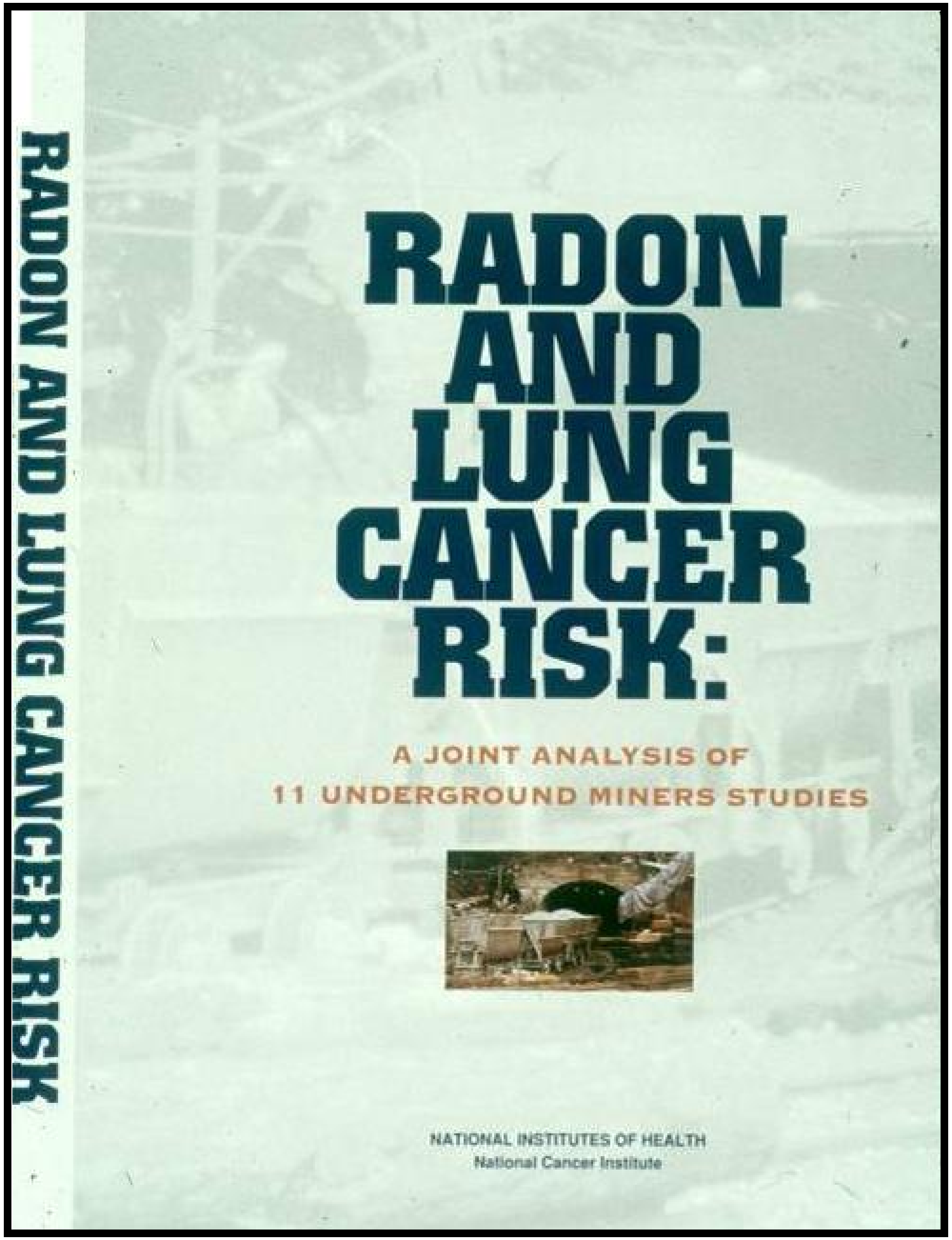
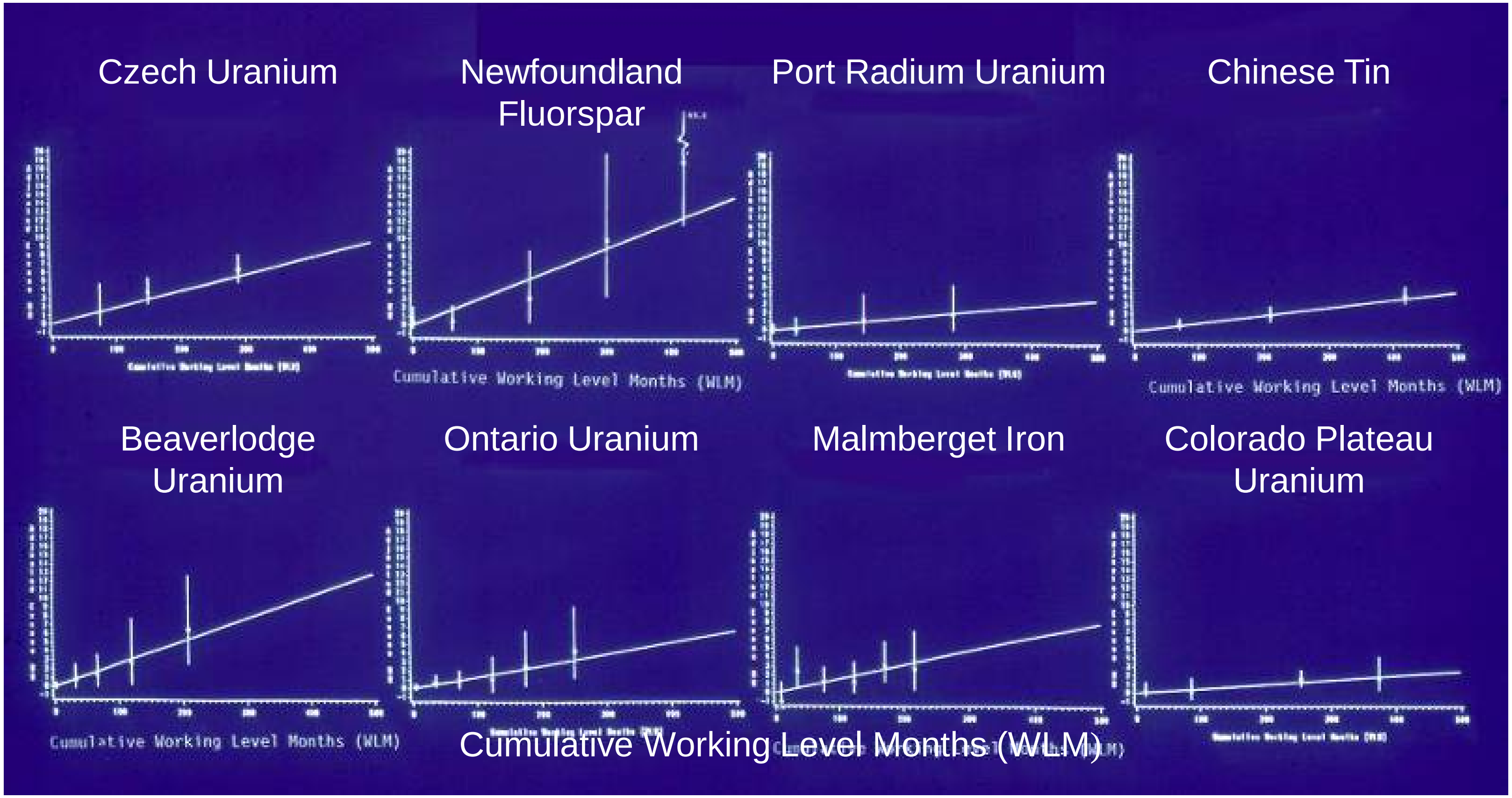
John D. Boice, Jr., Sc.D.
President, National Council on Radiation Protection and Measurements (NCRP), and Professor of Medicine, Vanderbilt University School of Medicine

Radiation Studies and Concepts II

Radiation Epidemiology & Dosimetry Course


RADON AND LUNG CANCER RISK
RADON AND LUNG CANCER RISK:
A JOINT ANALYSIS OF 11 UNDERGROUND MINERS STUDIES
NATIONAL INSTITUTES OF HEALTH
National Cancer Institute

Lung Cancer Dose Responses in Miners
Consistency in the Epidemiology



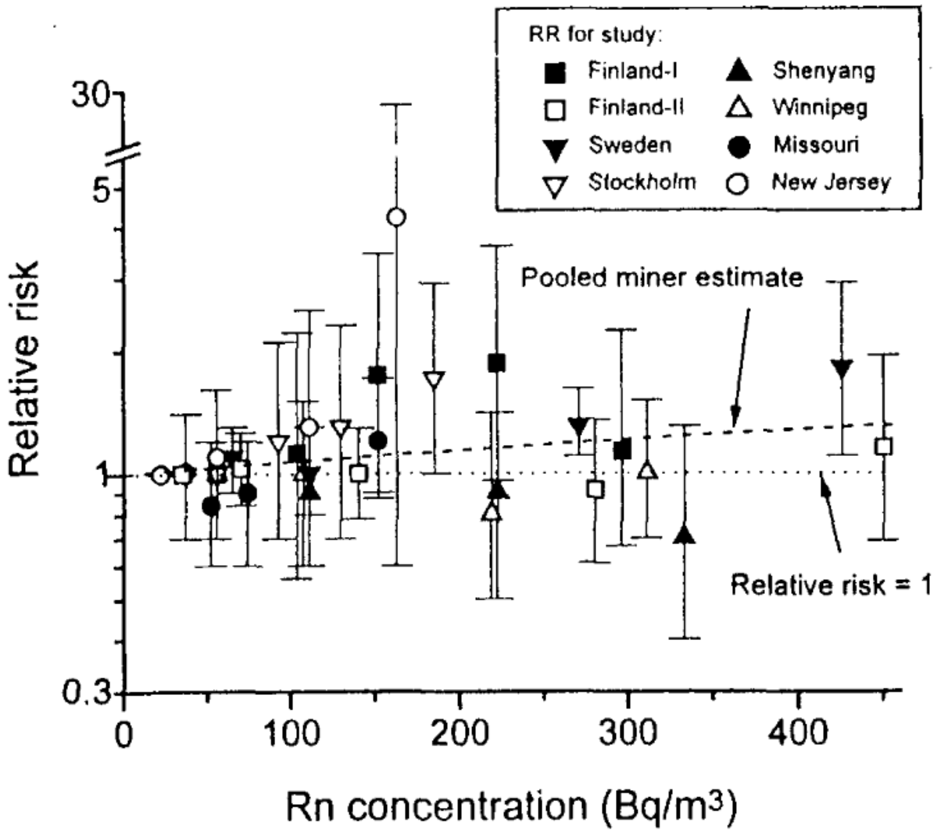
The Study Team - 1992

Radon Interacts with Smoking to Enhance Risk

A nearly multiplicative interaction

NRC, BEIR, 1999

Indoor Radon Meta-Analysis
4,263 Lung Cancers



Difficult to detect low-dose risks, yet significant trend when studies combined!

Lubin & Boice, *JNCI*, 89:49, 1997

4 pCi/l = 150 Bq/m^3

Featured in Junk Science

Batman: *Good work Robin. Let's see... a-ha...Lubin and Boice have concluded that by combining the radon epidemiologic studies together through a meta-analysis, "a lot of nothing" can become "something!" Lubin and Boice used the meta-analysis technique to report that higher levels of radon exposure increase the risk of lung cancer by a statistically significant 14 percent. Then Samet, the King of Radon, blessed the report in his editorial!*

Robin: *What... what's a meta-analysis?*

What will the RADdler do with this new junk science?
Is the Dynamic Duo too late?
How do Samet, Lubin and Boice sleep at night?
Will they ever get a life and forget about radon?

RADdler - a radon epidemiologist and descendant of the notorious criminal "Riddler"

http://junksciencearchive.com/news/batman.html

Radon Studies in Homes (Case-Control)

United States
- √ New Jersey
- √ Missouri
- Iowa
- Connecticut
- Utah/Idaho

Canada
- Winnipeg

Europe
- Southwest England
- Western Germany
- Czech (cohort)

Nordic Countries
- √ Sweden
- Finland

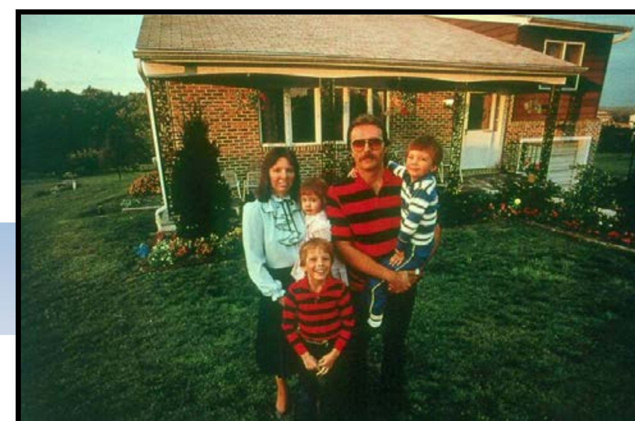
China
- √ Shenyang
- √ Gansu

Pooled
- √ Lubin (1997, 1999)
- North America (Krewski, 2005)
- Europe (Darby, 2005)
- √ China (Lubin, 2004)
- World (Darby, in progress)

BEIR VI, 1999; Field, *Rev Envir Health* 16, 2001

- Residents in the Center Valley area are urged to have radon tests done in their homes after recent testing revealed "record high" levels.
- Several homes had radon levels of over 1,000 picocuries per liter (pCi/L). One specific home tested at 2,750 pCi/L and is the one of the highest radon values ever recorded in the state. (Nov 2014)
- Pennsylvania has one of the most serious radon problems in the country.
- An estimated 40 percent of Pennsylvania homes have radon levels above Environmental Protection Agency's action guideline of 4 picocuries per liter.

Center Valley home registers highest radon level ever in Pennsylvania



Gold and Platinum Honors (1950+)

- Japanese Atomic Bomb Survivors
- Pooling – Thyroid
- Pooling – Breast

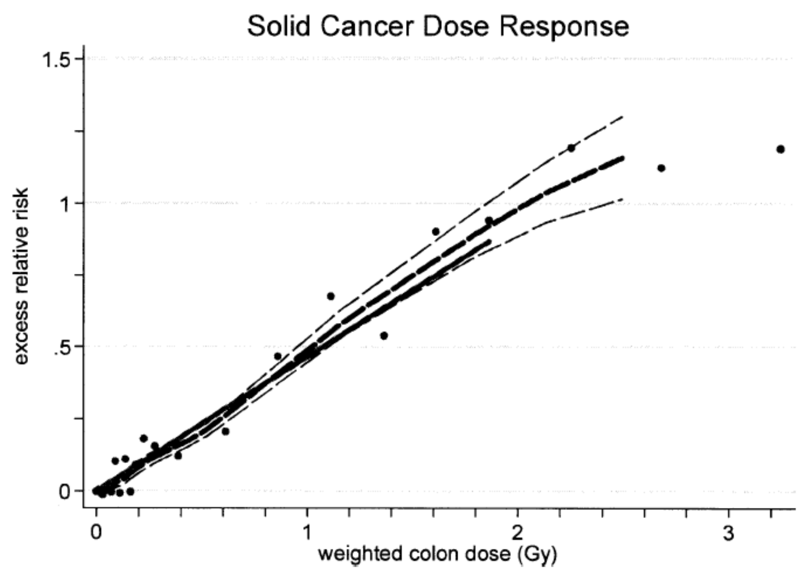
Vanderbilt-Ingram Cancer Center

ICRP

Epidemiologic Studies are the Basis for Cancer Risk Estimates.

" Radiation risk estimates are derived for incidence data for specific tumour sites when adequate dose response data are available from the Japanese Life Span Study (LSS), pooled analyses of multiple studies, or other sources." **ICRP Publ 103, 2007**

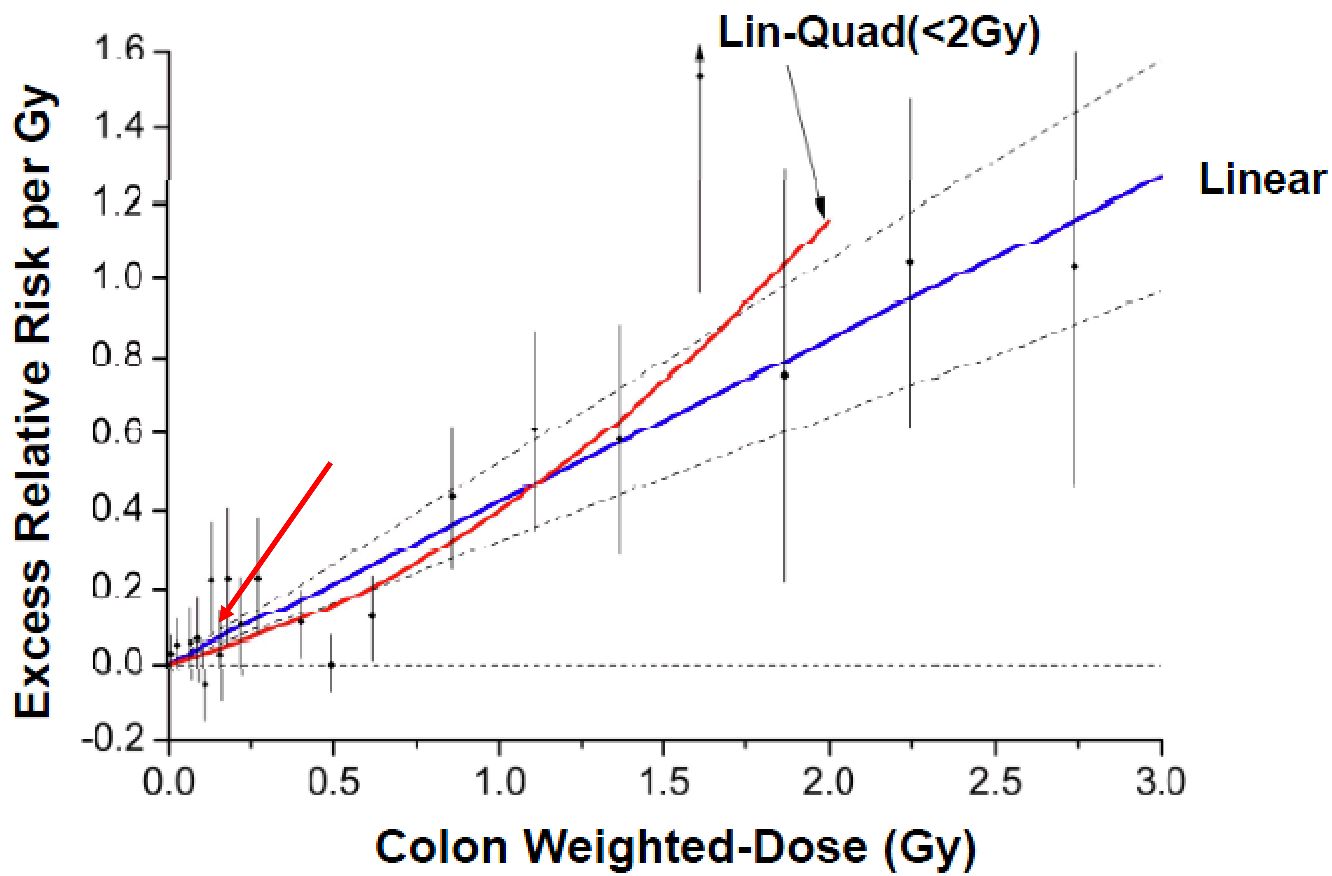
1945, Japan, war torn, acute exposure



Preston, *Rad Res* 168:1, 2007

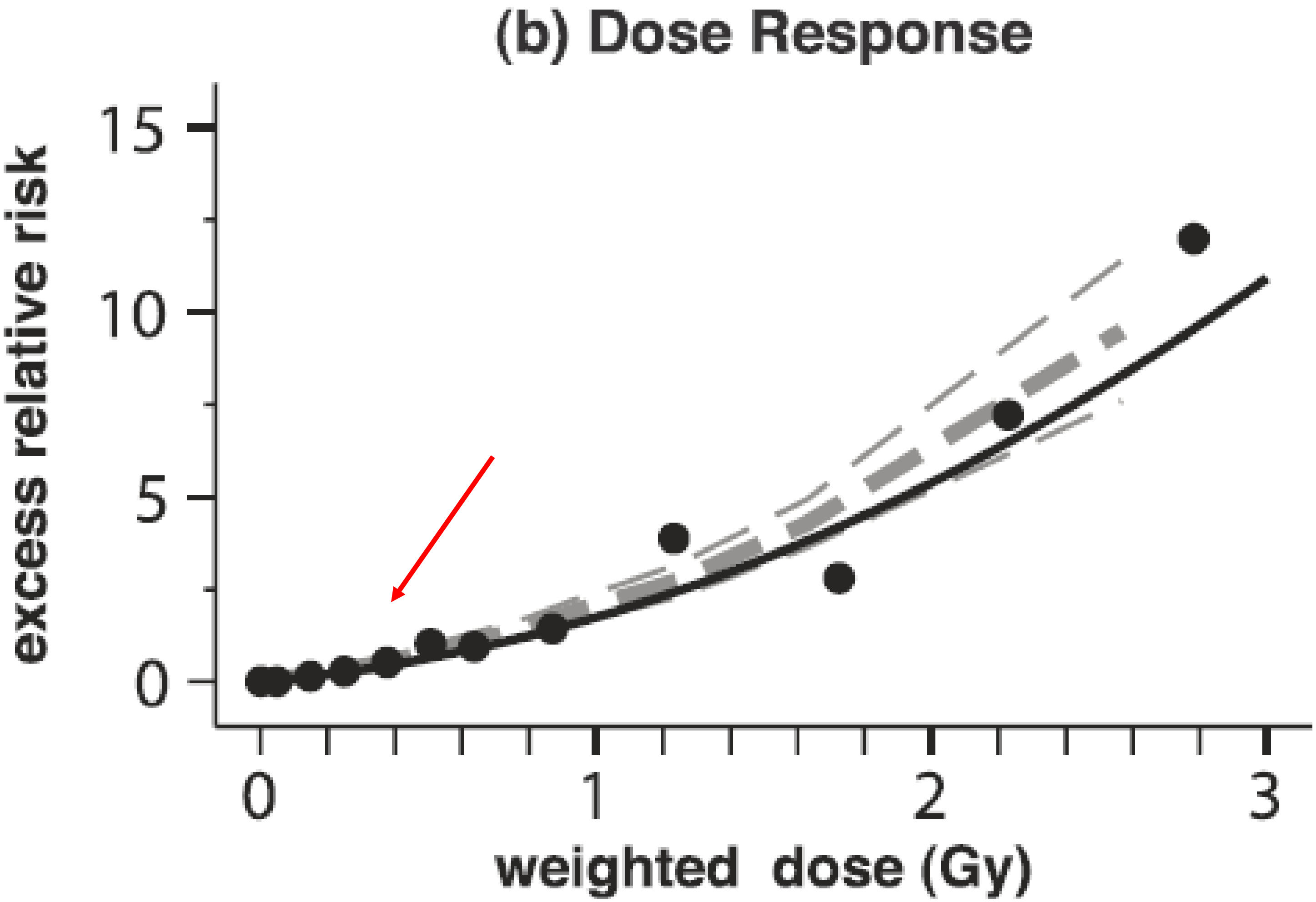
Cancer Incidence, 1958-1998

LSS Dose Response for Solid Cancer Mortality, 1950-2003



Ozasa et al, *Rad Res* 177; 2012

LSS Leukemia (other than CLL) Dose Response



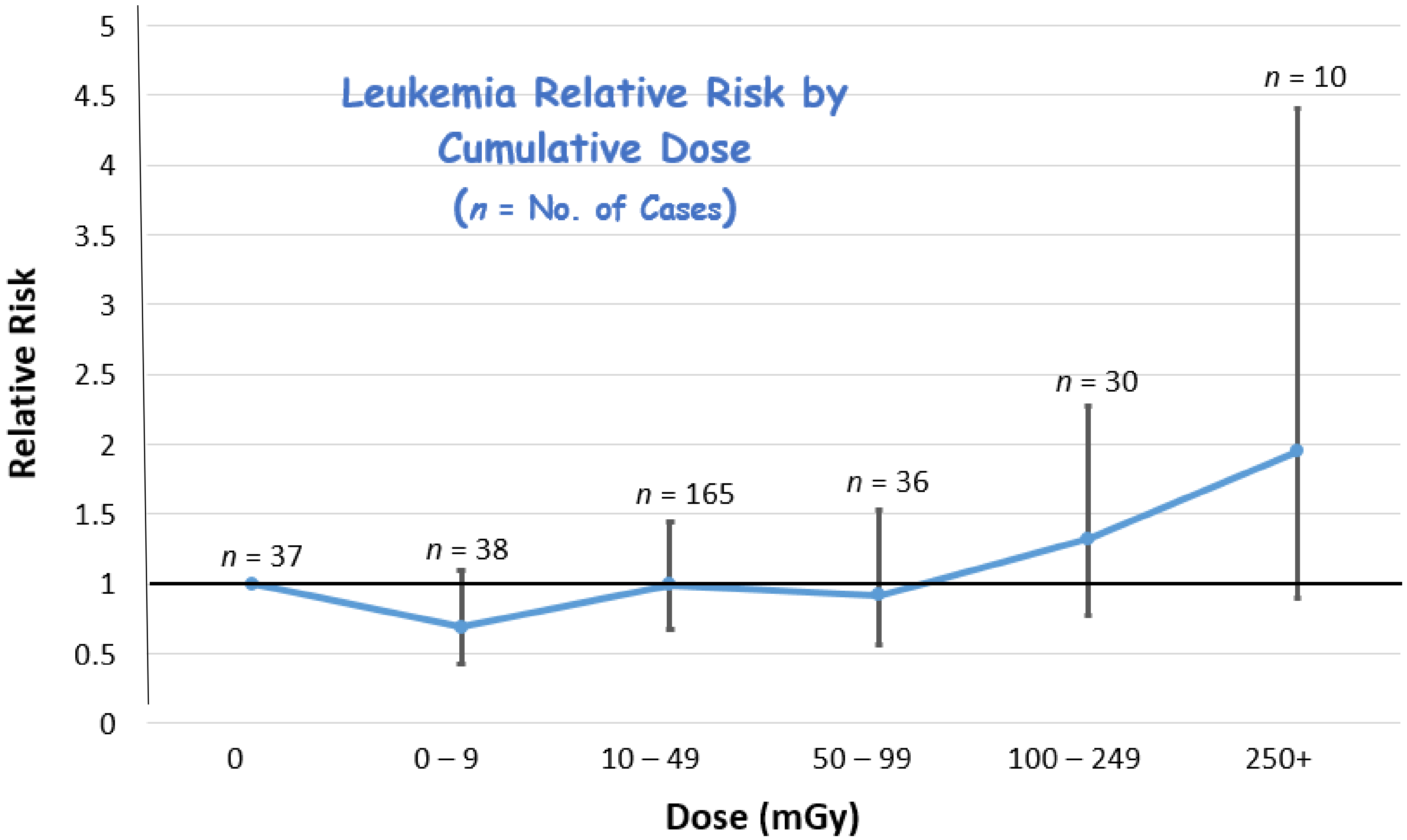
Nonlinear dose response. Much higher risk coefficient than solid cancer. Excess occurs early. Hsu et al. Radiat Res 2013.

