

CHAPTER 68

Is There a Reasonable Non-Radiation Explanation for the Observations?

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The key observations in this book are the strong, positive dose-responses, by Census Divisions, between Physicians-per-100,000 Population (PhysPop) and 1940 Cancer death-rates, and the strong, positive dose-responses in 1950 between PhysPop and Ischemic Heart Disease death-rates (age-adjusted to the 1940 reference year). So of course we asked, could reasons OTHER than medical radiation cause these tight, linear, positive correlations between PhysPop and each disease? This chapter presents our reasoning, about various alternative explanations.

● Part 1. High-Density of Physicians and High Density of Sick People?

WHY do the relationships, described above, occur? Are these observations explicable by proposing that the Census Divisions with the highest PhysPop values also had the highest densities of very sick people per 100,000 population --- in other words, by proposing that "doctors and sick people attract each other to the same location"? The explanation fails, because we also uncovered a significant NEGATIVE correlation between PhysPop and the 1950 MortRates from all NonCancer NonIHD causes combined (Chapter 25, Box 1).

And so we explored the proposition, that the strong POSITIVE correlations (PhysPop with Cancer MortRates and with IHD MortRates) are due to the combined force of the "attraction" speculation above PLUS the lack of effective treatments for Cancer and IHD at mid-century. But this modified proposition still provides no reasonable substitute for medical radiation as the correct explanation --- because several OTHER major diseases, which also lacked effective treatments at mid-century, do NOT have strong positive correlations with PhysPop. Reminder: A negative sign on the ratio (Xcoef/SE) reflects a DOWNWARD slope.

Chap.	Disease	Male R-sq.	Male Xcoef/SE	Fem R-Sq	Fem Xcoef/SE
27	CNS Vascular (Stroke)	0.40	-2.16	0.29	-1.68
28	Chronic Nephritis	0.46	-2.42	0.27	-1.60
30	Hypertensive Disease (1950)	0.35	-1.92	0.19	-1.28
31	Influenza + Pneumonia	0.83	-5.94	0.88	-7.34
34	RheumHeart + RheumFever	0.002	+0.12	0.06	+0.64
35	Syphilis + Sequelae	0.33	-1.85	--	--
36	Tuberculosis	0.21	-1.35	0.64	-3.51
29	Diabetes Mellitus is omitted due to the reason described in Chap. 29, Box 1.				

It is likely that the PhysPop-MortRates correlations for Cancer in 1940 would resemble the OTHERS on the list above, if it were not for the fact that physicians can CAUSE Cancer by causing medical irradiation. What distinguishes Cancer with certainty, from all the other diseases above, is Cancer's proven inducibility by ionizing radiation --- not its lack of effective treatment. So the "attraction" speculation does not explain the real-world observations --- whereas medical irradiation, caused by physicians, explains the observed correlation between Cancer MortRates and PhysPop very, very reasonably.

### ● Part 2. Some Other Carcinogenic/Mutagenic Activity of Physicians?

Besides causing irradiation of patients, did physicians also behave very commonly in some OTHER way, during the first half of the Twentieth Century, which could cause the extremely strong and positive correlations between PhysPop and 1940 Cancer MortRates, by Census Divisions? And between PhysPop and age-adjusted 1950 IHD MortRates, by Census Divisions? Although such an explanation can not be absolutely ruled out, it would be irrational to choose to explain the correlations by an imaginary carcinogen/mutagen, instead of explanation by a proven, potent, identified carcinogen/mutagen, very commonly dispensed by physicians to both male and female patients --- namely, medical radiation.

Of course, both radiotherapy and chemotherapy for Cancer are themselves carcinogens/mutagens, dispensed by physicians. But neither type of therapy can explain the mid-century dose-responses between PhysPop and Cancer MortRates, by Census Divisions. Both types of therapy are a RESULT of Cancer, and can not explain its occurrence in the first place. IHD is considered in Part 3.

### ● Part 3. A Causal Role for RadioTherapy and ChemoTherapy in IHD MortRates?

For both males and females, a positive correlation exists, by Census Divisions, between age-adjusted MortRates for Cancer and age-adjusted MortRates for IHD. The details are in Appendix-N. To a good approximation, the IHD MortRates are high in the same Census Divisions where the Cancer MortRates are high, and are low in other Census Divisions where Cancer MortRates are low. Smoking is an inadequate explanation (Appendix-N).

