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The Linear No-Threshold Model of Low-Dose Radiogenic Cancer: A Failed Fiction

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Abstract

The linear no-threshold (LNT) model for low-dose, radiogenic cancer has been a fixture of radiation protection and regulatory requirements for decades, but its validity has long been contested. This article finds, yet again, more questionable data and analyses purporting to support the model, this within the "gold-standard" data set for estimating radiation effects in humans. Herein is addressed a number of significant uncertainties in the Radiation Effects Research Foundation's Life Span Study (LSS) cohort of atomic bomb survivors, especially in its latest update of 2017, showing that the study's support of the LNT model is not evidence based. We find that its latest 2 analyses of solid cancer incidence ignore biology and do not support the LNT model. Additionally, we identify data inconsistencies and missing causalities in the LSS data and analyses that place reliance on uncertain, imputed data and apparently flawed modeling, further invalidating the LNT model. These observations lead to a most credible conclusion, one supporting a threshold model for the dose–response relationship between low-dose radiation exposure and radiogenic cancer in humans. Based upon these findings and those cited from others, it becomes apparent that the LNT model cannot be scientifically valid.

Keywords

low-dose radiation (LDR), linear no-threshold (LNT), threshold, Life Span Study (LSS), Hiroshima and Nagasaki atomic bomb survivors, radiogenic cancer, Radiation Effects Research Foundation (RERF), radiation protection, radiation regulatory requirements

Introduction

The linear no-threshold (LNT) model has been a fixture in radiation protection and regulatory requirements for decades, but its validity has long been contested, even repudiated, as a variety of studies clearly demonstrate.[1-5] Support for the LNT model relies on epidemiological studies suggesting its truth, on its acceptance by the BEIR VII Committee, or the Radiation Effects Research Foundation's (RERF) Life Span Study (LSS) of Hiroshima and Nagasaki atomic bomb survivors, considered the "gold-standard" data set for estimating radiation effects in humans.

Many epidemiological studies attempt to justify the LNT model, but a recent article has shown some studies compromise the scientific method, using incomplete data and invalid statistical methods for hypothesis testing, resulting in circular reasoning and rendering their conclusions indefensible.[6] Likewise, a recent study exposes the errors in the BEIR VII Committee Report, invalidating its conclusions in support of the LNT model.[7]

Objectives

This article reviews the LSS data's and analyses' shortcomings and inconsistencies, demonstrating their failure in applying the LNT model for low-dose radiation (LDR). The LSS data analyses generally concentrate on atomic bomb radiation exposure as a cause of cancer incidence or mortality, and RERF analyses seem to miss relevant, published data reflecting known biology regarding various other significant causalities likely far more responsible for carcinogenesis than LDR exposure. As we illustrate, the assumed low-dose cancer risk is not probable; the dose–effect relationship is nonlinear and the risk estimates exhibit large uncertainties, which include negative values.

The other causalities include extensive and long-term incidence of tobacco smoking, severe physical and psychological stress and distress, and widespread infectious diseases and

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dietary/physical conditions that have plagued Japan for decades. We appropriately account for these causalities and attempt to demonstrate that hypothetical solid tumor cancer risk attributed to LDR is not probable, potentially supporting, not the LNT model, but rather a hormetic one.

We first discuss the latest 2 analyses of solid cancer incidence among the LSS cohort, which do not support the LNT model, then consider the error of biologic omission, and briefly note that longevity may be a better measure of LDR health effects than cancer mortality. Finally, we consider some inconsistencies, errors, and missing causalities in LSS data and analyses that show RERF places reliance on uncertain, imputed data and apparently flawed modeling requiring correction, which further invalidates the LNT model.

Methods to Evaluate LSS Solid Tumor Cancer Data and the LNT Model

What the LSS Data Have Been Telling Us

Three analyses exist for solid cancer incidence among the LSS cohort of atomic bomb survivors in Hiroshima and Nagasaki. Comprehensive analyses of solid and hematopoietic cancer incidence data among the LSS cohort with follow-up through 1987 were first reported in 1994, then updated through 1998 in 2007, and again updated recently through 2009 in 2017. Below, we focus on the last 2 analyses, illustrating nonlinearity at low doses, thereby invalidating the LNT model.

(1) LSS data for solid cancer from 1958 to 1998 as presented in the RERF website (www.rerf.or.jp/en), see Figure 1, and as reported by Preston et al[8] and later reanalyzed by Furukawa et al.[9]

Furukawa et al[9] analyzed the LSS data employing a semiparametric, dose–response model that assumes no specific, parametric function form. Compared to the conventional LNT model, the semiparametric model estimated smaller risks with wider confidence interval estimates at low doses, indicating no clear evidence of an increased risk up to 100 mGy of exposure. Furukawa created an expanded graph (doses from 0 to 0.4 Gy) to better illustrate the low-dose data points, since they are obscured when examining the dose response over the entire dose range. This graph, modified by us to show only the reported low-dose solid cancer data points without the superimposition of the Furukawa models, is shown in Figure 2.