Nuclear Utility Worker Dose Distribution
Preliminary (REIRS & Landauer)

Lifetime dose (mSv)	Frequency	Percent
< 10 *	30,764	20.7
10 – 49 *	77,383	52.0
50 – 99	21,578	14.5
100 - 499	18,846	12.7
500 - 999	322	0.2
> 1,000	22	<0.1
Total	**148,915**	

*Sampled < 50 mSv

Leukemia (other than CLL) among 150,000 U.S. Nuclear Power Plant Workers - Preliminary



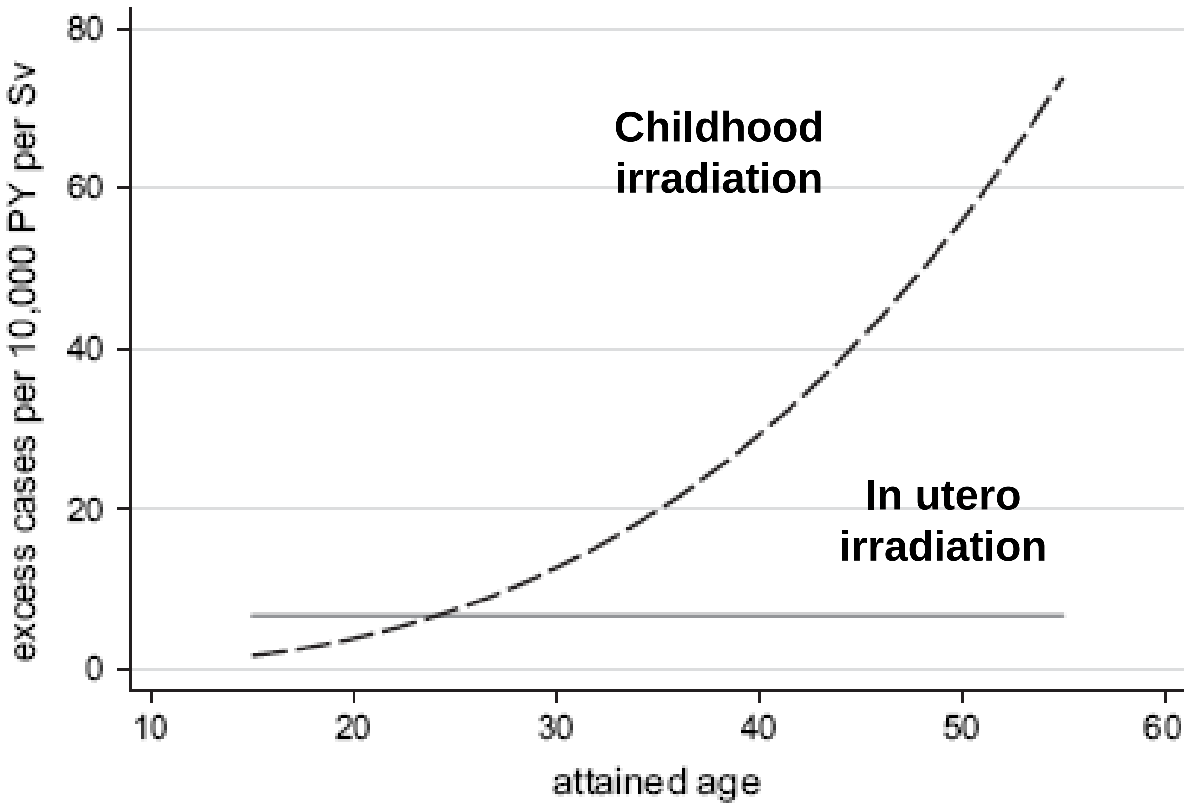
347 Leukemias among nuclear power plant workers

121 Leukemias among adult A-Bomb survivors

Atomic Bomb Survivors In Utero & Post-Natal Cancer Risk

Risk of

Cancer

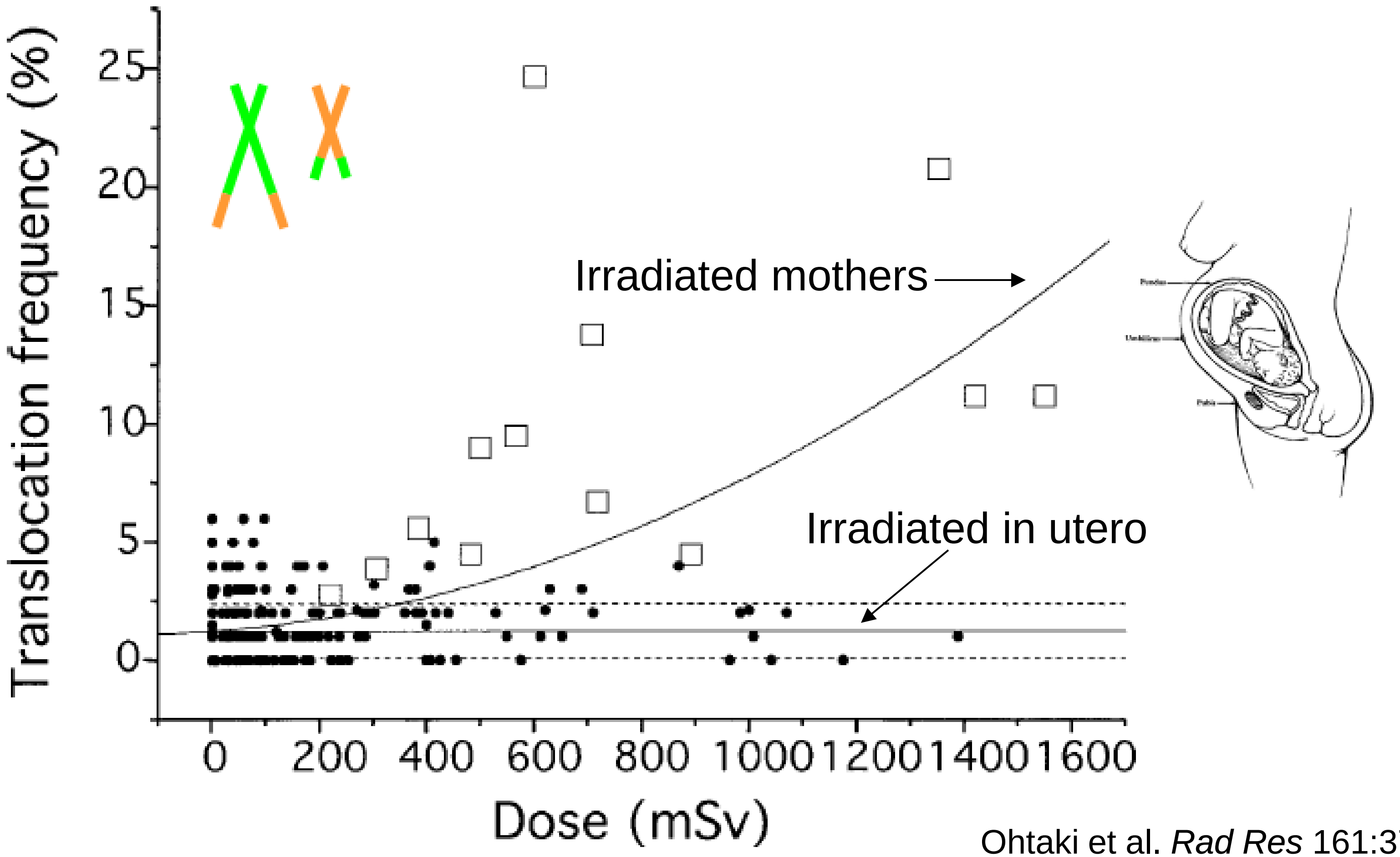


No apparent increased sensitivity

No childhood leukemia

Preston et al. *JNCI* 100:428, 2008

No Dose-Response for Chromosome Aberrations after *In Utero* Exposure, RERF

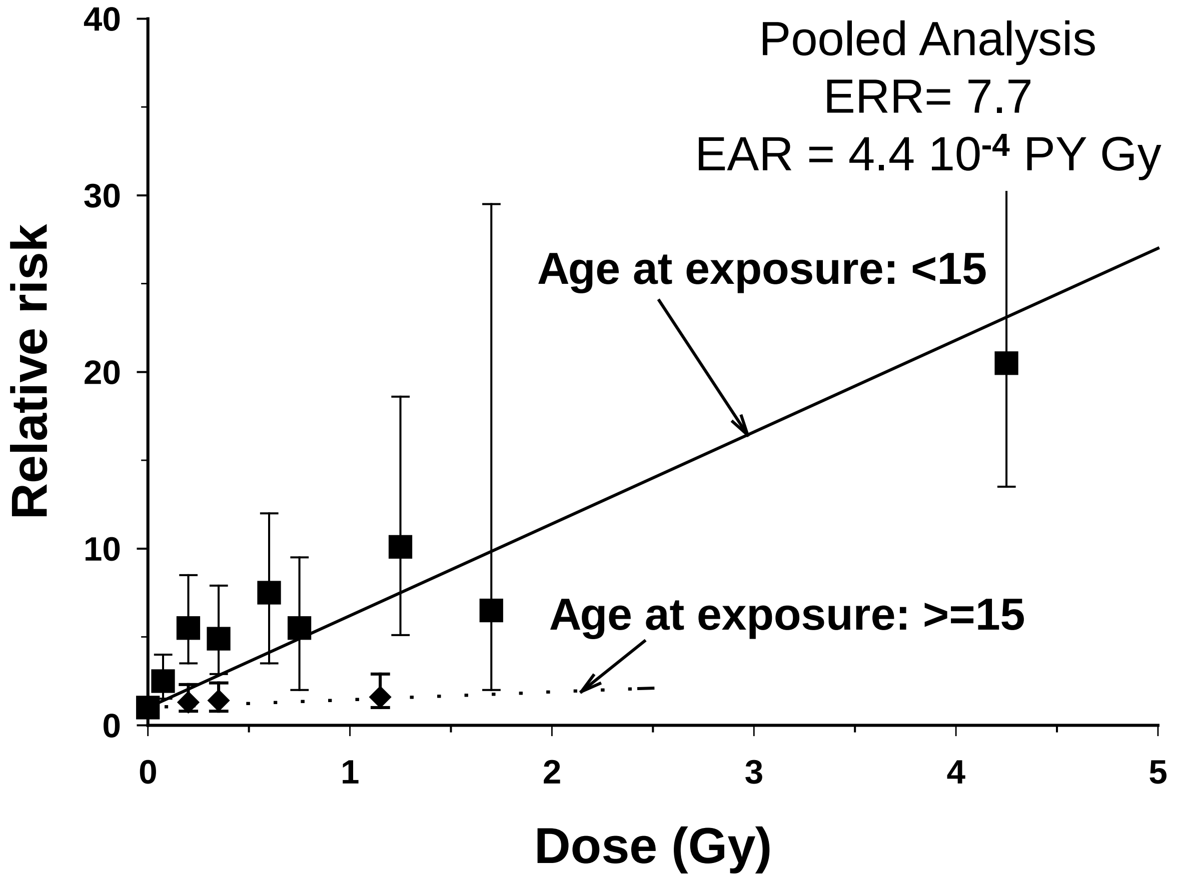


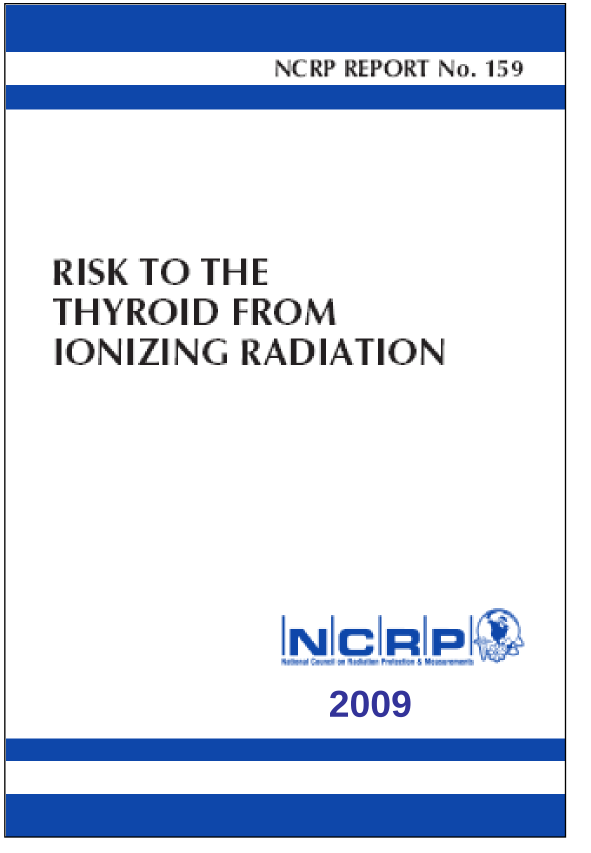
Ohtaki et al. *Rad Res* 161:373, 2004

Thyroid Cancer after Exposure to External Radiation: A Pooled Analysis of Seven Studies

Ron et al, 1995

Thyroid Cancer & External Radiation Risk
Dose Response by Age at Exposure





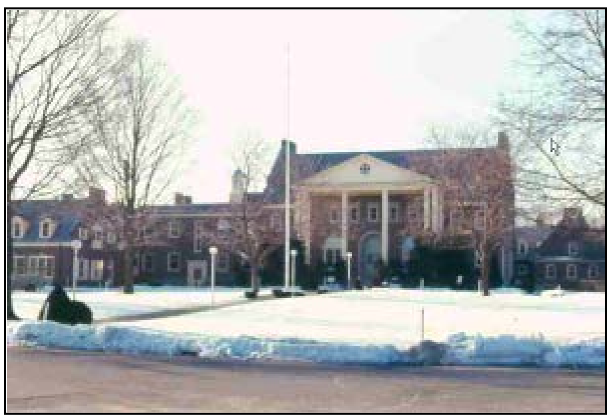
Ron E, Lubin J, Shore R et al, Thyroid cancer after exposure to external radiation: A pooled analysis of 7 studies. Radiat Res 1995

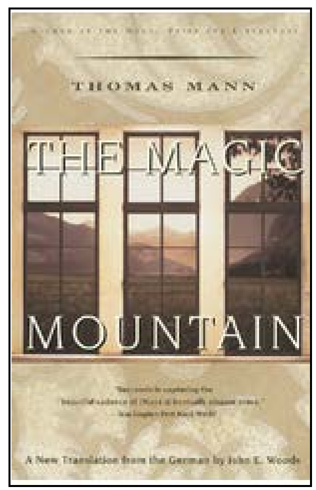
#5 On the Hit Parade !

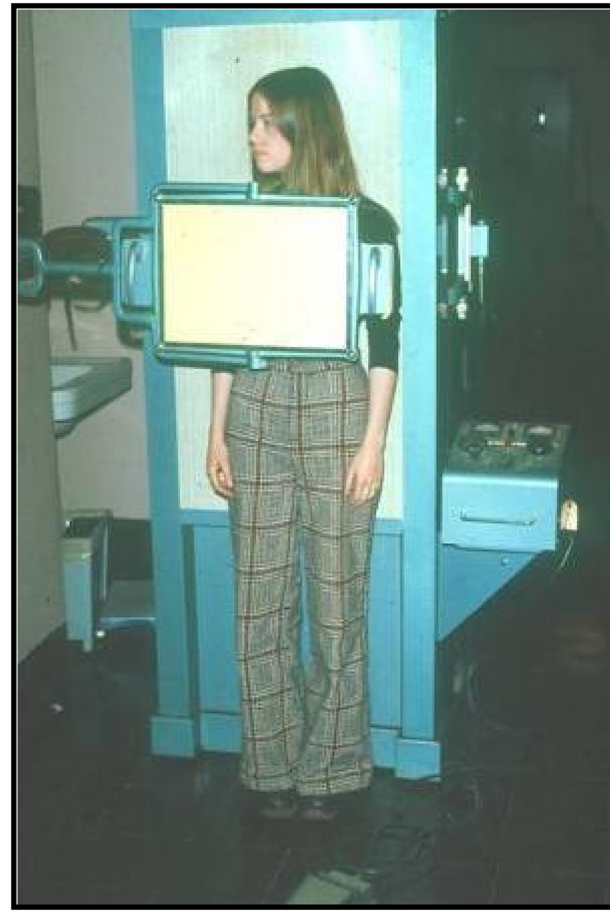
Radiation Research 1952–2012
Top 100 Articles

Studies of Low-Dose Exposures Accumulating to High Dose

Lung collapse therapy for tuberculosis and associated multiple chest fluoroscopic x-rays (1930-1954)







Breast Cancer
TB - Fluoroscopy, Massachusetts

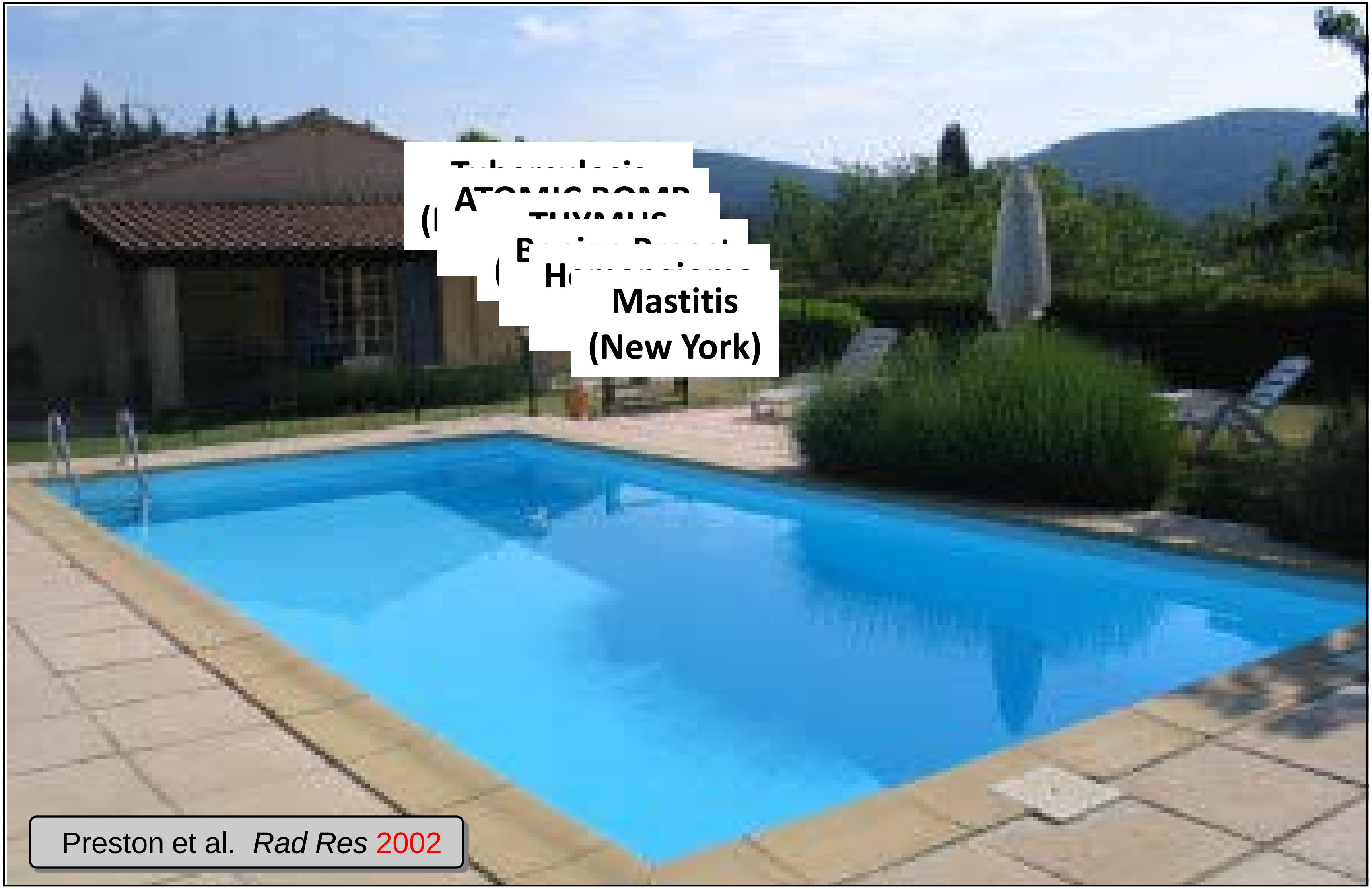
	Exposed	Nonexposed
No. of women	2,573	2,367
No. chest fluoroscopies, ave	**88**	--
Dose (ave) [*Dale Trout*]	790 mGy	--
Breast cancers		
Observed (O)	147	87
Expected (E)	114	101
O/E	**1.29**	0.86

29% Excess

ERR/Gy ~ 0.4

Boice et al, *Radiat Res* 126:214, 1991
Boice & Monson, *J Natl Cancer Inst* 59:823 1977

