February 7, 2022

Committee Members

Committee on Developing a Long-Term Strategy for Low-Dose Radiation Research in the United States, National Academies of Sciences, Engineering, and Medicine

Comment for the Committee's Report

Dear Committee Members,

I appreciate the committee's effort to develop a research strategy for Low-Dose Radiation Research. I am a professor of marketing science at Keio University who was born in Hiroshima, majored in nuclear engineering at the Graduate School of Engineering, Tokyo University, and changed my career to the field of marketing science. Since Fukushima nuclear disaster, I'm working on (re-)analysis of radiation epidemiologic data including a-bomb survivor, US nuclear worker, Fukushima thyroid cancer, and radiation biological data, then identified some limitations in their analysis. Based on my expertise and personal experience, I would like to comment on Low-Dose Radiation Research.

1 Background of My Comment

Starting with my personal experience would help to understand my concern for Low-Dose Radiation Research. I participated in the Low-dose 2018 conference that was cited in the OSTP report [1] as a panelist in the epidemiology session. The meeting was co-hosted by the American Nuclear Society and Health Physics Society, thus, I expected it would be an academic or scientific conference. Unfortunately, my expectations were disappointing. Some presenters in the nuclear industry said, "It's ridiculous to stay at home for fear of exposure to 1mSv," and "It's time to dump LNT." The recording of the meeting is available on YouTube[1], please take a look. It was a two-day meeting, so if you want to name one, check out Dr. Magwood's plenary who served DOE and NRC that I will summarize later. I assume that there is an intention among some people in Low Dose Research to reduce costs by abandoning LNT and introducing thresholds.

2 Specific Comment

The following are individual comments.

2.1 Misperception on uncertainty at a low dose based on inappropriate analysis

Through critical review on radiation epidemiology and radiation biology, I identified methodological limitations that cause misperception of uncertainty under 100 mSv.

- Categorization of dose and aggregation of individual-level data

[1] Low Dose Rad 2018
https://www.youtube.com/channel/UCfLpY9M-7bjznbaJoHENJLg

Although individual-level dose is estimated in a-bomb survivor study, the dose is categorized into 24 ranges and tabulated by dose, age, sex, and other covariates, then the Poisson regression model is applied[2] [3]. Categorization and aggregation cause a loss of information, inefficient estimation, and weaker statistical power when detecting the risk of a low dose.

To confirm the limitation of this approach, I applied the logit model and hazard model that can handle individual-level data to the US DOE nuclear worker data in Hanford, Oak Ridge, and Rocky Flats sites with that [4] failed to detect a significant effect of radiation with Mantel-Haenszel score test or the Poisson regression[2]. As shown in Table 1, significant coefficients were obtained with the individual-level model [5].
This "categorization & aggregation" approach is common among major radiation epidemiology, including analysis of a-bomb survivors[2] [3], nuclear workers [6], Mayak workers [7], and Techa River residents[8].

Table 1 Comparison between Aggregated Data Analysis and Individual-level Data Analysis[5]

		Gilbert et al(1993)			Re-Analysis		
		Trend statistics	ERR		Binomial Logit	Multinomial Logit	Hazard
ALL		-0.25			2.55**		
Cancer		-0.04	-0.0 (<0, 0.8)		2.22**		
(excluding leukemia)			0.0 (<0, 0.8)		2.37**		
	Solid cancer				1.88*	1.70*	0.091 *
	Leukemia		-1.0 (<0, 2.2)		-0.38	-0.40	
	Other cancer				2.02*	2.22**	
Non-cancer		-0.08			1.78*	2.50**	
External		-1.85*			-0.14	-0.29	
Unknown		-1.46			2.48**	2.50**	

