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Evaluating thyroid cancer risks for nuclear workers related to the Fukushima Daiichi Nuclear Power Plant accident based on LNT theory is problematic

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Dear Editor,

I read with great interest the recent study by Tatsuzaki *et al.* [1], which focused on abnormal thyroid function among seven Fukushima Daiichi Nuclear Power Plant (FDNPP) accident victims (emergency nuclear workers) from more than 24 000 workers, who had internal radiation exposure due to intakes of radionuclides (mainly I-131). The indicated seven individuals (all men) were followed for 10 years after the accident and were thought to have received the highest committed equivalent radiation doses to the thyroid (3.2–12 Sv). According to the researchers, none of the workers had symptoms demonstrating abnormal thyroid function. However, there are plans for longer follow-up of the seven workers. This letter intends to supplement the paper by Tatsuzaki *et al.* [1] by pointing out the need for a large epidemiologic study of thyroid cancer among the FDNPP workers and also pointing out biasing procedures (associated with poorly designed studies) to avoid. Including workers exposed to low radiation doses (e.g. 0–0.5 Sv) to the thyroid is recommended.

It is important to avoid a poorly designed epidemiologic study of cancer risk, especially when considering low radiation doses. Poorly designed studies that relate to cancer risks for low radiation doses (e.g. see literature [2–5]) employ misinforming procedures that yield results that promote radiation-phobia-related harm [6]. Radiation phobia has already caused enormous societal losses for Japanese citizens following the FDNPP accident, related to the highly stressed elderly evacuees [6]. The phobia is linked to the unscientific linear no-threshold (LNT) cancer risk model, whereby any amount of radiation, no matter how small, can cause cancer (e.g. thyroid cancer), and cancer risk increases linearly as radiation dose increases; however, extensive radiobiological data related to adaptive-response-associated, chemico-biological interactions in the body and their consequences essentially invalidate LNT as applied to cancer induction by ionizing radiation [7, 8].

Presently, justification for use of LNT in epidemiologic studies focused on low radiation doses is unfortunately based on misinforming procedures used that essentially guarantee an apparent LNT dose–response relationship for relative risk (*RR*) and related excess relative risk (*ERR*) for cancer induction (or cancer mortality) [6]. Some misinforming procedures employed by some epidemiologists are presented in Table 1 and elsewhere [6, 9]. A key misinforming procedure to avoid is using LNT as the null hypothesis (implied by using an LNT model and including high dose data [6, 9]), rather than assuming no radiogenic harm (e.g. for low doses). When LNT is considered the null hypothesis, uncertainty in *RR* and *ERR* is modeled to progressively vanishing as dose decreases toward the *assigned zero dose group*, with essentially no uncertainty about elevated risk remaining at a dose of 1 nGy; with 1 nGy being treated as definitely harmful for someone in a very large population. This is permitted because uncertainty for the estimate $RR = 1$ for the zero-dose group (actually exposed to natural background radiation) is omitted [9]. Including this uncertainty can lead to results that support a threshold [9], as clarified in the next paragraph. For examples of intentionally and unscientifically vanishing existing uncertainty, see these LNT applications [2–5] by epidemiologists. Reviewers for at least one of the papers [3] appear to be unaware of the use of misinforming procedures by the researchers, as evidenced by reviewer comments available via the journal.

The misleading nature of inappropriately vanishing risk uncertainty is reflected by the fact that absolute risk estimates, upon which *RR* and *ERR* estimates are based, have >0 uncertainties; thus, uncertainty should not vanish, even for the estimated $RR = 1$ for the assigned zero dose group [9]. The missing uncertainty can be evaluated by assuming a lognormal distribution of *RR* estimates or by using a binominal distribution of the cases count associated with absolute risk [9]. Both approaches would be expected to yield very similar results for the lower (*L95*) and upper (*U95*) 95% confidence interval values, respectively,