When focusing on the low-dose data, the dose response is neither as positively sloped as the high-dose data nor linear, even suggesting a hormetic response. The LSS data that have been touted as supporting the LNT model for years, in fact, do not—4 of the 5 excess relative risk (ERR) values (for solid cancer) below 100 mGy are less than 0, with a fit having negative slope, supporting a hormetic model. This is worth repeating—the ERR values, for the most part, are negative below 100 mGy, and this has generally been ignored or dismissed. Our independent analysis of these same LSS data confirmed these findings; as illustrated in Figure 2, positive-sloped linearity at low doses does not exist; rather, it is forced by the high-dose extrapolation of the LNT model.[4]

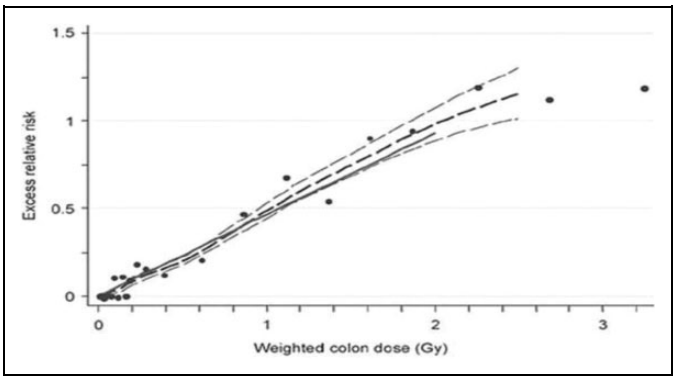

Figure 1. LSS solid cancer incidence, excess relative risk (ERR) by radiation dose, 1958 to 1998, using DS86 dosimetry system.[8] Note that doses <0.1 Gy appear to have ERRs <0. LSS indicates Life Span Study.

(2) LSS data from 1958 to 2009, latest update, and analysis of LSS data as reported by Grant et al.[10]

This study provides the most recent analyses of solid cancer incidence among the LSS cohort through 2009 using a revised dosimetry system (DS02R1). The dose response for males confined to the low-dose range (0-<200 mGy) is shown in Figure 3.

It is apparent again that when focusing only on low-dose data (<200 mGy), the dose response is not linear with a positive slope, invalidating the LNT model. Therefore, based on these studies, the dose–effect relationship is nonlinear and the risk estimates exhibit large uncertainties that include negative values. This clearly indicates the conventional wisdom is wrong—the associated cancer risk estimates are overly conservative and incorrect, invalidating the LNT model for predicting solid cancer risk in the 0 to 100 mGy dose range.

For completeness, a 2012 study by Ozasa et al reported and analyzed solid cancer mortality, as opposed to incidence, among the LSS cohort using the DS02 dosimetry system,[11] again exhibiting nonlinearity at low doses; in fact, statistically significant curvature at low doses was observed. It is apparent from Ozasa's Figure 4 that not only are the uncertainties extremely large for the ERR values, but these values are lower at high doses and higher at low doses when compared to the incidence dose–response data exhibited in Figure 1; the reason for both these latter findings is not well understood and has never been adequately described.

Mortality follow-up data have been reported 14 times since 1961, but, according to Grant et al,[10] these data, although highly valuable, do not provide adequate information on less fatal cancers. The LSS cancer incidence data enable risk estimates for both fatal and nonfatal cancers with better diagnostic accuracy and disease onset date.

Biology Matters: Modeling Must Follow the "Rules of Boxing"

The phrase "rules of boxing" was first presented in another publication[12] and simply expresses the "rules" for the proper

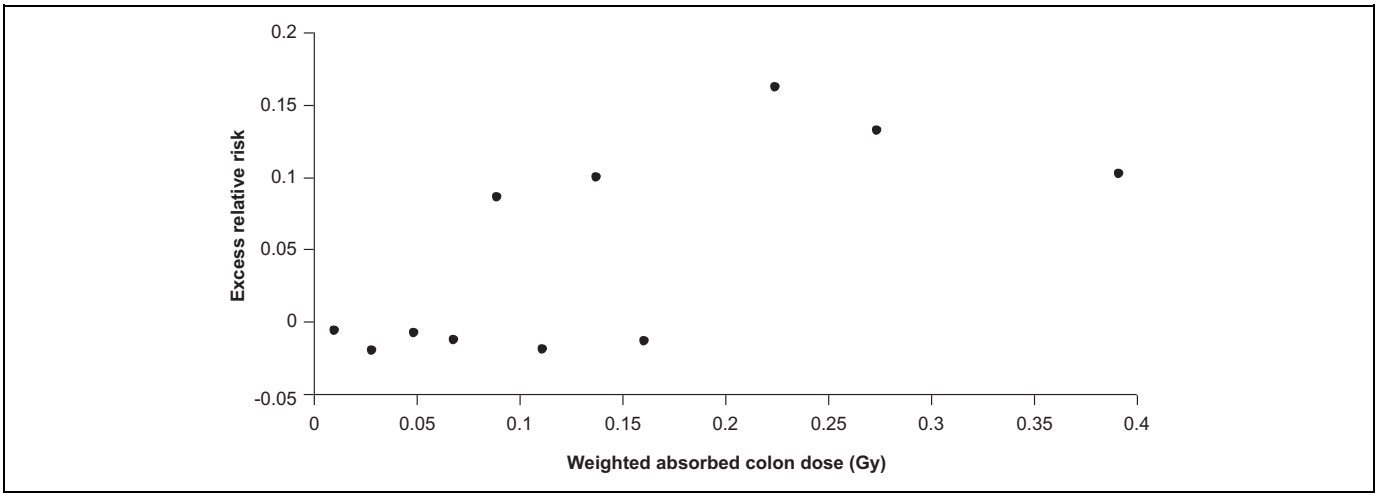

Figure 2. LSS solid cancer incidence in the 0 to 0.4 Gy dose range derived from that reported by Furukawa.[9] LSS indicates Life Span Study.

