Epidemiological Research with Special Reference to Nuclear Worker Studies: Commentary

Keywords: Cancer risk; Low-level radiation exposure; Nuclear workers; Hormesis

Abstract

Limitations of some epidemiological studies on low-dose low-rate exposures to ionizing radiation include dose comparisons disregarding natural radiation background, unfounded classification of sporadic diseases as radiogenic and conclusions about causality of dose-effect relationships. Other bias, confounders and inter-study heterogeneity have been pointed out. Some dose-effect correlations can be explained by a dose-dependent selection, self-selection and recall bias. It can be reasonably assumed that individuals knowing their higher doses would be more motivated to undergo medical examinations being at the same time given more attention. Reported dose-effect relationships between low-dose low-rate exposures and non-neoplastic diseases call in question the causality of such relationships for cancer detected by the same researchers. Reliable evidence in regard to biological effects of low radiation doses can be obtained in large-scale animal experiments with registration of life duration. The monitoring of human populations exposed to low-dose radiation is important but conclusions should be made with caution considering potential bias and economical motives to strangulate nuclear energy production in accordance with the interests of fossil fuel producers. Of note, health burdens are the greatest for power stations based on coal and oil; the burdens are smaller for natural gas and still lower for the nuclear power. The same ranking applies for the greenhouse gas emissions.

Introduction

According to the linear no-threshold hypothesis (LNT), the risk of cancer is proportional to the radiation dose; a dose-response correlation can be extrapolated down to low doses, where the relationship is unproven and can become inverse in accordance with hormesis. Among hormetic agents are numerous physical and chemical factors, light, ultraviolet as well as products of water radiolysis [1-3]. By analogy with other environmental factors, an evolutionary adaptation to the natural radiation background (NRB) can be reasonably assumed. Cells may have retained some capability to repair damage from higher radiation levels than today’s NRB [4]. The experimental evidence in favor of hormesis and adaptive responses to ionizing radiation is considerable [5-9] i.e. experimental data are partly at variance with the epidemiological research. The evidence supporting radiation hormesis has been obtained also in human studies [10-12]. In animal experiments, doses associated with carcinogenicity have been generally higher than averages in the Chernobyl, East Urals Radioactive ‘Trace cohorts and contemporary professional settings [13-18].

Some assessments of the data about survivors of atomic explosions in Hiroshima and Nagasaki (A-bomb survivors) do not support the LNT and are consistent with hormesis [19]. For solid cancers and leukemia, significant dose-response relationships were found among A-bomb survivors exposed to ≤500 mSv but not ≤ 200 mSv [20-22]. Artificial neural networks applied to the data on A-bomb survivors indicated a presence of thresholds ~200 mSv varying with organs [23,24]. The value 200 mSv has been referred to in reviews as a level, below which the cancer risk elevation is unproven [22,25]. According to the UNSCEAR, a significant risk increase was observed at doses ≥100-200 mGy [26]. This value may have been underestimated as a result of biased epidemiological research. Among limitations of some epidemiological studies on low-dose low-rate exposures have been unfounded classification of sporadic diseases as radiogenic, dose comparisons disregarding NRB, conclusions about incidence increase without valid comparison with control [27,28], inexact citation [29]. Other bias, confounders and inter-study heterogeneity have been pointed out [11,23,30-32]. Some dose-effect correlations may be explained by a dose-dependent selection, self-selection and recall bias noticed in different exposed cohorts [33-35]. It can be reasonably assumed that individuals knowing their higher doses would be more motivated to undergo medical examinations being at the same time given more attention. Therefore, diagnostics would be a priori more efficient in people with higher doses. For example, the dose-dependent incidence increase of cardio- and cerebro-vascular diseases among Mayak Production Association (MPA) workers was not accompanied by an increase in mortality [36-39], which can be explained by recording of mild cases in people with higher doses. Moreover, the excess relative risk per unit dose (ERR/Gy) for leukemia (excluding chronic lymphatic leukemia) among MPA workers using incidence data has been considerably higher than that using mortality data [40]. A more efficient detection of latent leukemia with occasional registration of unverified cases can provide an explanation. The author agrees with Dr. Little [41] that the research of questionable reliability “should therefore probably not be used for epidemiologic analysis, in particular for the Russian worker studies considered here [42-45]” and some others. The inter-study heterogeneity [32], mixture of more and less reliable data assessed together remains a problem of some systematic reviews and meta-analyses. As discussed previously [9,46], reported dose-effect relationships between low-dose low-rate exposures and non-neoplastic diseases call in question the causality of such relationships for cancer revealed by the same and other scientists. Certain data on enhanced cancer risk after low-rate exposures appear doubtful. For example, a significantly increased...
risk of non-melanoma skin cancer was reported by Azizova and co-
workers among MPA workers [47]. An observation bias was not
excluded. The workers and probably some medics knew individual
work histories, wherefrom accumulated doses could be inferred,
potentially influencing the diagnostic thoroughness. Skin doses were
unknown [47]. Among A-bomb survivors, non-melanoma skin
cancer incidence dataset was consistent with a threshold at ~1 Sv [48].
The MPA workers were exposed mainly to γ-rays that have a relatively
long penetration distance in tissues, so that the absorbed doses in
the skin must have been correspondingly low. Not surprisingly,
premalignant skin lesions and/or actinic keratoses were "very rare"
[47]. Considering the above, a cause-effect relationship between
radiation and skin tumors in the study [47] appears improbable. Risk
estimates by Azizova et al. [49] were found to be significantly higher
than those by other experts [50]. Reliability of some other studies has
been questioned previously [29,51,52].