Radiation Effects on Breast Cancer Risk: A Pooled Analysis of Eight Cohorts

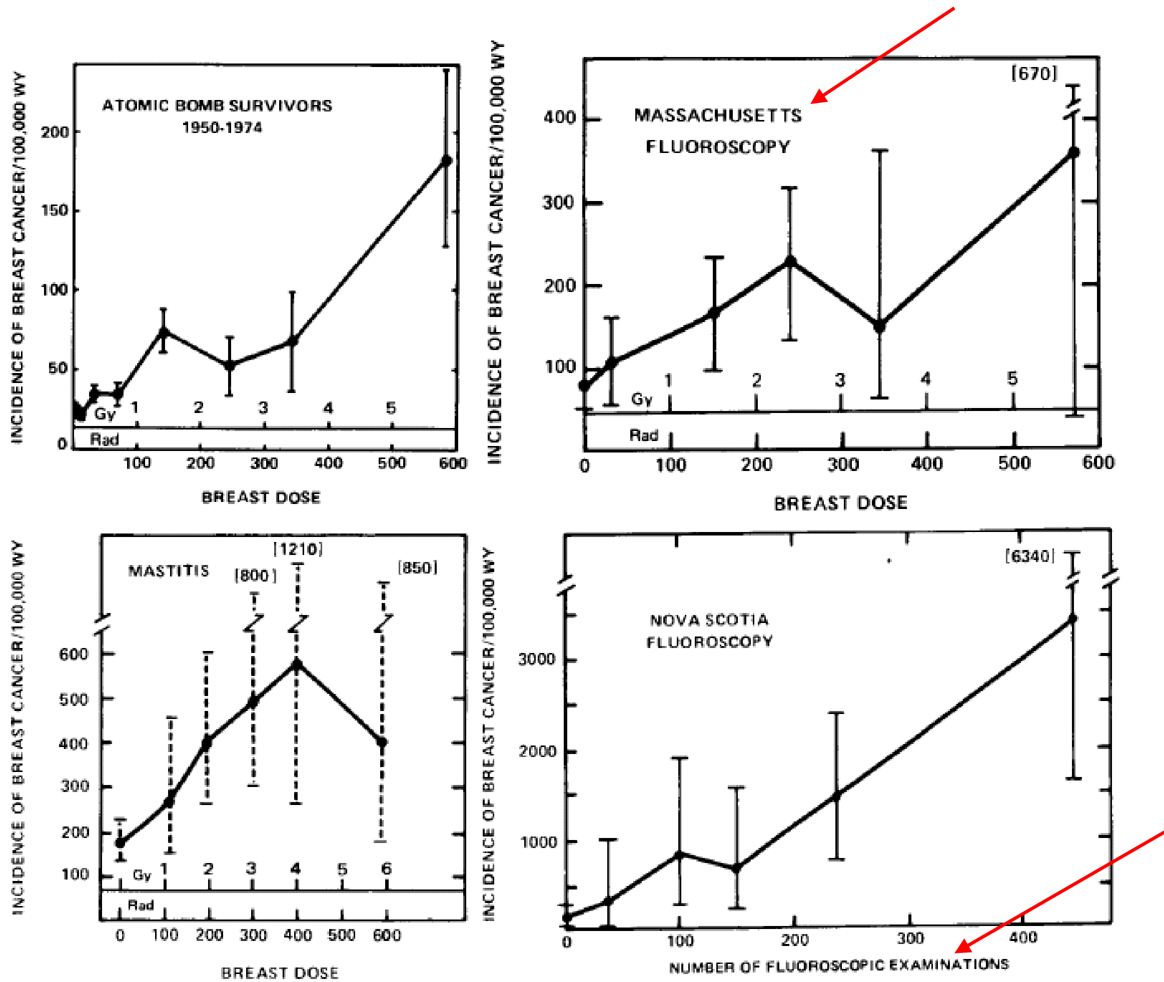


Preston et al. *Rad Res* 2002

Dose Response – Pooled Analysis of Breast Cancer Studies

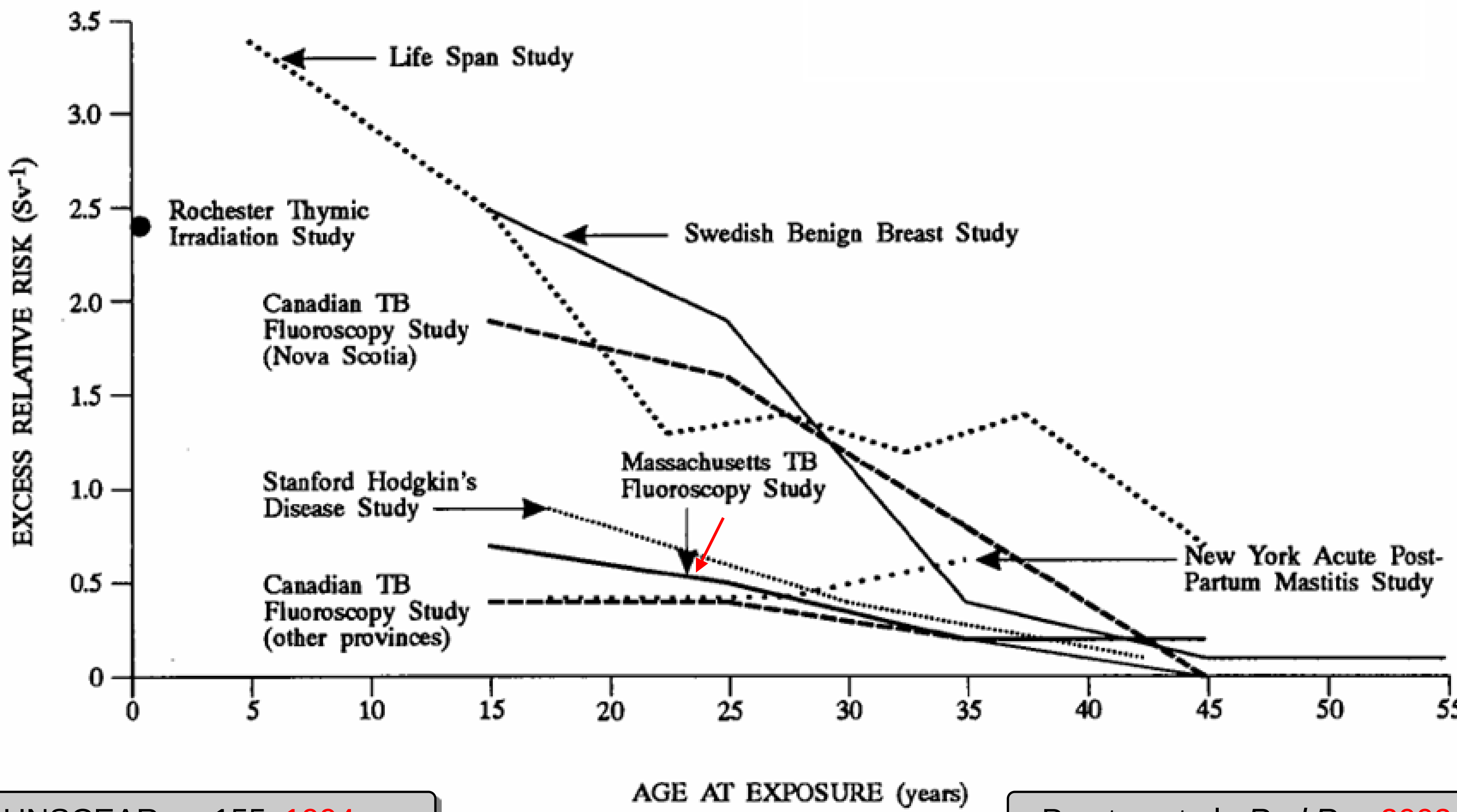
Breast Cancer

Consistent with linearity



Boice, *Radiology* 131:589, 1979

Age at Exposure
Radiation-Induced Breast Cancer Studies



UNSCEAR, p. 155, 1994

Preston et al. *Rad Res* 2002

Lung and Leukemia
TB - Fluoroscopy, Massachusetts

	Lung	Leukemia
No. exposed	6,285	6,285
No. unexposed	7,100	7,100
No. chest fluoroscopies (ave)	77	77
Dose to lung or marrow	840 mGy	90 mGy
Observed (O)	69	17
Expected (E)	86	19
RR (95% CI)	**0.8** (0.6-1.0)	**0.9** (0.5-1.8)

Davis et al, *Cancer Res* 49:6130, 1989

No excess lung or leukemia

Not all tissues respond similarly to fractionation.

Lung Cancer - Canada
TB - Fluoroscopy vs Atomic Bomb

	Relative Risk by Lung Dose (mGy)						ERR/Gy (95% CI)
	<10	10 -	500 -	1,000 -	2,000 -	3,000 -	
Multiple fluoroscopy	1.0	0.87	0.82	0.94	1.09	1.04	0.00 (–0.06, 0.07)
Atomic bomb	1.0	1.26	1.45	1.93	2.65	—	0.60 (0.27, 0.99)
	Numbers of Lung Cancer by Lung Dose (mGy)						
	<10	10 -	500 -	1,000 -	2,000 -	3,000 -	
Multiple fluoroscopy	723	180	92	114	41	28	
Atomic bomb	248	290	38	30	10	3	

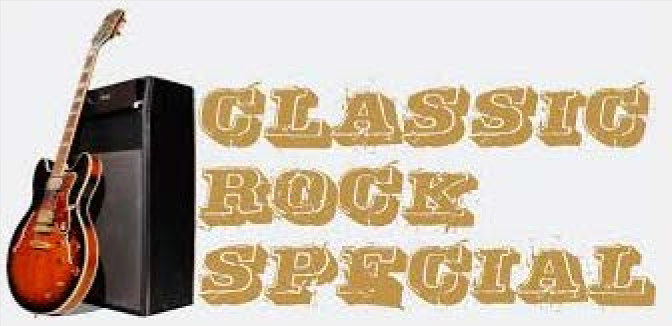
Howe, G. (1995). Radiat. Res. **142**, 295

Summary
TB Fluoroscopy

- Tissues respond differently to the effects of fractionated doses
- Age at exposure modifies effect
- Be cautious when generalizing – one size doesn't fit all – all models are wrong, some are useful

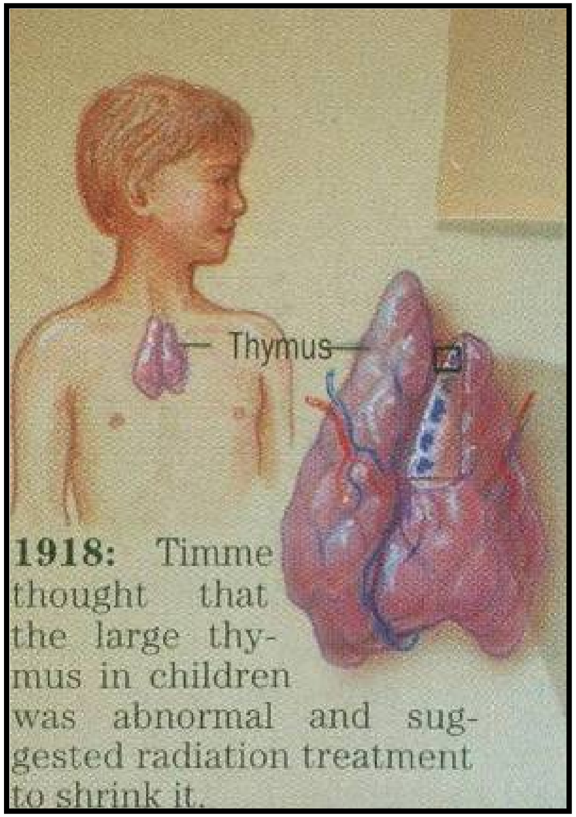
Hall of Fame (1950-1970s)

- Thymus
- Tinea Capitis
- Hemangioma
- I-131
- Tuberculosis



Thyroid Cancer Thymus Irradiation

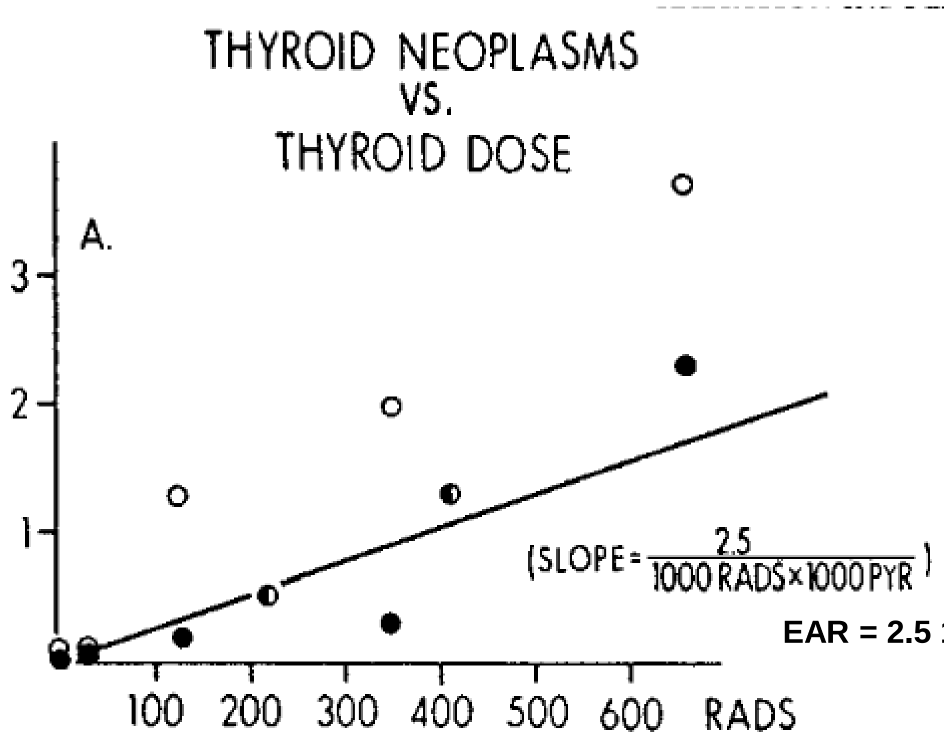
In 1950 Robert W Miller MD was assigned by Atomic Energy Commission to University of Rochester. In his Memoriam to Hempelmann (1993) he wrote:



"In 1950 he [Hempelmann] joined the faculty at the University of Rochester as an Associate Professor of Experimental Radiology. Benedict Duffy, who came to a neighboring department soon after, had just published on a case-series of 28 children who had developed thyroid cancer. Surprisingly, 10 had received thymic radiotherapy as infants.

Incidence of Thyroid Neoplasm (Hemplelmann et al. *Science* 1968; JNCI 1975)

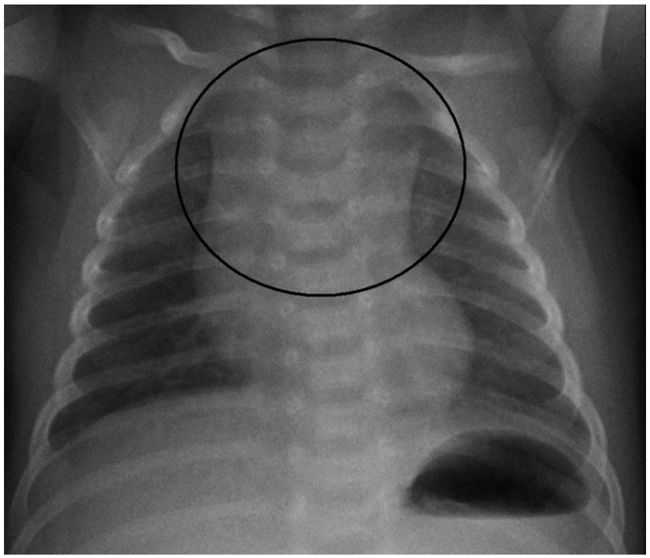
Louis Hempelmann with J Robert Oppenheimer

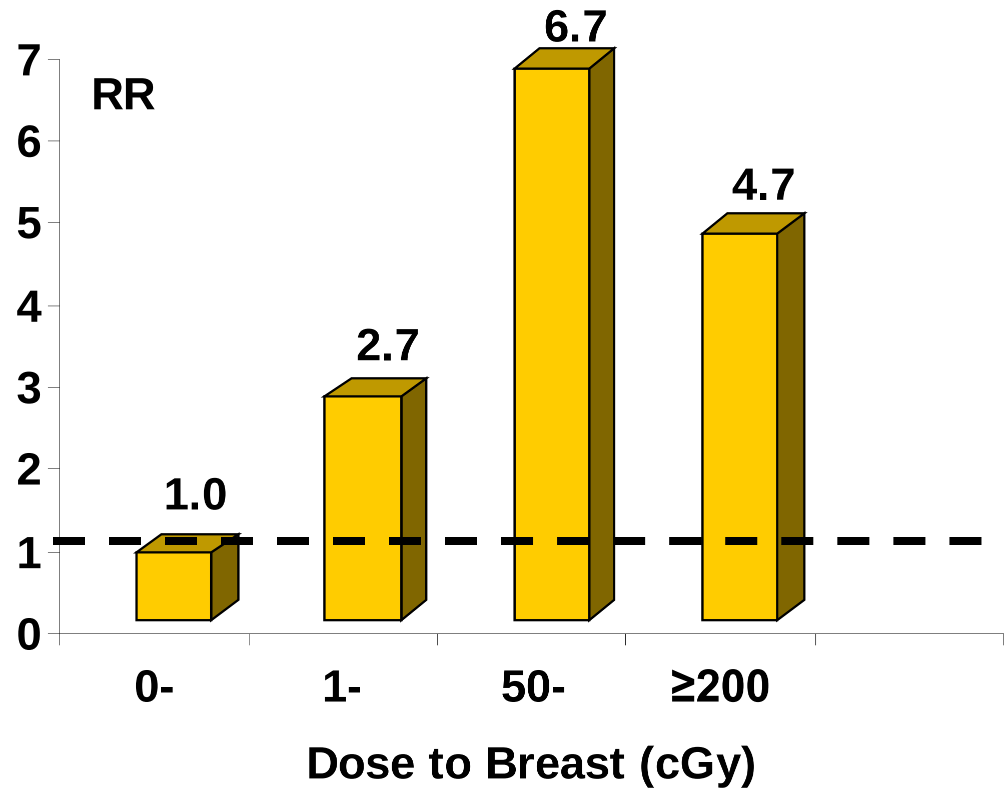


EAR = 2.5 10^{-4} PY Gy

Update: Adams et. al. *Rad Res* 2010

Breast Cancer Thymus Irradiation

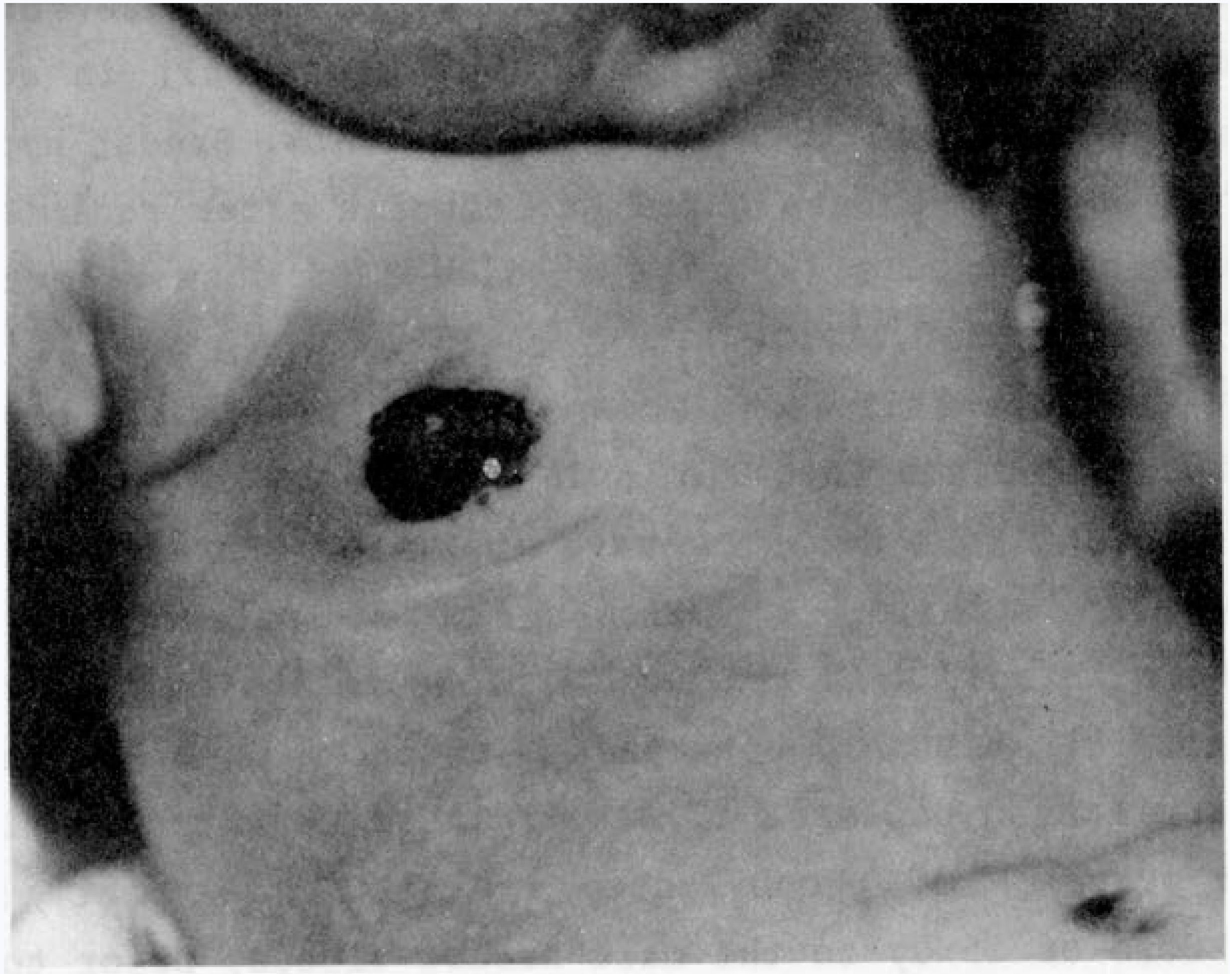




Hildreth et al, *NEJM* 321:1281, 1989

Immature breast tissue at risk but risk manifests many years later.

Update Adams et. al. *CEBP* 2010



Cavernous Hemangioma in girl, 6 months old
1936, Ra-226, 6.6 Gy to breast

Lundell et al Rad Res 1999

Breast Cancer After Infant Exposure
Dose Rate Reduction (DDREF = 7)

Study Exposure	Breast Dose (Gy)*	Number Treated	Breast Ca	Excess Risk (10^4 WY- Gy)
Thymus				
High-dose-rate X-rays	0.7	3,312	34	34.0
Hemangioma				
Low-dose-rate Gamma radiation	0.4	17,082	226	5.1

***Ranges (0.02-7.5 Gy) & (0.02-35 Gy)**

Preston et al, *Radiat Res*, 158:220, 2002

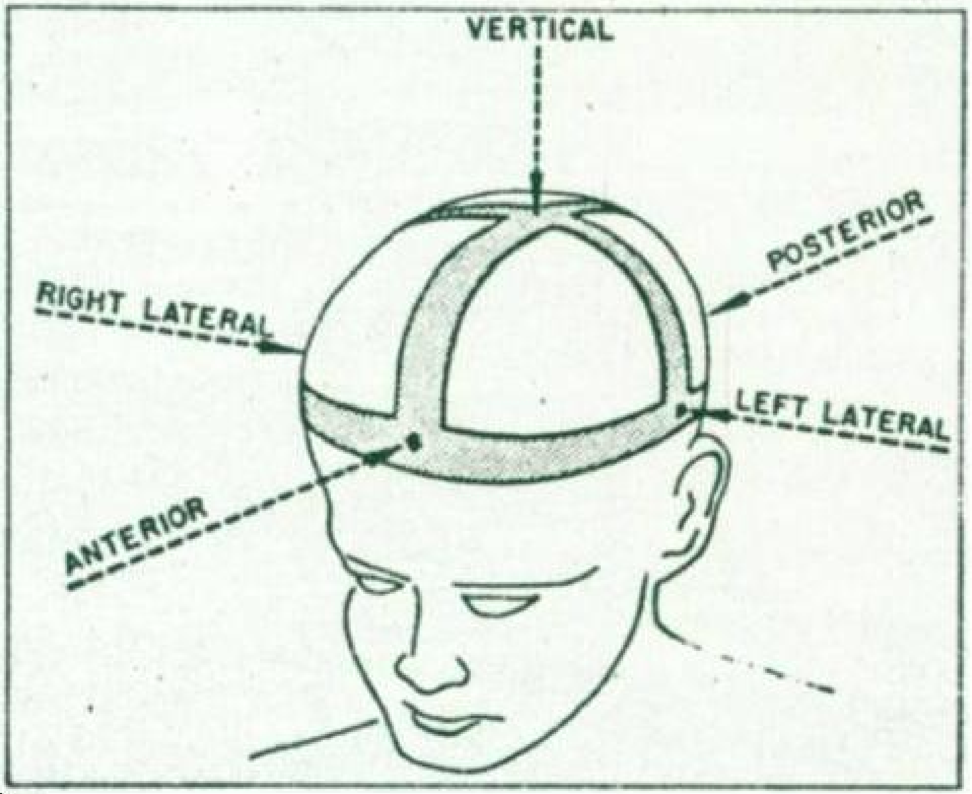
Consistent with a *low dose rate* having a smaller effect

Eidemüller M et al. Mutat Res. 2015 May--Risk estimates are a factor of 2 higher as a consequence of dosimetry re-evaluation.

Radiotherapy for Ringworm
5 treatments, 3-12 minutes each

TINEA CAPITIS WITH KERION FORMATION
II-YEAR-OLD BOY WITH 3 YEAR INFECTION

Fig 1.—Five Treatment fields used in the Adamson-Kienbock treatment were positioned with the aid of a "cap" made from steel bands.



