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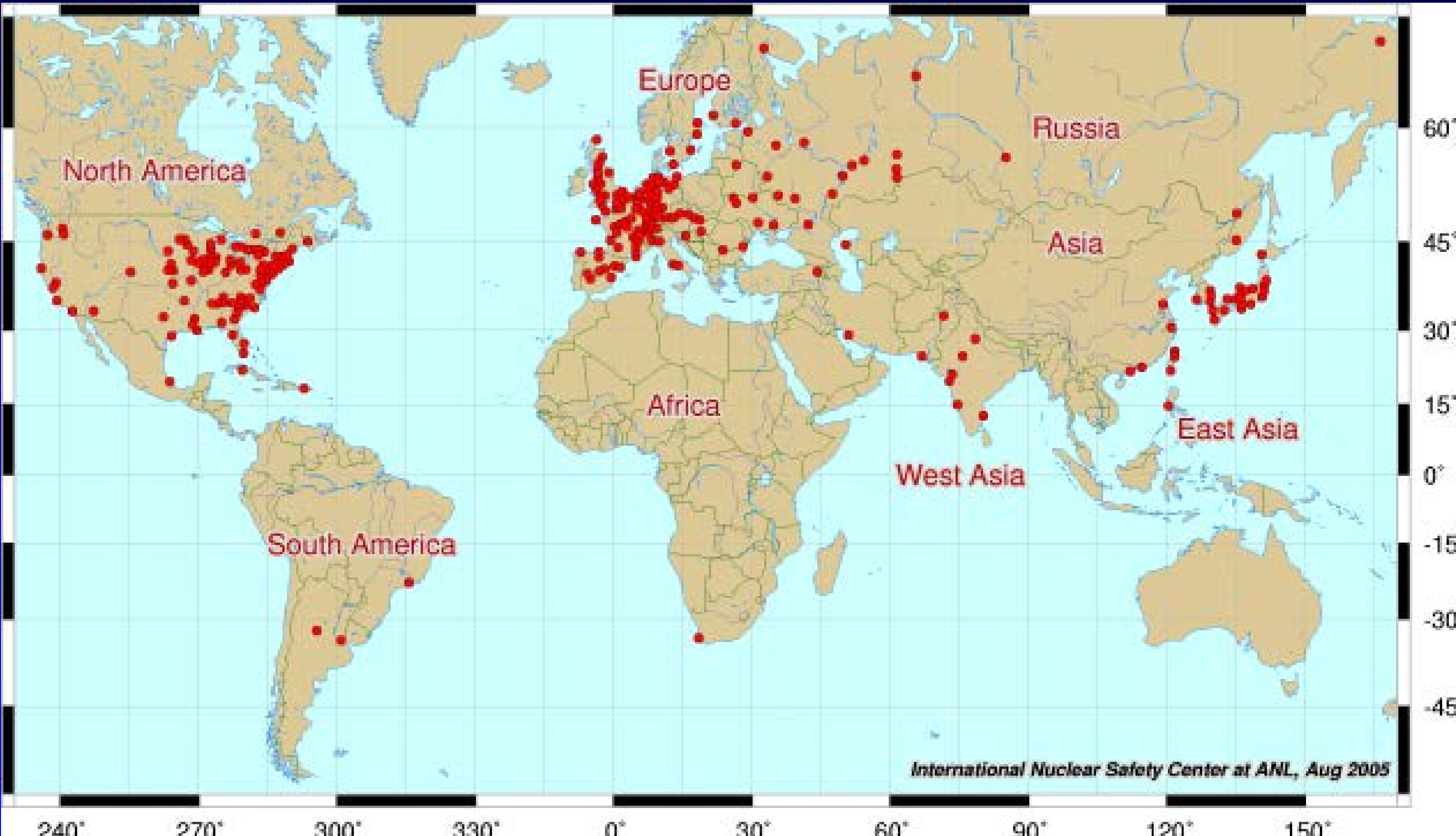
Radiation Workers Throughout the World

Radiation Epidemiology & Dosimetry Course

National Cancer Institute
www.dceg.cancer.gov/RadEpiCourse


Europe
Russia
North America
Asia
Africa
East Asia
West Asia
South America
International Nuclear Safety Center at ANL, Aug 2005
60°
45°
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240°
270°
300°
330°
0°
30°
60°
90°
120°
150°

Nuclear Workers

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

Nuclear Worker Studies

- Nuclear workers exposed to low doses of external radiation

- Mayak nuclear workers
  - Exposed to high protracted external doses
  - Plutonium

- Medical and dental workers

Why Study Nuclear 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

Advantages of Studying Workers

- Dose estimates obtained from personal dosimeters worn by workers

Advantages of Studying 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 rRate

Dose	Solid cancers	Leukemia
1 Gy	1.2	2.4
0.5 Gy	1.1	1.7
0.2 Gy	1.03	1.3
0.1 Gy	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, 2014
Los Alamos Nat'l Lab.	US	1994
Rocketdyne	US	1999, 2006, 2011
Mallinckrodt Chemical	US	2000

History of Studies of Workers

Population	Country	Publication Date
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