Concluding his recent review, Dr. Wakeford writes: "Ultimately,
it will be powerful epidemiological studies examining exposure
direct relevance to radiological protection against low-
level radiation exposure that will provide the most reliable evidence"
[40]. Neither exexperimental studies nor the NRB are mentioned
in this review. As discussed below, reliable data on the biological
effects of low radiation doses can be obtained in extensive animal
experiments rather than in epidemiological studies. Annual average
doses from NRB should be indicated if cohorts from different regions
are compared; otherwise exposures in a control group may turn out
to be not significantly different from those in "exposed" cohorts e.g.
from Colombia and Spain vs. Ukraine [53,54], discussed in [52]. In the
International Nuclear Workers Study (INWORKS), many workers
received 2-4 mSv/year [40]. Annual doses from the NRB are generally
expected to be in the range of 1-10 mSv, 2.4 mSv being the estimated
global average. The mean cumulative doses in the INWORKS (red
bone marrow - 17.6 mGy, colon - 19.2 mGy) protracted over years
(follow-up 1950-2005) [55] are comparable with the NRB. These
and other considerations about INWORKS have been expressed
previously: "Failure to account for natural background radiation
exposure, the differences in which potentially dwarf the occupational
exposures of the study cohort" [1].

Another example is a study of Bushehr nuclear plant workers in
Iran [56]. The average individual total dose received by workers
who developed cancer was 45.1 mSv; the median duration of follow-up
was 34.8 months. No doses from NRB are given. The data on the NRB
are of particular importance for Iran, where in some areas the natural
radiation background is relatively high. The mean individual annual
dose to the residents of high background radiation areas at Ramsar
(Mazandaran Province) is ~10 times higher than the public dose limit
recommended by the International Commission on Radiological
Protection (1 mSv/year); a part of the residents receive annual doses ~
260 mSv [57] i.e. much higher than nuclear workers at Bushehr. There
have been no consistent reports on any detrimental health effects in
the residents of the Ramsar area [57]. It can be reasonably assumed
that the screening effect and increased attention of exposed people
to their own health would result one day in an increase of the registered
cancer incidence in areas with enhanced natural or anthropogenic
radiation background, which would prove no causal relationship.
Another comparison: around 13,000 German uranium miners with
archived occupational data, who worked during 1946-1990 for the
Soviet nuclear industry, underwent average individual exposures of
725 WLM (3.7 Sv), including about 800 workers with levels >1800
WLM (>9.2 Sv). Annual exposures of some miners were >200 WLM
(>1 Sv) combined with silica dust that may act synergistically [58].
The working-level month is a dose unit used for cumulative exposures
from radon and its progeny; 1 WLM is equivalent to ~5.1 mSv [59].

