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Economic benefit-cost implications of the LNT model

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1. Introduction

As documented in this Special Issue, the linear no threshold (LNT) dose response model as a default model is scientifically invalid for both radiation and most chemicals. Consequently, there is no logical rationale to assume that the LNT model should be used to estimate health or safety benefits within benefit-cost analysis. Because thresholds are likely to exist for both radiation and chemicals, assuming that LNT is valid for economic analyses will lead to policy decisions with unnecessary costs imposed on society. From an economic perspective, a *policy threshold* is reached when the costs of decreasing exposures exceed the benefits. This paper investigates the use of LNT and policy thresholds using two examples to illustrate them, radon and formaldehyde.

EPA's present LNT-driven program to mitigate indoor air radon to prevent lung cancer from homes and buildings costs billions of dollars each year while the benefits of the program are, at best, negligible. EPA's program to reduce exposure from formaldehyde in composite wood products costs about $60 million each year, again, with negligible (or zero) benefits. Both programs demonstrate that the economic threshold for decreasing exposure has, for the most part, already been attained and would have been correctly identified if a threshold model had been employed. Thus, use of a threshold model, instead of an LNT model, would have resulted in a different policy.

Controversy over the use of LNT for risk assessment purposes goes back over 70 years to 1946 when Ernst Caspari reported a threshold response to radiation, based on the dose rate for gamma-ray-induced mutations in fruit flies [1]. Prior to that, ionizing radiation-induced mutations were assumed to be linear, down to zero (i.e., a single "hit" could induce cancer), with respect to the dose. Caspari's findings challenged the model originally created by Herman Muller.

In fact, Muller believed he had induced mutations by dosing fruit flies with X-rays when, in fact, he made "large gene deletions and other gross chromosomal aberrations [2]." After Mullers mistakes, Caspari's findings set off a temporary alarm amongst the radiation genetics community such that it prompted one radiation researcher to ask (about the LNT), "What can we do to save the (one) hit model? [1]" Their worry was misplaced; Muller's views eventually won the day.

But Ed Calabrese reports that "the LNT dose-response model, which drives cancer risk assessment, was based on flawed science, on ideological biases by leading radiation geneticists, on scientific misconduct by an NAS Genetics Panel during the atomic radiation scares of the 1950s, and on a 40 year mistaken assumption by yet another NAS Committee [3]."

The controversy is important for multiple reasons. Scientifically, as extensively discussed in this Special Issue, the LNT makes no sense biologically. Second, from a risk perspective, chemicals and radiation are regulated to very low levels and those regulations often replace a very low risk with a higher risk from a substitute product or activity. This is called a risk/risk trade-off. Finally, use of the LNT inappropriately can lead to the imposition of unnecessary, and often very large, costs.

It is no longer possible to ignore the costs of regulation. Today, nearly 300,000 federal workers (up from 57,000 in 1960 [4] put out 3–4000 regulations every year that have resulted in over 1 million restrictions (individual requirements) in the *Code of Federal Regulations* [5]. The cost of these regulations to the U.S. economy, although difficult to estimate, could be as high as $2 trillion each year [6]; nearly 11% of the U.S. GDP.

Inappropriate use of the LNT can lead to spending too much on regulations and, because it results in overestimation of risks, will in turn cause benefits to be overestimated. Most benefit analyses currently use the results of risk assessments as the starting point. To be useful with estimates of cost, risk assessments need to estimate actual risks and to factor in the probabilistic information when possible to properly characterize the expected and net risks [7].

Beyond costs and benefits, there are other problems with using the LNT when it is not appropriate. In a staff report, EPA declares that it seeks to adequately protect public and environmental health by preferring an approach that does not underestimate risk in the face of uncertainty and variability. In other words, EPA seeks to adequately protect public and environmental health by *ensuring that risk is not likely to be underestimated"* [emphasis in original] [8]. To ensure that they do not underestimate risk, EPA staff routinely employ conservative defaults and assumptions that result in substantial overestimates of risk. Employing the LNT when there is a threshold is also conservative (precautionary). But by doing so, they have "effectively usurped risk management since managers (are) often never made aware of

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uncertainties or the potential impact of these uncertainties on the results and (are) essentially forced to make decisions that began with an assumed overestimate of the risk [7]."

