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
IARC* 15-country		2005, 2007

- 96,000 workers in the US, UK, and Canada

*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

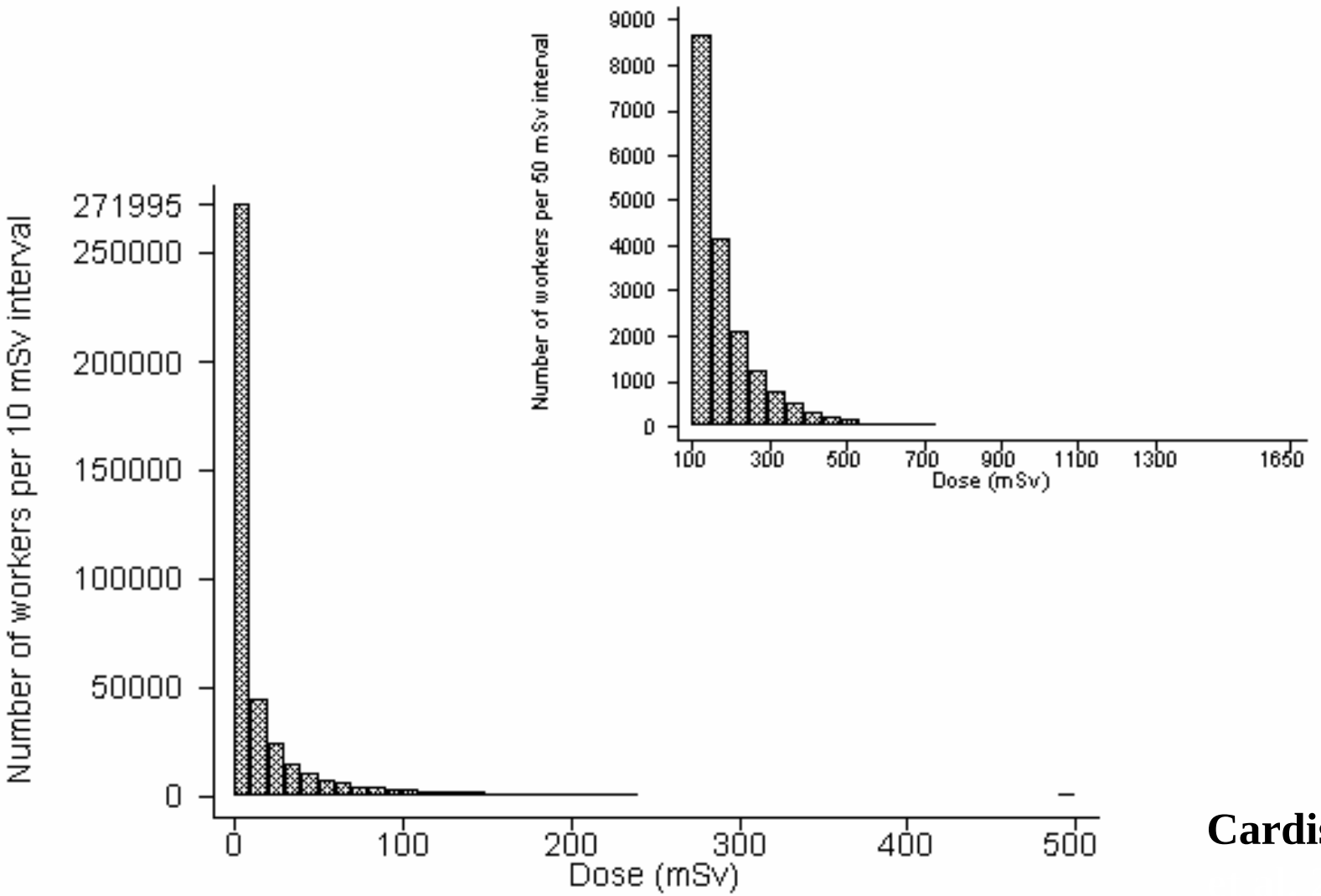
Dosimetry for 15-Country Study

