ANOTHER NOBLE LIE,

LINEAR NO-THRESHOLD RADIATION

AND GENERAL TOXICOLOGY,

NEEDS TO GO

John Dale Dunn MD JD

Applicability of Radiation-Response Models to Low Dose Protection Standards
Joint Topical Conference
American Nuclear Society and
Health Physics Society
Pasco, WA
September 30-October 3, 2018

American Nuclear Society/Health Physics Society meeting Sept 30-Oct 3, 2018

Pasco, Washington

Abstract

The United States Environmental Protection Agency (USEPA) has responsibility for toxins and risk management, including regulations and public education/guidance as well as policy making to reduce risks for the public and protect the environment. That includes ionizing radiation risks and mitigation of those risks. Currently, the USEPA linear no-threshold (LNT) modeling is based on the assumption that there is no safe level for radiation exposures in matters of cancer risks.

This paper and presentation will show why LNT modeling was never good science and it was based on serial misconduct and malfeasance by researchers and those they sought to influence. Dr. Muller misrepresented the results of his experiments and then tried to suppress the work of Stern, but beyond that he worked energetically to influence the BEAR and then the

BEIR committees during the 1950's and so now we not only have LNT for radiation biophysics but it has been inappropriately extended to general toxicology by means of common methodologies and data management combined with assumptions ignore the evidence that LNT is generally not a valid template for toxicology and oncological research. LNT is not good science as a foundation for risk management policy and it creates real problems since it asserts no threshold and no safe level of radiation or toxin exposure—two assertions that are patently untrue. The realities and the evidence of those realities refute the LNT template or protocol for radiation and general toxicology research in risk assessment and risk management. This presentation and monograph will focus on radiation biophysical oncological research and leave general toxicology for another time, in the interests of space and time and the nature of the audience that is concerned by radiation Health Physics and health issues related to nuclear physical phenomena.

The LNT model survives because of politics, and aggressive environmentalism in EPA policy making. It is time to abandon the LNT model in matters or radiation biophysics, but also in other areas of environmental toxicology since it is unscientific and creates excessive compliance burdens that cannot be justified.

The Central Role of the US EPA

The Clean Air Act; Safe Drinking Water Act; and the Comprehensive Environmental Response Compensation and Liability Act (CERCLA) include sections pertaining to ionizing radiation sources. The Public Health Service Act (PHSA) authorities the US EPA to study effects of ionizing and advise states on mitigation of any adverse effects on humans or the environment. environmental radiation, perform research on the environmental and human health effects of exposure to radiation.

This paper examines the radiation protection framework and policies of the USEPA as they are applied to low dose, low dose-rate (LDDR) radiation exposures. It focuses on current scientific literature, policy implications, public health impacts and future directions for developing a radiation protection framework based on sound scientific principles. I must give great credit to Carderelli and Ulsh, whose thorough going and comprehensive paper on LNT was liberally referenced and adopted as the basis for my efforts to outline the issues and arguments on LNT for this paper and my presentation to the American Nuclear Society/Health Physics Socity conference (Carderelli 2018).

Low dose is radiation exposure in excess of ambient that produces a cumulative lifetime dose of 100 mGy (10 rad) lifetime above natural background. Low dose rate is defined as less than 0.01 mGy min^{-1} (1 mrad min^{-1}) above natural background. The definitions for low dose and low dose rates have varied over time but generally fall below 200 mGy for low dose and <0.05 mGy min^{-1} for low dose rate (UNSCEAR 1993). For comparison annual ambient radiation exposure for Americans is

The USEPA relies on the linear no-threshold (LNT) dose-response model developed in the BEIR reports of the National Research Council of the National Academy of Sciences, but a review of the literature cited and relied shows that the present template is inappropriate. In 2015, several members of the group, Scientists for Accurate Information (SARI), submitted petitions to the US EPA to eliminate the use of the LNT paradigm and take radiation hormesis into account". The petition cited 36 references in support the petitioners' request. The basis of the petition were also presented in a peer-reviewed scientific article (Welsh *et al.* 2017). The USEPA response was little more than a hand wave (Edwards 2015) and declined to address all but two references

cited by the petitioners. SARI also recently submitted a letter to the administrator of the USEPA (Miller *et al.* 2017) that was ignored.

IN 2017, in response to Executive Order by the President establishing a policy to eliminate unnecessary regulatory burdens, the USEPA formed a Regulatory Reform Task Force and the Office of Air and Radiation (OAR) was ordered to provide recommendations regarding specific rules that could be repealed, replaced or modified to make them less burdensome by May 15, 2017.

OAR hosted a public meeting on April 24, 2017 to solicit proposals and the Health Physics Society (HPS) gave verbal comments during the meeting urging USEPA to reconsider their adherence to LNT and to improve several documents [*e.g.,* (USEPA 1988, 1993, 1999, 2001a, 2011)] by better addressing uncertainties in LDDR environments. The HPS also stated that reliance on the LNT model "…tends to foment the public's fear of all types of radiation". The HPS followed up with written comments, which stated,

> "As a scientific organization of professionals who specialize in radiation safety, the HPS believes the EPA's reliance on the LNT model, especially at very low doses and dose rates, is inappropriate and can exaggerate the risk. Of most concern to the HPS is the EPA's extrapolation of the LNT model to calculate collective dose and the use of collective dose as a metric for risk". (Kirner 2017) (Ring *et al.* 2017). I would emphasize there is no scientific basis for claiming that "collective" dose (cumulative) is a good metric for risk.

There is no good excuse or justification for continued use of LNT modeling in radiation risk management.

What is the science that pertains to LNT?

Sir Austin Bradford Hill, using common sense, mostly, but certainly science, established a set of objective criteria for proof of causation to be implied from a correlation or association.

He properly listed the criteria for the association/correlation being asserted as causal as requiring (1) temporal relation (2) strength of correlation (3) dose-response correlation, (4) consistency (reproducibility), (5) plausibility (reasonable scientific mechanism), (6) consideration of alternate explanation and confounding factors, (7) experimental evidence, (8) specificity, and (9) coherence [*e.g.*, is the association or correlation compatible with existing theory and knowledge?] (Hill 1965)

. Hill's Criteria when applied to Low Dose Radiation do not support the BEIR LNT template as applied to low dose radiation (Ulsh 2012). In its comments on SARI's petition to the NRC, the USEPA stated,

> "The U.S. Environmental Protection Agency strongly disagrees with the petition to the Nuclear Regulatory Commission (NRC) to cease using the linear no-threshold (LNT) model as a basis for regulating exposures to ionizing radiation. The USEPA's Carcinogen Assessment Guidelines specify that LNT should be used as a default assumption unless there is compelling evidence that the biological mechanism for carcinogenesis is inconsistent with LNT." (Edwards 2015)

This argument was also published by USEPA in a scientific article in justifying the Agency's reliance on the LNT model:

> "Radiation protection, like the regulation of other carcinogenic agents, is—in the absence of compelling evidence to the contrary—predicated on the linear, no-threshold (LNT) hypothesis…" (Puskin 2009)

The US EPA continued defense of LNT and adherence to LNT as the default theory in the absence of "compelling evidence to the contrary" ignores the evidence weight of the evidence and violates basic rules of the scientific method. As Einstein said we can never prove the negative we can only evaluate for the reasonable evidence of causation. The EPA and the LNT advocates can always argue that no threshold risk might exist, but that ignores evidence of no observable effect by the method of tunnel vision, a nice way to describe bullheadedness in the face of evidence and energetic confirmation bias.

The current USEPA policy takes the position that the LNT model is accurate unless "compelling evidence to the contrary" is presented. This approach is included in the agency's guidelines which direct the use of the LNT even if the scientific evidence cannot substantiate that conclusion. This is a circular argument which excludes the option of other alternative models from being considered. One could also describe it as a tautological argument, indicative of the anchoring and confirmation bias fallacies of fanatics, not scientists.

But there is more fallacious USEPA thinking that goes into the policy of LNT as the default—the first is magical thinking—closely related to confirmation bias and other fallacies for the USEPA says:

> "Biophysical calculations and experiments demonstrate that a single track of ionizing radiation passing through a cell produces complex damage sites in DNA, unique to radiation, the repair of which is error-

prone. Thus, no threshold for radiation-induced mutations is expected, and, indeed, none has been observed." **(**Edwards 2015)

This statement relies on a biological plausibility argument that is, in fact contradicted by knowledge of Cancer and causes of Cancer—DNA damage is not the explanation for cancer in the majority of types, instead modern oncology attributes cancer to the development of hyperploidy and multiploidy in cell lines due to telomeric dysfunction combined with failure of immune mechanisms to eliminate the malignant cell lines—the reason that aging has always been a very important correlation to cancer. The US EPA bites on the weak argument that ionizing radiation causes mutations that cause cancer—working from a research record that fails to support the theory.

The elimination of cell lines involves multiple established cellular and tissue defenses, even in those cell lines that develop without polyploid nuclei, since extensive protective biological processes are initiated upon any DNA damage caused by any toxic effect or even dysfunction of mitosis. The defenses are there to prevent potential development of cancer [*e.g.* cellular and tissue-level defense mechanisms including not only DNA damage repair, but also apoptosis, premature terminal differentiation, and immune surveillance (Ulsh 2010; Sacks and Siegel 2017; Welsh *et al.* 2017 Davoli 2011, Ioan Baba 2011, DaVita 2008, Weinberg, 2014). As explicitly acknowledged by the National Council on Radiation Protection and Measurements (NCRP) over 15 years ago (NCRP 2001),

Scientific evidence has accumulated in recent years that refutes critical elements of the

LNT model defended by the US EPA. For example:

> "Since the cell is able to repair a very high level of endogenous DNA damage without frequent mutagenic consequences, a further small increment of such DNA damage from low dose rate irradiation should, equally efficiently, be repaired. Mutation rates will only increase if due to higher dose and dose rate, the capacity for high fidelity DNA repair is exceeded. . . ."
>
> And;
>
> "The mechanism which induces "radiation-induced genomic instability" appears to involve a non-nuclear target and upregulation of oxidative stress, which also is the main mechanism of metabolic DNA damage. **These experimental observations are not compatible with a single hit mechanism which is the basis for the microdosimetric justification of the linear-non threshold dose response hypothesis."**
>
> (Trott and Rosemann 2000)

It would be reasonable to consider that biological effects are different at different exposures, and certainly with ionizing radiation at the LDDR level and so it is--current evidence demonstrates that biological responses to LDDR radiation are distinct from those occurring at high doses (Cohen 2008; Averbeck 2009; Ulsh 2010; Feinendegen 2011; Zhang *et al.* 2011; Ulsh 2012; Paunesku *et al.* 2017). Similarity of mechanisms the foundation of the claims of linearity and no threshold and the evidence is contrary, making the assumptions on mechanism incorrect.

The assertion that no threshold in radiation-induced mutations has been observed is inaccurate. The earliest data on mutations in fruit flies upon which adoption of the LNT model

was initially based indicated a threshold, but was *misrepresented* by Muller as supporting the LNT model (Siegel *et al.* 2015; Calabrese 2017a, 2017b).

Repeating similar experiments, more recent studies examining mutations in fruit flies confirm that the dose-response is characterized by a threshold, or even hormesis (Koana *et al.* 2004; Koana *et al.* 2007; Ogura *et al.* 2009; Koana and Tsujimura 2010; Koana *et al.* 2012). These studies relate to another of Hill's Criteria - Experiment, which can greatly strengthen the case for causation. However, these studies do not support the LNT model, but rather a threshold or hormesis model.

A threshold for radiation-induced mutations has also been observed in mice (Boreham *et al.* 2006; Sykes *et al.* 2006a; Sykes *et al.* 2006b; Zeng *et al.* 2006; Sykes and Day 2007), human-hamster hybrid cells (Ueno *et al.* 1996), and human cells (Manesh *et al.* 2015). These findings also relate to another of Hill's Criteria - Consistency, defined by Hill as generality or repeatability – but here again, they do not support the LNT model; instead they demonstrate thresholds.

The USEPA's own Scientific Advisory Board (Morgan and Lipoti 2008) has cautioned the Agency on taking this LNT position stating,

> "Radiation-induced genomic instability seems to be one of the early stages in the carcinogenesis process and has been seen both in vitro and in vivo. *These observations challenge the relative importance that initial mutations play in radiation-induced cancer* (Kadhim *et al.* 2004)",

and further,

"*Genomic instability and the ability to modify responses after the radiation exposure both challenge the linear relationship between initial DNA damage and cancer frequency*." (emphasis added)

Strength of association is another of Hill's Criteria. USEPA states the evidence is strong and consistent the LNT response at moderate and low doses. However, radiation in general is a weak carcinogen (Hall 2006; Hayes 2014) and the evidence that LDDR radiation exposure in particular increases cancer risk is lacking (Ulsh 2012). In fact, many professional organizations have explicitly warned against estimating risks from low dose radiation environments due to large uncertainties associated with the epidemiologic data (ICRP 2007; UNSCEAR 2012; HPS 2016). USEPA's position on this point appears to contradict their own guidance document (USEPA 2011), which states,

"Generally speaking, epidemiology cannot be used to detect and quantify the carcinogenic effects of radiation at doses below about 100 mGy of low-LET radiation because of limitations on statistical power (Land 1980; Brenner *et al.* 2003)."

Is the scientific community convinced on LNT?

"Over the last half century, numerous authoritative national and international bodies have convened committees of and repeatedly they have endorsed LNT as a reasonable approach to regulating exposures to low dose radiation. One exception was a French National Academy Report, which found low-dose radio biological effects in vitro indicative of nonlinearity in the dose response." (Edwards 2015)

US EPA appeal to authority and consensus

The USEPA "appeals to authority" (Hansen 2015), where the LNT model is asserted to be valid because some authority putatively endorses it, another form of confirmation bias—that ignores the evidence that the "consensus" may not be based on good evidence. There is plenty of dispute about LNT, and it is based on evidence that is reliable and there is disagreement about LNT that extends to individual scientists, professional societies, expert advisory bodies, US regulators, nor even within USEPA itself. As acknowledged above, contradictory recommendations based on cited evidence and studies were issued by the French National Academies of Science and Medicine (Aurengo *et al.* 2005) that contradict the "consensus" so, by definition there is no consensus. The US EPA's scientific argument relies on the BEIR VII document released by the National Research Council of the National Academy of Science, however, other organizations have repeatedly cautioned against application of the LNT model to calculate hypothetical risks from LDDR exposures (ICRP 2007; UNSCEAR 2012).