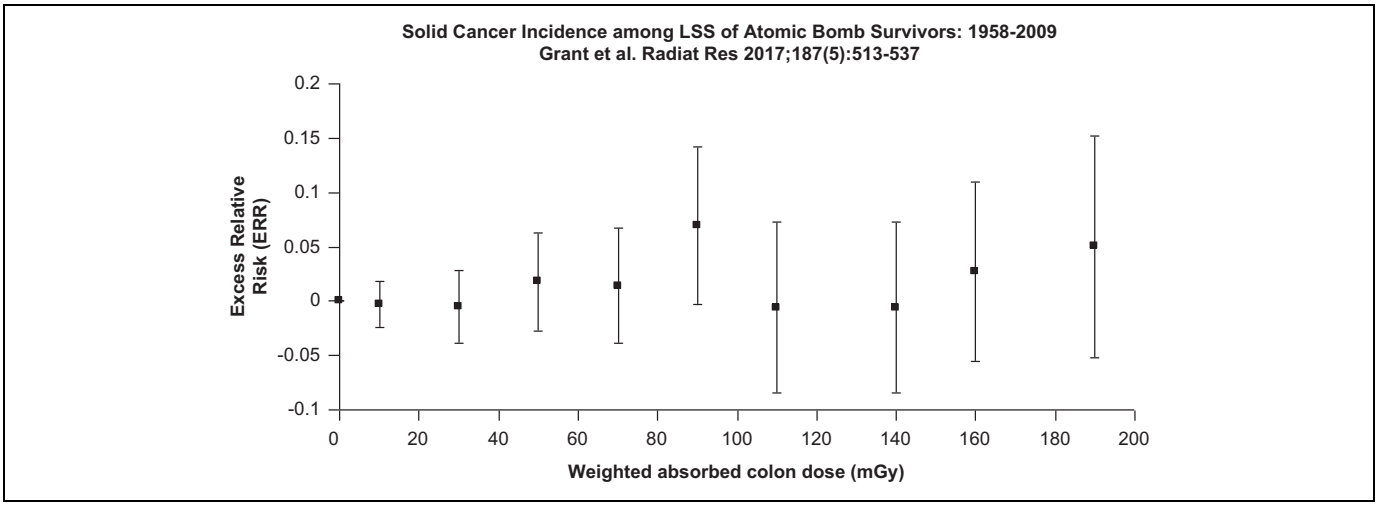

Figure 3. LSS data derived from Grant's reported data in Appendix Table E1.[10] ERR values are shown with 95% confidence intervals, indicating large uncertainties. LSS indicates Life Span Study; ERR, excess relative risk.

grouping (or binning) of dose–response data. Models explain the dose–response relationship of LDR with cancer incidence to reflect physical processes (rules) occurring in the range of data under consideration, which may be termed "the box." If the rules change, so will the resulting pattern of the data, such that some data (eg, low-dose data on the order of less than 200 mGy) belong in one box, while the higher dose data fall into a different box where different rules apply. Researchers often analyze data using statistical methods that inappropriately force the entire dose range's data into one box. The problem is that if one believes all the data fall under one set of rules when they do not (the LNT model problem), one will wrongly sort the data into a single box, yielding a faulty analysis.

At high doses, proven, adaptive, biological responses that reduce both LDR and metabolic damage are suppressed, while at low doses they are stimulated, repairing or eliminating much of all damage.[4,13] The LNT model demands that one box contain all doses, violating these rules of boxing and ensuring modeling linearity. But this is scientifically invalid for predicting LDR responses and precludes discovery of a threshold or hormetic dose–response.

The LSS dose–response data have been updated by the RERF over time, all the while reporting the dose response is essentially consistent with the LNT model down to 0 dose. To be fair, Grant et al[10] did report that for males, significant upward curvature over the full dose range was observed indicating a linear quadratic model is favored over the LNT model, raising unresolved questions. So much so that the authors concluded, "At this time, uncertainties in the shape of the dose response preclude definitive conclusions to confidently guide radiation protection policies."

Still, as shown in Figures 2 and 3, if only the low-dose data points ranging from 0 up to $\sim$400 mGy are examined, these data points do not display the high-dose, positive-sloped

linearity. Positive-sloped linearity at low doses is a fiction forced by extrapolating high-dose data based on the LNT model. If the low-dose data alone are analyzed, it is inescapable that the LNT model is incorrect. By forcing positive-sloped linearity from high-dose data, a no-harm or benefit-inducing threshold is rendered invisible by the preconception that none exists—a self-fulfilling prophecy. Therefore, the LNT model cannot and does not apply to LDR data. This conclusion is a direct consequence of the demonstration that the body responds to LDR exposure by repairing/eliminating any damage,[4] that is, since there is repair, it is unlikely that the LNT model is true. Further, spontaneous biological damage exists, and LDR-induced biological defenses operate on both radiogenic and spontaneous damage. Intact organisms possess a steady state of DNA-damaged cells that permit adaptive processes, stimulated further by LDR, to repair and/or remove, not only most of the added DNA-damaged cells due to the radiation, but also some of the preexisting, steady-state, DNA-damaged cells. The net effect is a decrease in the number of damaged cells relative to the preexposure steady-state number, indicating not only that a threshold exists but that the LDR is also supportive of hormesis. That such repair and/or removal may not be 100% efficient is correct, but it is incomplete when mention of the steady-state preexposure damage level is omitted from the argument.[14]