+ many more recent studies

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

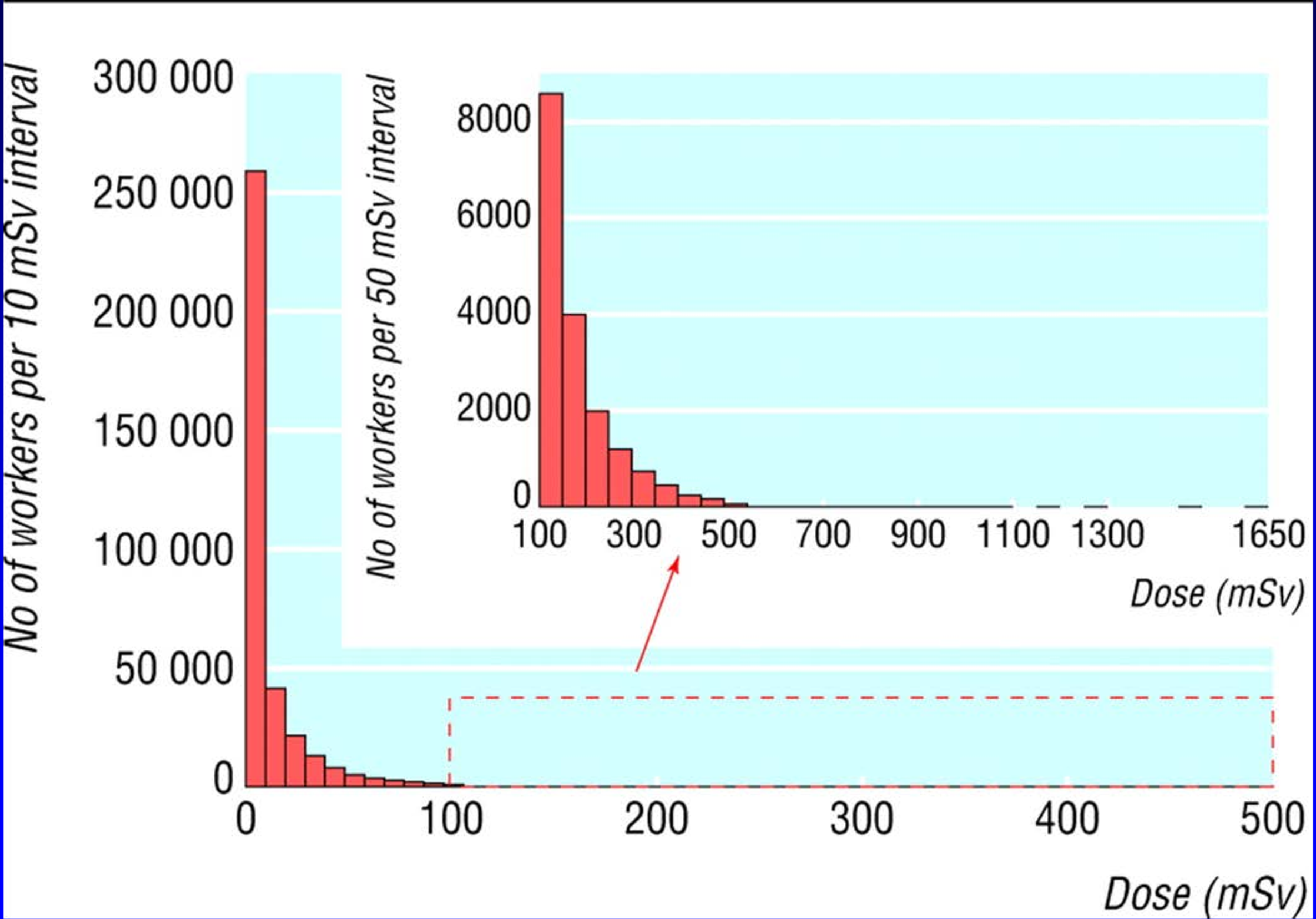
External Comparisons:

Compare cause-specific death rates with national rates (SMRs)

Internal comparisons:

Compare cause-specific death rates by level of cumulative radiation dose

Cumulative Dose Distribution



Internal Comparisons

- **Linear relative risk model:**
  RR = 1 + B dose, where B = ERR/Gy

- **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 studies Japanese A-bomb survivors

- **Leukemia:** Significant dose-response in some but not all studies.

- **Site-specific cancers:** No consistent pattern across studies

Interpreting Data from Multiple Studies

- Wealth of epidemiologic data pertaining to radiation workers
- How can be best summarize these data?

Pooled Analyses

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

Pooled Worker Studies

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 Nuclear Worker Study

- 407,391 workers (after exclusions)
  - 90% male
- Date of last follow-up: 1984-2000
- Mean cumulative dose of 19.4 mSv

*International Agency for Research on Cancer

Cardis et al. 2005, 2007

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 (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: ERR/Gy (90% CI)

	All cancer excluding leukemia	Non-CLL Leukemia
15-country	0.97 (.27, 1.8)	1.9 (<0, 7.1)
A-bomb survivors*	0.26 (0.14, 0.41) (linear)	1.4 (0.1, 3.4) (linear-quadratic)

