Dr Ian Fairlie
Consultant on Radioactivity in the Environment
LONDON
United Kingdom
www.ianfairlie.org

US Nuclear Regulatory Commission (NRC): Consultation

https://www.federalregister.gov/articles/2015/06/23/2015-15441/linear-no-threshold-model-and-standards-for-protection-against-radiation

Introduction

On June 26 2015, the US Nuclear Regulatory Commission (NRC) stated it was seeking public comments by September 8, on petitions stating that the Linear No Threshold theory of radiation's effects was not a valid basis for setting radiation standards and that the hormesis model should be used instead.

In more detail, the NRC has received three petitions for rulemaking requesting that the NRC amend its "Standards for Protection Against Radiation" regulations and change the basis of those regulations from the Linear No-Threshold (LNT) model of radiation protection to the hormesis model. (See the Appendix for details of the petitions.)

The LNT model assumes that biological damage from radiation is linearly related to exposure and is always harmful, ie without a threshold. The hormesis model assumes that exposures to low radiation levels is beneficial and protects the human body against deleterious effects of high levels of radiation.

The NRC has stated it is examining these petitions to determine whether they should be considered in rulemaking and is requesting public comments. US environmental groups are concerned that, if the NRC agreed with the petitions, it would introduce rules to weaken radiation protection standards at US nuclear facilities. On the other hand, according to two NRC staffers (Brock and Sherbini, 2012), the NRC apparently pays attention to the evidence on risks of low levels of radiation. See references at end.

Comments on Hormesis

It is true that some cell and animal experiments indicate that if small amounts of radiation were administered before later larger amounts, the damage done is less than if no previous small amount were given. (The word "tickle" is used in radiobiology lingo to denote such small amounts.) On the other hand, other cell and animal studies using different doses, durations and endpoints fail to show this effect, and there is no human evidence, ie from epidemiology. But it is true that some evidence from chemistry indicates the same effect, and there is some theoretical support for an adaptive effect in animals and plants.

Hormesis advocates typically argue that although radiation attacks DNA and causes mutations, DNA repair mechanisms quickly correct these. These mechanisms are certainly numerous and busy – it is estimated over 15,000 repairs per hour are carried out in each cell – but from the sheer number of repairs, many misrepairs occur and it is the misrepairs that cause the damage.

But even if the existence of hormesis were accepted, the question remains – what relevance would it have for radiation protection? The answer- as stated repeatedly in official reports by UNSCEAR and BEIR etc - is zero. For example, do we give "tickle" doses to people about to undergo radiation therapy, or to nuclear workers? Of course, we don't.

And what about background radiation? All of us receive small "tickle" doses of radiation – about 3 mSv per year of which about 1 mSv is from external gamma radiation. Do these somehow protect us from subsequent radiation? How would we notice? And if it did, so what? That is, what relevance would it have for radiation protection, eg setting radiation standards? The answer is again ….none. Indeed, as we show below, increasing evidence exists that even background radiation itself is harmful.

Comments on LNT

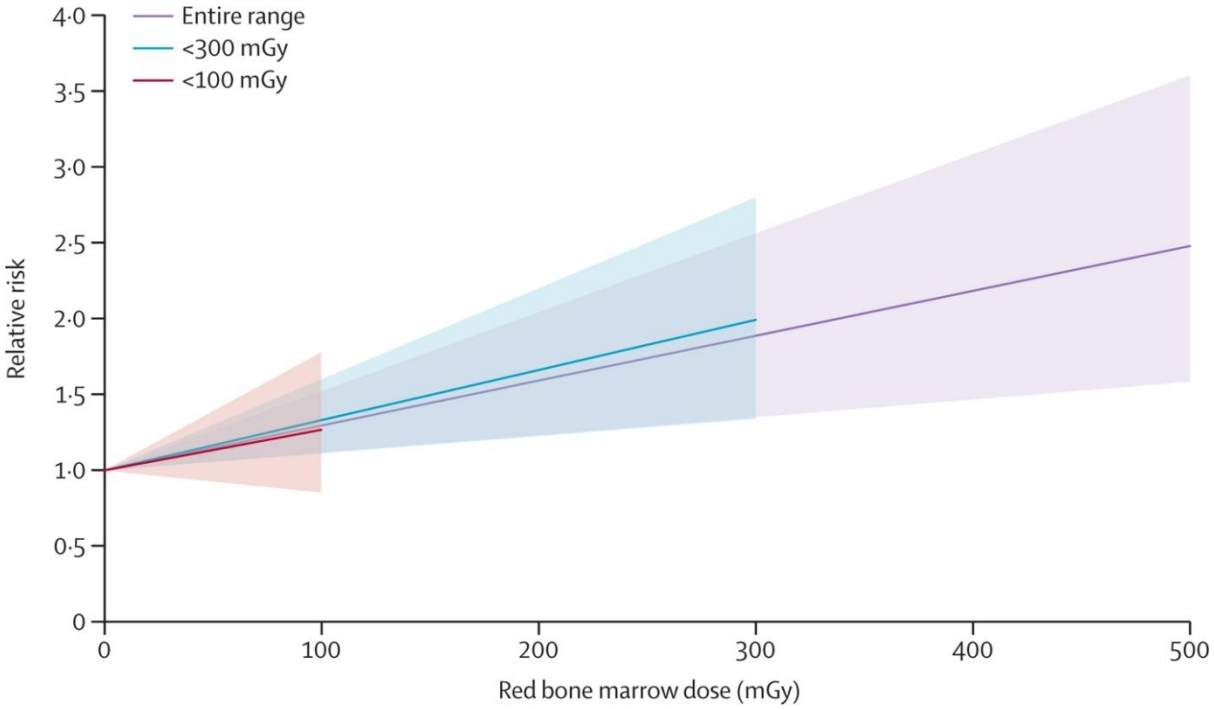
On the other hand, the scientific evidence for the LNT is plentiful, powerful and persuasive. It comes from epidemiological studies, radiobiological evidence, and official reports. Let's examine these in turn.