Results: LSS Solid Tumor Cancer Data Do Not Support the LNT Model

Enough Is Enough

The low-dose, LSS dose–response data set is generally obscured by graphing the full dose range. Any apparent nonlinearity at low doses can then simply be ignored in favor of the unequivocally erroneous observation that the data support the LNT model. The RERF's stated objectives from its Articles of Incorporation include "... to conduct research and studies for peaceful purposes on medical effects of radiation and associated diseases in humans, ..." (https://www.rerf.or.jp/uploads/2017/09/aie.pdf). To this end, the RERF has performed numerous studies calculating what they believe is a certain number of excess cancers, but, as discussed herein, these study results are questionable, as the cancers claimed to be due to radiation exposure are based on use of the LNT hypothesis and various flawed methodologies, including lack of consideration of various other significant causalities likely far more responsible for carcinogenesis than LDR exposure.

To further complicate RERF results, albeit in a more subtle way, its extensive use of ERR versus dose graphs likely shifts (moves) the *x*-axis right and left and the *y*-axis, up and down:

1. Doses are associated with large uncertainties—right and left shift. They are not measured but model based, which have changed over the years based on various dosimetry systems (DS)—DS86 to DS02 to DS02R1 (a revised DS02), amounting to an ill-defined (imprecise) shift along the *x*-axis.
2. ERR values are based on methods used to determine baseline rates that are variable (derived from 0 dose cohorts either not-in-city or in-city for the bombings or based on Poisson regression), causing *y*-axis shifts.

Incidence and mortality data have both been reported and the DS have been different. If one examines Figure 1 (incidence data by Preston using DS86), one will note that ERR values are <0 for doses <100 mGy. This is more easily appreciated in Figure 2. If one examines Ozasa's Figure 4 mortality data using DS02,[11] the ERR values are greater than 0 in this low-dose range, likely due to using the Poisson regression intercept that has been reported to underestimate the baseline mortality rate; that is, the ERR values are artificially inflated.[3]

Further, the LSS cohort doses may have been underestimated because fallout radioactivity was not accounted for. Sutou has reported that 10% of each bomb blast's energy was residual radiation,[15] the majority of which was fallout. Bomb survivor doses were estimated solely on the basis of initial blast radiation. This could mean LSS doses were underestimated, leading to overestimated cancer risk in the LSS cohort. Sakata et al[16] concede that fallout radiation data and its effects are quite difficult to determine, even over long years of research. They report the findings remain inconclusive, such that the "deleterious health effects from rain exposure immediately after the atomic bombing cannot be completely ruled out."

The final defense of the LNT model is that its "conservatism-derived" policies will be protective. But that has been proven to be untrue, as use of the LNT model has led to ignoring beneficial/no health effects from LDR, and the model's actual risks that are far greater than the hypothetical carcinogenic risk purportedly avoided (eg, radiation fear/fearmongering, degraded radiological imaging, nuclear event evacuation policies, etc, which have produced harmful effects in millions of people).[2,4]

We also note that some have suggested longevity is a better measure of the health effects of radiation than is cancer mortality.[17] As reported in a study by Cologne and Preston,[18]

> The average decrease in life expectancy for those in the Life Span Study cohort with non-zero dose estimates below 1 Gy (mean 0.14 Gy) is about 2 months. For the 40 403 (43%) of exposed survivors in the cohort with non-zero dose estimates less than 0.25 Gy (mean 0.055 Gy), the decrease in life expectancy is estimated as 21 days.

This decrease in 21 days is associated with a reported 95% confidence interval of approximately ± 5 years. The LSS data have indicated that the health effects at low doses are, therefore, not only highly uncertain but also, up to now, provide no documented evidence of either an increase in cancer or a decrease in longevity. Further, as reported by many, LDR effects could hardly have a role in any decreased life

Table 1. Abbreviated Form of Grant et al Table 8.[10] Radiation Dose Response for Both Males and Females: LSS Solid Cancer Incidence Cohort With Known Doses, 1958 to 2009.

Dose (Gy)	Person-Years	Cases	Background	Radiation-Only	AF Radiation (%)	Radiation–Smoking Interaction	AF Radiation–Smoking (%)	Smoking-Only	AF Smoking (%)
<0.005	1 794 130	12 592	10 646	3.3	0	0	0	1857	15
0.1	807 885	5674	4785	82	1	6	0	867	15
0.2	164 111	1217	996	80	7	6	1	179	15
0.5	169 177	1414	1023	188	13	16	1	191	13
1.0	88 992	889	526	228	26	22	2	99	11
2.0	42 236	560	239	211	38	29	5	54	10
2.0+	12 953	192	67	104	54	17	9	16	8
Total	3 079 484	22 538	18 284	895	10	97	1	3263	15 for cases >0.005 Gy

Abbreviations: AF, attributable fraction; LSS, Life Span Study.

expectancy in survivors, due to the physical injuries, burns, biological injuries, poor nutrition, bad hygienic conditions, and special psychological distress that led to early mortality.