Albert et al AJPH 1968; Modan et al Lancet 1974

Brain Tumor
Tinea Capitis - Israel

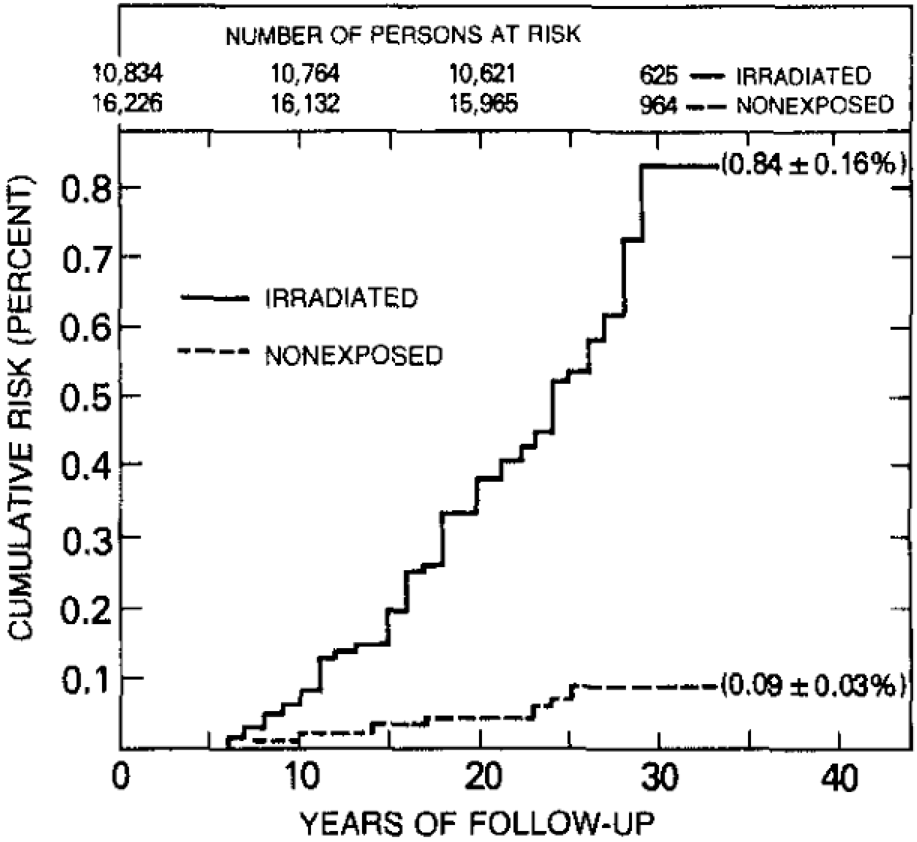
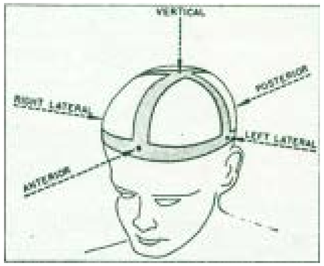


Figure 1. Cumulative Risk of Neural Tumors among Irradiated Subjects, as Compared with the Combined Control Groups.

Ron et al, *NEJM*, 1988

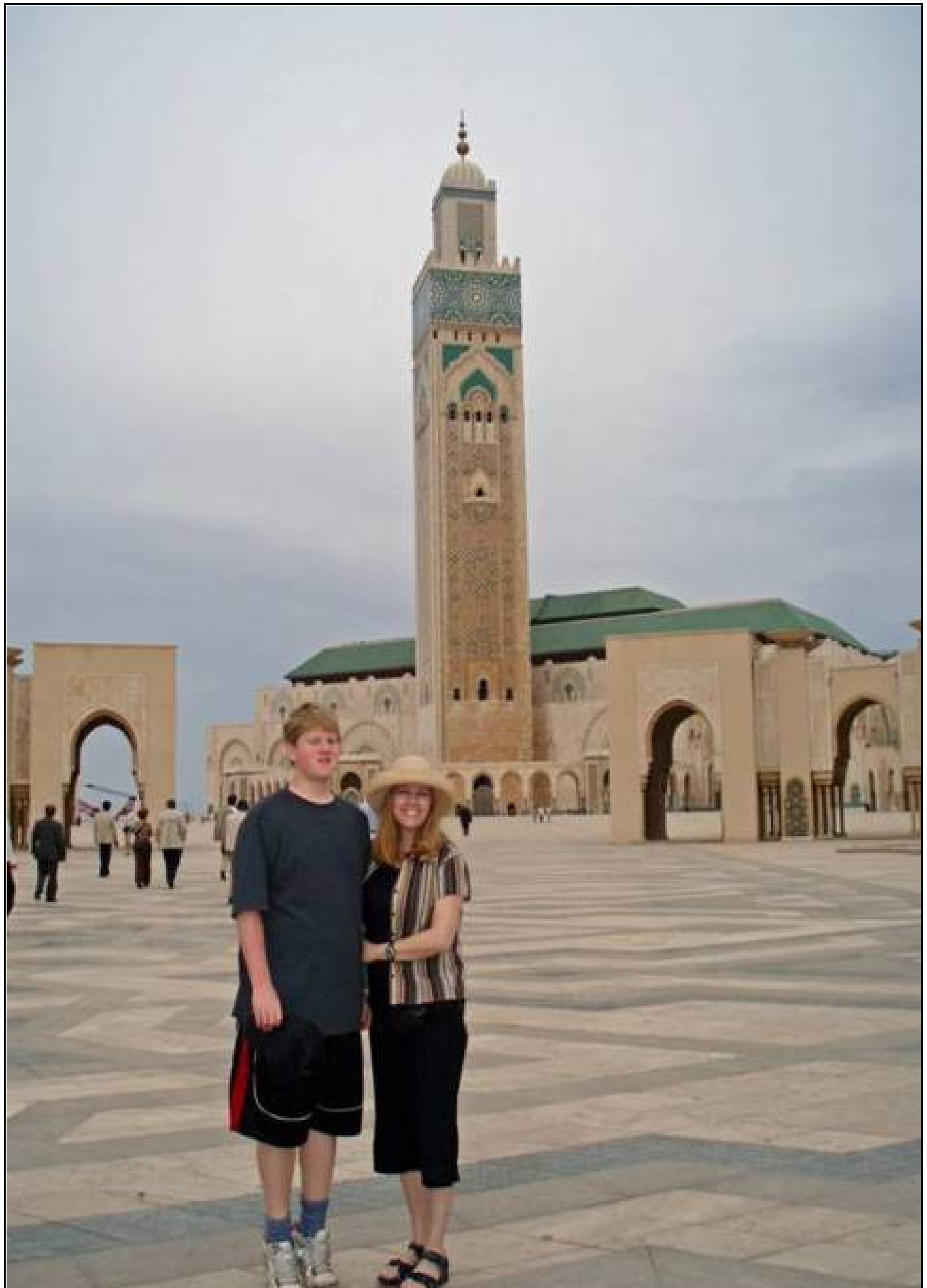
Thyroid
Tinea Capitis - Israel



Number Exposed:	10,834
Number Nonexposed:	16,226
Thyroid Dose (mean):	9 cGy
Observed Thyroid Cancers:	43
Expected:	10.7
RR (95% CI):	4.0 (2.3 - 7.9)

Ron et al, *Radiat Res* 120:516, 1989

Wiggle, Morocco, genetic

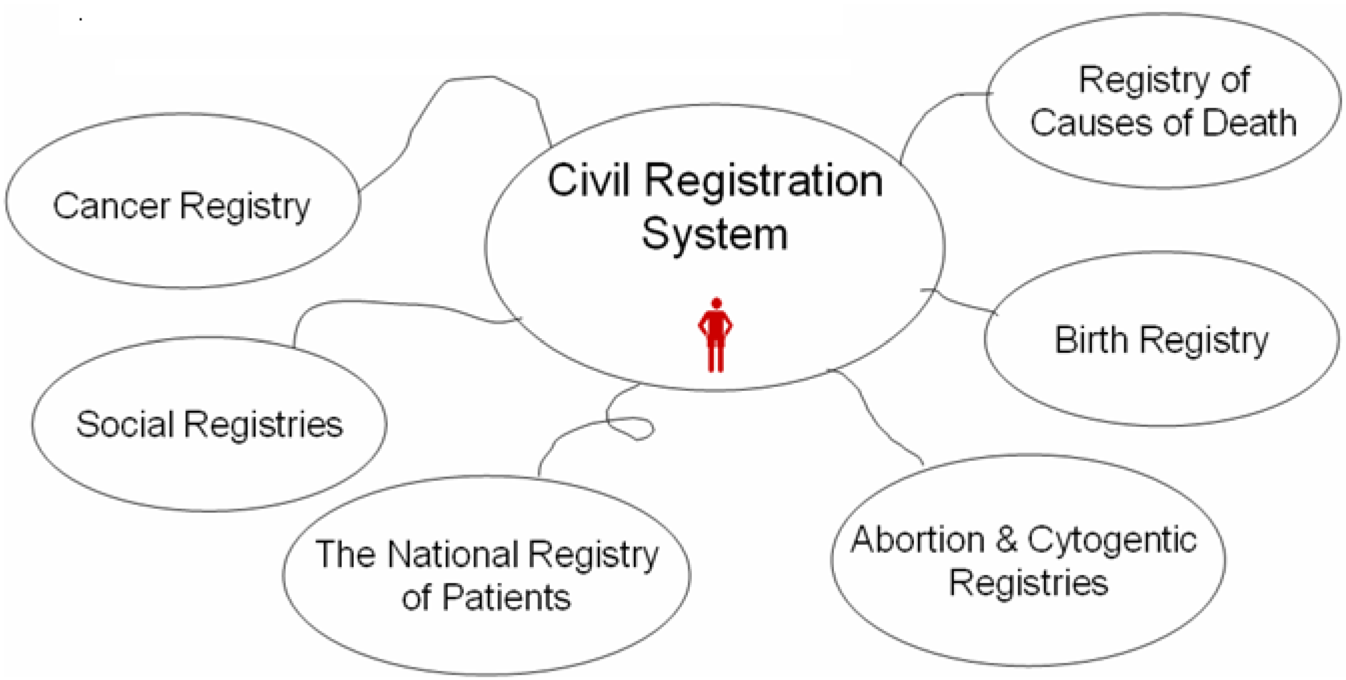


Some Uncertainties of Epidemiology…

- Effect primarily among immigrants, mainly from **Morocco**, not Israeli born (Ron, *Rad Res*, 1989)
- "Irradiation for tinea capitis was given to many Jews in **Morocco** prior to immigration…"(Modan, *JNCI* , 1980)
- **Genetic susceptibility** & family clustering (4 sisters thyroid disease)
- **Wiggle** could increase dose x 3
- Immigrants from Morocco came from Atlas Mt region, and **diets** deficient in stable iodine

Scandinavia – Epidemiologic Gold Mines

Kaiser J. Swedish bioscience. Working Sweden's population gold mine. Science. 2001



Leukemia Incidence
Swedish I-131 Studies

	Diagnostic I-131	Hyperthyroidism Therapy	Cancer Therapy
No. patients	36,326	9,860	802
Mean bone marrow dose (cGy)	0.02	4.8	25.1
Non-CLL			
No. cases	103	25	2
SIR	1.2	0.8	1.2
95% CI	(0.95-1.4)	(0.6-1.2)	(0.2-4.4)

Hall et al, *Lancet* 2:1, 1992

Thyroid Cancer
Swedish Diagnostic I-131 (Scans)

Number Exposed:	24,010
Years of Scans	1952-69
Thyroid Dose:	0.94 Gy (94 rad)
Observed Thyroid Cancer:	36
Expected:	39.5
RR (95% CI)	0.9 (0.6 - 1.3)

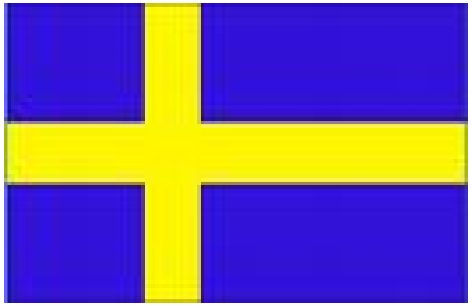
Dickman et al, *Int J Cancer,* 106:580, 2003

Hall et al, *Radiat Res,* 145:86, 1996

Confounding by Indication ?

- Thyroid cancer following I-131 scans for evaluation of suspected tumor in Sweden among 36,792 adults (ave thyroid dose 0.94 Gy)

Dickman PW, Holm LE, Lundell G, Boice JD Jr, Hall P. Thyroid cancer risk after thyroid examination with 131I: A population-based cohort study in Sweden. Int J Cancer 106(4):580–587; 2003.



We abstracted clinical data for all 36,792 patients, including thyroid size, I-131 activity administered and the reason for the examination. **Holm et al. JNCI (1988)**

Reason for I-131 Scan
All Reasons

Reason for I-131 Scan (No. Cancers)	RR of Thyroid Cancer by Years After I-131 Scan 2-	5-	10-	>20	All
All Reasons (105)	3.1*	2.5*	1.2	1.7*	1.8*

- Significant thyroid cancer risk overall (RR 1.8*)

Note that the adult thyroid gland is not considered radiosensitive.

Reason for I-131
Suspicion of Tumour

Reason for I-131 Scan (No. Cancers)	RR of Thyroid Cancer by Years After I-131 Scan 2-	5-	10-	>20	All
All Reasons (105)	3.1*	2.5*	1.2	1.7*	1.8*
Suspicion of Tumour (69)	6.3*	4.8*	2.3*	3.5*	3.5*

- Risk very high when reason for Scan was a suspicion of tumour (RR 3.5*)

Reason for I-131
Other Than Suspicion of Tumour

Reason for I-131 Scan (No. Cancers)	RR of Thyroid Cancer by Years After I-131 Scan				
	2-	5-	10-	>20	All
All Reasons (105)	3.1*	2.5*	1.2	1.7*	1.8*
Suspicion of Tumour (69)	6.3*	4.8*	2.3*	3.5*	3.5*
Other Reasons (36)	1.3	1.5	0.6	0.9	0.9

- No excess risk if Scan performed for “other reasons” (RR 0.9), e.g., hyperthyroidism and hypothyroidism.

Reverse Causation Bias Lasted for More than 20 years after 131-I Exam

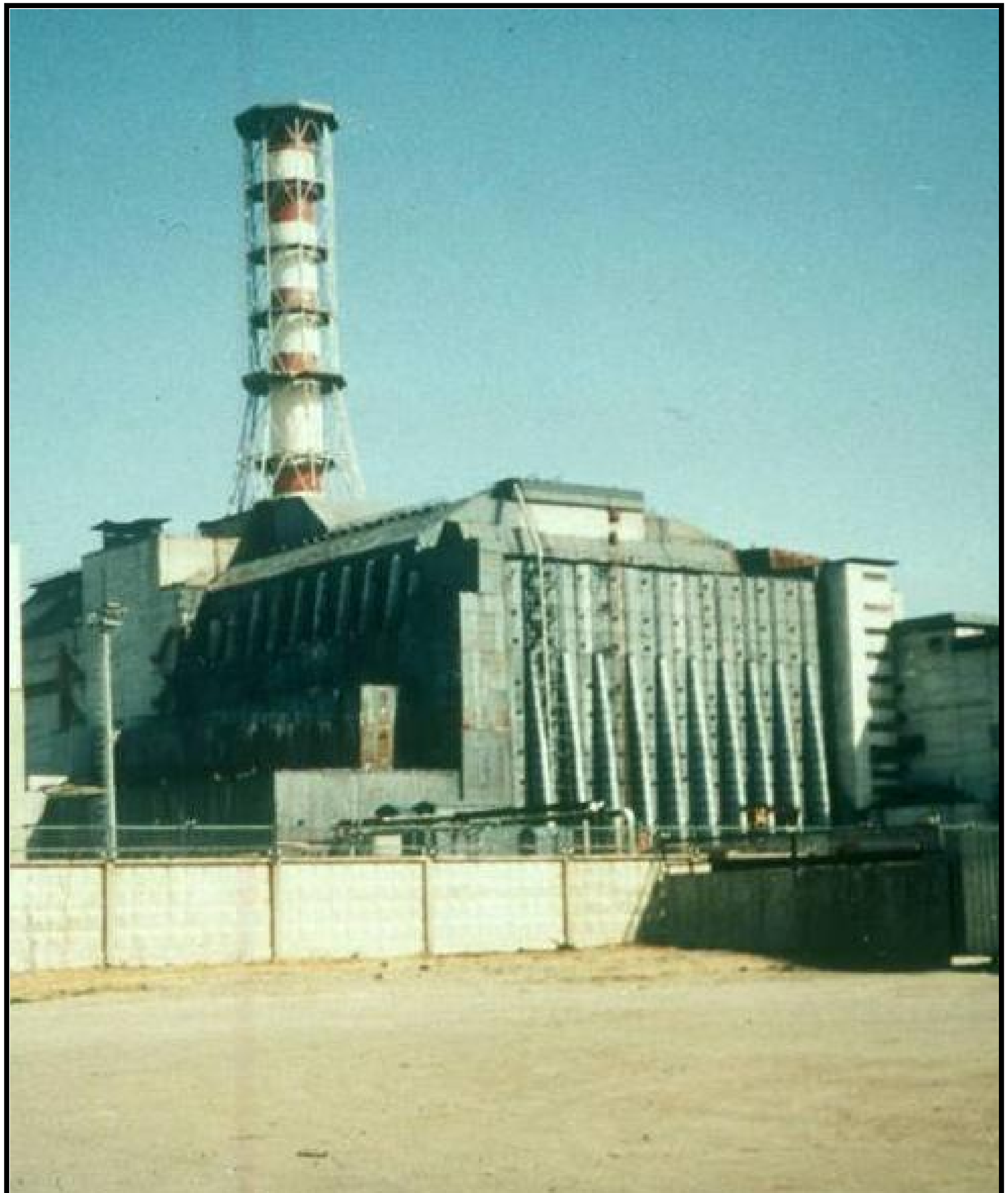
Reason for Scan (No. Cancers)	RR of Thyroid Cancer by Years After Scan				
	2-	5-	10-	>20	All
All Reasons (105)	3.1*	2.5*	1.2	1.7*	1.8*
Suspicion of Tumour (69)	6.3*	4.8*	2.3*	3.5*	3.5*
Other Reasons (36)	1.3	1.5	0.6	0.9	0.9

- The "suspicion of tumour" predicted future diagnoses of cancer even 20 years after examination

I-131 did not cause the thyroid tumors; the thyroid tumors caused the I-131 exams

Hits (1980 - 1990s)

- Chernobyl
- Hanford
- Mayak
- Hodgkin Lymphoma
- Retinoblastoma
- Childhood Cancer
- Rocketdyne (Atomics International)



Thyroid Cancers in Children in Belarus

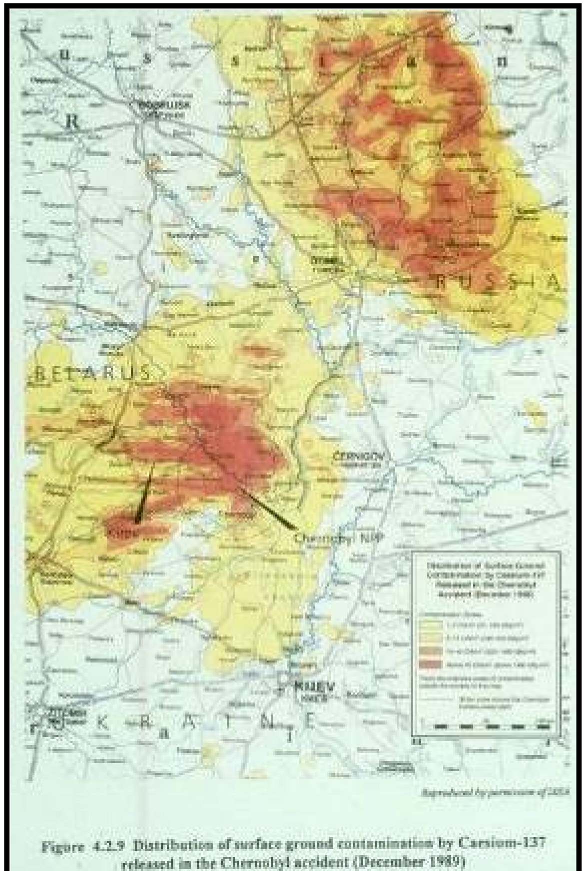
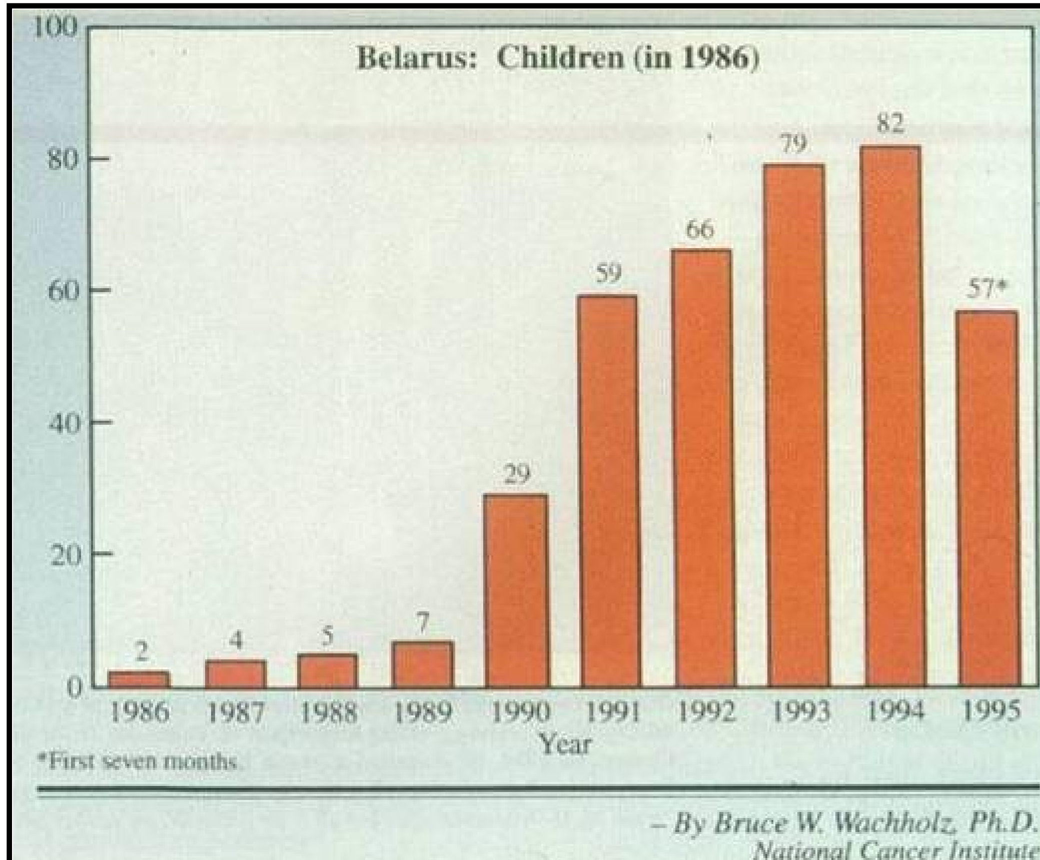


Figure 4.2.9 Distribution of surface ground contamination by Caesium-137 released in the Chernobyl accident (December 1989)

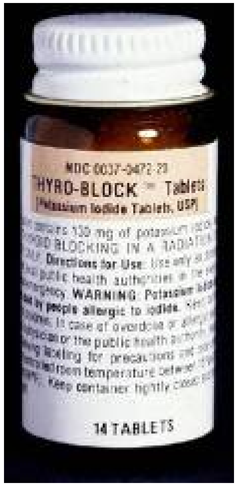


Belarus Milk
Japanese children - Fukushima
Washington State

Thyroid Cancer (IARC 2005)
Risk Varies by KI and Endemic Goiter

Consumption of potassium iodide	RR at 100 rad (95% CI): Highest two tertiles of soil iodine	RR at 100 rad (95% CI): Lowest tertile of soil iodine
No	**3.5 (1.8 to 7.0)**	**10.8 (5.6 to 20.8)**
Yes	1.1 (0.3 to 3.6)	3.3 (1.0 to 10.6)

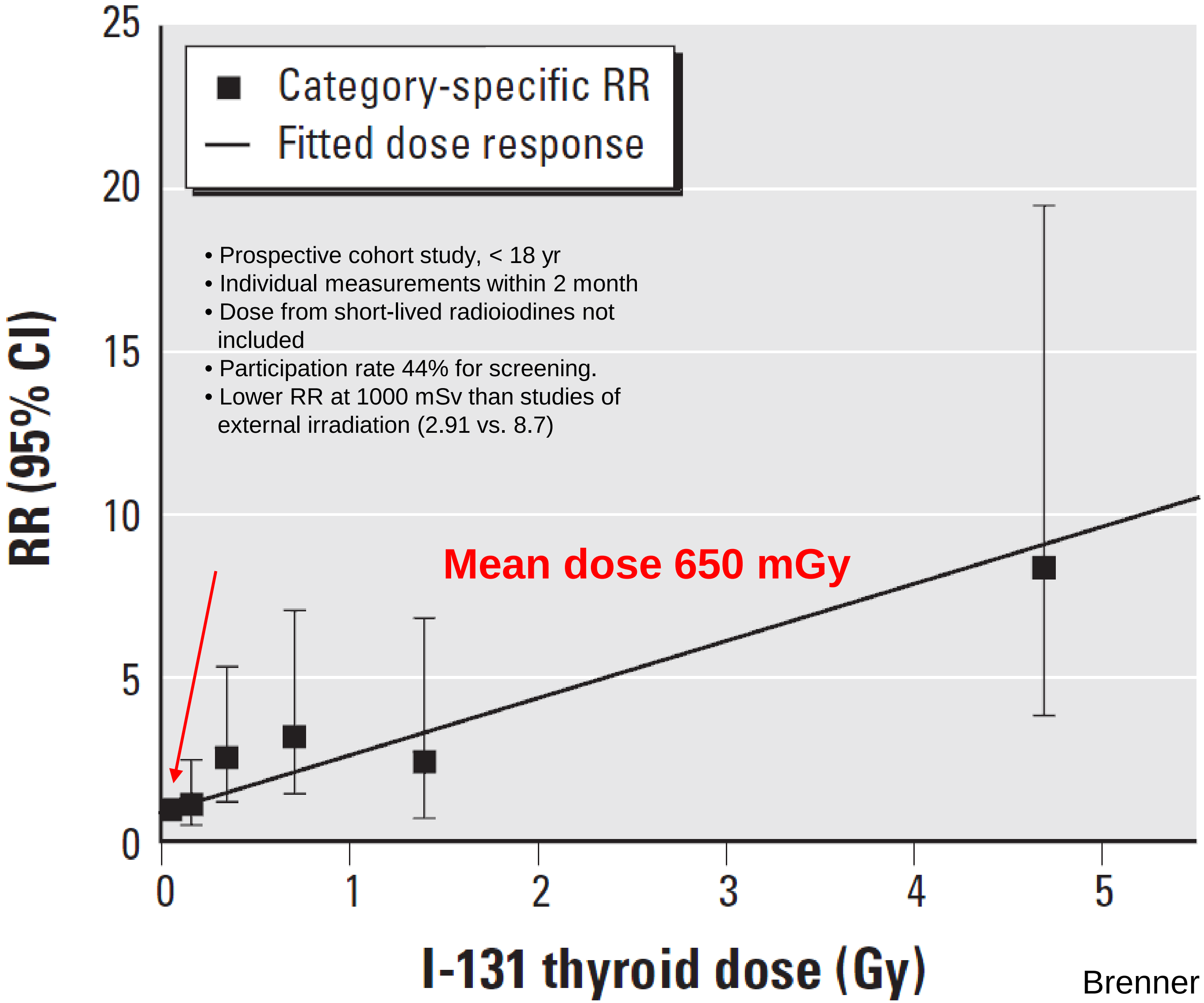
Lower risk seen among children with normal levels of stable iodine in diet.