A. Epidemiological Studies

Does the available epidemiological evidence show risks declining linearly with dose at low doses? Yes, recent epidemiology studies do indeed show this, and the important new points are that these are (a) **very large** studies with good confidence intervals, and (b) at **very low doses**, even down to background levels. In other words, the usual caveats about the validity of the linear shape of the dose response relationship down to low doses are unjustified.

The most recent evidence is from a particularly powerful study by Leuraud et al (2015) which shows linearly-related risks down to very low levels (average dose rate = 1.1 mGy per year). http://www.thelancet.com/journals/lanhae/article/PIIS2352-3026%2815%2900094-0/fulltext The main findings from the Leuraud study are shown in graph 1.

Graph 1

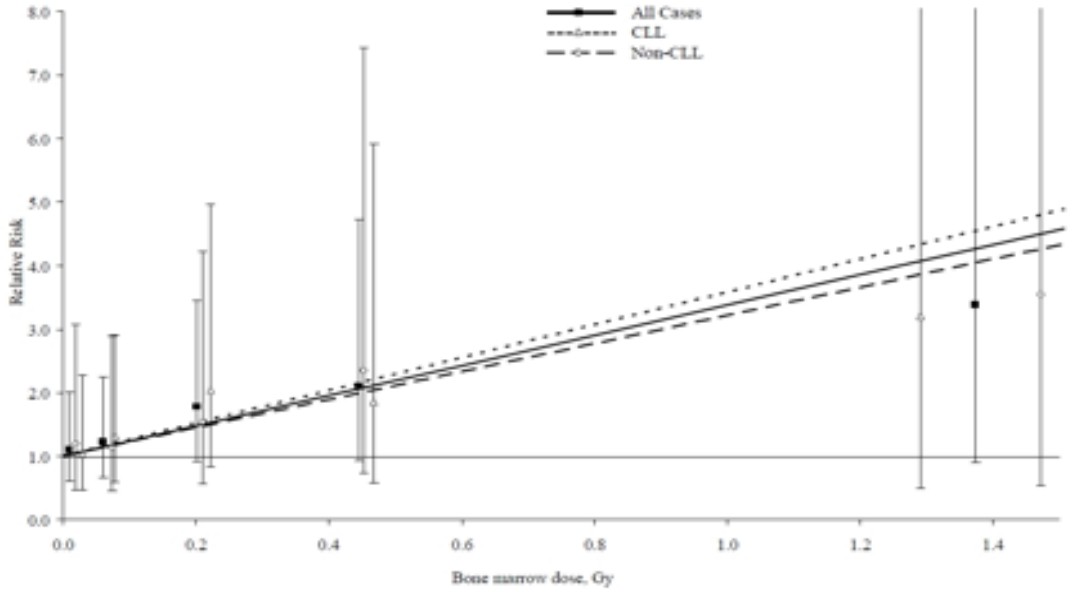


Two interesting things about this study are that 5 of the 13 authors are from US scientific institutes, including the Centers for Disease Control and Prevention, the National Institute for Occupational Safety and Health, the Department of Health and Human Services, University of North Carolina, and Drexel University School of Public Health. Also that the study was funded by many international agencies, including the US Centers for Disease Control and Prevention, US National Institute for Occupational Safety and Health, US Department of Energy, and the US Department of Health and Human Service.