Methods to Determine Inconsistencies and Omissions in LSS Data and Analyses

Who Are the Atomic Bomb Survivors?

The survivors of the Hiroshima and Nagasaki bombings are a cohort of special people known as the "hibakusha." They were treated as outcasts, exposed to extreme physical and psychological distress for decades by their countrymen and the occupation forces[19,20] who feared that these sick and injured people might be contagious or carriers of disease. The hibakusha suffered ongoing physical, economic, and emotional abuse arising from social and government discrimination due to society's fears.[21] A mental health assessment of 3756 atomic bombing survivors in 1997 indicated that they suffered from serious psychological distress (SPD).[21] Research in the United States has shown that SPD is a major factor in reduced life expectancy and is therefore likely the foremost contributor to reduced life expectancy within the hibakusha.[22] Adults with SPD have significantly higher age-adjusted death rates compared to those without SPD for each of the 3 leading causes of death: heart disease, cancer/malignant tumors, and assaults/accidents/unintentional poisonings. Low-dose radiation (LDR) cannot account on any biological basis for such reduced life expectancy.

Although the RERF acknowledges the issue,[23] essentially all of the LSS reports have neglected the study of SPD and its effects. Kamiya et al reported in 2016 the potential for increased mortality, but that, although the study of radiation effects has mostly focused on natural science and essentially ignored the psychosocial problems of radiation exposure, most accept the results of the LSS as is " . . . studies of psychosocial aspects of the bombings were very limited. Although . . . bomb-related injuries not caused by radiation might increase mortality risks, the results of the LSS are accepted by epidemiologists worldwide."[24]

However, the Chernobyl and Fukushima Daiichi nuclear power plant accidents provide convincing evidence of adverse psychological effects among people who experienced the trauma of the accidents. Even with estimates of low public doses and health effects, psychosocial problems around these plants have had devastating effects on millions of peoples' lives. Later, we will address this matter further. First, we present our analysis of the effects of smoking on the LSS cohort.

Observations on the Inconsistencies of Data and Analyses Associated With Smoking

For the first time in an LSS update report, the RERF offers tobacco smoking as a cause of cancer incidence among the LSS cohort.[10] Table 8 in that report (see abbreviated form in our Table 1) presents a breakdown of the LSS cohort's solid tumor cases.

All LSS cases are now divided into 4 subsets: those associated with radiation, those that arise only from smoking, those that have radiation–smoking interaction, and those that are background cases and not associated with radiation or smoking. No other causalities are identified. Importantly, radiation-only cases are the sole Table 1 entry that remains a variable in the LSS cohort's solid tumor cancer cases. Corrections increasing the smoking-related cases in the LSS cohort require an in-kind decrease in radiation-only cases. We show corrections resulting from both unreliable smoking data and the smoking model are necessary, thereby eliminating radiation-only cases at low doses. Other corrections imposed by new causalities not likely considered in the background cases, such as stress, also require a diminution in the radiation-only cases, as we show later.

Since the focus here is on LDR effects that the RERF has always insisted arise from the bomb blast radiation, the following applies in the 0 to 0.5 Gy dose range. The total number of solid tumor cases is 20 897: Of these, 17 450 are background cases, which are difficult to corroborate (apparently derived from modeling and attributed to nonradiation and nonsmoking causalities, their previous reporting remains unknown to us); 3094 are attributed to smoking-only; and 381.3 are attributed to radiation-only and radiation–smoking

interaction. Note also that the radiation-only, solid tumor case rate in this dose range is 1.82%.

With respect to smoking-only cases, significant issues arise, these being recognized and reported by the authors, including the smoking data are questionable and incomplete—the data were collected through questionnaires having only a 61% response rate; smoking status was unknown for about 60% of the total follow-up time and smoking status at the time of diagnosis was unknown for about 40% of the cases; almost half of the cases having smoking data and 40% of those without smoking data were imputed to be associated with smoking; among those responding to surveys, 86% of the men and 18% of the women indicated that they were ever-smokers, but Table 4 of the study by Grant et al[10] shows only 50% of men and 11% of women are ever-smokers; patients' smoking habits were assumed to be the same after the subjects' final response on smoking, which was no later than 1992; in 2009, the LSS cohort's average age was 78 years and it was simply assumed unlikely that many had begun smoking and likely that many had quit smoking by that age, but the impact on radiation effects was unclear; despite the large cohort and case numbers, the data permitting inference regarding radiation–smoking interaction were still limited by a highly skewed dose distribution and the unavailability of histology information for about 30% of the cases.[10,25-27]

It is clear the authors knew of substantial gaps in the smoking data, but these are not the only source of uncertainty regarding the results reported in Table 1. Issues within the smoking model make the smoking data results also questionable.

The smoking model has been earlier described as applicable to lung cancer, not all cancers, and how the model has been changed to accommodate smoking's many other organ targets is not addressed.[10,25-27] Additionally, the model ignores a major confounder regarding high levels of radionuclides in tobacco resulting from deposition of radon and its high linear-energy-transfer (LET), α-emitting decay products on, and adhering to, tobacco leaves; these decay products are released into cigarette smoke and transferred to smokers' lungs and other organs, being increasingly retained over years of smoking.[28] Omitting these high-LET doses means the modeling of low-dose, low-LET, bomb blast radiation, essentially dwarfed by smoking's high-LET doses, may inflate the bomb blast's radiation-only, solid tumor causality, overstating LDR's case rate.

