

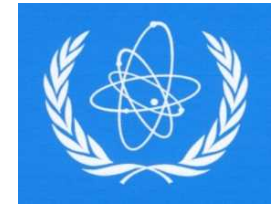
**Consultancy Meeting on Science, Technology and Society Perspectives
on Nuclear Science, Radiation and Human Health:**



The International Perspective

23 May 2017

Hiroshima, Japan



Long-term Epidemiological Studies on Radiation Effects in A-bomb Survivors

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Radiation Effects Research Foundation



Outline of Presentation

- 1. Epidemiological studies on health effects of atomic bomb radiation**
2. Study results
 - 1) Atomic bomb survivors
 - Cancers
 - Diseases other than cancers
 - 2) F1 offspring
3. Future perspectives

Studies on Health Effects of A-bomb Radiation - History -

1945

'47 '48

1975

2000



Hiroshima
6 August

Nagasaki
9 August

Atomic Bomb Casualty
Commission (ABCC)

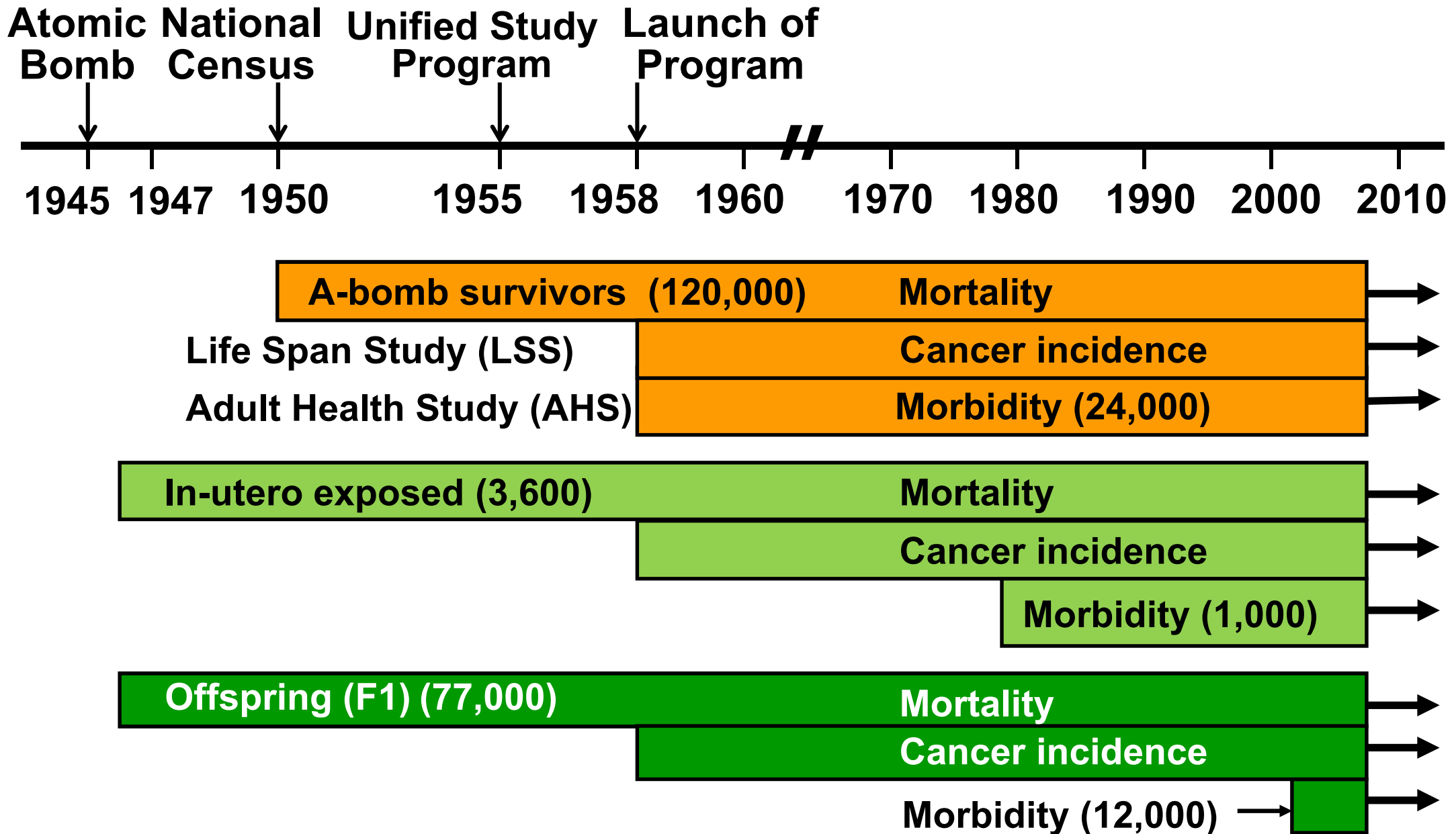
Japanese National
Institute of Health

28 years

Radiation Effects
Research Foundation
(RERF)

42 years

Long-term Epidemiological Studies of Atomic Bomb Survivors and Their Offspring