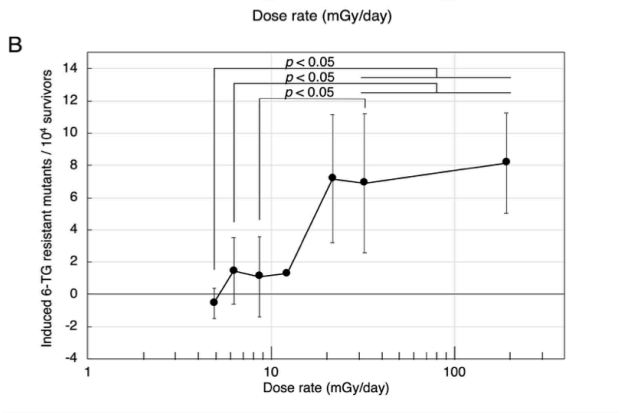
Significant Level ***:1% **:5% *:10%

- Improper scaling

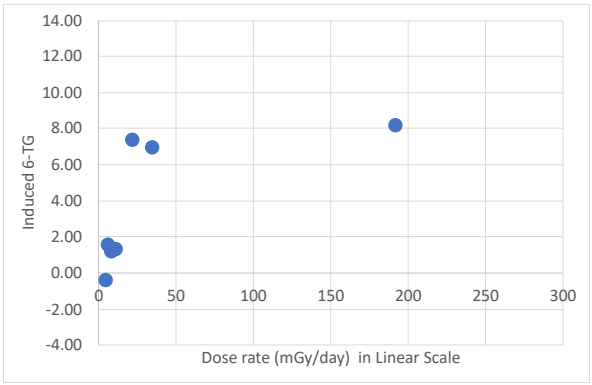
At Meeting 6, results of Japanese radiobiology that concluded the possibility of threshold in dose rate was introduced[3]. However, if I look closely at the graph, the dose rate is shown in logarithms (panel (a) in Figure 1), and if it was plotted on a linear scale, there is a linear relationship in the low dose rate range (panel (a') in Figure 1), thus the threshold was illusion with improper scaling. I identified similar mistakes in several radiation biological studies as shown below [9].

[2] Data is released under the CEDR project (Dataset HFMULA02)
[3] Presentation by Dr. Imaoka at Meeting 6
https://www.nationalacademies.org/event/11-16-2021/developing-a-long-term-strategy-for-low-dose-radiation-research-in-the-united-states-meeting-6-november-16-17-2021

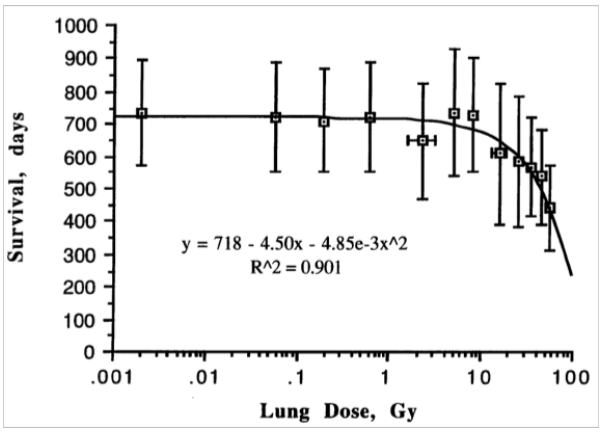
(a) Nagashima et al.(2021) [10]



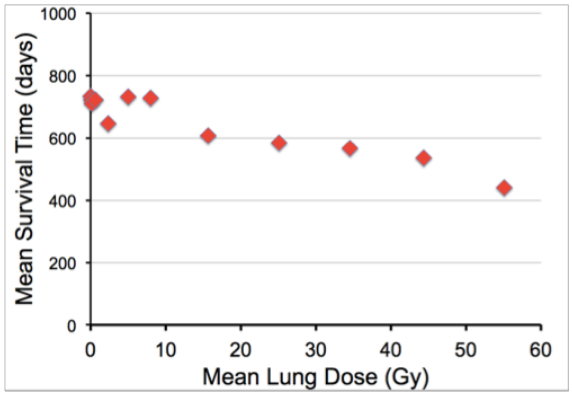
(a') Same data in Linear Scale



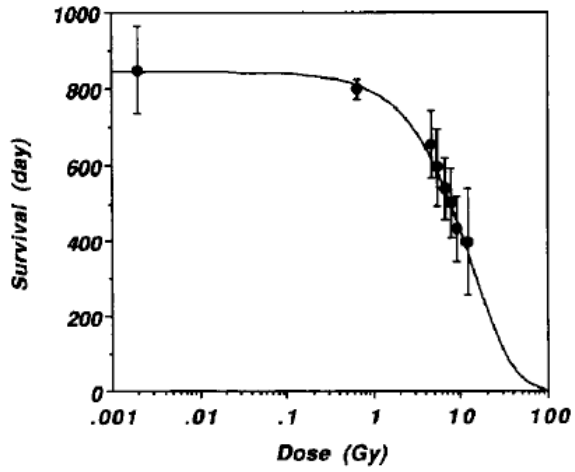
(b) Sanders et al. (1993) [11]



