 1940 MortRate	All-Cancers, Males Regression Output:	
Pacific	165.11	122.9	Constant	-27.0754
New England	142.24	135.5	Std Err of Y Est	18.0748
West North Central	140.93	110.9	R Squared	0.4630
Mid-Atlantic	137.29	140.9	No. of Observations	9
East North Central	136.06	119.6	Degrees of Freedom	7
Mountain	135.38	99.8		
West South Central	125.15	86.9	X Coefficient(s)	1.0086
East South Central	119.76	73.6	Std Err of Coef.	0.4105
South Atlantic	110.32	88.9	Coefficient / S.E.	2.4568

• - Part 2b.	1923 PhysPop	1940 MortRate	All-Cancers, Males Regression Output:	
Pacific	163.06	122.9	Constant	-24.8337
New England	137.39	135.5	Std Err of Y Est	16.6440
West North Central	138.31	110.9	R Squared	0.5447
Mid-Atlantic	138.92	140.9	No. of Observations	9
East North Central	131.82	119.6	Degrees of Freedom	7
Mountain	130.51	99.8		
West South Central	119.16	86.9	X Coefficient(s)	1.0198
East South Central	113.16	73.6	Std Err of Coef.	0.3524
South Atlantic	106.79	88.9	Coefficient / S.E.	2.8937

• - Part 2c.	1925 PhysPop	1940 MortRate	All-Cancers, Males Regression Output:	
Pacific	161.67	122.9	Constant	-16.5482
New England	138.31	135.5	Std Err of Y Est	15.7102
West North Central	133.92	110.9	R Squared	0.5943
Mid-Atlantic	134.36	140.9	No. of Observations	9
East North Central	127.54	119.6	Degrees of Freedom	7
Mountain	122.30	99.8		

West South Central	112.83	86.9	X Coefficient(s)	0.9879
East South Central	107.22	73.6	Std Err of Coef.	0.3085
South Atlantic	103.61	88.9	Coefficient / S.E.	3.2024

• - Part 2d.

	1927 PhysPop	1940 MortRate	All-Cancers, Males Regression Output:	
Pacific	157.83	122.9	Constant	-20.9399
New England	137.50	135.5	Std Err of Y Est	13.1094
West North Central	131.54	110.9	R Squared	0.7175
Mid-Atlantic	138.40	140.9	No. of Observations	9
East North Central	126.18	119.6	Degrees of Freedom	7
Mountain	118.75	99.8		
West South Central	108.25	86.9	X Coefficient(s)	1.0399
East South Central	102.07	73.6	Std Err of Coef.	0.2466
South Atlantic	102.13	88.9	Coefficient / S.E.	4.2168

• - Part 2e.

	1929 PhysPop	1940 MortRate	All-Cancers, Males Regression Output:	
Pacific	156.64	122.9	Constant	-19.27093
New England	138.46	135.5	Std Err of Y Est	12.0934
West North Central	128.72	110.9	R Squared	0.7596
Mid-Atlantic	138.49	140.9	No. of Observations	9
East North Central	126.51	119.6	Degrees of Freedom	7
Mountain	118.68	99.8		
West South Central	105.60	86.9	X Coefficient(s)	1.0351
East South Central	99.41	73.6	Std Err of Coef.	0.2201
South Atlantic	100.86	88.9	Coefficient / S.E.	4.7032

• - Part 2f.

	1931 PhysPop	1940 MortRate	All-Cancers, Males Regression Output:	
Pacific	159.97	122.9	Constant	-10.4041
New England	142.35	135.5	Std Err of Y Est	11.4992
West North Central	126.50	110.9	R Squared	0.7827
Mid-Atlantic	140.82	140.9	No. of Observations	9
East North Central	128.59	119.6	Degrees of Freedom	7
Mountain	118.89	99.8		
West South Central	105.95	86.9	X Coefficient(s)	0.9582
East South Central	96.73	73.6	Std Err of Coef.	0.1909
South Atlantic	99.59	88.9	Coefficient / S.E.	5.0207

• - Part 2g.

	1934 PhysPop	1940 MortRate	All-Cancers, Males Regression Output:	
Pacific	160.09	122.9	Constant	-2.6000
New England	148.60	135.5	Std Err of Y Est	8.8299
West North Central	125.96	110.9	R Squared	0.8718
Mid-Atlantic	149.62	140.9	No. of Observations	9
East North Central	129.36	119.6	Degrees of Freedom	7
Mountain	117.16	99.8		
West South Central	104.68	86.9	X Coefficient(s)	0.8903
East South Central	92.00	73.6	Std Err of Coef.	0.1290
South Atlantic	98.41	88.9	Coefficient / S.E.	6.9009

• - Part 2h.