Cardis *et al.* *JNCI* 97:724, 2005

Boice *JNCI* 97:703, 2005

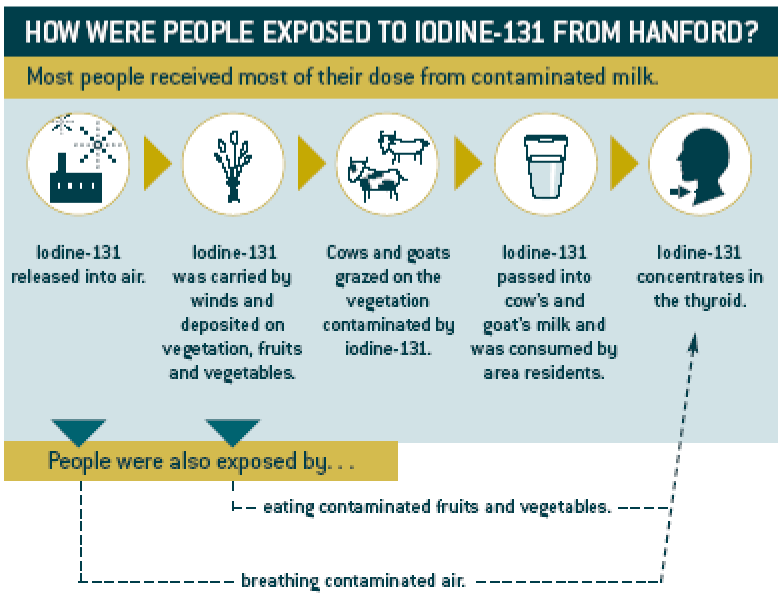
Ukrainian – American Chernobyl Thyroid Study

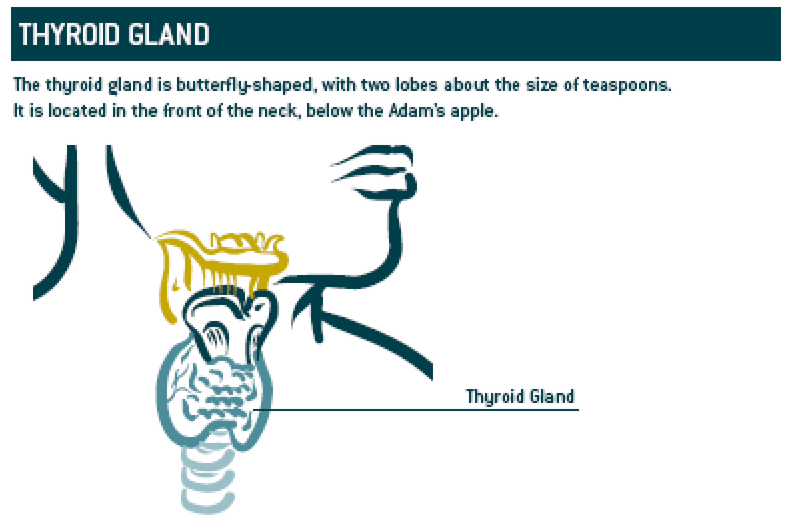


Brenner et al EHP 2011

Hanford Thyroid Disease Study

FINAL REPORT





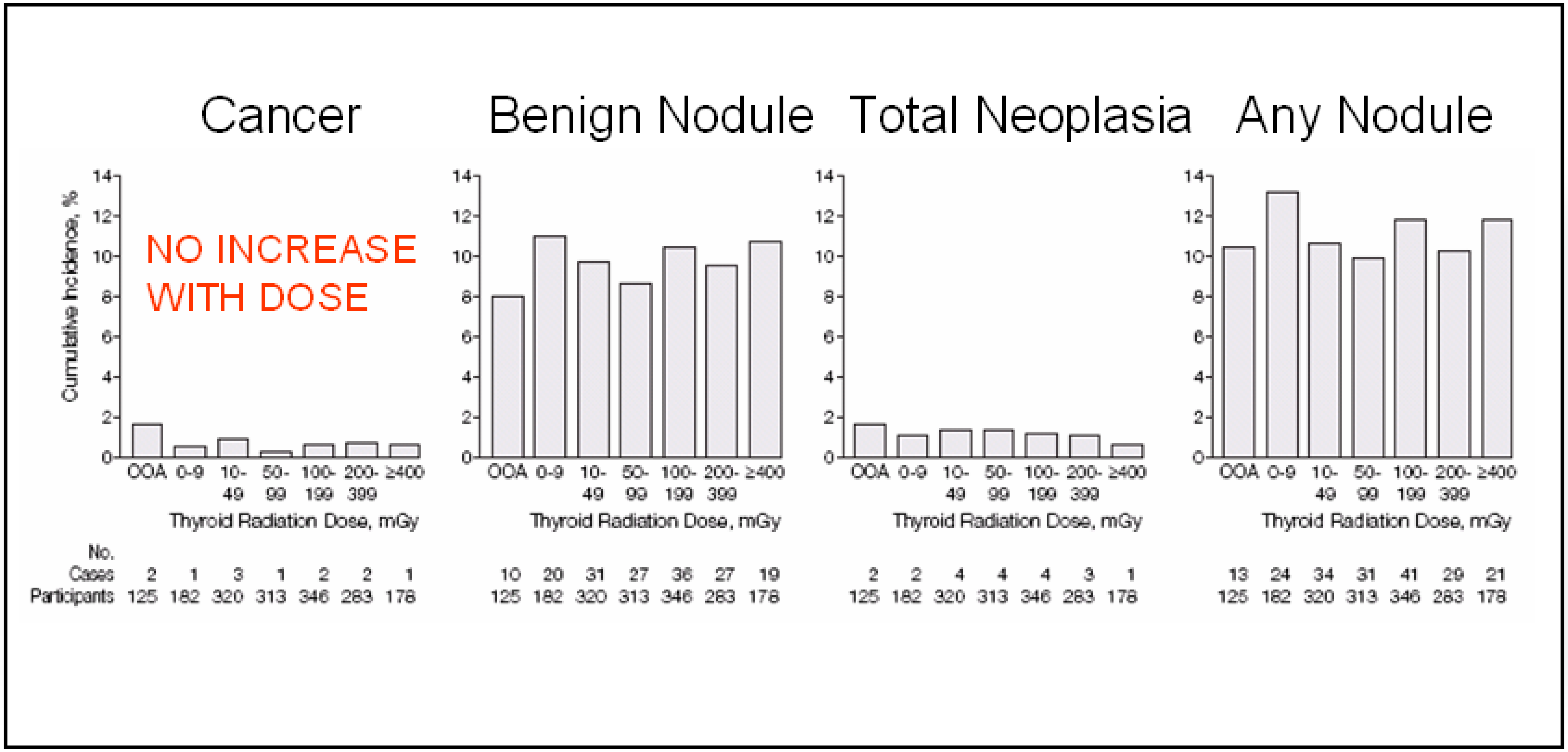
Davis S, Kopecky KJ, Hamilton TE. Hanford Thyroid Disease Study. Final Report. 2002. Fred Hutchinson Cancer Research Center, Seatle, WA. (CDC Conract No. 200-89-0716), June 21, 2002 (Available at: http://www.cdc.gov/nceh/radiation/hanford/htdsweb/pdf/htdsreport.pdf)

Hanford Thyroid Disease Study

- Exposure 1944-1957 (“pure” I-131)
- About 5,200 births in 1940-1946 selected
- 3,440 examined 1992-97
- Dose Reconstruction (174 mGy ave.; <1-1000+ mGy range)

Davis *et al.* Final Report, 2002; JAMA 292:2600, 2004

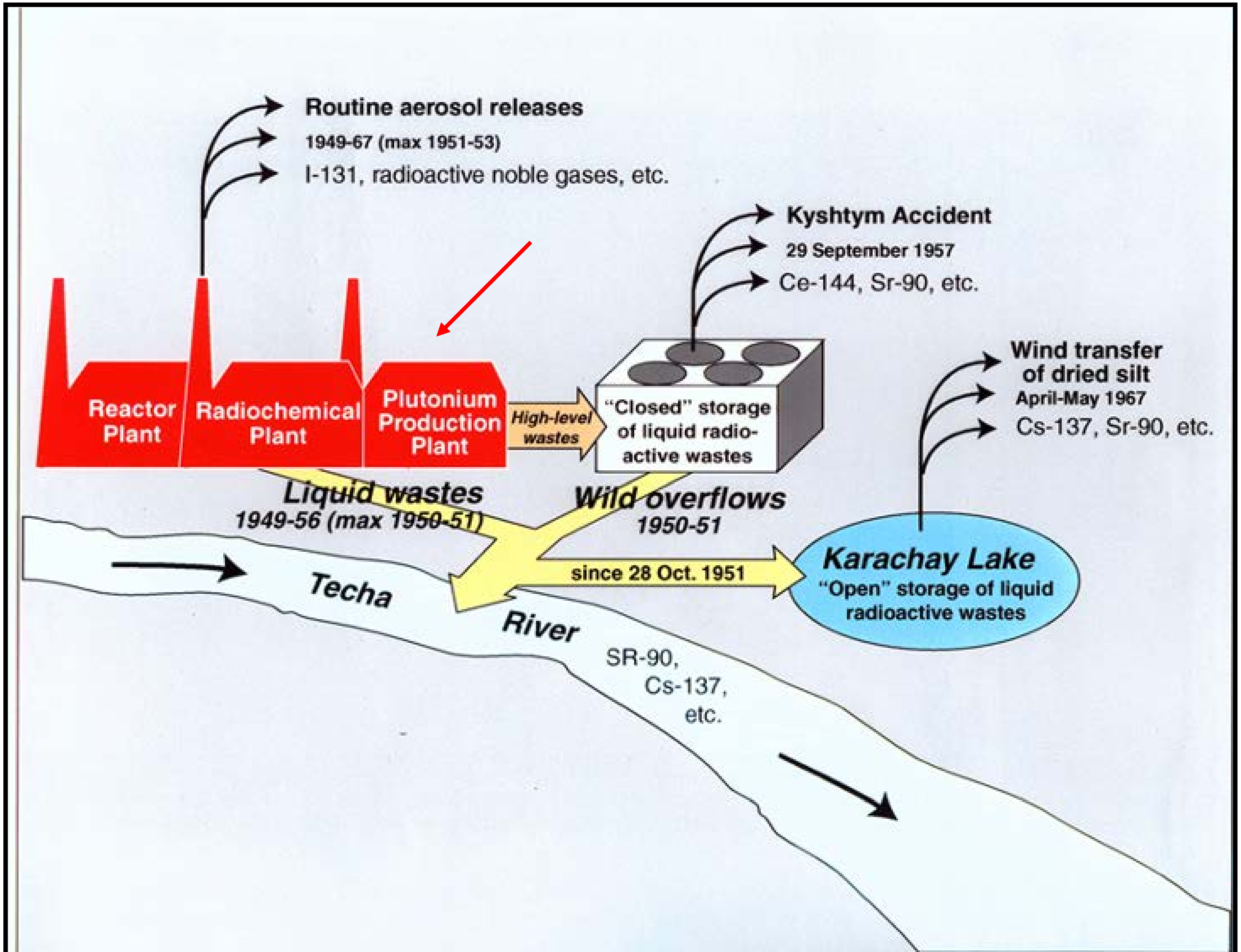
Cumulative Incidence of Thyroid Disease by Dose



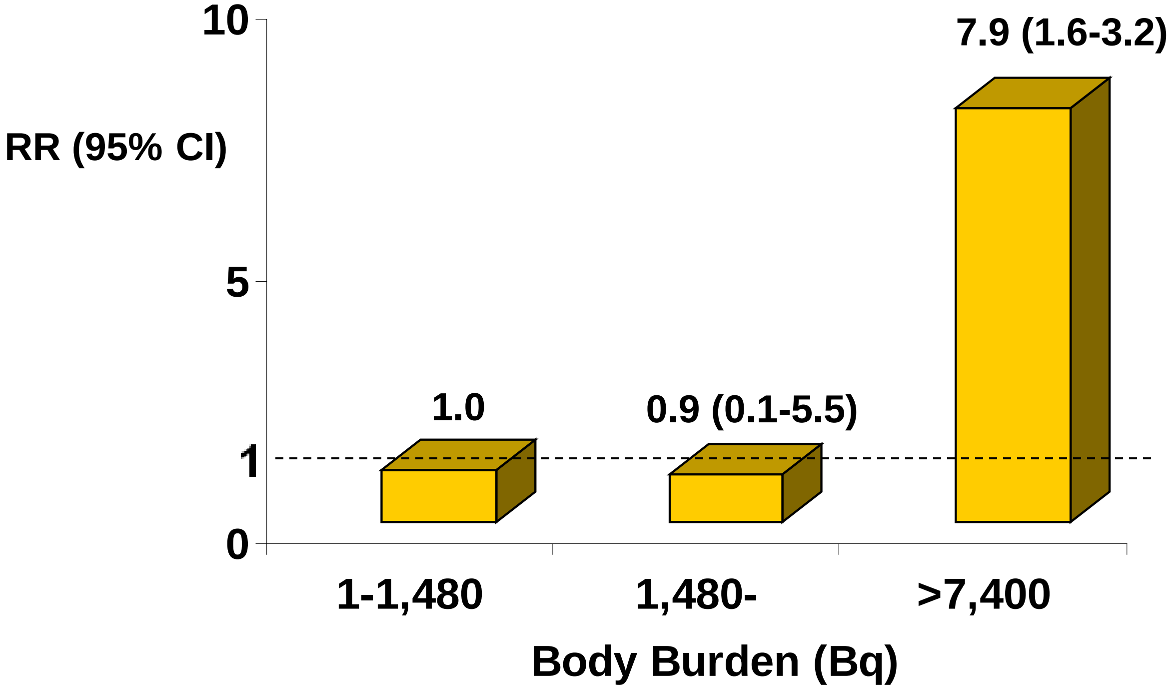
The percentage of people with thyroid disease is the same, regardless of dose.

Davis *et al.* Final Report, 2002; JAMA 292:2600, 2004

Mayak Nuclear Weapons Plant



Mayak - Plutonium - Bone



No. Bone Cancers	6	1	3
Person Years	162,540	15,614	4,410

Gilbert et al, *Radiat Res* 154:237, 2000

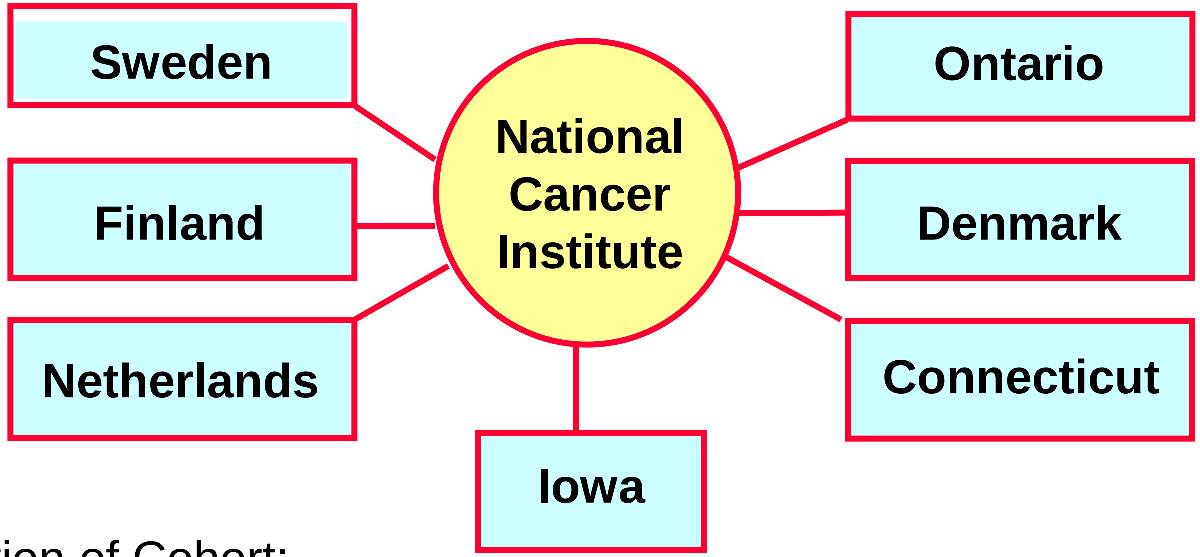
Alpha emitter, Bone threshold?
No leukemia excess. Shilnikova 2008

Sokolnikov et al, Int J Ca 2008– update_bone, liver, lung – same bone picture

Sokolnikov et al, PLos One, Feb 2015 – other than bone, liver, lung – low ERR/Sv

Hunter et al, Br J Ca PLos One, Oct 2013 – other than bone, liver, lung – no to low ERR/Sv

Lung Cancer Following Hodgkin Lymphoma International Case - Control Study (2002)



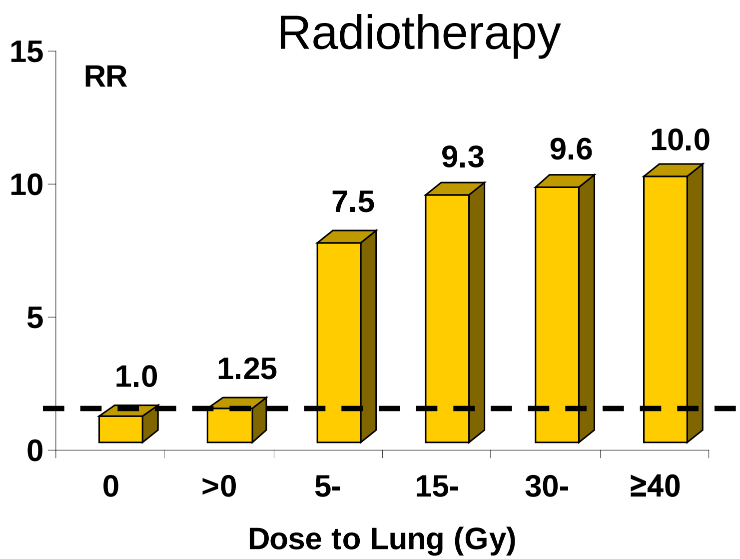
Definition of Cohort:

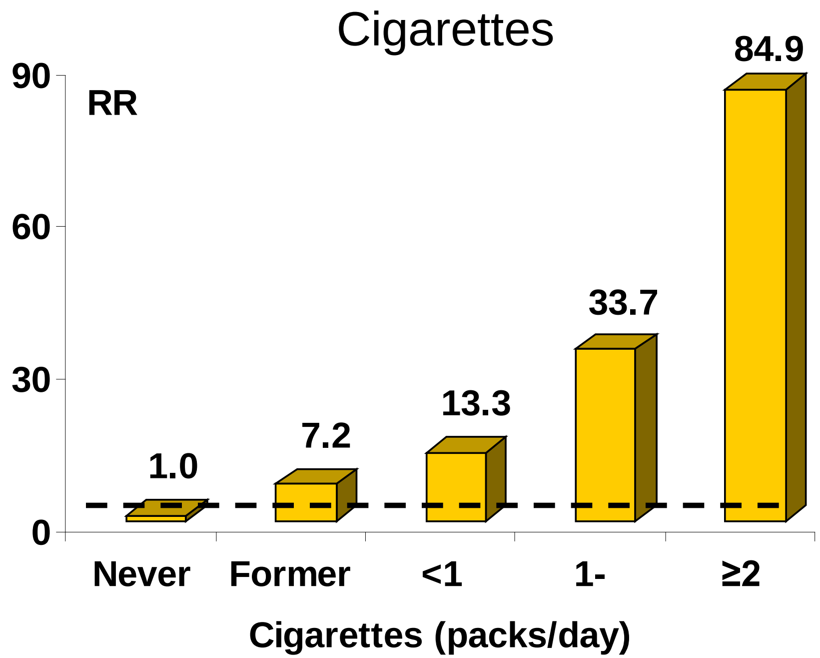
- Diagnosis of Hodgkin lymphoma: 1965-1994
- Survival of 1 or more years

Final Cohort: 22,977 (222 cases, 444 controls)

Travis et al. *JNCI* 94:182, 2002

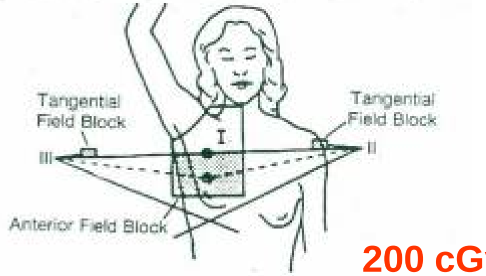
Lung Cancer After Hodgkin Lymphoma
Radiotherapy and Environmental Factors





<1 pack/day has greater risk than ≥40 Gy

Gilbert et al, *Rad Res* 159:161, 2003
Travis et al, *JNCI* 94:182, 2002



200 cGy (ave)

Radiotherapy for Breast Cancer
All Breast Cancers in Connecticut (1935-82)
Second Breast Cancer

	RR	95% CI
All Subjects*	**1.19**	0.9-1.5
Time After Exposure (Yr)		
5-9	0.99	0.7-1.4
≥10	**1.33**	1.0-1.8
Age at Exposure (Yr)		
<35	**2.26**	0.9-5.7
35 -	1.46	0.9-2.3
≥45	1.01	0.8-1.4

*655 Cases, 1,189 Controls

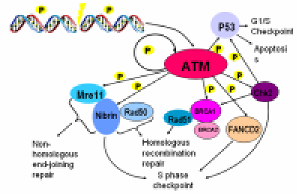
Boice et al, *NEJM* 326:781, 1992

Risk after 10 years among young.
Example of age modification.

Update: Stovall et al, Int J Radiat Oncol Biol Phys 72:1021-30,2008.

