Sievert Lecture
IRPA 14 – 50 Years of Practicing Radiation Protection
Cape Town, South Africa

How to Protect the Public When You Can't Measure the Risk — The Role of Radiation Epidemiology

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Monday, May 9, 2016

"And it was so typically brilliant of you to have invited a radiation epidemiologist."

The New Yorker, Nov 26, 2001, Wm Hamilton

But please don't bother if not so brilliant !

Thanks Steve Simon

Rolf Maximilian Sievert Lecturers (1973 - 2016)

- Bo Lindell, Sweden (1973)
- William Mayneord, UK (1977)
- Laurie Taylor, USA (1980)
- Bill Pochin, UK (1984)
- Wolfgang Jacobi, Germany (1988)
- Giovanni Silini, Italy (1992)
- Dan Beninson, Argentina (1996)
- Itsuzo Shigematsu, Japan (2000)
- Abel González, Argentina (2004)
- Christian Streffer, Germany (2008)
- Richard Osborne, Canada (2012)
- John Boice, USA (2016)

Sievert in the physics research laboratory in the Radiumhemmet.

Bo Lindell, Sweden:
1st Sievert Lecture (1973)

Giants I have known!

Health Physics Pergamon Press 1976. Vol. 31 (Sept.), pp. 265–272. Printed in Northern Ireland

RADIATION AND MAN

THE 1973 SIEVERT LECTURE*

BO LINDELL
National Institute of Radiation Protection, Fack, S-10401 Stockholm 60, Sweden

THE HONOUR that has been bestowed upon me by selecting me as the first lecturer in this new series of lectures must be a reflection of the admiration that my colleagues still feel for Rolf Sievert and their hope that one of his pupils might be able to pay him a proper tribute in this first Sievert Lecture.

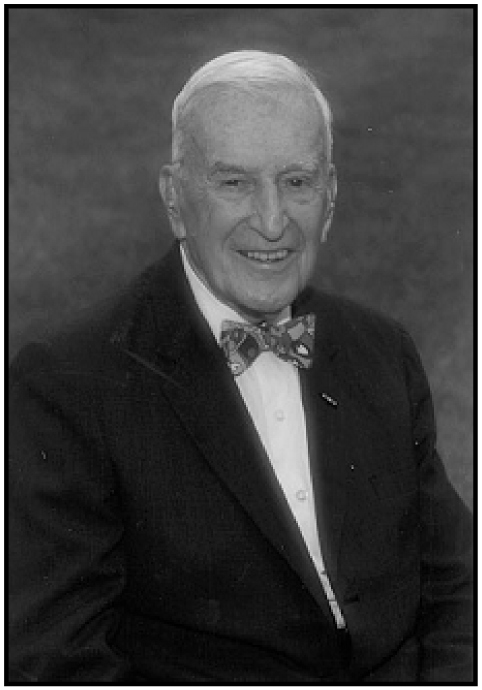
Let me, however, begin by claiming that this is an impossible task: no pictures, no descriptions, no quotations can do Rolf Sievert justice. Only life could bring into his stout body the vitality and the magnetism by which he mesmerized his environment. Those who were never subjected to that forceful vitality and to the cascade of ideas, innovations, plans and solutions that flowed from Rolf Sievert in a glittering, boisterous torrent will never be able to see in the dead pictures of Sievert the man he was to us who knew him.

Furthermore, it would not have pleased Sievert to have a lecture of this kind focussed on himself.

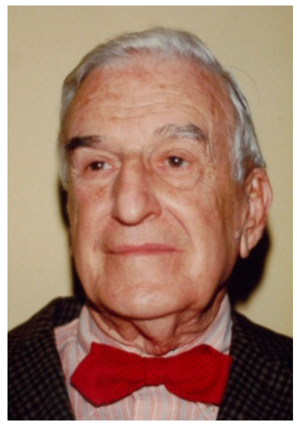
1928—we have had for almost 40 yr an internationally applied set of dose limits which guarantee that no harmful *acute* effects will result from normal uses of radiation. We should recall that the prevention of immediate toxic effects is still the main problem in many conventional types of occupational or environmental protection, we may just recall substances such as mercury and DDT.

With the conventional standards of thinking, small doses of radiation would be considered not only safe but also often non-existent. Let us not forget that laws on food additives in many countries until recently have completely forbidden any presence of carcinogenic substances, but that the definition of a "zero quantity" has been "a non-detectable quantity." Had radioactive substances been chemically toxic instead of radioactive, many of them would, in the terms of the law, not have existed until new scientific detection methods had revealed their existence and complicated life for the

Laurie Taylor, USA:
3rd Sievert Lecture (1980)

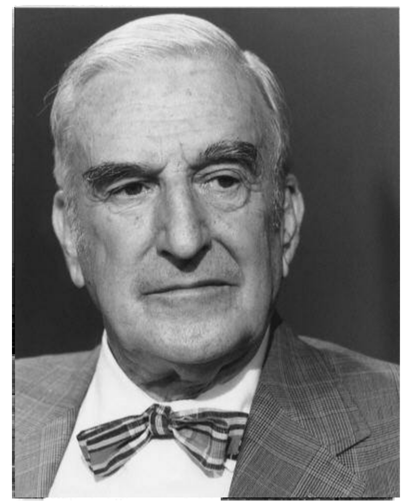


Giants I have known!



Age 3 y

SOME NONSCIENTIFIC INFLUENCES ON
RADIATION PROTECTION STANDARDS AND PRACTICE
THE 1980 SIEVERT LECTURE*



LAURISTON S. TAYLOR†

1. INTRODUCTION

IN THE practical application of the principles for achievement of protection against harmful radiation effects, our greatest obstacles today do not include a lack of knowledge about the biomedical effects of ionizing radiation. Today, we know about all we need to know for adequate protection from ionizing radiation.

Let me repeat that. Today we know about all we need to know for adequate protection against ionizing radiation. Therefore, I find myself charged to ask: why is there a radia-

