## Epidemiologic Studies of Nuclear Workers

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## Radiation workers

- **Nuclear industry workers**
- Chernobyl clean-up workers
- Airline and aerospace employees
- Medical and dental occupational exposures

## What is a Nuclear Worker?

Involved in the
- production of nuclear power
- manufacture of nuclear weapons
- enrichment and processing of nuclear fuel
- reactor or weapons research

Does not include medical and dental workers or underground miners

## What is a Nuclear Worker?

## Nuclear Worker Studies

- **Workers exposed to low doses of external radiation**
- Mayak workers
  - Exposed to high protracted external doses
  - Plutonium

## Why study workers exposed to low doses of external radiation?

- Current risk estimates based on A-bomb survivors and others exposed at high dose rates
- For risk assessment, interest is primarily in low doses and dose rates
- Uncertainty in the extrapolation process

## Why study workers?

- Dose estimates obtained from personal dosimeters worn by workers
- Exposures deliberately limited as a protection to the worker
- Provide a direct assessment of risks at low doses and dose rates
- Limitations, but worker studies can detect serious underestimation of risk

## Magnitude of Doses

Current risk estimates:
Driven by doses of 0.5+ Gy
Worker-based estimates:
Driven by doses 0.1-0.5 Gy
Of interest for risk assessment:
0 - 0.1 Gy

## Predicted relative risks* for adult male exposed at low dose rate

| Dose | Solid cancers | Leukemia |
|---|---|---|
| 1 Sv | 1.2 | 2.4 |
| 0.5 Sv | 1.1 | 1.7 |
| 0.2 Sv | 1.03 | 1.3 |
| 0.1 Sv | 1.02 | 1.1 |
| 0.01 Sv | 1.002 | 1.01 |

*Based on BEIR VII models developed from A-bomb survivor data

## History of Studies of Workers at Individual Facilities

| Population | Country | Publication Date(s) |
|---|---|---|
| Hanford Site | US | 1978, …, 1993 |
| Oak Ridge Nat'l Lab. | US | 1985, 1991 |
| Atomic Energy Authority | UK | 1985, 1993 |
| Sellafield Plant | UK | 1986, 1994, 1999 |
| Rocky Flats Weapons Plant | US | 1987 |
| Atomic Energy of Canada | Canada | 1987 |
| Atomic Weapons Establish. | UK | 1988 |
| Savannah River Plant | US | 1988, 1999 |
| Mound Laboratory | US | 1991 |
| Los Alamos Nat'l Lab. | US | 1994 |
| Rocketdyne | US | 1999, 2006 |
| Mallinckrodt Chemical | US | 2000 |

## History of Studies of Workers

| Population | Country | Publication Date |
|---|---|---|
| National Registry of Radiation Workers | UK | 1992, 1999 |
| National Dose Registry | Canada | 1998, 2001 |
| Nuclear reactor workers | Finland | 2002 |
| Nuclear industry workers | Japan | 1997, 2003 |
| Nuclear power workers | US | 2004 |
| Nuclear power workers | Canada | 2004 |
| Atomic Energy Commission | France | 2004 |
| National Electricity Co. | France | 2005 |
| Nuclear workers | Belgium | 2005 |
| Idaho National Engineering and Environmental Lab. | US | 2005 |
| Nuclear industry workers | Australia | 2005 |

## Approaches to Analyses

External Comparisons:
Compare cause-specific death rates with national rates (SMRs)

Internal comparisons:
Compare cause specific death rates by level of cumulative radiation dose

## Standardized Mortality Ratios (Numbers of Deaths)

| Population | All Causes | All Cancers |
|---|---|---|
| **United States:** | | |
| Hanford Site | 0.82 (9,452) | 0.86 (2,195) |
| Oak Ridge | 0.74 (1,524) | 0.79 (346) |
| Rocky Flats | 0.62 (409) | 0.71 (95) |
| Mound | 0.79 (309) | 0.88 (66) |
| Los Alamos | 0.63 (3,196) | 0.64 (732) |
| Savannah River | 0.78 (1,722) | 0.82 (413) |
| Rocketdyne | 0.68 (844) | 0.79 (248) |
| Mallinckrodt | 0.90 (1,013) | 1.05 (283) |

