The Latest Update on Atomic-Bomb Survivor Studies

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Subjects of Life Span Study

- Atomic-bomb survivors
  - National Census in 1950: 284,000 people answered that they met A-bomb in Hiroshima/Nagasaki
  - Master Sample: those who lived in Hiroshima/Nagasaki in 1950 (195,000)
  - A total of 120,000 were collected by stratified sampling for exposure status
    - Lived in Hiroshima or Nagasaki at the time of bombing
      - <2.5 km from the hypocenters: about 54,000
      - 2.5 to 10 km: about 40,000
    - Not in either city at the time of bombing: about 27,000
  - They have been followed-up since 1950
Estimation of Individual Radiation Dose (Evaluation of Exposure)
Radiation from Atomic Bomb

• Initial Radiation
  – At explosion (<1min)

• Residual Radiation
  – Induced radiation
  – Radioactive Fallout

➢ Factors Influencing Individual Dose from initial radiation
  – Non-shielded dose
    • Distance from the explosion center
  – Shielding condition
    • Building, Terrain
  – Personal condition
    • Body size, posture, direction
  – Individual dose for 15 organs
    • Weighted absorbed dose
      (neutron x10+gamma dose)
Non-Shielded Dose (Free-in-Air Tissue Kerma) by Distance from the Hypocenter by DS02(Gy)

<table>
<thead>
<tr>
<th>Distance (m)</th>
<th>Hiroshima</th>
<th></th>
<th>Nagasaki</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Neutron</td>
<td>Gamma-ray</td>
<td>Total (X10 for neutron)</td>
</tr>
<tr>
<td>1000</td>
<td>0.260</td>
<td>4.22</td>
<td>6.82</td>
</tr>
<tr>
<td>1200</td>
<td>0.067</td>
<td>1.81</td>
<td>2.48</td>
</tr>
<tr>
<td>1500</td>
<td>0.0090</td>
<td>0.527</td>
<td>0.617</td>
</tr>
<tr>
<td>1800</td>
<td>0.0013</td>
<td>0.165</td>
<td>0.178</td>
</tr>
<tr>
<td>2000</td>
<td>0.0004</td>
<td>0.076</td>
<td>0.080</td>
</tr>
<tr>
<td>2500</td>
<td>0.0000</td>
<td>0.013</td>
<td>0.013</td>
</tr>
</tbody>
</table>

Young RW, et al. DS02, RERF, 2005
# Estimated Individual Doses

<table>
<thead>
<tr>
<th>DS02 dose</th>
<th>Hiroshima</th>
<th>Nagasaki</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not-in-City</td>
<td>20,230</td>
<td>6,350</td>
<td>26,529</td>
</tr>
<tr>
<td>&lt;5 mGy</td>
<td>21,713</td>
<td>16,812</td>
<td>38,509</td>
</tr>
<tr>
<td>5-99</td>
<td>22,744</td>
<td>7,232</td>
<td>29,976</td>
</tr>
<tr>
<td>100-499</td>
<td>10,115</td>
<td>2,226</td>
<td>12,341</td>
</tr>
<tr>
<td>500-999</td>
<td>2,376</td>
<td>1,052</td>
<td>3,428</td>
</tr>
<tr>
<td>1000-1999</td>
<td>1,151</td>
<td>614</td>
<td>1,765</td>
</tr>
<tr>
<td>2000+</td>
<td>436</td>
<td>189</td>
<td>625</td>
</tr>
<tr>
<td>Unknown</td>
<td>3,449</td>
<td>3,621</td>
<td>7,070</td>
</tr>
<tr>
<td>Total</td>
<td>82,214</td>
<td>38,107</td>
<td>120,321</td>
</tr>
</tbody>
</table>
Other Risk Factors
(Confounding and Interaction)

• Mail surveys
  – Self-administered questionnaire
  – Lifestyle, etc
  – Conducted in 1965, 69, 79, 91, and 2008-11
  – Response rate; around 60% of whole LSS subjects
Results based on 1950-2003 (LSS 14)
## Follow-up, 1950-2003

<table>
<thead>
<tr>
<th>Age at bombing</th>
<th>No. of subjects</th>
<th>Observed person-years</th>
<th>No. of death*</th>
<th>Alive (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-9</td>
<td>17,833</td>
<td>910,347</td>
<td>2,200</td>
<td>88%</td>
</tr>
<tr>
<td>10-19</td>
<td>17,563</td>
<td>848,826</td>
<td>4,887</td>
<td>72%</td>
</tr>
<tr>
<td>20-29</td>
<td>10,891</td>
<td>494,021</td>
<td>5,178</td>
<td>52%</td>
</tr>
<tr>
<td>30-39</td>
<td>12,270</td>
<td>462,694</td>
<td>10,410</td>
<td>15%</td>
</tr>
<tr>
<td>40-49</td>
<td>13,504</td>
<td>365,240</td>
<td>13,397</td>
<td>1%</td>
</tr>
<tr>
<td>50+</td>
<td>14,550</td>
<td>213,079</td>
<td>14,548</td>
<td>0%</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>86,611</strong></td>
<td><strong>3,294,210</strong></td>
<td><strong>50,620</strong></td>
<td><strong>42%</strong></td>
</tr>
</tbody>
</table>

*Excluding the deletion by the authority office

+ Excluding NIC

Analytical Models

• Excess relative risk (ERR) model

\[ \lambda_{\text{exposed}} = \lambda_0 (c,s,a,b)[1+\text{ERR}(d,s,e,a)] \]