For example, UNSCEAR has stated,

> "In general, increases in the incidence of health effects in populations cannot be attributed reliably to chronic exposure to radiation at levels that are typical of the global average background levels of radiation. … the Scientific Committee does not recommend multiplying very low doses by large numbers of individuals to estimate numbers of radiation-induced health effects within a population exposed to incremental doses at levels

> equivalent to or lower than natural background levels". (UNSCEAR 2012)

Similarly, the ICRP has stated,

> "Collective effective dose is an instrument for optimization, for comparing radiological technologies and protection procedures. Collective effective dose is not intended as a tool for epidemiological studies, and it is inappropriate to use it in risk projections. This is because the assumptions implicit in the calculation of collective effective dose (*e.g.,* when applying the LNT model) conceal large biological and statistical uncertainties. Specifically, the computation of cancer deaths based on collective effective doses involving trivial exposures to large populations is not reasonable and should be avoided. Such computations based on collective effective dose were never intended, are biologically and statistically very uncertain, presuppose a number of caveats that tend not to be repeated when estimates are quoted out of context, and are an incorrect use of this protection quantity". (ICRP 2007)

USEPA's estimates of cancer incidence and mortality risks due to low doses of ionizing radiation for the U.S. population (2015), as well as their advice to the public and tools used to establish cleanup levels, are at odds with UNSCEAR's and ICRP's guidance. For example, USEPA states,

> "…overall, if each person in a group of 10,000 people exposed to 1 rem of ionizing radiation, in small doses over a life time, we would expect 5 or 6 more people to die of cancer than would otherwise. In this group of 10,000 people, we can expect about 2,000 to die of cancer from all non-radiation causes. The accumulated exposure to 1 rem of radiation, would increase that number to about 2005 or 2006." (USEPA 2015a)

This advice to the public is inconsistent with the intended purpose of effective dose (prospective dose estimation for the purpose of optimization), which is inappropriate for predicting future cancer risk (Fisher and Fahey 2017).

Advice undermining the claim of a pro-LNT consensus is not limited to external expert advisory bodies. USEPA's own Scientific Advisory Board (SAB) has expressed caution as well. USEPA has claimed that unfettered application of the LNT,

> "…is the position adopted by the USEPA after review by the Agency's Scientific Advisory Board, an independent group of distinguished outside scientists" (Edwards 2015)

However the SAB's Radiation Advisory Committee (RAC) cautioned (Morgan and Lipoti 2008):

- "...a major issue with the choice of the LNT model is whether it is appropriately applied at low doses."
- "…while the RAC endorses USEPA's use of the LNT model, the Agency is advised to continue to monitor the science of the biological mechanisms underlying cancer induction at low doses of ionizing radiation and of their influence on the biophysical models used to estimate the cancer risk in this dose range."
- "At radiation exposures in the range of natural background, it is difficult to distinguish radiation-induced changes in risk from the baseline. Thus, as a cautionary note, the RAC recommends that the USEPA discuss potential problems associated with the use of LNT dose response model risk estimates in very low dose settings. Currently at these low doses, statistically significant differences between the cancer rates among "exposed" (defined study populations) and "non-exposed" (defined comparison populations) are not observed."

- "As BEIR VII acknowledges, the epidemiological data below 100 mSv (0.1 Sv) are not sufficient by themselves for risk estimation, and considerable cellular and animal data suggest complexities beyond the application of a simplified DNA damage model which historically has been used as support for an LNT dose-response model."

It is important to note that since the SAB last took up this issue and advised USEPA to explicitly monitor developments on these topics, the NCRP has issued comprehensive reports on uncertainties in the measurement and dosimetry of external radiation (NCRP 2007b), internal radiation dose (NCRP 2009), and in the estimation of radiation risks (NCRP 2012).

Despite this guidance, the USEPA develops risk estimation tools based on the LNT model to determine cleanup policies and guidelines for its Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) Superfund sites. Because they multiply very small doses by large populations to predict excess cancer incidence or mortality, these tools also conflict with the scientific guidance provided by other governmental organizations and professional societies.

There also is no consensus among US regulators. The US General Accounting Office (GAO) has twice investigated whether or not there is a consensus among USEPA, the NRC, and the Department of Energy (DOE) on approaches to regulating LDDR radiation exposures to the public. Over twenty years ago, the GAO found,

> "the radiation standards that have been developed reflect a lack of overall interagency consensus on how much radiation risk to the public is acceptable"

and also,

> "Differences in radiation limits and risks, calculation methods, and protective strategies reflect the historical lack of a unified federal framework for protecting the public from radiation exposure" (GAO 1994).

The situation had not improved by 2000, with GAO finding (GAO 2000),

> "U.S. regulatory standards to protect the public from the potential health risks of nuclear radiation lack a conclusively verified scientific basis, according to a consensus of recognized scientists. In the absence of more conclusive data, scientists have assumed that even the smallest radiation exposure carries a risk. This assumption (called the "linear, no-threshold hypothesis" or model) extrapolates better-verified high-level radiation effects to lower, less well-verified levels and is the preferred theoretical basis for the current U.S. radiation standards. However, this assumption is controversial among many scientists"

and also,

> "…USEPA and NRC have disagreed on exposure limits. Although we recommended as far back as 1994 that the two agencies take the lead in pursuing an interagency consensus on acceptable radiation risks to the public, they continue to disagree on two major regulatory applications: (1) the proposed disposal of high-level nuclear waste in a repository at Yucca Mountain and (2) the cleanup and decommissioning of nuclear facilities."

There is also no consensus in support of the LNT model among relevant professional societies (SPR 2001; ARPS 2008; AAPM 2011; HPS 2016). Extrapolation of LDDR risks via the LNT model is at odds with the advice of professional societies around the world. For example, the Australasian Radiation Protection Society (ARPS) has stated,

> "There is insufficient epidemiological evidence to establish a dose-effect relationship for effective doses of less than a few tens of millisieverts in a year above the background level of exposure" and further, "…no inference may be drawn concerning the risk to health or risk of fatality of an individual from an effective dose below 10 mSv in a year. For individual doses less than some tens of millisieverts in a year, risk inferences are unreliable and carry a large uncertainty that includes the possibility of zero risk" (ARPS 2008).

In the United States, the Health Physics Society (HPS) has concluded,

> "In accordance with current knowledge of radiation health risks, the Health Physics Society recommends against quantitative estimation of health risks below an individual dose of 5 rem in one year or a lifetime dose of 10 rem above that received from natural sources. Doses from natural background radiation in the United States average about 0.3 rem per year. A dose of 5 rem will be accumulated in the first 17 years of life and about 25 rem in a lifetime of 80 years. Estimation of health risk associated with radiation doses that are of similar magnitude as those received from natural sources should be strictly qualitative and encompass a range of hypothetical health outcomes, including the possibility of no adverse health effects at such low levels" and further, "There is substantial and convincing scientific evidence for health risks following high dose exposures. However, below 5–10 rem (which includes occupational and environmental exposures), risks of health effects are either too small to be observed or are nonexistent" (HPS 2016).

Additional examples from medical physics and radiology professional societies are provided in Section V below.

In addition to expert advisory bodies and professional societies, studies have also been conducted of individual scientists' views regarding the accuracy of the LNT dose response model for radiation effects (Silva *et al.* 2007; Jenkins-Smith *et al.* 2009) (Table 1). A survey of scientists employed at US national laboratories revealed that 70% believed that a threshold model accurately reflected radiation effects, compared to only 12% who believed a LNT model is accurate (Silva *et al.* 2007). Even among members of the Union of Concerned Scientists, a group which has expressed concerns about the US nuclear power industry, 48% believed a threshold model accurately describes LDDR effects while only 21% favored a LNT model. The results were similar when scientists from the US and Europe who subscribe to the journal *Science* were surveyed (Jenkins-Smith *et al.* 2009): (1) 75% of U.S scientists believed a sublinear threshold model accurately described radiation effects, compared to only 19% who favored a LNT model; (2) for British scientists, the breakdown was 71% for sublinear threshold and 21% for LNT models; (3) for French scientists, 70% and 18% respectively; (4) for German scientists, 64% and 22% respectively, and (5) for other European scientists, 69% and 23%. These studies indicate that a majority of individual scientists are skeptical of the accuracy of the LNT model - exactly the opposite of a pro-LNT consensus claimed by USEPA (Puskin 2009).

I. Should the BEIR VII report continue to be used to justify the use of the LNT model for LDDR radiation environments?

The USEPA places great weight on a few scientific references to support its application of the LNT model, most notably, the BEIR VII report from the U.S. National Academy of Sciences (NAS) (USEPA 2011). For example, USEPA states,

> "The BEIR VII study, which was sponsored by several federal agencies including the USEPA and the NRC, determined that "the balance of evidence from epidemiologic, animal and mechanistic studies tend to favor a simple proportionate relationship at low doses between radiation dose and cancer risk." (Edwards 2015)

The NAS originally adopted the LNT model as the basis for its philosophy to protect against radiation-induced genetic mutations in the human population at the recommendation of its Biological Effects of Atomic Radiation (BEAR) Committee Genetics Panel in 1956 (Jones 2005). This recommendation was made in spite of the fact that radiation-induced genetic effects in the offspring of irradiated parents have never been observed in humans. Recent historical research has revealed that this recommendation was made under questionable circumstances [(Calabrese 2013; Calabrese 2015a; Calabrese 2015c, 2015b; Calabrese 2016), but see also (Beyea 2016a; Beyea 2016b; Beyea 2017)]. Even so, the LNT model was later expanded and applied to radiation-induced cancer risks. Controversial from the beginning, this recommendation nevertheless initiated decades of institutional inertia, with multiple iterations of NAS Committees repeatedly reaffirming the suitability of the LNT model as the basis of radiation protection philosophy, most recently in the BIER VII report over a decade ago (National Research Council 2005). The BEIR VII Committee concluded,

> "…current scientific evidence is consistent with the hypothesis that there is a linear, no-threshold dose-response relationship between exposure to ionizing radiation and the development of cancer in humans".

Even though they acknowledged that a linear-quadratic model fit the data better than the LNT model at low doses, they reported the improvement was not statistically significant. In large part because the NAS inappropriately treated the LNT model as if it were the null hypothesis rather

than appropriately treating it as an alternative hypothesis to be tested against the null of no effect, the LNT model became the Committee's preferred recommendation. In turn, the USEPA incorporated BEIR VII risk models into their policy and guidance (USEPA 2006).

However, two major pieces of evidence the BEIR VII Committee relied upon to support their endorsement of the use of the LNT model to estimate risks from low doses, the Lifespan Study (LSS) of the Japanese atomic bomb survivors and the 15-country study of nuclear workers, no longer support the LNT model (Harvey *et al.* 2015). We summarize the problems with continuing to cite these two pieces of evidence to justify risk estimates using the LNT model in LDDR environments below.

It is widely acknowledged (in the BEIR VII report and elsewhere) that the LSS was the most influential study in setting radiation protection guidelines around the world. It is also evident that even this dataset do not provide definitive evidence of increased cancer risk after exposure to low radiation doses (Kamiya *et al.* 2015). In fact, the most recent epidemiological study on cancer mortality in the Japanese survivors of the atomic bombings states,

> "the estimated lowest dose range with a significant ERR [excess relative risk] for all solid cancer was 0 to 0.20 Gy" (Ozasa *et al.* 2012b).

Another way of saying this is that no significant ERR was observed for doses below 0.20 Gy. The authors also concluded that,

> "…statistically significant upward curvature was observed when the dose range was limited to 0–2 Gy... The curvature over the 0–2 Gy range has become stronger over time".

This means the argument for a LNT relationship has weakened over time. This is an example of epidemiological data possibly reflecting dissimilarity of biological responses to LDDR and

HDDR, however it is not discussed by the authors in spite of explicit calls to integrate biology and epidemiology (NCRP 2015; Preston 2017). Despite that evidence, these authors concluded,

> "…a formal dose-threshold analysis indicated no threshold; *i.e.*, zero dose was the best estimate of the threshold" (Ozasa *et al.* 2012b, 2012a).

Reviewing their threshold analysis, others found that they excluded the possibility of negative values despite eight of the ten lowest data points having confidence intervals including negative values. Alternative analyses that did not exclude negative values revealed the possibility of a nonzero threshold (Doss *et al.* 2012; Sasaki *et al.* 2014; Siegel and Welsh 2015; Socol and Dobrzynski 2015; Ulsh 2015).

Similarly for cancer incidence in the LSS cohort,

> "The lowest dose range that showed a statistically significant dose response using the sex averaged, linear ERR model was 0–100 mGy" (Grant *et al.* 2017)

In other words, there are no detectable health effects below 100 mGy. It is evident that statistical power limitations preclude the selection of one alternative hypothesis over another (*e.g.*, LNT vs. linear with threshold), therefore the assertion that the LSS data provide definitive evidence in support of the LNT is not accurate. A threshold model is also consistent with both the latest solid cancer incidence and mortality data.

The second piece of evidence the BEIR VII Committee relied heavily upon was the so called "15-country study" (Cardis *et al.* 2007). This study initially concluded that,

> "Significantly increased risks were found for mortality from all cancers excluding leukemia and from lung cancers".

However, further analysis revealed that this conclusion is also no longer valid. The Canadian Nuclear Safety Commission (CNSC) concluded that Canadian Atomic Energy of Canada, Ltd.

(AECL) nuclear energy workers (NEWs) cohort included in the original 15-country study did,

> "… not have an increased risk of solid cancer mortality. Incomplete dose records are likely the cause for the apparent increased risk of solid cancer mortality in AECL NEWs first employed before 1965 (1956-1964)". (CNSC 2011)

Furthermore, (Zablotska *et al.* 2014) concluded:

> "Significantly increased risks for early AECL workers are most likely due to incomplete transfer of AECL dose records to the National Dose Registry. Analyses of the remainder of the Canadian nuclear workers (93.2%) provided no evidence of increased risk"

and,

> "Study findings suggest that the revised Canadian cohort, with the exclusion of early AECL workers, would likely have an important effect on the 15-country pooled risk estimate of radiation-related risks of all cancer excluding leukaemia by substantially reducing the size of the point estimate and its significance".

These findings should serve as a warning against relying on BEIR VII to justify the use of the LNT model for LDDR risk estimation purposes.

In summary, two influential pieces of evidence relied upon by the BEIR VII Committee (the LSS cohort, and the 15-country study) no longer support the LNT model based on the latest scientific literature. However, the USEPA relies heavily upon the recommendations of the BEIR VII report on this issue and continues to use it to support is current policies and risk assessment strategies.

II. What other information is available in the scientific literature and does it support the

continued use of the LNT model for LDDR environments?

The USEPA has cited studies published after BEIR VII, which they assert provides support for the LNT model in LDDR environments (Pawel 2015; Puskin 2016):

> "Since publication of BEIR VII, additional evidence has accumulated supporting the use of LNT to extrapolate risk estimates from high acute doses to lower doses and dose rates. In this connection, we would note, inter alia, results of epidemiological studies on: nuclear workers in the United States, France and the United Kingdom (Leuraud *et al.* 2015); residents along the Techa River in Russia who were exposed to radionuclides from the Mayak Plutonium Production Plant (Krestinina *et al.* 2010; Davis *et al.* 2015); and children who had received CT scans (Pearce *et al.* 2012). These studies have shown increased risks of leukemia and other cancers at doses and dose rates below those which LNT skeptics have maintained are harmless - or even beneficial." (Edwards 2015)

Follow up studies of a selected part of the cohort included in the 15-country study has recently been published to examine leukemia (Leuraud *et al.* 2015) and solid cancer (Richardson *et al.* 2015) risks. These studies, also known as the INWORKS studies, examined risk in worker cohorts from the USA, France, and the UK (a subset of the larger cohort included in the 15-country study). The leukemia study (Leuraud *et al.* 2015) concluded,

> "This study provides strong evidence of positive associations between protracted low-dose radiation exposure and leukemia".