Long-term Epidemiological Studies of Atomic Bomb Survivors

- The cohort study of the Japanese survivors of the atomic-bombings of Hiroshima and Nagasaki is broadly considered one of the most reliable sources of information on radiation health effects because of the size and nature of the population investigated and the scale of the data available.**
- For this reason, the study has become fundamental to the risk assessment of radiation exposure and study results have been utilized by the international organizations, such as UNSCEAR, ICRP, IAEA and other authorities.**

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RADIATION RESEARCH **187**, 000–000 (2017)
0033-7587/17 \$15.00
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DOI: 10.1667/RR14492.1

Solid Cancer Incidence among the Life Span Study of Atomic Bomb Survivors: 1958–2009

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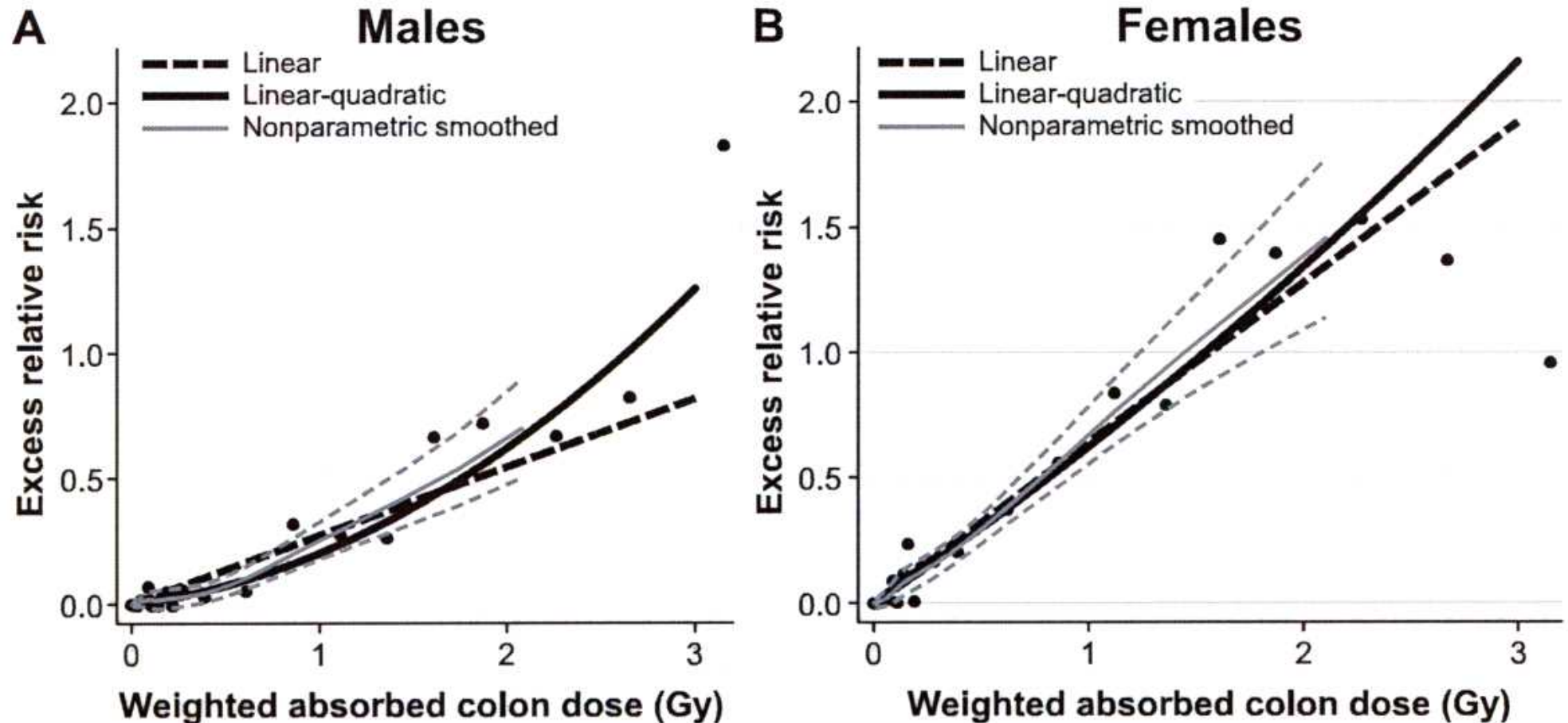
(Grant EJ et al: Radiat Res 2017; 187: DOI: 10.1667/RR14492.1)