	1936 PhysPop	1940 MortRate	All-Cancers, Males Regression Output:	
Pacific	158.44	122.9	Constant	-1.4212
New England	150.18	135.5	Std Err of Y Est	7.3226
West North Central	126.14	110.9	R Squared	0.9119
Mid-Atlantic	155.05	140.9	No. of Observations	9
East North Central	130.42	119.6	Degrees of Freedom	7
Mountain	119.80	99.8		
West South Central	103.52	86.9	X Coefficient(s)	0.8756
East South Central	89.94	73.6	Std Err of Coef.	0.1029
South Atlantic	99.16	88.9	Coefficient / S.E.	8.5104

• - Part 2i.

	1938 PhysPop	1940 MortRate	All-Cancers, Males Regression Output:	
Pacific	157.62	122.9	Constant	3.0512
New England	154.08	135.5	Std Err of Y Est	6.0043
West North Central	124.95	110.9	R Squared	0.9407

Mid-Atlantic	160.69	140.9	No. of Observations	9
East North Central	131.98	119.6	Degrees of Freedom	7
Mountain	119.88	99.8		
West South Central	102.79	86.9	X Coefficient(s)	0.8351
East South Central	88.21	73.6	Std Err of Coef.	0.0792
South Atlantic	99.26	88.9	Coefficient / S.E.	10.5419

● - Part 2j.	1940 PhysPop	1940 MortRate	All-Cancers, Males Regression Output:	
Pacific	159.72	122.9	Constant	11.5484
New England	161.55	135.5	Std Err of Y Est	5.4727
West North Central	123.14	110.9	R Squared	0.9508
Mid-Atlantic	169.76	140.9	No. of Observations	9
East North Central	133.36	119.6	Degrees of Freedom	7
Mountain	119.89	99.8		
West South Central	103.94	86.9	X Coefficient(s)	0.7557
East South Central	85.83	73.6	Std Err of Coef.	0.0650
South Atlantic	100.74	88.9	Coefficient / S.E.	11.6275

● Part 3. Maximum Relationship (Box 1), Best-Fit Equation (Box 2), and Graph

The regression analysis of Part 2j produces the strongest correlation --- which is the appropriate one to use (Chapter 5, Part 8b; and Chapter 22, Part 5). From the output, we can write the best-fit equation, as we did for the MX and MX+C models in Chapter 5. (We use the symbol * to denote multiplication.)

- ● - All-Cancer MortRate, Males = (X-Coefficient * PhysPop) + Constant.
- ● - All-Cancer MortRate, Males = (0.7557 * PhysPop) + 11.55.

Using the equation of best fit, we can calculate a best-fit MortRate for any value of PhysPop. In Box 2, we show best-fit MortRates which have been calculated for the nine actual PhysPop values of Part 2j, and also for lower PhysPop values, down to zero PhysPop (Chapter 5, Part 5e).

Figure 6-A, shows the line of best fit --- which connects these pairs of x,y values (various PhysPops, best-fit MortRates). The graph also shows nine boxy symbols (the nine actual observations from Part 2j). Per 100K means per 100,000 population.

Relationship between the Census-Division List and the Graph's Boxy Symbols

Emphasis belongs on the fact that the permanent sequence of the Census-Division list has no effect upon the regression analysis and no effect upon the graph. Graph-related example: Although the Pacific Census Division is at the top of the PhysPop list, the boxy symbol which is farthest to the right on the graph does NOT represent the Pacific Census Division. That boxy symbol represents Mid-Atlantic, because by 1940, Mid-Atlantic (not Pacific) is the Division with the highest PhysPop value.

Identification of the boxy symbols is completely unnecessary for visual recognition of their scatter and sequence around the best-fit line --- and those are the features which largely determine the quality of a dose-response. However, if some readers wish to know "who" each boxy symbol represents, a good way to begin is to identify the two Census Divisions with the highest and lowest PhysPop values in Box 2 --- or the two Divisions with the highest and lowest Observed MortRates. All the boxy symbols in Figure 6-A are identified on its replica, Figure 22-C. In that same chapter, Figure 22-A depicts the dose-response between the earlier (1921) PhysPops and the 1940 MortRates. The lower quality of the dose-response in Figure 22-A, compared with Figure 22-C, is visually obvious.

