New insight into cancer risks from radiation exposure of low-dose and low dose rate

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Radiation risk estimation

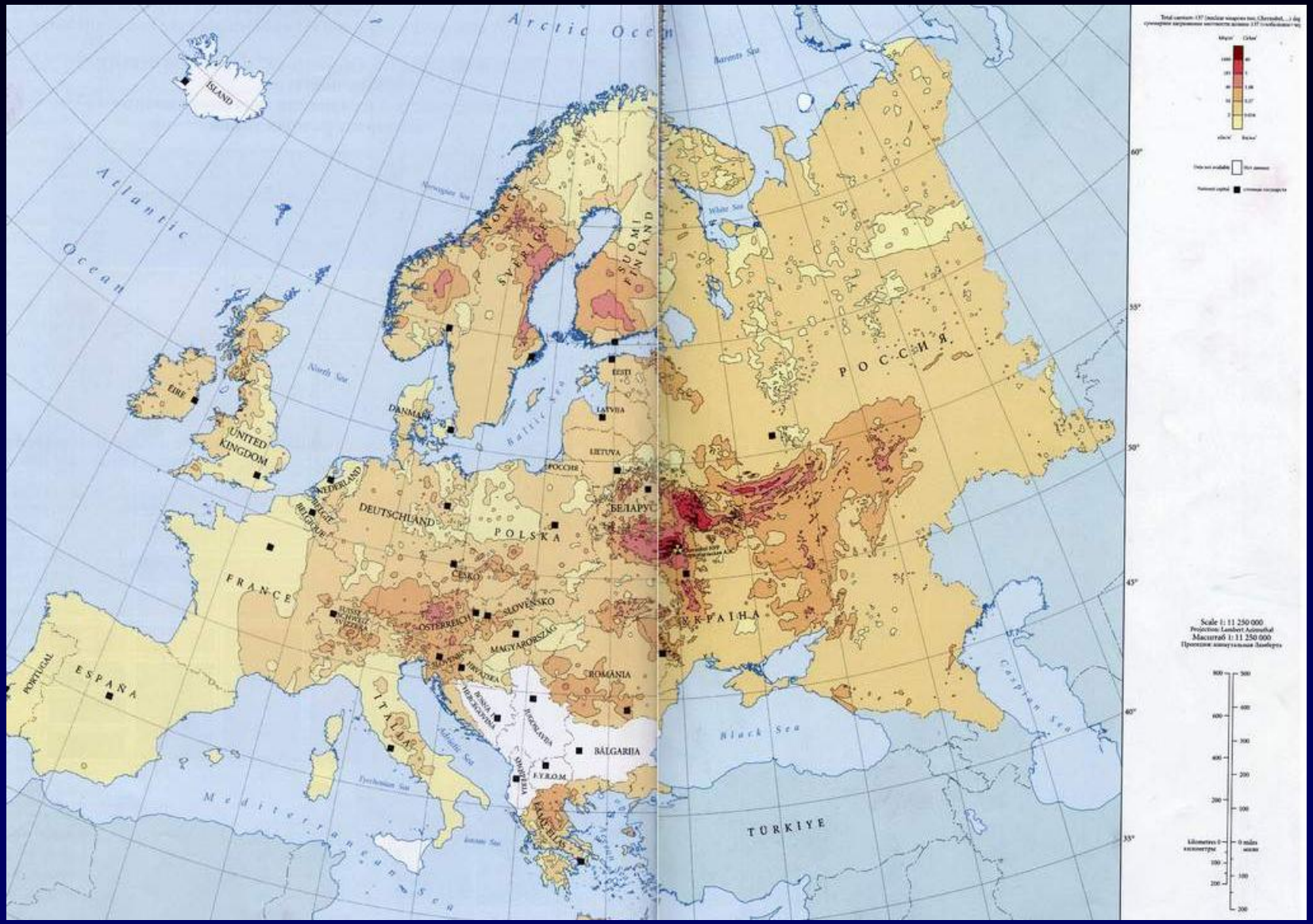
Estimation of radiation cancer risks generally signifies evaluating the *probability* of stochastic late effects.

Risk estimation involves not only estimation of a *risk coefficient* (e. g., relative risk- RR), but also requires accounting for spontaneous (background) rates of disease or dearth and assessment of effect modification by age of exposure, time, gender, attained age and other factors.

The most common risk model is the excess relative risk (ERR) model. The simplest ERR model is linear ERR model.

[Encyclopedia of Quantitative Risk Analyses and Assessment (edited by E. L. Melnick and B. S. Everitt), 2008.]