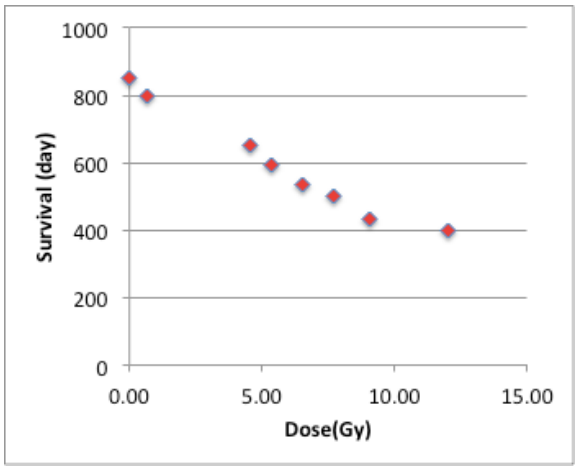
(b') Linear Scale



(c) Oghiso et al. (1994) [12]



(c') Linear Scale



Note) Data was digitized from the original graph, then plotted with a linear scale.

Figure 1 Wrong Scaling Leads to Threshold Illusion

- Limited sample analysis

Furthermore, I believe the finding of no significant effect below 100 mSv is based on an inadequate analysis that limits the sample to the lower dose range without using all samples[13]. Of course, If the sample size was limited, threshold-like results are obtained due to a lack of statistical power.

Table 2 Limited Sample Analysis Cause Threshold Like Behavior[13]

Excess Relative Risk Estimates for Selected Dose Ranges

Dose	ERR/Sv (SE)[a]	*P* value[b]
0–0.05	0.93 (0.85)	0.15
0–0.1	0.64 (0.55)	0.30
0–0.125	0.74 (0.38)	0.025
0–0.15	0.56 (0.32)	0.045
0–0.2	0.76 (0.29)	0.003
0–0.5	0.44 (0.12)	<0.001
0–1	0.47 (0.10)	<0.001
0–2	0.54 (0.07)	<0.001
0–4	0.47 (0.05)	<0.001

[a] Sex-averaged estimates at age 70 after exposure at age 30.
[b] One-sided *P* value for a test of the hypothesis that the slope is 0.

- Analysis with old or limited case data that could conclude hormesis effect

In addition, studies that emphasize hormesis use data from an era when the number of deaths among atomic bomb survivors was small. As shown in panel (b) of Figure 2, it has been found that the fit of the linear model is good after subsequent cases are added.

(a) A Graph that insists Hormesis with 1950's A-bomb Survivor Data [14]

(b) Dose response function for atomic bomb Survivor Data in Early and Latest Data. [2]

