Studies on Atomic Bomb Survivors
--- Cancer and non-cancer Diseases

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Introduction

- Epidemiological Studies of the Japanese A-bomb survivors provide the single largest set of information on the late health effects of radiation exposure

- These studies largely form the basis of current radiation risk estimates (eg. those made by United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) and International Commission on Radiological Protection (ICRP))

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Background Information

A Japan-US Research Organisation: The Radiation Effects Research Foundation (RERF) was established to study the effects of radiation in the survivors of the atomic bombings of Hiroshima and Nagasaki.

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Background Information

- Fixed cohorts were established to provide epidemiological and clinical data on the health status and mortality of the survivors and their children

- Some of the datasets are available at the RERF web site, through which other organisations can conduct their own research

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Life Span Study

- The Life Span Study consists of a large cohort of both sexes and all ages
- The risks of cancer incidence, cancer mortality, and non-cancer diseases have been studied in relation to radiation dose.

Offspring

- About 88 500 persons born between May 1946 and December 1984
- No association demonstrated to date between radiation and either hereditary disease or cancer in offspring

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Mortality Dataset (Preston et al., 2003)

- Total Number of subjects: 86,572
- Follow-up: 1950-1997
- 52% of subjects had died by end of 1997
- Dosimetry system: DS86 (unit in Sv)

  DS02 is now available, but this leads to little change in overall findings
- Death certification: Koseki uses ICD codes
- Follow-up: 0.2% lost