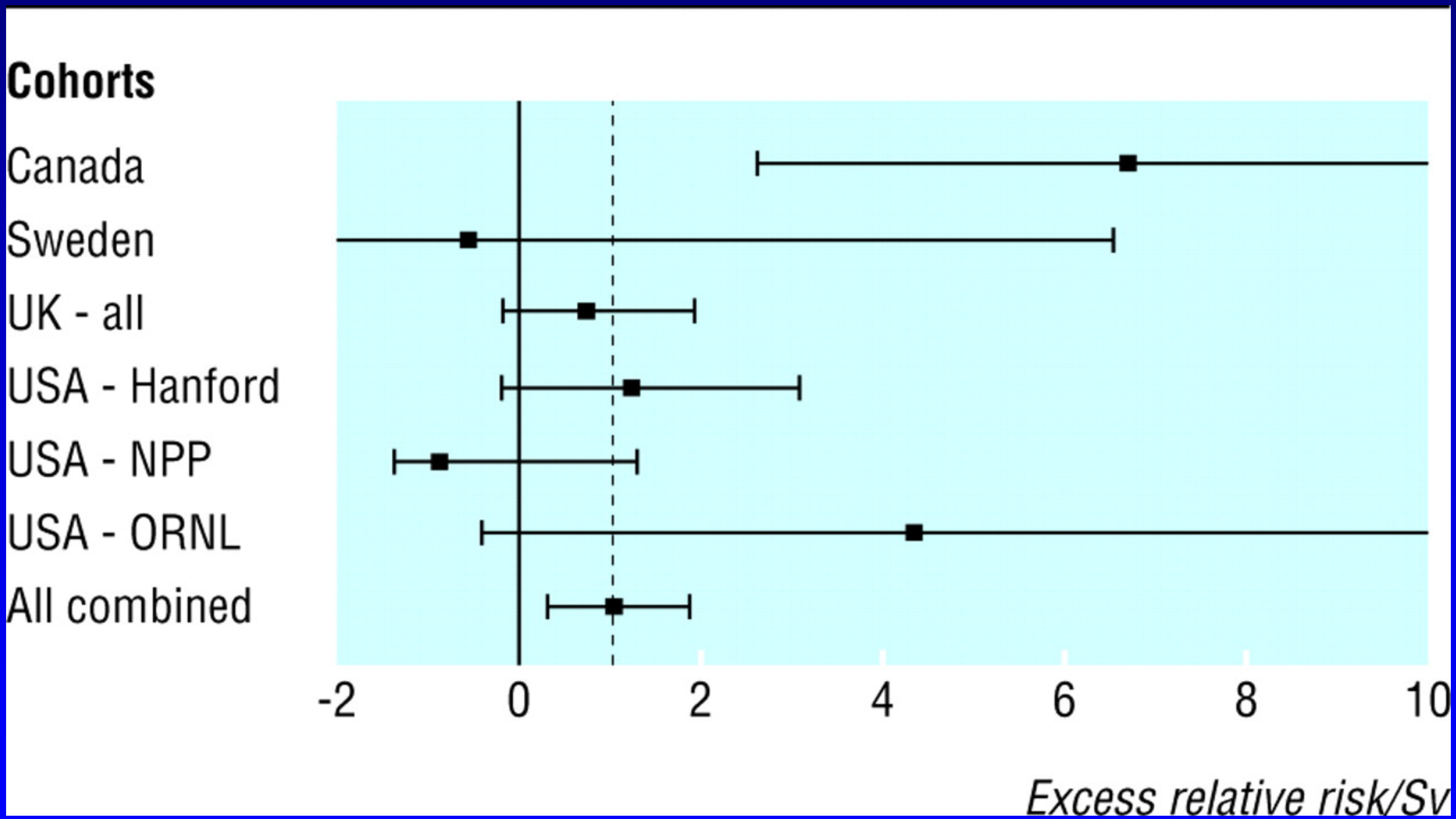
*BEIR VII for adult males

Cardis et al. 2007

Comments on 15-Country Nuclear Worker Study

- Generally well-conducted study
  - Strong dosimetry
- Common core protocol set out details of study including
  - Which workers to be included
  - How analyses to be conducted
- Subject to limitations of low dose epidemiologic studies
  - Likely bias due to confounding by smoking
  - Possible problems with Canadian data

15-Country Study: ERR/Gy



Cardis et al. 2005

15-country Study: Bias in Estimates for All Cancers Excluding Leukemia?

Estimate with all countries:	0.97 (0.14, 2.0)
Canada:	6.7 (2.6, 13)
Estimate with Canada excluded:	0.58 (–0.2, 1.6)
Lung cancer:	1.85 (0.26, 4.0)
Other smoking-related cancers	0.21 (<0, 2.0)
Solid cancers unrelated to smoking	0.62 (–0.5, 2.2)

Cardis et al. 2005, 2007

More Recent Pooled Analyses

Population	Publications	Follow-up through
NRRW* (UK)	2009	2001
BNFL** (UK)	2014	2005
US pooled	2015	2005
France pooled	2013	2004

*National Registry of Radiation Workers
**British Nuclear Fuels plc

Muirhead et al. 2009; Giles and Haylock 2014; Schubauer-Berigan et al. 2015; Metz-Flamant et al. 2014

Characteristics of Recent Studies

	Number of worker	Mean Dose (Sv)	Number of cancers
15-country	407,391	0.019	5,024
NRRW	174,541	0.025	8,107
(BNFL	64,956	0.053	3, 026)
US pooled	119,195	0.020	10,877
France	59,021	0.023	2,312

15-Country Study (Cancer deaths)

[Cancer deaths in recent country-specific analyses]

United States (2,841)	10,877	Hungary (40)
United Kingdom (2,273)	8,107	Finland (34)
Japan* (432)		Lithuania (25)
Canada (417)		Spain (25)
France (348)	2,312	Korea (21)
Sweden (194)		Switzerland (24)
Belgium (90)		Australia (20)
		Slovakia (10)

*Included only in leukemia analyses

Cardis et al. 2005, 2007

US Facilities in Pooled US Analyses

	Number of workers	Mean Dose (Gy)	Number of cancers
Portsmouth Naval Shipyard	9,625	0.025	1499
Hanford Site	34,278	0.026	3971
Oak Ridge NL	18,830	0.014	1916
Savannah River	22,485	0.022	1772
Idaho NL	33,978	0.016	2374
Total	119,195	0.020	11,332

Schubauer-Berigan et al. 2015

Country specific pooled analyses: ERR/Gy

	All cancer excluding leukemia	Leukemia excluding CLL
NRRW (UK)	0.28 (0.02, 0.6)	1.7 (0.1, 4.3)
US	0.14 (-0.2, 0.5)	1.7 (-0.2, 4.7)
France	0.34 (-0.6, 1.4)	4.0 (<0, 17)

Muirhead et al. 2009; Schubauer-Berigan et al. 2015; Metz-Flamant et al. 2014

Country specific pooled analyses: ERR/Gy

	All cancer excluding leukemia	Leukemia excluding CLL
NRRW (UK)	0.28 (0.02, 0.6)	1.7 (0.1, 4.3)
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*BEIR VII for adult males

Muirhead et al. 2009; Schubauer-Berigan et al. 2015; Metz-Flamant et al. 2014

Country specific pooled analyses: ERR/Gy

	All cancer excluding leukemia	Lung cancer
NRRW (UK)	0.28 (0.02, 0.6)	0.11 (-0.04, 0.8)
US	0.14 (-0.2, 0.5)	0.07 (-0.4, 0.7)
France	0.34 (-0.6, 1.4)	1.2 (-0.6, 3.6)

Muirhead et al. 2009; Schubauer-Berigan et al. 2015; Metz-Flamant et al. 2014

Specific Solid Cancers with Significant Dose-Response Relationships

- NRRW (UK):
  - Mortality: Uterus
  - Incidence: Rectum, multiple myeloma,
    Non-melanoma skin cancer
- US pooled: Multiple myeloma
- France: Mouth and pharynx