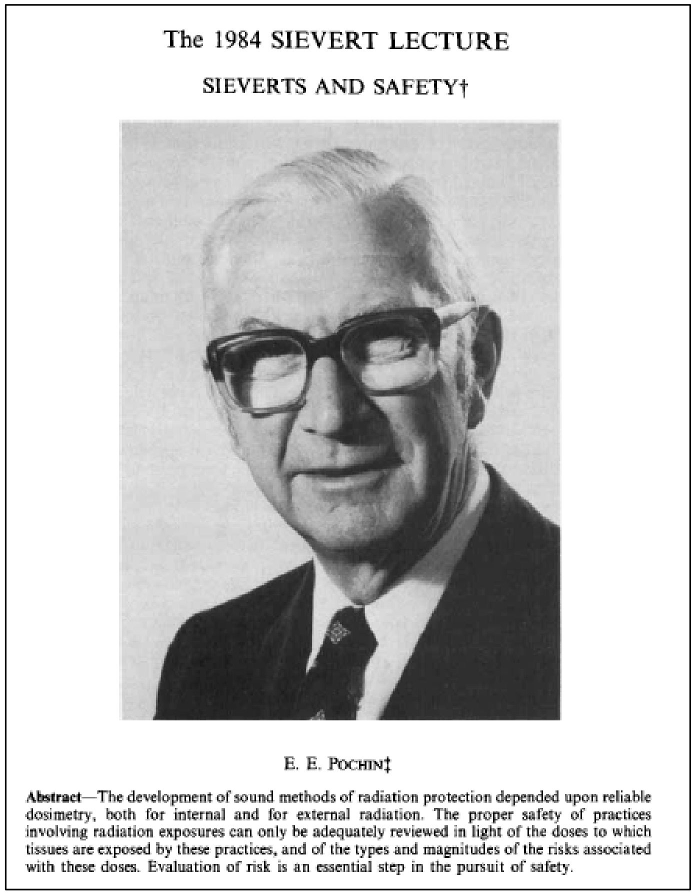
*This lecture was delivered at the Fifth International Congress of the International Radiation Protection Association, Jerusalem, Israel, 9–14 March 1980.

†Past President, National Council on Radiation Protection and Measurements.

851

Bill Pochin, UK:
4th Sievert Lecture (1984)

Giants I have known!



The 1984 SIEVERT LECTURE

SIEVERTS AND SAFETY†

E. E. POCHIN‡

Abstract—The development of sound methods of radiation protection depended upon reliable dosimetry, both for internal and for external radiation. The proper safety of practices involving radiation exposures can only be adequately reviewed in light of the doses to which tissues are exposed by these practices, and of the types and magnitudes of the risks associated with these doses. Evaluation of risk is an essential step in the pursuit of safety.

Thanks Fred Mettler

Dan Beninson, Argentina:
7th Sievert Lecture (1996)

Giants I have known!

RISK OF RADIATION AT LOW DOSES

D. Beninson*

INTRODUCTION

RISK AND risk sources have been increasingly studied in recent years. The essentials of risk consist of a combination of the idea of loss with that of chance or probability. The idea of chance is crucial: the inevitable can be utterly unpleasant but, lacking the element of chance, is not a risk.

Even without analyzing the different components of the concept of "loss," it should be recognized that to be exposed to risk is not necessarily bad. The achievements of modern life imply the exposure to several sources of risk, and past evolution would have been impossible without the risk incurred by our ancestors.

A special type of risk, pertinent to our discussion, is exemplified by the health threats due to low levels of natural or man-made chemicals and low radiation levels. It constitutes a risk very difficult to analyze, not because the effects are unknown but because they are already very familiar, and exposed groups only manifest a slightly increased frequency of such effects.

RADIATION RISK

at all below such doses. This, of course, could be true but certainly not because of the lack of observation.

Statistical detectability and claims of threshold

Even assuming a non-threshold linear relation between risk (here used in a loose way meaning probability as the considered effect is only cancer) and dose, the required number of individuals, N, incurring a dose D, for achieving detectability increases steadily with a reduction of dose. If all other influencing factors are kept constant, the excess number of cancers attributable to radiation and its standard deviation are given by

$$\text{Excess} = rDN \quad \text{and} \quad \sigma = \sqrt{2bN + rDN} \qquad (1)$$

where b is the "natural" risk of cancer, appropriate to the group under study, and r is the risk per unit dose in the group.

In order to be detectable the excess must be larger than a stipulated number of standard deviations (usually two, for a level of significance of about 95%). Therefore,

$$rDN \geq 2\sqrt{2bN + rDN}. \qquad (2)$$

In most cases, the "natural" cancer risk is substan-

Itsuzo Shigematsu, Japan: 8th Sievert Lecture (2000)

Giants I have known!

THE 2000 SIEVERT LECTURE—LESSONS FROM ATOMIC BOMB SURVIVORS IN HIROSHIMA AND NAGASAKI

I. Shigematsu*

SHORT HISTORY OF STUDIES ON ATOMIC BOMB SURVIVORS

People in Hiroshima and Nagasaki, without distinction of age or sex, experienced for the first time in human history exposure to massive doses of instantaneous ionizing radiation that was produced by the detonation of atomic bombs in August 1945. Such tragedies should never be repeated, but it is true that these unfortunate experiences have greatly enhanced our knowledge of the health effects due to exposure to ionizing radiation. Immediately after the atomic bombings, Japanese researchers initiated studies on the casualties caused by the bombings. Soon thereafter, Japan was occupied by the Allied Forces and initiative for the conduct of these studies was placed in the hands of the United States military mission, and the Japanese researchers were requested to join this mission for cooperation.

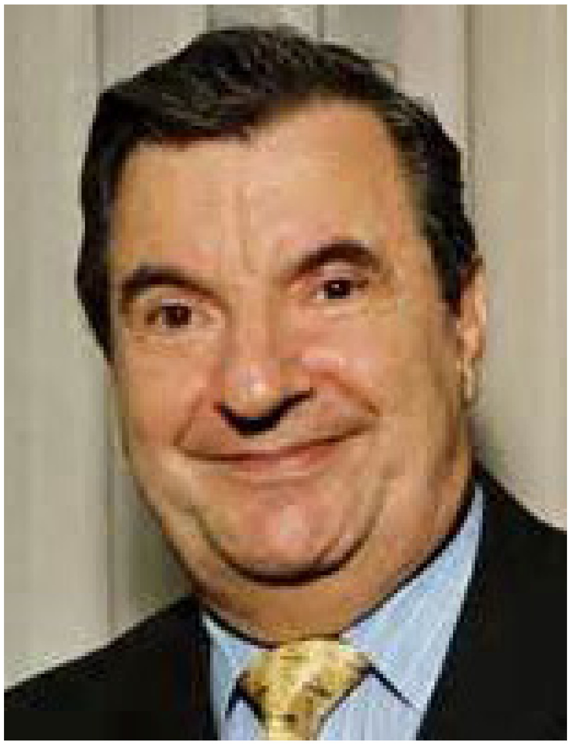
Based on the findings of this mission, the United States government established the Atomic Bomb Casualty Commission (ABCC) in Hiroshima and Nagasaki in 1947 and 1948, respectively, under the auspices of the National Academy of Sciences (NAS). The purpose was to study late health effects in the people exposed to the atomic bomb radiation. To attain this purpose smoothly, branch laboratories of the Japanese National Institute of Health (NIH) were attached to ABCC in 1948.

ABCC conducted studies on the atomic bomb survivors there were many restrictions for Japanese researchers in conducting studies on atomic bomb survivors, but after the Peace Treaty became effective in 1952, these restrictions were removed and active programs began in various institutions including local universities in Hiroshima and Nagasaki. The results of these studies have been summarized annually since 1959 at the meetings of the Research Council on Late Health Effects of Atomic Bomb Radiation.