- **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

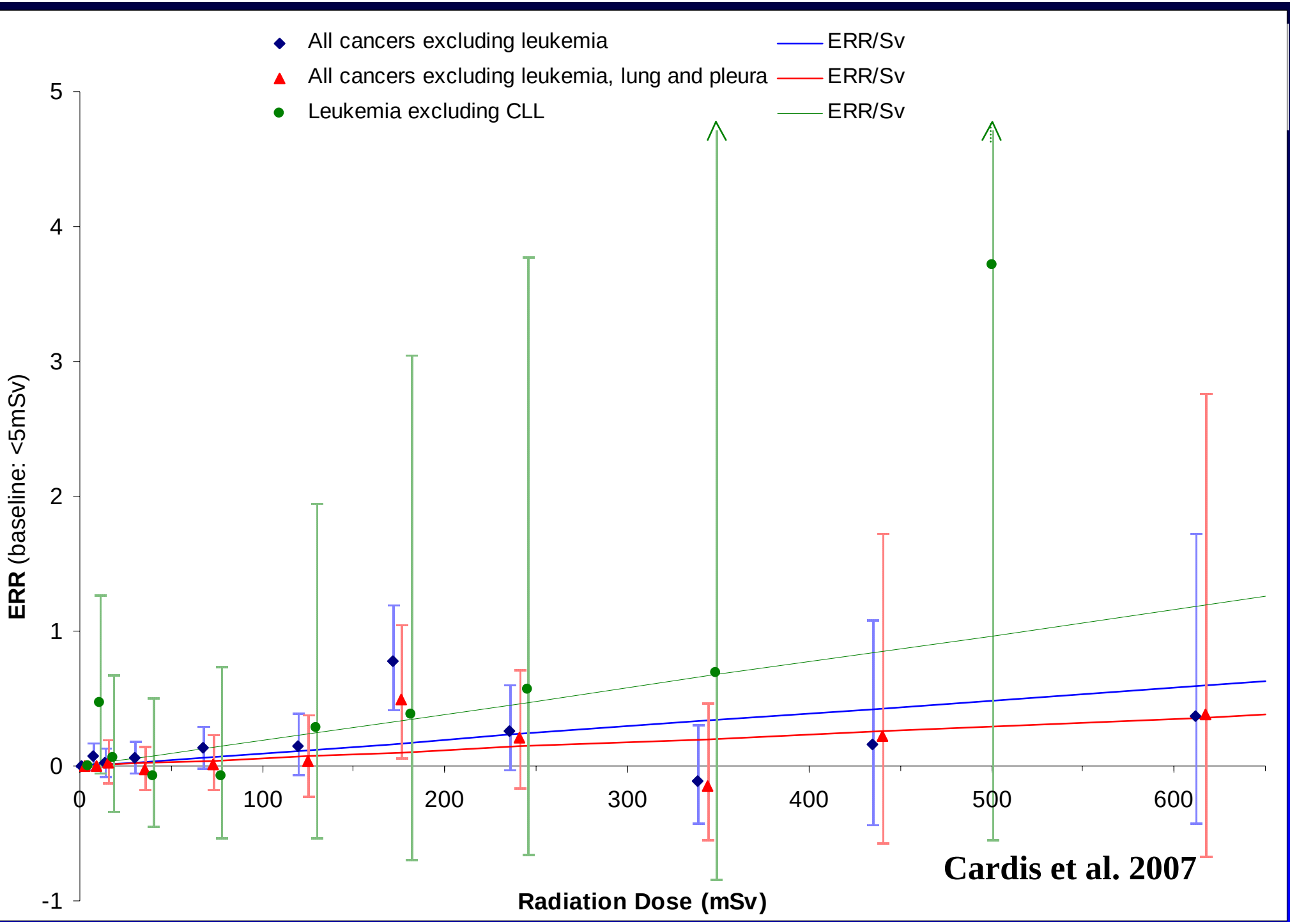
Cumulative Dose (mSv)	IARC 3-country	IARC 15-country
0-	2234	3547
10-	462	500
20-	445	476
50-	276	249
100-	196	165
200-	161	75
400+	56	12
Total	3830	5024