Muirhead et al. 2009; Schubauer-Berigan et al. 2015; Metz-Flamant et al. 2014

Circulatory Disease

- NRRW
  - Statistically significant dose-response relationship for circulatory disease mortality
  - ERR/Gy similar in magnitude to that for cancer
- US, France
  - No evidence of dose-response for circulatory disease

Muirhead et al. 2009; Schubauer-Berigan et al. 2015; Metz-Flamant et al. 2014

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 Worker Studies

- Nuclear workers exposed to low doses of external radiation

- Mayak nuclear workers
  - Exposed to high protracted external doses
  - Plutonium

- Medical and dental workers

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
  - Largest doses in 1940's and 1950's

Mayak nuclear facility

Mayak Worker Cohort

- 26,000 workers hired 1948-82
- 25% female
- 12,400 deaths
- 3,000 deaths from cancer

- Exposed to both external radiation and to plutonium

- Protracted low dose rate exposure similar to that of interest for radiation protection

Gaps Filled by Mayak Worker Cohort

- Large protracted external doses
  - Doses much larger than those received by nuclear workers in other countries

Mean external dose (Gy)	
Mayak workers	0.35
15-country	0.02

  - Greater statistical power
  - Less potential for confounding

Gaps Filled by Mayak Worker Cohort-2

- Substantial exposure from internally deposited plutonium
  - No other human data that are adequate for estimating cancer risks from plutonium
- Both male and female workers exposed

Mayak Dosimetry

- Extensive collaborative effort of US and Russian scientists to improve both external and internal dose estimates
- Improved doses known as MWDS-2008
- Most results in this presentation based on MWDS-2008

Mayak Worker Cohort (MWC): External Doses

- Focus on solid cancers other than lung, liver, and bone, the main sites of plutonium deposition
- Solid cancer mortality analyses based on follow-up period 1948-2008.
- Solid cancer incidence analyses 1948-2004
- Monitored for external exposure with individual film badges

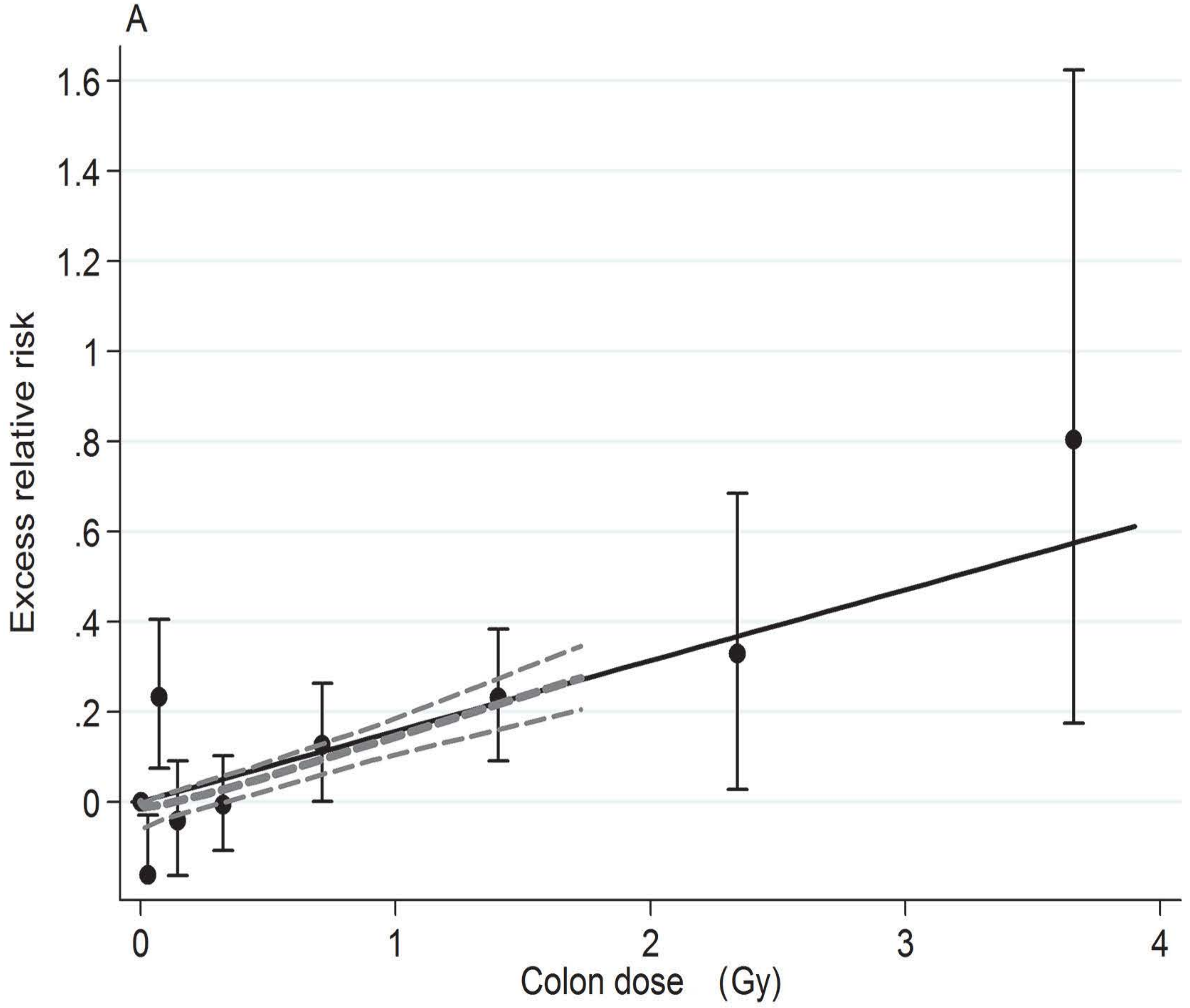
Mortality from Solid Cancers other than Lung, Liver, and Bone: External Dose

Dose (Gy)	Person-years	Observed deaths	Excess* deaths
<0.1	516,997	627	3.0
0.1-	248,626	558	22.9
0.5-	93,270	282	28.0
1-	72,944	271	48.9
2-	15,146	63	17.5
3+	3,913	24	7.7
Total	**950,894**	**1825**	**127.9 (7.1%)**

*Estimated excess due to external exposure based on the assumption of a linear dose-response.