Ranges of Values for the Y-Axis in Our Graphs

On the y-axis in Figure 6-A, values range from 0 to 150 annual deaths per 100,000 males. In later chapters where we study only a single group of Cancers, the height of the y-axis will be the same, but its range of values will be very much smaller. For example, in Chapter 12, the highest value on the y-axis will be 10 per 100,000. In graphs such as these, the visual steepness of best-fit lines is tied to the scales for the y-axis and x-axis. We can keep the x-scale (PhysPops) the same throughout

Section Two of the book, but we must adjust the y-scale according to the magnitude of the MortRates.

• Part 4. Best Estimate (Box 3): 90% of Male Cancers in 1940 due to Medical Radiation

The data have revealed a linear dose-response relationship in 1940 of immense strength between medical radiation and male cancer mortality. And now to test Hypothesis-1, we must ask:

"What would be the estimated male cancer mortality-rate in 1940 if there were NO dosage of medical radiation?"

No medical irradiation would occur if there were NO PHYSICIANS per 100,000 population. So we want to know the value of the y-variable (cancer MortRate) when the value of the x-variable (PhysPop) is equal to zero. This value is, of course, called the Constant in the regression output of Part 2j. On the graph, the Constant is the value of the MortRate where the line of best-fit intersects the y-axis. This "intercept" occurs where the value of PHYSPOP equals zero. No medical radiation at all.

Since every Census Division has physicians, there can be no real-world datapoint in our study of the male cancer MortRate when PhysPop = zero. But the calculated or "estimated" MortRate, if PhysPop were zero, certainly does not come out of thin air. It is extrapolated from nine real-world observations which reflect a very strong linear relationship. It merits emphasis that the raw data which reveal this relationship are neutral --- by which we mean they were collected long ago by people having no conceivable bias with respect to the studies in this monograph.

4a. Percentage Caused by Medical Radiation: "Fractional Causation"

Fractional Causation has been defined in this book's Introduction, Part 5. Fractional Causation is the fraction of the cancer mortality rate which would be ABSENT (prevented) in the ABSENCE of a specified carcinogen --- which is medical radiation, in the studies of this monograph. Therefore, Fractional Causation is the fraction of the cancer MortRate attributable to medical radiation --- or caused by medical radiation, in ordinary parlance. Here, Part 4a explains the procedure for obtaining the estimate of Fractional Causation, by medical radiation, of the 1940 National All-Cancer MortRate (males). The same procedure is also presented at the top of Box 3, in the format to be used in subsequent chapters.

The estimated cancer MortRate, if PhysPop were zero, is the Constant. The increments in MortRate above the Constant occur in proportion to accumulated dose of medical radiation, and such increments occur BECAUSE of medical radiation. That is the meaning of dose-response, of course. Therefore:

- The total National All-Cancer MortRate in 1940, minus the MortRate to which medical radiation did NOT contribute (the MortRate indicated by the Constant), is the MortRate induced by medical radiation. Radiation-induced cases of Cancer are defined as cases which would be absent in the absence of radiation exposure (Introduction, Part 5).

- The MortRate induced by medical radiation, divided by the entire National MortRate, is the fraction of the total caused by medical radiation (Box 3). We express that fraction as a percentage.

- When we subtract the Constant of 11.55 (Part 2j) from the National MortRate of 115.0 (Table 6-B), we have the rate of 103.45 per 100,000 from medical radiation. The fraction of the total is thus (103.45 / 115.0), or 0.8996. In other words, the "best estimate" which falls out of the data is that 90% of All-Cancer deaths in males, at approximately mid-century, are attributable to medical radiation (Box 3).

Comments: Use of 1940 PhysPops, and Treatment of Negative Constants

Use of the 1940 PhysPops: The 1940 PhysPop values are very highly correlated with the PhysPop values of 1929, 1931, 1934, 1936, and 1938, as demonstrated in Table 3-C. Although we do NOT believe that additional radiation received during 1940 contributes to the 1940 cancer mortality-rates, if the 1940 PhysPops produce the best correlation with the 1940 MortRates, we use that combination to estimate Fractional Causation (Chapter 5, Part 8b; Chapter 22, Part 5).

Negative Constants: In some chapters, the best-fit equations produce negative Constants. This is bound to happen occasionally if the true Constant is zero or near zero. In such cases, we will assume the Constant's value to be zero, since in the real world, mortality rates cannot go below zero. Chapter 22, Part 3, examines negative Constants and their probable origin.

Comment: Speculation versus the Evidence at Hand

In Chapter 1 (Part 6), we have already explained why we have a high level of confidence in our findings. Here, we discuss whether evidence should be discarded in favor of groundless speculation.