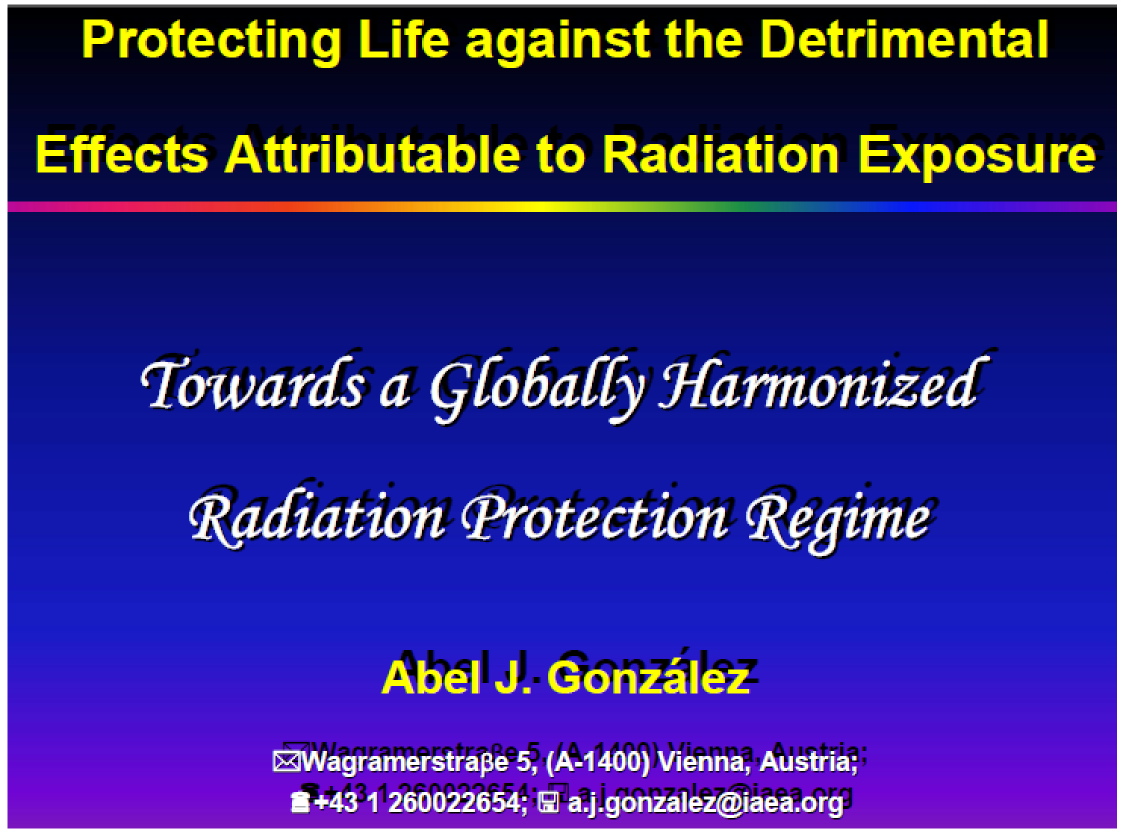
From the need to further continue the research studies for an extended period, ABCC was reorganized in April 1975 into the Radiation Effects Research Foundation (RERF) based on Japanese law, with its finance, operation, and scientific responsibilities shared equally by the governments of Japan and the United States through the Japanese Ministry of Health and Welfare and the United States NAS under contract with the U.S. Department of Energy. The objective of RERF is clearly given in its Act of Endowment, which prescribes that it will contribute to the maintenance of the health and welfare of atomic bomb survivors and to the enhancement of the health of all mankind. RERF succeeded the research program of ABCC, adding to the latter's existing program new study projects beneficial to atomic bomb survivors.

ABCC-RERF studies are necessarily limited to the effects of acute, single-dose, whole-body, mixed gamma-neutron radiation, but their comprehensiveness and long

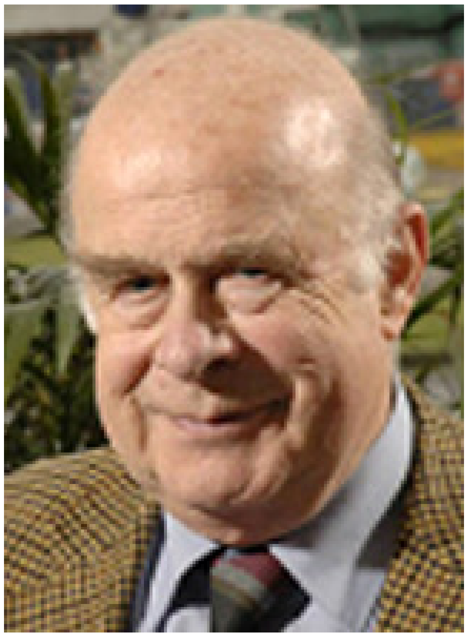
Abel (González), Argentina:
9th Sievert Lecture (2004)

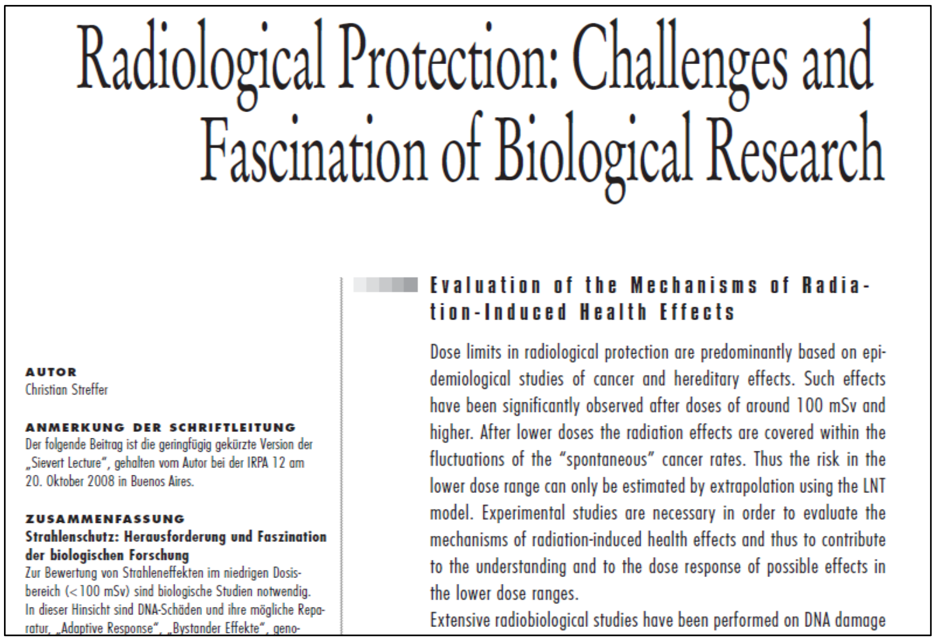


Giants I have known!