Surface ground deposition of ^{137}Cs throughout the Europe as a result of the Chernobyl accident



[De Cort et al., 1998]

Characteristics of Life Span Study Cohort (LSS) in Japan

- ✓ Survivors with dose estimates in excess of 1Gy comprise less than 3% of the cohort.
- ✓ Among 105,000 members of the LSS included in the current analysis, about 35,000 received doses between 5 and 200 mGy.
- ✓ In fact, they comprise about 75% of the cohort members with dose above 5 mGy.

[D.L. Preston, E. Ron, S. Tokuoka, S. Funamoto, N. Nishi, M. Soda, K. Mabuchi, K. Kodama. Solid cancer incidence in atomic bomb survivors: 1958-1998 // Radiat Res. – 2007. – V. 168, № 1. – P. 1–64.]

Second general report on radiation effects on the incidence of solid cancers among members of LSS cohort

Analyses were based on more than 40 years of cancer incidence data for the members of the LSS. 34% of the cancers included in the current analyses were diagnosed during 1988-1998.

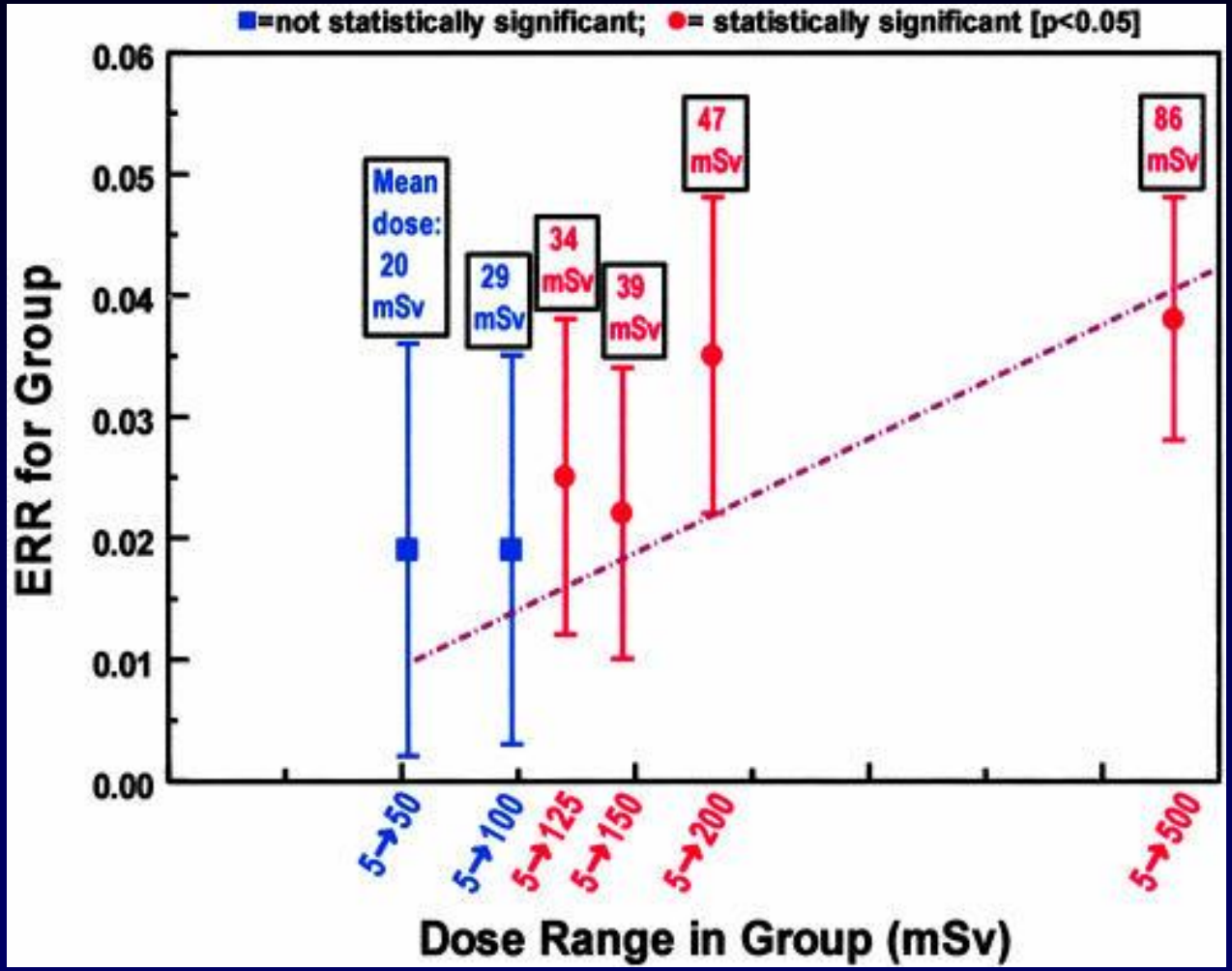
Conclusions.