2. Thresholds

Studies have shown that the same mechanisms that work at high doses for cancer causing substances, do not work at low doses because "we have evolved molecular systems that continuously monitor and repair DNA." [9] Others have argued, however, that because there is an underlying rate of spontaneous cancers, that induced cancers (from toxic substances and radiation) add to the probability of getting cancer. However, a recent evaluation of the mechanisms by which cancer is produced from spontaneous and induced cancers shows that they have completely different mechanisms. Therefore, they cannot be additive [10].

All chemicals will have a threshold because assaults to biological systems arise continuously and from everywhere - plants and animals we eat, environmental stressors, sunlight and other background radiation, oxygen, and microorganisms such as pathogens and viruses. Whether there are potentially negative effects from a stressor depends on dose, medical status and other factors.

3. Benefit-cost thresholds

Policy thresholds underlie the decision thresholds used by risk managers to determine when exposure is low enough to stop regulating. The key economics concept behind benefit-cost thresholds is "opportunity cost." Opportunity costs arise because decisions must be made among regulatory options. The opportunity cost of choosing one course of action is not choosing a different option. For example, if a regulation requires managers to switch from creating a new product to complying with a regulation, the opportunity cost is forcing them to spend their time on the regulation rather than their preferred option, creating the new product. Social opportunity costs include preventing people from using their existing resources on current activities as well as preventing them from buying something new. For example, if we require money to be spent on a federal regulation to reduce the risk of formaldehyde, the opportunity cost might be that worker safety could be improved elsewhere.

Policy decisions that employ benefit-cost thresholds could be, for example, how low a level to set for limiting exposure to a harmful chemical, whether to force a manufacturer to buy a certain kind of equipment to make a product or plant safer, how clean fill dirt must be in a Superfund site, how long to give manufacturers to comply with a regulation, or whom should be covered by a regulation or law. Each policy decision causes organizations, and possibly consumers, to change behaviors that, in turn, affects the type and magnitude of risks (benefits) they face. Costs are the forced changes in behaviors (e.g., new management or labor requirements, new capital) that move people away from their preferred option.

In a health and safety benefit-cost analysis, benefits are calculated as the (expected) reduced risk of morbidity or mortality for a population multiplied by the value people place on those reduced risks. People value each unit of risk reduced and those values can be estimated. For example, buying a car with more costly safety features implies a tradeoff for other features, such as a larger engine.

The opportunity costs of choosing a very low level for limiting exposure to a chemical or radiation are that the resources might have been spent reducing exposure elsewhere. When the additional costs of reducing exposure to a lower level (i.e., what has been given up) is more than the additional benefits of that reduction, i.e., the marginal costs are greater than the marginal benefits, then the economic threshold has been reached. This explains why the results of a benefit-cost analysis are said to generate an "efficient" choice. An efficient choice means that every dollar spent obtains the maximum possible benefit, i.e., the biggest bang for the buck. Morrall has shown how opportunity costs can be illustrated by the cost per life saved for various risk-reducing regulatory actions [11].

Crump describes an economic threshold as one that is "a societal decision rather than a purely scientific one [12]." Although not always the case, as regulation attempts to decrease exposure to a hazard, each reduction in exposure costs more than the previous reduction. Another way to say this is, each dollar spent will reduce exposure less than the previous dollar.[1]

An example of this principle comes from Superfund. When cleaning up a Superfund site, the deeper the ground that must be cleaned, the more it costs to go an additional yard deeper. Supreme Court Justice Stephen Breyer explained why the marginal costs and marginal benefits of cleaning Superfund sites matter in *Breaking the Vicious Circle.*

The first comes from a case in my own court, *United States v. Ottati & Goss,* arising out of a ten-year effort to force cleanup of a toxic waste dump in southern New Hampshire. The site was mostly cleaned up. All but one of the private parties had settled. The remaining private party litigated the cost of cleaning up the last little bit, a cost of about $9.3 million to remove a small amount of highly diluted PCBs and 'volatile organic compounds' (benzene and gasoline components) by incinerating the dirt. How much extra safety did this $9.3 million buy? The forty-thousand-page record of this ten-year effort indicated (and all parties seemed to agree) that, without the extra expenditure, the waste dump was clean enough for children playing on the site to eat small amounts of dirt daily for 70 days each year without significant harm. Burning the soil would have made it clean enough for the children to eat small amounts daily for 245 days per year without significant harm. But there were no dirt-eating children playing in the area, for it was a swamp. Nor were dirt-eating children likely to appear there, for future building seemed unlikely. The parties also agreed that at least half of the volatile organic chemicals would likely evaporate by the year 2000. To spend $9.3 million to protect non-existent dirt-eating children is what I mean by the problem of "the last 10% [13]."