• Excess absolute risk (EAR) model

\[ \lambda_{\text{exposed}} = \lambda_0 (c,s,a,b) + \text{EAR}(d,s,e,a) \]
- c: city, s: sex, a: attained age (follow-up period), b/e: birth year/age at exposure
- \( \lambda_0(c,s,a,b) \): rate at non-exposure defined by c,s,a,b

• Main effects of radiation (\( \rho \)) and effect modification (\( \varepsilon \))

\[ \text{ERR, EAR} = \rho(d) \varepsilon(e,s,a) \]
- \( \rho(d) = \beta d \) (linear), \( \gamma d^2 \) (quadratic), \( \beta+\gamma d^2 \) (linear-quadratic)
- \( \varepsilon(e,s,a) = \exp(\tau e) \cdot a^{\nu \sigma s} \)
ERR by Dose for All Solid Cancer, LSS, 1950-2003

- The linear (L) model provides the best fit over the full-dose range

- $\text{ERR/Gy}=0.42$ (95%CI: 0.32, 0.53) for the gender-averaged risk estimates at age 70 after radiation exposure at age 30, based on the model with effect modification by sex, age at exposure and attained age

- The lowest dose range with a statistically significant trend is $0-0.20\text{Gy}$ with ERR/Gy of 0.56

- Estimated threshold dose is $0.0\text{Gy}$ and upper 95% confidence limit is 0.15Gy

Modification of ERR and EAR of All Solid Cancer by Age at Exposure and Attained Age

• Both ERR and EAR were higher in the young at the time of the bombings
• ERR decreased along with attained age while EAR increased

Confounding and Interaction of Radiation Effects with Life Style and Other Factors

Risk of radiation for lung cancer:

- ERR at 1 Gy was around 0.7 in non-smokers
- ERR at 1 Gy was around 2.0 in light smokers who consumed 7-8 cigarettes per day (positive interaction)
- No additional increase in risk by radiation in heavy smokers (negative interaction, risk of lung cancer seemed to be saturated by smoking)
Issues on Risk Estimation at Low-dose Radiation Exposure

• Small effects at low-dose levels
  – Low power of detection needs a large number of subjects
• Effects of non-radiation risk factors
  – Lifestyle such as smoking, and geographical factors
    • Bias and confounding
      – Proximal/high dose survivors lived in urban area in Hiroshima and rather vice versa in Nagasaki
    • Non-differential effects (i.e., widen the confidence intervals)
    • Interaction (i.e., alter the risks of radiation between different strata of non-radiation risk factors)
• Effects of residual radiation and medical radiation exposure, revision of dose estimates, etc
Non-cancer Diseases
### Risk of Circulatory Diseases, 1950-2003

<table>
<thead>
<tr>
<th>Disease category (ICD-9 code)</th>
<th>No of deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Circulatory disease (390-459)</td>
<td>19,054</td>
</tr>
<tr>
<td><strong>Heart disease</strong> (390-398, 402, 404, 410-429)</td>
<td>8,463</td>
</tr>
<tr>
<td>Ischemic heart disease (410-414)</td>
<td>3,252</td>
</tr>
<tr>
<td>Myocardial infarction (410)</td>
<td>1,735</td>
</tr>
<tr>
<td>Hypertensive heart disease (402, 404)</td>
<td>922</td>
</tr>
<tr>
<td>Rheumatic heart disease (393-398)</td>
<td>242</td>
</tr>
<tr>
<td>Heart failure (428)</td>
<td>2,983</td>
</tr>
<tr>
<td>Other heart diseases</td>
<td>1,064</td>
</tr>
<tr>
<td><strong>Hypertensive disease without heart diseases</strong> (401, 403, 405)</td>
<td>411</td>
</tr>
<tr>
<td><strong>Stroke</strong> (430-438)</td>
<td>9,622</td>
</tr>
<tr>
<td>Cerebral infarction (433, 434)</td>
<td>2,659</td>
</tr>
<tr>
<td>Cerebral hemorrhage (431)</td>
<td>4,060</td>
</tr>
<tr>
<td>Subarachnoid hemorrhage (430)</td>
<td>461</td>
</tr>
<tr>
<td>Others or unspecified</td>
<td>2,442</td>
</tr>
<tr>
<td><strong>Other circulatory disease</strong></td>
<td>558</td>
</tr>
</tbody>
</table>

- Heart disease and stroke as a whole had significantly increased risks
- Specific disease types except for hypertensive and rheumatic heart diseases had no increased risks, but rather ill-defined diseases had them


(this figure was made by the presenter using the numbers in e-table)
Risk of Possible Chronic Renal Failure Death, 1950-2003

- Several diagnostic criteria of chronic kidney disease were applied and the broadest chronic renal failure had a significant risk of radiation in a quadratic model (ERR/Gy²=0.091, 95%CI: 0.05, 0.198)
- Renal dysfunction could be part of the mechanism causing increased risk after whole-body irradiation, which hypothesis deserves further study

Issues on Circulatory Diseases

- Risk of radiation exposure increased for rather ill-defined diseases
- Additional analyses on dose-response is being investigated by disease type, study period, age at exposure, attained age, etc
  - Prolonged effects of deterministic effects at high dose level?
  - Confounding by socioeconomic status and other factors related to spatial distribution of survivors?
  - Influence of changes of dominant non-cancer diseases in Japan during these decades?
  - Suspicious underlying malignancies?
  - Diagnostic preciseness of death certificates?
- These effects would be prominent especially at low-dose levels
References