It is legitimate to ask whether the NRC is in contact with these official US agencies about its consultation.

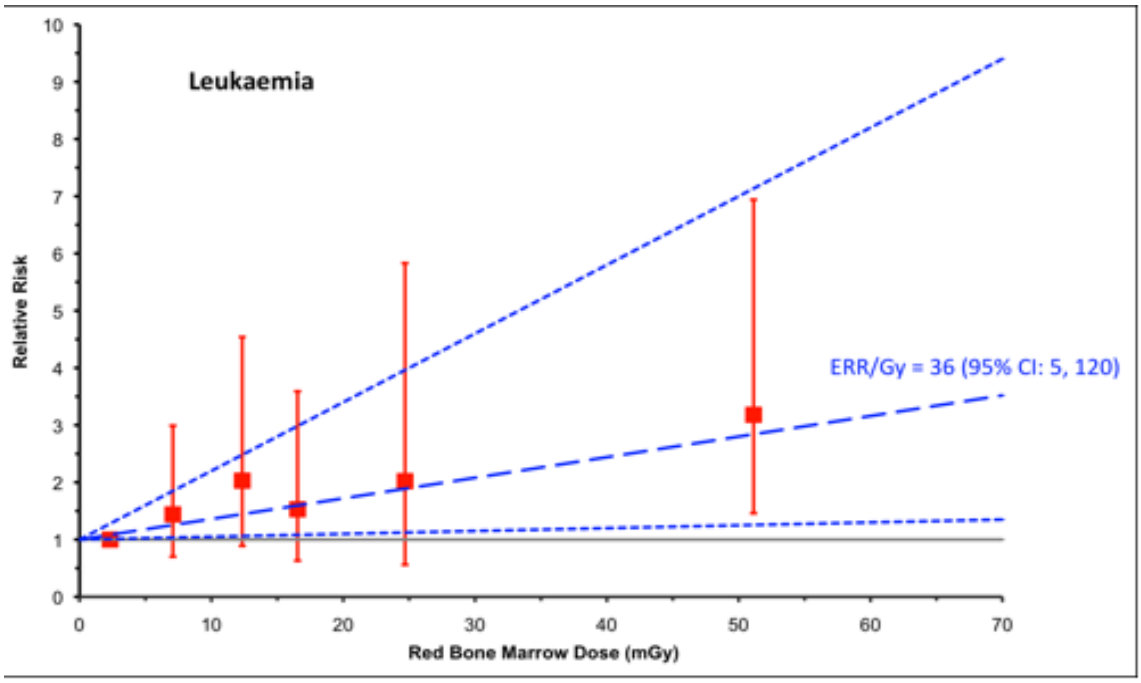
The Leuraud et al study is merely the latest of many studies providing good evidence for the LNT model. Second is the Zablotska study after Chernobyl. Graph 2 below, reproduced from Zablotska et al (2012), shows statistically significant risks for all leukemias and for chronic lymphocytic leukemia (CLL) in over 110,000 Chernobyl cleanup workers. It can also be seen that there are 6 data points showing increased risks below 100 mSv - a commonly cited cut-off point.

Graph 2



Third is the very recent cohort study of radiation exposures from medical CT scans in the UK by Pearce et al (2012). 74 out of 178,604 patients diagnosed with leukaemia and 135 out of 176,587 patients diagnosed with brain tumours were analyzed. As shown in graph 3 reproduced from their study, the authors noted a positive association between radiation doses from CT scans and leukaemia and brain tumours .The large dashed line showed a linear fit to the data with a 95% confidence interval shown by small dashed lines.