Sokolnikov et al. 2015

Dose-Response for Solid Cancers other than Lung, Liver, and Bone



Sokolnikov et al. 2015

Solid Cancers other than Lung, Liver and Bone: External dose (MWC)

	Not adjusted for Pu dose	Adjusted for Pu dose
Mortality*	0.16 (0.07, 0.36)	0.11 (0.03, 0.21)
Colon dose	1825 deaths (1948-2008)	

*Sokolnikov et al 2014

Solid Cancers other than Lung, Liver and Bone: External Dose (MWC)

	Not adjusted for Pu dose	Adjusted for Pu dose
Mortality*	0.16 (0.07, 0.36)	0.11 (0.03, 0.21)
Colon dose	1825 deaths (1948-2008)	
Incidence*	0.07 (0.01, 0.15)	0.06 (−0.01, 0.14)
Hp(10)	1447 cases (1948-2004)	

*Sokolnikov et al 2014; **Hunter et al. 2013

Solid Cancers other than Lung, Liver and Bone: External Dose (MWC)

	Not adjusted for Pu dose	Adjusted for Pu dose
Mortality*	0.16 (0.07, 0.36)	0.11 (0.03, 0.21)
Colon dose	1825 deaths (1948-2008)	
Incidence*	0.07 (0.01, 0.15)	0.06 (−0.01, 0.14)
Hp(10)	1447 cases (1948-2004)	

A-bomb survivors: 0.35 (0.19-0.55)

*Sokolnikov et al 2014; **Hunter et al. 2013

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

Cardiovascular Disease: External Dose (MWC)

	Ischemic heart disease*	Cerebro-vascular disease**
Mortality	0.03 (−0.04, 0.10) 2557 deaths	0.05 (-0.03, 0.16) 1578 deaths
Incidence	0.15 (0.08, 0.21) 6219 cases	0.46 (0.37, 0.57) 8717 cases

*Moseeva et al. 2014 Radiat Environ Biophy; **Azizova et al. 2014 Radiat Res

Mayak Workers: In Utero Exposure

- 8000 offspring of female Mayak workers born 1948-1988
  - 3226 were exposed in utero: Mean dose – 54.5 mGy
- Based on cumulative gamma radiation dose to the uterus during pregnancy
- No evidence of dose-response but not inconsistent with other risk estimates

Schonfeld et al. 2012

In Utero Exposure: Solid Cancers

In Utero Dose (mGy)	RR (95% CI)	Deaths
0	1.0 (ref)	47
>0 – 10	0.9 (0.4 - 1.9)	8
10-	1.8 (0.7 - 3.7)	7
20-	0.5 (0.1 - 1.2)	3
50-	1.1 (0.3 - 2.6)	4
100+	0.9 (0.3 - 1.9)	6

ERR/Gy = −0.1 (<-0.1, 4.1)

Schonfeld et al. 2012

In Utero Exposure: Leukemia

In Utero Dose (mGy)	RR (95% CI)	Deaths
0	1.0 (ref)	6
>0 – 10	0.0	0
10-	2.1 (0.1 - 12)	1
20-	5.9 (1.5 - 21)	4
50-	2.6 (0.2 - 15)	1
100+	0.0	0

ERR/Gy = −0.8 (<-0.8, 47)