For example, we and others can speculate that, prior to 1940, exposure to some nonxray carcinogen (which we will name NX) was quite unequal in the Nine Census Divisions, AND that this failure in matching was such that, as PhysPop values rose, exposure to NX also rose (producing a positive correlation between PhysPop and NX). If this occurred, then the observed dose-response in Figure 6-A would include some fatal cases produced by co-action between medical radiation and NX, but it would also include some fatal cases produced by co-action between NX and nonxray carcinogens, without any participation by medical radiation. Thus, our estimated Fractional Causation of 90%, by medical radiation, could be too high. How much too high would depend on what fraction of persons were exposed to NX and the potency of NX in combination with nonxray co-actors. We note that not many persons would be exposed to NX who were not ALSO exposed to xrays at some time --- because the rate of xray examinations was so high in the USA (Appendix-K, Part 2).

What is the customary way to consider the "what if" types of speculation? One checks them out, if possible. But we know of no way in which anyone CAN undertake a reality-check on the speculation that some nameless carcinogen may have had a persistent positive correlation with PhysPop in the decades leading up to 1940.

Moreover, in the absence of any BASIS for suspicion that such a situation existed prior to 1940, confidence belongs with the 90% estimate which is grounded in the real-world evidence provided in Chapters 2 and 6 of this monograph.

4b. Determining the Range of the X-Coefficient (Box 3)

Our central estimate, of Fractional Causation by medical radiation, is tightly tied to the value of the Constant, so we want to know the range of the Constant's likely value.

One way to estimate the range of the Constant is to work with the Standard Error of the X-Coefficient (the slope of the best-fit line). Using the Standard Error (SE) from Part 2j, we can learn the range of values within which 90% of the measured X-Coefficients would fall, if a great number of samples were measured (Chapter 5, Part 5g). Then, we can use the two extremes of this range, in the equation of best fit, in order to calculate the matching Constants. The calculations are tabulated in Box 3, below the dotted line, and also stated below:

In Part 2j, the X-Coefficient is 0.7557 with a Standard Error of 0.0650. The confidence limits on the X-Coefficient lie 1.645 Standard Errors away from the central value of 0.7557. Therefore, the lower 90% confidence limit on the X-Coefficient is (0.7557) - (1.645 times 0.0650) = 0.6488 --- which means a flatter slope than 0.7557. We do a comparable calculation to obtain the upper 90% confidence limit, except we ADD to the central value of 0.7557 instead of subtracting from it. The upper 90% confidence limit on the X-Coefficient is (0.7557) + (1.645 times 0.0650) = 0.8626 --- which means a steeper slope than 0.7557.

4c. Fractional Causation at the High 90% Confidence Limit (Box 3)

Now we can write the equation of best fit, using the National MortRate from Table 6-B, the upper 90% confidence-limit on the X-Coefficient from Part 4b, and the National PhysPop from Box 4 (the sum of Column D).

Nat'l All-Cancer MortRate = (X-Coef. * Nat'l PhysPop) + Constant.
Then we re-arrange:
Constant = (Nat'l All-Cancer MortRate) - (X-Coef * Nat'l PhysPop)

Constant = 115.0 - (0.8626 * 132.04)
Constant = 115.0 - 113.9
Constant = 1.10

So, at the upper 90% Confidence Limit on the X-Coefficient, we subtract 1.1 (the new Constant) from 115.0 (the National MortRate), to arrive at 113.9 per 100,000 males as the All-Cancer MortRate ascribed to PhysPop (medical radiation). At this limit, Fractional Causation is (113.9 / 115.0), or 99.0% by medical radiation (Box 3).

If the Constant here had turned out negative, we would have treated it as if its value were zero, since cancer mortality-rates cannot be less than zero in the real world. With "zero" to subtract from the National All-Cancer MortRate, the Fractional Causation would have been ~ 100 % by medical radiation.

4d. Fractional Causation at the Low 90% Confidence Limit (Box 3)

We repeat Part 4c, except that the X-Coefficient changes from 0.8626 to 0.6488 (Part 4b).

Constant = (Nat'l All-Cancer MortRate) - (X-Coef * Nat'l PhysPop)
Constant = (115.0) - (0.6488 * 132.04)
Constant = 115.0 - 85.7
Constant = 29.3

So, at the lower 90% Confidence Limit on the X-Coefficient, we subtract 29.3 from 115.0, to arrive at 85.7 per 100,000 males as the All-Cancer MortRate ascribed to PhysPop (medical radiation). At this limit, Fractional Causation is (85.7 / 115.0) = 0.745, or 74.5 % by medical radiation (Box 3).

