Japanese A-bomb Survivor Data and Studies of Low-Dose Effects

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Why is the A-bomb cohort considered a benchmark for assessment of radiation risks?
Residents in Hiroshima and Nagasaki at Explosions: \(\approx500,000\)

Residents at 1950 National Census
A-bomb survivors: \(\approx280,000\)

**Life Span Study**
120,000 (1950-)

**Adult Health Study**
17,000 (1958-)

**In Utero Exposed**
3,600

**In Utero Clinical**
1,600 (1978-)

**F1: Offspring of Survivors**
77,000

**F1 Clinical**
12,000 (2002-)
A-bomb Studies as a Benchmark for Radiation Risk Assessment

Characteristics of the radiation-exposed cohort:

- Large, prospective cohort (~120,000) consisting of all ages at exposure and both sexes
- Wide range of radiation exposure with relatively accurate estimated dosimetry
- Cohort is unselected with respect to medical conditions, occupational fitness, etc.
- High rates of follow-up and disease ascertainment for ~60 years
- Information on potential confounding risk factors
- Adult Health Study – biennial clinical examinations and biospecimen collection for a subset of about 17,000 – study correlates and mechanisms of radiation-related disease through biomarkers, etc.
Life Span Study (LSS) Cohort
(120,321 people)
Are the excess risks of cancer at low doses proportional to those at high doses? – i.e.,
Is there dose-response linearity, less-than or more-than linear risk at low doses, or a dose threshold?
LSS dose response: Solid-cancer incidence

- No evidence of non-linearity in the dose response
- Significant dose response on 0-150 mGy
- Low dose-range slope consistent with full range

\[
\text{ERR/Gy} = 47\% \ (95\% CI: 40-54\%)
\]

Dose-threshold: 40 mGy
(CI: <0, 85 mGy)


LSS Mortality Estimates of Relative Risk at 1 Gy for Various Dose Ranges (0 to Plotted Dose)

(Ozasa et al, Unpublished, 2010)
LSS Leukemia Dose Response

Linear-quadratic fits better than Linear model.
Dose-threshold estimate: 80 mGy (95% CI: 30, 190 mGy)

(Hsu et al, Unpublished, 2010)
Which organs are at risk of radiation-related cancer?

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th># Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>All solid cancers</td>
<td>10755</td>
</tr>
<tr>
<td>Esophagus</td>
<td>334</td>
</tr>
<tr>
<td>Stomach</td>
<td>3103</td>
</tr>
<tr>
<td>Colon</td>
<td>609</td>
</tr>
<tr>
<td>Rectum</td>
<td>419</td>
</tr>
<tr>
<td>Liver</td>
<td>1485</td>
</tr>
<tr>
<td>Gall bladder</td>
<td>410</td>
</tr>
<tr>
<td>Pancreas</td>
<td>495</td>
</tr>
<tr>
<td>Lung</td>
<td>1535</td>
</tr>
<tr>
<td>Breast</td>
<td>316</td>
</tr>
<tr>
<td>Uterus</td>
<td>544</td>
</tr>
<tr>
<td>Ovary</td>
<td>155</td>
</tr>
<tr>
<td>Prostate</td>
<td>125</td>
</tr>
<tr>
<td>Bladder</td>
<td>177</td>
</tr>
</tbody>
</table>

Note: Estimates standardized to age 70 after exposure at age 30 and averaged, where appropriate, over sex.

(Ozasa, Shimizu et al, Unpublished, 2010)
Do certain subgroups have greater risk of cancer from radiation exposure?
LSS Cancer Incidence: Site-specific Excess Relative Risk (ERR) Estimates by Gender

Excess Rates of Solid Cancer Mortality by Age at Exposure and Attained Age

(Ozasa, Shimizu et al, Unpublished)
How great is the cancer risk following *in utero* exposure?
Very large risks from *in utero* exposure have been predicted

- Based mostly on the large Stewart-Kneale case-control study of fetal radiation exposure and childhood cancer, it was predicted that an additional 6% of persons would die from cancer after 1 Gy of *in utero* radiation. (Doll & Wakeford, *Br J Radiol*, 70:130-39, 1997)

- 6% lifetime cancer mortality risk per Gy is:
  - ~3 times as large as the corresponding estimated A-bomb risk after exposure at age 10, or
Solid Cancer Risk Patterns for *In Utero* and Childhood Exposure, A-bomb Survivors

**In utero ERR/Gy = 1.0 (95%CI: 0.2, 2.3)**

Leukemia after *In Utero* or Childhood A-bomb Exposure

### Childhood exposure, ages 0-5
- 39 cases, 22 with estimated bone marrow doses >500 mGy
- Steep dose response (ERR/Gy = 15, 95%CI: 6, 36)

### *In Utero* Exposure
- 4 cases, all with estimated bone marrow doses <40 mGy
- No dose response (ERR/Gy = 0, 95%CI: <0, 7)

(Kasagi, Ozasa, et al, Unpublished, 2010)
Is the magnitude of radiation risk altered by other environmental exposures?
Models of Lung Cancer Risk: Radiation Dose and Smoking

** Gender-averaged excess risk relative to unexposed never-smokers

Liver Cancer Risk from Hepatitis C Virus (HCV) and Radiation

Are there noncancer risks from radiation exposure at low doses?
Radiation and Heart Disease Mortality

- Clear evidence of heart disease risk at doses below 4-5 Gy
- Dose-response for heart disease mortality appears linear, but there is considerable uncertainty below about 0.5 Gy.

Corroborative Clinical Evidence for Radiation Effects

- ↑ Circulatory system inflammation – numerous markers of inflammation are ↑
- Blood lipids – ↑ total cholesterol, triglycerides; ↓ HDL cholesterol
- Cardiovascular risk factors – ↑ blood pressure and calcification of arteries

Heart Disease Mortality

ERR = 14% per Gy†
(95% CI: 6, 23%)  
L: linear  
LQ: linear-quadratic

†Adjusted for gender, age at exposure, attained age, diabetes, etc.

Radiation protection agencies had long believed there was no risk for vision-impairing cataracts below about 5 Gy and set safety standards accordingly. More protective safety standards for the eye are now being considered.

\[
\text{ERR/Gy} = 21\% \ (95\% \text{CI}: 9-36\%)
\]

Dose-Threshold: \(~0.5 \text{ Gy} \ (95\% \text{CI}: 0.1-1.0)\)

\(P < 0.001\)

(Adjusted for city, gender, age at exposure, attained age and diabetes)

(Nakashima, Neriishi et al, Unpublished, 2010)
How large is the risk to offspring from parental gonadal irradiation?
Relative Risk for Non-cancer and Cancer Mortality in 41,000 Offspring of Atomic Bomb Survivors, 1946-2003

- To date, the frequencies of cancer and other diseases in the offspring are unrelated to parental radiation dose, but 20-30 more years of follow-up are needed to provide definitive evidence.

(Suyama, et al, Unpublished, 2009)