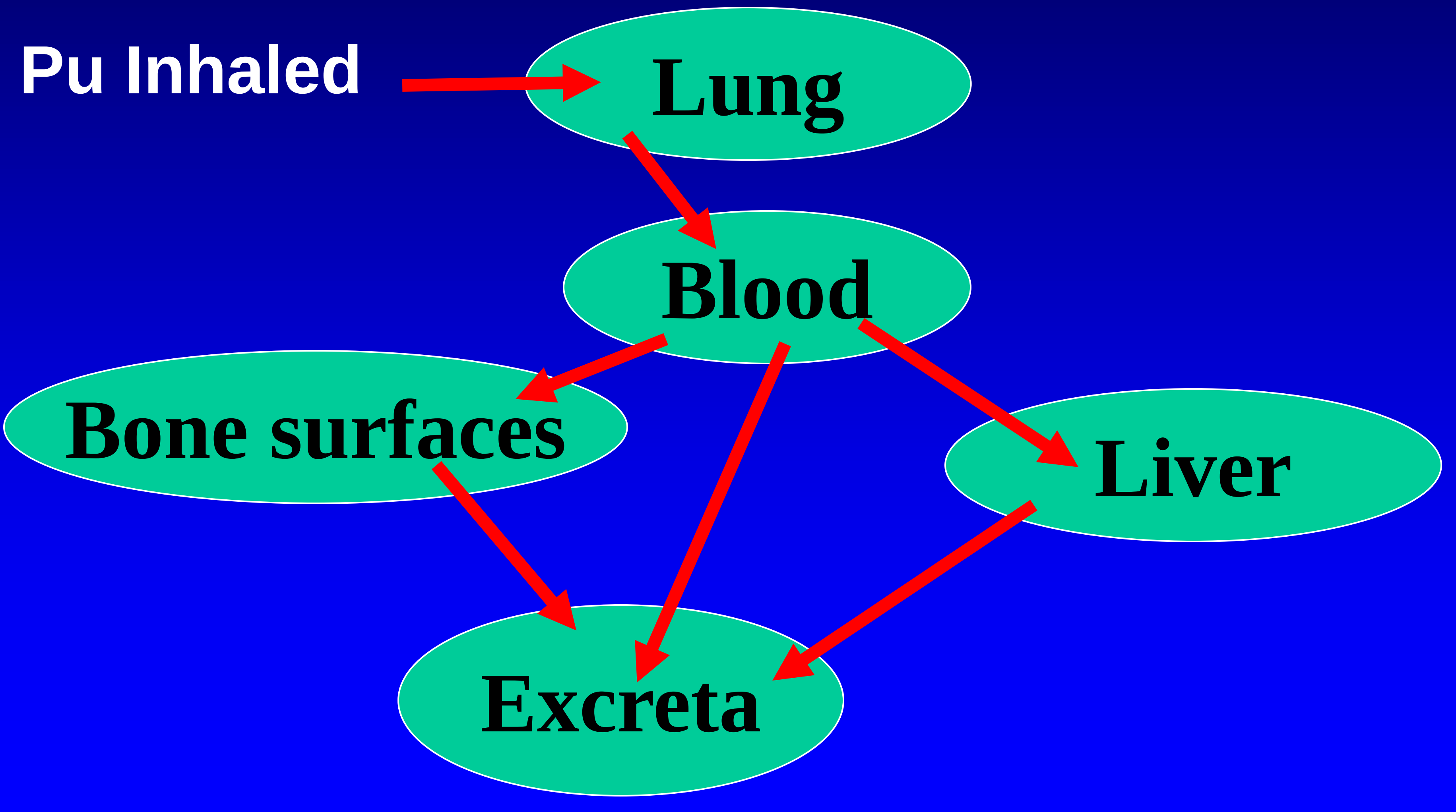
Schonfeld et al. 2012

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

Simple View of Inhaled Plutonium Dynamics



Plutonium Dosimetry

- Dose estimates based on urine monitoring data in combination with occupational history
- Urine monitoring data available for only 40% of those with potential for plutonium exposure
- Biokinetic models used to estimate deposition and clearance in organs of the body

Mayak Worker Results: Internal Plutonium Dose

- Lung cancer dose-response based on MWDS-2008
- Plutonium dose-response based on workers with plutonium doses that could be estimated
  - Monitored or never worked in places with potential for Pu exposure
- Adjusted for external dose

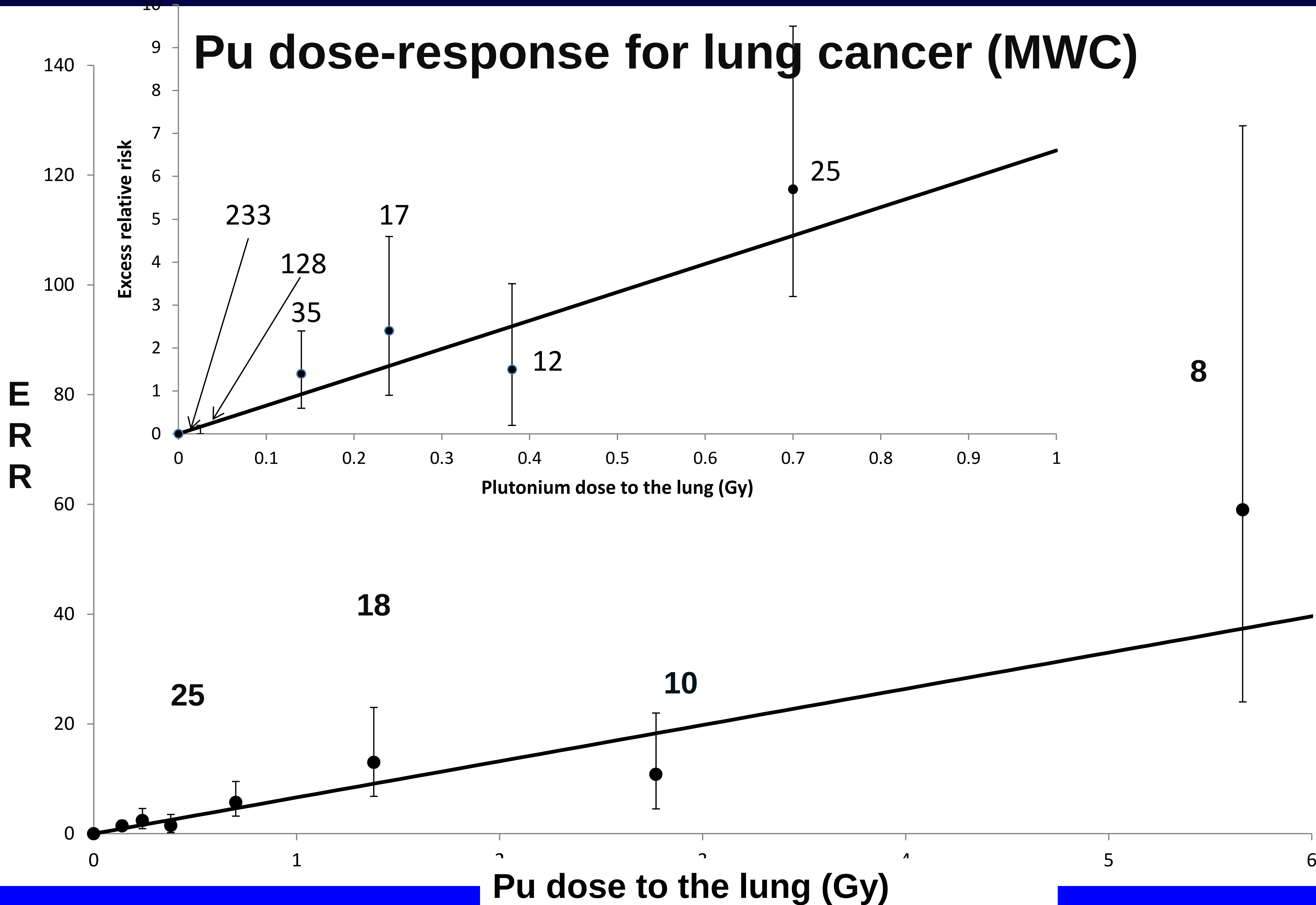
Lung Cancer: Plutonium Dose-Response

Lung Dose (Gy)	RR (95% CI)	Deaths
0	1.0	233
>0 - .1	0.99 (<1 - 1.2)	128
.1-	2.4 (1.6 – 3.4)	35
.2-	3.4 (1.9 – 5.6)	17
.3-	2.5 (1.2 – 4.5)	12
.5-	6.7 (4.2 - 11)	25
1-	14 (7.8 - 24)	18
2-	12 (5.5 – 23)	10
4+	60 (25 - 130)	8