Similarly, the solid cancer study (Richardson *et al.* 2015) concluded,

> "The study provides a direct estimate of the association between protracted low dose exposure to ionizing radiation and solid cancer mortality".

Several methodological questions have been raised about these studies (Doss 2015; Nagataki and Kasagi 2015), and the authors have replied (Schubauer-Berigan *et al.* 2015). In addition, numerous methodological shortcomings have been identified by (Sacks *et al.* 2016). These include:

(1) failure to account for natural background radiation exposure, the differences in which potentially dwarf the occupational exposures of the study cohort;

(2) failure to account for medical exposures experienced by the public;

(3) failure to account for dose-rate effects;

(4) the *a priori* assumption of a LNT dose-response;

(5) mischaracterization of the y-intercept as zero total dose, when in fact, it was zero occupational dose;

(6) arbitrary exclusion of all dose responses except LNT and linear-quadratic (which actually provided a better fit to their observed data, but the authors claimed the improvement was not statistically significant);

(7) dismissing six of seven disease outcomes as being highly imprecise rather than stating that they are not statistically significantly different from no-effect;

(8) creating an artificial disease category by arbitrarily combining three forms of leukemia and excluding a fourth, then characterizing this artificial grouping as an additional statistically significant association;

(9) providing misleading characterizations of the data above 200 mGy as statistically significant when in fact, only the 200-300 mGy dose category was significantly elevated, while the highest dose category was not (nor was any other dose category);

(10) insufficient consideration of age as a possible confounder;

(11) *a priori* and arbitrary consideration only of the possibility of increased risks, and excluding the possibility of decreased risks;

(12) the arbitrary choice of a 90% confidence limit rather than the more conventional 95%, thus increasing the possibility of significance, then mischaracterizing the results as strong evidence of risk from LDDR radiation exposure.

To this list of methodological shortcomings, we add the omission of *occupationally required* medical imaging exams (which are distinct from medical doses received by the public at large – raised as #2 above), resulting in potential significant underestimation of external radiation dose. With regard to potential confounding by diagnostic medical dose, the INWORKS authors state,

> "…for confounding to occur, medical radiation exposures would need to be associated with occupational doses…which is unlikely to be the case" (Schubauer-Berigan *et al.* 2015).

The basis for the authors' conclusion that such confounding is unlikely is not provided. The omission of dose from medical imaging received by workers as a condition of employment presents one of the most serious questions about the methodology of these studies, as it likely resulted in potentially significant underestimation of external radiation dose. At several of the US sites included in the study, workers were required to undergo a medical exam at least yearly, which included medical imaging exams. Of particular concern is the use of photofluorography in the early years (*e.g.* 1940s to 1950s). Photofluorography delivered high dose-rate radiation exposures to workers at the Savannah River Site [1951-1960, 0.46 mGy per exam to male red bone marrow](Thomas 2009), Hanford [1943-1962, 1.41 mGy](Thomas 2009), and the three Oak Ridge Sites: Y-12 [at least 1943-1947, 2.76 mGy](Murray 2009), X-10 [at least prior to

1947, 2.58 mGy](Burns 2009), and K-25 [1945-1956, 2.0 mGy](Thomas 2013). So for example, a worker at Hanford from 1943-1962 could have received a red bone marrow dose of ~27 mGy from photofluorography alone. While these are not especially large doses, the authors reported recorded mean occupational external bone-marrow doses of only 16 mGy and median doses of only 2.1 mGy, and they claim to have observed increased leukemia risks. If that is true, then even larger potential doses from occupationally-required medical exams cannot be casually dismissed. The impact of medical imaging exams workers received as a condition of employment has been specifically studied at one of the sites included in the INWORKS study (Cardarelli 2000; Cardarelli *et al.* 2002). Work-related medical imaging exams were the predominant source of radiation exposure among workers at the K-25 site. In fact, the work-related medical imaging dose was on average 50 times higher than the recorded occupational dose (Cardarelli *et al.* 2002). Occupationally-required medical imaging could certainly influence the estimation of possible thresholds (which the authors of the INWORKS studies did not report), estimates of risk per unit dose, and the shape of the dose-response relationship (Cardarelli *et al.* 2002). Furthermore, at some sites, workers judged to be at high risk (*e.g.* those performing jobs where they received higher occupational radiation dose) were examined more frequently, which indicates nonrandom distribution of medical radiation exposure among the cohort, and subsequent bias. Neglecting this important source of exposure seriously compromises the conclusions of the INWORKS study. At least for the US sites, workers' medical records are available, so including this dose should be feasible. The importance of this issue for the UK and French cohorts included in the INWORKS study should also be examined.

For the Techa River cohort, it is unclear why USEPA chose to cite an outdated reference (Krestinina *et al.* 2010) when there is a more recent update (Krestinina *et al.* 2013), however risk

estimates in the most recent update are less than half of the estimates in the earlier reference USEPA cited. Furthermore, (Krestinina *et al.* 2013) states,

> "For the basic dose–response model, the ERR was assumed to be linear in dose but we also considered models where the dose response was taken as a linear-quadratic, a pure quadratic function of dose, or threshold models in which the ERR was assumed to be 0 up to some threshold dose and taken as linear for higher doses".

No further details are provided on their analysis of thresholds. It is not clear whether the authors allowed ERR to assume negative values, which would certainly be indicated given that the total leukemia rates reported for the five lowest dose groups were lower than the control group (those who received <0.01 Gy). Only the two highest dose groups (those receiving 0.5-1 Gy and 1+ Gy) exceeded controls. For leukemia excluding CLL, the rates for two of the three lowest dose groups were below that for the control group, suggesting a threshold or even potential hormetic effect which is often dismissed as a potential health worker effect. The authors reported that their data, "…are consistent with a linear dose response…", however they do not report whether or not their data are also consistent with a threshold or hormetic dose-response, which would seem to be the case given these results. If multiple models adequately describe the observed dose-response, then USEPA should not cite these results as supporting the LNT model and excluding the threshold model as petitioned by SARI.

For solid cancers in the Techa River Cohort, the situation is similar. USEPA cited (Davis *et al.* 2015), and again, the authors claimed,

> "There is a statistically significant (P=0.02) linear trend in the smoking-adjusted all-solid cancer incidence risks".

However, a closer look at the data in this study reveals that the two lowest dose categories have ERR estimates lower than the zero dose controls, consistent with a hormetic dose-response, or at least a threshold (Figure 1). This is another example of epidemiological data possibly reflecting the dissimilarity of biological responses to LDDR and HDDR, but again it is not discussed by the authors.

Within the past few years, new studies of pediatric patients receiving computed tomography (CT) medical imaging exams claimed to observe increases in risks from relatively low doses (though delivered at a high dose-rate)(Pearce *et al.* 2012; Mathews *et al.* 2013). These studies received extensive press coverage, and almost immediately, claims were made that,

> "…the new data confirm that the cancer risk associated with the radiation from a CT scan is very small, but not zero" (Hall and Brenner 2012).

In presentations to the Interagency Steering Committee on Radiation Standards (ISCORS), USEPA has referenced these studies to suggest potential adverse health effects from LDDR radiation (Pawel 2015; Puskin 2016). However, these early enthusiastic pronouncements have not held up to scientific scrutiny. A number of significant methodological issues have been identified in these studies (Cohen 2013; Boice 2015; Siegel and Welsh 2015), including: (1) individual doses were not directly assessed, but rather "typical" doses were assumed; (2) doses applied were for adults and assumed no decrease for pediatric patients, even though this is the standard of care; (3) the reason for the CT was not considered, and it is possible that the underlying condition indicating the CT has associated cancer susceptibility [this point was acknowledged in the slides from one of the USEPA presentations (Pawel 2015), but not the other (Puskin 2016)]. On the latter point, as explained by (Ulsh 2015),

> "One of the strongest associations (Pearce *et al.* 2012) observed was for gliomas,

but they did not control for prior head injury. Head injuries are a common reason for head CT in children.., and head injury may be associated with brain tumors."

This assessment agrees with (UNSCEAR 2013a), which concluded

> "... There are concerns about the risk estimates because of lack of information about indications for the CT scans and the consequent potential for 'reverse causation' (*i.e.,* cancers may have been caused by the medical conditions prompting the CT scans rather than by the CT dose)".

The NCRP came to similar conclusions, stating:

> "Children who receive frequent examinations may have some underlying disability related to the outcome of interest. That is, a child who receives multiple CT examinations of the head may have a central nervous system disorder that is prompting such examinations and it is these underlying disorders that are related to the cancer diagnosis and not the CT radiation dose" (NCRP 2012).

Furthermore, two recent studies from France (Journy *et al.* 2015) and Germany (Krille *et al.* 2015) have demonstrated that failing to account for the underlying reason requiring the exam can inflate risk estimates in studies of populations exposed to CT scans.

In spite of the UNSCEAR and NCRP conclusions, and multiple papers pointing out the limitations of these studies, [*e.g.*, (Boice 2015; Ulsh 2015)], they continue to be cited by USEPA and others as providing strong or definitive evidence of risks of very low radiation doses and supportive of the LNT model (Pawel 2015; Puskin 2016). However, the application of the LNT model and the ALARA principle to medical imaging has come under heavy criticism (Siegel *et al.* 2017a; Siegel and Sacks 2017; Siegel *et al.* 2017b; Siegel *et al.* 2017c). Professional societies with expertise in medical imaging continue to unanimously maintain that the carcinogenicity of

low radiation doses has not been demonstrated, and estimates of risks from low doses like those associated with medical imaging exams remain speculative and unproven. For example:

- **American Association of Physicists in Medicine (AAPM):** "Discussion of risks related to radiation dose from medical imaging procedures should be accompanied by acknowledgement of the benefits of the procedures. Risks of medical imaging at effective doses below 50 mSv [5 rem] for single procedures or 100 mSv [10 rem] for multiple procedures over short time periods are too low to be detectable and may be nonexistent. Predictions of hypothetical cancer incidence and deaths in patient populations exposed to such low doses are highly speculative and should be discouraged. These predictions are harmful because they lead to sensationalistic articles in the public media that cause some patients and parents to refuse medical imaging procedures, placing them at substantial risk by not receiving the clinical benefits of the prescribed procedures" (AAPM 2011).
- **International Organization for Medical Physics: "**Prospective estimates of cancers and cancer deaths induced by medical radiation should include a statement that the estimates are highly speculative because of various random and systematic uncertainties embedded in them. These uncertainties include dosimetric uncertainties; epidemiological and methodological uncertainties; uncertainties from low statistical power and precision in epidemiology studies of radiation risk; uncertainties in modeling radiation risk data; generalization of risk estimates across different populations; and reliance of epidemiological studies on observational rather than experimental data. Such uncertainties cause predictions of radiation-induced cancers and cancer deaths to be susceptible to biases and confounding influences that are unidentifiable." (Pradhan 2013)
- **The Society for Pediatric Radiology:** "To prevent misconceptions and public alarm, it

is important to realize that the radiation used in CT scans has not been proven to cause cancer during a child's lifetime. The very small risk of cancer from radiation exposure is an estimate and is based on information and statistics that are debatable" (SPR 2001).

USEPA has also cited studies of natural background and other environmental LDDR radiation exposures. Studies to understand health effects on people exposed to LDDR radiation are especially important since they more closely reflect the environment following a radiological cleanup effort. They also serve to help the agency determine if the cleanup policies are adequate to protect human health and environment while accounting for social and economic factors (*i.e.,* do they do more good than harm to society?). USEPA cited a study of leukemia risk due to natural background radiation exposure (Kendall *et al.* 2013), and noted that this study claimed to have observed significant excess risk associated with dose rates as low as 1 mGy y^{-1} (Pawel 2015; Puskin 2016). We reviewed (Kendall *et al.* 2013), and have identified several methodological issues:

1. The authors conclude:

> "The possibility of confounding by some unidentified factor can never be entirely disproved, and is of particular concern when dealing, as here, with small RRs. However, we were unable to identify any mechanism whereby such confounding might plausibly account for the observed magnitude and specificity of effect in this study".

Socio-economic status was the only confounder considered. There is evidence that paternal smoking is also associated with increased risk of childhood leukemia (Milne *et al.* 2012), yet the authors did not consider this. USEPA presented Kendall et al. as evidence of a LNT relationship for LDDR exposures despite the fact that it ignored

potential confounding due to exposure to tobacco smoke. It is also worth noting that USEPA explicitly criticized other ecological LDDR studies that contradicted the LNT model (Cohen 1987, 1995) for not accounting for smoking [(Puskin 2003, 2010), but see also (Cohen 2004a; Cohen 2004b)]. In the same presentation citing Kendall *et al*., USEPA acknowledged the potential role of confounding factors, stating "variations in cancer rates due to other causes tend to swamp out those due to [ionizing radiation] exposure", but apparently did not consider the potential for smoking to confound this study by noting this limitation.

2. Kendall *et al*. estimated background gamma and radon doses based on the residence location of the mother, using county measurements. This information was available for cases both at birth, and at time of diagnosis. It was discovered that about half of the cases had moved between birth and diagnosis. For controls, only the residence location at time of birth was available, so the number of the controls who moved after birth is unknown. UNSCEAR warned that,

   > "*The study should be interpreted with caution because of the large uncertainties associated with using an ecological measure of dose."*(UNSCEAR 2013c)

3. The study considers only radiation exposure from natural background gamma radiation and radon. It ignores other, potentially larger sources of radiation exposure, *e.g*. medical exposure. This is in spite of the fact that one of the co-authors of this study (M.P. Little) was a co-author of a separate study which claimed that exposure of British children to CT scans has increased their leukemia risk (Pearce *et al.* 2012). If it is true that exposure to CT scans is an important risk factor for childhood leukemia in this population, how can omitting it from the Kendall study be justified? How can the authors claim an inability to

identify other possible sources of bias or confounding?

4. The number of cases with a gamma-ray dose-rate different from their control(s) was 14,308 (52% of all cases). This means that for 48% of the cases, the gamma-ray dose-rate was not different from their controls. This is not a result that strongly demonstrates a causal relationship between background gamma-ray dose-rate and leukemia. This observation does not satisfy Hills Criteria of Strength of Association.
5. The authors used a log-linear logistic model for data analysis. But use of such a model to analyze dose-risk relationships contains the intrinsic assumption that dose is linearly related to leukemia risk without threshold. They did not report testing other possible dose-response relationships. The authors assumed the validity of the LNT model, and citing this study in support of the LNT model is therefore a circular argument (Hansen 2015).