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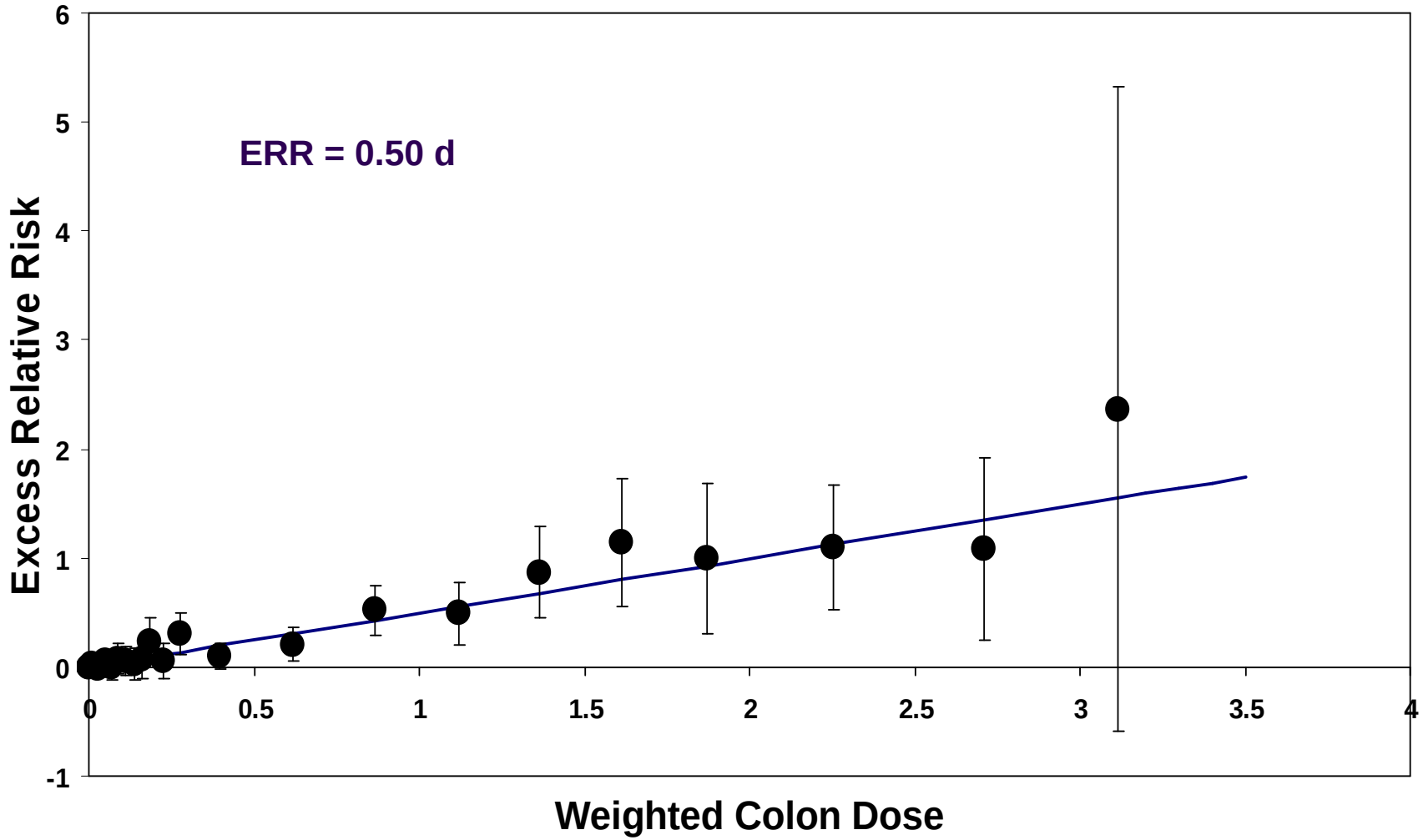
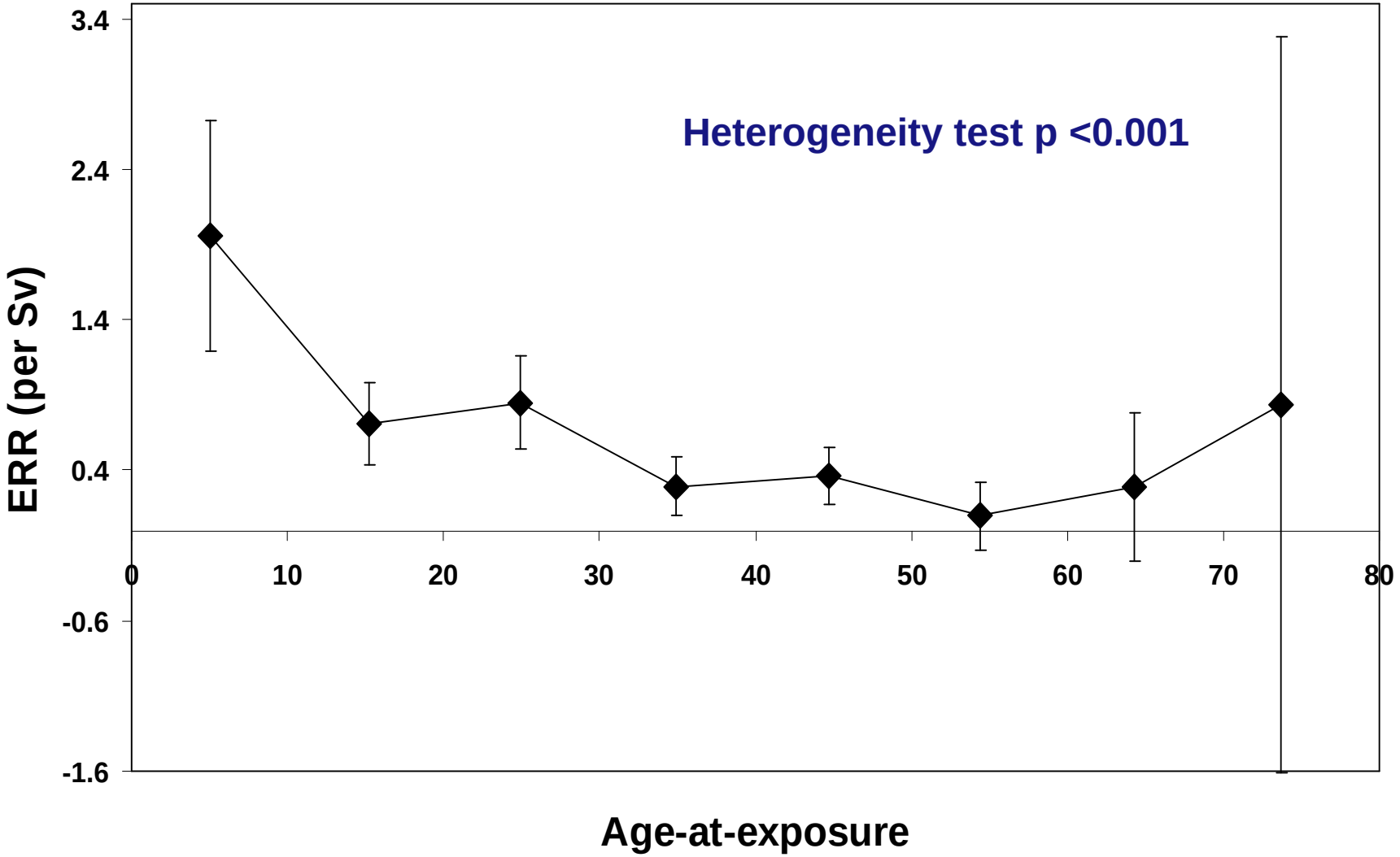
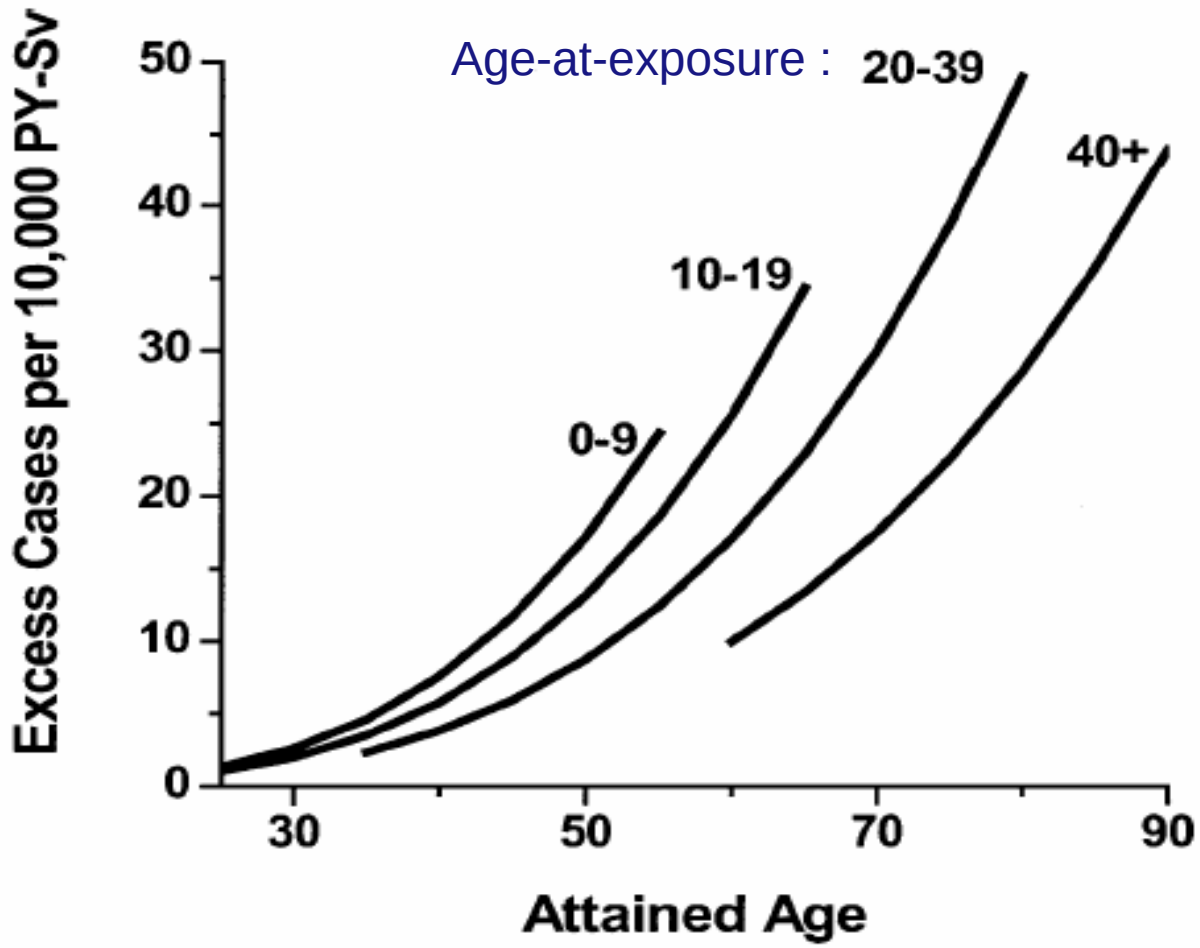
Dose-response for All Solid Cancer Mortality