Estimates for males at age 60

Gilbert et al. 2013

Pu dose-response for lung cancer (MWC)



Lung Cancer: Plutonium Dose-Response

- Dose-response well described by a linear function
- Linear-quadratic function did not improve fit over linear function ($p > 0.5$)
- Power function: $\beta_1 \, d_{plu}^{\eta}$
  - Power (η) estimated to be 1.02 (0.84 – 1.23)

Gilbert et al. 2013

Lung Cancer PU ERR/Gy for Restricted Dose Ranges

Plutonium Dose Range	Number of lung cancer with Pu doses >0	ERR/Gy (95% CI)
All doses	253	7.4 (5.2-10)
< 1 Gy	217	7.2 (4.8-11)
< 0.5 Gy	192	6.5 (3.4-11)
< 0.3 Gy	180	8.1 (4.1-13)
< 0.2 Gy	163	7.0 (2.5-13)
< 0.1 Gy	128	1.3 (<0-9.4)

Lung Cancer: Modification by Attained Age

- ERR per Gy declined sharply with attained age (ERR/Gy at attained age 50 is about 3 times that for age 70)
- Pattern very similar to that observed for underground miners (BEIR VI)

Lung Cancer: Modification by Sex

ERR per Gy for plutonium

Males: 7.1 (4.9 – 10)

Females: 15 (7.6 – 29)

Female/Male ratio = 2.1 (1.0 – 4.3)

Results shown are for attained age 60

Gilbert et al. 2013

Lung Cancer: Modification by Smoking

ERR per Gy for plutonium

Smokers: 6.9 (4.6 – 10)

Non-smokers: 29 (9.8 – 83)

Non-smoker/Smoker ratio = 4.1 (1.4 – 12)

Results shown are for attained age 60

Gilbert et al. 2013

Lung Cancer:
Modification by Smoking

ERR per Gy for plutonium

Smokers:	6.9 (4.6 – 10)
Non-smokers:	29 (9.8 – 83)

Interaction was sub-multiplicative (0.011)

Additional analyses showed the interaction was more than additive (<0.001)

Results shown are for attained age 60

Gilbert et al. 2013

Excess Lung Cancer Deaths Attributed to Smoking and to Pu exposure

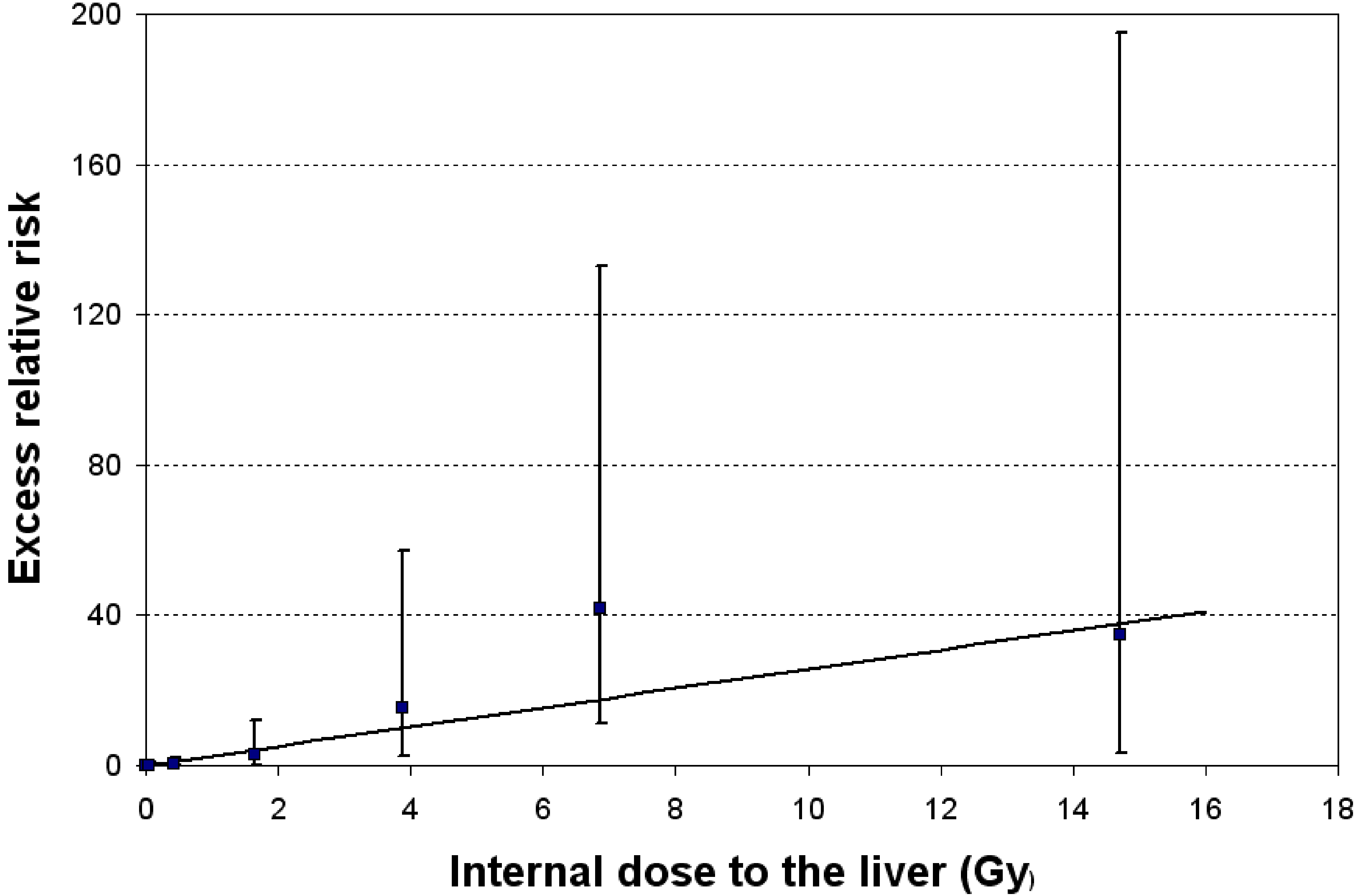
Plutonium Dose Range	Males	Females
Observed deaths	416	35
Excess from		
Smoking alone	302.4	5.3
Plutonium alone	27.9	17.8
Plutonium and smoking	53.7	2.3
<		