Memorial Sloan Kettering Cancer Center

WECARE Study Collaborative Group



Genetic Susceptibility Second Breast Cancer

	Exposure	RR	95% CI
Genes	*BRCA1* mutation	5.1	3.0-8.5
	BRCA2 mutation	3.9	2.2-7.0
Radiation	1 Gy (age <40 y)	**1.6**	1.1-2.5
	1 Gy (age ≥45 y)	1.0	0.9-1.3

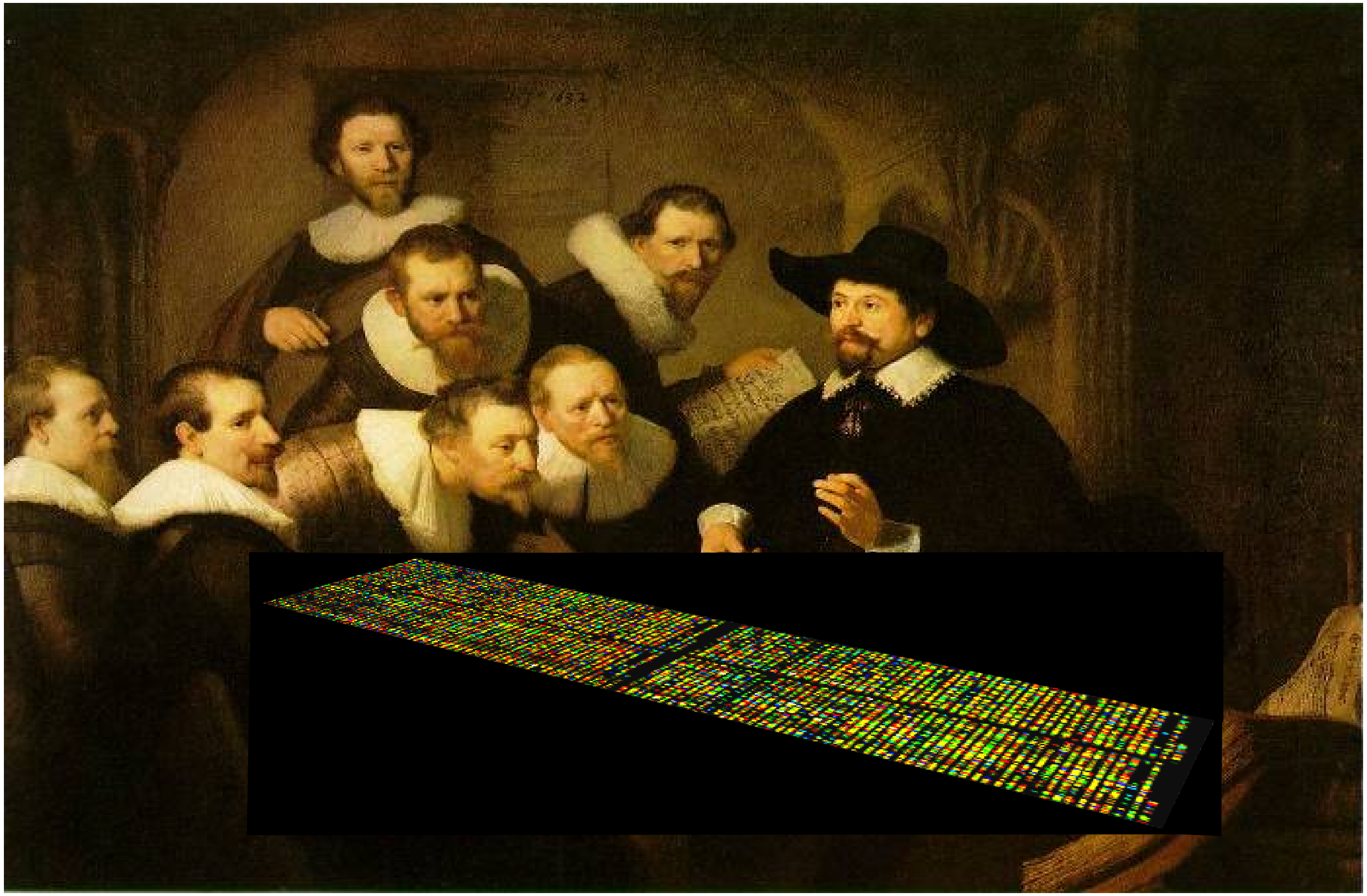
Bernstein J et al. BRCA1_Eur J Ca 2013
Bernstein J et al. ATM_JNCI 102, 2010
Concannon et al. *Cancer Res* 68, 2008

Stovall, *IJROBP* 72, 2008
Begg et al, *JAMA* 2008

1 – Genes Predispose to Breast Cancer – *BRAC1*/2, *PALB2*…
2 – Radiation Risk When Exposures Occur Early, < 40 y
3 – Some Women may be Particularly Sensitive by Virtue of their Genetic Backdrop

- Genetics more important than dose
- Risk only among young women at Rx
- Doses lower than in the past

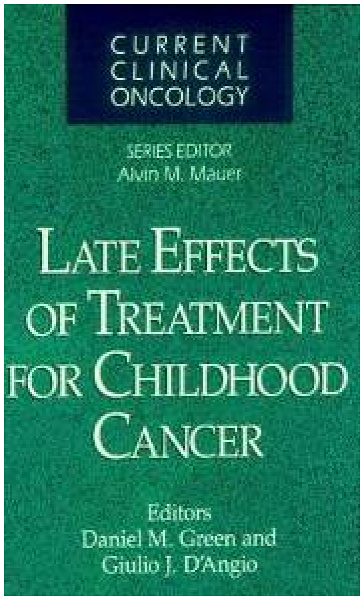
If Rembrandt were alive Today
The *Genomics* “Anatomy Lesson”

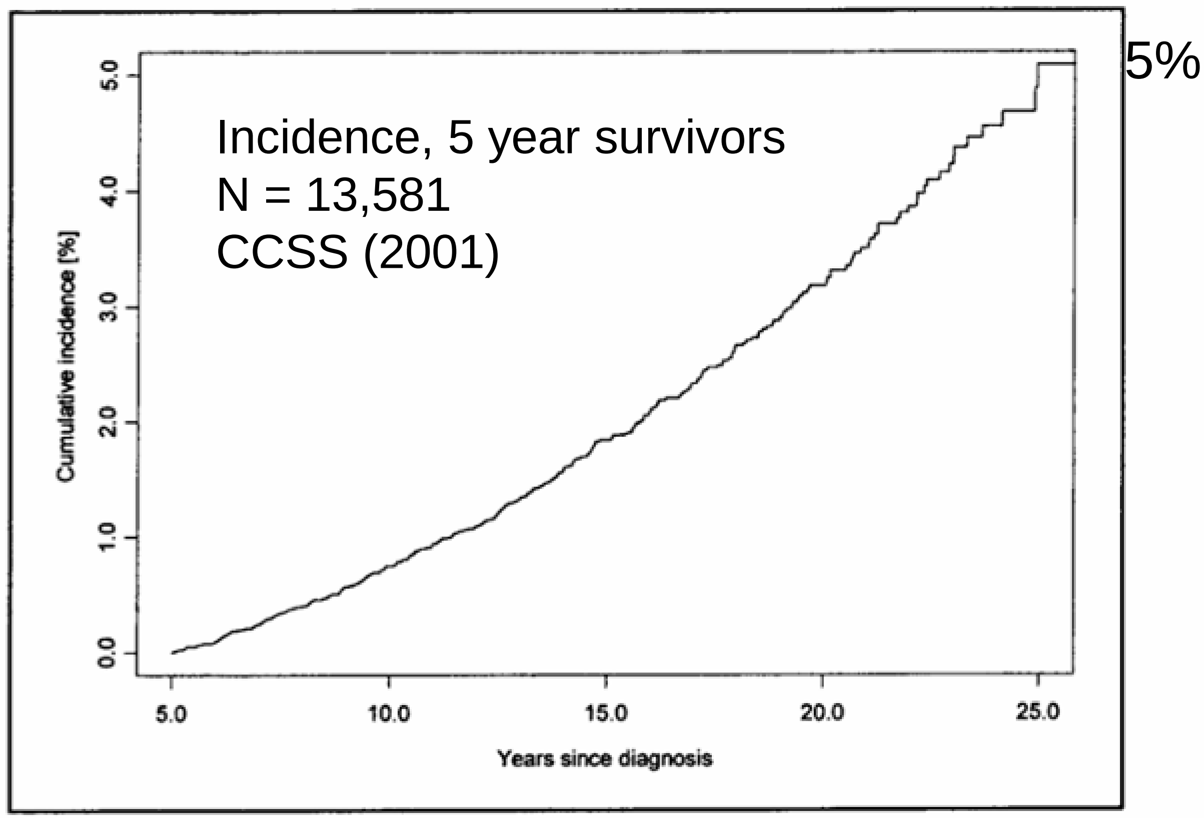


Methods have focused on candidate genes, pathways and across the genome.

Courtesy of Dr Lois Travis, Roswell Park Medical Center

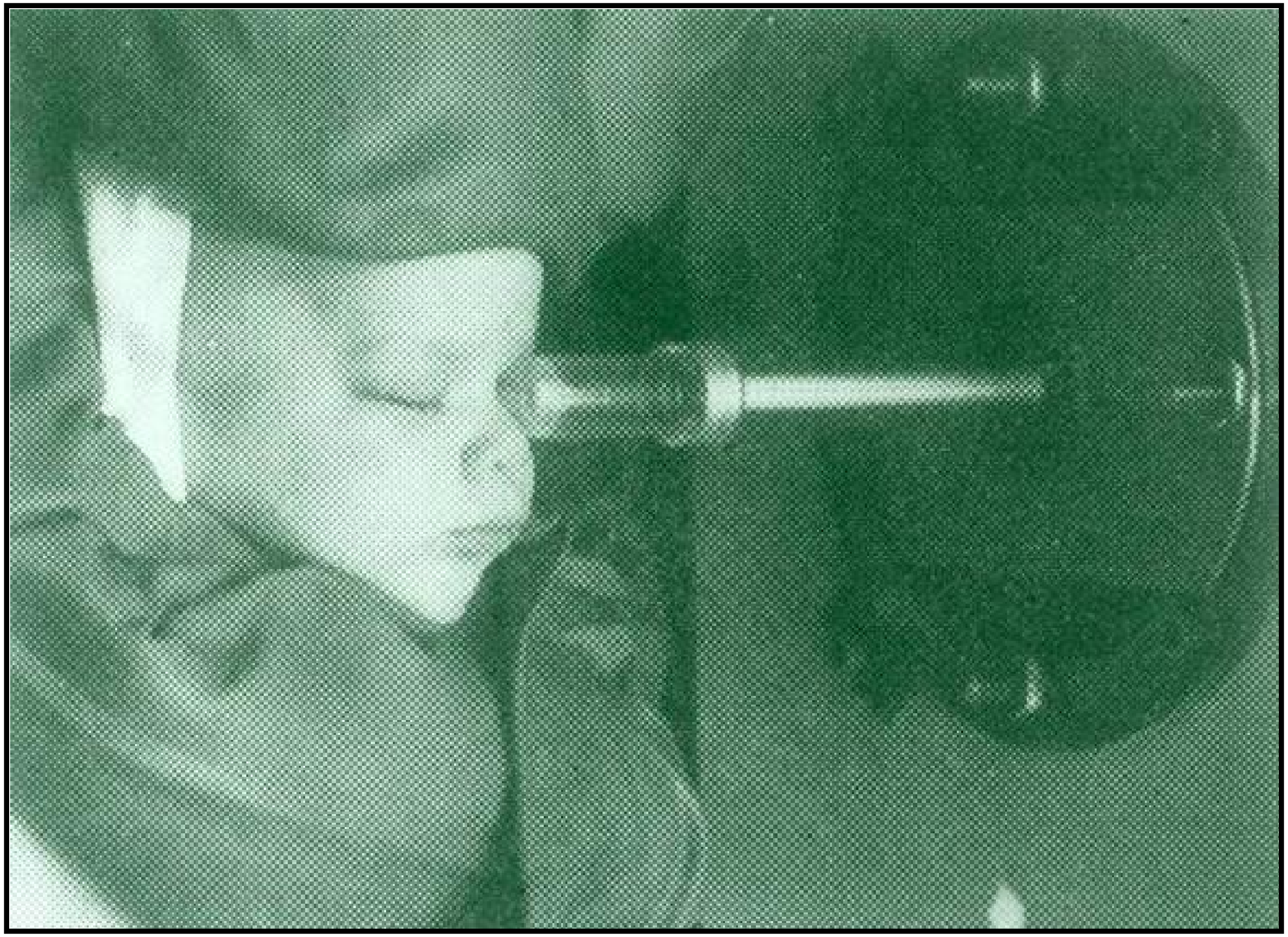
2nd Cancers After Childhood Cancer (CCSS)



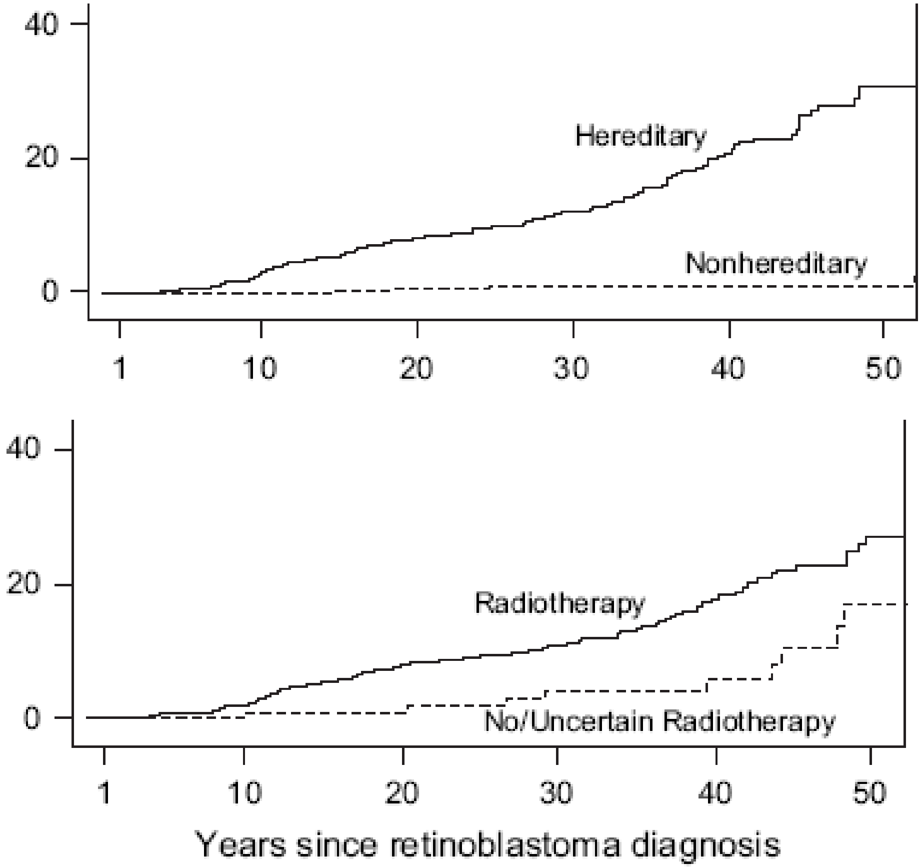


Neglia, *JNCI* 93:618, 2001

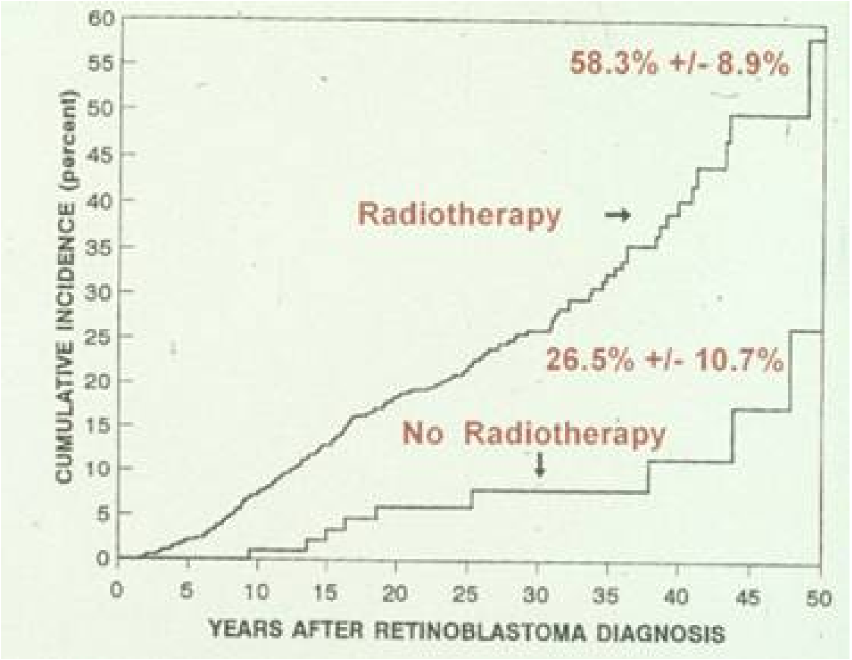
Early Treatment of Retinoblastoma



Second Cancer after Retinoblastoma



Possible high dose interaction with genetic susceptibility

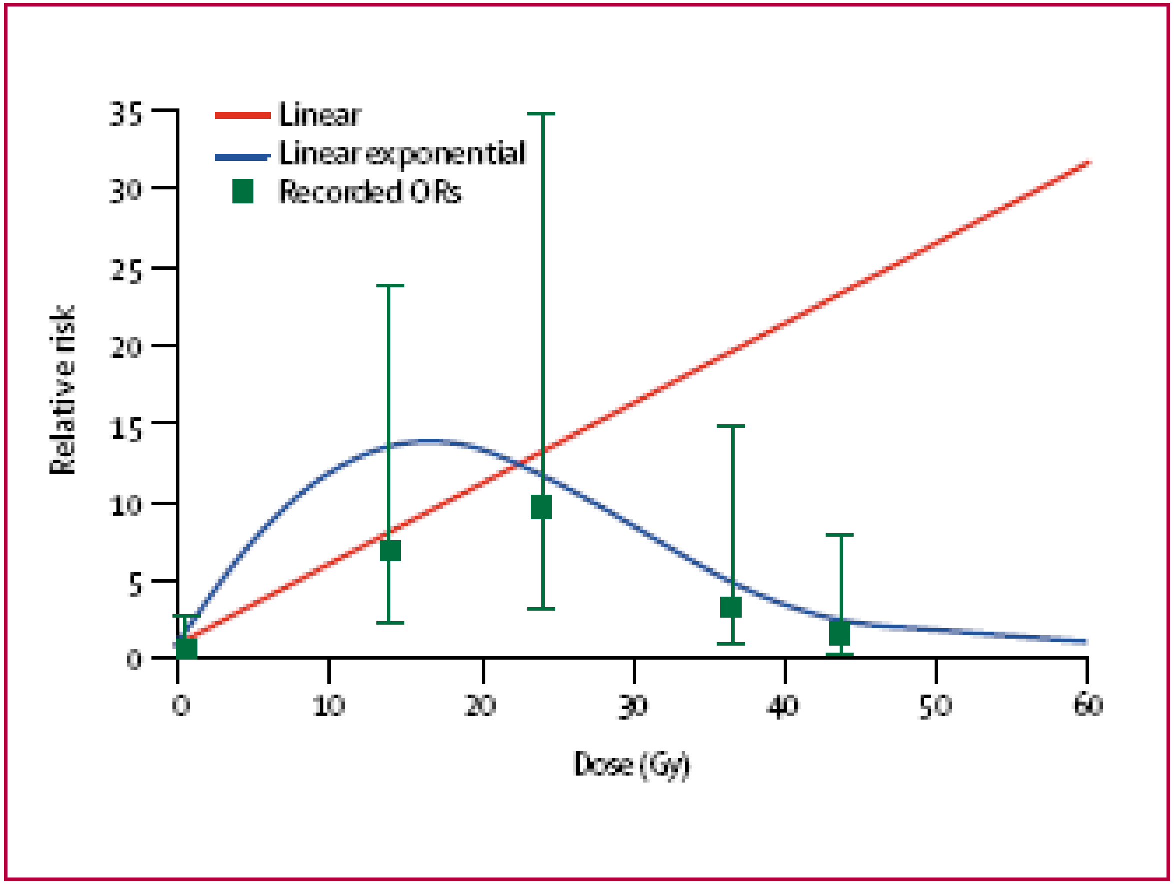


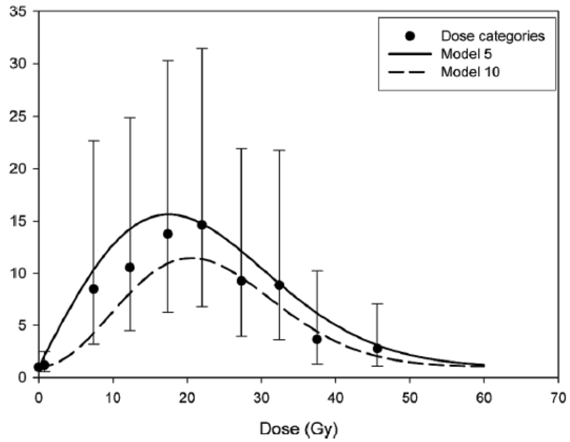
Updated. Yu et al.
***JNCI 101:581,* 2009**

Updated. Kleinerman et al.
***JCO 23:2272,* 2005**

Wong et al.
***JAMA 278:1262,* 1997**

Thyroid Cancers After Childhood Cancer (CCSS) Cell Killing



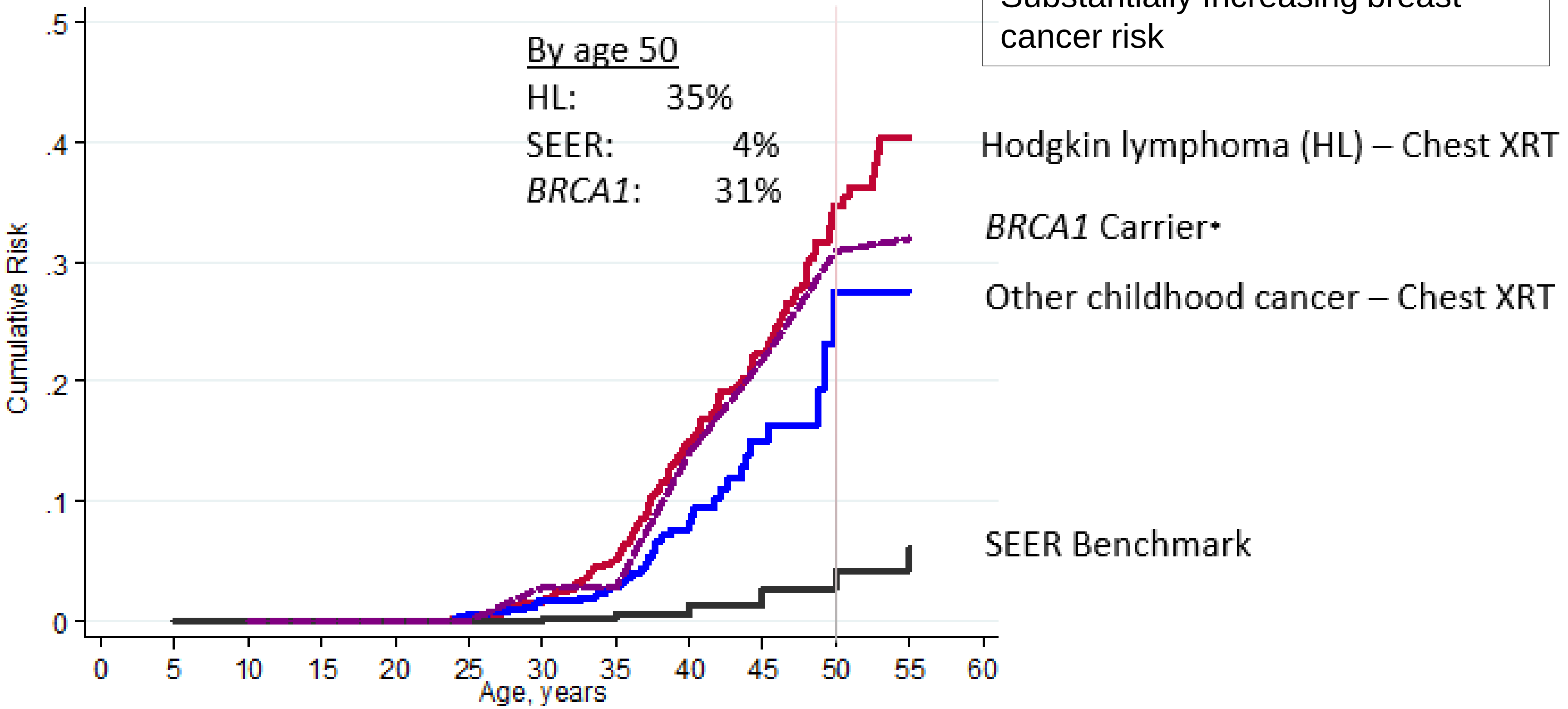


Sigurdson, *Lancet* 365:2014, 2005
Tucker, *Cancer Res* 51:2885, 1991
Meadows, *JCO* 27, 2009
Bhatti, Rad Res 174, 2010

Childhood Cancer Survivor Study and WECARE Study

Cumulative Breast Cancer Risk

Chest radiotherapy equivalent to Germline genetic mutations Substantially Increasing breast cancer risk