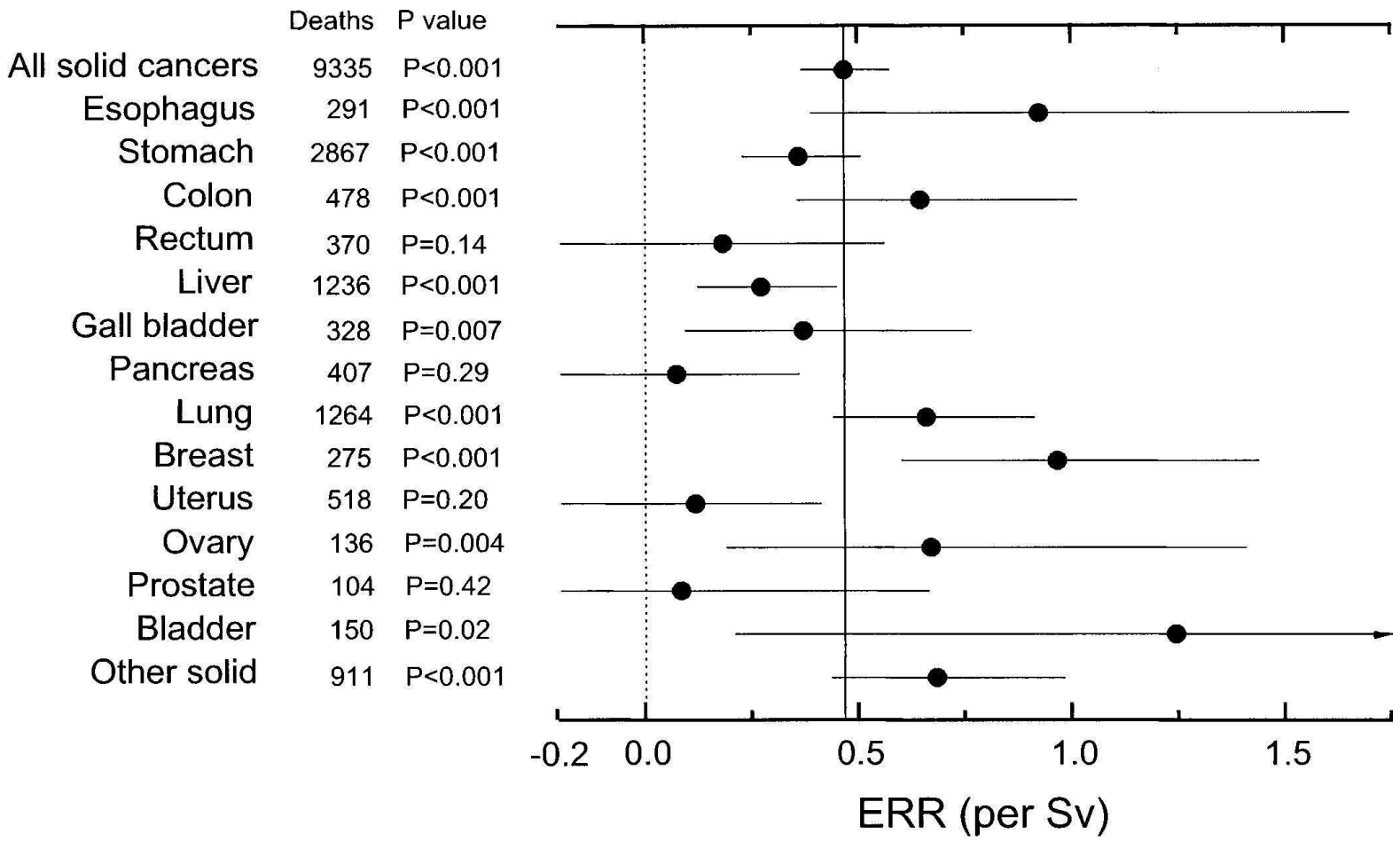
Excess Relative Risk (ERR) per Sv for all solid cancer mortality versus age-at-exposure



Excess solid cancer deaths per 10,000 PY-Sv versus attained age (Preston et al., 2003)



Excess relative risk by cancer site in the LSS mortality data (Preston *et al*, 2003)



Observed and radiation associated solid cancer deaths 1950-1997 by dose group (Preston et al. 2003)

Dose	People	Deaths	Excess
<0.005	37,458	3,833	0
0.005-0.1	31,650	3,277	44
0.1-0.2	5,732	668	39
0.2-0.5	6,332	763	97
0.5-1	3,299	438	109
1-2	1,613	274	103
2+	488	82	48
Total	86, 572	9,335	440

Summary of cancer mortality in A-bomb study

- The excess risk of solid cancer appears to be linear in dose
- ERR depends on age-at-exposure and is highest for those exposed as children
- The solid cancer risk is elevated by 47% per Sv at age 70 for those exposed at age 30 (Preston et al, 2003)
- There were 249 leukaemia deaths in this cohort. The attributable risk is about 53%. Many of the excess deaths occurred during the earlier years of the follow-up. The excess risk appears to be linear-quadratic in dose.