#### 3a. Is RadioTherapy the Explanation?

In light of the well-known heart damage by high-dose medical radiation (Appendix-J), we asked ourselves: If deaths due to high-dose cardiac damage have been routinely mis-reported as deaths from IHD, could radioTHERAPY for Cancer explain the correlations between Cancer MortRates and IHD MortRates? Are IHD MortRates high where Cancer MortRates are high, simply because radiation-treated cancer patients are switched --- by their radiation treatment --- from the Cancer death-stream into the "Heart Disease" death-stream? No. We will explain how we reach that conclusion.

High-dose radiogenic heart lesions require radiation therapy to a Cancer existing near the HEART. Otherwise, the heart will not receive the very high doses used in cancer therapy. The two frequent cancers in the heart-region are Respiratory-System Cancers and Breast Cancer. But Respiratory-System Cancers are explicitly excluded from Difference Cancers. By definition, Difference Cancers are All-Cancers-Combined EXCEPT respiratory-system cancers (Chapter 18). That leaves, for males, no high-frequency chest cancer within the Difference-Cancer MortRates. Hodgkin's disease, lymphomas, and leukemia are too infrequent to enter these considerations.

Therefore, if a high positive correlation exists between male MortRates for Difference-Cancers and for IHD, by Census Divisions, we can conclude reasonably that radiotherapy to the chest is not the explanation. Such correlation does exist. Based on the Observed MortRates (from Chapters 18 and 40), the R-squared values are: 0.81 in 1950; and 0.96 in 1960; and 0.94 in 1970; and 0.76 in 1980; and 0.53 in 1990. So we can say with assurance that radiotherapy to the chest does not explain the MortRate-MortRate (Cancer,IHD) correlations for males. And if radiation therapy is not the explanation for males, it is very unlikely to be an adequate explanation for females --- despite radiotherapy for some Breast-Cancers.

#### RadioTherapy for Breast-Cancer: The Cuzick Study, 1994; the Clarke Report, 1995

A reminder here may be helpful: "Cardiac-related" deaths and IHD deaths are not the same entity. When someone reports an excess of "cardiac-related" deaths, it is possible that NONE of those deaths are IHD deaths. For instance, in 1994, Cuzick and co-workers reported an elevated death-rate from "cardiac-related" causes among breast-cancer patients who received surgical and radiation therapies (circa 1950 to 1976), by comparison with breast-cancer patients in the same studies who received only surgical therapy ( $P < 0.001$ ) (Cuzick 1994, p.447; pp.451-452). Cuzick specified that

"cardiac-related" causes included all the entities with ICD/9 codes 390-429 --- a range which includes many more entities than IHD. Fortunately for breast-cancer patients, current techniques of radiation therapy result in lower radiation doses to the heart than such therapy in the past (Cuzick 1994, p.451; see also "Radiotherapy for Breast Cancer" on the Internet at <<http://oncolink.upenn.edu/cancernet/>> ).

Regarding radiotherapy for "Early Breast Cancer," a 1995 meta-analysis involving 10-year survival --- for 17,273 women treated surgically for "Early Breast Cancer" --- produced no significant difference between women who had both surgery and radiotherapy and women who had only surgery ( $p = 0.3$ ; Clarke 1995, p.1444, pp.1445-1447). Radiotherapy was associated with a lower risk of death from Breast Cancer (Odds Ratio = 0.94) but a higher risk of death from other causes (Odds Ratio = 1.24) which were not specified in the report.

### 3b. Radiation-Conversion of IHD Patients to Cancer Deaths

There is no doubt that IHD patients receive a lot of xray procedures (diagnostic and interventional) to parts of the chest.

For male IHD patients, xray procedures associated with IHD are undoubtedly converting some patients from IHD death to Respiratory-Cancer death. But since Difference-Cancers exclude Respiratory-Cancers, such conversions can not explain the persistent correlations, by Census Divisions, between male IHD MortRates and male Difference-Cancer MortRates.

For female IHD patients, xray procedures associated with IHD are undoubtedly converting some female IHD patients from IHD deaths into Breast-Cancer deaths, which ARE included with female Difference-Cancers. But we doubt very, very much that such conversions suffice to explain the following positive correlations between female MortRates for Difference-Cancers and for IHD, by Census Divisions (MortRates from Chapters 19 and 41): 0.90 in 1950; and 0.98 in 1960; and 0.94 in 1970; and 0.72 in 1980; and 0.59 in 1990.