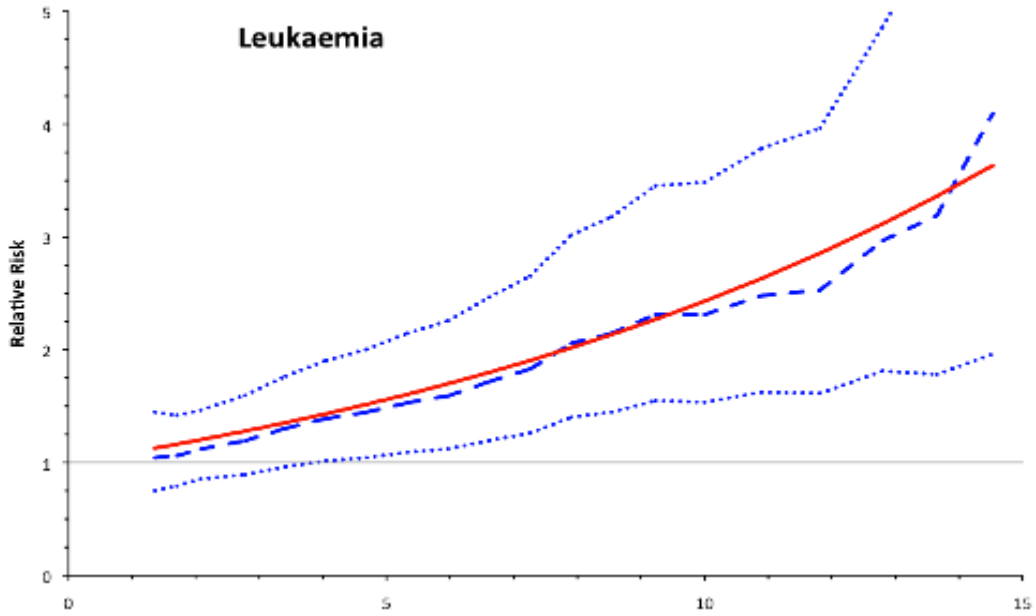
Graph 3



Fourth are the risks from background radiation – yes, even from background radiation. Kendall et al in 2012 conducted a large UK record-based case–control study testing associations between childhood cancer and natural background radiation with over 27,000 cases and 37,000 controls. Surprisingly, they observed an elevated risk of childhood leukaemia with cumulative red bone marrow dose from natural background gamma radiation. See the similar findings in a very recent study by Spycher et al (2015) discussed on page 10 below.

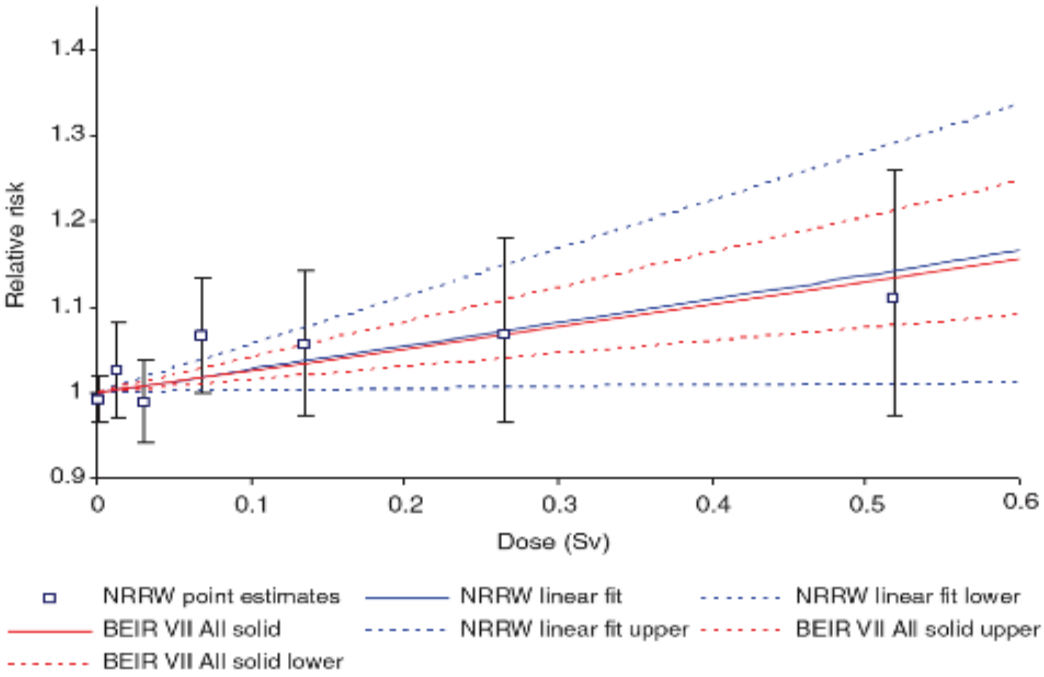
In graph 4 below reproduced from the Kendall et al study, the x-axis represents cumulative gamma ray doses in mGy. The red line shows not merely a linear but a slightly supralinear curve fitted to the data. The small dotted lines mark a 95% confidence interval.