Radiation Risks of All Solid Cancers

ERR per Gy		
Sex-averaged (95% CI)	Males (95% CI)	Females (95% CI)
Unadjusted for smoking		
0.50 (0.42 to 0.59)	0.36 (0.28 to 0.45)	0.65 (0.53 to 0.77)
Adjusted for smoking, additive joint effect		
0.56 (0.46 to 0.66)	0.48 (0.36 to 0.61)	0.64 (0.52 to 0.76)
Adjusted for smoking, multiplicative joint effect		
0.47 (0.39 to 0.55)	0.33 (0.25 to 0.42)	0.60 (0.49 to 0.72)

(Grant EJ et al: Radiat Res 2017; 187: DOI: 10.1667/RR14492.1)

Solid Cancer Incidence - Dose Response -



Sex-averaged at age 70 for exposure at age 30

(Grant EJ et al: Radiat Res 2017; 187: DOI: 10.1667/RR14492.1)

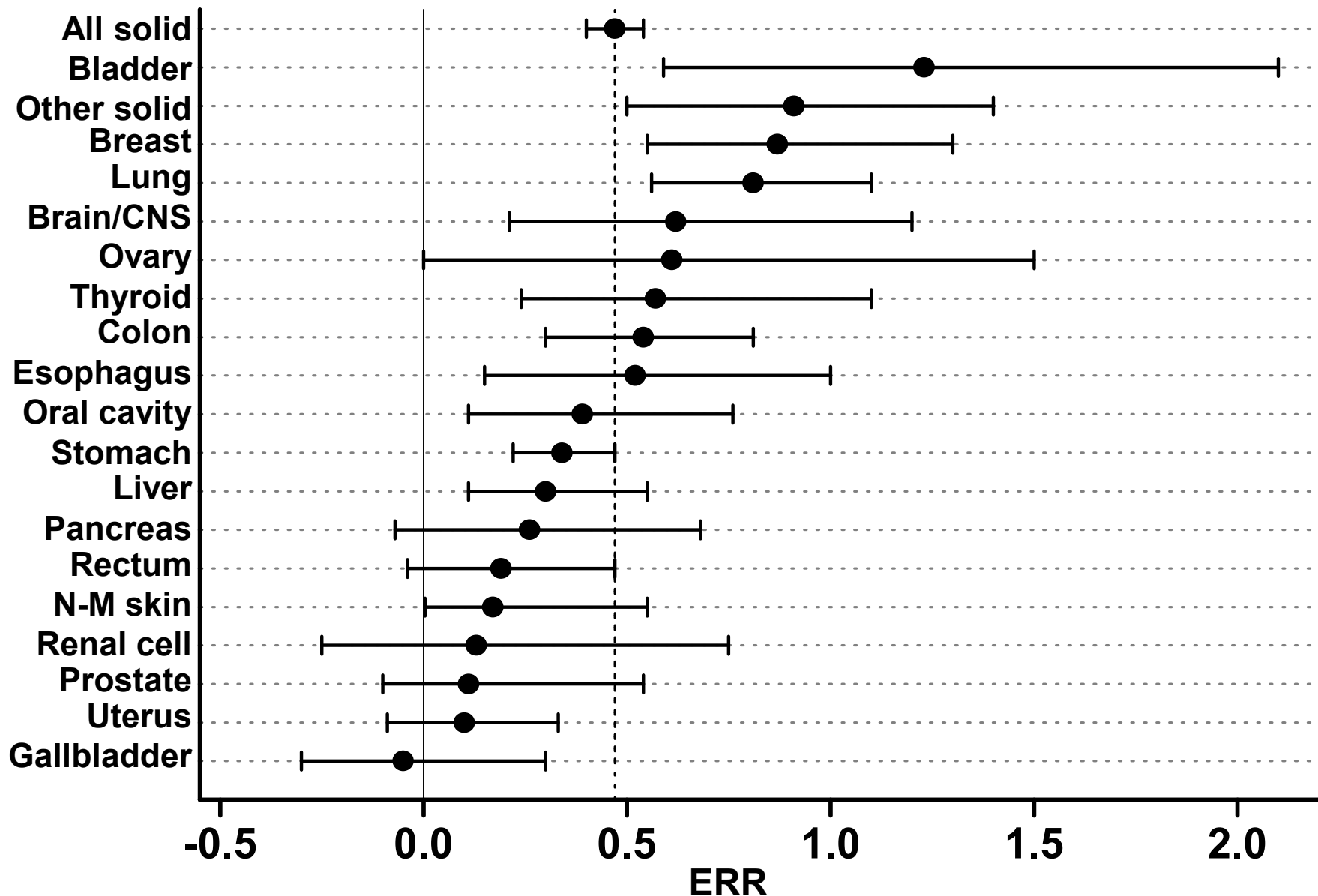
Lowest Significant Dose Range (LSS, Cancer Incidence, 1958-2009)

The lowest dose range for which there are statistically significant risks:

- **0-100 mGy**
- **Sex-averaged linear ERR model**
- **No adjustment for smoking**
- **ERR = 0.49/Gy (95%CI:0.026-1.01)**

(Grant EJ et al: Radiat Res 2017; 187: DOI: 10.1667/RR14492.1)

Site-specific Cancer Risk (LSS, Incidence, 1958-1998)



gender-averaged for 1 Gy at age 70 after exposure at age 30

(Preston DL et al. RERF UPDATE 2007; 18: 9-13)

Cancer and leukemia

Other findings:

- **Cancer risk elevation associated with A-bomb radiation exposure seems to continue for the lifetime.**
- **Leukemia risk elevation also persists.**
- **Myelodysplastic Syndrome (MDS) risk appears to be increased.**
- **The increases in the risk of first primary and second primary cancers seem comparable.**
- **Radiation effects on lung cancer risk seem to be stronger among smokers.**



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RADIATION RESEARCH **187**, 319–332 (2017)
0033-7587/17 \$15.00
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DOI: 10.1667/RR14347.1