Christian Streffer, Germany: 10th Sievert Lecture (2008)





Radiological Protection: Challenges and Fascination of Biological Research

AUTOR
Christian Streffer

ANMERKUNG DER SCHRIFTLEITUNG
Der folgende Beitrag ist die geringfügig gekürzte Version der „Sievert Lecture", gehalten vom Autor bei der IRPA 12 am 20. Oktober 2008 in Buenos Aires.

ZUSAMMENFASSUNG
Strahlenschutz: Herausforderung und Faszination der biologischen Forschung
Zur Bewertung von Strahleneffekten im niedrigen Dosisbereich (< 100 mSv) sind biologische Studien notwendig. In dieser Hinsicht sind DNA-Schäden und ihre mögliche Reparatur, „Adaptive Response", „Bystander Effekte", geno-

Evaluation of the Mechanisms of Radiation-Induced Health Effects

Dose limits in radiological protection are predominantly based on epidemiological studies of cancer and hereditary effects. Such effects have been significantly observed after doses of around 100 mSv and higher. After lower doses the radiation effects are covered within the fluctuations of the "spontaneous" cancer rates. Thus the risk in the lower dose range can only be estimated by extrapolation using the LNT model. Experimental studies are necessary in order to evaluate the mechanisms of radiation-induced health effects and thus to contribute to the understanding and to the dose response of possible effects in the lower dose ranges.
Extensive radiobiological studies have been performed on DNA damage

Giants I have known!

“If I have seen farther than others, it is because I was standing on the shoulders of giants”

Isaac Newton 1642 – 1727

… really Bernard of Chartres 1159

Thanks Fred Mettler

The alternative …

“If I have not seen as far as others, it is because giants were standing on my shoulders”

Harold Abelson

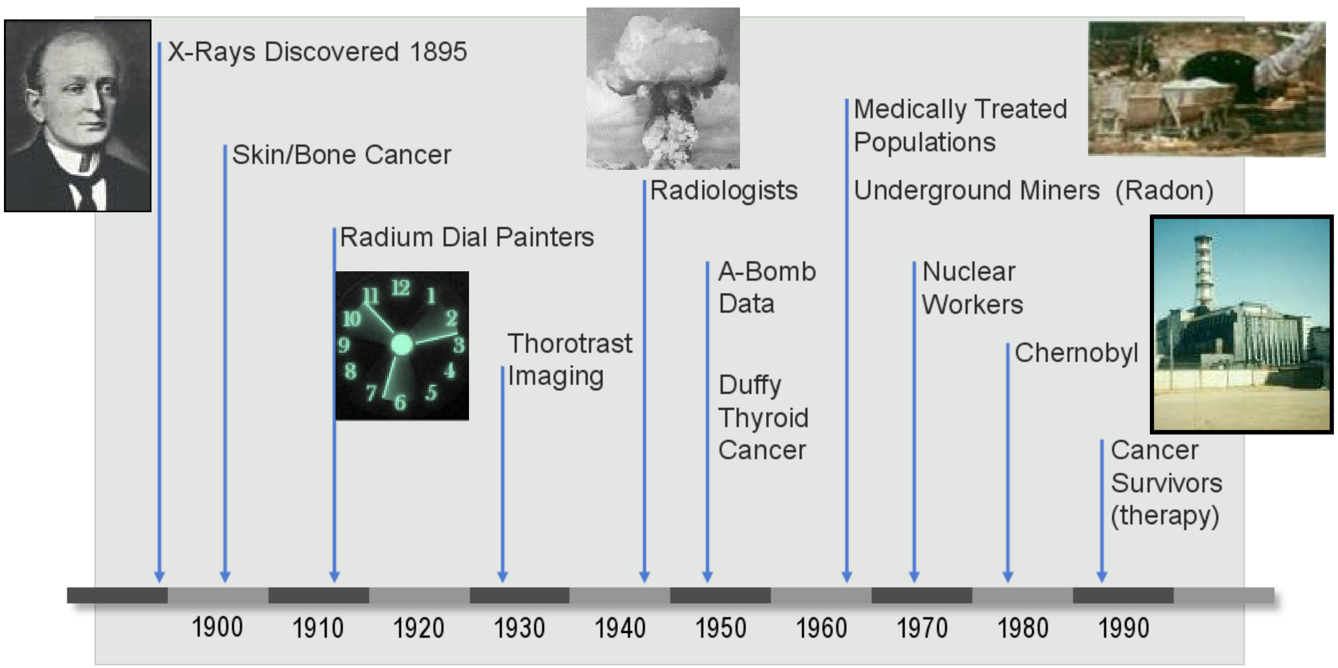
Thanks Fred Mettler

Protection & Radiation Epidemiology

- Radiation Epidemiology
- Heritable Effects and Protection
- From Science to Protection
- Radium
- Occupation
- Leukemia – past to present
- Breast and Thyroid Cancer
- Radon
- A Million Person Study
- What's Next?

Epidemiology is the Study of the Distribution and Causes of Disease in Humans

Radiation Epidemiology Dates Back 100 Years



Epidemiologic Studies of Exposed Human Populations

JAPANESE ATOMIC BOMB SURVIVORS

RADIOTHERAPY - CANCER
- Cervical
- Endometrial
- Childhood
- Breast
- Hodgkin Lymphoma

RADIOTHERAPY - NON-MALIGNANT
- Spondylitis
- Thymus
- Tonsils
- Menstrual Disorders
- Scalp Ringworm
- Mastitis
- Infertility
- Otitis Media
- Ulcer
- Hemangioma