## Approaches to Analyses

**External Comparisons:**
Compare cause-specific death rates with national rates (SMRs)

**Internal comparisons:**
Compare cause-specific death rates by level of cumulative radiation dose

## Internal comparisons

- Linear relative risk model:
  RR = 1 + B dose, where B = ERR/Sv
- Choice of models driven by findings from A-bomb and other high dose studies

## Results of Dose-Response Analyses for Studies of Individual Facilities

- **All cancers:** Most studies consistent both with no risk and risks several times those predicted from high dose studies
- **Leukemia:** Significant dose-response in some but not all studies.
- **Site-specific cancers:** No consistent pattern across studies

## Combined Analyses

- Obtain more precise estimates of risk
- Opportunity for understanding differences and similarities in studies
  - Comparable statistical methods
  - Results in comparable format
- Best overview or summary of studies

## Combined Studies of Workers

| Population | Country | Publications |
|---|---|---|
| Hanford/Oak Ridge/Rocky Flats | US | 1989, 1993 |
| AEA/AWE/Sellafield | UK | 1994 |
| IARC* 3-country | US/UK/Canada | 1994, 1995 |
| • 96,000 workers in the US, UK, and Canada | | |
| IARC* 15-country | | 2005, 2007 |

*International Agency for Research on Cancer

## IARC 15-Country Study

- Main findings published in British Medical Journal (Cardis et al. 2005)
- 3 papers published in Radiation Research
  - Cancer risks (Cardis et al. 2007)
  - Methods (Vrijheid et al. 2007)
  - Dosimetry (Thierry-Chef et al. 2007)

## IARC* 15-Country Nuclear Worker Study

- Nearly 600,000 workers employed in 154 facilities in 15 countries
- Exclusions
  - Employed < 1 year (113,711 workers)
  - Not monitored for external radiation (38,521 workers)
  - Potential for internal contamination (39,720 workers)
  - Potential for substantial neutron dose (19,041 workers)
- Main study population includes 407,291 workers
  - Largest worker study ever conducted

*International Agency for Research on Cancer

Cardis et al. 2005

## IARC* 15-Country Nuclear Worker Study

- 407,391 workers (after exclusions)
  - 90% male
  - Includes most workers in previous studies in US, UK, and Canada
  - Several new studies in US and other countries
- Mean cumulative dose of 19.4 mSv
- Collective dose of 7892 person-Sv

*International Agency for Research on Cancer

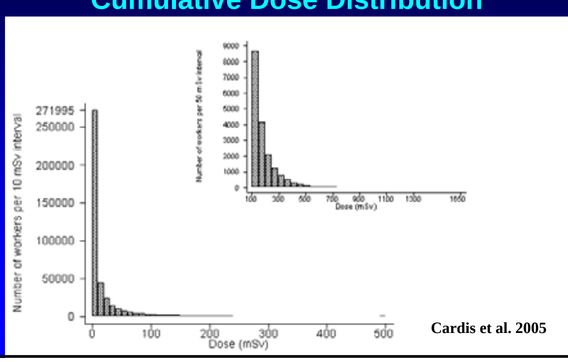
Cardis et al. 2005

## Dosimetry for 15-Country Study

- Extensive attention given to dosimetry
  - Dosimetry subcommittee
  - Questionnaires on dosimetry practices and radiation environments
  - Special studies of representative facilities
  - Testing of several representative dosimeters
- Objective: Develop factors for converting recorded doses to organ doses and evaluate uncertainties in these factors

Thierry-Chef et al. 2007

## 15-Country Study: Cumulative Dose Distribution




Cardis et al. 2005

## 15-Country Study (Cancer deaths)

United States (2,841)
United Kingdom (2,273)
Japan* (432)
Canada (417)
France (348)
Sweden (194)