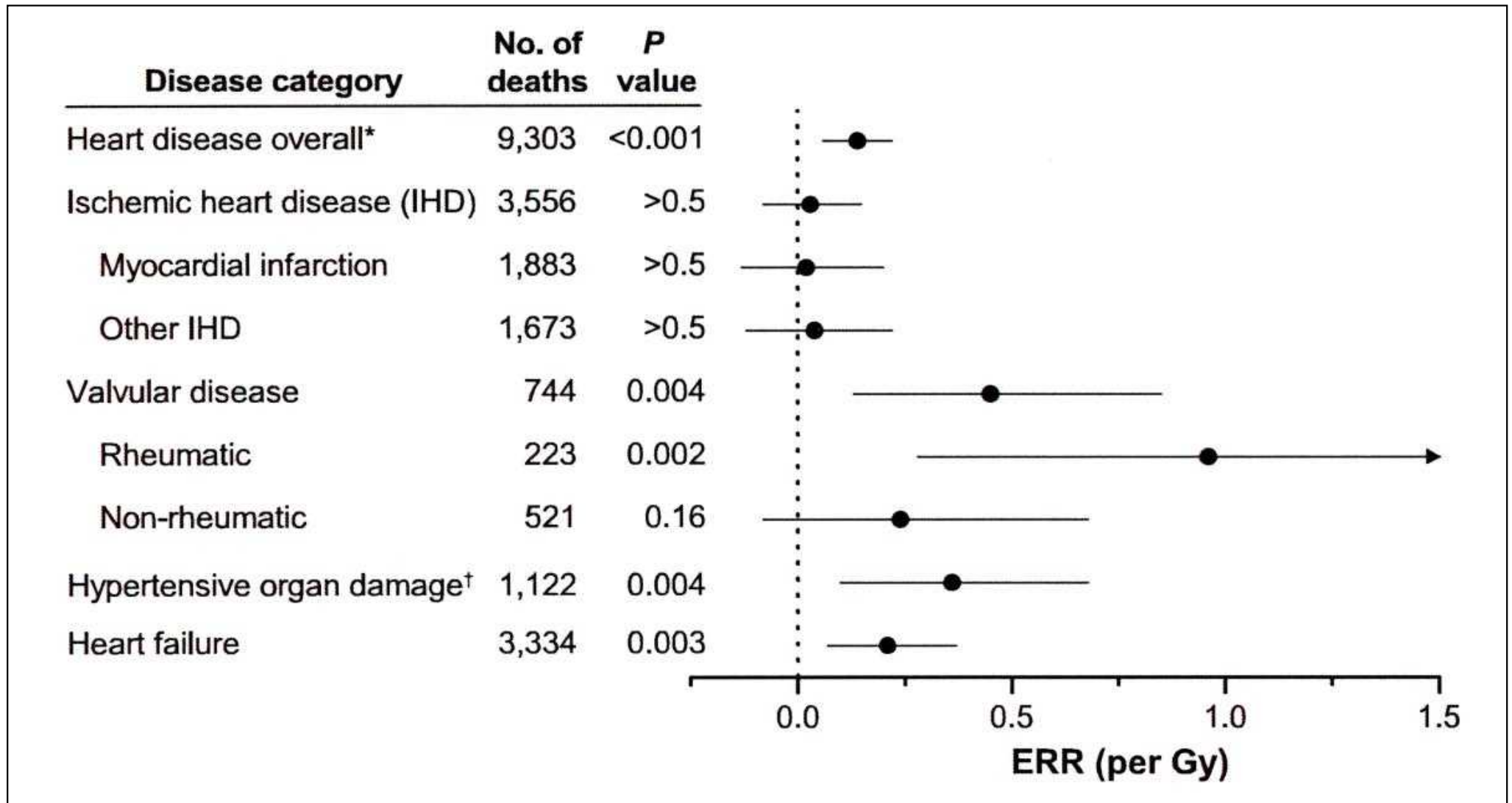
Heart Disease Mortality in the Life Span Study, 1950–2008