All the steps to obtain the best estimate of Fractional Causation, and the Confidence-Limits, are abbreviated in Box 3. In subsequent chapters, Box 3 by itself will suffice.

• Part 5. Looking for Consistencies (Box 4): Error-Checks on Input and Output

We can use the National 1940 MortRate for All-Cancers (male) from Table 6-B, in order to verify that we have not made any serious errors in our work so far. Absent errors, our own work must produce a National MortRate which is reasonably close to the value in Table 6-B.

In calculating the National All-Cancer MortRate (male) in 1940 for the USA as a whole, we must weight the MortRate in each Census Division by multiplying it by its share of the total population. We also needed, for Parts 4c and 4d of this chapter, the weighted-average National PhysPop in 1940. We do both calculatons in Box 4.

The National MortRate of 112.65 (calculated in Box 4, Column F) is in good agreement with the National MortRate of 115.0 in Table 6-B. We can also check the reasonableness of our 1940 National PhysPop value (calculated in Box 4) and the X-Coefficient and Constant in our dose-response study of 1940 PhysPops and 1940 MortRates (Part 2j). If these three values are "good," then they too should produce a reasonable national MortRate for 1940, when we insert them into the appropriate best-fit equation (1940 PhysPops with 1940 MortRates):

1940 Nat'l All-Cancer MortRate = (X-Coefficient * Nat'l PhysPop) + Constant.
1940 Nat'l All-Cancer MortRate = (0.7557 * 132.04) + 11.55
1940 Nat'l All-Cancer MortRate = 111.33. This value, too, is in reasonable agreement with 115.0 from Table 6-B, and we are assured that there cannot be any serious errors in the work so far.

All the checks in Part 5 are abbreviated in Box 4. In subsequent chapters, Box 4 by itself will suffice.

• Part 6. Fractional Causation by Medical Radiation and by NonXray Causes: Co-Action

The estimate, that 90% of the males' National All-Cancer MortRate in 1940 was caused by medical radiation, may result in readers thinking, "That leaves only 10% for other causes!" Not true.

Because of co-action, the finding that Cancer has a high Fractional Causation by medical radiation does not limit any other cause of Cancer to a low Fractional Causation. This important point, already explained in the book's Introduction (Part 5), merits the additional discussion of co-action below.

6a. Co-Action among Causes: Views from the BEIR Reports of 1990 and 1999

With respect to the likelihood that co-action occurs between causes of Cancer, the Introduction (Part 4) has already presented "the general wisdom." Here, we add the views from the two most recent BEIR Reports. Of course, not all readers of this monograph will be familiar with the BEIR Reports. They are a series of six monographs issued during the 1972 - 1999 period by six (different) Committees on the Biological Effects of Ionizing Radiation --- all funded by the federal government and organized under the National Research Council.

BEIR 1990 states (p.152): "As discussed in the preceding section, the carcinogenic process includes the successive stages of initiation and promotion. The latter phase, promotion, appears to be particularly susceptible to modulation, with cigarette smoking being a conspicuous example of a modulating factor. Susceptibility to the carcinogenic effects of radiation can thus be affected by a number of factors, such as genetic constitution, sex, age at initiation, physiological state, smoking habits, drugs, and various other physical and chemical agents (UNSCEAR 1982)." The alteration of carcinogenic potency per rad of exposure, by nonradiation agents, is not speculation; there is experimental evidence (for instance, Segaloff 1971; BEIR 1990, pp.145-147). Our Chapter 49 (Part 2) discusses HOW co-actors can modify each other's potency.

BEIR 1999 (p.5) re-affirms the same view as BEIR 1990, even though the BEIR Committees which issued the two reports differ almost completely in their memberships: "Radiation carcinogenesis, in common with any other form of cancer induction, is likely to be a complex multistep process that can be influenced by other agents and genetic factors at each step."

6b. The Meaning of Co-Action: More Than One Cause per Case

The statements from BEIR reflect co-action among multiple causes. For example (from BEIR 1990): "Susceptibility to the carcinogenic effects of radiation can thus be affected by ... various other physical and chemical agents." This can be true only if the radiation and nonradiation agents are co-actors in the same case.

If a factor contributes to an outcome (say, a death from Stomach Cancer at age 55), the meaning of "contributes" is that the factor is a necessary cause of the outcome. If the additional factor is NOT necessary --- if the outcome would happen as it does anyway --- then the factor contributes nothing to the outcome. A contributor is a cause. And multiple causes per case are co-actors.