The following citations should be commented: the "puzzling
finding from INWORKS is that the primary EER/Gy estimate for
photon doses and all cancers except leukemia, which was adjusted for
neutron monitoring status, 0.48 (95% CI: 0.15, 0.85), reduced by ~60%
to 0.20 (95% CI: -0.07, 0.51) when no such adjustment was made...
A further perplexing result from INWORKS is that when the analysis
was confined to the 83% of workers who were not monitored for
intakes of radionuclides, the ERR/Gy for all cancers except leukemia
increased by 50% to 0.72 (95% CI: 0.21, 1.28); similar increases in
external exposure risk estimates for workers not monitored for
potential exposure to internal emitters when compared with those for
workers who were monitored for internal exposures has been noted in
other studies" [40]. The answer to the "puzzle" seems to be as follows.
The workers monitored for intakes of radionuclides and those under
the "neutron monitoring" probably received averagely more attention
from medics and were better supervised. Consequently, there must
have been fewer undiagnosed diseases among them. As a result, the
mechanism of dose-dependent diagnostic/observation quality would
be less efficient as fewer neglected cases are left to be preferentially
found in persons with higher doses. Of note, 6% of workers with
doses >100 mGy, received predominantly at an early date (years
1960-1979), were influential in a downwards [emphasis added]
leverage of the dose-response. In the range of low doses, EER/Gy
for cancer in the INWORKS was even higher than in the Life Span Study
(LSS) of A-bomb survivors [40,55]. The LSS data originated from
earlier times. Apparently, the non-radiation-related dose-dependent
mechanisms were less efficient in the remote past, when diagnostic
possibilities were limited. It can be speculated that modern methods,
diversification, more differences between the superior and inferior
diagnostic quality at a later time provided more opportunities for the
dose-dependent selection and self-selection. Fitted (under a simple
linear excess relative rate model) excess deaths from solid cancer
were higher in the INWORKS than in the LSS among individuals
with average colon doses in the range 1-78.3 mGy, while in those
with mean doses ≥ 143.1 mGy the aforesaid index was higher in the
LSS [55]. This indicates that some cancers were radiogenic in the LSS
but not in the INWORKS as the doses ~100 mGy have never been
satisfactorily proven to be carcinogenic. Logically, the dose-response
relationship must be stronger at >200 mGy than at <200 mGy. In
the INWORKS, the tendency was vice versa [55]. By analogy, in the
epidemiologic study [35] a curve of the linear-exponential dose-
response model, providing an improved fit to the data, is most steep
at low doses, becomes more gently sloping with increasing doses and
nearly horizontal at the level of 5-7 Gy. Similar proportions were
reported also earlier, but the leveling of the dose-response curve
occurred at >10 Gy [60]. The decrease in the risk increment per
dose unit at higher doses was explained by the cell killing [61,62],
which seems to be the only thinkable radiation-related mechanism.
However, no leveling of thyroid cancer risk was noticed at doses
10 Gy [63]. In children after radiotherapy, exposures to 60 Gy were associated with a high risk of thyroid cancer [64]. In a series of studies in rats, the carcinogenic effect of 11 Gy from acute x-ray exposure was comparable to that of 1.1 MBq of iodine-131, which would produce a thyroid dose of ~100 Gy, when a significant cell killing effect might be expected [65]. The cell killing concept is obviously inapplicable to low doses, when tissues remain morphologically intact. Apparently, both the dose–effect relationships at low doses and their reduction at higher doses in [35,55] were caused by non-radiation factors.