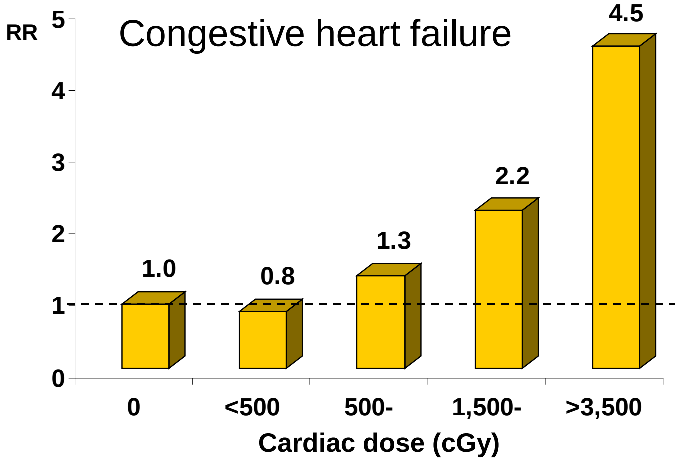


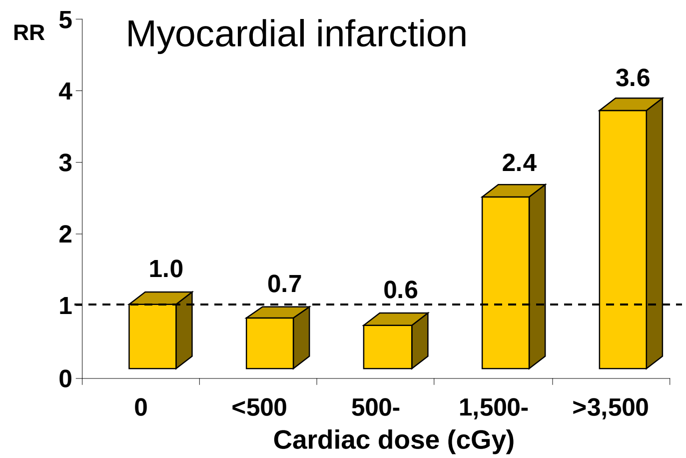
* Population-based estimate

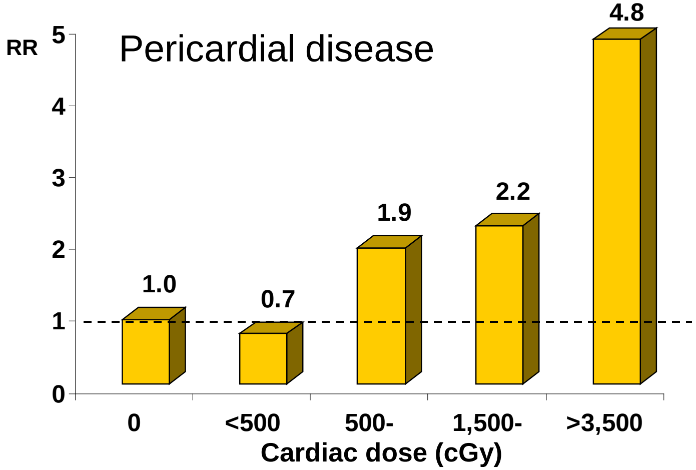
Courtesy of Greg Armstrong, St Jude

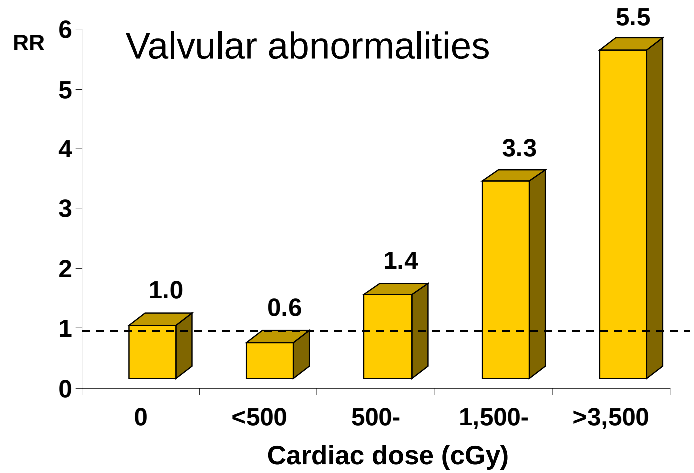
Moskowitz et al, J Clin Oncol, 2014

Dose Response – Heart Disease (CCSS)









Mulrooney et al. BMJ 2009

A Model for Dosimetry
Rocketdyne/Atomics International
Santa Susana Field Laboratory

Simi Valley
Sodium reactor
Moorpark 1957
Edward R Murrow
'See it Now'
Accident 1959
Saturn Engine

Leggett et al. J Radiol Prot 2005
Boice et al. Health Physics 2006
Boice et al. Radiat Res 2006
Boice et al. Radiat Res 2011

Sodium Reactor Experiment (1956)

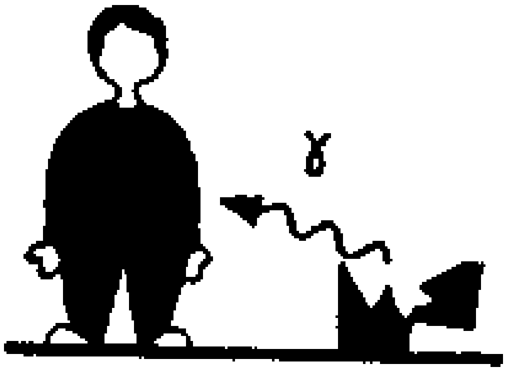
Hot Laboratory (1978)

- Gamma
- X-ray (radiographers)
- Neutrons

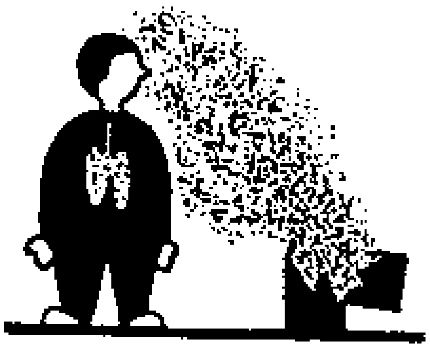
Types of Exposure

- Uranium, Plutonium
- Americium, Polonium
- Thorium, Strontium
- Cesium, Tritium

External



Internal



Uniform dose
Delivered during exposure
Film (TLD) badge reading

Non uniform dose
Protracted in time
Bioassay measurements

Leggett et al. J Radiol Prot 2005
Boice et al. Health Physics 2006

Discussion Sessions with Former Radiation Workers

Career Doses
Sources of Additional Radiation Exposure

Rocketdyne Workforce 46,970 — Monitored Workers 5,801

- **Department of Energy** 2,058
- **NRC – REIRS** 1,039
- **Landauer Dosimetry Co.** 1,792
- Other Sources

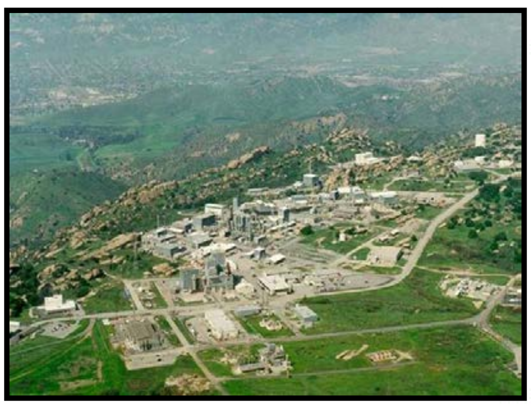
Known Facilities

- Hanford (1,194)
- Idaho National Engineering Lab (237)
- Albuquerque Operation (11)
- Argonne National Lab (74)
- Brookhaven National Lab (8)
- Chicago Operations (17)
- Fermilab (8)
- Fernald (26)
- Lawrence Berkeley Lab (22)
- Lawrence Livermore National Lab (73)
- Los Alamos National Lab (92)
- Mound (13)
- Nevada Test Site (103)
- Oak Ridge Reservation (95)
- Oakland Operations (250)
- PanTex (14)
- Pittsburgh Naval Reactor (34)
- Portsmouth Gaseous Diffusion Plant (6)
- Rocky Flats (160)
- Sandia National Lab (38)
- Savannah River (72)
- Schenectady Naval Reactor (KAPL) (30)
- Stanford Linear Accelerator (12)
- West Valley (6)

Other Sources

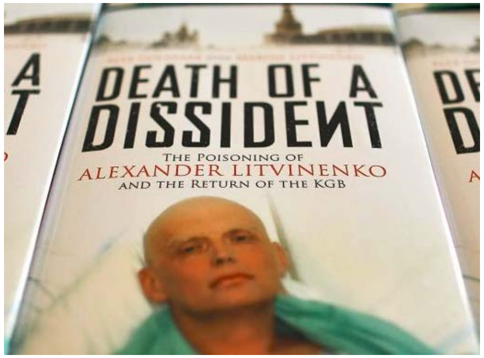
- Oak Ridge (66)
- Mallinckrodt (13)
- Fernald (11)
- Savannah River (26)
- Rochester Files (6)
- 5 REM Study (14)
- US Army (152)
- US Air Force (152)
- US Navy (26)

Military



26.5% of total occupational dose was received at other facilities both prior to and after employment at Rocketdyne.

Boice et al. Health Physics 2006

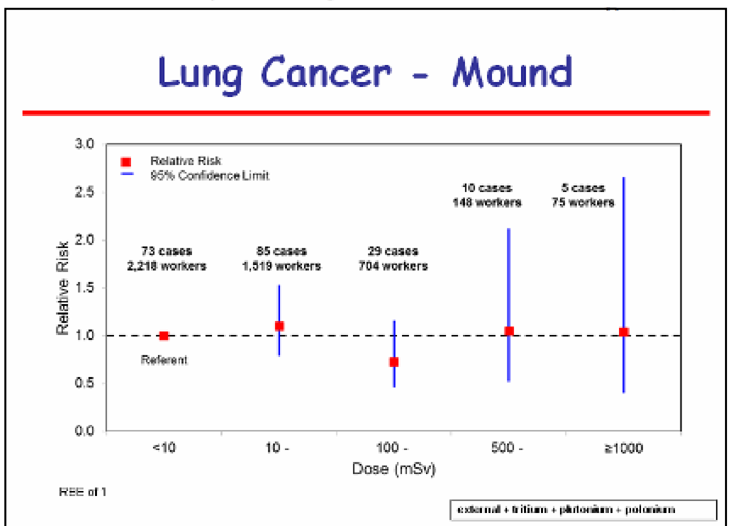


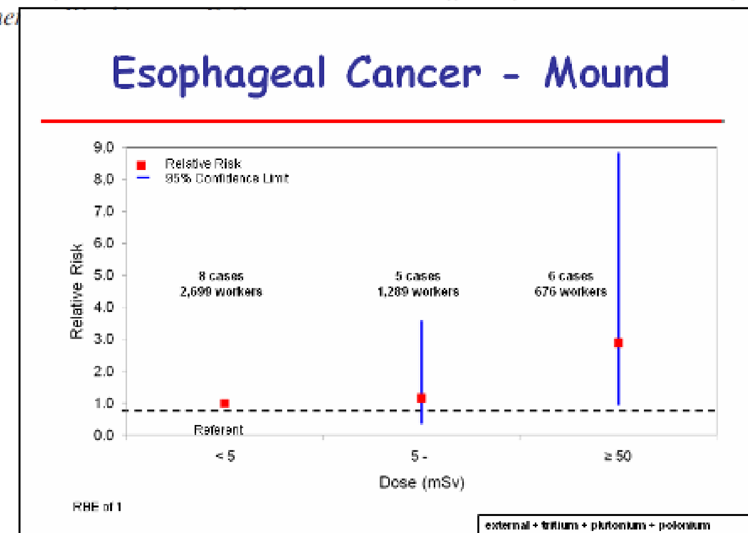
Mound (Polonium) - 2014

Mortality Among Mound Workers Exposed to Polonium-210 and Other Sources of Radiation, 1944–1979

John D. Boice, Jr.,[a,b,1] Sarah S. Cohen,[c] Michael T. Mumma,[d] Elizabeth Dupree Ellis,[e] Donna L. Cragle,[e] Keith F. Eckerman,[f] Phillip W. Wallace,[e] Bandana Chadda,[d] Jennifer S. Sonderman,[d] Laurie D. Wiggs,[g] Bonnie S. Richter[h] and Richard W. Leggett[f]

[a] National Council on Radiation Protection and Measurements, Bethesda, Maryland; [b] Division of Epidemiology, Department of Medicine, Vanderbilt Epidemiology Center and Vanderbilt-Ingram Cancer Center, Nashville, Tennessee; [c] EpidStat Institute, Ann Arbor, Michigan; [d] International Epidemiology Institute, Rockville, Maryland; [e] Oak Ridge Associated Universities, Oak Ridge, Tennessee; [f] Oak Ridge National Laboratory, Oak Ridge, Tennessee; [g] Los Alamos National Laboratory, Los Alamos, New Mexico; and [h] Office of Health and Security, ... of Ene...





Executive Summary

Mr Litvinenko died on 23.11.06 following an intake of polonium-210, assumed here to have been on 1.11.06. Intake and doses to Mr Litvinenko were estimated on the basis of measurements on post-mortem tissue samples of liver, kidney, spleen and lung and a single urine measurement. Blood count results were provided for the time that Mr Litvinenko was in Barnett & Chase Farm Hospital from 3.11.06 to 17.11.06.

Doses were calculated using biokinetic and dosimetric models developed by the International Commission on Radiological Protection (ICRP) for the alimentary and respiratory tracts (ICRP 1994, 2006) **and a systemic model for the distribution and retention of ^{210}Po absorbed to blood developed by Leggett and Eckerman (2001).**

A best estimate of intake by ingestion was obtained using the kidney, liver and urine measurements. The value obtained was 4.4 GBq, or more correctly, 440 MBq absorbed to blood,

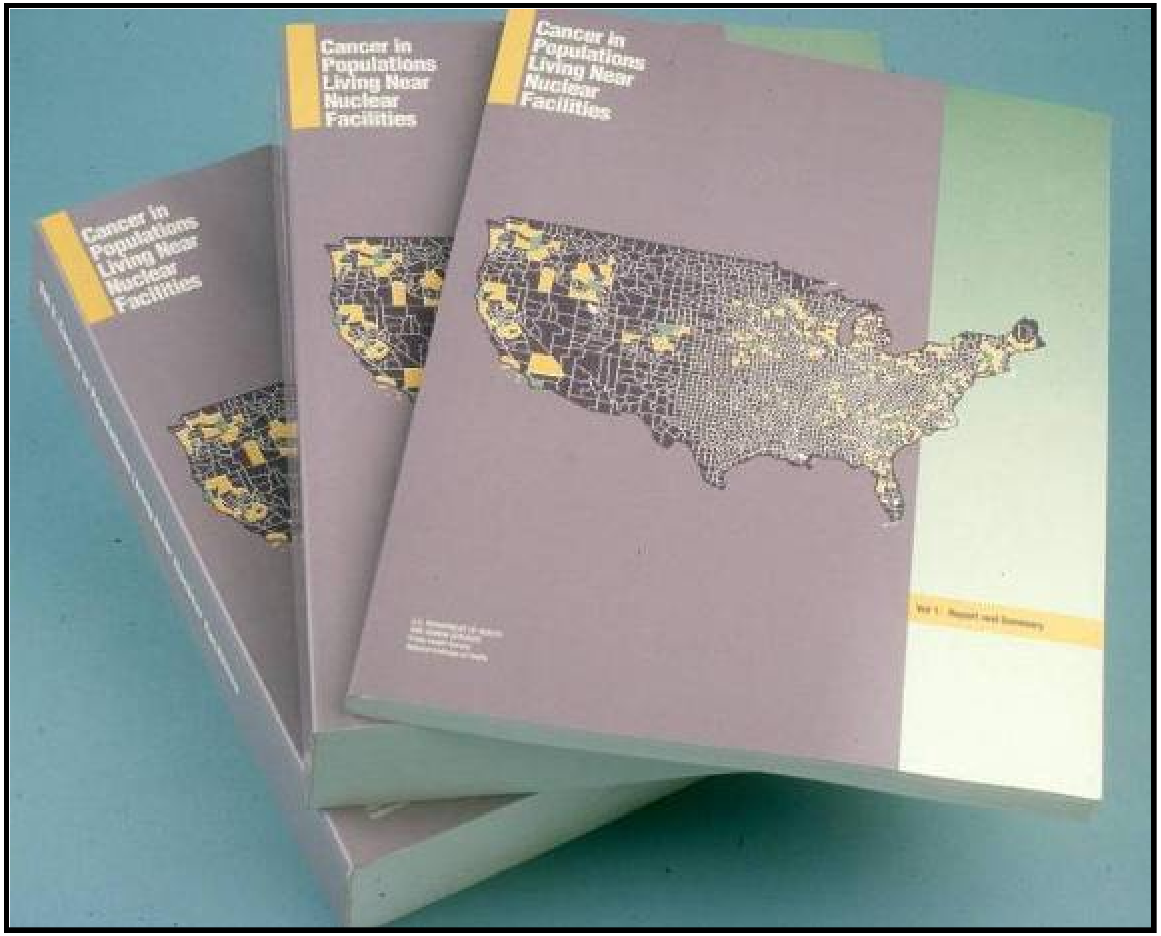
The estimated *LD/50* value of 3 Gy with supportive treatment was reached after about 3 days and the *LD/100value* of about 4 Gy in less than 5 days (estimated 4.5 Gy by 5 days). The cumulative dose to bone marrow after one week was estimated as about 6 Gy, increasing to about 12 Gy after 2 weeks and about 17 Gy by the time of death (22 days). …. Andrei Lugovoi charged

One Hit Wonders? (1990 - 2000s)

- Nuclear Facilities
- UK and International Worker Studies
- Natural Background Areas

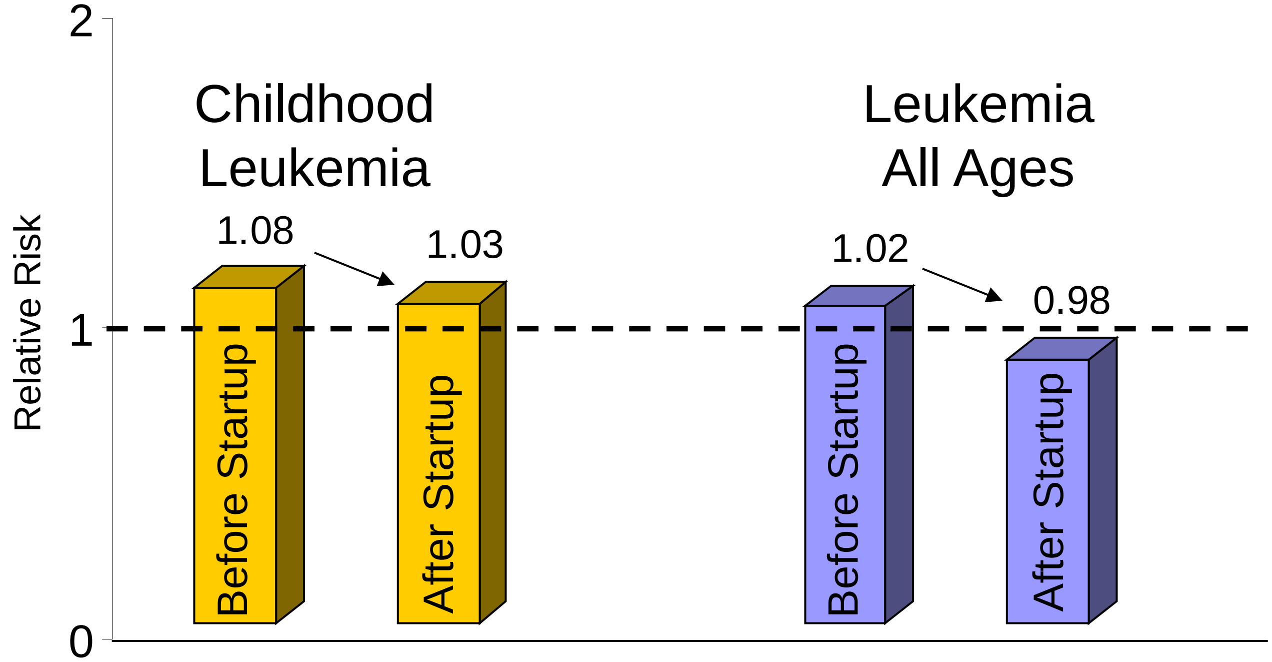
Descriptive Studies
Nuclear Facilities (Sellafield, U.K.)

Cancer in Populations
Living Near Nuclear Facilities
Jablon, *JAMA* 256: 1991



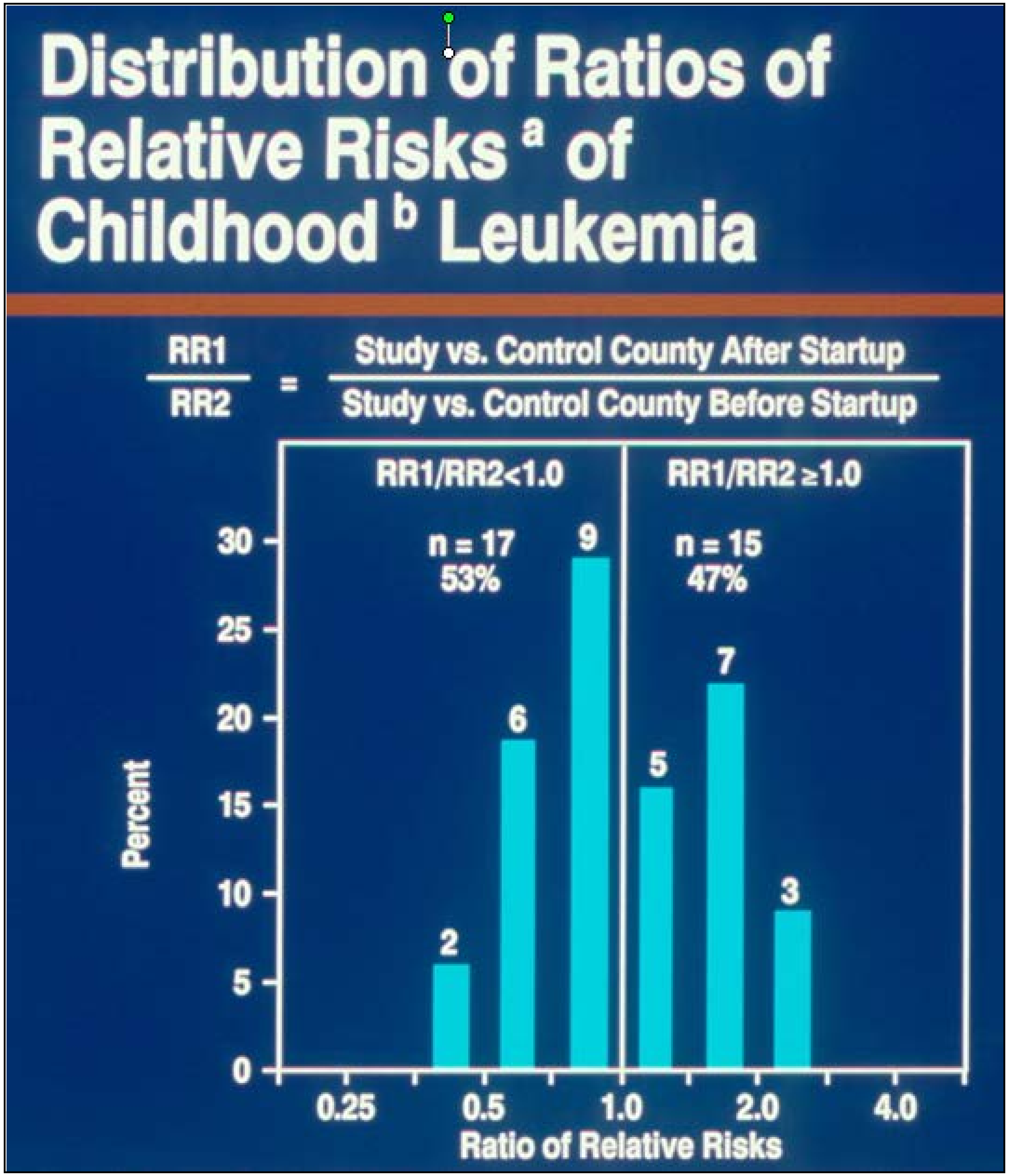
Digitally re-mastered VHS→DVD released 2011

Overall Relative Risk of Leukemia Before and After Nuclear Facility Startup



Risk higher before than after facilities began operating

Jablon et al, *JAMA* 265:1403-1408, 1991



Concern – subgroup analyses

- multiple comparisons
- chance

COMARE 14th Report: Further consideration of the incidence of childhood leukaemia around nuclear power plants in Great Britain 6 May 2011

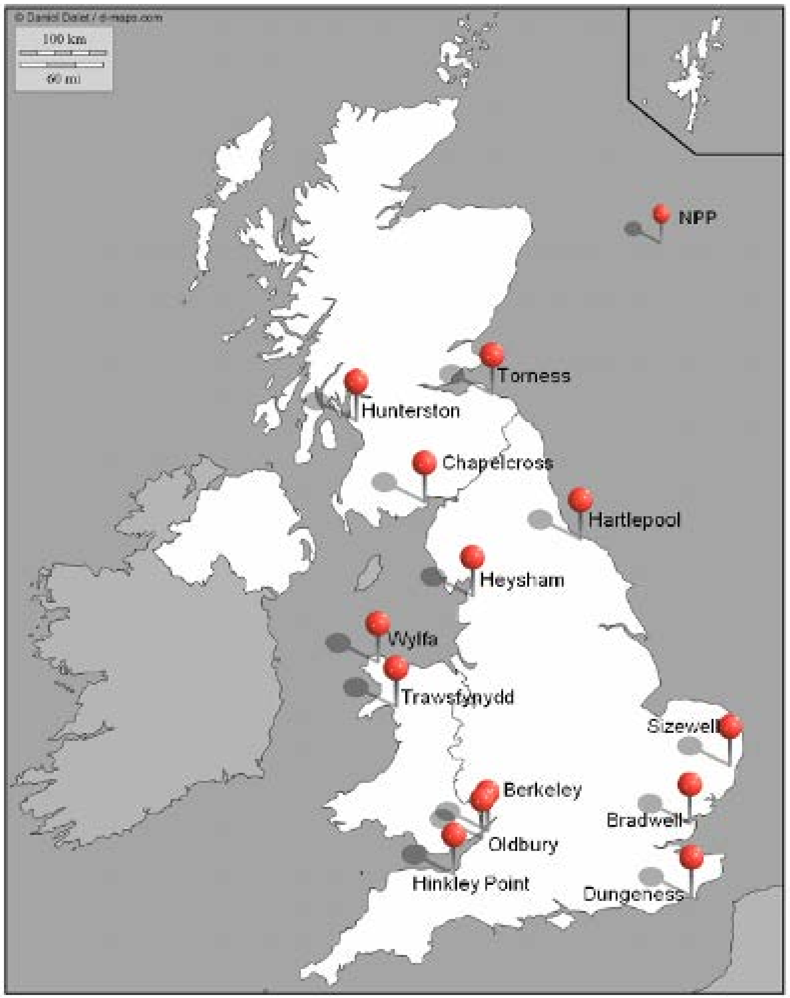


Figure 3.1 NPP sites in Great Britain

In this, the 14th COMARE report, the incidence of childhood leukaemia in the vicinity of nuclear power plants (NPPs) in Great Britain has been reviewed and it has been concluded that the risk estimate for childhood leukaemia associated with proximity to an NPP is extremely small, if not zero.