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Box 1 of Chap. 6
Summary: Regression Outputs for All-Cancers, Males.

Below are the summary-results from regressing the 1940 cancer MortRates upon the ten sets of PhysPops (1921-1940), as presented in Parts 2a-2j of this chapter. We are searching for the maximum correlation. Even the maximum will tend to understate the true correlation (Chapter 5, Part 8b).

Part	PhysPop	R-squared	Constant	X-Coef	Std Err	X-Coef/SE
2a	1921	0.4630	-27.08	1.0086	0.4105	2.4568
2b	1923	0.5447	-24.83	1.0198	0.3524	2.8937
2c	1925	0.5943	-16.55	0.9879	0.3085	3.2024
2d	1927	0.7175	-20.94	1.0399	0.2466	4.2168
2e	1929	0.7596	-19.27	1.0351	0.2201	4.7032
2f	1931	0.7827	-10.40	0.9582	0.1909	5.0207
2g	1934	0.8718	-2.60	0.8903	0.1290	6.9009
2h	1936	0.9119	-1.42	0.8756	0.1029	8.5104
2i	1938	0.9407	3.05	0.8351	0.0792	10.5419
2j --->	1940 Max	0.9508	11.55	0.7557	0.0650	11.6275

Related text = Part 2.

Box 2 of Chap. 6
Input-Data for Figure 6-A. All-Cancers. Males.

Part 2j, Best-Fit Equation: Calc. MortRate = (0.7557 * PhysPop) + (11.55)

Census Divisions	1940 Observed PhysPops	1940 Observed MortRates	Best-Fit Calc. MortRates
Pacific	159.72	122.9	132.250
New England	161.55	135.5	133.633
West No. Central	123.14	110.9	104.607
Mid-Atlantic	169.76	140.9	139.838
East No. Central	133.36	119.6	112.330
Mountain	119.89	99.8	102.151
West So. Central	103.94	86.9	90.097
East So. Central	85.83	73.6	76.412
South Atlantic	100.74	88.9	87.679
Additional PhysPops	70.00		64.449
--- not "observed" ---	60.00		56.892
down to zero PhysPop	50.00		49.335
(zero medical radiation).	40.00		41.778
For each, we calculate	30.00		34.221
a best-fit MortRate.	20.00		26.664
These additional x,y pairs	10.00		19.107
are also part of the	0		11.550
best-fit line (Chap 5, Part 5e).			

Related text = Part 3.

Box 3 of Chap. 6
Presumptive Fraction of Cancer MortRate Attributable to Medical Radiation.

Please see text in Chapter 6, Parts 4 and 6.

All-Cancers. MALES. * denotes multiplication.

• MALE National MortRate (MR) 1940, from Table 6-B	115.0	National MortRate
• Constant, from regression, Part 2j	11.5484	Constant
• Fractional Causation, Best Est. = (Natl MR - Constant) / Natl MR	90.0%	Frac. Causation

....

90% Confidence-Limits (C.L.) on Fractional Causation. See text in Chapter 6, Part 4b, please.

X-Coefficient, from Part 2j	0.7557	X-Coef., Best Est.
Standard Error (SE) of X-Coefficient, from Part 2j	0.0650	Standard Error
Upper 90% C.L. on X-Coef. = (Coef) + (1.645 * SE) =	0.8626	New X-Coefficient
New Constant = (Natl MR) - (New X-Coef * 1940 Natl PhysPop) =	1.0990	New Constant
Frac. Causation, High-Limit = (Natl MR - New Constant) / Natl MR =	99.0%	New Frac. Caus'n.
Lower 90% C.L. on X-Coef. = (Coef) - (1.645 * SE) =	0.6488	New X-Coefficient
New Constant = (Natl MR) - (New X-Coef * 1940 Natl PhysPop) =	29.3351	New Constant
Frac. Causation, Low-Limit = (Natl MR - New Constant) / Natl MR =	74.5%	New Frac. Caus'n.

Related text = Part 4a.

Related text = Parts 4b-4d.

Box 4 of Chap. 6
Error-Check on Our Own Work: All-Cancers, Males.

Please see text in Chapter 6, Part 5.

Below, Columns A, C, and E come directly from the regression input in Part 2j. Column B, the fraction of the whole 1940 population in each Census Division, comes from Table 3-B in Chapter 3. Each Column-D entry is the product of (B-entry times C-entry). Each Column-F entry is the product of (B-entry times E-entry). PhysPops and MortRates are each "per 100,000."