Cardis et al. 2007

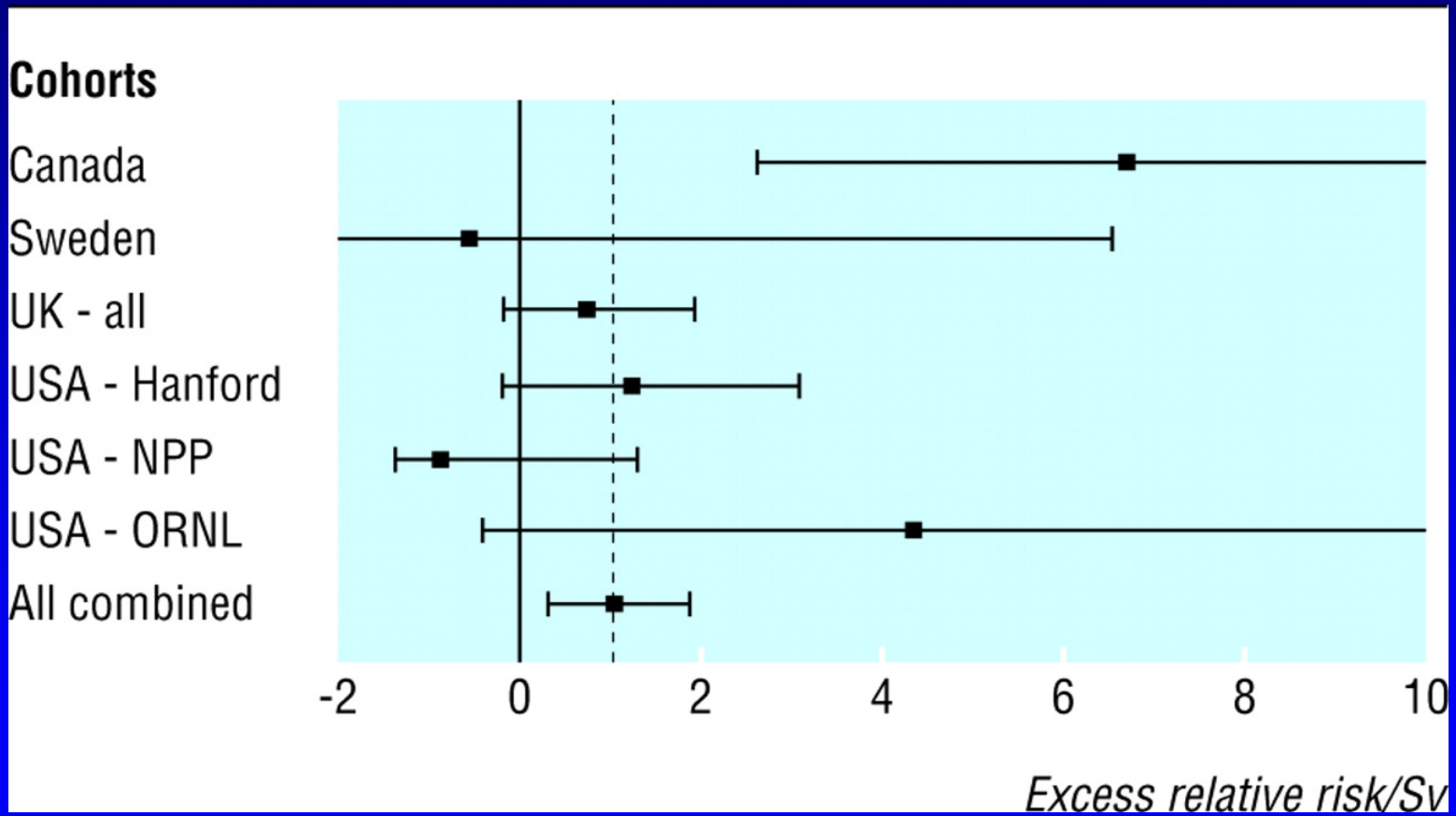
Excess Relative Risk (ERR) per Gy for 15-Country Study

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


All cancers excluding leukemia
ERR/Sv
All cancers excluding leukemia, lung and pleura
ERR/Sv
Leukemia excluding CLL
ERR/Sv
ERR (baseline: <5mSv)
5
4
3
2
1
0
-1
0
100
200
300
400
500
600
Radiation Dose (mSv)
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

