Risk of cancer mortality in an international study of nuclear workers (INWORKS)

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Extrapolation from acute to protracted low doses

Transposition of risks from acute to chronic exposure is a major hypothesis of the radiation protection system.

Lack of information on health effects of low dose.
Advantages of nuclear worker studies

- Well defined populations, since mid 40s
- Large size
- Stable work history and good quality of follow-up
- Individual monitoring of external radiation exposure

Very good capacity to characterize the shape of the dose-risk relationship associated with low dose protracted exposure

Epidemiological cohorts first implemented in the 70s

Previous pooling studies (Cardis et al. Rad Res 1995; Cardis et al. BMJ 2005)
INWORKS population

National cohort
n = 59,003

UK NRRW
n = 147,866

US combined cohort
n = 101,428

Workers employed at least 1 year and monitored for external exposure to ionizing radiation (individual dosimeters)

- CEA civil
- AREVA NC
- EDF

- UK Atomic Energy Authority
- British Nuclear Fuels plc
- British Energy Generation and Magnox Electric Ltd
- Atomic Weapons Establishment
- Ministry of Defence

- Hanford Site
- Idaho National Laboratory
- Oak Ridge National Laboratory
- Portsmouth Naval Shipyard
- Savannah River Site

308,297 workers
Objectives of INWORKS

To improve the quantification of the dose-risk relationship associated with low dose protracted external radiation exposure

- What is the gain in statistical power provided by the pooling of the 3 cohorts?

- Are dose-risk relationships observed among nuclear workers similar to those derived from the A-Bomb survivors?

- What does it bring regarding the current radiation protection system?
## Characteristics of the INWORKS cohort 1943-2005

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of workers</td>
<td>308,297</td>
</tr>
<tr>
<td>Males</td>
<td>87%</td>
</tr>
<tr>
<td>Mean age at last observation</td>
<td>58</td>
</tr>
<tr>
<td>Mean duration of employment in years</td>
<td>15</td>
</tr>
<tr>
<td>Mean duration of follow-up in years</td>
<td>27</td>
</tr>
<tr>
<td>Total person years (million)</td>
<td>8.2</td>
</tr>
<tr>
<td>Mean cumulative whole body dose (mSv)</td>
<td>24 (max 1.6 Gy)</td>
</tr>
<tr>
<td>Vital status</td>
<td></td>
</tr>
<tr>
<td>Deceased</td>
<td>66,632 22%</td>
</tr>
<tr>
<td>Cancers excluding leukemia</td>
<td>19,064</td>
</tr>
<tr>
<td>leukaemia excluding CLL*</td>
<td>531</td>
</tr>
<tr>
<td>circulatory diseases</td>
<td>27,848</td>
</tr>
<tr>
<td>Emigrated or lost to follow-up</td>
<td>4,752 &lt;2%</td>
</tr>
</tbody>
</table>

### Good homogeneity of data quality
Increased statistical power
Long duration of follow-up

* chronic lymphocytic leukaemia
RR per Gy : cancer excluding leukemia

Note: The number of cancers in the lowest dose category (10,433 deaths) has not been annotated on this figure for reasons of legibility.
Colon dose – lag 10 years
Stability of the dose-risk relationship

Sensitivity analyses

- Excluding females
- Excluding specific cancer sites
- Exclusion one of the three countries
- Changing lag (5 or 15 years)
- Replacing colon dose by recorded photon dose
- Testing different shapes of dose-risk response (linear, quadratic, LQ)
- Excluding individuals with neutron flag
- Excluding individuals with internal contamination flag
- Testing alternative stratification
ERR of cancer excluding leukemia over restricted ranges

ERR/Gy cancer excluding leukemia

<table>
<thead>
<tr>
<th></th>
<th>ERR per Gy</th>
<th>CI 90%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whole dose range</td>
<td>0.48</td>
<td>0.20, 0.79</td>
</tr>
<tr>
<td>Cumulative dose &lt; 200 mGy</td>
<td>1.04</td>
<td>0.55, 1.56</td>
</tr>
<tr>
<td>Cumulative dose &lt; 150 mGy</td>
<td>0.69</td>
<td>0.10, 1.30</td>
</tr>
<tr>
<td>Cumulative dose &lt; 100 mGy</td>
<td>0.81</td>
<td>0.01, 1.64</td>
</tr>
</tbody>
</table>

Colon dose, 10-y lag

[Richardson et al, BMJ 2015]

Relationship statistically significant over dose range 0 - > 100 mSv

Large uncertainty remains at very low doses (below few tens of mGy)
Quantifying the dose-risk relationship at low dose
Quantifying the dose-risk relationship at low dose

Risk

Dose

Were are we?
Comparison with LSS

15-country study

INWORKS

Life Span Study
(men exposed at age 20-60 years)

Solid cancer

ERR per gy

-0.5  0  0.5  1  1.5  2

0.87 (4 770)

0.47 (17 957)

0.37 (3 475)
Conclusion

- Large capacity to demonstrate a dose-risk relationship associated with protracted exposure to external radiation (statistical power, homogeneity of data quality). Presents limits as every epidemiological study (dose uncertainties, no data on other risk factors, only mortality, limited age at end of follow-up)

- Dose-risk relationship observed between cumulated external exposure and mortality from cancer risk. No more significant below several tens of mGy

- Relationship appears stable (small heterogeneity between countries, small variation in sensitivity analyses)

- Risk coefficients similar to those derived from the A-bomb survivors study

- Results compatible with the extrapolation from acute high dose to low chronic dose, which is a main underlying hypothesis of the current radiation protection system.

- Results are not in favour of the hypothesis of a reduction of radiation effect at low dose and low dose rate (DDREF)

- Complementary to radiobiological research
Publications


- Other papers in preparation
INWORKS partners

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