Ikuno Takahashi,^{a,b,1} Yukiko Shimizu,^b Eric J. Grant,^b John Cologne,^c Kotaro Ozasa^b and Kazunori Kodama^{a,d}

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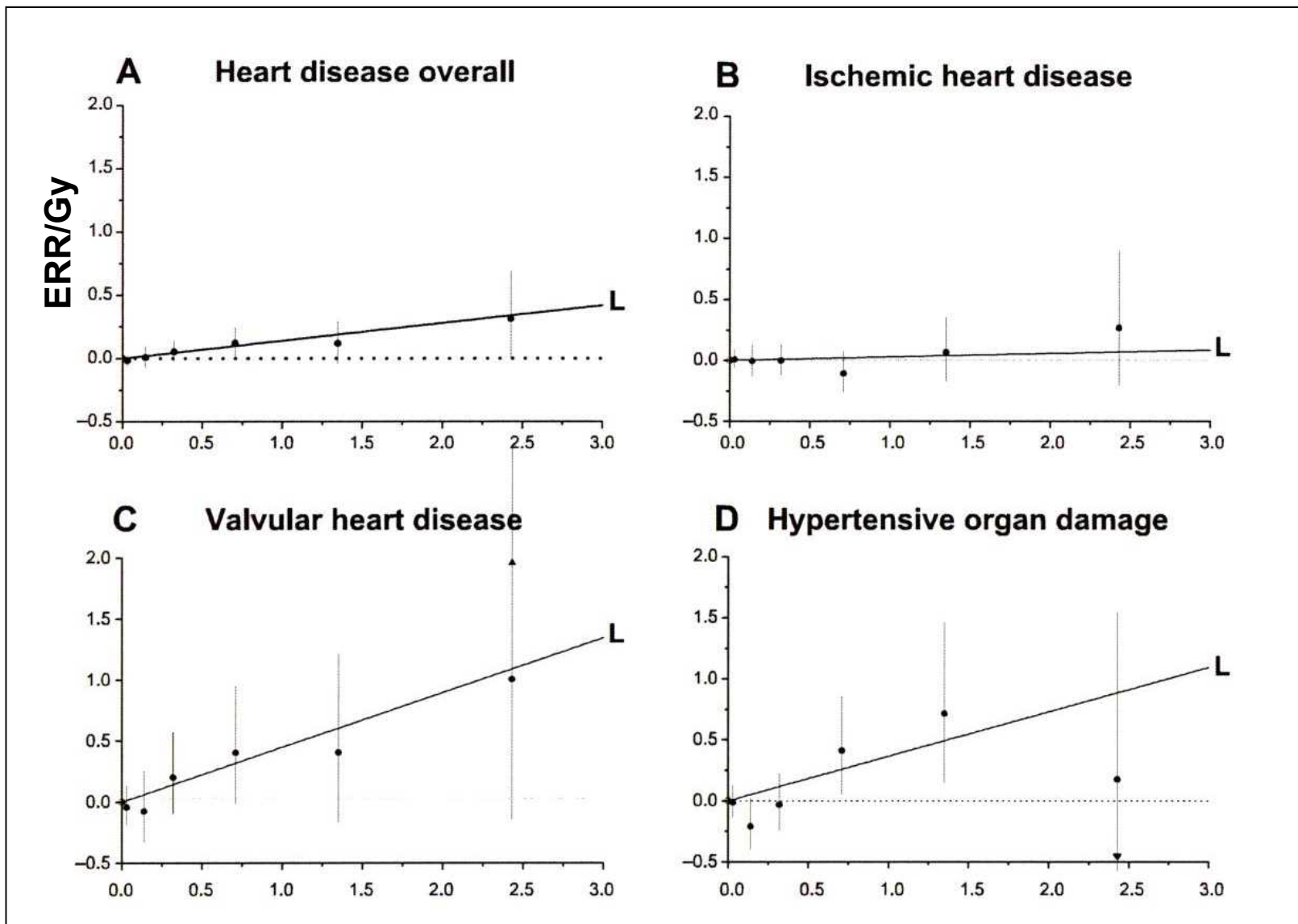
(Takahashi I et al. Radiat Res 2017;187: 319-332)