Belgium (90)
Hungary (40)
Finland (34)
Lithuania (25)
Spain (25)
Korea (21)
Switzerland (24)
Australia (20)
Slovakia (10)

*Included only in leukemia analyses

Cardis et al. 2005

## 15-Country Study (Cancer deaths)

- United States Studies (2,841)
  - Hanford (1,279)
  - Idaho National Engineering Laboratory* (886)
  - Nuclear Power Plant Workers (314)
  - Oak Ridge National Laboratory (225)

*Included only in leukemia analyses

Cardis et al. 2005

## Excess Relative Risk (ERR) per Gy for All Cancers Excluding Leukemia

| | |
|---|---|
| 3-country study: | –0.07 (–0.29, 0.30) |
| 15-country study: | 0.97 (0.14, 1.97) |
| A-bomb survivors*: | 0.32 (0.01, 0.50) |

*Estimates for males exposed at ages 20-60

Cardis et al. 2005

## Excess Relative Risk (ERR) per Gy for Leukemia excluding CLL

| | |
|---|---|
| 3-country study: | 2.2 (0.13, 5.7) |
| 15-country study: | 1.9 (< 0, 8.5) |
| A-bomb survivors*: | |
| Linear | 3.2 (1.6, 5.7) |
| Linear-quadratic | 1.5 (<0, 5.3) |

*Estimates for males exposed at ages 20-60

Cardis et al. 2005

## Number of leukemias (excluding CLL) by 2-year lagged cumulative dose

| Cumulative Dose (mSv) | IARC 3-country | IARC 15-country |
|---|---|---|
| 0- | 60 | 135 |
| 10- | 19 | 23 |
| 20- | 14 | 19 |
| 50- | 8 | 9 |
| 100- | 8 | 6 |
| 200- | 4 | 3 |
| 400+ | 6 | 1 |
| Total | 119 | 196 |

Cardis et al. 2007

## Number of cancers excluding leukemia by 10-year lagged cumulative dose

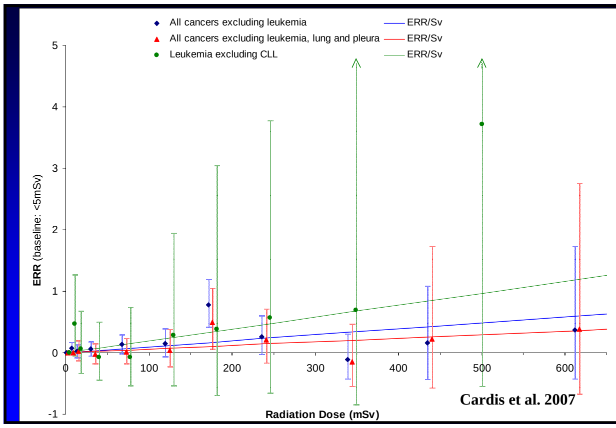
| Cumulative Dose (mSv) | IARC 3-country | IARC 15-country |
|---|---|---|
| 0- | 2234 | 3547 |
| 10- | 462 | 500 |
| 20- | 445 | 476 |
| 50- | 276 | 249 |
| 100- | 196 | 165 |
| 200- | 161 | 75 |
| 400+ | 56 | 12 |
| Total | 3830 | 5024 |

Cardis et al. 2007

## Excess Relative Risk (ERR) per Gy for 15-Country Study

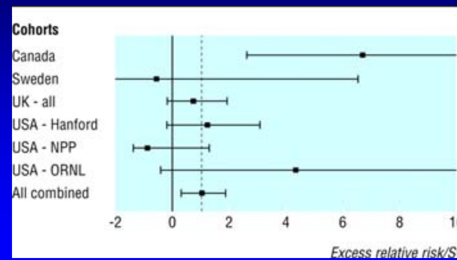
| | |
|---|---|
| All solid cancers (4770) | 0.87 (0.02, 1.9) |
| Solid cancers unrelated to smoking (2033) | 0.62 (–0.5, 2.2) |
| Smoking related cancers (2737) | 0.91 (–0.1, 2.2) |
| Lung cancer | 1.85 ( 0.26, 4.0) |
| Other smoking-related cancers | 0.21 (< 0, 2.0) |