The monitoring of populations exposed to low-dose radiation is important but conclusions should be made with caution considering known and unknown bias. For example, “the very high rates of circulatory disease” [66] in some nuclear worker cohorts from the former Soviet Union are probably caused by habitual overdosage of cardiovascular diseases in unclear cases, which is a known confounder [67]. Reliable evidence in regard to biological effects of low radiation doses can be obtained in extensive animal experiments rather than in epidemiological studies. It is unnecessary to examine each mouse or rat; it would suffice to maintain large groups of animals to record the average life duration. Such experiments would objectively characterize the net harm or potential benefit (as per hormesis model) at various doses and dose rates [1,13,68]. Among other things, the Dose and Dose Rate Effectiveness Factor (DDREF) can be evaluated in such experiments. The argumentation about DDREF based on the epidemiological research [40] is questionable because radiogenic nature of discussed conditions is unproven. Certain models suggested that protracted exposures are between 2.0 and infinitely times safer than acute ones [69]. The latter would correspond to a threshold or hormesis concept. DDREF assessments should be based primarily on direct comparisons of acute and protracted exposures [69]. Further research in this direction would better quantify the radiosensitivity of different animal species enabling more precise extrapolations to humans [70].

Conclusion

Evidently, some epidemiological research has been influenced by economical motives to boost gas and oil prices [46,71]. The Chernobyl accident has been exploited to strangle the “cleanest, safest and practically inexhaustible” nuclear energy [31]. Hidden conflicts of interest, ideological bias and research quality should be taken into account deciding about inclusion of studies into systematic reviews and metaanalysis. Not construed e.g. [72, 73] (commented [28,71]) but obvious Chernobyl consequences are coming - the increasing cardiovascular diseases in unclear cases, which is a known confounder [67]. Reliable evidence in regard to biological effects of low radiation doses can be obtained in extensive animal experiments rather than in epidemiological studies. It is unnecessary to examine each mouse or rat; it would suffice to maintain large groups of animals to record the average life duration. Such experiments would objectively characterize the net harm or potential benefit (as per hormesis model) at various doses and dose rates [1,13,68]. Among other things, the Dose and Dose Rate Effectiveness Factor (DDREF) can be evaluated in such experiments. The argumentation about DDREF based on the epidemiological research [40] is questionable because radiogenic nature of discussed conditions is unproven. Certain models suggested that protracted exposures are between 2.0 and infinitely times safer than acute ones [69]. The latter would correspond to a threshold or hormesis concept. DDREF assessments should be based primarily on direct comparisons of acute and protracted exposures [69]. Further research in this direction would better quantify the radiosensitivity of different animal species enabling more precise extrapolations to humans [70].