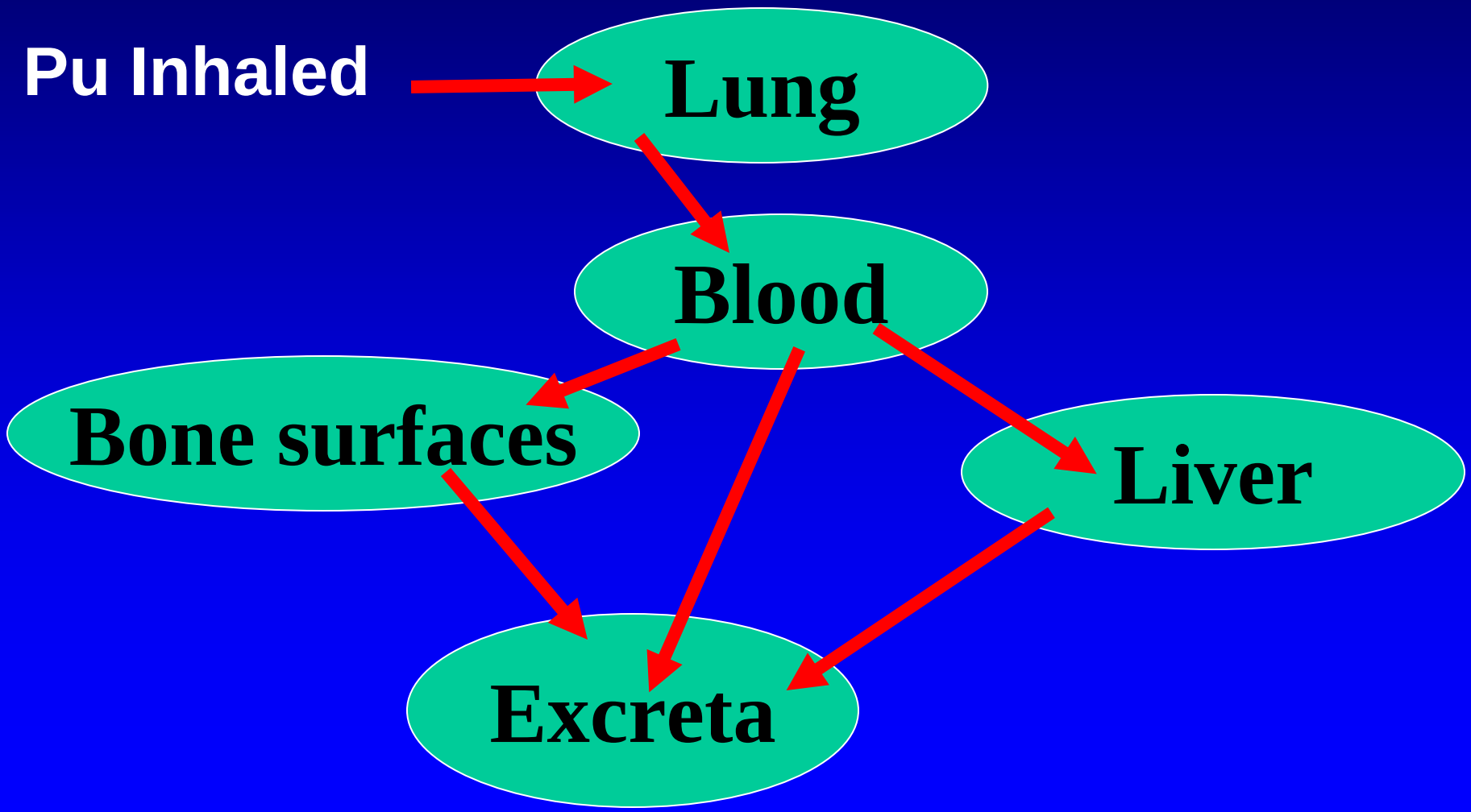
- Analyses based on improved dose estimates (Doses 2005) underway
- Includes evaluation of site-specific cancer risks
  - External dose
  - Plutonium exposure

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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