Graph 4



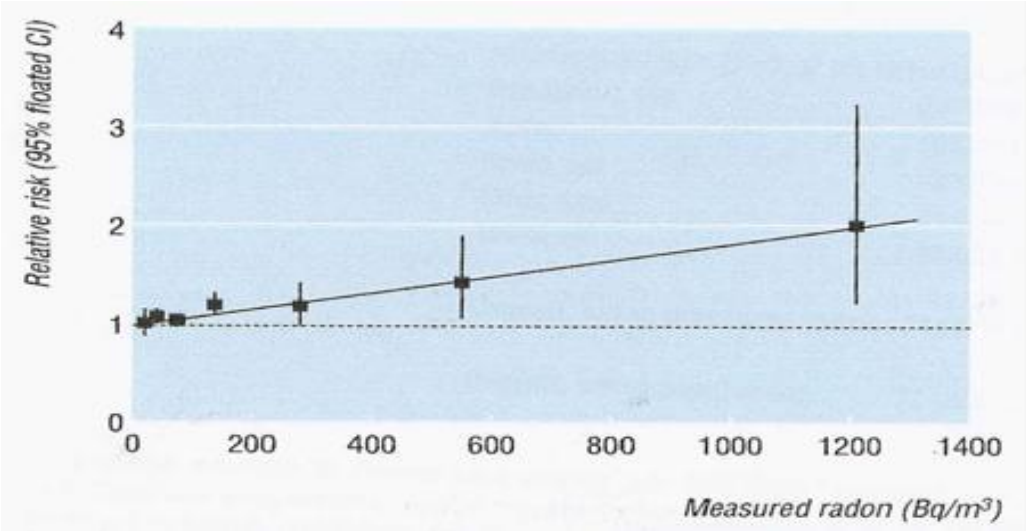
Fifth is the final analysis of the UK National Registry for Radiation Workers (NRRW). This study of observed 11,000 cancer cases and 8,000 cancer deaths in 175,000 UK radiation workers with an average individual cumulative dose of 25 mSv and an average follow-up of 22 years. Graph 5 reproduced from the study shows the relative risks for all solid cancers with the continuous blue line representing the NRRW data, and the continuous red line the results from the US BEIR VII report for comparison – the two are very similar, as can be seen. An estimated ERR of 0.27 per Sv can be derived from this graph.

Graph 5



Sixth is the meta-analysis of 13 European studies in 9 EU countries on indoor radon exposure risks by Darby et al (2005). This examined lung cancer risks at measured residential Rn concentrations with over 7,000 cases of lung cancer and 14,000 controls. The action level for indoor radon in most EU countries is 200 Bq per m^3, corresponding to about 10 mSv per year. (This is derived from a UNSCEAR (2000) reference value of 9 nSv per Bq·h/m^3. This means that people living 2/3rds of their time indoors (5,780 h/year) at a Rn concentration of 200 Bq/m^3 would receive an effective dose of ~10 mSv/year. Graph 6 reproduced from the study shows elevated risks at concentrations well below this level. The solid line is the authors' linear fit to the data.

Graph 6



No evidence below 100 mSv?

It is necessary at this point to directly address the argument often raised by hormesis advocates – that there is little evidence of effects below 100 mSv. This is incorrect. Older evidence exists -see http://www.ianfairlie.org/news/a-100-msv-threshold-for-radiation-effects/ for a list of studies and the newer evidence, as we have just seen, clearly shows this fact as well.

B. Radiobiological Evidence

Current radiobiological theory is consistent with a linear dose-response relationship down to low doses (ie below ~10 mSv).

The radiobiological rationale for linearity comes from the stochastic nature of energy deposition of ionising radiation. It was explained by 15 of the world's most eminent radiation biologists and epidemiologists in a famous article (Brenner et al, 2003) as follows:

"1. Direct epidemiological evidence demonstrates that an organ dose of 10 mGy of diagnostic x-rays is associated with an increase in cancer risk.

2. At an organ dose of 10 mGy of diagnostic x-rays, most irradiated cell nuclei will be traversed by one or, at most, a few physically distant electron tracks. Being so physically distant, it is very unlikely that these few electron tracks could produce DNA damage in some joint, cooperative way; rather, these electron tracks will act independently to produce stochastic damage and consequent cellular changes.

3. Decreasing the dose, say by a factor of 10, will simply result in proportionately fewer electron tracks and fewer hit cells. It follows that those fewer cells that are hit at the lower dose will be subject to (i) the same types of electron damage and (ii) the same radiobiological processes as would occur at 10 mGy.

4. Thus, decreasing the number of damaged cells by a factor of 10 would be expected to decrease the biological response by the same factor of 10; i.e., the response would decrease linearly with decreasing dose. One could not expect qualitatively different biological processes to be active at, say, 1 mGy that were not active at 10 mGy, or vice versa. The argument suggests that the risk of most radiation -induced endpoints will decrease linearly, without a threshold, from ~10 mGy down to arbitrarily low doses."