References

1. Cardarelli JJ, Ulsh BA (2018) It is time to move beyond the linear no-threshold theory for low-dose radiation protection. Dose Response 16: 1559325818779651.
2. Le Bourg É, Rattan SI (2014) Hormesis and trade-offs: a comment. Dose Response 12: 522-524.
3. Kaludercic N, Deshwal S, Di Lisa F (2014) Reactive oxygen species and redox compartmentalization. Front Physiol 5: 285.
4. Karam PA, Leslie SA (1999) Calculations of background beta-gamma radiation dose through geologic time. Health Phys 77: 662-667.
5. Baldwin J, Grantham V (2015) Radiation hormesis: historical and current perspectives. J Nucl Med Technol 43: 242-246.
6. Calabrese EJ (2015) Model uncertainty via the integration of hormesis and LNT as the default in cancer risk assessment. Dose Response 13: 1559325815621764.
7. Doss M (2013) Linear no-threshold model vs. radiation hormesis. Dose Response 11: 480-497.
8. Mitchell RE (2009) The dose window for radiation-induced protective adaptive responses. Dose Response. 8: 192-208.
9. Jargin SV (2018) Hormesis and radiation safety norms: Comments for an update. Hum Exp Toxicol. 37: 1233-1243.
10. Doss M (2018) Are we approaching the end of the linear no-threshold era? J Nucl Med 59: 1786-1793.
11. Shibamoto Y, Nakamura H (2018) Overview of Biological, Epidemiological, and Clinical Evidence of Radiation Hormesis. Int J Mol Sci 19: 2387.
12. UNSCEAR 2017 Report to the General Assembly. Annex B: Epidemiological studies of cancer risk due to low-dose-rate radiation from environmental sources. New York: United Nations.
13. Braga-Tanaka I 3rd, Tanaka S, Kohda A, Takai D, Nakamura S, et al. (2018) Experimental studies on the biological effects of chronic low dose-rate radiation exposure in mice: overview of the studies at the Institute for Environmental Sciences. Int J Radiat Biol 94: 423-433.
14. Rühm W, Azizova T, Bouffier S, Cullings HM, Grosche B, et al. (2018) Typical doses and dose rates in studies pertinent to radiation risk inference at low doses and low dose rates. J Radiat Res 59.
15. UNSCEAR (1962) Report to the General Assembly. Annex D: Somatic effects of radiation. New York: United Nations.
16. UNSCEAR (1986) Report to the General Assembly. Annex B: Dose-response relationships for radiation-induced cancer. New York: United Nations.
17. UNSCEAR (1994) Report to the General Assembly. Annex B: Adaptive responses to radiation in cells and organisms. New York: United Nations.
18. UNSCEAR (2000) Report to the General Assembly. Annex G: Biological effects at low radiation doses. New York: United Nations.
19. Doss M (2016) Future of radiation protection regulations. Health Phys 110: 274-275.
20. Little MP, Muirhead CR (1996) Evidence for curvilinearity in the cancer incidence dose-response in the Japanese atomic bomb survivors. Int J Radiat Biol 70: 83-94.
21. Little MP, Muirhead CR (1998) Curvature in the cancer mortality dose response in Japanese atomic bomb survivors: absence of evidence of threshold. Int J Radiat Biol 74: 471-480.
22. Heidenreich WF, Paretzek HG, Jacob P (1997) No evidence for increased tumour rates below 200 mSv in the atomic bomb survivors data. Radiat Environ Biophys 36: 205-207.
23. Sacks B, Meyerson G, Siegel JA (2016) Epidemiology without biology: False paradigms, unfounded assumptions, and specious statistics in radiation science. Biol Theory 11: 69-101.
24. Sasaki MS, Tachibana A, Takeda S (2014) Cancer risk at low doses of...
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ionizing radiation: artificial neural networks inference from atomic bomb survivors. J Radiol Prot 55: 391-406.

25. González AJ (2004) Radiation safety standards and their application: international policies and current issues. Health Phys 87: 259-272.

26. UNSCEAR (2010) Scientific report. Summary of low-dose radiation effects on health. New York: United Nations.

27. Jargin SV (2010) Overestimation of Chernobyl consequences: poorly substantiated information published. Radiat Environ Biophys 49: 743-745.

28. Jargin SV (2017) Debate on the Chernobyl disaster. Int J Health Serv 47: 150-159.

29. Jargin SV (2013) Unfounded statements tending to overestimate Chernobyl consequences. J Radiol Prot 33: 881-884.

30. Watanabe T, Miyao M, Honda R, Yamada Y (2008) Hiroshima survivors exposed to very low doses of A-bomb primary radiation showed a high risk for cancers. Environ Health Prev Med 13: 264-270.

31. Jaworowski Z (2010) Observations on the Chernobyl Disaster and LNT. Dose Response 8: 148-171.

32. Little MP, Tawn EJ, Tzoulaki I, Wakeford R, Hildebrandt G, et al. (2010) Review and meta-analysis of epidemiological associations between low/moderate doses of ionising radiation and circulatory disease risks, and their possible mechanisms. Radiat Environ Biophys 49: 139-153.

33. McGeough D, Binks K, Gillies M, Jones S, Whaley S (2008) The non-cancer mortality experience of male workers at British Nuclear Fuels plc, 1946-2005. Int J Epidemiol 37: 506-518.

34. Zablotska LB, Bazyka D, Lubin JH, Gudzenko N, Little MP, et al. (2013) Radiation and the risk of chronic lymphocytic and other leukemias among Chernobyl cleanup workers. Environ Health Perspect. 121: 59-65.

35. Zablotska LB, Ron E, Rozhko AV, Hatch M, Polyanskaya ON, et al. (2011) Thyroid cancer risk in Belarus among children and adolescents exposed to radiocarbon after the Chernobyl accident. Br J Cancer. 104: 181-187.