The opportunity cost of the resources spent on that last 10% might have been better spent on reducing risks of unintentional injuries to children (the leading cause of death for children aged 1–4) [14].

The marginal costs and marginal benefits of reducing exposure are illustrated in Fig. 1.

In Fig. 1, point A is where marginal costs of reducing exposure equal marginal benefits. Any decision to reduce exposure below point A (to the right) has marginal costs exceeding marginal benefits. Point B is the effect threshold, where any reduced exposure beyond that has only costs, no benefits.

When using an LNT model and ignoring a threshold, perhaps to be *protective* as EPA attempts to be, false benefits will be attributed to a reduction in exposure. Using the LNT inappropriately moves the benefit-cost threshold to the right of point A where, in actuality, marginal costs exceed marginal benefits. What's worse, this fact is obscured. As radiation and most chemicals have a toxicological threshold, inappropriate use of the LNT as a default is not only inaccurate but costly. The two examples below demonstrate how ignoring thresholds generates costs that vastly exceed benefits.

4. Radon

Radon-222 is a gas, a so-called "daughter" of radium 226 that is ubiquitous in the earth's crust and can be found in many homes and commercial buildings. EPA cites the Surgeon General's Health Advisory that "Indoor radon is the second leading cause of lung cancer in the United States [15] …"

Some states and localities have produced their own radon laws

[1] See, for example, Miller, Wilhelmine et al., National Academy of Sciences, "Valuing Heath for Regulatory Cost-Effectiveness Analysis," 2006, p. 267.

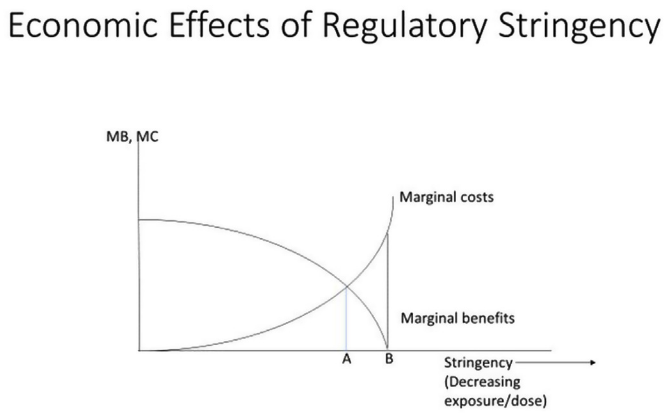

Fig. 1. Economic effects of regulatory stringency.

including 37 states with their own requirement for real estate transaction disclosure [16]; 11 states requiring radon resistant new construction; 2 states requiring testing in day care centers; and 18 states having radon mitigation laws [16].

At the federal level, EPA has a national program for testing and remediating radon for both homes and commercials buildings, particularly if they are present at levels at or above 4 pCi/L.[2] EPA based their 2003 reassessment of the risk of lung cancer from radon on the National Academy of Science BEIR VI (Biological Effects of Ionizing Radiation) report that used the LNT model [17]. EPA has data showing that 6% of all homes have "elevated levels" of indoor radon (above 4 pCi/L) [18]. CDC estimates that 7 million homes have high radon levels [19]. Because radon levels may vary considerably between counties and even adjacent homes, EPA warns that, "All homes should be tested, regardless of (radon) zone designation [20]." Sale of homes is typically contingent on the seller providing certification of a low radon home (or building) and proof of such shows up in most real estate contracts.

It is estimated that there are approximately 600,000 homes sold in the U.S. each year [21]. With an average testing cost of about $500 per home [22], the total cost to test all homes is about $30 million per year. If a seller must provide remediation for radon, EPA estimates that the average cost is between $800 and $2500 per house ($1600 average) [15]. Assuming that only those homes above 4 pCi/L are remediated, then 36,000 homes are remediated each year at a cost of $58 million annually. Together, testing and remediation are estimated to cost $89 million annually.[3]

In 2012, there were 5.6 million new commercial buildings in the U.S. comprising 87 billion square feet [23]. Assuming the same percentage of buildings as homes need radon remediation (6%), 336,000 buildings with an average of 15,536 square feet would be remediated each year. However, as radon cannot be tested until a building is built, it may be that in the 26 states that have high radon levels (average over 4 pCi/L), new buildings in these states may be built to eliminate radon during construction [24].