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Cancer Incidence (Preston et al. 2007)

- Information available from 1958-1998 on solid cancers in Hiroshima and Nagasaki (from 1950 for haematological cancers)
- Incidence data are particularly informative about cancers with good cure rates
  - *eg. breast, thyroid*
- For all solid cancers combined, the ERR and EAR at 1 Sv are higher in the incidence than in the mortality data, owing to:
  - *the greater diagnostic accuracy of the incidence data*
  - *the under-representation of cancers such as breast and thyroid in the mortality data*

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Comparison radiation risks between incidence and mortality studies (BEIR VII)

ERR Models	No. of Cases or Deaths	ERR/Sv (95% CI) at Age 30 and attained age 60 Males	Females
Incidence [a]	12,778	0.33 (0.24, 0.47)	0.57 (0.44, 0.74)
Mortality [b]	10,127	0.23 (0.15, 0.36)	0.47 (0.34, 0.65)

EAR Models		Excess cases per 10^4 PY-Sv (95%CI) Males	Females
Incidence [a]	12,778	22 (15, 30)	28 (22, 36)
Mortality [b]	10,127	11 (7.5, 17)	13 (9.8, 18)

[a]Based on analyses of LSS incidence data 1958-1998 for solid cancers excluding thyroid and nonmelanoma skin cancer.

[b]Based on analyses of LSS mortality data 1950-2000 for all solid cancers.

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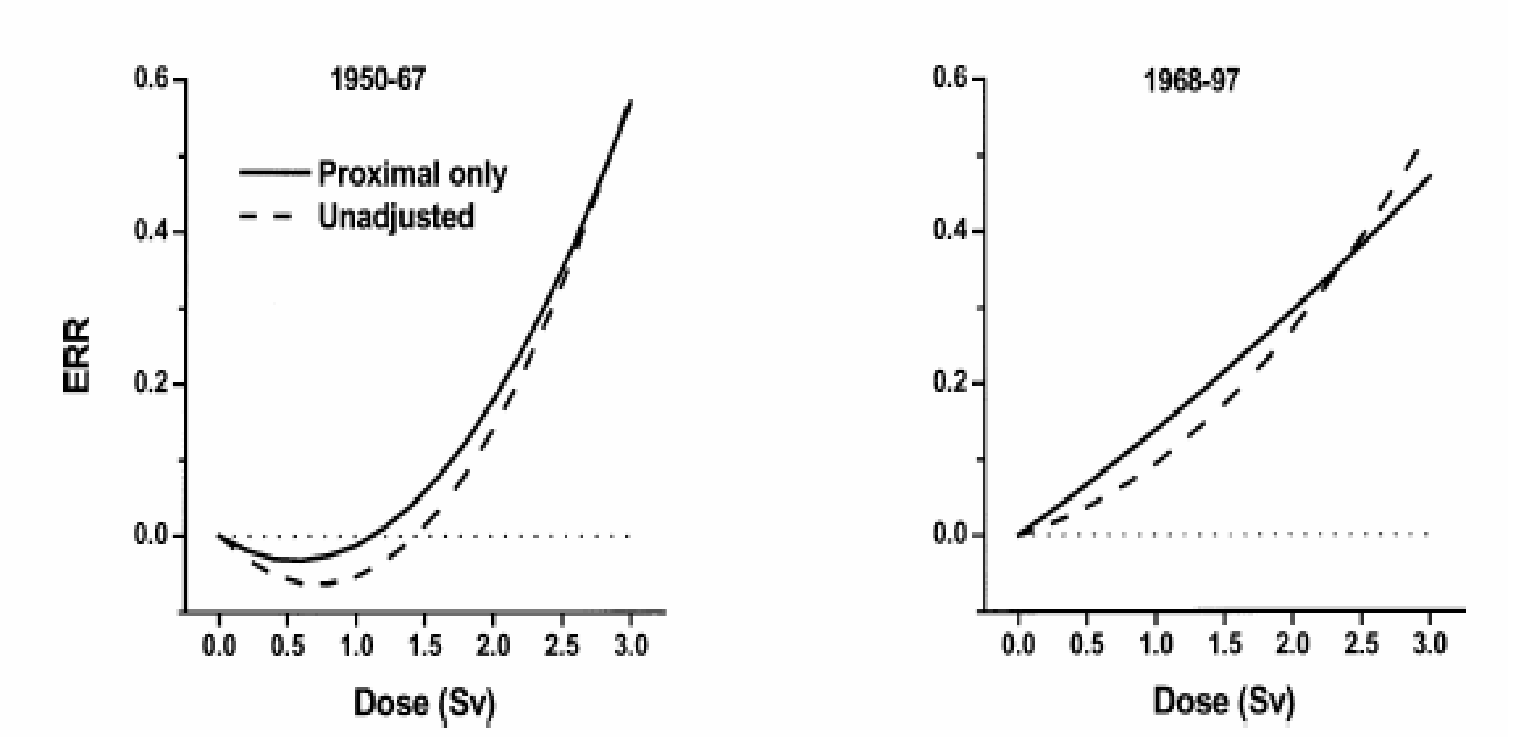
Risks of Non-cancer diseases Mortality

- A “healthy survivor” selection effect was reported during the first two decades after the bombs (Preston et al, 2003; Shimizu et al, 1999).

- RERF’s analyses of risks (Preston et al. 2003) therefore focused on the time period 1968-97.