The LSS data also differ from Japanese national smoking and cancer incidence data. For example, the smoking attributable fractions (AFs) shown in Table 1 are well below Japanese national cancer surveys and research,[29-31] when they should be higher due to the prevalence of smoking in the 1950s to 1980s; and the smoking AFs tend to decline remarkably in the LSS data with increased smoking prevalence, the opposite of what has been reported.[29,30] These inconsistencies force a misperception that radiation above 0.5 Gy is a greater cause of solid tumor incidence than heavy smoking, which is in disagreement with what is known by medical science.[29]

Two noteworthy statistical aberrations arise when comparing the data in Table 1 with the research from national Japanese studies of smoking and cancer.[29-31] First, smoking's AF of the cases is quite low; indeed, for the highest dose categories, the AF dips as low as 8%, though it is 14.5% of smoking-only cases for dose categories greater than 0.005 Gy. A significant national study by the National Cancer Center (NCC) shows that smoking's age-adjusted, population-attributable fraction (PAF) of solid tumor cancer cases is 0.201.[29] Adjusting for the LSS smoking prevalence and the male and female population percentage differences in the LSS cohort, this PAF becomes 0.215, almost 50% higher than the Table 1 AFs. The understated AFs in Table 1 yield a solid tumor incidence rate for smoking of only 11 in 10 000 persons per year, even when including the radiation–smoking interaction cases with smoking-only cases.

The second statistical aberration arises when the Table 1 solid tumor incidence rate is compared to Japan's annual mortality rate for smoking-associated, solid tumor cancers, as reported by Funatogawa et al,[30] which provides data through 2010 for lung cancer mortality (not including other cancers associated with smoking) in its Figure 2 for the same average age as the LSS cohort. Using those data, adjusted for the male and female population percentages for the LSS cohort, the Japanese annual lung cancer mortality rate is estimated to be 26 in 10 000 persons. Kaneko et al[31] also provides similar data through 2001 in its Figures 1 and 2. Appropriately adjusting these data, the Japanese annual, lung cancer mortality rate for the same average age as the LSS cohort is estimated to be 28 in 10 000 persons. It is clear that such smoking-associated, lung cancer-only mortality rates are not consistent with the cancer incidence rates of Table 1 for all smoking-related, solid tumor cancers. Mortality rates for lung cancer 130% to 150% higher than the incidence rate for all smoking, solid tumor cancers are physiologically inexplicable. Toyoda et al's Figure 1 offers compelling data close to what the LSS's lung cancer incidence rate should be, using the city of Osaka's lung cancer-only, annual incidence rate (a population of similar smoking habits and average age as the LSS cohort).[32] This rate is estimated to be 34 in 10 000 persons, more than 200% above the Table 1-derived rate for incidence of all smoking-related cancers. That annual incidence rate is about 20% to 30% more than the national, annual, mortality rate, a rational, physiological relationship for lung cancer. Clearly, the smoking-only, Table 1 cancer incidence rate is likely well underestimated and thus flawed. This calls into question the putative radiation-associated cases, which should, therefore, be much lower than reported.

Considering these observations, it is interesting that one error may cause both of these statistical aberrations, namely, that there are too few smoking-only cases included in the LSS smoking data. A simple correction to this problem would be to use the NCC's Japanese national data set of tobacco smoking's adjusted PAF of 0.215 for solid tumor cancer incidence, rather than the likely flawed LSS smoking data and its calculational model.[29] The total cases in the LSS cohort from smoking-only would then be 4846 cases due to smoking-only, compared to

Table 2. Table 8.[10] Derived Low-Dose Solid Tumor Cases From LSS Data on Smoking and Cases Determined Herein: Comparative LSS Low-Dose Cancer Incidence.

Dose Range: Weighted Colon Dose in Gy	LSS Cases	Background Cases	Cases Less Background	Radiation-Associated Cases	Smoking-Only Cases	Smoking Cases Derived[29]	(Cases Less Background) Less Smoking Cases Derived[29] = Radiation-Associated Cases
NIEC + 0-0.005	12 592	10 646	1946	4	1857	2372	(426)
0.005-0.1	5674	4785	889	88	867	1354	(465)
0.1-0.2	1217	996	221	86	179	312	(91)
0.2-0.5	1414	1023	391	204	191	362	29
Total				382	3094	4404	

Abbreviations: LSS, Life Span Study; NIEC, Not in Either City.

the Table 1 LSS-derived 3360 cases, including the radiation–smoking interaction cases.

Table 2 shows the impact of NCC's smoking and cancer data to determine a more credible set of smoking-only cases and LDR-associated cases.

Clearly, with unreliable smoking data and an unsupportable smoking model, the LSS's LDR cases are nonexistent and should, instead, be considered as smoking-only or other background cases, up to a weighted colon dose of at least 0.2 Gy and likely approaching 0.5 Gy. That is, there are no bomb blast radiation, solid tumor cases below this threshold (the number of these cases is actually negative and shown in parentheses in Table 2), thus invalidating the LNT model based on the LSS cohort.

Because other studies have even higher age-adjusted PAFs,[33] this approach likely represents the most conservative threshold estimate for the LSS radiation-associated cases. Using higher PAFs produces even fewer radiation cases and a higher dose threshold, below which no radiation-associated cases are likely.