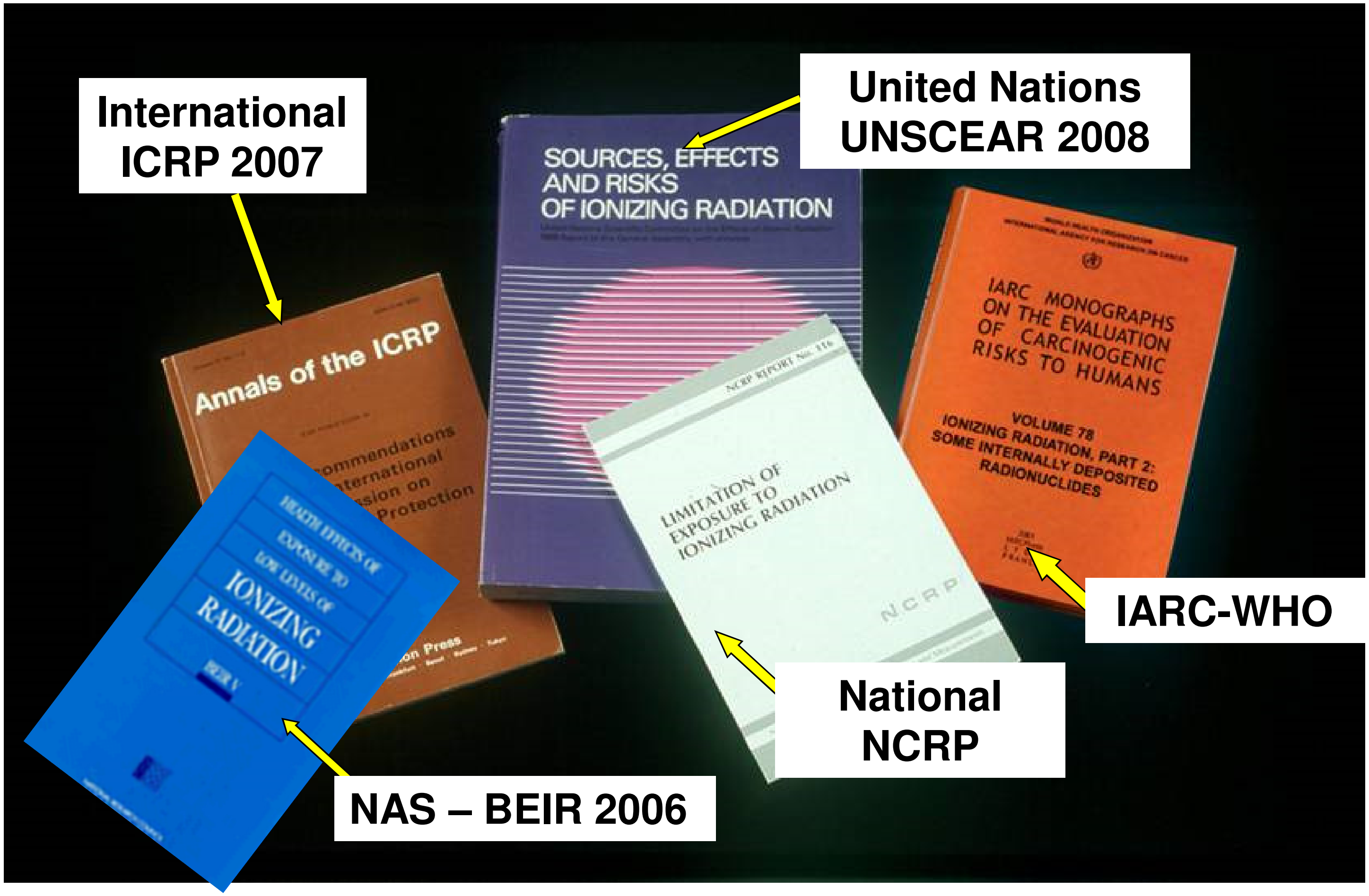
DIAGNOSTIC
- TB - Fluoroscopy
- Pelvimetry
- Scoliosis
- General

RADIONUCLIDES
- Thorotrast
- I - 131
- Uranium
- P - 32
- Ra - 224
- Plutonium

OCCUPATION
- Ra Dial Painters
- Miners (Radon)
- Radiologists
- Technologists
- Nuclear Workers
- Atomic Veterans

ENVIRONMENT
- Chernobyl
- Weapons Fallout
- Natl Background
- Techa River

Radiation Reports and Recommendations



The Role of Radiation Epidemiology

- Radiation epidemiology is now so sophisticated that human studies are the basis for radiation protection standards and for compensation schemes in response to claims of ill health from prior exposures

- Consensus judgment is needed to translate the epidemiology into recommendations and then into standards/regulations, especially when risks are cannot be detected

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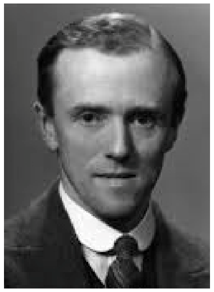
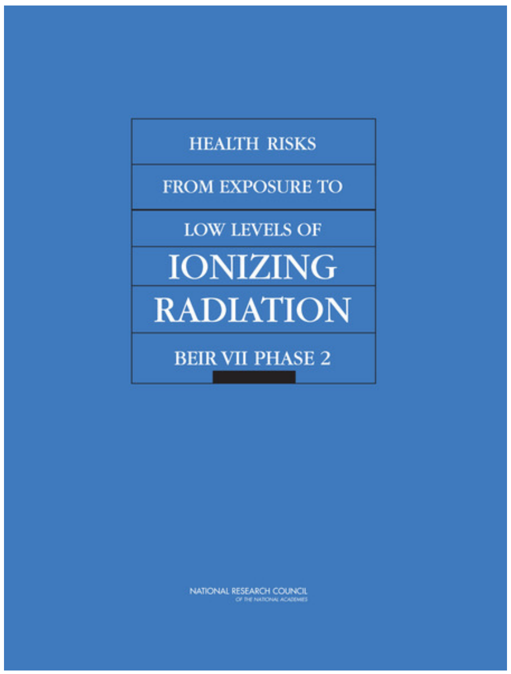


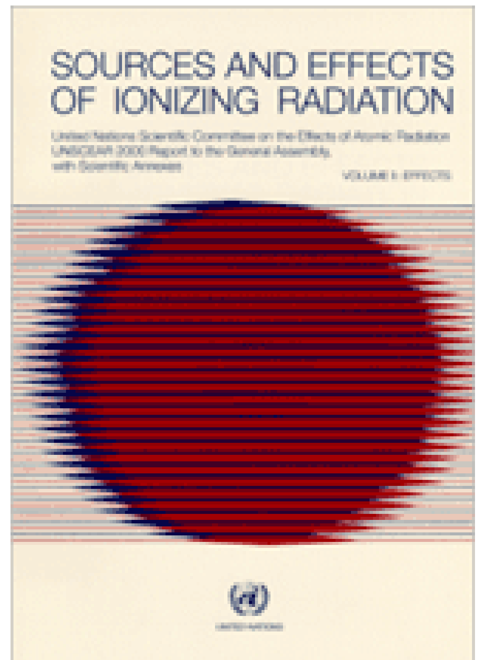
Bill Mayneord, UK,
2nd Sievert 1977

Step 1 – The Science: BEIR VII and UNSCEAR

NAS BEIR VII (2005)