36. Azizova TV, Muroed CR, Druzhininina MB, Grigor'eva ES, Vlasenko EV, et al. (2010) Cerebrovascular diseases in the cohort of workers first employed at Mayak PA in 1948-1958. Radiat Res 174: 851-864.

37. Azizova TV, Moseeva MB, Grigor'eva ES, Muirhed CR, Hunter N, et al. (2012) Mortality risk of cardiovascular diseases for occupationally exposed workers. Radiat Biol Radioecol 252: 158-166.

38. Azizova TV, Haylock R, Moseeva MB, Pikulina MV, Grigor'eva ES (2015) Cerebrovascular diseases incidence and mortality in an extended Mayak Worker Cohort: 1948-1982. Medical Radiology and Radiation Safety 43:61.

39. Soloviev VV, Krasnyuk VI (2018) On possible mistakes in the estimation of radiation risk non-cancer effects in Mayak plant workers. Medical Radiology and Radiation Safety. 2018;6(6): 83-84.

40. Wakeford R (2021) Overview of epidemiological studies of nuclear workers: opportunities, expectations, and limitations. J Radiol Prot 41.

41. Little MP (2016) Radiation and circulatory disease. Mutat Res 770: 299-318.

42. Azizova TV, Grigor'eva ES, Haylock RG, Pikulina MV, Moseeva MB (2015) Ischaemic heart disease incidence and mortality in an extended cohort of Mayak workers first employed in 1948-1982. Br J Radiol. 88: 20150169.

43. Ivanov VK, Maksioutov MA, Chekin SY, Petrov AV, Biryukov AP, et al. (2006) The risk of radiation-induced cerebrovascular disease in Chernobyl emergency workers. Health Phys 90: 199-207.

44. Kashcheev VV, Chekin SY, Maksioutov MA, Tumanov KA, Menyaylo AN, et al. (2016) Radiation-epidemiological study of cerebrovascular diseases in the cohort of Russian recovery operation workers of the Chernobyl accident. Health Phys 111: 192-197.

45. Moseeva MB, Azizova TV, Grigor'eva ES, Haylock R (2014) Risks of circulatory diseases among Mayak PA workers with radiation doses estimated using the improved Mayak Worker Dosimetry System 2008. Radiat Environ Biophys 53: 469-477.

46. Jargin SV (2021) The overestimation of medical consequences of low-dose exposures: Cui bono? Environ Dis 8: 101-107.

47. Azizova TV, Bannikova MV, Grigor'eva ES, Rybkina VL (2018) Risk of malignant skin neoplasms in a cohort of workers occupationally exposed to ionizing radiation at low dose rates. PLoS One 13: e0205060.

48. Little MP, Charles MW (1997) The risk of non-melanoma skin cancer incidence in the Japanese atomic bomb survivors. Int J Radiat Biol 71: 589-602.

49. Azizova TV, Muirhead CR, Moseeva MB, Grigor'eva ES, Sumina MV, et al. (2011) Cerebrovascular diseases in nuclear workers first employed at the Mayak PA in 1948-1972. Radiat Environ Biophys 50: 539-552.

50. Rühm W, Breckow J, Dietze G, Friedl A, Greinert R, et al. (2020) Dose limits for occupational exposure to ionising radiation and genotoxic carcinogens: a German perspective. Radiat Environ Biophys 59: 9-27.

51. Jargin SV (2019) Ionizing radiation: dose tolerability and hormesis. Annals of Ecology and Environmental Science 3: 20-26.

52. Jargin SV (2021) Markers of radiogenic cancer vs. tumor progression: an overview of Chernobyl studies. J Cancer Sci 81: 7.

53. Ruiz-Sauri A, Valencia-Villa G, Romanenko A, Pérez J, García R, García H, et al. (2016) Influence of exposure to chronic persistent low-dose ionizing radiation on the tumor biology of clear-cell renal-cell carcinoma. An immunohistochemical and morphometric study of angiogenesis and vascular related factors. Pathol Oncol Res 22: 807-815.