The average costs for radon remediation including engineering (vapor barriers), installation, first-year maintenance, and administrative costs for a new commercial building is $67,000, with an additional $7500 beginning in the second year in annual maintenance costs [25]. If only 6% of new buildings are remediated (the same percentage as homes above 4 pCi/L), the costs would be $23 billion per year. If half of all new buildings are remediated (in high radon states), the cost would be $189 billion per year. These figures only include new buildings, not existing buildings that test high and must be remediated.

Despite the Surgeon General's finding, on-going benefits of this program are suspect due to the high degree of uncertainty in the attributable levels of lung cancer related to radon. In fact, the threshold level for radon is most likely much higher than the EPA "action level." Higher minimum levels for carcinogenic effects have been reported, 8.1 pCi/L [26] and 14.7 pCi/L [27]. In addition, a recent paper that reanalyzed 32 case-control and two ecological studies concerning radon's effect on lung cancer risk concluded that exposure to radon concentrations below about 27 pCi/L (1,000 /bq/m^3) were not associated with any "statistically significant increase in lung cancer incidence [28]." Exactly where the threshold lies is uncertain, but it is likely to be somewhere between 8 and 27 pCi/L, or more than twice EPA's action level of 4 pCi/L. In fact, 4 pCi/L appears to be a level that is protective, not harmful [17].

Maps of average radon levels in "high" radon states (averages above 4 pCi/L) show that only two states have averages above the likely lowest threshold, 8 pCi/L [29]. South Dakota has an average of 9.6 pCi/L and Pennsylvania has an average of 8.6 pCi/L [29]. Both states have average levels well below 27 pCi/L, although, there is no available data as to how many individual homes and buildings exceed that concentration.

Fig. 2 indicates that the majority of lung cancer is caused by smoking, not radon.

Based on Fig. 2, a more efficient (cost effective) way to reduce lung cancer would be to address smoking directly. For example, to reduce the number of smokers, the Centers for Disease Control created a program (Tips from Former Smokers) that ran for 3 months in 2012. CDC estimated the program was likely to cause 100,000 people to quit smoking [31]. The campaign cost $54 million or about $540 per quitter, assuming the number of quitters' estimate proved to be correct. Given that most of the homes and buildings have radon levels far below the thresholds that have been discussed in this paper, it's likely that the number of cases of lung cancer reduced by radon mitigation are far less than the BEIR report shows suggesting that trying to reduce cases of lung cancer by mitigating radon results in expenditures of billions of dollars per case avoided. This means that the expenditures (costs) are likely to vastly exceed the benefits.

5. Formaldehyde

EPA recently finalized a regulation governing formaldehyde emissions for composite wood products (Formaldehyde Standards for Composite Wood Products Act, or Title VI of TSCA, 15 U S C. 2697) [32]. The primary health effect quantified by EPA in this regulation was for nasopharyngeal cancer (NPC). EPA's risk estimates were derived from the International Agency for Research on Cancer [33,34], the National Toxicology Program [35] and the US EPA [36](2010a), which concluded that formaldehyde is a known human carcinogen for NPC. However, that conclusion was based almost exclusively on the results of a single study conducted by the National Cancer Institute (NCI), which reported 9 deaths from NPC among more than 25,000 workers exposed [37]. Notably, five deaths came from one plant (Plant 1), while the remaining 4 were randomly distributed in the other 9 plants.

EPA presented an economic analysis (RIA) for its composite wood products regulation the LNT model-based IRIS Inhalation Unit Risk factor of 1.3×10^{-5} cancer cases per μg/m3 of formaldehyde (an upper bound) [38]. Using a unit risk factor implies that any reduction in risk would be the same for every reduction in exposure, and that there is no threshold for its cancer potency (i.e., the LNT model).