Cardis et al. 2005




Cardis et al. 2007

## Heterogeneity Among Countries
## All Cancer Excluding Leukemia




Cardis et al. 2005

## Heterogeneity Among Countries
## All Cancer Excluding Leukemia

- p-value for heterogeneity = 0.18
- Estimate with all countries: 0.97 (0.14, 2.0)
  Estimate with Canada excluded: 0.58 ( –0.2, 1.6)
- Estimate remained statistically significant when other studies were excluded individually

Cardis et al. 2005

## IARC 3-Country Study

| | All cancer excluding leukemia | Leukemia excluding CLL |
|---|---|---|
| Standard* | 0.97 (0.27, 1.8) | 1.9 (<0, 7.1) |
| No SES | 1.24 (0.52, 2.1) | 2.2 (<0, 7.6) |
| No employment duration | 0.31 (-0.2, 0.9) | 0.8 (<0, 4.6) |

*Adjusted for age, calendar year, sex, SES, and employment duration

Cardis et al. 2007

## IARC 3-Country Study:
## Site-specific cancers

- 31 site-specific cancers evaluated
- Dose-response relationships suggested for
  - Lung cancer: 0 = 0.01
  - Multiple myeloma: p = 0.06
  - Ill defined and secondary cancers: p =0.06

Cardis et al. 2007

## Number of leukemias multiple myelomas by 10-year lagged cumulative dose

| Cumulative Dose (mSv) | IARC 3-country | IARC 15-country |
|---|---|---|
| 0- | 28 | 68 |
| 10- | 3 | 4 |
| 20- | 1 | 3 |
| 50- | 5 | 4 |
| 100- | 3 | 3 |
| 200- | 2 | 1 |
| 400+ | 2 | 0 |
| Total | 44 | 83 |

Cardis et al. 2007

## IARC 15-Country Study Modifying Factors

- Little evidence that risks modified by
  - Sex
  - Type of facility
  - Attained age
  - Age at exposure
- Statistical power for detecting such modification limited

## Limitations of Low Dose Worker Studies

- Increase in risk likely to be at most a few percent
- Low statistical power and imprecisely estimated risks
- Strong potential for confounding

## What is the Role of Low-Dose Nuclear Worker Studies?

- Most informative of studies of persons exposed at low doses and dose rates
- Statistical uncertainties and high potential confounding impose important limitations

## Radiation workers

- Nuclear industry workers
- Chernobyl clean-up workers
- Airline and aerospace employees
- Medical and dental occupational exposures

## Medical Radiation Workers

| Population | Number of workers |
|---|---|
| US radiologists | 6500 |
| UK radiologists | 2700 |
| US technologists | 146,000 |
| US Army technologists | 6600 |
| Chinese x-ray workers | 27,000 |
| Danish radiation therapy workers | 4200 |
| Japanese technologists | 12,200 |
| Canadian radiation workers | 73,100 |

Yoshinaga et al. 2004

## US Radiologic Technologist Cohort

- 146,000 radiologic technologists 1926-82
  - 73% females
- Health endpoints
  - Cancer mortality
  - Non-cancer mortality
  - Cancer incidence
  - Some benign diseases
    - Cataracts

Collaborative study – NCI and U. of Minnesota

## US Radiologic Technologist Cohort

- Fractionated external exposure
  - Doses quite high in early calendar years (before 1950)
- Excesses for early years identified for
  - Breast cancer
  - Thyroid cancer
  - Melanoma
  - Basal cell carcinoma
  - Non-CLL leukemia