We also note that the USEPA presentations do not discuss the numerous studies of high natural radiation background areas that have observed no excess risks of cancer, even in populations exposed to dose-rates well in excess of 100 mGy y^{-1} [*e.g.* (Wei and Sugahara 2002; Mortazavi *et al.* 2005; Mosavi-Jarrahi *et al.* 2005; Zou *et al.* 2005; Nair *et al.* 2009; Tao *et al.* 2012)], except to categorically characterize them as "specious" (Puskin 2016). An objective evaluation of these studies is warranted to better understand any health effects from LDDR exposure to ionizing radiation, especially following the large-scale accidents in Chernobyl and Fukushima.

A similar LDDR situation, but involving a man-made elevated radiation background, occurred in Taipei, Taiwan where construction materials contaminated with ^{60}Co were used to build hundreds of structures throughout the city (Chang *et al.* 1997). These buildings included

schools and nearly 1,000 apartments. More than 4,000 people were chronically exposed to elevated radiation levels in this incident, some estimated as high as 1.2 Gy of cumulative dose (Chang 1993). It has also been the basis of legal action against the Taiwanese government (Hwang *et al.* 2001). USEPA cited a study of this population as supporting the LNT model.

Doses to the apartment-dwellers were estimated by survey instrument measurements in the affected apartments, and compared to doses measured by personal dosimeters (Cardarelli *et al.* 1997). This study found agreement to within 10-15% for adults, but only to within 60% for children. Large uncertainties were also noted in other dose reconstruction efforts (Tung *et al.* 1998), which found that children received the smallest radiation doses compared to other family members. Reconstructed doses were found to agree with measured doses to within a factor of three (Hsu *et al.* 2003). Radiation dose-rates have also been measured using thermoluminescent dosimeters (TLD's) (Chen and Yeh 2003), and studies have been conducted to determine how to convert TLD measurements to dose-rates received by residents using phantoms (Lee *et al.* 1999).

Epidemiological studies of this population reveal evidence that low doses of radiation not only failed to increase cancer risk, but actually provided a protective effect (Sanders 2010). A study of cancer mortality in this population observed,

> "The experience of these 10,000 persons suggests that long term exposure to radiation, at a dose rate of the order of 50 mSv (5 rem) per year, greatly reduces cancer mortality…" (Chen *et al.* 2004).

A separate study of cancer incidence was also conducted (Hwang *et al.* 2006). The abstract of this paper highlighted the few specific cancer subtypes which yielded increased standardized incidence ratios (SIRs), based on very low numbers of cases (*e.g.* leukemia, 7 cases vs. 3.3 expected). No mention was made in the abstract of the lack of increase for the other 19 types of

cancer which showed no statistically increased risks, nor more importantly, the observation of statistically significantly lower SIRs for all cancers (95 observed vs. 114.9 expected), all cancers except leukemia (88 observed vs. 111.6 expected), and all solid cancers (82 observed vs. 109.5 expected). The USEPA's presentation highlighted only the result for leukemia and breast cancer from a follow-up study which arbitrarily excluded the possibility of lower risks in the exposed population, and forced a linear fit to the data on selected cancers to estimate hazard ratios at 100 mGy (Hwang *et al.* 2008). The hazard ratio at 100 mGy for leukemia excluding chronic lymphocytic leukemia was just barely significant at the 90% alpha level (CI: 1.01-1.31), but not at the more conventional 95% level. The USEPA presentations did not discuss that no statistically significant increases were observed in all cancers, all cancers excluding leukemia, all solid cancers, or cancers of the cervix, lung, thyroid, liver, stomach, or rectum, even when the data was forced to follow a LNT model. Further, the USEPA presentation did not mention two other studies, including a larger study of cancer incidence by the same authors, which found statistically significantly *reduced* mortality (Chen *et al.* 2004) and incidence (Hwang *et al.* 2006) of all cancers combined and all solid cancers, suggesting not only a lack of cancer risk from low radiation doses, but in fact a protective effect. This creates the misleading impression that the Taiwan studies support the LNT model, when in fact, they directly contradict it.

> Another update on this cohort was recently published (Hsieh *et al.* 2017), which claimed, "Dose-dependent risks were statistically significantly increased for leukaemia excluding chronic lymphocytic leukaemia (HR100mSv 1.18; 90% CI 1.04-1.28), breast cancers (HR100mSv 1.11; 90% CI 1.05-1.20), and all cancers (HR100mSv 1.05; 90% CI 1.0-1.08, P=0.04)".

However, as observed by Doss [GET REFERENCE TO MOHAN'S LTE],

"The (Hsieh, 2017) publication claims increased hazard ratios for breast cancer and leukemia using LNT model based analysis of the cancer data (using 90% confidence intervals) – a conclusion that is similar to that of (Hwang, 2008) publication. However, if we examine the total number of cancers observed, and compare to expected number of cancers, estimated using age dependence of cancer rates in Taiwan cancer registry, relative risk is calculated to be 0.83 (with 95% C.I. being 0.73 to 0.94). Their use of the LNT model for analysis allows them to hide this hormetic decrease in overall cancers. The publication also claims younger irradiated subjects (age < 20) have a higher risk of cancer but this conclusion is based on low statistics (a few cancers)."

III. Is it appropriate to regulate ionizing radiation in the same manner as toxic chemicals?

In 1992, the USEPA SAB provided guidance on ways to harmonize risk assessment and risk reduction strategies for radiation and chemicals (Loehr and Nygaard 1992a). They noted that the regulations for radiation and chemical risks developed under different paradigms and stated:

"USEPA's priorities should be directed towards reducing the greatest risks first, especially when that can be accomplished economically. The corollary to that principle is that similar risks should be treated similarly, which calls for harmonization, in so far as is possible, of risk reduction strategies between chemical and radiation. *Harmonization does not necessarily imply identical treatment, but it does imply that any differences in treatment are clearly explained and justified***.**" (emphasis added)

The options noted in the SAB Commentary were:

1. Bring risk-reduction strategies for excess radiation exposures consistently in line with the chemical paradigm, a direction which it noted that some parts of the agency were already headed;
2. Bring chemical risk-reduction strategies more in line with the radiation paradigm; or
3. Achieve harmony between the two systems by modifying both in appropriate ways, explaining residual differences, and placing more emphasis on what can reasonably be achieved. In this case, background risk could be incorporated and the balancing of benefits and costs of risk-reduction measures could be strengthened while maintaining much of the Agency's current approach to chemicals.

The radiation paradigm approach to control radiation exposures is based on principles developed over many decades by the ICRP and the NCRP (Jones 2005). These principles are:

1. JUSTIFICATION: the need to justify any radiation exposures on the basis that the benefits to society exceed the overall societal cost.
2. ALARA (Optimization): maintain any exposures as low as reasonably achievable, economic and social factors being taken into account; and
3. LIMITATION: radiation exposures are kept to levels of *acceptable risk*.

As described by the ICRP,

> "For any situation where intervention is considered, some protective actions might be justified while others are not justified. Of those protective actions which are justified, it is necessary to establish the level at which the best protection will be provided. In other words the radiation detriment averted by each protective action should be balanced against the cost and other detriments of the action in such a way that the net benefit achieved by the protective action is maximized (*i.e.* optimization of protection)". (ICRP 1992)

The principles of ALARA (Optimization) and LIMITATION can be viewed as a "top-down" approach to limit radiation exposure and health risk (Figure 2). Therefore, radiation exposures are considered acceptable if they are less than a specific limit and they are as low as reasonably achievable. Compliance with a dose limit alone does not define acceptable exposures or risk.

The chemical paradigm approach can be viewed as a "bottom-up" approach. The historical use of this paradigm by the USEPA is based on the Delaney Clause of the Federal Food, Drug and Cosmetic Act Food Additives Amendment of 1958. This clause set a standard of *zero* risk to the public from carcinogenic food additives, (*e.g.*, pesticides) that concentrate in processed foods. This was interpreted in terms of a "negligible" but nonzero lifetime cancer risk of 10^{-8}, which was later increased to 10^{-6} due to pesticide measurement difficulties at levels corresponding to the lower risk. This lifetime cancer risk criterion and the concept of risk goals were later incorporated into various USEPA regulations [*e.g.,* CERCLA, Safe Drinking Water Act (SDWA), Clean Air Act (CAA), and Resource Conservation and Recovery Act (RCRA)]. This paradigm has two basic elements:

1) A goal for acceptable risk; and
2) Allowance for an increase (relaxation) in risks above the goal, based primarily on considerations of technical feasibility and cost.

The USEPA made the decision to regulate radiation the same way it regulates toxic chemicals for consistency purposes (USEPA 2014), despite advice from the SAB describing problems with such an approach (Loehr and Nygaard 1992b):

- "To many radiation scientists, reducing excess exposures much below 100 mrem/yr seems unnecessary and in any case exceedingly difficult to monitor for compliance because it is within the natural variability of background."

- "The application of standard chemical risk-reduction criteria to radionuclides in these situations leads to limitations on excess radiation dose that are small in comparison to natural background radiation."
- "In calculating excess risk from human sources of a chemical, background levels, if any, are therefore frequently seen as irrelevant…." This is in marked contrast to radiation, which is universally distributed in the natural environment.

The USEPA treats inorganic metals differently than other chemicals (USEPA 2015a). In the assessment of human risks from exposures to inorganic metals, USEPA takes into account metals that are naturally occurring and vary in concentrations across geographic regions. According to USEPA, the implications of this property include,

"Humans, other animals, and plants have evolved in the presence of metals and are adapted to various levels of metals. Many animals and plants exhibit geographic distributions that reflect variable requirements for and/or tolerance to certain metals. These regional differences in requirements and tolerances should be kept in mind when conducting toxicity tests, evaluating risks, and extrapolating across regions that differ naturally in metals levels."

USEPA also acknowledges that some metals are essential for maintaining proper health of humans, animals, plants, and microorganisms. As a result, USEPA considers the following implications for risk assessment:

- "Adverse nutritional effects can occur if essential metals are not available in sufficient amounts. Nutritional deficits can be inherently adverse and can increase the vulnerability of humans and other organisms to other stressors, including those associated with other metals",

- "Excess amounts of essential metals can result in adverse effects if they overwhelm an organism's homeostatic mechanisms. Such homeostatic controls do not apply at the point of contact between the organism and the environmental exposure", and
- "Essentiality thus should be viewed as part of the overall dose-response relationship for those metals shown to be essential, and the shape of this relationship can vary among organisms. For a given population, "reference doses" designed to protect from toxicity of excess should not be set below doses identified as essential. Essential doses are typically life-stage and gender specific".

These properties are analogous to those ascribed to radiation by the threshold and hormesis response models. An exception has been made to treat risk assessment for inorganic metals differently because of their essential characteristics or natural existence in background. Radiation has not been afforded the same consideration despite the similarities with inorganic metals. Instead, USEPA has stated,

> "…as the purpose of a risk assessment is to identify risk (harm, adverse effect, etc.), effects that appear to be adaptive, non-adverse, or beneficial *may not be mentioned*" (USEPA 2004) (emphasis added)

and further,

> "As a general principle, our practice is not to base risk assessments on adaptive, non-adverse, or beneficial events" (USEPA 2004).

Applying this guidance to radiation risk assessment excludes any scientific evidence on potential benefits from radiation exposures simply by policy mandate. That introduces bias by allowing only information claiming support for the LNT model while prohibiting evidence that contradicts it. Excluding evidence of adaption or benefits, and only considering evidence of harm, is

contrary to radiation protection philosophy as described by the ICRP (Calabrese 2012). National and international expert advisory bodies acknowledge adaptive and hormetic effects, and their consideration has even been formally included in new European standards for protection of the environment against radiation (Garnier-Laplace *et al.* 2010).

Regulating radiation the same way as toxic chemicals also does not take into account that risks from radiation exposure have been established based largely on observations in humans exposed to well-known individual doses, whereas chemical risks are more often based on projections from experiments on animals or human epidemiology that suffer from poorly characterized individual exposures. Since background radiation is an underlying factor that isn't present for most toxic chemicals, the USEPA SAB acknowledged the existence of threshold models for radiation carcinogenesis (*e.g.*, the radium dial painters) or at least "practical thresholds" (*e.g.*, the idea that cancer latency was inversely related to dose such that manifestation of risks at low doses could be delayed so long that no cancers would occur during a normal lifetime)(Loehr and Nygaard 1992a).

> Radiation protection philosophy is distinct from toxic chemical protection philosophy: "The precautionary principle is an alternative risk management strategy that gives disproportionate weighting to technological risks. It is often summarized by the phrase 'better safe than sorry' and requires forgoing, postponing or otherwise limiting a product or activity until uncertainty about potential risks has been resolved in favor of safety (Mossman 2007). ALARA, on the other hand, treats risks and benefits on a level playing field. Accordingly there is no prescribed dose goal. The end result of an ALARA practice is a residual dose and risk that is considered acceptable." (Mossman 2014)

The distinguishing hallmark of the ALARA philosophy is that interventions and radiation protection policies must be low, reasonable, and achievable. The USEPA application of the LNT model for determining risk and developing clean up levels often result in very low numbers that are nearly three orders of magnitude below where adverse effects are reliably observed, and significantly lower than those recommended by national and international expert advisory bodies. For example, the USEPA suggests that radiation exposures above $3x10^{-4}$ risk (about 0.12 mSv per year based on the LNT) is not protective to human health or the environment. As mentioned earlier, even BEIR VII acknowledges that epidemiological data below 100 mSv (0.1 Sv) are not sufficient by themselves for risk estimation, yet the USEPA maintain policies that require cleanup to levels where no net benefit to human health or the environment can be detected.

The USEPA SAB recognized in 1992 that the USEPA Superfund policy documents, like the risk assessment guidance for Superfund (USEPA 2001b) were being developed to be more consistent with the chemical risk paradigm. In contrast, it also noted that the USEPA radon policy was applying a rule of practicality based on the difficulty of reducing radon levels below 150 Bq per m^{-3} (4 picocuries per liter) within a reasonable budget. The associated risk for its' radon policy translates to a lifetime risk of over 1 in 100 for an average person (USEPA 1991) based on the LNT model. More recently, USEPA's approach to radon regulation has been challenged (Siegel *et al.* 2016).

IV. Should the current USEPA regulatory radiation policies be reconsidered and harmonized with the radiation protection

philosophy given the lessons learned from Fukushima?

The NCRP issued reports providing guidance on responding to a radiological or nuclear terrorism incident (NCRP 2010; Nisbet and Chen 2015), and decision making for late-phase recovery from nuclear and radiological incidents (NCRP 2007a). These recommendations from the NCRP endorse the strategy laid out by the ICRP (ICRP 2009), and apply them to the situation in the United States. This new strategy presents a,

> *"marked contrast to the current clean-up approach carried out under statutory regulatory provisions that focuses on radiological risk, precautionary decision making, and clean-up goals close to background"* (Nisbet and Chen 2015).