### 3c. Does CHEMOtherapy for Cancer Explain the IHD-Cancer Correlations?

The second part of Hypothesis-2 proposes that multiple mini-tumors, induced by ionizing radiation in the walls of the coronary arteries, probably constitute the mechanism by which very-low to moderate doses of medical radiation become a cause of IHD. Of course, the coronary arteries are exposed to non-radiation mutagens too. Some of the chemical agents used in cancer therapy are mutagens. Since these chemicals circulate in the blood-stream, a patient's Cancer need not be located in the CHEST in order for the therapeutic chemicals to have a tumorigenic impact on the coronary arteries.

So we asked ourselves: Could CHEMOtherapy for Cancer (rather than low-and-moderate doses of medical radiation) be the explanation for the the observed MortRate-MortRate correlations (IHD with Cancer, by Census Divisions)?

There is an overwhelming reason to answer "No." It is the timing. We have shown a strong correlation in 1950 (Appendix-N), the earliest year for which IHD data are available. Chemotherapy was very rarely used for Cancer in 1950, so it could not possibly explain the 1950 correlation between MortRates for IHD and for Cancer, by Census Divisions. Indeed, the first hundred cancer patients who underwent chemotherapy did so in 1943 (Moss 1995, p.18). Between 1945 and the present time, use of chemotherapy against various Cancers has grown dramatically, but by 1960 or 1970, it was still not common enough to explain the extremely strong correlations (IHD MortRates and Cancer MortRates, by Census Divisions) observed in 1960 and 1970.

"I'll eat my hat" if a good share of IHD deaths in 1960 or 1970 had a prior history of chemotherapy for Cancer. If chemotherapy for Cancer cannot explain the 1950, 1960, or 1970 observations, why ask chemotherapy to explain the 1980 and 1990 correlations? By contrast, if Hypothesis-2 is valid, then all ten sets of observations (1950, 1960, 1970, 1980, 1990, for males and females separately) can be explained by exposure to low-and-moderate doses of medical radiation --- a phenomenon whose effects have been in operation since 1896.

#### ● Part 4. Pressure Not to Report Cancer in Low-PhysPop Census Divisions?

At mid-century, the general wisdom which I heard in medical school was that having a cancer-death in the family was, at least among some families, regarded as somehow shameful. No one can possibly evaluate how common this attitude may have been, nor can anyone evaluate how often a family pleaded successfully with a physician to report a cancer-death as something else. Still, we asked ourselves: Could this attitude explain why age-adjusted Cancer MortRates in 1940 were low in the Census Divisions where PhysPop was low, and high where PhysPop was high?

To take this speculation seriously, we would need to believe firmly that the frequency of the attitude was proportional to PhysPop, and also that physicians routinely helped to cover-up cancer deaths when asked. And what about Ischemic Heart Disease? An explanation is required also for IHD's irrefutable and strong positive correlation with PhysPop in 1950, by Census Divisions. So we would need not only a second stigma --- but also one whose frequency was proportional to PhysPop. And what about tuberculosis-death? It has a NEGATIVE relationship with PhysPop at mid-century. So we would also need to believe that stigma was ABSENT for tuberculosis-death and all other causes of death which had negative relationships with PhysPop at mid-century (Chapter 38, Box 1). The "stigma" speculation can not compete, in evidence or reasonableness, with medical radiation as the correct explanation for our findings.

#### ● Part 5. A Consequence of Autopsy Rates?

We consider it likely that wherever PhysPop was higher, the autopsy-rate was higher. In Chapter 4, Part 3a, we related reports which attempt to quantify how often Cancer was first discovered at autopsy to be the cause of a death. The statements of Hill (1992, p.48) suggest that hospital autopsies in the first half of the Twentieth Century produced a net increase of about 25% in deaths assigned to Cancer, compared to clinical pre-autopsy counts. Additionally, Hill relates (p.51) that at mid-century in the USA, more than half of patients dying IN HOSPITALS were autopsied. We cannot independently verify either piece of information, but we can use both pieces to explore some implications of an "autopsy" speculation.