54. Romanenko A, Morell-Quadrey L, Ramos D, Nepomnysachyi V, Vozianov A, et al.(2006) Extracellular matrix alterations in conventional renal cell carcinomas by tissue microarray profiling influenced by the persistent, long-term, low-dose ionizing radiation exposure in humans. Virchows Arch 448: 584-590.

55. Leuard K, Richardson DB, Cardis E, Daniels RD, Gillies M, Haylock R, et al. (2021) Risk of cancer associated with low-dose radiation exposure: comparison of results between the INWORKS nuclear workers study and the A-bomb survivors study. Radiat Environ Biophys 60: 23-39.

56. Javinani A, Abolghasemi H, Hamidi H (2021) Five year mortality trend among Bushehr nuclear plant workers exposed to ionizing radiation: Does sanctions impact mortality rate? Journal of Clinical & Medical Case Reports 2021.

57. Abbasi S, Mortazavi SAR, Mortazavi SMJ (2019) Martian residents: mass media and Ramsar high background radiation areas. J Biomed Phys Eng 5: 483-486.

58. Taeger D, Fritsch A, Wiethege T, Johnen G, Eisenmenger A, et al. (2006) Role of exposure to radon and silica on the cell type of lung carcinomas in German uranium miners. Cancer 106: 881-889.

59. Sanders CL, Scott BR (2006) Smoking and hormesis as confounding factors in radiation pulmonary carcinogenesis. Dose Response 6: 53-79.

60. Ron E, Lubin JH, Shore RE, Mabuchi K, Modan B, et al. (1995) Thyroid cancer after exposure to external radiation: a pooled analysis of seven studies. Radiat Res 141: 259-277.

61. Boice JD Jr (2005) Radiation-induced thyroid cancer - what's new? J Natl Cancer Inst 97: 703-705.

62. UNSCEAR (2006) Report to the General Assembly. Annex A: Epidemiological studies of radiation and cancer. New York: United Nations.

63. Shore RE, Woodard E, Hildreth N, Dvoretsky P, Hempelmann L, et al. (1985) Thyroid tumours following thymus irradiation. J Natl Cancer Inst 71: 1177-1184.

64. UNSCEAR (1994) Report to the General Assembly. Annex A: Epidemiological studies of radiation carcinogenesis. New York: United Nations.

65. UNSCEAR 1993 Report to the General Assembly. Annex F: Influence of dose and dose rate on stochastic effects of radiation. New York: United Nations.

66. Little MP, Azizova TV, Hamada N (2021) Low- and moderate-dose non-cancer effects of ionizing radiation in directly exposed individuals, especially circulatory and ocular diseases: a review of the epidemiology. Int J Radiat Biol 97: 782-803.
67. Jargin SV (2017) Cardiovascular mortality in Russia: a comment. Cardiovasc Diagn Ther 7: 13-14.

68. Calabrese E (2017) The threshold vs. LNT showdown: dose rate findings exposed flaws in the LNT model. Part 2. How a mistake led BEIR I to adopt LNT. Environ Res 154: 452-458.

69. Haley BM, Paunesku T, Grdina DJ, Woloschak GE (2015) The increase in animal mortality risk following exposure to sparsely ionizing radiation is not linear quadratic with dose. PLoS One 10: e0140989.

70. Higley KA, Kocher DC, Real AG, Chambers DB (2012) Relative biological effectiveness and radiation weighting factors in the context of animals and plants. Ann ICRP 41: 233-245.

71. Jargin SV (2012) Hormesis and radiation safety norms. Hum Exp Toxicol 31: 671-675.

72. Nesterenko AB, Nesterenko VB, Yablokov AV (2009) Consequences of the Chernobyl Catastrophe for Public Health. Ann N Y Acad Sci 1181: 31-220.

73. Bertell R (2006) The death toll of the Chernobyl accident. In: Busby CC, Yablokov AV, editors. Chernobyl: 20 Years On. Health Effects of the Chernobyl Accident. Documents of the ECCR, N 1. Aberystwyth: Green Audit Books 245-248.

74. Markandya A, Wilkinson P (2007) Electricity generation and health. Lancet 370: 979-990.