The LSS's Missing or Incomplete Data and Evaluations

Missing Evaluation of High Stress and Cancer Incidence

The RERF has peripherally recognized that physical and psychological stress resulting from the bomb blasts has some role in the LSS data.[11,23] However, this issue is no less important than getting the LSS smoking data corrected, and the RERF interest has never seemed to recognize the incredibly unusual and protracted SPD of the hibakusha, as discussed herein. Based upon its absence in Grant et al,[10] the role of stressors in the LSS data as an important causality of cancer incidence may have been ignored. Therefore, we offer this preliminary accounting for such data within the background cases.

In a recent 2017 report, Song et al[34] present the results of a prospective cohort study by the Japan Public Health Center on perceived stress levels from everyday life (work, family, health, etc) and the risk of solid tumor cancer incidence in a Japanese population. The study included 111 257 eligible patients having complete information on perceived stress level at a baseline and, using baseline and 5-year follow-up data, measured dynamic stress levels. A subcohort of 79 301 participants with repeated stress data in 6 groupings was also used to measure long-term perceived stress. The association between perceived stress and solid tumor cancer incidence was measured by a Cox proportional hazards regression model (representing the ratio of outcomes in the test group to outcomes occurring in the control group), adjusted for all known confounders.

Using these data, the study examined several areas of interest, including (1) the association between dynamic perceived stress level and solid tumor cancer incidence and (2) the association between long-term perceived stress level and solid tumor cancer incidence. For the first area, after controlling for all available confounders, a small but significant increase in the risk of cancer incidence was observed for patients under either a medium- or high-level of stress, compared to the reference group (low stress level), with multivariable, adjusted hazard ratios (HRs) of 1.04 for the medium stress-level group and 1.06 for the high stress-level group, showing a clear trend to increase.

For the second area, analyses were conducted on the subcohort patients who had repeated data on stresses. The relative risk of cancer incidence increased with higher long-term stress levels. Individuals with constantly high perceived stress level had an 11% excess risk for cancer incidence compared to those with persistently low stress levels.

Therefore, if the SPD stressors experienced among the hibakusha from protracted social ostracism and government discrimination, arising from society's fears, are taken into consideration, the excess solid tumor cancer incidence is likely to be significantly affected.

A recent observational, epidemiological study of Holocaust survivors who had emigrated to Israel determined that the population had experienced an increased risk for solid tumor cancer incidence due to a variety of stressors, including extended physical harm, psychological abuse, and thorough physical and mental deprivation, earlier discussed as SPD.[35,36] A Cox proportional hazards model was used for the analyses. The study included 152 622 people and the conditions identified are strikingly similar to, but of shorter duration than, those experienced by the hibakusha: physical harm, intake restriction, exposure to

biologic agents/infectious diseases, intense physical stress, physical and emotional abuse from society and government, and psychological responses to such stressors.[19,20]

The reported results show that, as has been surmised in other studies,[21] the stressors did increase the incidence of certain cancers. Further, other studies show that more typical stress levels of life produce fewer cancers in populations.[22] Using the Holocaust survivor main study's results, cancer incidence in the hibakusha could be estimated by applying the HRs for the test cohort to the same cancer sites in the LSS data to determine the number of cancer cases in the LSS cohort attributable to SPD. Further, since the Not in Either City control group was not hibakusha, the Song et al[34] study offers Japanese background stressor cancer data for use with that group. Although there is some complexity introduced by the ethnic differences between Holocaust survivors and a Japanese population that must be addressed by further study before direct application of the Holocaust survivor data to the LSS cohort can be fully credible, higher solid tumor cancer incidence from higher stresses is certainly a rational expectation.

Results: Data and Analyses Omissions/Errors Show LSS Doesn't Support the LNT Model

After adjusting the HRs from the Song et al[34] Tables 2 and 3 for the associations in (1) and (2) for the male and female population percentages of the LSS cohort population and applying those adjusted HRs to the LSS cohort data from Table 1 to estimate the excess solid tumor cancer incidence risk to the LSS population from typical stresses of living, we found the LSS cohort solid tumor excess cancer incidence from perceived stress fell in the range of 800 to 1200 cases, which then should be extracted from the cases associated with bomb blast radiation (if they were not previously accounted for in the background cases).

Yet, applying the data from the epidemiological study of Holocaust survivors to the impact of stressors on the LSS cohort, it was estimated that as many as 2150 solid tumor cancers might arise from the protracted SPD of the LSS cohort. Such a result would further diminish the number of LSS radiation-associated cases at low doses, showing the application of the LNT model to LDR and radiogenic cancer within the LSS cohort is fatally flawed.

In summary, these adjustments to the LSS solid tumor cancer incidence rates for smoking and stressors perhaps miss some overlap and therefore require a more formalized and rigorous analysis. However, although preliminary and requiring validation, the adjusted LSS cohort, smoking-only cases using the NCC data,[29] presented herein, likely exhibit a solid tumor cancer incidence, threshold radiation effect. Further, until now, unaddressed, solid tumor cancer incidence arising from SPD stressors provides further compelling evidence that the current LSS database does not support the LNT model for LDR.

