Low Dose/Low Dose Rate Environmental Exposures Studies

Beebe Symposium on the Future of Low-Dose Radiation Research in the United States
National Academies
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Hirosoft International
Overview

• Introductory remarks
• Studies of environmentally-exposed populations (a fly-over view)
• Issues in the design, analysis, and interpretation of studies of radiation health effects in (environmentally) exposed populations
# Nuclear Power Plant Accidents

<table>
<thead>
<tr>
<th>Study</th>
<th>Type</th>
<th>Cancer</th>
<th>Cases</th>
<th>Cohort size /Controls</th>
<th>Mean/Median Dose (mGy)</th>
<th>ERR @ 100mGy</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Three Mile Island</td>
<td>Cohort</td>
<td>Solid Inc</td>
<td>1,643</td>
<td>21,494</td>
<td>0</td>
<td>-1</td>
<td>(-1; 30)</td>
</tr>
<tr>
<td>Chornobyl-Ukraine</td>
<td>Cohort</td>
<td>Thyroid</td>
<td>65</td>
<td>12,415</td>
<td>650/200</td>
<td>0.19</td>
<td>(0.04; 0.63)</td>
</tr>
<tr>
<td></td>
<td>Case-Control</td>
<td>Thyroid</td>
<td>66</td>
<td>835</td>
<td>cases 44 controls 16</td>
<td>4.9</td>
<td>(0.5; 12)</td>
</tr>
<tr>
<td>Chornobyl-Belarus</td>
<td>Cohort</td>
<td>Thyroid</td>
<td>23</td>
<td>12,504</td>
<td>770</td>
<td>0.21</td>
<td>(0.03; 1.0)</td>
</tr>
<tr>
<td></td>
<td>Cohort (prevalence)</td>
<td>Thyroid</td>
<td>87</td>
<td>11,970</td>
<td>560/230</td>
<td>0.21</td>
<td>(0.08; 0.54)</td>
</tr>
<tr>
<td>Chernobyl Bel, Ukr, Rus</td>
<td>Case-Control</td>
<td>Leukemia</td>
<td>421</td>
<td>824</td>
<td>11/0.9 (cases) 4/0.7 (controls)</td>
<td>3.2</td>
<td>(0.9; 8.4)</td>
</tr>
</tbody>
</table>
## Weapons Production and Testing

<table>
<thead>
<tr>
<th>Study</th>
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<th>ERR @ 100mGy</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Techa River</td>
<td>Cohort</td>
<td>Solid Inc</td>
<td>1,933</td>
<td>17,435</td>
<td>52/15</td>
<td>0.08</td>
<td>(0.01; 0.15)</td>
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<tr>
<td></td>
<td>Cohort</td>
<td>Solid Mort</td>
<td>2,303</td>
<td>29,730</td>
<td>35</td>
<td>0.06</td>
<td>(0.004; 0.13)</td>
</tr>
<tr>
<td></td>
<td>Cohort</td>
<td>Leukemia</td>
<td>72</td>
<td>28,233</td>
<td>250/410</td>
<td>0.22</td>
<td>(0.08; 0.54)</td>
</tr>
<tr>
<td>Hanford I131</td>
<td>Cohort (prevalence)</td>
<td>Thyroid</td>
<td>19</td>
<td>3,191</td>
<td>174/97</td>
<td>0.07</td>
<td>(-0.03; 0.6)</td>
</tr>
<tr>
<td>Utah Fallout</td>
<td>Case-Control</td>
<td>Leukemia</td>
<td>939</td>
<td>4,302</td>
<td>2.9 cases 2.7 controls</td>
<td>4.5</td>
<td>(-0.4; 14)</td>
</tr>
<tr>
<td>Study</td>
<td>Type</td>
<td>Cancer</td>
<td>Cases</td>
<td>Cohort size/Controls</td>
<td>Mean/Median Dose (mGy)</td>
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<tr>
<td>UK</td>
<td>Case-Control</td>
<td>Leukemia</td>
<td>27,447</td>
<td>36,793</td>
<td></td>
<td>12</td>
<td>(3; 22)</td>
</tr>
<tr>
<td>Yiangjing, China</td>
<td>Cohort</td>
<td>Solid</td>
<td>941</td>
<td>31,604</td>
<td>85 High 22 Low</td>
<td>-0.1</td>
<td>(-0.25; 0.3)</td>
</tr>
<tr>
<td>Switzerland</td>
<td>Cohort</td>
<td>Cancer</td>
<td>1,782</td>
<td>2,093,660</td>
<td>9</td>
<td>3</td>
<td>(1; 5)</td>
</tr>
<tr>
<td></td>
<td>Cohort</td>
<td>Leukemia</td>
<td>530</td>
<td></td>
<td></td>
<td>4</td>
<td>(0; 8)</td>
</tr>
<tr>
<td></td>
<td>Cohort</td>
<td>Lymphoma</td>
<td>328</td>
<td></td>
<td></td>
<td>1</td>
<td>(-4; 5)</td>
</tr>
<tr>
<td>Finland</td>
<td>Case-Control</td>
<td>Leukemia</td>
<td>1,093</td>
<td>3,027</td>
<td>1.96 cases 1.90 controls</td>
<td>-1</td>
<td>(-1; 6)</td>
</tr>
<tr>
<td>India, Kerala</td>
<td>Cohort</td>
<td>Solid cancer</td>
<td>1,349</td>
<td>69,958</td>
<td>110</td>
<td>-0.01</td>
<td>(-0.06; 0.05)</td>
</tr>
<tr>
<td>Taiwan Buildings</td>
<td>Cohort</td>
<td>Cancer</td>
<td>117</td>
<td>6,242</td>
<td>48</td>
<td>0.19</td>
<td>(0.01; 0.31)</td>
</tr>
</tbody>
</table>
Issues – Design

• Power is not the only (or in many cases the primary) consideration
• Seek identifiable populations with different levels of exposure
  • Oversample higher dose groups
  • Consider impact of screening
  • Case-cohort designs should be considered (especially with biospecimens or complex dosimetry)
• Consider dosimetry (and uncertainty) in the design phase
  • Focus on (broadly) shared multiplicative errors
  • Seek to keep study-participant data-provision burden reasonable and practical
• Follow-up
  • Identify sources and methods to determine vital status and migration
  • Linkage to cause of death, cancer diagnosis info
Issues -- Confounding

• Not all risk factors are confounders
• Confounding more likely to impact exposed-unexposed comparisons than dose response analyses
• Vague suggestions of confounding are often baseless
• Ascertainment bias can distort risk estimates
  • Stratification can often (but not always) help deal with this
Issues – Dose Uncertainty

• Dose uncertainty unlikely to induce a spurious dose response
• Good, practical methods to adjust for measurement error exists
  • Should be incorporated into the dosimetry system
  • Tend to increase risk estimates and their standard error to the same extent
• Shared multiplicative error (bias) is the most important source of error
  • Adjustment possible but not trivial
    • Increases width of confidence intervals mainly by increasing the upper bound
  • Shared error has essentially no effect on tests of the null hypothesis
References for Specific Studies (1)


References for Specific Studies (2)


Dose uncertainty issues and methods