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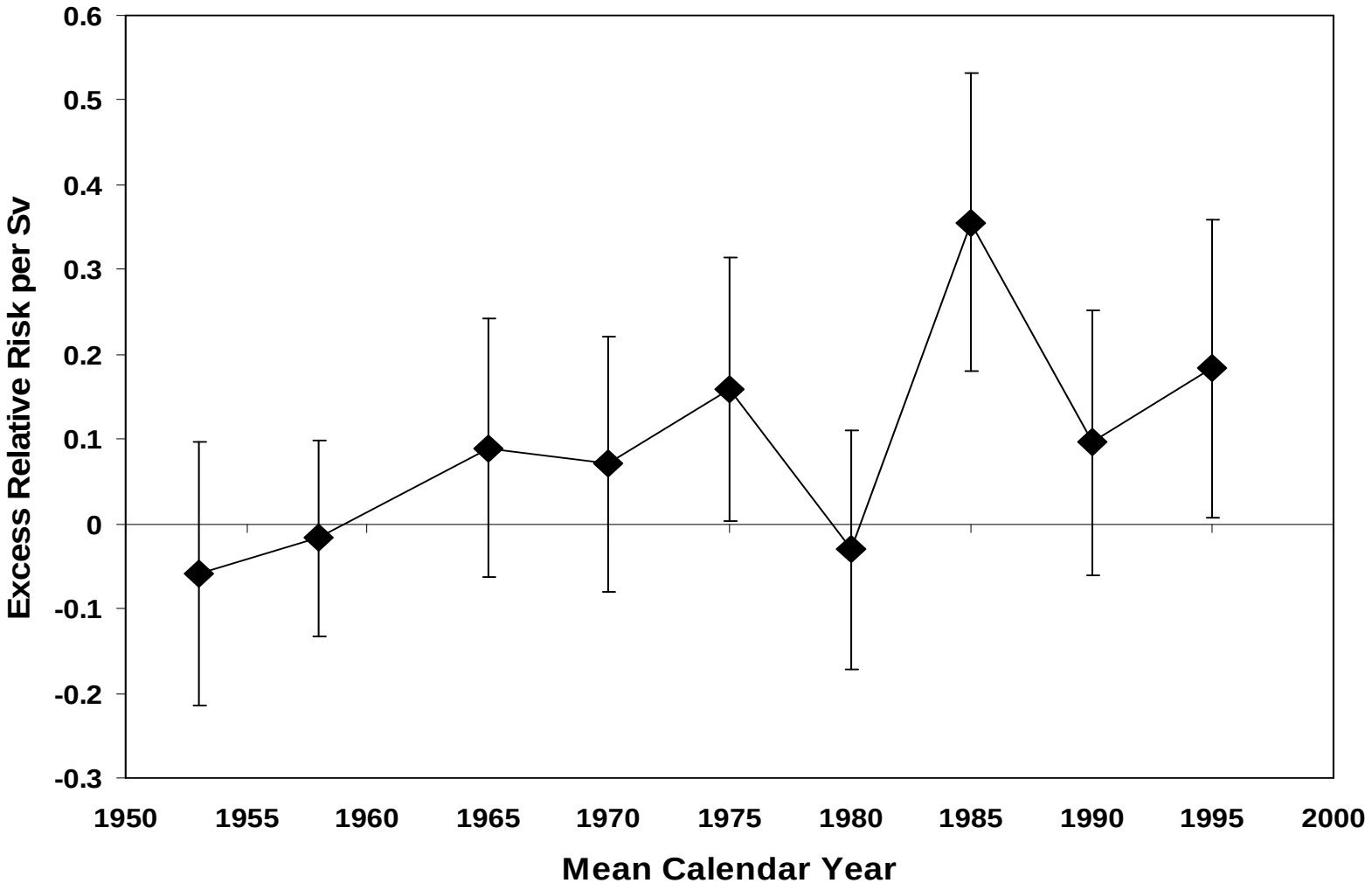
Excess relative risk for total non-cancer disease mortality versus calendar period (Zhang et al. 2005)



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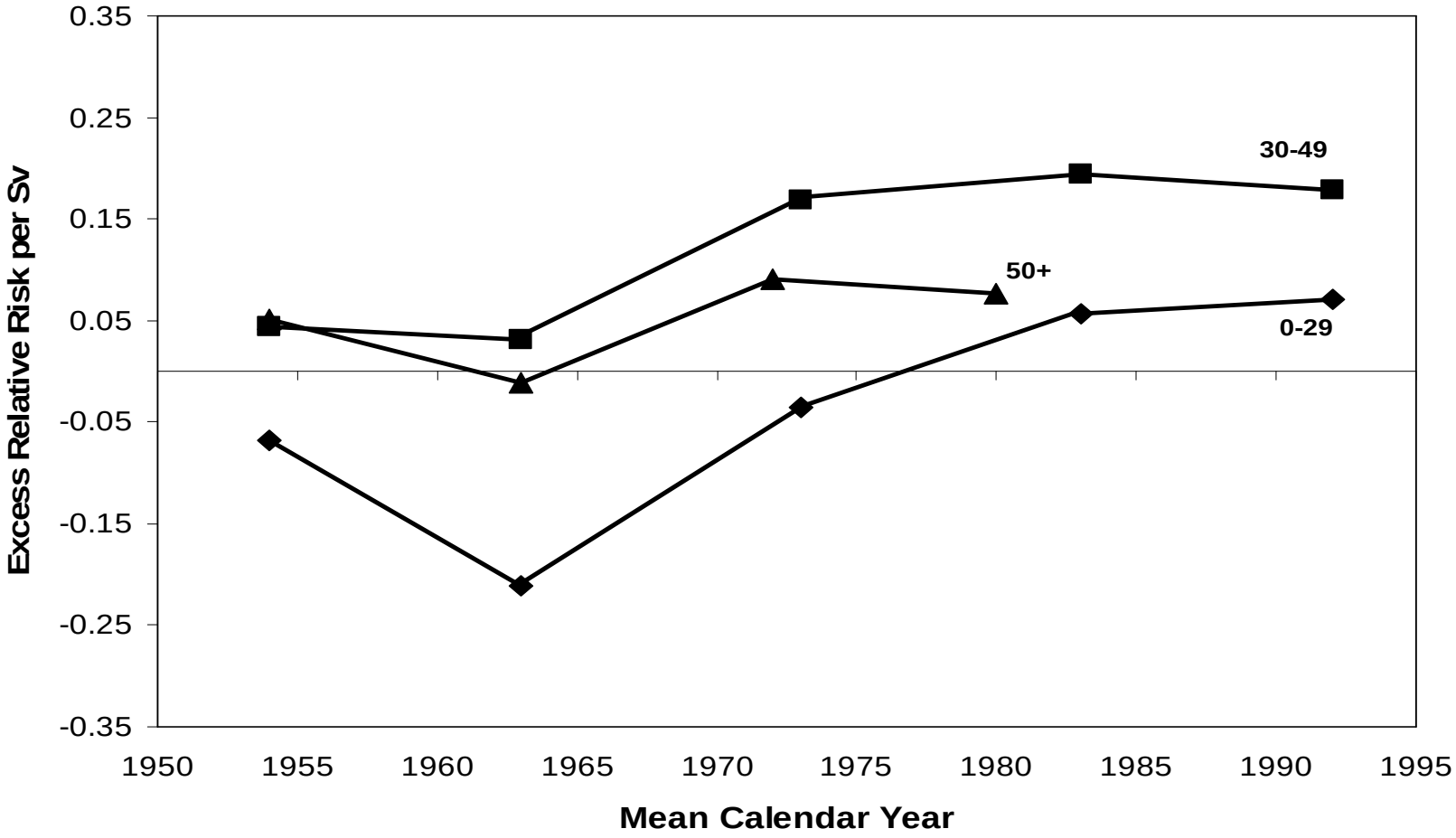
Excess relative risk for total non-cancer disease mortality versus calendar period for three age-at-exposure groups