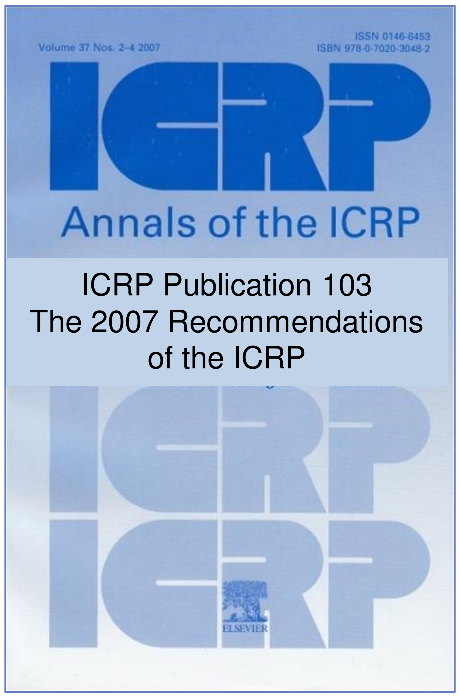
UNSCEAR 2000 REPORT, VOL. 2



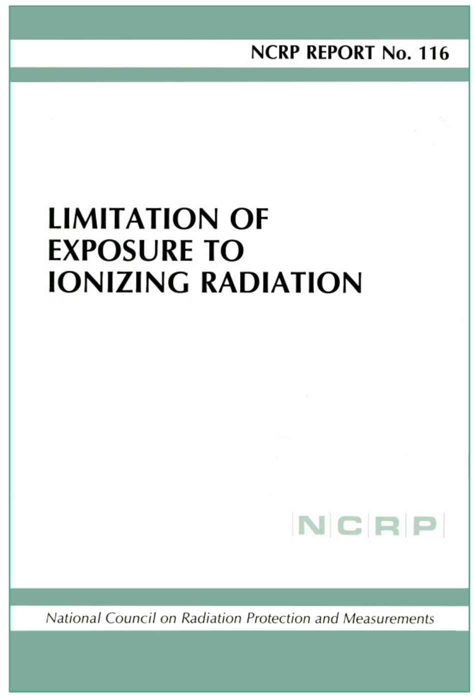
Thanks Mike Boyd

Step 2:
ICRP and NCRP Recommendations

ICRP PUBLICATION 103

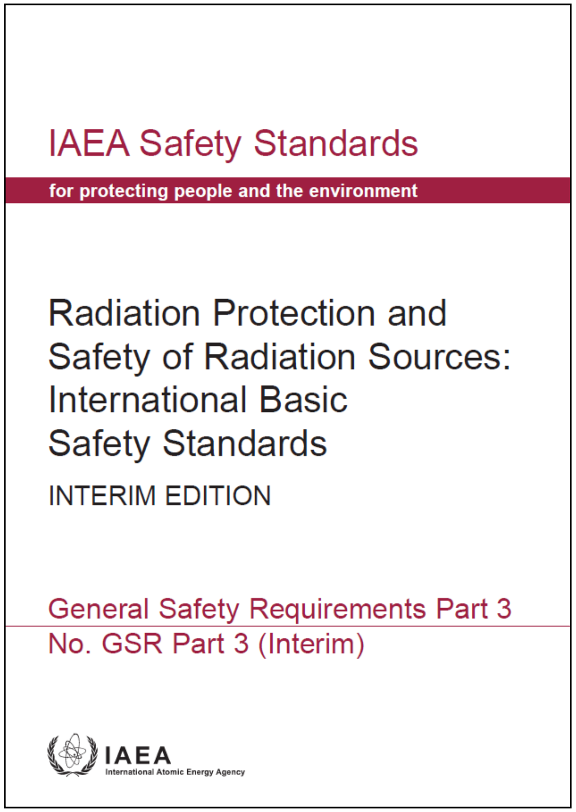


NCRP REPORT NO. 116



Thanks Mike Boyd

Step 2½:
IAEA Basic Safety Standards (2011)


IAEA Safety Standards

for protecting people and the environment

Radiation Protection and
Safety of Radiation Sources:
International Basic
Safety Standards

INTERIM EDITION

General Safety Requirements Part 3
No. GSR Part 3 (Interim)

IAEA
International Atomic Energy Agency

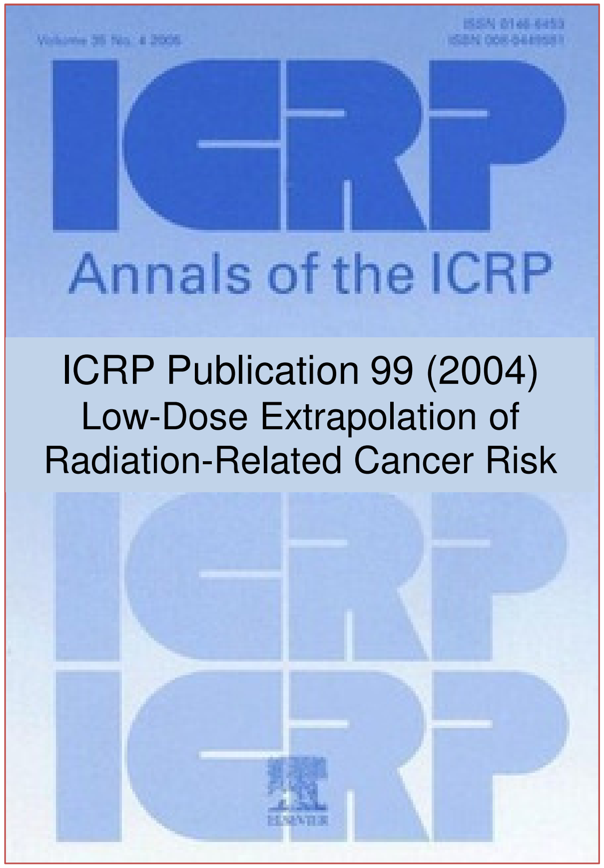
Thanks Mike Boyd

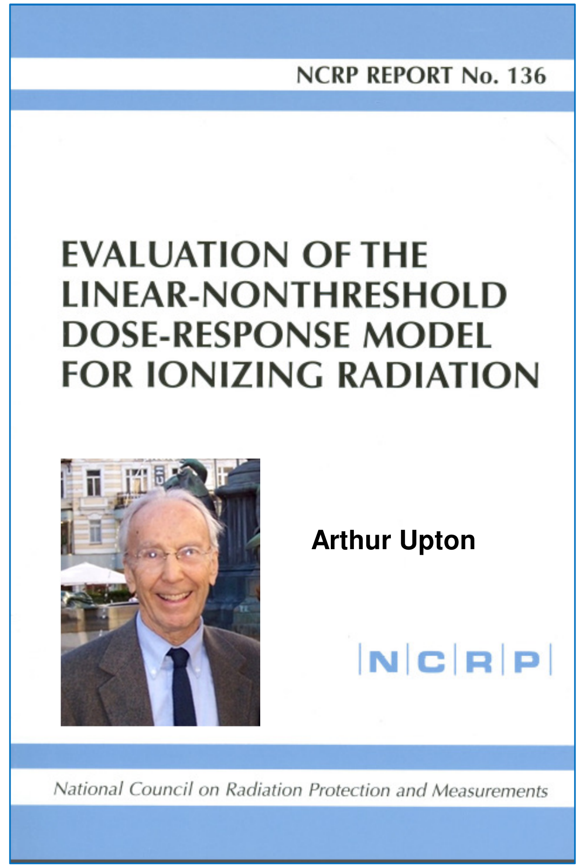
Step 3:
U.S. Radiation Protection Regulations