Collaborative study – NCI and U. of Minnesota

## US Radiologic Technologist Cohort

- 3 surveys conducted
- Provide information on
  - Disease incidence
  - Work history and practices
  - Cancer risk factors
    - smoking
    - physical activity
    - weight
    - several factors

Collaborative study – NCI and U. of Minnesota

## US Radiologic Technologist Cohort

- Estimates of dose (and uncertainties) have recently been developed
- Make use of
  - Monitoring data
  - Survey data on work histories and practices
  - Historical information on occupational doses
- Dose-response analyses underway

Collaborative study – NCI and U. of Minnesota

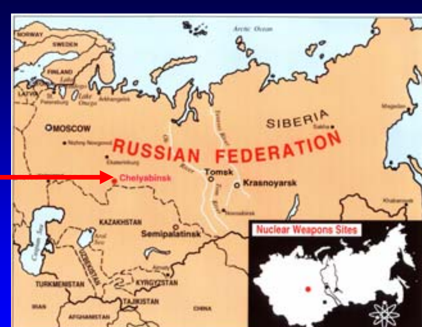
## Nuclear Worker Studies

- Workers exposed to low doses of external radiation
- Mayak workers
  - Exposed to high protracted external doses
  - Plutonium

## Mayak Nuclear Facility

- Located in the town of Ozyorsk (formerly Chelyabinsk-65) in the Chelyabinsk region of the Russian Federation
- Began operations in 1948
- Mission was to produce plutonium for USSR nuclear weapons program
- Large exposures to both workers and general public, mostly in the 1940's and 1950's

Mayak nuclear facility



## Mayak, Ozyorsk, Chelyabinsk, Russia

## Important Features of Mayak Cohort

- Large protracted external doses
- Both male and female workers exposed
- Substantial exposure from internally deposited plutonim

## Mayak Nuclear Facility

- 21,800 workers hired 1948-72
- 24% female

| Plant | Workers | Exposure |
|---|---|---|
| Reactor | 4400 | External |
| Radiochemical | 7900 | External + Plutonium |
| Plutonium | 6500 | External + Plutonium |
| Auxiliary | 2700 | Little potential |

## Mayak Dosimetry

**External exposure**

- Monitored for external exposure with individual film badges

**Plutonium exposure**

- Dose estimates based on urine monitoring data
- Initial models and methods developed by Russian scientists

## Plutonium Dosimetry

- Urine monitoring data available for only 40% of those with potential for plutonium exposure
- Plutonium surrogate based on work history developed
  - Not used for quantifying the plutonium dose-response
  - Used to adjust analyses addressing external dose

## Mayak Dosimetry

- Extensive collaborative effort of US and Russian scientists to improve both external and internal dose estimates
- Improved doses known as Doses 2005

## Mayak Workers: Mean External Lung Dose (Gy)

| | |
|---|---|
| All main plant workers | 0.54 |
| Males | 0.57 |
| Females | 0.44 |
| Hired 1948-58 | 0.74 |
| Hired 1959-72 | 0.18 |
| IARC 15-country study | 0.02 |

## Mayak Workers: Number with External Lung Doses Exceeding 1 Gy

| | |
|---|---|
| All main plant workers | 3174 |
| Males | 2491 |
| Females | 688 |
| Hired 1948-58 | 3052 |
| Hired 1959-72 | 127 |

## Results: External Dose

Reference:

- Shilnikova et al. Cancer mortality risk among workers at the Mayak nuclear complex (Radiat. Res. 2003)
- Not based on most recent dose estimates (Doses 2005)
- Analyses adjusted for plutonium exposure

## Solid Cancer and External Dose

- Statistically significant increase in solid cancer risk with dose (p < .001)
- Remained statistically significant when lung, liver, and bone cancers were excluded

Shilnikova et al. 2003

## Leukemia and External Dose

- Statistically significant increase in leukemia risk with dose (p < .001)
- No evidence of modification by sex or age at hire
- Strong evidence (p < .001) of dependence on time since exposure with larger risks for more recent doses