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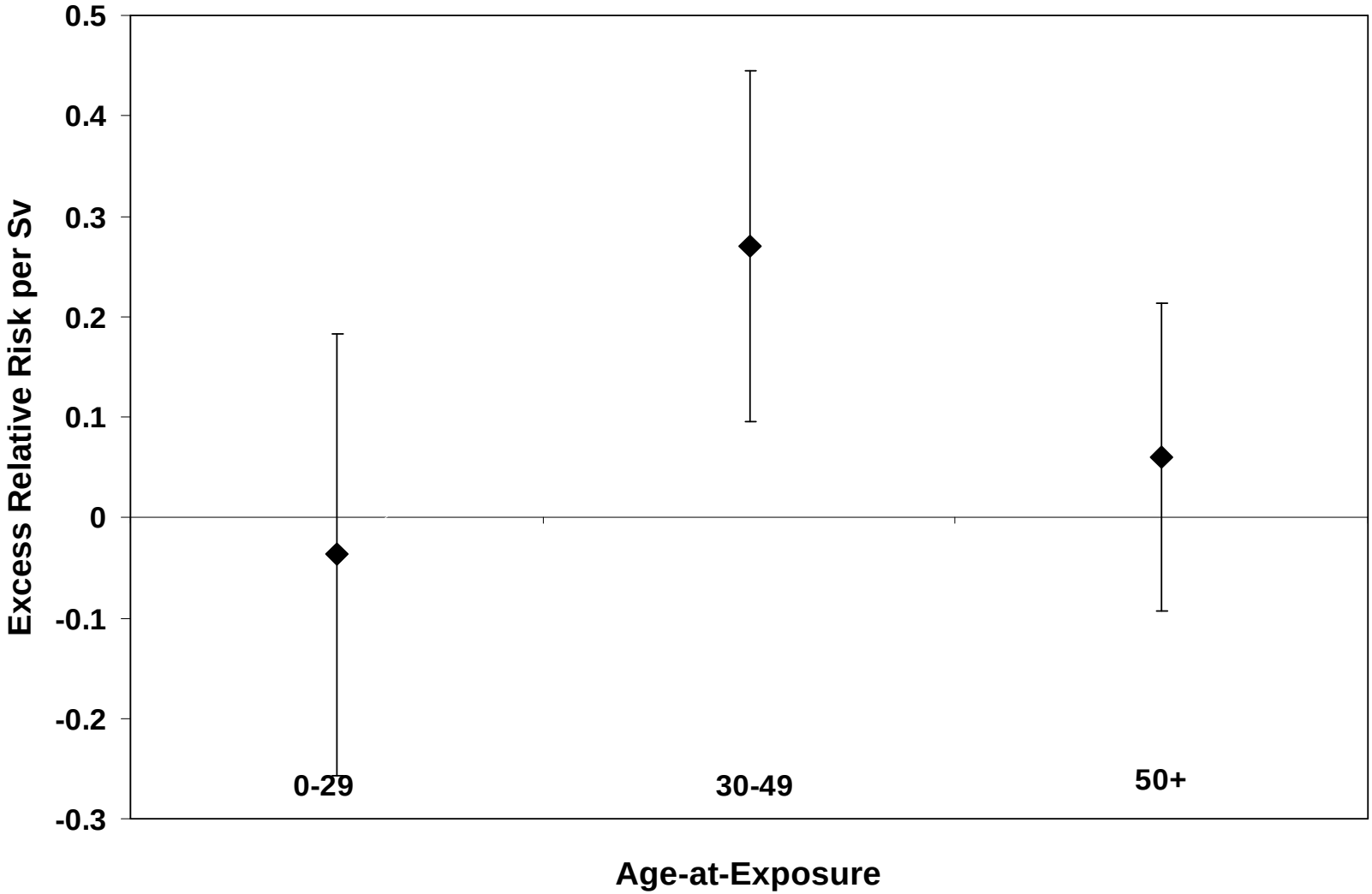
ERR for total non-cancer disease mortality for three age-at-exposure groups (Heterogeneity test p=0.04)