EPA estimated that reducing formaldehyde exposure to 1 ppm from current levels would, using the IRIS unit risk factor, result in 26–65 cases of NPC avoided per year (with annual benefits of between $19.3 to $47.6 million per year) [38]. However, the expected cases avoided are greater than the number of NPC cases from all exposure sources by a factor of more than 20 [39]. In fact, the World Health Organization concluded that there is no evidence of NPC caused by exposure to

[2] There are many ways to measure radiation, picocuries per liter. pCi/L, is a measure of the rate of radioactive decay of radon.

[3] EPA recommends remediation even down to 2 pCi/L.

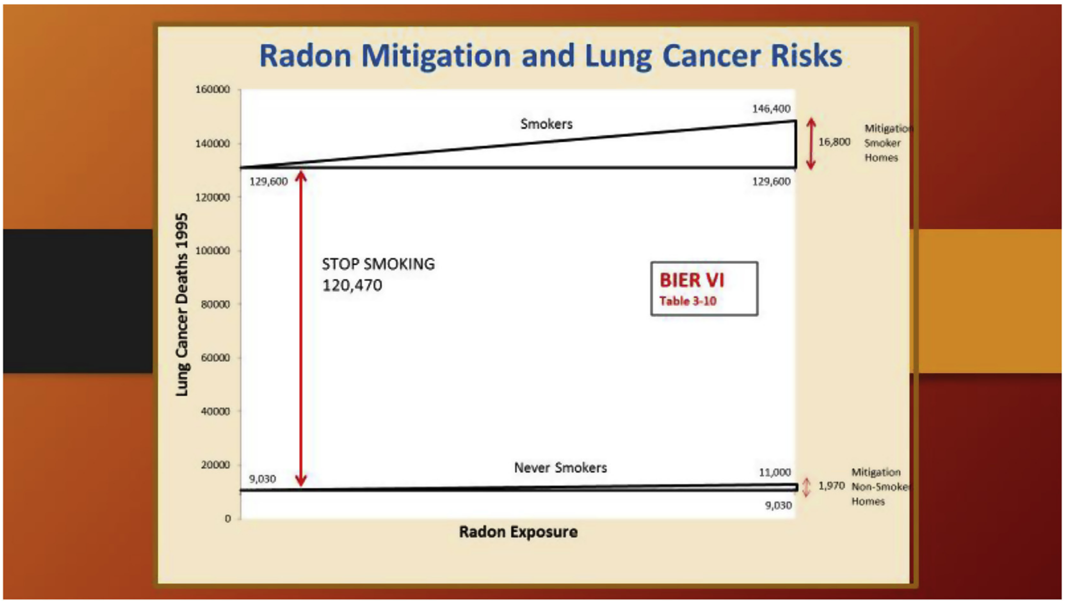

Fig. 2. Radon Mitigation and lung cancer risks [30].

formaldehyde at mean concentrations below 1.25 mg/m^3 [40].

Following the IRIS assessment (that produced formaldehyde's inhalation unit risk factor), McGregor determined that the mode-of-action elements (i.e., cytotoxicity, cell proliferation, and DNA effects) for formaldehyde-induced nasal tumors are not linear but, in fact, highly non-linear and do not occur unless a threshold dose (6 ppm) has been exceeded (well above EPA's action level of 1 ppm) [41]. In addition, Conolly found that upper respiratory tract cancers most likely had a *de minimis* level of 10^{-6} or less at relevant workplace exposure levels [42].

Careful investigation of the previous employment history of Plant 1 workers who died from NPC determined that four of the five NPC cases had worked previously in silver-smithing occupations involving substantial exposures to potential known risk factors for upper respiratory system cancers, including sulfuric acid mists and metal dusts [43]. In fact, in an updated re-analysis of the mortality risk from NPC in the NCI formaldehyde worker cohort Marsh [44] (2016) concluded that there was "little or no evidence to support NCI's suggestion of a persistent association between FA exposure and mortality from NPC. NCI's suggestion continues to be driven heavily by anomalous findings in one study plant (Plant 1)."

In another study of more than 14,000 British chemical workers with elevated formaldehyde exposures (including some 4000 workers with exposures > 2 ppm), there was no evidence of elevated NPC. The authors of this study (which involved formaldehyde exposures in excess of the NCI cohort) concluded that the evidence for formaldehyde carcinogenicity in humans was unconvincing [45]. In a study by the National Institute of Occupational Safety and Health (NIOSH) of more than 11,000 garment workers occupationally exposed to formaldehyde, no cases of NPC were observed [46]. Finally, a study from NCI conducted by Hauptmann [47] of formaldehyde-exposed embalmers reported no excess of NPC in the cohort.