Suppose that in the Census Division with the lowest 1940 PhysPop, no autopsies at all were performed. And suppose that in the Census Division with the highest 1940 PhysPop, 100% of all deaths were autopsied. We know that both suppositions are preposterous, but we are just exploring. In these unrealistic circumstances, we could expect that the 100% autopsy-rate would increase the reported Cancer MortRate in the high-PhysPop Census Division to a value about 25% higher than the reported Cancer MortRate in the low-PhysPop no-autopsy Census Division. But we know that a 25% increment would be a highly exaggerated expectation, because there never really was a 1940 autopsy-rate of zero in any Census Division, and there never really was an autopsy-rate of 100% in any Census Division (many people died AT HOME). So --- still assuming that autopsy-rates were higher where PhysPop values were higher --- we will approximate that higher autopsy-rates could cause reported cancer MortRates to be 13% higher in the the Census Division with the highest PhysPop than in the Census Division with the lowest PhysPop. Thirteen percent still may be quite an exaggerated expectation. Then we make a reality-check:

Males, All-Cancers (data from Chapter 6, Part 2j): For males in 1940, the Cancer MortRate is 73.6 where PhysPop is lowest. Therefore, due to a higher autopsy-rate where PhysPop is highest, the expected Cancer MortRate might be (73.6 times 1.13), or 83.2. In reality, the observed Cancer MortRate is 140.9 where PhysPop is highest.

Females, All-Cancers (data from Chapter 7, Part 2j): For females in 1940, the Cancer MortRate is 102.5 where PhysPop is lowest. Therefore, due to a higher autopsy-rate where PhysPop is highest, the expected Cancer MortRate might be (102.5 times 1.13), or 115.8. In reality, the observed Cancer MortRate is 142.9 where PhysPop is highest.

Our reality-check on a potential "autopsy effect" indicates that, in all likelihood, it is far from adequate to account for the observed increment in either the male or female 1940 Cancer MortRate, between the lowest PhysPop Census Division and the highest PhysPop Census Division. In other words, the "autopsy" speculation does not explain the observed, tight, positive correlations between PhysPop and 1940 All-Cancer MortRates. Something else was at work. The superior explanation is

medical radiation --- which is a proven cause of Cancer and is an explanation which ALSO accounts for the observation that PhysPop shows a dramatically different relationship with the NonCancer NonIHD causes of death.

#### ● Part 6. An Aspect of Urbanization as the Explanation?

We know a peer-reviewer who is fond of invoking "urbanization" as a possible explanation for many physical and mental afflictions. So we asked ourselves: What would be required, for urbanization to explain our mid-century findings?

First, it would require evidence that urbanization and physician-density per 100,000 population were very highly and positively correlated in the decades before mid-century. And then it would require evidence that city-life in the years 1900-1950 was a potent risk factor both for Cancer and for IHD. With such EVIDENCE, it would become reasonable to propose that PhysPop was a surrogate, in our mid-century regression analyses, for the accumulated health effects of city-life.

And then, if such evidence were at hand, we would have to ask ourselves: What ASPECT of city-living might elevate the MortRates from Cancer and IHD? With respect particularly to Cancer --- because ionizing radiation is a proven carcinogen --- a reasonable answer would be that the extra medical radiation administered by the extra city-based physicians would be a very reasonable explanation.

#### ● Part 7. What about Migration between High and Low PhysPop Census Divisions?

There is no doubt that, both before and after mid-century, migration from one Census Division to another has occurred. And when people receive, say, half of their medical irradiation in one Census Division, and then move to another Census Division, they carry with them the xray-induced mutations already inscribed upon their genetic molecules.

If 20 million people (illustrative number) move from the three High-PhysPop Census Divisions to the three Low-PhysPop Census Divisions, where they die, the effect would be to elevate the Cancer MortRate in the Low-PhysPop Divisions without any increase in PhysPop values --- even though the migrants from High-PhysPop Divisions had caused an increase in the average accumulated per capita dose of medical radiation in the population of the Low-PhysPop Census Divisions. And likewise, if 20 million other people migrate from the three Low-PhysPop Census Divisions to the three High-PhysPop Census Divisions, where they die, the effect would be to lower the Cancer MortRate in the High-PhysPop Divisions without any decrease in PhysPop values --- even though the migrants from Low-PhysPop Divisions had caused a decrease in the average accumulated per capita dose of medical radiation in the population of the High-PhysPop Census Divisions.

Under the above circumstances, the TRUE difference between High-PhysPop and Low-PhysPop Census Divisions, in average accumulated per capita dose of medical radiation, would be less than indicated by the ratio of their PhysPop values. Because of less dose-difference, the Cancer MortRates would become more similar in High-PhysPop and Low-PhysPop Census Divisions.