Liver Cancer: Plutonium Dose-Response

Dose to liver (Gy)	RR (95% CI)	Deaths
0	1.0	14
>0 – 0.2	1.03 (<1 - 1.8)	9
0.2-	1.5 (<1 - 3.2)	2
1-	4.0 (1.2 - 13)	3
3-	16 (3.3 – 58)	3
5-	43 (12 – 134)	7
10+	36 (4.5 – 196)	2

Estimates for males
Estimates for females are a factor of 11 higher

Sokolnikov et al. 2008


200
160
120
80
40
0
Excess relative risk
0
2
4
6
8
10
12
14
16
18
Internal dose to the liver (Gy)

Bone Cancer: Plutonium Dose-Response

Dose to bone surface (Gy)	RR (95% CI)	Deaths
0	1.0	5
>0 - 1	0.9 (<1 – 4.3)	3
1-	0.0 (0.0 – 8.7)	0
5-	0.0 (0.0 – 61)	0
10+	82 (17 – 338)	3*

*Doses of bone cancer deaths were 21, 37, and 85 Gy
Estimates for both sexes.

Sokolnikov et al. 2008

Lung Cancer Incidence

- Information on lung cancer histology
- 414 lung cancer cases
  - 111 adenocarcinoma
  - 101 squamous cell
  - 97 other epithelial
  - 103 unknown

- ERR/Gy significantly higher for squamous-cell than for adenocarcinoma

Labutina et al. 2013

Liver Cancer Incidence

- **414 lung cancer cases**
  - **18 hepatocellular cancers**
  - **6 cholangiocarcinomas**
  - **8 hemangiosarcoma**

- **7 of 8 hemangiosarcomas were in highest dose category of 4+ Gy**

Labutina et al. 2013

Limitations in Mayak Data

- Data on male smokers dominate results
- For liver and bone cancer
  - Number of excess cases is small
  - Risk at low doses very uncertain
- Limited data on confounders
- Pu dosimetry uncertainties

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

The Future: Mayak Plutonium Data

- Uncertainties in Pu doses are being quantified
- Take account of dosimetry uncertainties in dose-response analyses
- Uncertainties could affect both magnitude of risk and shape of dose-response

Summary Comments on Mayak

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

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**

Mean internal plutonium dose to the lung (Gy)

Mayak workers	0.12
Sellafield workers (UK)	0.01

Radiation Worker Studies

- Nuclear workers exposed to low doses of external radiation
- Mayak nuclear workers
  - Exposed to high protracted external doses
  - Plutonium
- Medical and dental workers

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 RadiologicTechnologist Cohort

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

Collaborative study – NCI and U. of Minnesota

US RadiologicTechnologist 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

- 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

Liu et al. 2014

Collaborative study – NCI and U. of Minnesota

US RadiologicTechnologist Cohort

- Estimates of dose (and uncertainties) are now available (Simon et al, Radiat Res 2014)

- 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

The Future

- Million Worker Study
  - Led by John Boice, NCRP

- International Nuclear Worker Study (INWORKS)
  - Combine data from the UK, US, and France

One Million U.S. Radiation Workers and Veterans

Robert Oppenheimer, General Leslie Groves, Enrico Fermi, Hans Bethe, Theodore Hall

- Manhattan Project 360,000
- Atomic Veterans 115,000
- Nuclear Utility Workers 150,000
- Industrial Radiographers 130,000
- Medical & other >250,000

Health Physics News October 2012; Health Physics (2014 in Press)

Manhattan Project and other Workers (Selected U.S. Nuclear Facilities)

- ✔ Atomics International / Rocketdyne (1948)
- ✔ Mound Laboratory (1947)
- Mallinckrodt (1942)
- Los Alamos National Laboratory (1942)
- Hanford Reservation (1943)
- Savannah River Site (1950)
- Oak Ridge Reservation K-25, X-10 and Y-12 (1942)
- Sandia National Laboratories (1945)
- Rocky Flats Environmental Technology Site (1951)
- Paducah Gaseous Diffusion Plant (1953)
- Fernald Environmental Management Project (1953)

Mound Plant, Dayton, Ohio
Innovations & Polonium

- Dosimetry: Polonium, Plutonium, Tritium, 200,000 urine samples, External radiation
- Tracing: 98.7 % of 7,291 workers (1944+), 98% CODs
- Cancer incidence - linkage with Ohio Cancer Registry (1996+)
- Renal Disease Registry linkage (1976+)

The Future

- Million Worker Study
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- International Nuclear Worker Study (INWORKS)
  - Combine data from the UK, US, and France

Country specific pooled analyses: ERR/Gy

	All cancer excluding leukemia	Leukemia excluding CLL
NRRW (UK)	0.28 (0.02, 0.6)	1.7 (0.1, 4.3)
US	0.14 (-0.2, 0.5)	1.7 (-0.2, 4.7)
France	0.34 (-0.6, 1.4)	4.0 (<0, 17)
Combined	To be provided by INWORKS	

What Have We Learned from Studies of Radiation Workers?

Protracted low-LET external exposure

- Provide direct evidence that protracted exposure increases cancer risks
- Magnitude of risks compatible estimates obtained from A-bomb survivors
- Need to consider study limitations
  - Small risks lead to strong potential for confounding
  - Epidemiology not up to providing direct evidence for very low doses (< ~ 0.1 Gy)

What have we learned from studies of radiation workers?

Plutonium exposure

- Mayak worker cohort has demonstrated clear dose-response relationships for lung, liver and bone cancer

- For lung cancer, data strong enough to
  - Quantify dose-response reasonably precisely
  - Evaluate effect modification by smoking and other variables

Thank you for your attention!

Questions?

Questions and Answers

U.S. Department of Health and Human Services
National Institutes of Health | National Cancer Institute
www.dceg.cancer.gov/RadEpiCourse
1-800-4-CANCER
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