

(1,4,5). In doing so, Weber and Zanzonico one-sidedly focus on risk in the low-dose region as the default assumption, neglecting benefit.

Most tellingly, they imply that prospective studies are the only valid basis on which to decide, but they simultaneously say that such studies may be “logistically and financially prohibitive,” not to mention possibly unethical. Thus, as the basis of regulatory policy and medical practice, they ensconce LNT in a position impervious to further (obtainable) evidence and implicitly reject the mounting nonprospective evidence against it.

Indeed, many, if not most, medical conclusions and practices have been arrived at without prospective studies, which would often be unethical. For example, in the 19th century a stunning insight by Dr. John Snow, that cholera was caused by sewage in the water supply, led to the purification of the water supply with salutary results. No prospective trial was ever performed, nor could it be performed ethically. Without the practical or ethical possibility of prospective studies, Bayesian estimates of probability have successfully been used to reach conclusions that have held as the best medical practices.

Moreover, many experimental and epidemiologic studies show benefit, rather than risk, from low-dose exposures (1,3). Furthermore, no ill health effects associated with natural background radiation levels have been documented anywhere in the world (5,6). The assertion of BEIR (Biological Effects of Ionizing Radiation) VII that such ecologic metastudies are meaningless puts the burden on the committee to identify confounders or other factors that can account for these consistent findings, rather than simply dismissing them a priori.

It should be noted that, whereas all medical procedures require justification and optimization, the International Commission on Radiological Protection recommendation that this apply to lowering radiation exposure (to as low as reasonably achievable) is scientifically unjustified and medically counteroptimal.

As we reported, in a recent study of young adults undergoing body CT, the observed risk of death was found to be more than an order of magnitude greater than the hypothetical LNT-predicted risk of dying from radiation-induced cancer. Underlying morbidity, rather than CT-induced cancer, is the dominant factor driving adverse outcomes. A controlled randomized trial comparing outcomes of patients who did and did not undergo CT would be the definitive prospective study to measure the benefits (versus risks) incurred by imaging. However, withholding CT for such a trial would be unethical.

Weber and Zanzonico conclude with the hopeless statement that “the debate over LNT will not be resolved anytime soon.” With agnosticism being forcefully injected into the evidential imbalance that characterizes the LNT-versus-hormesis debate, it will never be resolved. The all too common reticence to accept the available and mounting evidence that is decidedly in favor of hormesis and soundly against LNT, and the displacement of the burden of proof from the evidence-absent LNT to the evidence-rich hormesis, are unscientific, as well as assuredly unethical.

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REPLY: Despite their critical nature, we very much appreciate the comments by Dr. Marcus and Drs. Siegel and Sacks on our Invited Perspective (1). We further appreciate the unmistakable passion they bring to the issue of dose–response relationships in the context of low-level radiation. Importantly, our commentary was not intended as either an endorsement or a refutation of the linear no-threshold (LNT) dose–response model or of any alternative model. Rather, our intent was to provide some background on this issue for the readership of *The Journal of Nuclear Medicine*. The publication by Siegel et al. (2) had already made a compelling case for the fallacy of the LNT model, and it would have been inappropriate, we feel, to simply ignore the large body of scientific literature that supports or at least does not refute the LNT model—even if this model is ultimately discredited. Such an effort inevitably results in the citation of publications that bolster as well as undermine different scientific positions. Our commentary concluded as follows: “. . . even if one concedes the validity of the LNT model, it cannot be applied reliably to individuals but only to large populations. . . and application with certitude of population-derived risk factors to individual patients or even defined patient populations is simply not justified.” Although ignored in the letters from Dr. Marcus and Drs. Siegel and Sacks, and despite our presumed agnosticism, the foregoing conclusion amounts to a tangible refutation of the LNT model in a very important context, that of clinical practice.

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