The ICRP suggests that the reference level should be selected in the lower part of the 1–20 mSv $year^{-1}$ range [100 – 2,000 mrem per year (ICRP 2009)]. This is much more realistic and achievable than the LNT 10^{-6} risk-based preliminary remediation goals (PRGs) developed by USEPA, which are approximately two to three orders of magnitude lower than other guidance provided by NCRP and ICRP.

Although the simplicity of the LNT model used for risk assessment has traditionally been thought to be reasonably conservative, its application has led many to believe that any amount of radiation brings unwarranted risk. This contributes to society's response to make personal decisions to avoid any radiation exposures at all costs thus potentially resulting in more societal harm than good. It also drives down cleanup levels, resulting in extraordinary cleanup costs. Furthermore, USEPA has provided guidance stating "approaches that do not follow the remedial program's policies and guidance should not be used at CERCLA remedial sites" (USEPA 2014). It specifically targets any guidance developed by other Federal, State or Tribal Agencies or by

international or national organizations (*e.g,* ICRP, NCRP and other scientific or professional organizations) and leaves only USEPA guidance available for consultation.

The more recent example of where LNT-based guidance may have caused more harm than good is the evacuation in Fukushima, Japan (Thomas and May 2017). The Fukushima accident involved no deaths directly related to radiation exposure (UNSCEAR 2013), however the evacuation itself caused increased mortality, primarily among the elderly (Nomura et al. 2013, Yasumura et al. 2013, Uchimura et al. 2014). Well over a thousand people died from causes related to the evacuation (Ichiseki 2013), and the continued exclusion of residents from their homes for extended periods of time. This occurred in spite of the fact that "no significant contamination was found in the patients evacuated from the 20 km zone despite the fact that 48 h had passed between the first explosion and their evacuation" (Tanigawa et al. 2012). During the Fukushima incident, the public exhibited distrust of radiation experts, and confusion regarding what risks radiation from the accident actually presented (Clancy and Chhem 2015). The population that evacuated from the area around the Fukushima plant is now at increased risk for mental health problems and other social and psychological problems because of their continued exclusion from their homes, and they are subject to social stigma (Clancy and Chhem 2015; Hasegawa *et al.* 2015).

The application of the LNT to estimate cancer risks associated with residual contamination, without appropriately considering the uncertainties involved (*i.e.,* LNT predictions represent an upper bound estimate of risks, and real risks might in fact be zero), has contributed to continued exclusion of the evacuated Fukushima population from their homes. The same situation occurred at Chernobyl (Jaworowski 2008). In addition, recent research has indicated that even when hypothetical radiation risks from residual radioactive contamination are calculated via the LNT

model, mass evacuations and relocations like those following Chernobyl and Fukushima have been unjustifiably extensive (Thomas 2017; Waddington *et al.* 2017b), and are almost never part of the optimal response strategy (Gale 2017; Thomas and May 2017; Yumashev *et al.* 2017). Therefore, it is reasonable to question the perceived protectiveness of the LNT model for LDDR radiation environments (Siegel *et al.* 2017c). The long term response to the Fukushima accident will undoubtedly involve, and in fact emphasize, providing accurate information about radiation risks to returning residents and dealing with their fears (Ohtsuru *et al.* 2015; Reich and Goto 2015). These fears are exacerbated by strident statements that "there is no safe dose" and "doses outside the USEPA risk range are not protective", and by inaccurate and incomplete information about the uncertainties involved in estimating risks from very low residual radiation doses (Kai 2015).

While some of the remedial strategies in response to the Fukushima accident have been retrospectively analyzed and determined to be justified based on a LNT calculation of risk from residual contamination (Waddington *et al.* 2017c), others response measures have been found to be unjustified (Waddington *et al.* 2017a). Unrealistic cleanup standards, which fail to properly account for the real possibility that risks from such low doses may very well be zero, exacerbate public fears, fail to optimize response strategies by ignoring the economic and public health consequences of these actions (Ashley *et al.* 2017), and can distort the allocation of resources in the recovery effort. The mission of the USEPA is to protect human health and the environment and the status of the science of applying the LNT model in risk estimation and determining cleanup levels is showing that it has the real potential to cause more economic and environmental harm than good to society.

A comprehensive review of the application of ICRP guidelines and the problems encountered

at Fukushima have been documented (Gonzalez *et al.* 2013) and offer many lessons. Among the highlights are the following:

- "It has been noted that the uncertainties surrounding the crisis itself, in addition to the absence of demonstrated risk at the tiny exposures to the population and the uncertain validity of the linear extrapolation of risk down to such tiny doses, raise serious questions about whether these calculations could provide even an order-of-magnitude guess as to possible health consequences. Further, given the wide range of uncertainties in the risk models used, it is likely that zero effects should be included as a lower bound to the estimates, or even as a central estimate of the likely future effects."
- "These hypothetical computations of effects are based on assumptions that cannot be validated because the estimated doses are substantially below the level where epidemiology has the ability to detect increases above the natural occurrence. The large number of deaths reported following these theoretical predictions, especially when not contrasted with the normal high occurrence of death, is alarmist and unfounded and has caused severe anxiety and emotional distress in the Japanese population."
- "It should be recognized, however, that *'balancing' good and harm is not confined to issues associated with radiation exposure. Other non-radiation-related benefits and detriments arising from the protective action must also be considered,* thus going far beyond the scope of radiological protection." (emphasis added)

Fukushima and Chernobyl offer very rare opportunities to learn from the application of radiation protection guidance and strategies in challenging, real-world situations. A frank assessment of the successes and shortcomings of these strategies and how they may impact the agency's cleanup policies is necessary.

USEPA has taken the position that any residual contamination concentration exceeding the upper risk range of $3x10^{-4}$ (a dose of about 0.12 mS y^{-1} [12 mrem y^{-1}]) is "not protective". Is this a valid interpretation given the very different advice given by the ICRP? Gonzalez et al. state:

- "Thus, the public has doubts about what type of exposure the inhabitants of the rehabilitated area will be subject to when the rehabilitation starts. If these people are regarded as members of the public and if the exposure situation is regarded as a planned one, the dose limit of 1 mSv $year^{-1}$ and the corresponding dose constraint could in principle be considered as applicable, therefore *requiring annual doses to the residents to be kept below a few tenths of a millisievert, a restriction that might be considered unrealistic and furthermore rather strange and unreasonable."* (emphasis added) (Gonzalez *et al.* 2013)
- "There was a particular misunderstanding about the appropriate use and application of the dose value of 1 mSv $year^{-1}$. The public tended to regard a dose above this value as dangerous, which created challenges in coping with the aftermath of the accident. The fact that there is little convincing evidence for human health effects below 100 mSv $year^{-1}$ (or 100 times the dose limit) appeared to hold little sway over the level of concern." (Gonzalez *et al.* 2013)

USEPA's interpretation is clearly at odds with the views of the ICRP, which stated,

"The Commission's recommended limits are set at a level which is thought to be associated with a low degree of risk; thus, *unless a limit were to be exceeded by a considerable amount, the risk would still be sufficiently low as not to warrant such countermeasures as would themselves involve significant risks or undue cost.* It is therefore clear that it is not obligatory to take remedial action if a dose-equivalent limit has been or might be exceeded." (ICRP 1977) (emphasis added)

In answer to the question, "Is any amount of radiation safe?", USEPA has explained,

> "In setting limits, USEPA makes the conservative (cautious) assumption that any increase in radiation exposure is accompanied by an increased risk of stochastic effects." (USEPA 2015a)

Similarly, USEPA has explained,

> "LNT also has the great advantage of simplicity, risks from multiple exposures being proportional to the total dose. Given these features of protectiveness and convenience, there is very wide support for LNT in the context of radiation protection, even among scientists and regulators who harbor serious doubts about its scientific validity" (Puskin, 2009).

Note that these explanations are based on the assumption that LNT is "conservative" and "cautious". In light of the Fukushima experience, these assumptions are no longer tenable. Others have argued that radiation protection guidelines are confusing and overly stringent, based on the application of LNT at doses far below where risks can actually be observed, and that this had directly observable negative public health consequences (Siegel *et al*. 2017c; Welsh *et al*. 2017).

IX. Conclusions

The USEPA is the lead federal agency responsible for protecting human health and the environment from hazardous agents. It should carry out its mandate by applying scientific information to promulgate regulations and policies that other federal agencies (*e.g.,* NRC and DOE) and states incorporate into their regulations or policies where appropriate or applicable. The USEPA has a tremendous responsibility to ensure its radiation regulations, policies, and guidance as well as its toxicology regime are scientifically sound while providing adequate

protection without placing an unnecessary burden on the affected population or organizations subject to them.

The only reasonable conclusion is that the US EPA has been irresponsible in its conduct with regards to assessing radiation biophysics matters, and equally irresponsible in applying the Linear No Threshold template for general toxicological matters.

The research that the US EPA claims to support the LNT model for LDDR radiation environments is unreliable, disproven by research since and was wrongly extrapolated from from high dose and high dose rate environments. The application of the LNT model to determine health risks has created a culture where a few clicks on a radiation dose-rate meter equates to cancer in the minds of the public. Society has become so fearful of radiation that unnecessary steps are taken, and other risks are accepted, compliance costs are tolerated so that even trivial radiation exposures are pursued energetically and expensively in an environment of zero tolerance and the precautionary principle. This public panic has now compromised the use of potentially life-saving medical exams, which is recognized as a problem by the many scientific and professional organizations specializing in radiation.

Since the Three Mile Island Nuclear Power Plant accident in 1979, the world has experienced what were dealt with as several large-scale nuclear or radiological accidents (*e.g.,* Chernobyl, 1986; Goiania, 1987; Fukushima, 2011) affecting millions of people and contaminating millions of hectares of land. The 2011 Fukushima nuclear power plant accident is the most recent radiological accident. Any sensible scientist or engineer would distinguish these incidents as to risk for the plant, its workers and the surrounding area. Fukishima was not

Chernobyl, but even with that proviso, the actual radiation harm created by the worst of the incidents, Chernobyl was limited—stunningly limited considering the nature of the event.

The Fukishima event itself caused no radiation-related deaths (UNSCEAR 2013b), however the evacuation in response to the accident, combined with the extended exclusion of area residents from their homes, has increased mortality from various stress-related causes. The elderly are especially vulnerable to these effects (Nomura *et al.* 2013; Yasumura *et al.* 2013; Uchimura *et al.* 2014), and over 1,600 people died as a result (Ichiseki 2013) of the response to the Fukushima accident. A retrospective evaluation has concluded that the risk from the evacuation outweighed any hypothetical risk of radiation exposure calculated using the LNT model (Thomas 2017; Waddington *et al.* 2017b), particularly among the elderly (Murakami *et al.* 2015), the evacuation did not protect human health, and was therefore unethical (Akabayashi and Hayashi 2012).

Scientists and society do not appear to be able to overcome the precautionary principle—that continues to dominate any reactions to "events" of all kinds. The atmosphere of anxiety and fear created by modern day politically motivated science is not to be underestimated and the scares of the past almost 70 years that have led to the continued use of LNT and its progeny—fear—will prevent societies from a proper assessment of risk and proper reactions. The German decision to shut down nuclear plants that produced vital energy is a classic example of policy governed by the fear factor and not sensible risk assessment and management.

Changes, long overdue, on the matter of LDDR radation risk management must go forward with the knowledge that adverse health effects are not detectable and that radiation exposures have a no effect, a harmful threshold of effect and even a sweet spot where radiation

produces hormetic beneficial effects. LNT model-based predictions are a failed endeavor that must be discarded.

Is it time for the USEPA to reconsider the use of the LNT model in LDDR radiation environments in the regulatory process, especially in the tools it has developed to determine cleanup levels? We have presented scientific information addressing this question. Change does not occur quickly or easily within government frameworks. It took decades of institutional inertia to arrive at the current irresponsible and unscientific regulatory framework. The USEPA SAB recommended "change in the agency culture, change in how the agency works, and increased support for scientists and managers in programs and regional offices responsible for science integration" (Swackhamer and Burke 2012) to occur and thereby improve its regulations and polices.

Objectively evaluating and incorporating the latest scientific evidence on LDDR dose-response relationships for application to the regulatory and policy-making process for risk assessment purposes will: (1) ensure science remains the foundation for its decision making; (2) reduce the unnecessary burden of costly cleanups; (3) provide a much needed platform to educate the public on the risks or benefits from LDDR radiation exposures; and (4) harmonize the agency's policies with those recognized by the rest of the radiation scientific community.

References

Supreme Court of the United States. 2015. Michigan et al v. Environmental Protection Agency et al. Docket No. 14-46.

AAPM. 2011. AAPM position statement on radiation risks from medical imaging procedures. Available at http://www.aapm.org/org/policies/details.asp?id=318&type=PP&current=true

Akabayashi A and Hayashi Y. 2012. Mandatory evacuation of residents during the Fukushima nuclear disaster: an ethical analysis. J Public Health (Oxf) 34:348-351

ARPS. 2008. Low dose radiation. Available at http://www.arps.org.au/?q=content/low-dose-radiation

Ashley SF, Vaughan GJ, Nuttall WJ and Thomas PJ. 2017. Considerations in relation to off-site emergency procedures and response for nuclear accidents. Proc Safety Environ Prot 112:77-95

Aurengo A, Averbeck D, Bonnin A, LeGuen B, Masse R, Monier R, Tubiana M, Valleron AJ and de Vathaire F. 2005. Dose-effect relationships and estimation of the carcinogenic effects of low doses of ionizing radiation. Paris

Averbeck D. 2009. Does scientific evidence support a change from the LNT model for low-dose radiation risk extrapolation? Health Phys 97:493-504

Beyea J. 2016a. Response to "The birth of the illegitimate linear no-threshold model: An invalid paradigm for estimating risk following low-dose radiation exposure". Am J Clin Oncol 39:425–426

Beyea J. 2016b. Response to, "On the origins of the linear no-threshold (LNT) dogma by means of untruths, artful dodges and blind faith.". Environ Res

Beyea J. 2017. Lessons to be learned from a contentious challenge to mainstream radiobiological science (the linear no-threshold theory of genetic mutations). Environ Res 154:362-379

Boice JD, Jr. 2015. Radiation epidemiology and recent paediatric computed tomography studies. Ann ICRP 44:236-248

Boreham DR, Dolling JA, Somers C, Quinn J and Mitchel RE. 2006. The adaptive response and protection against heritable mutations and fetal malformation. Dose-Response 4:317-326

Brenner DJ, Doll R, Goodhead DT, Hall EJ, Land CE, Little JB, Lubin JH, Preston DL, Preston RJ, Puskin JS, Ron E, Sachs RK, Samet JM, Setlow RB and Zaider M. 2003. Cancer risks attributable to low doses of ionizing radiation: assessing what we really know. Proc Natl Acad Sci USA 100:13761-13766

Burns RE. 2009. Oak Ridge National Laboratory - occupational medical dose, ORAUT-TKBS-0012-3 Rev. 02. Available at http://www.cdc.gov/niosh/ocas/pdfs/tbd/ornl3-r2.pdf