Epidemiology is an observational science, it is not experimental

Epidemiology is an observational science for which small biases and confounding factors become much more important at low doses (UNSCEAR 2008).

Further, the effect to be detected at low doses is, not surprisingly, very low and the statistical power of epidemiology is insufficient to demonstrate excesses.

Some biases/confounding to recognize include: selection, screening, response, survival, follow-up completeness, outcome ascertainment, confounding by smoking, chemicals, and by indication (UNSCEAR).

Low Dose Studies are More Susceptible to – Bias and Confounding and Chance

81. … there are a number of studies of occupationally exposed persons, who generally receive low doses of ionizing radiation at low dose rates. For example, in the IARC 15-country study, average cumulative doses were 19.4 mSv, and fewer than 5% of workers received cumulative doses exceeding 100 mSv. (UNSCEAR 2008)

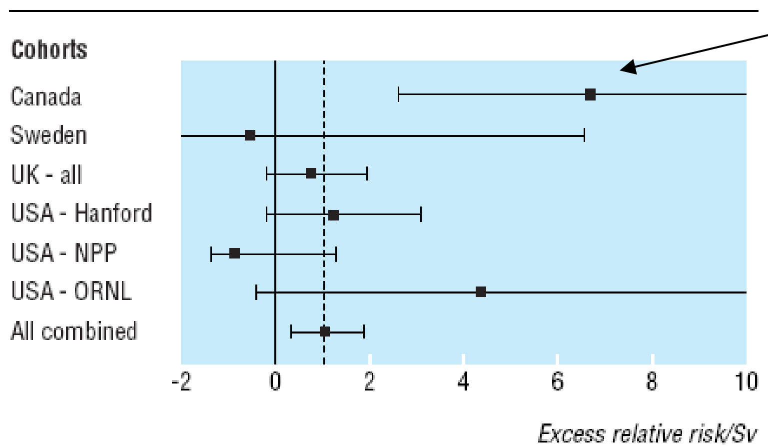


Fig 2 Excess relative risks per Sv for all cancer excluding leukaemia in cohorts with more than 100 deaths (NPP=nuclear power plants, ORNL=Oak Ridge National Laboratory)

Canada

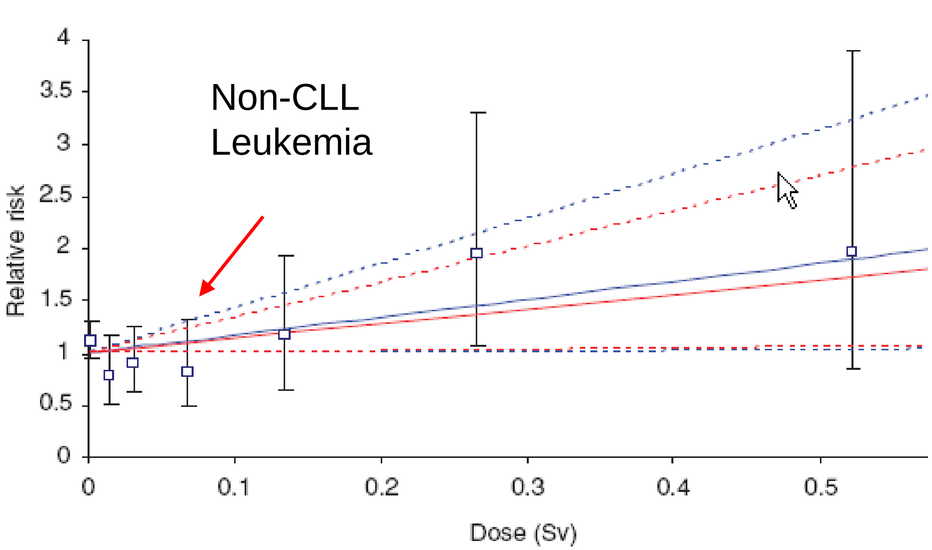
- One country of 15 (Canada)
- One cancer of 28 (lung)
- Leukemia not significant
- Low dose (19.4 mSv) and narrow dose distribution

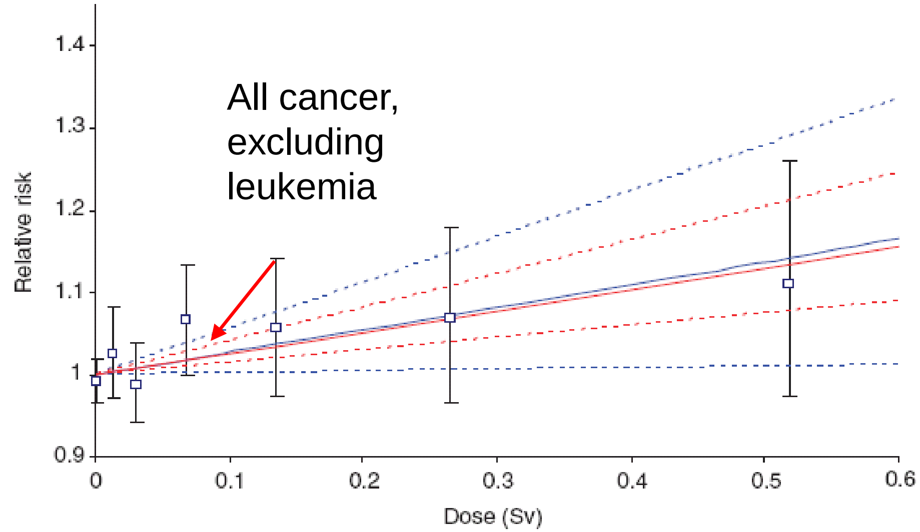
Cardis et al. BMJ 2005
Ashmore et al. JRP 2010
Boice JRP 2010

Zablotska BJC 2014

Leukemia and Cancer Dose Response in the U.K. National Registry of Radiation Workers - 2009

"Within the cohort, mortality and incidence from both leukaemia excluding CLL and the grouping of all malignant neoplasms excluding leukaemia increased to a statistically significant extent with increasing radiation dose. Estimates of the trend in risk with dose were similar to those for the Japanese A-bomb survivors, with 90% confidence intervals that excluded both risks more than 2–3 times greater than the A-bomb values and no raised risk." Muirhead et al. BMJ 2009





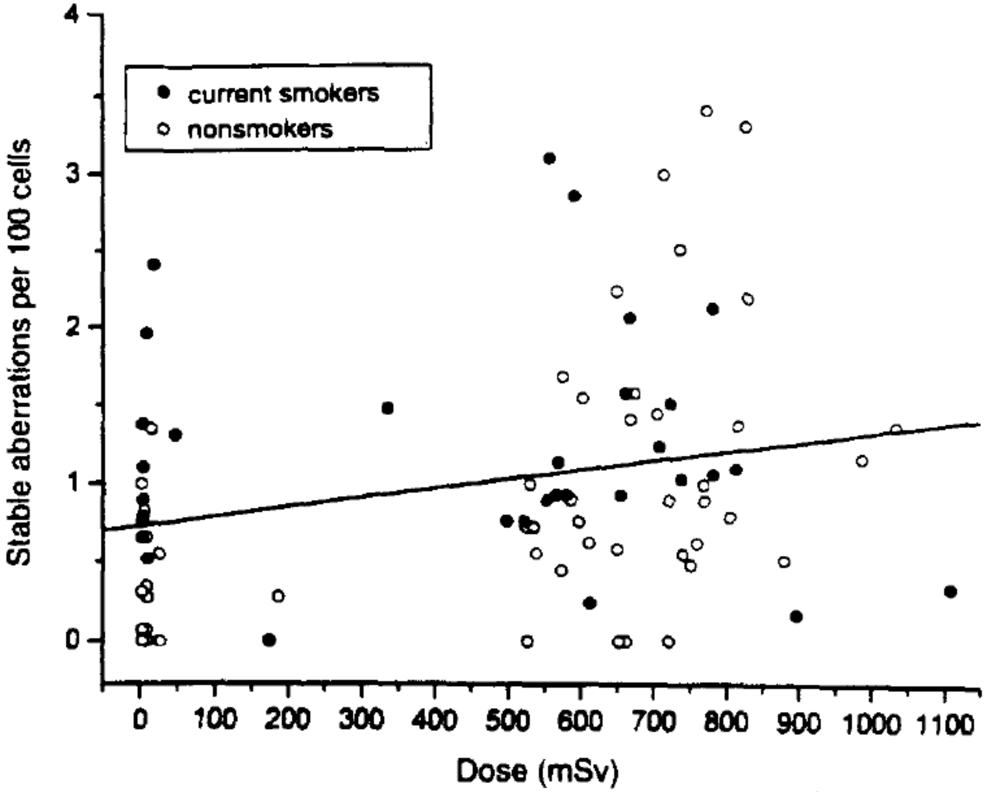
Muirhead et al. BMJ 2009

The remarkable influence of Sellafield, workers – studies aren't independent, IARC 1996, 2007, NRRW 2009, BNFL 2014.

Unexpected cancers drive the dose response (ERR/Sv): rectum (1.7), pleura (1.3), uterus (17.0), larynx (4.1), thyroid (3.1), testes (3.3). Mean 24.9 mSv

Aberrations (& Leukemia) and DDREF of 6

81 workers, mean ~500 mSv



"The slope of the dose response for stable aberrations is 0.79 aberrations per 100 cells per sievert, which is less than that observed among atomic bomb survivors, and suggests a dose and dose-rate effectiveness factor for chronic exposure of about 6."

Tucker JD, Tawn EJ, et al. *Rad Res* 148, 1997

Sellafield workers

Yangjiang County, Guangdong Province, bordering on South China Sea, 2 regions with thorium-containing monazites

Natural Background Radiation
China, Thyroid Nodules

	High Background	Low Background
Number examined	1,001	1,005
Thyroid dose (rad)	14	5
Nodular disease	9.5%	9.3%
RR (95% CI)	**1.02** (0.8-1.4)	

Low Dose Rate
External

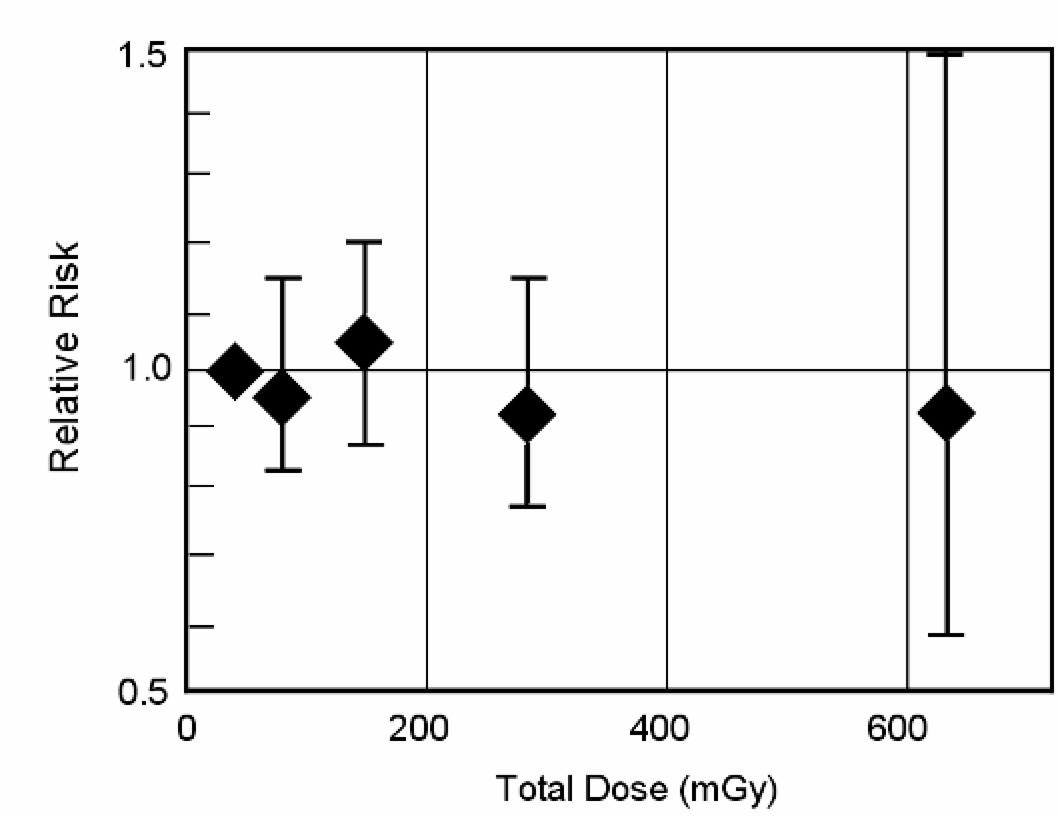
Wang et al. *JNCI* 82, 1990

Karunagappally Study – Kerala, India

- 400,000 population
- cancer registry, established in 1990
- questionnaire survey of all residents

- radiation measurements in 70,000 homes
- personal dosimetry and biodosimetry
- individual dose estimates (mean, 161 mGy)

Relative Risk of All Cancer Excluding Leukemia by Cumulative Dose to High Background Radiation in Kerala



Nair et al. *Health Physics*, 2009;
Boice et al. *Radiation Research* 2010

Epidemiology has shifted the focus from genetic effects in future generations to somatic effects on the individuals exposed.

Radiation epidemiology (UNSCEAR 2008) tells us that:

- a single exposure can increase your cancer risk for life
- the young are “somewhat” more susceptible than the old
- in-utero susceptibility is no greater than early childhood
- females are more susceptible than males.
- risks differ by organ or tissue and
- some sites have not been convincingly increased after exposure.

Radiation epidemiology has yet to tell us about low dose and low dose rate exposures

National Study of 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 115,000
- Medical & other >250,000

OAK (HARDTACK I), Enewetak, 8.9 MT, 28 Jun 1958

Bouville et al. Health Physics Feb 2015

Comparison with Atomic Bomb Survivor Study

External Dose (mSv)	Million Worker Study Total to Date	Atomic Bomb Survivor Study (Ozasa 2012)
< 5 mSv	6,507,275	38,509
5 -	963,652	29,961
100 -	53,211	5,974
200 -	24,456	6,356
500 -	4,120	3,424
1000 -	1,007	1,763
> 2000 mSv	211	624
TOTAL	7,553,932*	86,611

> 100 mSv	83,005	18,141

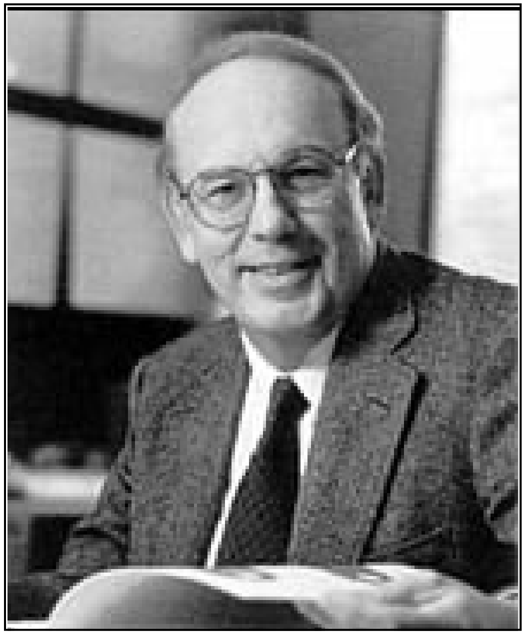
*3000 rolls of microfilm to come

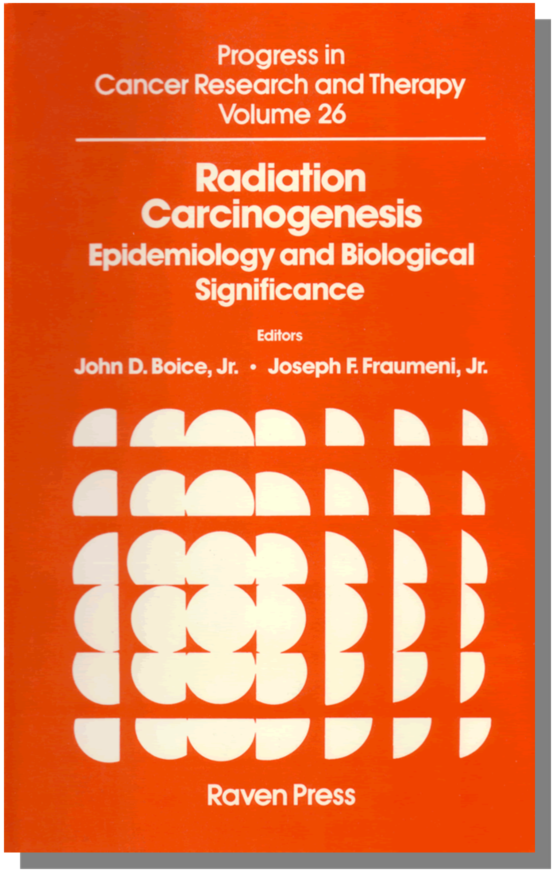
4x more High Dose Subjects

As of Oct 2013


LUCY, AS YOUR MANAGER, I MUST INSIST THAT YOU SEE A DOCTOR ABOUT YOUR ARM
HE WON'T HURT YOU...ALL HE'LL DO IS TAKE A FEW X-RAYS...
ARE YOU CRAZY?!
THOSE X-RAYS DESECRATE YOUR BONES!
SCHULZ

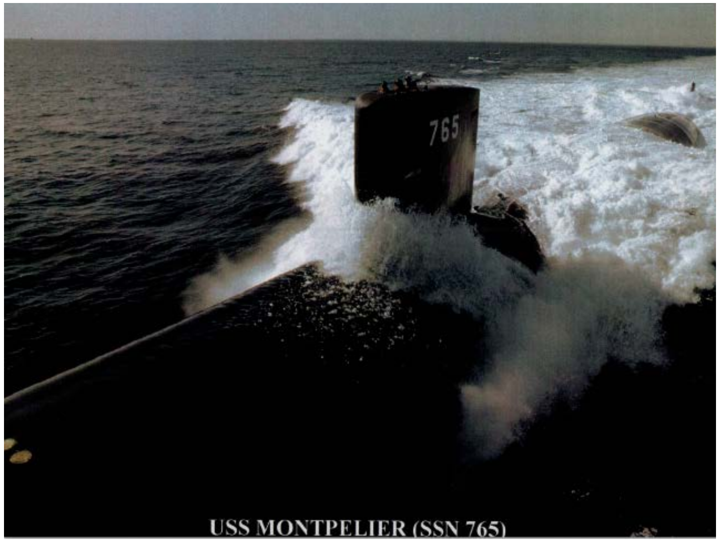
Thank You!




Progress in
Cancer Research and Therapy
Volume 26
Radiation
Carcinogenesis
Epidemiology and Biological
Significance
Editors
John D. Boice, Jr. • Joseph F. Fraumeni, Jr.
Raven Press

Epidemiologists will go to any DEPTH in the Public Interest - 85, 033 Nuclear Submariners

USS Montpelier



At 600 feet

Bibliography - 1

Amundson S, et al. Low-dose radiation risk assessment. Report of an International Workshop on Low Dose Radiation Effects held at Columbia University Medical Center, New York, April 3-4, 2006. *Radiat Res* 166:561-565, 2006.

Boice JD Jr. Ionizing radiation. In: *Cancer Epidemiology and Prevention, 3rd Edition*. (Schottenfeld D, Fraumeni JF Jr, eds). New York, Oxford University Press, 2006.

Boice JD Jr. Lauriston S. Taylor lecture: Radiation epidemiology: the golden age and future challenges. *Health Phys* 100:59-76, 2011.

Boice JD Jr. Implications of radiation dose and exposed populations on radiation protection in the 21st century. *Health Phys* 106:313-28, 2014.

Boice JD Jr. Radiation epidemiology and recent paediatric computed tomography studies. *Ann ICRP*. March 24, 2015.

Bouville A, Toohey RE, Boice JD Jr., et al. Dose reconstruction for the Million worker Study: status and guidelines. *Health Phys* 108:206-20, 2015.

Cardis E, et al. The 15-Country collaborative study of cancer risk among radiation workers in the nuclear Industry: estimates of radiation-related cancer risk. *Radiat Res* 167:396, 2007.

Bibliography - 2

Darby S, et al. Radon in homes and risk of lung cancer: collaborative analysis of individual data from 13 European case-control studies. *BMJ* 330:223, 2005.

Fry RJM, Boice JD Jr. Radiation carcinogenesis. In: *Oxford Textbook of Oncology, Second Edition* (Souhami RL, Tannock I, Hohenberger P, Horiot J-C, eds). New York: Oxford Press, pp 167-184, 2002.

Hall EJ, Metting N, Puskin J, Ron E. Low dose radiation epidemiology: what can it tell us? *Radiat Res* 172:134-138, 2009.

International Agency for Research on Cancer. IARC monographs on the evaluation of carcinogenic risks to humans. Vol 75. *Ionizing Radiation, Part 1: X- and Gamma (γ) – Radiation, and Neutrons*. Lyon, France: IARC, 2000.

International Agency for Research on Cancer. IARC monographs on the evaluation of carcinogenic risks to humans. Vol 78. *Ionizing Radiation, Part 2: Some Internally Deposited Radionuclides*. Lyon, France: IARC, 2001.

Nair RR, et al. Background radiation and cancer incidence in Kerala, India-Karanagappally cohort study. *Health Phys* 96:55-66, 2009.

Bibliography - 3

National Academy of Sciences. Committee on Health Risks of Exposure to Radon. (BEIR VI). Washington, DC: National Academies Press, 1999.

National Research Council. Committee on the Biological Effects of Ionizing Radiation. (BEIR VII). Washington, DC: National Academies Press, 2006.

National Council on Radiation Protection and Measurements (NCRP). *Evaluation of the Linear-Nonthreshold Dose-Response Model for Ionizing Radiation*. NCRP Report 136. Bethesda, MD: NCRP, 2001.

NCRP. *Second Primary Cancers and Cardiovascular Disease after Radiation Therapy*. NCRP Report 170. Bethesda, MD: NCRP, 2011.

NCRP. *Uncertainties in the Estimation of Radiation Risks and Probability of Disease Causation*. NCRP Report 171. Bethesda, MD: NCRP, 2012.

NCRP. *Preconception and Prenatal Radiation Exposure*. NCRP Report 174. Bethesda, MD: NCRP, 2013.

Ozasa K, et al. Studies of the mortality of atomic bomb survivors, Report 14, 1950-2003: an overview of cancer and noncancer diseases. *Radiat Res* 177:229-43, 2012.

Bibliography - 4

Preston RJ. Integrating basic radiobiological science and epidemiological studies: why and how. *Health Phys* 108:125-30, 2015.

Preston DL, et al. Effect of recent changes in atomic bomb survivor dosimetry on cancer mortality risk estimates. *Radiat Res* 162:377, 2004.

Preston DL et al. Solid cancer incidence in atomic bomb survivors: 1958-1998. *Radiat Res* 168:1, 2007.

Tubiana M, et al. *Dose-effect Relationships and the Estimation of Carcinogenic Effects of Low Doses of Ionizing Radiation*. Joint Report 2. Paris: Academie Nationale de Medecine, Institut de France-Academie des Sciences, 2005.

United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR). *UNSCEAR 2006 Report to the General Assembly with Scientific Annexes, Effects of Ionizing Radiation*. Vol 1: Report and Annexes A and B. New York: United Nations, 2008; Vol 2: Annexes C, D and E, 2009, 2011.

UNSCEAR. *Effects of Radiation Exposure of Children*. E.14.IX.2. United Nations, New York, 2013.

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
Produced May 2015