Notably, the excess of NPC cases in the NCI cohort (Plant 1), quite reasonably now attributable to other exposures, appear unlikely to be related to formaldehyde. It is difficult to envision a scenario in which the 6 cases of NPC in the approximately 7000 workers in Plant 1 were due to formaldehyde when none occurred among 25,000 plus occupationally exposed workers reported in the other studies.

Interestingly, EPA's use of the IRIS unit risk factor implies that there is a 1 in one million risk of NPC at a formaldehyde exposure concentration of 0.08 parts per *billion.* This level is more than 50 times lower than the median concentration people (and all animals) exhale in each breath (4.3 ppb) resulting from normal endogenous metabolic processes [48]. In fact, Golden concluded that "a formaldehyde concentration of 0.1 ppm would be *protective* for leukemia or cancer at any other site within the body [28,49]."

Since the IARC (2006) decision concluding that formaldehyde is a known human carcinogen based on NPC, several comprehensive quantitative evaluations of the epidemiological literature have carefully documented that the weight of human evidence does not support a causal association between formaldehyde exposure and NPC [50,51]. EPA's reliance on the single NCI study now seems to be entirely unwarranted and the benefits of this rule are likely to approach zero.

The costs of EPA's composite wood products rule included "changes to production process and raw materials that are needed to meet the emissions standards, as well as the costs of the testing, third-party certification, rule familiarization, recordkeeping, labeling, and chain of custody activities required by the rule." were estimated to be from $38 million to $83 million per year [42]. Golden has concluded, "Despite numerous epidemiology studies that have raised a specter of formaldehyde-induced NPC and leukemia, both endpoints now appear more likely to be false positives, as these findings are inconsistent with an ever-increasing body of data demonstrating that such effects simply cannot occur under any real-world exposure scenario [49]." If Golden's conclusion is correct, the likely benefits of the composite wood products rule are negligible, if not zero, meaning that the net costs of the rule are $38 to $83 million per year.

5.1. *Leukemia and formaldehyde*

EPA also considered the risk of leukemia and formaldehyde. However, in their Regulatory Impact Analysis, they concluded, "EPA did not have sufficient information to derive a concentration-response function for myeloid leukemia and thus could not estimate the number of cases that would be avoided by reducing formaldehyde exposure [32]." While EPA did not quantify the effects of formaldehyde on leukemia in their most recent regulation, the International Agency for Research on Cancer (IARC 2009) has concluded that there is "sufficient evidence" to link formaldehyde with leukemia [33].

While a number of chemicals (e.g., benzene and some anti-cancer drugs) have been associated with leukemia, all share the ability, following inhalation, to enter the blood with subsequent transport to the bone marrow where leukemia develops. Given the prodigious metabolism and detoxification of formaldehyde in the upper respiratory tract, no inhaled exogenous formaldehyde, even at high concentrations, can be detected in the blood to increase the concentrations already present naturally. Since leukemia is far more prevalent that NPC, it is feasible that EPA, will at some point rely on LNT to reduce exposure limits to mitigate potential risks of this endpoint as well.

6. Conclusion

Risk management decisions can be based on different factors, such as the need to protect a highly exposed or sensitive group of people or a legal requirement. Because different legal requirements and values affect risk management decision-making, different thresholds may need to be considered in benefit-cost determinations. For policy decisions based on benefit-cost analysis, using the LNT model when it is biologically inappropriate causes benefits to be over-estimated and results in costs more than what they would be worth to consumers, who ultimately pay for regulations. Use of the LNT for risk management may be viewed as "conservative" because it overestimates risk to ensure public health protection. However, spending scarce resources to prevent some risks means that we may not be addressing others. In other words, the more regulators try to lower exposure to chemicals or radiation, particularly past their toxicity thresholds, the more likely they are to get the policy wrong. As extensively addressed in the other papers in this Special Issue, because LNT is an invalid dose-response descriptor for potentially carcinogenic effects from both chemicals and radiation, it should not be used in economic analyses.

Transparency document

Transparency document related to this article can be found online at https://doi.org/10.1016/j.cbi.2019.01.028.

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