Calabrese E. 2015a. On the origins of the linear no-threshold (LNT) dogma by means of untruths, artful dodges and blind faith. Environ Res 142:432-442

Calabrese E. 2017a. The threshold vs LNT showdown: Dose rate findings exposed flaws in the LNT model Part 1. The Russell-Muller debate. Environ Res

Calabrese E. 2017b. The threshold vs LNT showdown: Dose rate findings exposed flaws in the LNT model part 2. How a mistake led BEIR I to adopt LNT. Environ Res

Calabrese EJ. 2012. NEPA, EPA and risk assessment: Has EPA lost its way? Regul Toxicol Pharmacol 64:267-268

Calabrese EJ. 2013. How the US National Academy of Sciences misled the world community on cancer risk assessment: new findings challenge historical foundations of the linear dose response. Arch Toxicol

Calabrese EJ. 2015b. An abuse of risk assessment: how regulatory agencies improperly adopted LNT for cancer risk assessment. Arch Toxicol
Calabrese EJ. 2015c. Cancer risk assessment foundation unraveling: New historical evidence reveals that the US National Academy of Sciences (US NAS), Biological Effects of Atomic Radiation (BEAR) Committee Genetics Panel falsified the research record to promote acceptance of the LNT. Arch Toxicol
Calabrese EJ. 2016. LNTgate: How scientific misconduct by the U.S. NAS led to governments adopting LNT for cancer risk assessment. Environ Res
Cardarelli J, 2nd, Elliott L, Hornung R and Chang WP. 1997. Proposed model for estimating dose to inhabitants of 60Co contaminated buildings. Health Phys 72:351-360
Cardarelli J, Spitz H, Rice C, Buncher R, Elson H and Succop P. 2002. Significance of radiation exposure from work-related chest X-rays for epidemiological studies of radiation workers. Am J Ind Med 42:490-501
Cardarelli JJ. 2000. A potential consequence of excluding work-required X-ray exposures when computing cumulative occupational radiation dose at a uranium enrichment plant, in: Environmental and Occupational Health, University of Cincinnati, Cincinnati, OH,
Carderelli JJ, 2018 Ulsh BA. It is time to move beyond the linear no-threshold theory for low-dose radiation protection. Dose Response an International Journal, April-June 2018 pp. 1-24. http://journals.sagepub.com/doi/full/10.1177/1559325818779651

Cardis E, Vrijheid M, Blettner M, Gilbert E, Hakama M, Hill C, Howe G, Kaldor J, Muirhead CR, Schubauer-Berigan M, Yoshimura T, Bermann F, Cowper G, Fix J, Hacker C, Heinmiller B, Marshall M, Thierry-Chef I, Utterback D, Ahn YO, Amoros E, Ashmore P, Auvinen A, Bae JM, Bernar J, Biau A, Combalot E, Deboodt P, Diez Sacristan A, Eklof M, Engels H, Engholm G, Gulis G, Habib RR, Holan K, Hyvonen H, Kerekes A, Kurtinaitis J, Malker H, Martuzzi M, Mastauskas A, Monnet A, Moser M, Pearce MS, Richardson DB, Rodriguez-Artalejo F, Rogel A, Tardy H, Telle-Lamberton M, Turai I, Usel M and Veress K. 2007. The 15-Country Collaborative Study of Cancer Risk among radiation workers in the nuclear industry: estimates of radiation-related cancer risks. Radiat Res 167:396-416
Chang WP. 1993. Spread of Taiwan radiation panic. Lancet 342:1544-1544
Chang WP, Chan CC and Wang JD. 1997. 60Co contamination in recycled steel resulting in elevated civilian radiation doses: causes and challenges. Health Phys 73:465-472
Chen WL, Luan YC, Shieh MC, Chen ST, Kung HT, Soong KL, Yeh YC, Chou TS, Mong SH, Wu JT, Sun CP, Deng WP, Wu MF and Shen ML. 2004. Is chronic radiation an effective prophylaxis against cancer? J Amer Physicians and Surgeons 9:6-10
Chen WL and Yeh SH. 2003. The measurement of Co-60-contaminated rebar buildings with thermoluminescence dosemeters. Radiat Prot Dosim 103:235-240
Clancy G and Chhem R. 2015. Hiroshima, Nagasaki, and Fukushima. Lancet 386:405-406
CNSC. 2011. Verifying Canadian nuclear energy worker radiation risk: a reanalysis of cancer mortality in Canadian nuclear energy workers (1957–1994) summary report. Ottawa, Canada
Cohen BL. 1987. Tests of the linear, no-threshold dose-response relationship for high-LET radiation. Health Phys 52:629-636
Cohen BL. 1995. Test of the linear-no threshold theory of radiation carcinogenesis for inhaled radon decay products. Health Phys 68:157-174

Cohen BL. 2004a. The Puskin observation on smoking as a confounder in ecologic correlations of cancer mortality rates with average county radon levels. Health Phys 86:203-204; author reply 204-205
Cohen BL. 2004b. Response to "Residential radon exposure and lung cancer risk: commentary on cohen's county-based study". Health Phys 87:656-658

Cohen BL. 2008. The linear no-threshold theory of radiation carcinogenesis should be rejected. J Am Physicians and Surg 13:70-76
Cohen M. 2013. Cancer risks from CT radiation: is there a dose threshold? J Am Coll Radiol 10:817-819
Davis FG, Yu KL, Preston D, Epifanova S, Degteva M and Akleyev AV. 2015. Solid cancer incidence in the Techa River Incidence Cohort: 1956-2007. Radiation Research 184:56-65

DaVita VT, Lawrence TS, Rosenberg S, *Cancer: Principles and Practice eof Oncology*. (Phil Balt. Wolters Kluwer/Lippincott 8th ed 2008).

Davoli T, de Lange T, The Causes and Consequences of Polyploidy in Normal Development and Cancer. Annu. Rev. Cell Dev. Biol. 2011. 27:585‑610 First published online as a Review in Advance on July 21, 2011 The *Annual Review of Cell and DevelopmentalBiology* is online at cellbio.annualreviews.org doi: 10.1146/annurev-cellbio-092910-154234Doss M. 2015. INWORKS study: risk of leukaemia from protracted radiation exposure. Lancet Haematology 2:E404-E405

Doss M, Adams R, Allison W, Cohen MD, Corris L, Cuttler JM, Davey C, Dobrzynski L, Dube S, Esposito VJ, Feinendegen LE, Fornalski KW, Gomez LS, Hargraves R, Janiak MK, Jennetta A, Mahn J, Miller ML, Orient JM, Pennington CW, Sacks B, Sanders CL, Strupczewski A and S. S. 2015. Incoming petition for rulemaking (PRM-20--30) from Mohan Doss et al. Washington DC

Doss M, Egleston BL and Litwin S. 2012. Comments on "Studies of the Mortality of Atomic Bomb Survivors, Report 14, 1950-2003: An Overview of Cancer and Noncancer Diseases" (Radiat Res 2012; 177:229-43). Radiat Res

Edwards JD. 2015. U.S. Environmental Protection Agency's comments on linear no-threshold model and standards for protection against radiation; notice of docketing and request for comment id: nrc-215-0057-0010. Docket ID-2015-0057. Washington, D.C.

Feinendegen LE. 2011. 2010 Marie Curie prize lecture: low-dose induced protection invalidates the linear-no-threshold model in mammalian bodies – a system-biology approach. Int J Low Radiat 8:78-95
Fisher DR and Fahey FH. 2017. Appropriate use of effective dose in radiation protection and risk assessment. Health Phys 113:102–109
Gale RP. 2017. Medical and policy considerations for nuclear and radiation accidents, incidents and terrorism. Curr Opin Hematol 24:496-501
GAO. 1994. Nuclear health and safety: Consensus on acceptable radiation risk to the public is lacking. Washington, D.C.

GAO. 2000. Radiation standards: Scientific basis inconclusive, and EPA and NRC disagreement continues. Washington, D.C.
Garnier-Laplace J, Della-Vedova C, Andersson P, Copplestone D, Cailes C, Beresford NA, Howard BJ, Howe P and Whitehouse P. 2010. A multi-criteria weight of evidence approach for deriving ecological benchmarks for radioactive substances. Journal of Radiological Protection 30:215-233
Gonzalez AJ, Akashi M, Boice JD, Chino M, Homma T, Ishigure N, Kai M, Kusumi S, Lee JK, Menzel HG, Niwa O, Sakai K, Weiss W, Yamashita S and Yonekura Y. 2013. Radiological protection issues arising during and after the Fukushima nuclear reactor accident. Journal of Radiological Protection 33:497-571
Grant EJ, Brenner A, Sugiyama H, Sakata R, Sadakane A, Utada M, Cahoon EK, Milder CM, Soda M, Cullings HM, Preston DL, Mabuchi K and Ozasa K. 2017. Solid cancer incidence among the life span study of atomic bomb survivors: 1958–2009. Radiat Res
Hall EJ. 2006. Radiobiology for the Radiologist. Lippincott Williams & Wilkins, Philadelphia
Hall EJ and Brenner DJ. 2012. Cancer risks from diagnostic radiology: the impact of new epidemiological data. British Journal of Radiology 85:E1316-E1317
Hansen H. 2015. Fallacies. In: The Stanford Encyclopedia of Philosophy.
Harvey HB, Brink JA and Frush DP. 2015. Informed consent for radiation risk from CT is unjustified based on the current scientific evidence. Radiol 275:321-325
Hasegawa A, Tanigawa K, Ohtsuru A, Yabe H, Maeda M, Shigemura J, Ohira T, Taominaga T, Akashi M, Hirohashi N, Ishikawa T, Kamiya K, Shibuya K, Yamashita S and Chhem RK. 2015. Health effects of radiation and other health problems in the aftermath of nuclear accidents, with an emphasis on Fukushima. Lancet 386:479-488
Hayes WA. 2014. Hayes' Principles and Methods of Toxicology. CRC Press, Boca Raton, FL
Hill AB. 1965. The environment and disease: association or causation? Proc R Soc Med 58:295-300
HPS. 2016. Radiation risk in perspective: position statement of the Health Physics Society. Available at http://hps.org/documents/risk_ps010-2.pdf
Hsieh WH, Lin IF, Ho JC and Chang PW. 2017. 30 years follow-up and increased risks of breast cancer and leukaemia after long-term low-dose-rate radiation exposure. Br J Cancer 1-5
Hsu FY, Tsai HY, Hsu CY, Tung CJ, Liao CC and Tsay YS. 2003. Dose reconstruction for residents living in buildings with moderate and minor 60Co contamination in rebar. Health Phys 85:357-364
Hwang JY, Chang JBH and Chang WP. 2001. Spread of Co-60 contaminated steel and its legal consequences in Taiwan. Health Phys 81:655-660
Hwang SL, Guo HR, Hsieh WA, Hwang JS, Lee SD, Tang JL, Chen CC, Chang TC, Wang JD and Chang WP. 2006. Cancer risks in a population with prolonged low dose-rate gamma-radiation exposure in radiocontaminated buildings, 1983-2002. Int J Radiat Biol 82:849-858
Hwang SL, Hwang JS, Yang YT, Hsieh WA, Chang TC, Guo HR, Tsai MH, Tang JL, Lin IF and Chang WP. 2008. Estimates of relative risks for cancers in a population after prolonged low-dose-rate radiation exposure: a follow-up assessment from 1983 to 2005. Radiat Res 170:143-148
Ichiseki H. 2013. Features of disaster-related deaths after the Great East Japan Earthquake. Lancet 381:204-204
ICRP. 1977. Recommendations of the ICRP: Publication 26. Ann ICRP 1:

ICRP. 1992. Principles for intervention for protection of the public in a radiological emergency. ICRP Publication 63. Ann ICRP 22:
ICRP. 2007. ICRP Publication 103: The 2007 recommendations of the International Commission on Radiological Protection. Ann ICRP 37:1-332
ICRP. 2009. Application of the Commission's recommendations to the protection of people living in long-term contaminated areas after a nuclear accident or a radiation emergency. ICRP Publication 111. Ann ICRP 39:
Ioan Baba A, Catoi C, Annu. Rev. Cell Dev. Biol. 2011. 27:585‑610

First published online as a Review in Advance on

July 21, 2011 The *Annual Review of Cell and Developmental*

Biology is online at cellbio.annualreviews.org doi: 10.1146/annurev-cellbio-092910-154234

https://www.ncbi.nlm.nih.gov/books/NBK9557/

Comparative Oncology Comparative Oncology Bucharest: The Publishing House of the Romanian Academy; 2007. ISBN-10: 973-27-1457-3ISBN-13: 978-073-27-1457-7

Jaworowski A. 2008. The paradigm that failed. Int J Low Radiat 5:151-155
Jenkins-Smith HC, Silva CL and Murray C. 2009. Beliefs about radiation: scientists, the public and public policy. Health Phys 97:519-527
Jones CG. 2005. A review of the history of U.S. radiation protection regulations, recommendations, and standards. Health Phys 88:697-716
Journy N, Rehel JL, Ducou Le Pointe H, Lee C, Brisse H, Chateil JF, Caer-Lorho S, Laurier D and Bernier MO. 2015. Are the studies on cancer risk from CT scans biased by indication? Elements of answer from a large-scale cohort study in France. Br J Cancer 112:185-193
Kadhim MA, Moore SR and Goodwin EH. 2004. Interrelationships amongst radiation-induced genomic instability, bystander effects, and the adaptive response. Mutat Res 568:21-32
Kai M. 2015. Experience and current issues with recovery management from the Fukushima accident. Ann ICRP 44:153-161
Kamiya K, Ozasa K, Akiba S, Niwa O, Kodama K, Takamura N, Zaharieva EK, Kimura Y and Wakeford R. 2015. Long-term effects of radiation exposure on health. Lancet 386:469-478
Kendall GM, Little MP, Wakeford R, Bunch KJ, Miles JC, Vincent TJ, Meara JR and Murphy MF. 2013. A record-based case-control study of natural background radiation and the incidence of childhood leukaemia and other cancers in Great Britain during 1980-2006. Leukemia 27:3-9
Kirner NP. 2017. EPA Request for Regulatory Reform Task Force. McLean, VA
Koana T, Okada MO, Ogura K, Tsujimura H and Sakai K. 2007. Reduction of background mutations by low-dose X irradiation of Drosophila spermatocytes at a low dose rate. Radiation Research 167:217-221
Koana T, Takahashi T and Tsujimura H. 2012. Reduction of spontaneous somatic mutation frequency by a low-dose X irradiation of Drosophila larvae and possible involvement of DNA single-strand damage repair. Radiation Research 177:265-271
Koana T, Takashima Y, Okada MO, Ikehata M, Miyakoshi JJ and Sakai K. 2004. A threshold exists in the dose-response relationship for somatic mutation frequency induced by X irradiation of Drosophila. Radiation Research 161:391-396

Koana T and Tsujimura H. 2010. A U-shaped dose-response relationship between x radiation and sex-linked recessive lethal mutation in male germ cells of Drosophila. Radiation Research 174:46-51

Krestinina L, Preston DL, Davis FG, Epifanova S, Ostroumova E, Ron E and Akleyev A. 2010. Leukemia incidence among people exposed to chronic radiation from the contaminated Techa River, 1953-2005. Radiat Environ Biophys 49:195-201

Krestinina LY, Davis FG, Schonfeld S, Preston DL, Degteva M, Epifanova S and Akleyev AV. 2013. Leukaemia incidence in the Techa River Cohort: 1953-2007. British Journal of Cancer 109:2886-2893

Krille L, Dreger S, Schindel R, Albrecht T, Asmussen M, Barkhausen J, Berthold JD, Chavan A, Claussen C, Forsting M, Gianicolo EA, Jablonka K, Jahnen A, Langer M, Laniado M, Lotz J, Mentzel HJ, Queisser-Wahrendorf A, Rompel O, Schlick I, Schneider K, Schumacher M, Seidenbusch M, Spix C, Spors B, Staatz G, Vogl T, Wagner J, Weisser G, Zeeb H and Blettner M. 2015. Risk of cancer incidence before the age of 15 years after exposure to ionising radiation from computed tomography: results from a German cohort study. Radiat Environ Biophys 54:1-12

Land CE. 1980. Estimating cancer risks from low doses of ionizing radiation. Science 209:1197-1203

Lee JS, Dong SL and Wu TH. 1999. Estimation of organ dose equivalents from residents of radiation-contaminated buildings with Rando phantom measurements. Appl Radiat Isot 50:867-873

Leuraud K, Richardson DB, Cardis E, Daniels RD, Gillies M, O'Hagan JA, Hamra GB, Haylock R, Laurier D, Moissonnier M, Schubauer-Berigan M, Thierry-Chef I and Kesminiene A. 2015. Ionising radiation and risk of death from leukaemia and lymphoma in radiation-monitored workers (INWORKS): an international cohort study. Lancet Haematology 2:e276-e281

Loehr RC and Nygaard OF. 1992a. Personal communication with Reilly WK.