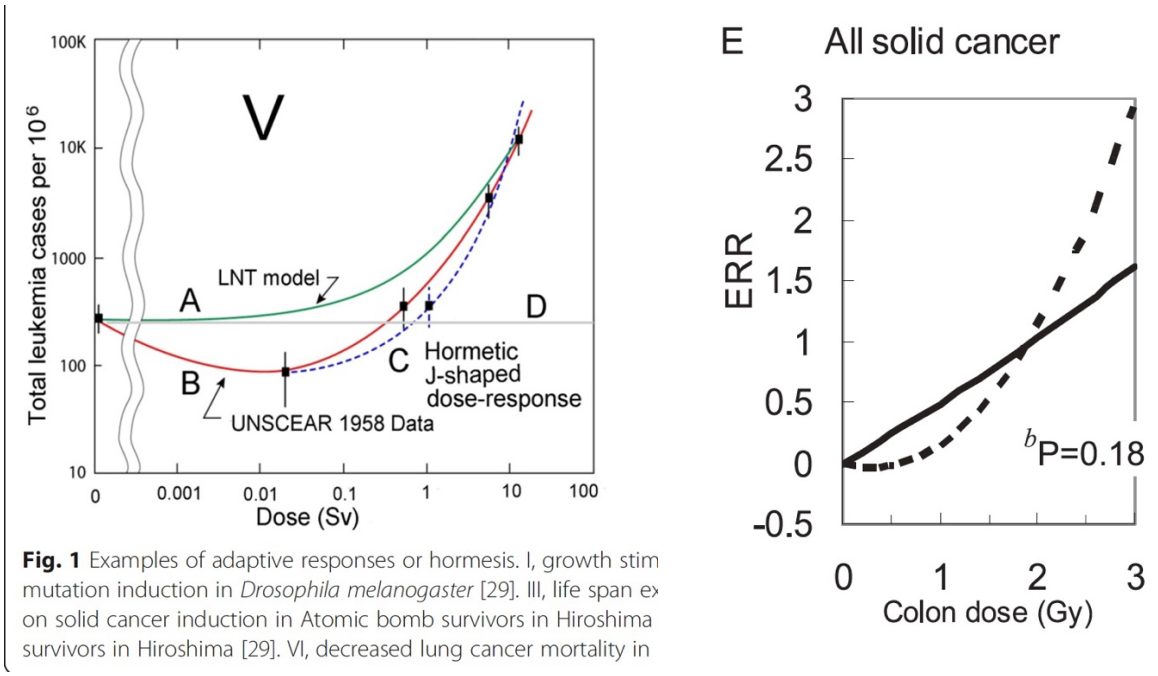


Fig. 1 Examples of adaptive responses or hormesis. I, growth stim mutation induction in *Drosophila melanogaster* [29]. III, life span ex on solid cancer induction in Atomic bomb survivors in Hiroshima survivors in Hiroshima [29]. VI, decreased lung cancer mortality in

Figure 2. Hormesis like Responsee was Observed in Old data but Disappeared in the Later Data

2.2 Wrong perception of uncertainty that could lead to an ill-defined problem

As Dr. Ulrich of RERF introduced in Meeting 7[4], in the analysis of solid cancer in atomic bomb survivors, significant effects have been observed under 100 mSv[2] [3] with categorized and tabulated data. A recent NCRP report[15] has also concluded LNT is supported in large epidemiological studies. Nevertheless, the OSTP/NSTC report[1] is misunderstood, citing uncertainty as cited below.

> "The risk estimates for adverse health outcomes from low-doses and low-dose rates of radiation are uncertain which, in turn, leads to uncertainty inappropriate regulations for protection from radiation (OSTP/NSTC 2022, p. v)."

The problem setting itself that there is uncertainty in the low-dose region is incorrect. Since the Fukushima accident, the human rights of radiation-exposed citizens have been violated by false statements such as "no statistically significant effects below 100 mSv is identified" or "no effects below 100 mSv" in Japan. The perception of uncertainty in low-dose should be corrected.

2.3 Inappropriate research purpose

The OSTP/NTSC report[1] states that the health effects below 100 mSv are uncertain, and as cited below, the report even states that finding a threshold would save money. This study may be intended to deny LNT.

> "If, as some experts believe, a threshold level for low-dose exposure could be demonstrated, it may be possible to revise regulatory guidance in ways that would provide significant cost savings by reducing compliance costs while mitigating risks(OSTP/NSTC 2022, p.2)."

2.4 Impossible or time-consuming research goal

The attempt to integrate radio-epidemiology and radiobiology seems to be an interesting scientific approach. However, this approach does not solve the problem of sample size or statistical power, which is one of the reasons why low dose effects cannot be detected in epidemiology[15]. Just as the application areas of Newtonian dynamics and quantum mechanics are different, their integration is unlikely and time-consuming.

2.5 Irrelevance with Policy Making

Economics can be classified into microeconomics and macroeconomics, but economic policies are formulated based on variables that can be observed at the macro level. Regulations for radiation protection are also based on epidemiological rather than biological findings. First and foremost are the epidemiological findings.

If biological mechanisms are to be studied and to be related to regulation, policy should reflect micro-level findings, such as compensating for defects at the DNA level, even though no health hazards have been

[4] https://www.nationalacademies.org/event/01-24-2022/developing-a-long-term-strategy-for-low-dose-radiation-research-in-the-united-states-meeting-7-january-24-25-2022

identified. As mentioned above, failure to recognize damage without understanding the mechanism leads to an increase in damage for humans.

2.6 The distinction between human and biological research

The integration of epidemiology and biology is an interesting research approach, but the results of biology cannot be applied directly to humans, as is evident from the fact that medicines are not certified in animal studies alone. Especially in animal experiments, it is being tested on animals that do not exist naturally, such as mice genetically modified to be susceptible to cancer. As Dr. Ulrich warned in Meeting 7, when incorporating the results of animal experiments, careful examination is necessary.

2.7 Need for an education program on data analysis methodology for researchers

As I pointed out above, some studies appealing to uncertainties below 100 mSv are problematic. Data from radiobiology, epidemiology, and other studies collected so far should be shared and reanalyzed properly before new studies are initiated.

Outreach to the general public is intended, but statistical education of researchers and peer review of research results should be improved to avoid inappropriate analysis as described above.

2.8 Necessity of individual-level data sharing and re-analysis

I am aware of some individual-level data on radiation workers[5] and radiation biology[6] are shared in the US. However, other important data, such as a-bomb survivor[7], Chernobyl, Mayak, medical exposure, DNA-level experiment, and so on, are not shared. Before initiating a new study program, a re-analysis of shared data should be conducted to confirm possible misunderstandings as pointed out above.