The Weighted-Avg. Nat'l PhysPop, 1940, is the sum of Column-D entries = 132.04

The Weighted-Avg. Nat'l Male MortRate, 1940, is sum of Col.F entries = 112.65
The Nat'l Male MortRate is also (X-Coef * Nat'l PhysPop) + Constant = 111.33
Comparison: The Nat'l Male MortRate, 1940, in Table 6-B = 115.00

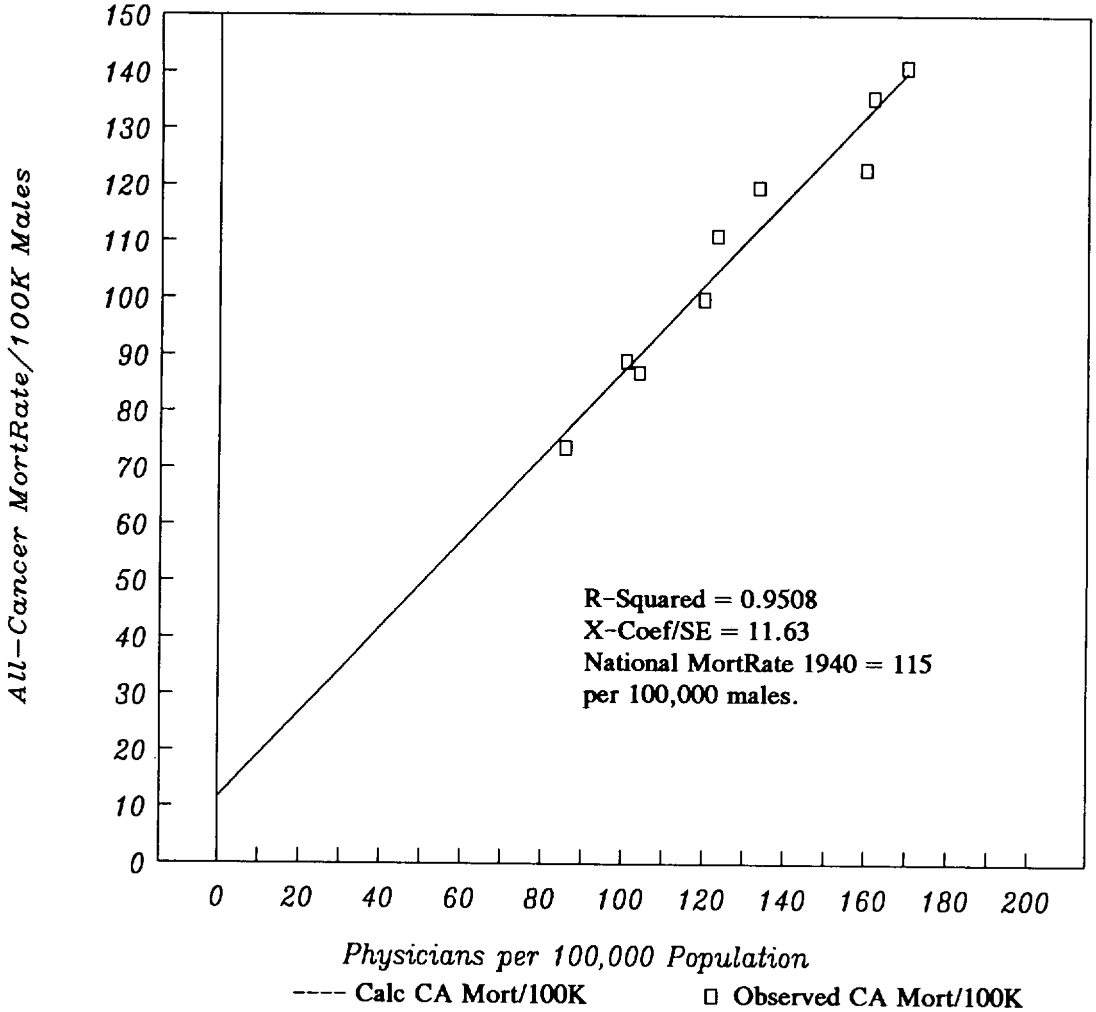
(A) Census Division	(B) Pop'n Fraction	(C) PhysPop 1940	(D) 1940 Weighted PhysPop	(E) MortRate 1940	(F) Weighted MortRate
Pacific	0.0739	159.72	11.80	122.9	9.08
New England	0.0641	161.55	10.36	135.5	8.69
West No. Central	0.1027	123.14	12.65	110.9	11.39
Mid-Atlantic	0.2092	169.76	35.51	140.9	29.48
East No. Central	0.2022	133.36	26.97	119.6	24.18
Mountain	0.0315	119.89	3.78	99.8	3.14
West So. Central	0.0992	103.94	10.31	86.9	8.62
East So. Central	0.0819	85.83	7.03	73.6	6.03
South Atlantic	0.1354	100.74	13.64	88.9	12.04
Sums	1.0000		132.04		112.65

Related text = Part 5.