Loehr RC and Nygaard OF. 1992b. Personal communication with Reilly WK.

Manesh SS, Sangsuwan T, Wojcik A and Haghdoost S. 2015. Studies of adaptive response and mutation induction in MCF-10A cells following exposure to chronic or acute ionizing radiation. Mutat Res 780:55-59

Marcus C. 2015. Personal communication with Vietti-Cook AL.

Mathews JD, Forsythe AV, Brady Z, Butler MW, Goergen SK, Byrnes GB, Giles GG, Wallace AB, Anderson PR, Guiver TA, McGale P, Cain TM, Dowty JG, Bickerstaffe AC and Darby SC. 2013. Cancer risk in 680 000 people exposed to computed tomography scans in childhood or adolescence: data linkage study of 11 million Australians. Brit Med J 346:f2360

Miller M, Adams R, Allison WM, Bhat M, Church BW, Cohen M, Cravens G, Cuttler JM, Dobrzynski L, Doss M, Esposito VJ, Feinendegen LE, Fellman A, Feitham C, Frey SR, Hargraves R, Hauer JM, Hoe GL, Janiak MK, Mahn J, Marcus CS, Mortazavi SMJ, Pennington C, Philbin J, Quinn T, Rangacharyulu C, Sacks B, Sanders CL, Sutuo S, Stabin MG, Strupczewski A and Waltar AE. 2017. Establishing scientific bases for risk-based radiation regulations.

Milne E, Greenop KR, Scott RJ, Bailey HD, Attia J, Dalla-Pozza L, de Klerk NH and Armstrong BK. 2012. Parental prenatal smoking and risk of childhood acute lymphoblastic leukemia. Am J Epidemiol 175:43-53

Morgan MG and Lipoti J. 2008. Personal communication with Johnson SL.

Mortazavi SMJ, Ghiassi-Nejad A and Rezaiean A. 2005. Cancer risk due to exposure to high levels of natural radon in the inhabitants of Ramsar, Iran. In: Sugahara T, Morishima H, Sohrabi M, Sasaki Y, Hayata I and Akiba S (eds) High Levels of Natural Radiation and Radon Areas: Radiation Dose and Health Effects, pp 436-437.
Mosavi-Jarrahi A, Mohagheghi M, Akiba S, Yazdizadeh B, Motamedi N and Monfared AS. 2005. Mortality and morbidity from cancer in the population exposed to high level of natural radiation area in Ramsar, Iran. In: Sugahara T, Morishima H, Sohrabi M, Sasaki Y, Hayata I and Akiba S (eds) High Levels of Natural Radiation and Radon Areas: Radiation Dose and Health Effects, pp 106-109. Elsevier Science Bv, Amsterdam
Mossman KL. 2007. Radiation risks in perspective. CRC/Taylor & Francis, Boca Raton, FL
Mossman KL. 2014. Cancer complexity and radiation protection. Health Phys 107:73-79
Murakami M, Ono K, Tsubokura M, Nomura S, Oikawa T, Oka T, Kami M and Oki T. 2015. Was the risk from nursing-home evacuation after the Fukushima accident higher than the radiation risk? PLOS One 10:e0137906
Murray WE. 2009. Y-12 National Security Complex - occupational medical dose, ORAUT-TKBS-0014-3 Rev. 01. Available at http://www.cdc.gov/niosh/ocas/pdfs/tbd/y123-r1.pdf
Nagataki S and Kasagi F. 2015. INWORKS study: risk of leukaemia from protracted radiation exposure. Lancet Haematology 2:E404-E404
Nair RRK, Rajan B, Akiba S, Jayalekshmi P, Nair MK, Gangadharan P, Koga T, Morishima H, Nakamura S and Sugahara T. 2009. Background radiation and cancer incidence in Kerala, India-Karunagappally cohort study. Health Phys 96:55-66
National Research Council. 2005. Health risks from exposure to low levels of ionizing radiation: BEIR VII Phase 2. Washington, DC
NCRP. 2001. Evaluation of the linear-nonthreshold dose-response model for ionizing radiation. 7910 Woodmont Avenue, Suite 800, Bethesda, MD 30814
NCRP. 2004. Approaches to risk management in remediation of radioactively contaminated sites. 7910 Woodmont Avenue, Suite 800, Bethesda, MD 30814
NCRP. 2007a. Decision making for late-phase recovery from major nuclear or radiological incidents. Bethesda, MD
NCRP. 2007b. Uncertainties in the measurement and dosimetry of external radiation 158. Bethesda, MD
NCRP. 2009. Uncertainties in internal radiation dose assessment. 164. Bethesda, MD
NCRP. 2010. Responding to a radiological or nuclear terrorism incident: A guide for decision makers. NCRP Report No. 165. Bethesda, MD
NCRP. 2012. Uncertainties in the estimation of radiation risks and probability of disease causation. 171. Bethesda, MD
NCRP. 2015. Health effects of low doses of radiation: Perspectives on integrating radiation biology and epidemiology. Bethesda, MD
Nisbet AF and Chen SY. 2015. Decision making for late-phase recovery from nuclear or radiological incidents: new guidance from NCRP. Ann ICRP 44:162-171
Nomura S, Gilmour S, Tsubokura M, Yoneoka D, Sugimoto A, Oikawa T, Kami M and Shibuya K. 2013. Mortality risk amongst nursing home residents evacuated after the Fukushima nuclear accident: a retrospective cohort study. PLOS One 8:e60192
Office of the Press Secretary. 2017. Presidential executive order on enforcing the regulatory reform agenda. Available at https://www.whitehouse.gov/the-press-office/2017/02/24/presidential-executive-order-enforcing-regulatory-reform-agenda

Ogura K, Magae J, Kawakami Y and Koana T. 2009. Reduction in mutation frequency by very low-dose gamma irradiation of drosophila melanogaster germ cells. Radiation Research 171:1-8
Ohtsuru A, Tanigawa K, Kumagai A, Niwa O, Takamura N, Midorikawa S, Nollet K, Yamashita S, Ohto H, Chhem R and Clarke M. 2015. Nuclear disasters and health: lessons learned, challenges, and proposals. Lancet 386:489-497
Ozasa K, Shimizu Y, Suyama A, Kasagi F, Soda M, Grant EJ, Sakata R, Sugiyama H and Kodama K. 2012a. Errata. Radiat Res 179:e0040-e0041
Ozasa K, Shimizu Y, Suyama A, Kasagi F, Soda M, Grant EJ, Sakata R, Sugiyama H and Kodama K. 2012b. Studies of the mortality of atomic bomb survivors, Report 14, 1950-2003: an overview of cancer and noncancer diseases. Radiat Res 177:229-243
Paunesku T, Haley B, Brooks A and Woloschak GE. 2017. Biological basis of radiation protection needs rejuvenation. Int J Radiat Biol 93:1056-1063
Pawel D. 2015. New information on radiogenic cancer risks since BEIR VII, is it time for BEIR VIII? Available at http://www.iscors.org/doc/david-pawel-11-9-2015.pdf
Pearce MS, Salotti JA, Little MP, McHugh K, Lee C, Kim KP, Howe NL, Ronckers CM, Rajaraman P, Craft AW, Parker L and Berrington de Gonzalez A. 2012. Radiation exposure from CT scans in childhood and subsequent risk of leukaemia and brain tumours: a retrospective cohort study. Lancet 380:499-505
Perrin AD. 2017. Personal communication with Miller ML.
Pradhan AS. 2013. On the risk to low doses (<100 mSv) of ionizing radiation during medical imaging procedures - IOMP policy statement. J Med Phys 38:57
Preston RJ. 2017. Can radiation research impact the estimation of risk? Int J Radiat Biol 93:1-6
Puskin JS. 2003. Smoking as a confounder in ecologic correlations of cancer mortality rates with average county radon levels. Health Phys 84:526-532
Puskin JS. 2009. Perspective on the use of LNT for radiation protection and risk assessment by the U.S. Environmental Protection Agency. Dose Response 7:284-291
Puskin JS. 2010. Letter to the Editor: Reply to Cohen's Response to EPA Position on Cancer Risk from Low Level Radiation. Dose Response 8:387-388
Puskin JS. 2016. LNT: Overview and update.
Reich MR and Goto A. 2015. Towards long-term responses in Fukushima. Lancet 386:498-500
Richardson DB, Cardis E, Daniels RD, Gillies M, O'Hagan JA, Hamra GB, Haylock R, Laurier D, Leuraud K, Moissonnier M, Schubauer-Berigan MK, Thierry-Chef I and Kesminiene A. 2015. Risk of cancer from occupational exposure to ionising radiation: retrospective cohort study of workers in France, the United Kingdom, and the United States (INWORKS). BMJ 351:
Ring JP, Tupin EA, Elder D, Hiatt J, Sheetz MA, Kirner NP and Little C. 2017. Health Physics Society comments to EPA Regulatory Reform Task Force. Health Phys in press:
Rothman KJ and Greenland S. 1998. Modern Epidemiology. 2nd ed., Lippincot Williams & Wilkins, Philadelphia, PA
Sacks B, Meyerson G and Siegel JA. 2016. Epidemiology without biology: false paradigms, unfounded assumptions, and specious statistics in radiation science (with commentaries by Inge Schmitz-Feuerhake and Christopher Busby and a reply by the authors). Biol Theory
Sacks B and Siegel JA. 2017. Preserving the anti-scientific linear no-threshold myth: Authority, agnosticism, transparency, and the standard of care. Dose Response 15:1559325817717839

Sanders CL. 2010. Radiation Hormesis and the Linear-No-Threshold Assumption. Springer, New York
Sasaki MS, Tachibana A and Takeda S. 2014. Cancer risk at low doses of ionizing radiation: artificial neural networks inference from atomic bomb survivors. J Radiat Res 55:391-406
Schubauer-Berigan MK, Leuraud K, Richardson DB, Cardis E, Daniels RD, Gillies M, O'Hagan JA, Hamra GB, Haylock R, Laurier D, Moissonnier M, Thierry-Chef I and Kesminiene A. 2015. INWORKS study: risk of leukaemia from protracted radiation exposure Reply. Lancet Haematology 2:E405-E406
Siegel JA, Pennington CW and Sacks B. 2017a. Subjecting radiological imaging to the linear no-threshold hypothesis: a non sequitur of nontrivial proportion. J Nucl Med 58:1-6
Siegel JA, Pennington CW, Sacks B and Welsh JS. 2015. The birth of the illegitimate linear no-threshold model: an invalid paradigm for estimating risk following low-dose radiation exposure. Am J Clin Oncol
Siegel JA, Pennington CW, Sacks B and Welsh JS. 2016. Rectifying radon's record: An open challenge to the EPA. Int J Radiol Imaging Tech 2:1-5
Siegel JA and Sacks B. 2017. Eliminating use of the linear no-threshold assumption in medical imaging. J Nucl Med 58:1014-1015
Siegel JA, Sacks B, Pennington CW and Welsh JS. 2017b. Dose optimization to minimize radiation risk for children undergoing CT and nuclear medicine imaging is misguided and detrimental. J Nucl Med 58:865-868
Siegel JA, Sacks B and Welsh JS. 2017c. Time to terminate LNT: Radiation regulators should adopt LT. J Radiol Oncol 1:49-53
Siegel JA and Welsh JS. 2015. Does imaging technology cause cancer? debunking the linear no-threshold model of radiation carcinogenesis. Technol Cancer Res Treat
Silva CL, Jenkins-Smith HC and Barke RP. 2007. Reconciling scientists' beliefs about radiation risks and social norms: explaining preferred radiation protection standards. Risk Anal 27:755-773
Socol Y and Dobrzynski L. 2015. Atomic bomb survivors life-span study: insufficient statistical power to select radiation carcinogenesis model. Dose Response 13:1
SPR. 2001. Risks and benefits in pediatric CT. Pediatric Radiol 31:387-387
Swackhamer DL and Burke TA. 2012. Personal communication with Jackson LP.
Sykes PJ and Day TK. 2007. Requirements for identification of low dose and non-linear mutagenic responses to ionising radiation. Dose Response 5:308-314
Sykes PJ, Day TK, Swinburne SJ, Lane JM, Morley AA, Hooker AM and Bhat M. 2006a. In vivo mutagenic effect of very low dose radiation. Dose-Response 4:309-316
Sykes PJ, Morley AA and Hooker AM. 2006b. The PKZ1 recombination mutation assay: a sensitive assay for low dose studies. Dose-Response 4:91-105
Tao Z, Akiba S, Zha Y, Sun Q, Zou J, Li J, Liu Y, Yuan Y, Tokonami S, Morishoma H, Koga T, Nakamura S, Sugahara T and Wei L. 2012. Cancer and non-cancer mortality among Inhabitants in the high background radiation area of Yangjiang, China (1979-1998). Health Phys 102:173-181
Thomas EM. 2009. Savannah River Site - occupational medical dose, ORAUT-TKBS-0003-3 Rev. 04. Available at http://www.cdc.gov/niosh/ocas/pdfs/tbd/srs4.pdf
Thomas EM. 2013. Oak Ridge Gaseous Diffusion Plant (K-25) - occupational medical dose, ORAUT-TKBS-0009-3 Rev. 01. Available at http://www.cdc.gov/niosh/ocas/pdfs/tbd/k253-r1.pdf