C. Official Reports

Both types of evidence (epidemiology and radiobiology) have been examined in 4 international official reviews: UNSCEAR (2008), US NCRP Report No 136 (2001), US BEIR VII (2006) and ICRP 99 (2006). These reports confirmed the LNT as being the most prudent assumption for radiation protection purposes.

For example in 2006, the chair of BEIR VII, Richard R. Monson, associate dean for professional education and professor of epidemiology, Harvard School of Public Health, Boston stated "The scientific research base shows that there is no threshold of exposure below which low levels of ionizing radiation can be demonstrated to be harmless or beneficial". http://hps.org/documents/BEIRVIIPressRelease.pdf

Recently, the US-based scientist Mark Little and his colleagues (Little et al, 2009) examined the matter in considerable detail. They discussed (i) the degree of curvature in the cancer dose response within the Japanese atomic bomb survivors and other groups, (ii) the consistency of risks between the Japanese and other low-dose cohorts, and (iii) biological data on mechanisms. They concluded linearity was the best bet.

Also in 2009, the head of the US Environmental Protection Agency's radiation section reviewed the matter in an influential article (Puskin, 2009). He stated "Although recent radiobiological findings indicate novel damage and repair processes at low doses, LNT is supported by data from both epidemiology and radiobiology. Given the current state of the science, the consensus positions of key scientific and governmental bodies, as well as the conservatism and calculational convenience of the LNT assumption, it is unlikely that EPA will modify this approach in the near future".

The Importance of LNT in Radiation Protection

Regardless of dissenting views on LNT, the reality is that most concepts used in radiation protection today are fundamentally based on the LNT theory. For example, LNT underpins the concepts of absorbed dose, effective dose, committed dose, and the use of dose coefficients (ie Sv per Bq of a radionuclide). It also allows radiation doses (i) to be averaged within an organ or tissue, (ii) to be added from different organs, and (iii) to be added over time.

LNT also permits annual dose limits; optimization -ie comparison of practices; radiation risk assessment at low and very low doses; individual dosimetry with passive detectors; collective dose, and dose registers over long periods of time.

In fact, the LNT underpins all legal regulations in radiation protection in the US and in the rest of the world. Indeed, if the LNT were not used, it's hard to imagine our current radiation protection systems existing at all. However this statement should not be misconstrued to mean that the LNT is used just because it's convenient: the LNT is used because the scientific evidence for it is comprehensive, cogent and compelling.

Statistical Significance

It is necessary to discuss the vexed issue of statistical significance, as hormesis advocates (eg http://atomicinsights.com/leukemia-and-lymphoma-study-recently-published-in-lancet-being-strong-challenged-by-sari/) often dismiss studies stating they show "no significantly" raised risks at low levels, or that excess risks are "not significant" at low levels, or similar phrases.

Let's examine these phrases because they can mislead readers into incorrectly thinking that the reported increase is "unimportant" or "irrelevant". The word "significant" is a specialist adjective used in statistical tests to convey the narrow meaning that the likelihood of an observation being a fluke is less than 5% (assuming a p = 5% test was used). It does not mean important or relevant.

Secondly, such phrases are often glibly used by hormesis advocates without explaining that the test level used is quite arbitrary. There is no scientific justification for using a 5% or any other test level: it is merely a matter of convenience. In other words, it is quite possible for results which are "not significant" when a 5% test is applied, will become "significant" when a 10% test is used. For this reason, good epidemiologists nowadays have stopped using the words "significant" or "significance" altogether. Instead they use confidence intervals: hormesis advocates should follow suit.

There is a third reason why these phrases shouldn't be used. Scientifically speaking, it's bad practice to dismiss results (or to imply this) just because they do not meet a statistical test. This is because the probability (ie p value) that an observed effect may be a fluke is affected by both magnitude of effect and size of study (Whitely and Ball, 2002). This means statistical tests must be cited with caution, as the use of an arbitrary cut-off point for statistical significance (often p = 5%) can lead to incorrectly accepting the null hypothesis - ie that there's no effect (Sterne and Smith, 2001). This is called a type II error in statistics, and it often occurs in studies due to low numbers[1] of observed cases (Everett et al, 1998) rather than lack of effect. In other words, the rejection of findings for statistical reasons can often hide real risks (Axelson, 2004; Whitley and Ball, 2002).