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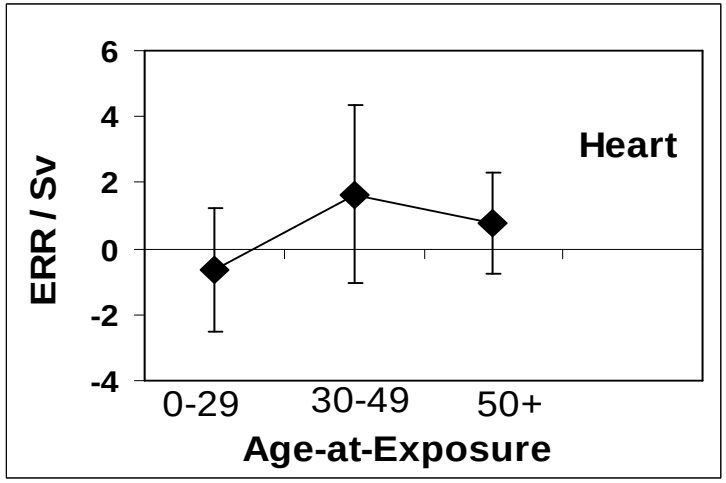
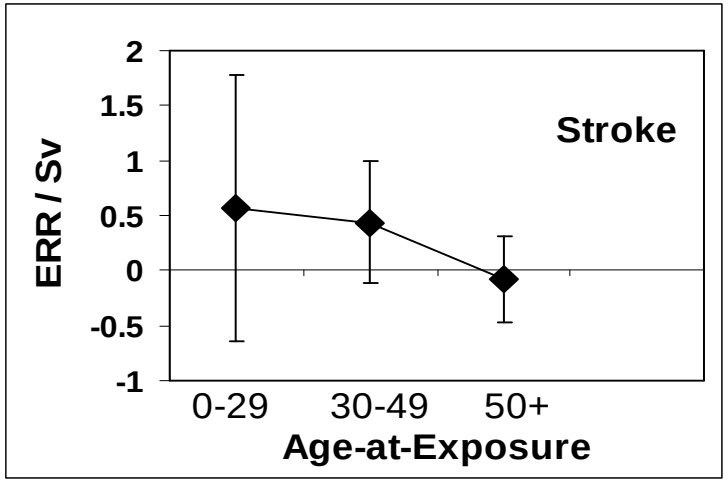
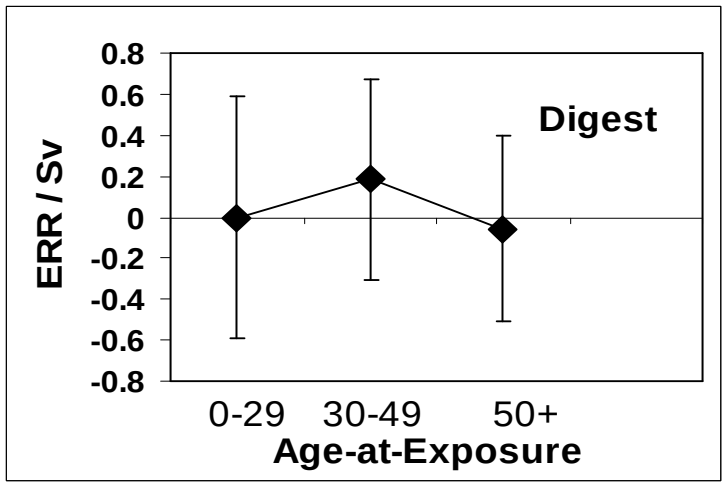
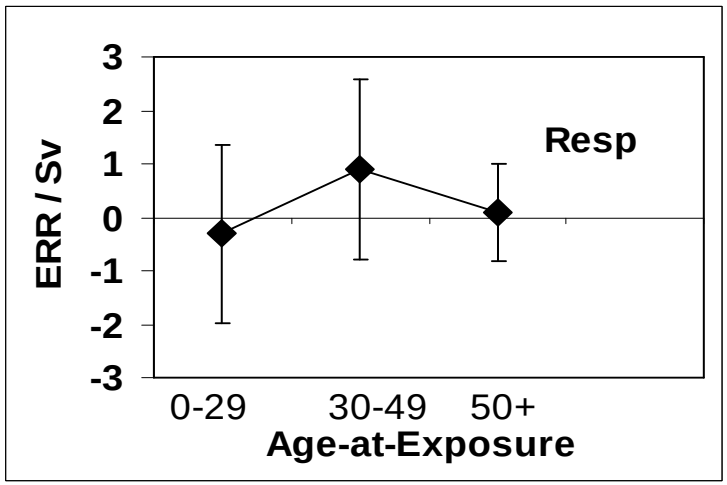
ERR versus age-at-exposure for heart, stroke, digestive and respiratory diseases









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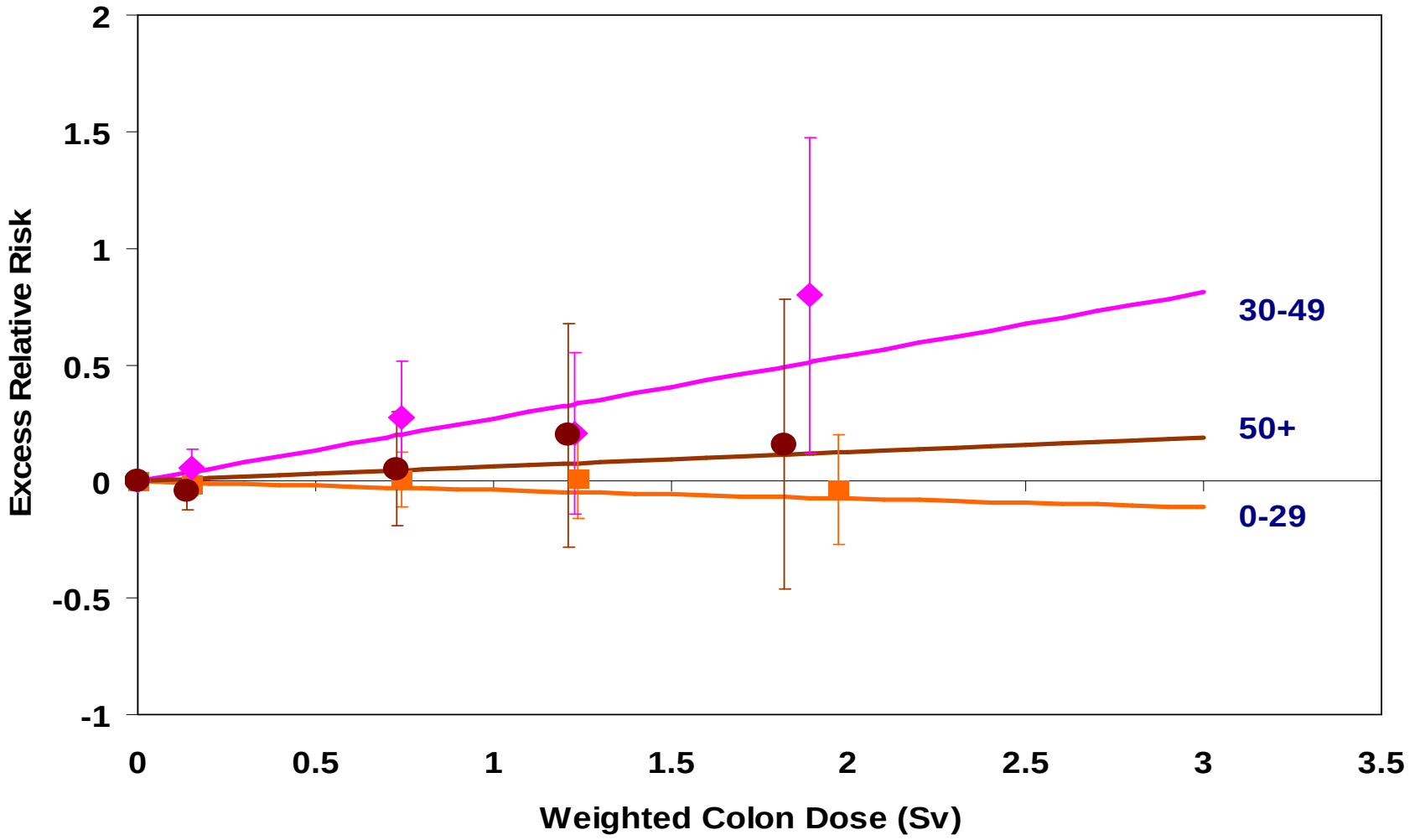
Dose response for total non-cancer disease mortality for each of three age-at-exposure groups (Zhang et al. 2005)