- There is a statistically significant dose response when analyses were limited to cohort members with doses of 0.15 Gy or less.

- Radiation-associated increases in cancer rates persist throughout life regardless of age at exposure.

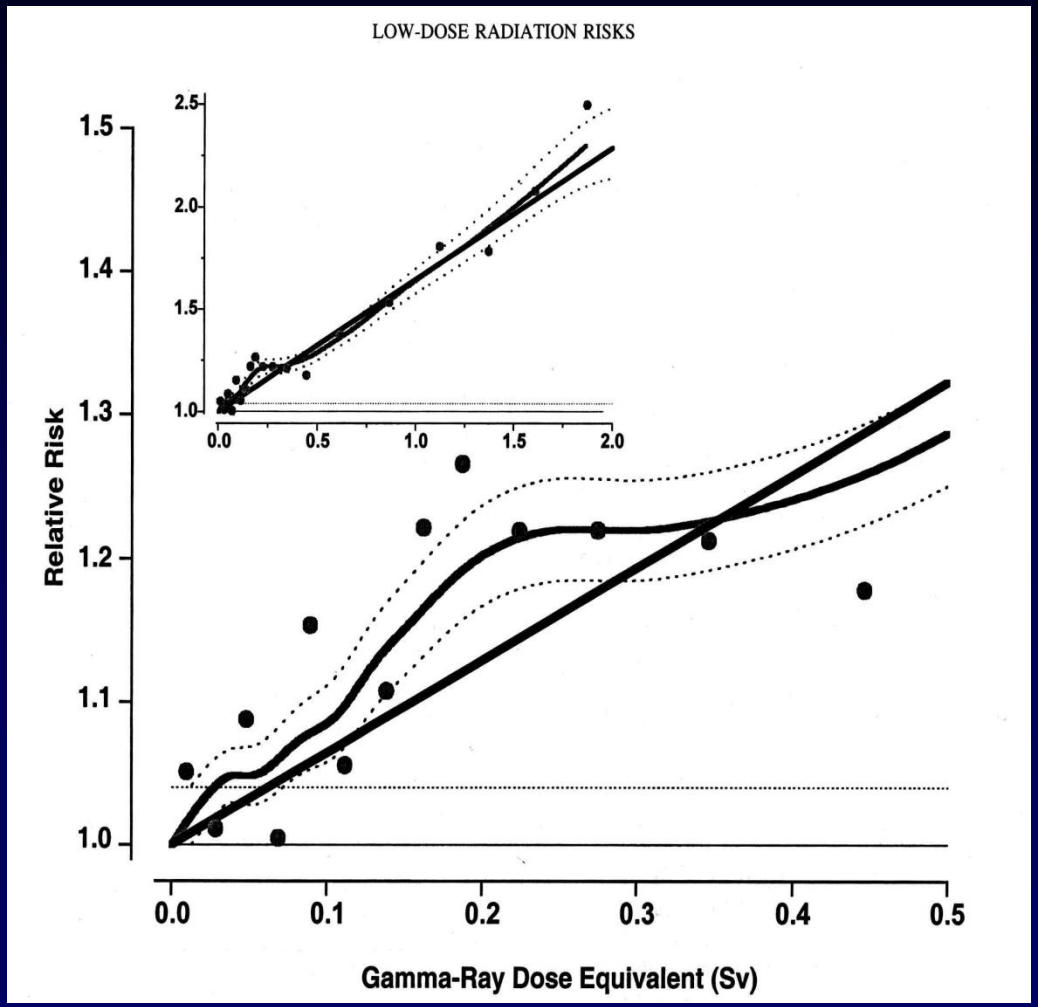
[D.L. Preston, E. Ron, S. Tokuoka, S. Funamoto, N. Nishi, M. Soda, K. Mabuchi, K. Kodama. Solid cancer incidence in atomic bomb survivors: 1958-1998 // Radiat Res. – 2007. – V. 168, № 1. – P. 1–64.]

Excess relative risk (ERR) of mortality (1950-1957) from solid cancers among groups of survivors in the LSS cohort



[D.J. Brenner et al. Cancer risks attributable to low doses of ionizing radiation: Assessing what we really know // PNAS. – 2003. – V. 100, № 24. – P. 13761–13766.]