Table 1. Misinforming procedures used by some epidemiologists when trying to justify use of the LNT risk model for assessing cancer risk for low radiation doses [6, 9]

Number	Misinforming procedure
1	For the supposedly un-irradiated group, assigning the estimate $RR = 1$ no uncertainty, even though the absolute risk used to evaluate RR has >0 uncertainty.
2	Lagging the protracted exposure dose (i.e. discarding some of the dose) even when the dose is too small to likely cause any harm, thereby blaming each cancer on radiation exposure irrespective of the true cause.
3	Treating the assigned unexposed group as having never been irradiated via natural background or other radiation sources.
4	Including high-dose data to guarantee a positive slope to the forced fitted LNT line.
5	Using dose groups with a wide range of doses, which can hide nonlinearity. Modern data analysis methods allow for individual data points to be used with risk replaced with a Bernoulli random variable (1 for cancer present; 0 for cancer absent), in which case individual-specific doses rather than dose groups can be used along with conditional logistic regression in modeling cancer risk. For an example of modern data analysis methods, see Thompson's analysis of lung cancer probability related to radon inhalation in the home [10].
6	Using LNT for cancer induction as the null hypothesis rather than assuming no radiation harm (e.g. for low doses).

associated with the estimated $RR = 1$. When evaluating *ERR*, adjustment for the indicated missing uncertainty for $RR = 1$ for the assigned zero dose group needs to be performed, which unfortunately is seldom done [e.g. see literature 2, 5] by LNT-using epidemiologists. The cited reference [9] relates to alpha-radiation-caused lung cancer in humans. Making the needed adjustment can lead to results supportive of a population threshold (i.e. the greater than zero radiation dose needed to cause cancer of a specific type in the most radiosensitive member of a population). When only risk increases above the *U95* were considered scientifically defendable *ERR* for lung cancer induction, a population threshold dose >20 mGy was implicated for alpha radiation [9]. Note that a 20 mGy absorbed dose corresponds to a 400 mSv equivalent dose. For doses below a population threshold, no cancers of the type of interest are induced by radiation in anyone in an irradiated population; however, the threshold likely differs for different populations, cancer types and radiation exposure scenarios [9].

The need to account for the missing risk uncertainty was apparently recognized by Tatsuzaki *et al.* [1] when discussing results of an epidemiologic study of thyroid cancer among Chernobyl liquidators [11]. Hopefully the information provided in this letter will help in designing additional studies of cancer risk associated with radiation exposures related to the FDNPP accident that do not by design promote more potentially harmful radiation phobia on top of what already exists in Japan [12]. Possibly, suggestive evidence for a population threshold for cancer induction will be found, as was the case for Chernobyl liquidators, where no evidence of harm for doses <300 mGy to the thyroid were pointed out by Tatsuzaki *et al.* [1]. If so, it will be important to characterize the population threshold dose uncertainty, as has now been done for lung cancer among Mayak plutonium facility workers exposed internally to high-LET alpha radiation [9].

Unlike modern-science-devoid LNT theory, the notion of a population dose threshold for cancer induction is consistent with modern radiobiology associated with radiation adaptive responses after low radiation doses and dose rates, as reviewed elsewhere [7, 8]. The multiple natural defenses enhanced by low radiation doses and dose rates that are linked to radiation adaptation *in vivo* are gifts of evolution that serve as barriers against cancer [7, 13]. Below the population threshold dose, these radiation adaptive responses can provide health benefits, including a significant reduction in cancer risks associated with exposure to other carcinogens [7, 13–15] and possibly reducing, for a period of time, the severity of some diseases including Alzheimer's [16, 17].

It is quite important to be aware of the harm that radiation phobia, linked to LNT theory, can cause for emergency nuclear workers exposed to I-131 and other radiation sources following the FDNPP accident. Hopefully, this letter will help prevent such avoidable harm from occurring.

CONFLICT OF INTEREST

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PRESENTATION AT CONFERENCE

None.

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