2.9 Potential conflicts of interest for DOE

The DOE, which has been conducting nuclear research, is the source of funding. Although at Meeting 1, Dr. Todd Anderson of DOE explained that DOE would not interfere with the content of the study, there is a high possibility that the research will be biased in favor of industry. In his Keynote speech at the Lowdose 2018 conference[8], Dr. William D. Magwood[9]: former director of the civilian nuclear energy program at DOE, former NRC, and now OECD/NEA Director-General, stated the rejection of LNT and the collective dose is his hope. Judging from this, the neutrality of DOE is suspected. Research should be conducted under the budget of a neutral or regulatory government body, such as EPA.

> "that we were then to be able to assume that below some this threshold level that there be no risk that there would be a case that below this threshold we could even say there was a benefit this could be a significant"[10]

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[5] https://oriseapps.orau.gov/cedr/
[6] http://janus.northwestern.edu/janus2/index.php
[7] Tabulated data is released, but individual-level data is not released.
[8] https://www.youtube.com/watch?v=Pp-CHrp8dpY
[9] https://www.oecd-nea.org/jcms/pl_36718/nea-director-general-william-d-magwood-iv?details=true
[10] Automatic superimpose by YouTube.

"we could all do is look for any opportunity to attack mercilessly anyone who dares put out a number use the collective dose"

" we were then to be able to assume that below some this threshold level that there be no risk that there would be a case that below this threshold, we could even say there was a benefit this could be a significant easing and the need to manage a lot of operational effluences. We could with the easy to clean up facilities, we would be able to deal with very very very low-level waste in a very different way."

2.10 Incorporating Japanese citizen's experience: expert and government fails

At Meeting 5, citizens from the Navajo Nation, downwinders of US nuclear tests, Marshall island, and others were invited to comment as Stakeholders. I appreciate this opportunity. However, I think you should also invite the survivors of the atomic bombs in Hiroshima and Nagasaki and the victims of the nuclear power plant accident in Fukushima. Although there was a report from a Japanese researcher on the Fukushima accident, it was very biased. You can start now, so please listen to the voices of the citizens.

At Meeting 6, Dr. Imaoka, a Japanese researcher, reported on risk communication to non-expert groups in Japan, which was extremely biased. The introductory supplemental text on radiation was published in 2011, 2014, and 2018. In the 2011 edition immediately after the accident, there was little mention of the Fukushima Daiichi Nuclear Power Plant accident, emphasis on the use of radiation, and failure to convey the danger of radiation exposure. This did not reflect facts and lessons learned and was therefore criticized by many people, including disaster victims, citizens, and researchers. Although these points were added in the 2014 edition, there are problems such as the lack of a description of the responsibility of the Japanese government, the failure of response to the accident, and the lack of information on the seriousness of the accident at the Fukushima Daiichi Nuclear Power Station [16]. However, these are not introduced in the presentation.

At the time of the Fukushima nuclear accident, nuclear experts incorrectly explained that nuclear power plants do not explode sound was due to the intentional explosion to reduce the pressure in the reactor, and that radiation exposure up to 100 mSv had no effect on health. The presentation failed to report that the expert also failed.

In Hiroshima, black rain containing radioactive fell in a wide area immediately after the atomic bombing, but only residents in a limited area were given certificates of exposure (medical expenses, etc., are paid). Those who had been exposed to the black rain but had not been given a certification as a-bomb exposure filed a lawsuit and were finally granted it in 2021. In this way, people who have been exposed to radiation are suffering greatly.

As pointed out above, there is a danger that DOE funds could be used to conduct research based on the logic of industry, but I do hope that this research will be conducted from the viewpoint of protecting citizens.

3 Key questions

To summarize my comment, I would like to list key questions for low-dose radiation research.

- Is the statement "effect of low dose exposure is uncertain" right?

- Can we confirm the conclusion of previous studies that concluded non-linear, threshold, or hormesis with a re-analysis of individual-level data?
- Can we share collected data in previous studies to conduct a re-analysis?

- Is it feasible or meaningful to integrate epidemiological and biological knowledge?

- Are there effective teaching methods to enable researchers to conduct methodologically and ethically sound research?

- Are the objectives of low-dose research sound? Wouldn't that be a good study for the industry?
- How do build transparent and trusted research entities to conduct low-dose radiation research?

- Are we ready to incorporate to compensate DNA or molecular level damage caused by radiation without health damage?
- Do we have a rational method to measure and weigh cost, benefit, and human rights for radiation exposure-related consequences?

I hope my comment is considered for your research strategy.

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