Infectious Disease and Cancer Incidence in the LSS Data

Some LSS solid tumor cancer incidence data from infectious disease are likely included in Table 1 background cases, but the 2005 data from the NCC of Japan regarding Japanese cancer incidence from infectious diseases and other causalities may not have been.[29] Infectious diseases were widespread and a serious public health problem among many Japanese, including the hibakusha, before, during, and after World War II.[29] In 2005, 55% of cancer among men was attributable to preventable risk factors in Japan,[29] including smoking. The corresponding figure for women was lower, but still accounted for nearly 30% of cancer.[29]

The NCC information regarding the linkage between several infectious bacteria/viruses and solid cancers, along with some examples of the bacterial or viral infections and their influence on increased cancer risk, are summarized by Inoue et al,[29] as follows:

> Another important finding from our study is its confirmation of the notion that infectious agents are a major cause of cancer in the East Asian region [16]. Its advanced socioeconomic status and high degree of hygiene and sanitation notwithstanding, Japan is not an exception: H. pylori [Helicobacter pylori] and HCV [hepatitis C virus] are major infectious causes that account for a relatively large share of preventable cancers . . . The prevalence of these infectious agents shows a strong cohort effect, namely a huge variation by birth cohort, and has been declining rapidly among younger birth cohorts.
>
> The majority of gastric cancer in Japan is derived from the noncardia stomach (91% in men and 94% in women in 2000) [32], and the prevalence of H. pylori is >80% in the birth cohort born before 1950 and 40%–50% in those born after 1950 [33, 34] . . . . Hepatocellular carcinoma, which accounts for 90% of all liver cancer cases, is primarily caused by chronic HCV infection in Japan. The peak incidence between the 1970s and the 1990s in Japanese men was affected by the birth cohort effect among those born during 1931–1935, which was attributed to HCV outbreaks in Japan [35].

Further, Inoue et al[29] provide more detailed data that show the range of the solid tumor cancer incidence associated with many of the infectious diseases that have plagued Japan for decades. For example, hepatitis C and B have been shown to be associated with liver cancer; the human papillomavirus with cancers of the oral cavity, oropharynx, anus, genitalia, and cerix uteri; and the Epstein-Barr virus with nasopharyngeal cancer, Burkitt lymphoma, and Hodgkin lymphoma.

For 2005, these NCC infectious disease data for Japan[29] resulted in a PAF of 0.206 for all solid cancer incidence arising from this generations-old abundance of these bacteria and viruses. This PAF is higher than that for smoking, showing the immense impact that infectious disease has on solid tumor cancer incidence in the Japanese population.[29]

The NCC data also show other causalities of solid tumor cancers in Japan, including alcohol intake, salt intake, fruit and vegetable intake deficiencies, body mass index, physical

inactivity, and exogenous hormone use, with a 2005 PAF greater than 0.1.[29] The impact of these other factors on hibakusha compared with controls remains unknown and requires further study.

Combining the NCC's solid cancer incidence causalities in Japan from preventable risk, more than 50% of such cancers arise from smoking, infectious diseases, and the other causalities identified above. The SPD stresses should also be included as a preventable risk factor, which would likely push solid cancer incidence in Japan arising from preventable risk even higher.

The LNT Model Is a Failed Fiction and Not Scientific Knowledge

Conventional wisdom says there are 2 LDR applications for the LNT model: one for risk assessment as a scientifically defensible hypothesis and one for radiation protection/management. Regulatory and advisory agencies such as the National Council on Radiation Protection and Measurements (NCRP) and the International Commission on Radiological Proection (ICRP) and other advisory agencies/organizations support the LNT model's use for LDR protection, but not risk assessment. As Lauriston Taylor, a past president of the NCRP, noted in 1980,[37] LNT model risk-based calculations are "deeply immoral uses of our scientific knowledge." Unfortunately, they defend the use for LDR protection on the fallacious grounds that it protects by "erring on the side of caution."

This claim of "prudence" is a dangerously ill-informed illusion, failing to consider a range of possible outcomes, as discussed earlier. Either the LNT model accurately describes responses to LDR, or it doesn't, and if it doesn't, as shown herein and elsewhere, then its use in risk management will regularly produce harmful effects.

We have herein shown the robust, counter-epistemological evidence against the LNT model for LDR, and scientific empiricism requires robust, epistemological evidence in order for the LNT model to be science. The LNT model is simply without empirical basis, and it is no longer science, if ever it was.

Conclusion

With the disclosures of the errors and false conclusions in BEIR VII, the flawed analyses and statistics in epidemiological and mechanistic LDR studies, the demonstration herein that the LDR dose response is nonlinear with negative ERR values, and the possible threshold we show when significant causalities, heretofore ignored in the LSS data's low-dose range, are considered, there exists irrefutable evidence that invalidates the LNT model. As we have reported,[7] BEIR VII asserts that "at relatively low doses, there is still uncertainty as to whether there is an association between radiation and disease, and if there is an association, there is uncertainty about whether it is causal or not." Our work demonstrates there is likely neither association nor causality. Therefore, the LNT model is now on a level beneath that of empirical knowledge, where logic is constrained by verification. Using the LNT model as the basis for regulation and practice within medicine and nuclear energy remains a continuing *non sequitur*, applying nonscience to regulate the highest levels of science within medicine and energy.

In science, what is true is unrestrainable and what is error is unsustainable. Herein lies the hope science offers all humanity: That truth must always be science's standard of practice.

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