- U.S. Nuclear Regulatory Commission
  - 10 CFR Part 20
  - 10 CFR 50 Appendix I
- U.S. Environmental Protection Agency
  - 40 CFR Part 190
  - Other dose-based standards found in Clean Air Act regulations, Safe Drinking Water Act MCLs, and various waste management standards

Thanks Mike Boyd

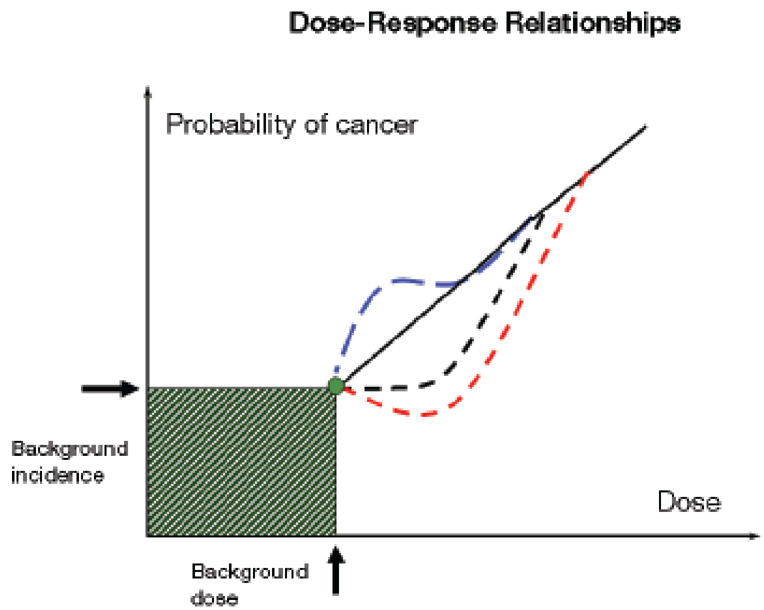
The Science Behind LNT Hypothesis





The Judgment on LNT — Plausible and Practical Although Risk Below 100 mSv Uncertain

(67) … the adoption of the LNT model combined with a judged value of a dose and dose rate effectiveness factor (DDREF) provides a prudent basis for the practical purposes of radiological protection, *i.e.*, the management of risks from low-dose radiation exposure (ICRP Publ 103, 2007)



The Linear Nonthreshold (LNT) Hypothesis

- May be true or not. "No conclusive evidence to reject the assumption" NCRP Report No. 136
- (66) … whilst the LNT model remains a scientifically plausible element in its practical system of radiological protection, biological/epidemiological information that would unambiguously verify the hypothesis that underpins the model is unlikely to be forthcoming. ICRP Publication 103
- Continually being re-assessed, e.g. NCRP SC 1-25, with angst !

Thanks Fred Mettler

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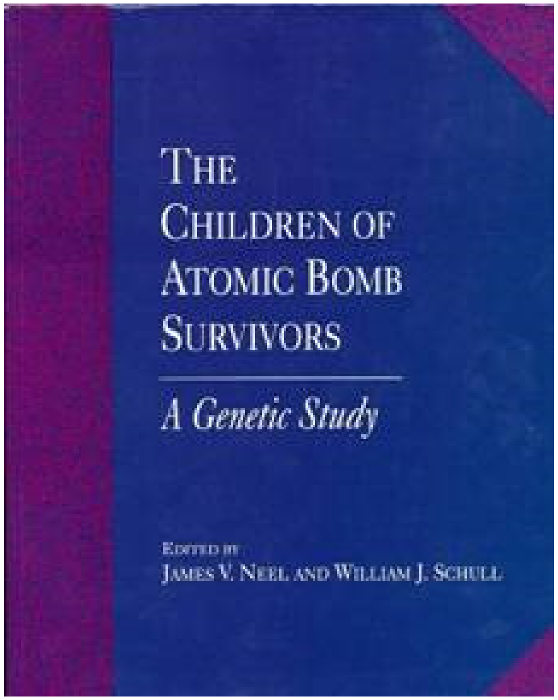
Radiation Epidemiology Has Shifted the Focus from Genetic Effects in Future Generations to Somatic Effects on the Individuals Exposed

- Untoward pregnancy outcomes (major congenital malformations, and/or stillbirths and/or neonatal deaths)
- Sex of child
- Childhood cancer (F1 cancer)
- Death of offspring (F1 mortality)
- Growth and development
- Cytogenetic abnormalities
  - chromosome number (sex-aneuploidy or Down)
  - chromosome structure (translocations)
- Protein mutations
- DNA microarray-based comparative genomic hybridization
- Mortality after 62 years of follow-up (2015)



Neel, Teratology 59:216, 1999

Schull, J Rad Prot 23:369, 2003

Grant et al Lancet Oncol 2015

Preconception Studies – Heritable Effects
Children of Cancer Survivors

Will I be able to have children of my own?
Will my children be healthy?
Will they have birth defects or malignancies?

Children of Cancer Survivors
Genetic Consequences of Cancer Treatment

NIH

Scientific Advisory Committee

USA/CCSS

St. Jude | MDACC | U OKLA

Denmark

Danish Cancer Society | MDACC | U OKLA | Westlakes

Expansion

Finland | Vanderbilt | Young Adults 20-34-yr

Boice et al, *Health Phys* 85:65, 2003

Genetic Disease in Children of Survivors & Sibling Controls (CCSS: self-reports, verification by medical records)

14,054 children with cancer
126 cGy mean dose ovaries, 46 cGy testes

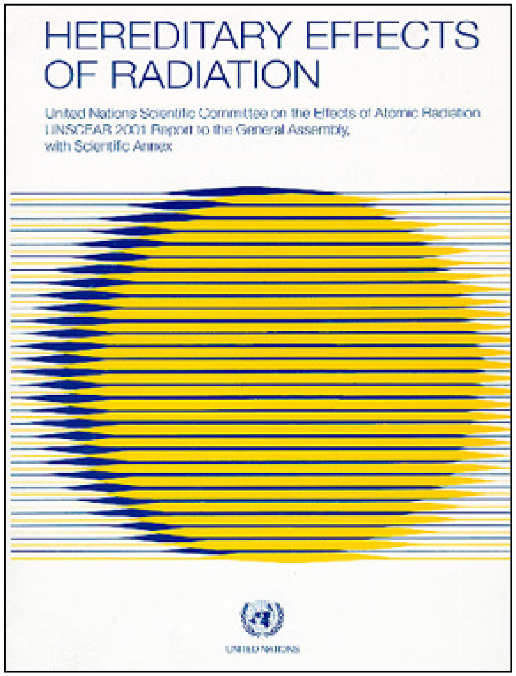
Type of Genetic Disease	Survivors (n = 6,129)	Controls (n = 3,101)
Cytogenetic	7 (0.1%)	6 (0.1%)
Single gene disorder	14 (0.2%)	8 (0.3%)
Simple malformation	136 (2.2%)	97 (3.1%)
Total	157 (2.6%)	111 (3.6%)