So what should hormesis advocates do with a study having positive findings which do not meet their self-selected 5% test? First of all, they should NOT reject the findings. Instead they should report the observed increase and add there's a greater than 5% possibility this could be a chance finding. And then they should discuss

[1] It should be borne in mind that low case numbers are not the fault of researchers but often due to the fact that many conditions are rare (eg child leukemia) and very large numbers of exposed people are needed to pick up the few observed cases.

whether their interpretation would change if a slightly less strict 10% test were chosen (as is increasingly used nowadays). And they should discuss the confidence interval so that readers can make up their own minds. For example, they could say that the relative risk was, say, 1.55 with a 90% confidence interval of 1.01 to 1.98. This would mean that the observed relative risk was 1.55 and that we are 90% sure that the real value lies between 1.01 and 1.98. The key point is that the loaded words "significant" or "significance" are therefore avoided.

Conclusions

(i) the debate

The validity or otherwise of LNT and hormesis have been the subject of hundreds of scientific articles and debates over several decades. Unfortunately, much of the literature on hormesis or adaptive response is based on faulty science or on misconceptions, or on misinterpretations, or on all three. This is particularly the case with several US and UK journalists who write with confidence on how radiation risks are exaggerated. Their knowledge and experience of radiogenic risks are limited to say the least, but these journalists, almost on a weekly basis, misinform and mislead the public about radiation risks, so the existence of the US petitions is perhaps unsurprising.

However real scientists are increasingly standing up and opposing the poor science used by hormesis advocates. Very recently, four Swiss scientists from the Institute of Social and Preventive Medicine at the University of Bern; the Swiss Tropical and Public Health Institute, Basel and the University of Basel published a study which revealed that exposure to high rates of background radiation resulted in increased cancer risks to children (Spycher et al, 2015). http://ehp.niehs.nih.gov/1408548/

In reply, 17 scientists (Siegel et al, 2015) mostly from the US, some of whom were members of a hormesis pressure group "Scientists for Accurate Radiation Information" objected to these findings. They alleged that the government would have to evacuate children living in higher radiation areas and relocate them to lower radiation areas. They stated that studies like this should not be taken seriously without public health policy implications being examined. (http://ehp.niehs.nih.gov/1510111/)

The Swiss scientists in turn responded (http://ehp.niehs.nih.gov/1510111R/) that the proposed evacuation was "nonsensical" in view of the very low numbers involved. In a spirited rejoinder, they refuted the poor science cited and added that "the Scientists for Accurate Radiation Information *a priori* exclude the possibility that low-dose radiation could increase the risk of cancer. They will therefore not accept studies that challenge their foregone conclusion".

(ii) the petitions

After briefly examining the three US petitions, my conclusion is that they do not merit serious consideration. It seems that the petitioners, who may or may not have axes to grind about radiation risks, have seized on the possible phenomenon of hormesis

to make ill-considered claims that radiation is protective or even good for you. In other words, the petitions appear to be based on preconceptions, or even ideology, rather than the scientific evidence which points in the opposite direction.

The petitions should not be used by the NRC to justify weakening regulatory standards at US nuclear facilities. A question remains whether the NRC should have accepted the petitions for review. Presumably the NRC has discretion not to review or to refer back spurious, mischievous, or ill-founded petitions.

The NRC should seek guidance from the five US scientific agencies and Government departments mentioned above whose scientists have published evidence on the matter.

Credits. Thanks to Dr Jan Beyea, Cindy Folkers, Dr Alfred Körblein, Xavier Rabilloud, Dr Marvin Reznikoff and Dr Gordon Thompson for comments on drafts. Any errors are my responsibility.

References

Axelson O. Negative and non-positive epidemiological studies. Int J Occup Med Environ Health. 2004;17:115-121.

BEIR VII (2006) http://www.nap.edu/catalog/11340/health-risks-from-exposure-to-low-levels-of-ionizing-radiation

Brenner David J, Richard Doll, Dudley T. Goodhead, Eric J. Hall, Charles E. Land, John B. Little, Jay H. Lubin, Dale L. Preston, R. Julian Preston, Jerome S. Puskin, Elaine Ron, Rainer K. Sachs, Jonathan M. Samet, Richard B. Setlow and Marco Zaider (2003) Cancer risks attributable to low doses of ionizing radiation: Assessing what we really know. PNAS. vol.100 no.24. pp 13761-13766. www.pnas.orgjcgijdoij10.1073jpnas.2235592100

Brock TA and Sherbini SS (2012) Principles in practice: Radiation regulation and the NRC. Bulletin of the Atomic Scientists 2012 68: 36. http://bos.sagepub.com/content/68/3/36

Cardis et al (2005) Risk of cancer after low doses of ionizing radiation: retrospective cohort study in 15 countries. BMJ. 2005 Jul 9;331 (7508).

Darby et al (2005) Radon in homes and risk of lung cancer: collaborative analysis of individual data from 13 European case-control studies. BMJ 2005;330:223.