In Chapters 49 through 65 (exception: female Genital Cancers), the Boxes 1 always reveal that after mid-century, something caused more upward pressure on the Cancer and IHD MortRates in the Low-PhysPop Census Divisions than in the High-PhysPop Census Divisions. Even when National MortRates fell relative to 1940 or 1950, they fell by a smaller factor in the Low-PhysPop Divisions. Sometimes MortRates fell by just a LITTLE in the High-PhysPop Divisions while RISING in the Low-PhysPop Divisions. The Boxes 1 are consistent with inspection of Tables 6-A and 7-A (and subsequent MortRates tables, including 40-A and 41-A), with attention to the row marked "Ratio, Hi5/Lo4." It is obvious that, over time, Cancer MortRates grew more similar among the Census Divisions, and so did IHD MortRates.

We had to ask ourselves: Are these observations more consistent with extra smoking in the Low-PhysPop Divisions, or with a net migration from Higher-PhysPop Divisions to Lower-PhysPop Divisions?

### Regression-Output without the Smoking Adjustment

We answered the question by studying the regression-outputs (not shown) of post-1940 "raw" Cancer and IHD MortRates ("raw" meaning without a smoking-adjustment) regressed upon Mean PhysPop values (Table 47-A). Those R-squared values decline with every decade --- and for MALES, a few of the X-coefficients turn negative. By the time one arrives at raw 1988 Cancer MortRates (1993 for IHD), regressed upon 1940-1990 Mean PhysPop values, the R-squared values range all over the place, even though most R-squared values were in a tight range of 0.85 to 0.95 in 1940 (for IHD, in 1950) --- with only positive slopes.

	Male R-sq	Xcoef/SE	Fem R-sq	Xcoef/SE
All-Cancers 1988	0.11	-0.91	0.22	+1.41
Respiratory 1988	0.31	-1.78	0.06	+0.70
Diff-Cancers 1988	0.03	+0.43	0.24	+1.48
Digestive-Ca 1988	0.32	+1.79	0.42	+2.23
Breast Cancer 1990	--	--	0.57	+3.07
IHD 1993	0.06	-0.67	0.0011	+0.09

### The Better Explanation: The Inverse Relationship of PhysPop with Smoking

In the preceding tabulation, the opposite slopes and wide range of R-squared values are not indicative of migration as the explanation. If migration were the explanation, the correlations should degrade about equally for all types of Cancer, per gender. For example, migrants from one Census Division to another can not decide to carry their xray-induced mutations for Digestive-System Cancers WITH them, but choose to leave BEHIND their xray-induced mutations for Respiratory-System Cancers --- or vice versa.

By contrast, the tabulated results are very reasonably explained by the rising post-1940 impact of the inverse relationship between PhysPop (the x-variable) and smoking-intensity. By 1988-1993, the inverse PhysPop-Smoking relationship not only conceals the true PhysPop-MortRate relationships, but does so UNEQUALLY --- with the most intense impacts exactly where they are expected: Upon the PhysPop correlations with Respiratory-Cancer and IHD MortRates.

Of course, we also asked ourselves: Could the explanation of the tabulated values be that medical radiation just lost its importance, relative to some new and independent cause of Cancer? No. We have already demonstrated (Chapter 5, Part 6a) that a high correlation between PhysPop and Cancer MortRates, by Census Divisions, would NOT be lowered just by addition of a new and independent cause of Cancer --- if the intensity of the new cause were MATCHED across the Census Divisions.

### ● Part 8. A Reminder about the Law of Minimum Hypotheses

In logic and science, the Law of Minimum Hypotheses (Ockham's Razor) advises: To explain a phenomenon, invoke only as many explanations as required. This monograph has revealed certain phenomena:

- For Cancer, powerful positive correlations exist between PhysPop values and Cancer MortRates, by Census Divisions, for males and females separately.
- For Ischemic Heart Disease, powerful positive correlations exist between PhysPop values and IHD MortRates, by Census Divisions, for males and females separately.
- For NonCancer NonIHD causes of death, powerful positive correlations with PhysPop do NOT exist across the Census Divisions; instead, the relationships are NEGATIVE.

These three facts "demand" an explanation. This chapter has reviewed various explanations which do NOT appear reasonable. By contrast, medical radiation is almost certainly the correct and sufficient explanation, for the reasons which we have presented earlier. From this it follows (by the logic demonstrated in this book) that medical radiation is a highly important cause of both Cancer and Ischemic Heart Disease, in the USA, for most of the Twentieth Century --- including the present day.

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