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Observed and radiation associated non-cancer deaths 1950-1997 by dose group (Preston et al. 2003)

Dose	People	Deaths	Excess
<0.005	37,458	13,832	0
0.005-0.1	31,650	11,633	17
0.1-0.2	5,732	2,163	17
0.2-0.5	6,332	2,423	47
0.5-1	3,299	1,161	61
1-2	1,613	506	68
2+	488	163	40
Total	86, 572	31,881	250

Summary of non-cancer mortality in A-bomb study

- An excess of deaths from non-cancer diseases has been observed in the Japanese Atomic Bomb Survivors cohort.
- The excess relative risk is highest amongst the 30-49 years age-at-exposure group, but is close to zero for the 0-29 years age-at-exposure group. This need to be taken into consideration while modelling the ERR.
- Given that these persons exposed at ages 0-29 had reached 52-81 years of age by 1997 and that they had not shown a raised ERR in relation to radiation exposure, does that mean the excess of non-cancer mortality amongst A-bomb survivors is largely over ? --- Need to look at longer follow-up.

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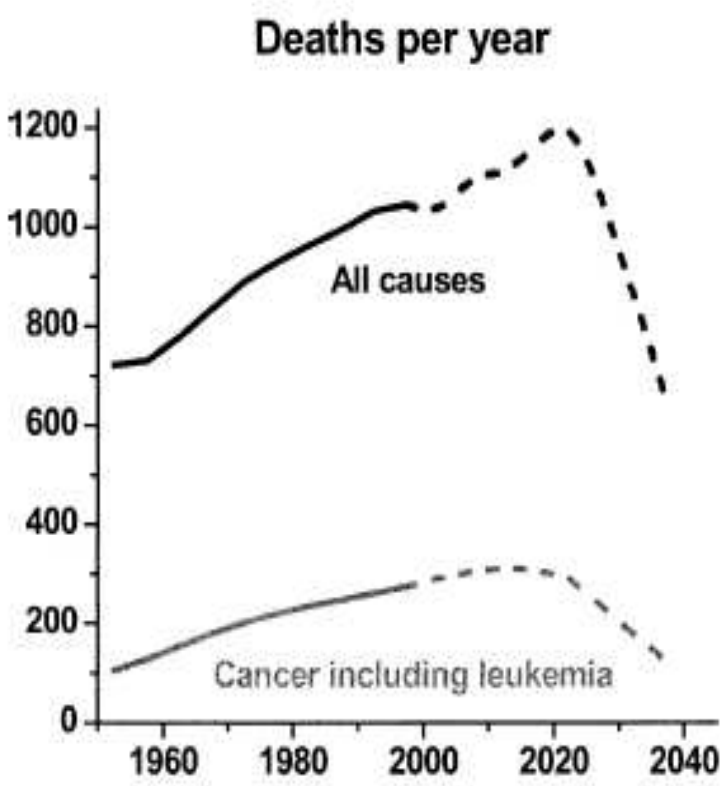
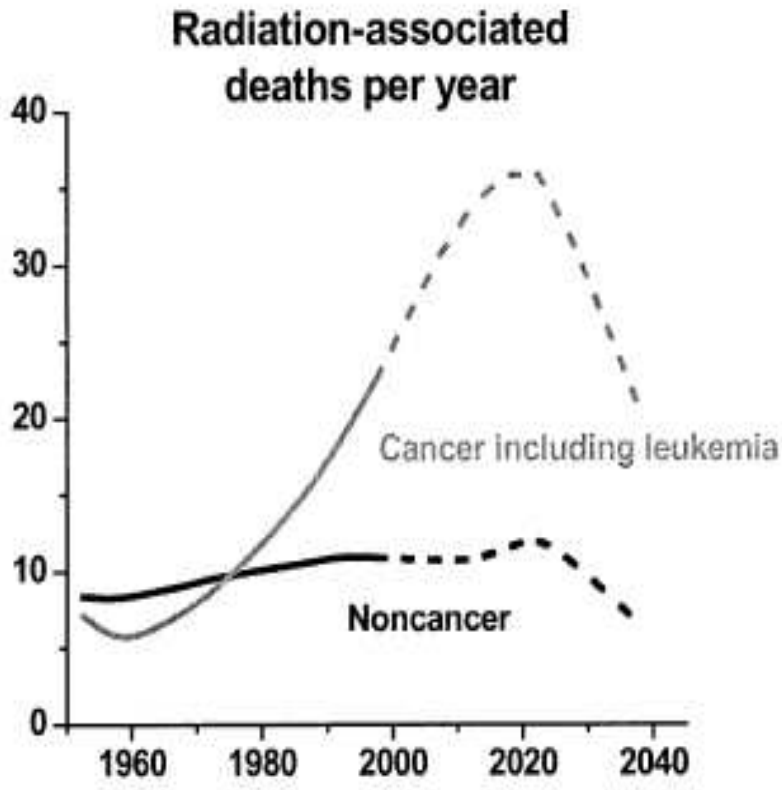
Total and radiation-associated deaths per year for all causes and for cancer including leukemia (Preston et al. 2003)





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Perspectives

- Notwithstanding the time since the bombings, continued follow-up of the A-bomb survivors will be important for risk estimation; 48% were still alive in 1997.
- Future pattern of risks
  - *important in determining lifetime cancer risks for those exposed when young*
- Shape of dose-response
  - *both for cancer and non-cancer*
- Site-specific cancer risks and transfer to other populations

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