Heart Disease Subtype-Specific Risk (LSS, Mortality, 1950-2008)



(Takahashi I et al. Radiat Res 2017;187: 319-332)

Heart Disease Subtype-Specific Dose Response (LSS, Mortality, 1950-2008)



(Takahashi I et al. Radiat Res 2017;187: 319-332)



A-bomb Radiation and CVD

- Summary of RERF Findings -

- **Mortality study indicated an elevated risk of heart disease at doses above 0.5 Gy.**
- **Among heart diseases, hypertensive heart disease and rheumatic heart disease are showing elevated risk in mortality.**
- **There are additional findings indicating elevated risk of stroke mortality, myocardial infarction incidence, CKD mortality, and elevation of risk factor levels, presence of inflammation, and alteration of immune function associated with radiation dose.**



A-bomb Radiation and CVD

- Summary of RERF Findings -

- Dose-response relationship appeared to be linear for HD mortality. However, there are indications that dose-response could be linear-quadratic or quadratic for other CVD endpoints, such as stroke mortality, incidence of myocardial infarction, incidence of hypertension and mortality of renal failure.**
- However, it is still unclear that the observed association has causal link or not.**
- It is also unclear whether the biological mechanisms operating at high doses of radiation apply to lower doses.**

Radiat Environ Biophys (2013) 52:425–434
DOI 10.1007/s00411-013-0489-2

CONTROVERSIAL ISSUE

Cardiovascular effects after low-dose exposure and radiotherapy: what research is needed?

**Jan Wondergem · Marjan Boerma ·
Kazunori Kodama · Fiona A. Stewart ·
Klaus R. Trott**

(Wondergem J et al. Radiat Environ Biophys 2013;52:425-434)

Cardiovascular effects after low-dose exposure and radiotherapy: what research is needed?

- Recommendation for Epidemiological Studies -

1. Subtype specific risk estimations

- Epidemiological studies, evaluating all heart diseases together, are not expected to solve the important questions.**
- Each disease may have a different pathogenesis, a different clinical manifestation and a different prognosis.**
- Once specific radiation-induced heart diseases are identified and risk estimation has been made, measures for primary and secondary prevention can be implemented.**

(Wondergem J et al. Radiat Environ Biophys 2013;52:425-434)

Cardiovascular effects after low-dose exposure and radiotherapy: what research is needed?

- Recommendation for Epidemiological Studies -

2. Dose response analysis

- With regard to the risk estimation in prospective cohort studies, attention should be placed on dose-response analysis based on individual dose to identify whether dose responses are linear or nonlinear.**
- In the A-bomb survivor's data, the dose response of some specific heart diseases may well be nonlinear such as the linear-quadratic or quadratic dose dependence of the incidence of myocardial infarction.**

(Wondergem J et al. Radiat Environ Biophys 2013;52:425-434)



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Health Effects among F1 Offspring of A-bomb Survivors

- **Past studies (e.g., studies of birth defects, sex ratio, and chromosome aberrations, and biochemical studies) reported no genetic effects.**
- **Ongoing studies (mortality, cancer incidence, and health examination studies) have yet to show evidence that parental radiation exposure increases disease risks among F1 offspring.**



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Future Perspectives

- **Radiation-associated cancer and noncancer diseases will likely increase in the next 10-15 years.**
- **Accumulated epidemiological data will continue to lead to important findings on radiation-associated cancer and noncancer disease risks.**
- **Continued epidemiological studies are essential for risk assessment among A-bomb survivors exposed at age 20 or under.**
- **For elucidation of mechanisms of radiation-associated diseases, research based on stored biosamples and animal experiment will become increasingly important.**

Peace Memorial Park, Hiroshima

Thank you for listening!