1940 All–Cancer Mortality–Rates versus 1940 PhysPop Values for the 9 Census Divisions, USA.

Dose–Response Relationship

PhysPop is a surrogate for accumulated dose from medical irradiation.



Related text = Parts 3 + 4.

On the X–axis, PhysPop values = Physicians per 100,000 Population in the Nine Census Divisions of the USA Population, Year 1940. This variable is a surrogate for accumulated radiation dose --- the more physicians per 100,000 people, the more radiation procedures are done per 100,000 people.

On the Y–axis, All–Cancer Mortality–Rate per 100,000 males = the reported rates in USA Vital Statistics for the Nine Census Divisions, Year 1940.

Shown above is the strongest relationship between these two variables (Part 2j). The nine datapoints (boxy symbols) were collected long ago for other purposes, and are free from potential bias with respect to this dose–response study. Fractional causation is (Natl MortRate minus the Y–intercept) / (Natl MortRate).

Fractional Causation of All–Cancer Mortality–Rate in Males

by Medical Radiation = 90 % from Best Estimate (Box 3).

74.5% at Lower 90% Conf. Limit (Box 3). *99% at Upper 90% Conf. Limit (Box 3).*

Table 6–A.
All–Cancer Mortality Rates by Census Divisions: Males.

Rates are annual deaths per 100,000 male population, USA, age–adjusted to the 1940 reference year. There are no exclusions by color or "race." Sources are stated in Table 6–B, and described in Chap. 4, Part 2. The Nine Census–Division MortRates are population–weighted (Chap. 4, Part 2b). The averages below them are not.

Census Division	1940	1950	1960	1970	1980	1988
Pacific	122.9	127.2	140.7	147.2	153.7	148.5
New England	135.5	152.4	164.6	167.5	170.3	167.1
West North Central	110.9	125.3	135.6	143.8	152.0	155.9
Mid–Atlantic	140.9	156.0	164.0	167.9	171.8	168.4
East North Central	119.6	138.3	150.7	160.1	169.5	171.2
Mountain	99.8	108.1	118.7	126.7	134.7	139.1
West South Central	86.9	112.7	133.8	148.3	162.9	172.9
East South Central	73.6	104.7	125.1	149.6	174.1	188.2
South Atlantic	88.9	116.3	137.1	154.2	171.4	175.8
Average, ALL	108.8	126.8	141.1	151.7	162.3	165.2
Average, High–5	126.0	139.8	151.1	157.3	163.5	162.2
Average, Low–4	87.3	110.5	128.7	144.7	160.8	169.0
Ratio, Hi5/Lo4	1.44	1.27	1.17	1.09	1.02	0.96

The declining Hi5/Lo4 ratio is explained in Chapters 48 and 49.

Related text = Part 2.

Table 6–B.
All–Cancer Mortality Rates, USA National.

Rates are age–adjusted to the 1940 reference year. Both sexes: Deaths per 100,000 population (males + females). Males: Deaths per 100,000 male population. Females: Deaths per 100,000 female population. No exclusions by color or "race."

	Both Sexes	Male	Female
1940	120.3	115.0	126.1
1950	127.7	132.8	123.2
1960	129.1	145.7	114.9
1970	129.8	155.1	111.7
1979–81	131.9	164.5	108.5
1987–89	135.0	162.7	111.3

● – 1940, 1950, 1960: All rates come from Grove 1968, Table 67, p.676, "Malignant neoplasms, including neoplasms of lymphatic and hematopoietic tissues (140–205)" ICD/7.

● – 1970: All rates are interpolations (Chap. 4, Parts 2b, 2c); except that the 1970 National "Both Sexes" rate comes from PHS 1995, Table 30, p.110.

● – 1980: All rates (ICD/9, 140–208) come from the reference NatCtrHS 1980.

● – 1988 rates by Divisions and National come from Monthly Vital Statistics Vol.41, No.6, November 12, 1992. Exception: National "Both Sexes" is for 1990, and comes from PHS 1995, Table 39, p.132.

Related text = Part 4a. Also Box 3.