Shilnikova et al. 2003

## Leukemia and External Dose

| Years since dose received | ERR* per Gy |
|---|---|
| 3 - 5 years | 7.6 (3.2, 17) |
| 5 + years | 0.45 (0.1, 1.1) |
| 5 - 10 | 0.3 |
| 10 - 20 | 0.8 |
| 20+ | 0.4 |

*Excess relative risk

Shilnikova et al. 2003

## Results: External Dose

- Analyses based on improved dose estimates (Doses 2005) underway
- Includes evaluation of site-specific cancer risks
  - External dose
  - Plutonium exposure

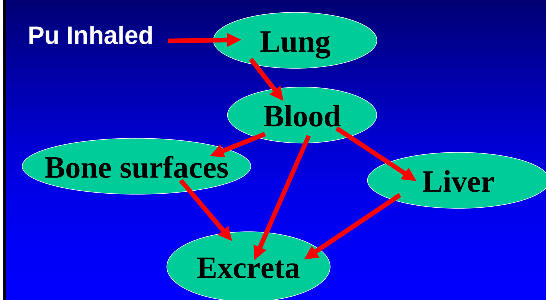
## Plutonium: "The most hazardous substance known to man?"



## Plutonium Concerns

- Occupational Exposure
  - Plutonium production
  - Nuclear Fuel Reprocessing
  - Clean-up operations
- General Public
  - Reactor accidents
  - Nuclear wastes
  - Space accidents


## An Overly Simple View of Inhaled Plutonium Dynamics




## Studies of Workers Exposed to Low Doses from Plutonium

- US: Los Alamos, Rocky Flats Mound, Hanford
- UK: Sellafield

## Studies of Workers Exposed to Low Doses from Plutonium: Summary

- Strong "healthy worker effect" (US)
- No clear evidence of adverse effects
- Sample sizes and exposures too small for meaningful risk assessment

## Mayak Workers: Previous analyses of lung, liver and bone cancer risks

- Lung cancer risks evaluated by
  - Tokarskaya et al. (1997)
  - Koshurnikova et al. (1998)
  - Kreisheimer et al. (2000)
  - Gilbert et al. (2003)
- Bone and liver cancer risks evaluated by
  - Koshurnikova et al. (2000)
  - Gilbert et al. (2000)
  - Tokarskaya et al. (2006)

## Plutonium doses for Mayak and Sellafield workers

| | Mayak | Sellafield |
|---|---|---|
| Mean dose (Gy) to | | |
| Lung | 0.19 | 0.010 |
| Liver | 0.27 | 0.005 |
| Bone surfaces | 0.98 | 0.036 |

## Plutonium body burdens for Mayak and US workers

| Exposure | Number of Mayak workers |
|---|---|
| 1.5 – 3.7 kBq | 446 |
| 3.7 – 7.4 kBq | 172 |
| 7.4 – 18.5 kBq | 107 |
| 18.5 – 173 kBq | 94 |
| 1.5+ kBq | 819 |

- Highest burden among US workers: 3.2 kBq

## Features of Mayak plutonium analyses

- Analyses adjusted for
  - sex
  - attained age
  - birth cohort
  - smoking status (lung cancer)
  - external dose
- Based on Doses 2005

## Limitations in Mayak Data

- For liver and bone cancer
  - Number of excess cases is small
  - Risk at low doses very uncertain
- Limited data on confounders
- Dosimetry
  - Uncertainties could affect both magnitude of risk and shape of dose-response

## Uncertainties in Plutonium Dosimetry

- Imprecision in urine measurements
- Uncertainties in when plutonium exposure occurred and form of plutonium
- Uncertainties in biokinetic models and parameter values used to estimate deposition and clearance in organs of the body
- Models can only approximate behavior of plutonium in a given individual

## Summary Comments

- Mayak worker cohort is a unique resource for evaluating the risk of cancer from
  - Protracted external exposure
  - Plutonium exposure
- Recognize limitations

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