Radiation-related cancer risks at low doses among atomic bomb survivors



Estimated low-dose relative risks. Age-specific cancer rates over the 1958–1994 follow-up period relative to those for unexposed persons, averaged over the follow-up and over sex, and for age at exposure 30. ***The dashed curves*** represent 1 standard error for the smoothed curve. ***The straight line*** is the linear risk estimate computed from the range 0–2 Sv. Because of an apparent distinction between distal and proximal zero-dose cancer rates, ***the unity baseline*** corresponds to zero-dose survivors within 3 km of the bombs. ***The horizontal dotted*** line represents the alternative baseline if the distal survivors were not omitted. ***The inset*** shows the same information for the fuller dose range.

[D.A. Pierce, D.L. Preston II Radiat Res, 2000]

Excess relative risk (ERR) of solid cancer mortality in the Semipalatinsk Historical Cohort (1960-1999)

Outcome	ERR/Sv (95% CI) Total cohort	ERR/Sv (95% CI) Exposed group
Size of cohort	19 545	9 850
Dose range	20 mSv – 4 Sv	70 mSv – 4 Sv
All solid cancers	1.77 (1.35; 2.27)	0.81 (0.46; 1.33)
Esophagus cancers	2.37 (1.47; 3.63)	0.18 (-0.09; 0.66)

[Bauer et al. // Radiat Res, 2005]

For comparison:

ERR/Gy of mortality for all solid cancers in LSS cohort – 0.35 (0.22; 0.55); sex averaged; exposure at ages 30 - 45.

[Committee to Assess Health Risks from Exposure to Low Levels of Ionizing Radiation (2006). Health Risks from Exposure to Low Levels of Ionizing Radiation. ***BEIR VII Phase 2****]*

Estimates of excess relative risk (ERR) of mortality in the NRRW, the IARC study and the Japanese A-bomb survivors

Analysis	ERR/Sv (90% CI) for all malignant neoplasms excluding leukaemia	ERR/Sv (90% CI) for leukaemia excluding CLL
2nd NRRW* analysis [Muirhead et al., 1999]	0.09 (-0.28; 0.52)	2.55 (-0.03; 7.16)
1st NRRW analysis [Kendall et al., 1992]	0.41 (-0.17; 1.15)	4.28 (0.40; 13.56)
IARC** Intern. Study [Cardis et al., 2005, 2007]	0.97 (0.27; 1.80)	1.93 (<0; 7.14)
Japanese A-bomb survivors [Pierce et al., 1996]	0.24 (0.12; 0.37)	2.15 (0.43; 4.68)

* NRRW – the UK National Registry for Radiation Workers

** IARC – the International Agency for Research of Cancer

[Muirhead C.R., O'Hagan J.A., Kendall G.M. // Radiat Biol Radioecol, 2008]

Excess relative risks of cancer mortality and cancer incidence in the Techa River cohort (1956-2002)

Outcome	Size of cohort	Average cumulative dose, mGy	ERR/Gy (95% CI)
Cancer mortality [a]	29 873	30	0.92 (0.2; 1.7)
All solid cancer incidence [b]	17 433	40	1.0 (0.3; 1.9)

[[a] Krestinina, Preston et al. // Radiat Res, 2005.;
[b] Krestinina, Davis et al. / / Int J Epidemiol, 2007]

For comparison:

ERR/Gy of mortality for all solid cancers in LSS cohort – 0.35 (0.22; 0.55); sex averaged; exposure at ages 30 - 45.

*[Committee to Assess Health Risks from Exposure to Low Levels of Ionizing Radiation (2006). Health Risks from Exposure to Low Levels of Ionizing Radiation. **BEIR VII Phase 2**]*

Conclusions

- Doses of the whole body irradiation of affected populations of the Republic of Belarus, Ukraine and contaminated regions of the Russian Federation are in the dose range of **0–0.15 Gy**, i. e. within the range of doses that caused statistically significant increase in cancer incidence in the Life Span Study (LSS) cohort of atomic bomb survivors.

- There is an increasing set of data showing that radiation risks of chronic irradiation of populations at low doses and low dose rates may be higher than radiation risks in the LSS cohort.

- The 15-country collaborative study of cancer risk among radiation workers of the nuclear industry gives evidence that excess relative risks (ERR) of all malignant neoplasms excluding leukemia and lung cancer is approximately **3 times higher** than cancer risk in the LSS cohort.

- The results of some studies do not suggest that cancer risks associated with low-dose-rate exposure are less than those in the LSS cohort exposed to acute radiation at high dose rate.

- Thus, cancer risks in the LSS cohort and especially use of Dose and Dose Rate Effectiveness Factor (DDREF) above 1 are not applicable for prognosis estimates of radiation induced cancers in the case of long-term radiation exposure of populations at low dose rate such as the Chernobyl fallout exposure.