Thomas PJ. 2017. Quantitative guidance on how best to respond to a big nuclear accident. Proc Safety Environ Prot 112:4-15
Thomas PJ and May J. 2017. Coping after a big nuclear accident. Proc Safety Environ Prot 112:1-3
Trott KR and Rosemann M. 2000. Molecular mechanisms of radiation carcinogenesis and the linear, non-threshold dose response model of radiation risk estimation. Radiation and Environmental Biophysics 39:79-87
Tubiana M, Feinendegen LE, Yang C and Kaminski JM. 2009. The linear no-threshold relationship is inconsistent with radiation biologic and experimental data. Radiology 251:13-22
Tung CJ, Chao TC, Chen TR, Hsu FY, Lee IT, Chang SL, Liao CC and Chen WL. 1998. Dose reconstruction for residents living in 60Co-contaminated rebar buildings. Health Phys 74:707-713
Uchimura M, Kizuki M, Takano T, Morita A and Seino K. 2014. Impact of the 2011 Great East Japan Earthquake on community health: ecological time series on transient increase in indirect mortality and recovery of health and long-term-care system. J Epidemiol Community Health 68:874-882
Ueno AM, Vannais DB, Gustafson DL, Wong JC and Waldren CA. 1996. A low, adaptive dose of gamma-rays reduced the number and altered the spectrum of S1- mutants in human-hamster hybrid AL cells. Mutat Res 358:161-169
Ulsh BA. 2010. Checking the foundation: recent radiobiology and the linear no-threshold theory. Health Phys 99:747-758
Ulsh BA. 2012. The new radiobiology: returning to our roots. Dose Response 10:593-609
Ulsh BA. 2015. Are risks from medical imaging still too small to be observed or nonexistent? Dose-Response 13:1-27
UNSCEAR. 1993. Effects of Ionizing Radiation. UNSCEAR Report to the General Assembly, with Scientific Annexes. New York, NY
UNSCEAR. 2012. Report of the United Nations Scientific Committee on the Effects of Atomic Radiation Fifty-ninth Session (21-25 May 2012). New York, NY
UNSCEAR. 2013a. Biological mechanisms of radiation ations at low doss. New York, NY
UNSCEAR. 2013b. Report to the General Assembly with Scientific Annexes: Volume I. New York, NY
UNSCEAR. 2013c. Report to the General Assembly with Scientific Annexes: Volume II. New York, NY
USEPA. 1988. Limiting values of radionuclide intake and air concentration and dose conversion factors for inhalation, submersion, and ingestion. Washington, D.C.
USEPA. 1991. Proposed revisions in EPA estimates of radon, risks and associated uncertainties, in, USEPA,
USEPA. 1992. Revised radon risk estimates and associated uncertainties, in: Board SA (Ed.), USEPA, Washington D.C.,
USEPA. 1993. External exposure to radionuclides in air, water, and soil. Washington, D.C.
USEPA. 1999. Cancer risk coefficients for environmental exposure to radionuclides. Washington, D.C.
USEPA. 2000. Radiation Protection at the EPA, The First 30 Years, in: Air OoRaI (Ed.), United States Environmental Protection Agency, United States Environmental Protection Agency,
USEPA. 2001a. Radionuclide carcinogenicity slope factors for HEAST. Washington, D.C.

USEPA. 2001b. Risk Assessment Guidance for Superfund (RAGS): Part D, Volume I - Human Health Evaluation Manual (Part D, Standardized Planning, Reporting and Review of Superfund Risk Assessments) Final, in,
USEPA. 2004. An examination of risk assessment principles and practices, in: Force RAT (Ed.), USEPA Office of the Science Advisor, Washington D.C.,
USEPA. 2006. Modifying EPA radiation risk models based on BEIR VII. Air OoRaI, Washington D.C.
USEPA. 2011. EPA radiogenic cancer risk models and projections for the U.S. population, in: Air OoRaI (Ed.), USEPA, Washington D.C.,
USEPA. 2014. Distribution of the Radiation Risk Assessment At CERCLA Sites: Q&A.
USEPA. 2015a. Health effects. Available at http://www.epa.gov/radiation/understand/health_effects.html
USEPA. 2015b. U.S. Environmental Protection Agency Scientific Integrity Policy. Available at http://www2.epa.gov/sites/production/files/2014-02/documents/scientific_integrity_policy_2012.pdf
Waddington I, Taylor RH, Jones RD and Thomas PJ. 2017a. J-value assessment of the cost effectiveness of UK sheep meat restrictions after the 1986 Chernobyl accident. Proc Safety Environ Prot 112:114-130
Waddington I, Thomas PJ, Taylor RH and Vaughan GJ. 2017b. J-value assessment of relocation measures following the nuclear power plant accidents at Chernobyl and Fukushima Daiichii. Proc Safety Environ Prot 112 Part A:16-49
Waddington I, Thomas PJ, Taylor RH and Vaughan GJ. 2017c. J-value assessment of remediation measures following the Chernobyl and Fukushima Daiichi nuclear power plant accidents. Proc Safety Environ Prot 112:50-62
Weil and Sugahara T. 2002. Risk assessment based on an epidemiological study in a high background radiation area A China–Japan cooperative research. Int Congress Series 1225:267-275
Weinberg RA, *The Biology of Cancer*. (NY London, GS Garland Science, 2nd ED. 2014.
Welsh JS, Sacks B and Siegel JA. 2017. Time to eliminate LNT: The NRC needs to adopt LT and eliminate ALARA. Nucl Med Biomed Imaging 2:1-5
Yasumura S, Goto A, Yamazaki S and Reich MR. 2013. Excess mortality among relocated institutionalized elderly after the Fukushima nuclear disaster. Public Health 127:186-188
Yumashev D, Johnson P and Thomas PJ. 2017. Economically optimal strategies for medium-term recovery after a major nuclear reactor accident. Proc Safety Environ Prot 112:63-76
Zablotska LB, Lane RS and Thompson PA. 2014. A reanalysis of cancer mortality in Canadian nuclear workers (1956-1994) based on revised exposure and cohort data. Br J Cancer 110:214-223
Zeng G, Day TK, Hooker AM, Blyth BJ, Bhat M, Tilley WD and Sykes PJ. 2006. Non-linear chromosomal inversion response in prostate after low dose X-radiation exposure. Mutat Res 602:65-73
Zhang C, Jin S, Guo W, Li C, Li X, Rane MJ, Wang G and Cai L. 2011. Attenuation of diabetes-induced cardiac inflammation and pathological remodeling by low-dose radiation. Radiat Res 175:307-321
Zou JM, Tao ZF, Sun QF, Akiba S, Zha YR, Sugahara T and Wei LX. 2005. Cancer and non-cancer epidemiological study in the high background radiation area of Yangjiang, China. In:

Sugahara T, Morishima H, Sohrabi M, Sasaki Y, Hayata I and Akiba S (eds) High Levels of Natural Radiation and Radon Areas: Radiation Dose and Health Effects, pp 97-101.

Footnotes

Figure legend

Figure 1

Solid cancer ERR estimates for the Techa River Cohort plotted against stomach dose

[reproduced from Figure 1 of (Davis *et al.* 2015), red circle added for emphasis]

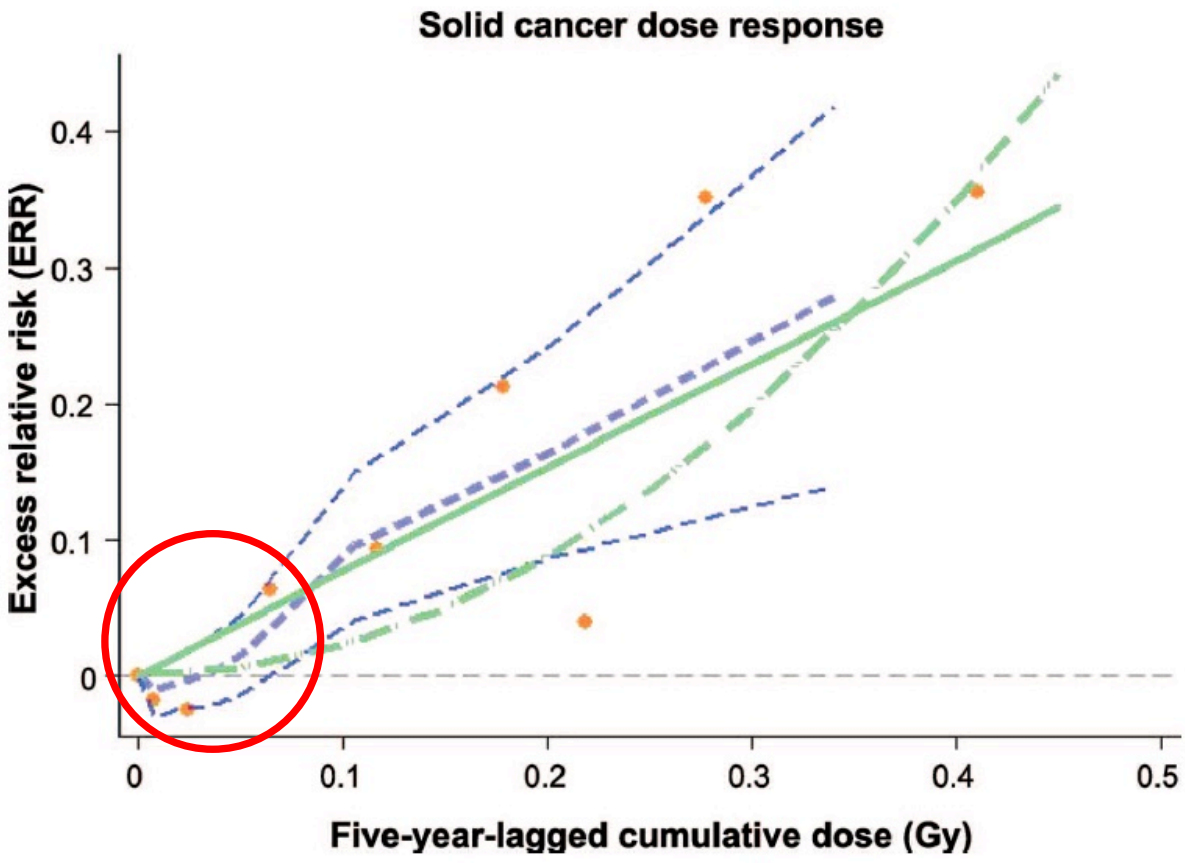

Figure 2.

Cancer Risk Management Paradigms

[reproduced from Figure X of (NCRP 2004)]

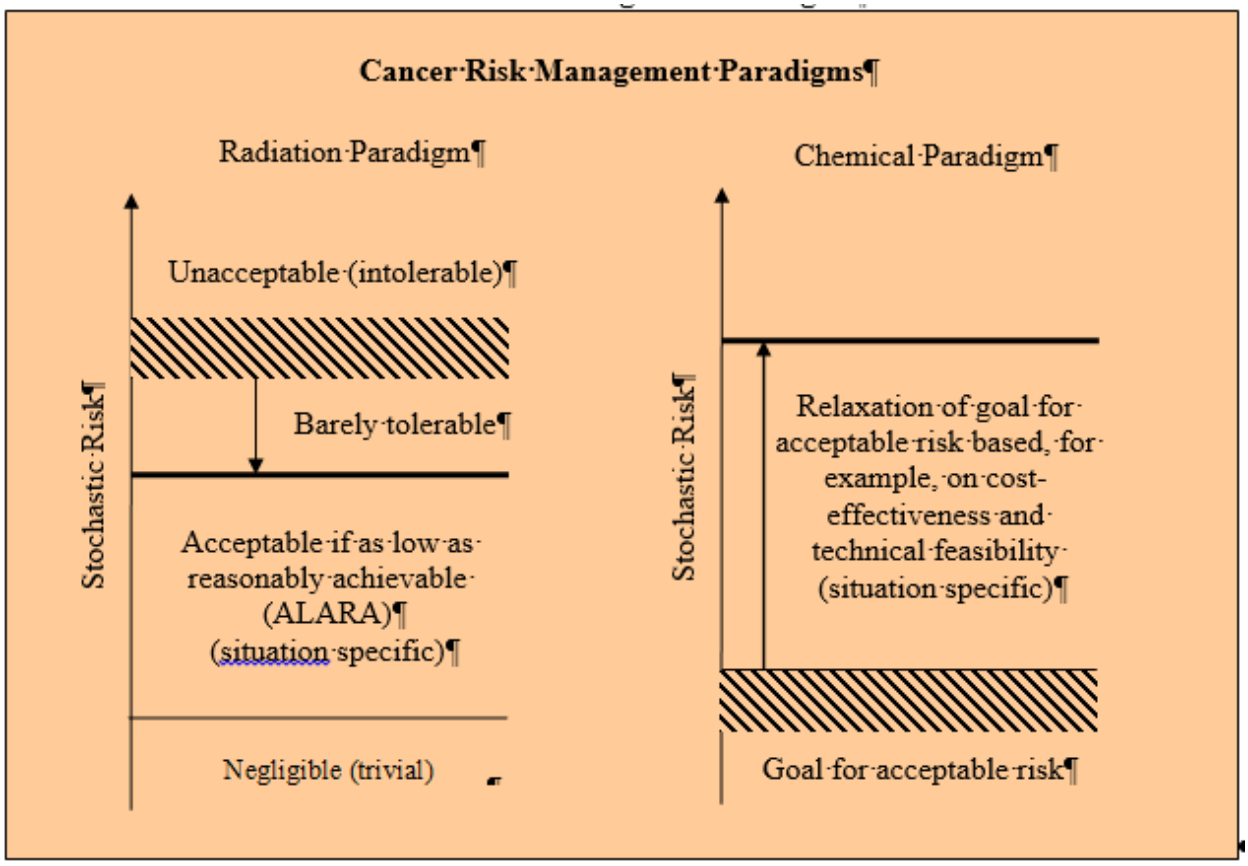

Table legend

Table 1

Survey of scientists regarding the most accurate radiation dose-response model for cancer (Silva *et al.* 2007; Jenkins-Smith *et al.* 2009).

Surveys	Respondents	Percent supporting LNT Model	Percent supporting Threshold Model	Other
United States	National Labs	12	70	18[a]
	Union of Concerned Scientists	21	48	31[a]
Subscribers to *Science*	United States	19	75	6[b]
	Britain	21	71	8[b]
	France	18	70	13[b]
	Germany	22	64	13[b]
	Other EU	23	69	8[b]

a: The "other" category includes "supralinear" and "don't know" responses.

b: The "other" category includes "supralinear" responses.