Everett DC, Taylor S, Kafadar K. Fundamental Concepts in Statistics: Elucidation and Illustration. J of Applied Physiology 1998; 85(3):775-786.

Kendall G M, M P Little, R Wakeford, K J Bunch, J C H Miles, T J Vincent, J R Meara and M F G Murphy (2012) 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 (5 June 2012) | doi:10.1038/leu.2012.151

Leuraud, Klervi et al (2015) Ionising radiation and risk of death from leukaemia and lymphoma in radiation-monitored workers (INWORKS): an international cohort study. The Lancet Haematology. Published Online: 21 June 2015.

Little MP, Wakeford R, Tawn EJ, Bouffler SD, Berrington de Gonzalez A. Risks associated with low doses and low dose rates of ionizing radiation: why linearity may be (almost) the best we can do. Radiology. 2009 Apr;251(1):6-12. doi: 10.1148/radiol.2511081686.

Muirhead et al (2009) Mortality and cancer incidence following occupational radiation exposure: third analysis of the National Registry for Radiation Workers. Br J Cancer 2009; 100: 206-212.

Pearce et al (2012) Radiation exposure from CT scans in childhood and subsequent risk of eukaemia and brain tumours: a retrospective cohort study. The Lancet. June 7, 2012. **380**: 499-505. DOI:10.1016/S0140-6736(12)60815-0, http://press.thelancet.com/ctscanrad.pdf

Puskin J (2009) Dose-Response Vol 7:284–291. Perspective On The Use Of LNT For Radiation Protection And Risk Assessment by the U.S. Environmental Protection Agency.

Siegel JA et al (2015) Comment on "Background Ionizing Radiation and the Risk of Childhood Cancer: A Census-Based Nationwide Cohort Study" Environ Health Perspect*; DOI:10.1289/ehp.1510111*

Spycher BD, Martin Röösli, Matthias Egger and Claudia E. Kuehni (2015) Response to "Comment on 'Background Ionizing Radiation and the Risk of Childhood Cancer: A Census-Based Nationwide Cohort Study'. Environ Health Perspect; DOI:10.1289/ehp.1510111R

Sterne JAC, Smith GD. Sifting the evidence--what's wrong with significance tests? Phys Ther (2001) 81(8):1464-1469.

United Nations Scientific Committee on the Effects of Atomic Radiation (2008). UNSCEAR Report to the General Assembly, with scientific annexes – Annex B, § 153.

Whitley E, Ball J. Statistics Review 1: Presenting and summarising data. Crit. Care 2002; 6:66-71.

Zablotska et al (2012) Radiation and the Risk of Chronic Lymphocytic and Other Leukemias among Chornobyl Cleanup Workers. Environmental Health Perspectives http://dx.doi.org/10.1289/ehp.1204996 Online 8 November 2012.

Appendix: Views of US Petitioners

On February 9, 2015, Dr. Carol S. Marcus, a Professor of Radiation Oncology, of Molecular and Medical Pharmacology (Nuclear Medicine), and of Radiological Sciences at the David Geffen School of Medicine at the University of California-Los Angeles, filed a petition for rulemaking with the Commission, PRM-20-28 (ADAMS Accession No. ML15051A503). Dr. Marcus was a member of the NRC's Advisory Committee on the Medical Uses of Isotopes from 1990 to 1994. The petitioner indicated that "[t]here has never been scientifically valid support for this LNT hypothesis since its use was recommended by the U.S. National Academy of Sciences Committee on Biological Effects of Atomic Radiation (BEAR I)/Genetics Panel in 1956" and that "[t]he costs of complying with these LNT based regulations are enormous."

On February 13, 2015, Mr. Mark L. Miller, a Certified Health Physicist, filed a petition for rulemaking with the Commission, PRM-20-29 (ADAMS Accession No. ML15057A349). The petitioner indicated that "[t]here has never been scientifically valid support for this LNT hypothesis" and that "[t]he costs of complying with these LNT-based regulations are incalculable." In addition, the petitioner suggests that the use of the LNT hypothesis has "led to persistent radiophobia [radiation-phobia]."

On February 24, 2015, Dr. Mohan Doss, filed a petition for rulemaking with the Commission, PRM-20-30 (ADAMS Accession No. ML15075A200). Dr. Doss filed this petition on behalf of Scientist for Accurate Radiation Information, whose mission is to "help prevent unnecessary, radiation-phobia-related deaths, morbidity, and injuries associated with distrust of radio-medical diagnostics/therapies and from nuclear/radiological emergencies through countering phobia-promoting misinformation spread by alarmists via the news and other media including journal publications."