Green et al, *J Clin Oncol*, 2009

No increase in birth defects

Epidemiology Has Not Revealed Heritable Effects in Humans

No radiation-induced genetic diseases have so far been demonstrated in humans ... estimates of risk have to be based on mouse experiments. UNSCEAR 2001



Preconception Radiation – When no Risk

Liane Russell

- But heritable effects are seen in animal studies
- A small risk is assumed for radiation protection
- ICRP 103 (A 124) The gonadal dose to the total detriment is reduced from 18% to 3–4%

Bill Russell

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Wolgang Jacobi
Germany
5th Sievert 1988

Marie Curie at Memorial NYC (1921)

After resting at Mrs. Meloney Brown's home Curie left 'to have a few hours of pure pleasure inspecting the radium laboratories in the **Memorial Hospital** in New York City ...

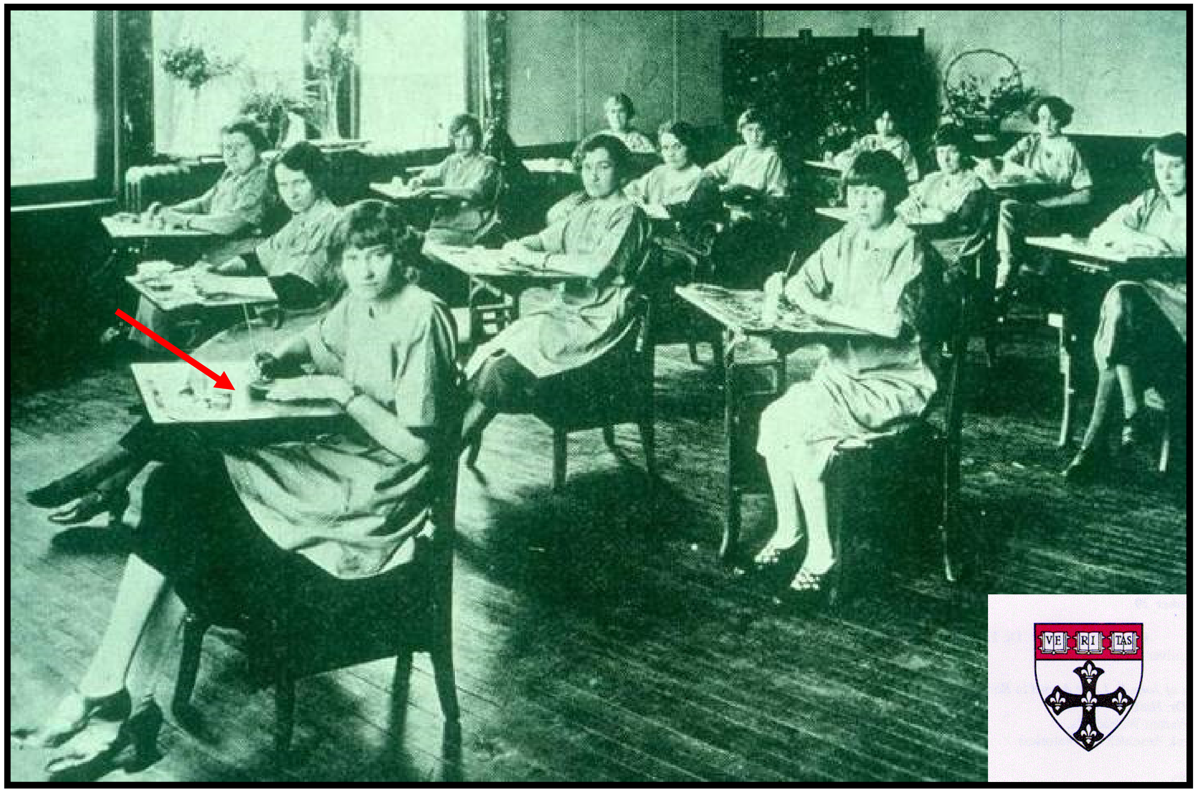
There is no case on record of any one being injured in health by radium ... Mme. Curie has been working with radium twenty year ... If it had any deleterious effects, they would have been noted long ago ...

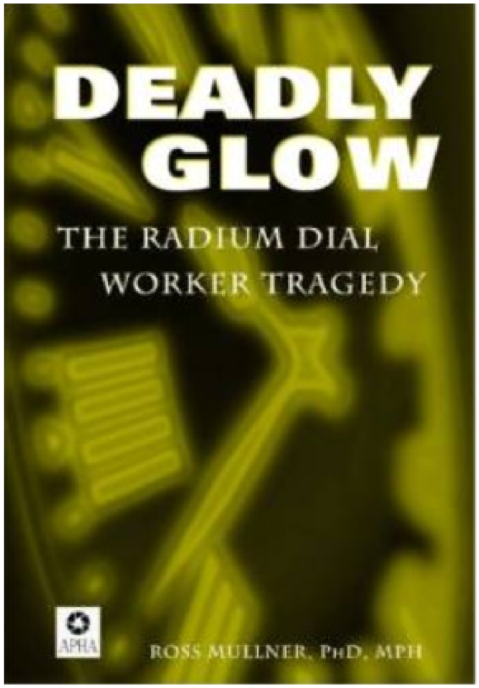
Mme. Curie is somewhat anaemic as nearly all persons of confined, studious pursuits are. About half of the people are more or less so.

NY Times, May 29, 1921

Figure 2. Smith College was the first stop of Marie Curie's visit and the first of seven women's colleges she visited. College President William Neilson accompanies her to the May 13, 1921 convocation conferring an honorary Doctor of Science.

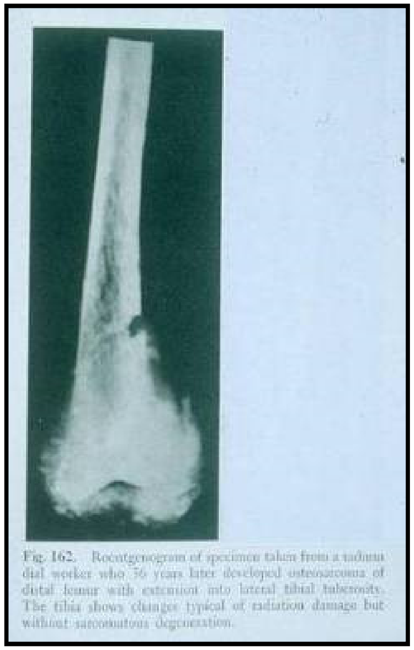
Radium Dial Painters – Years Later

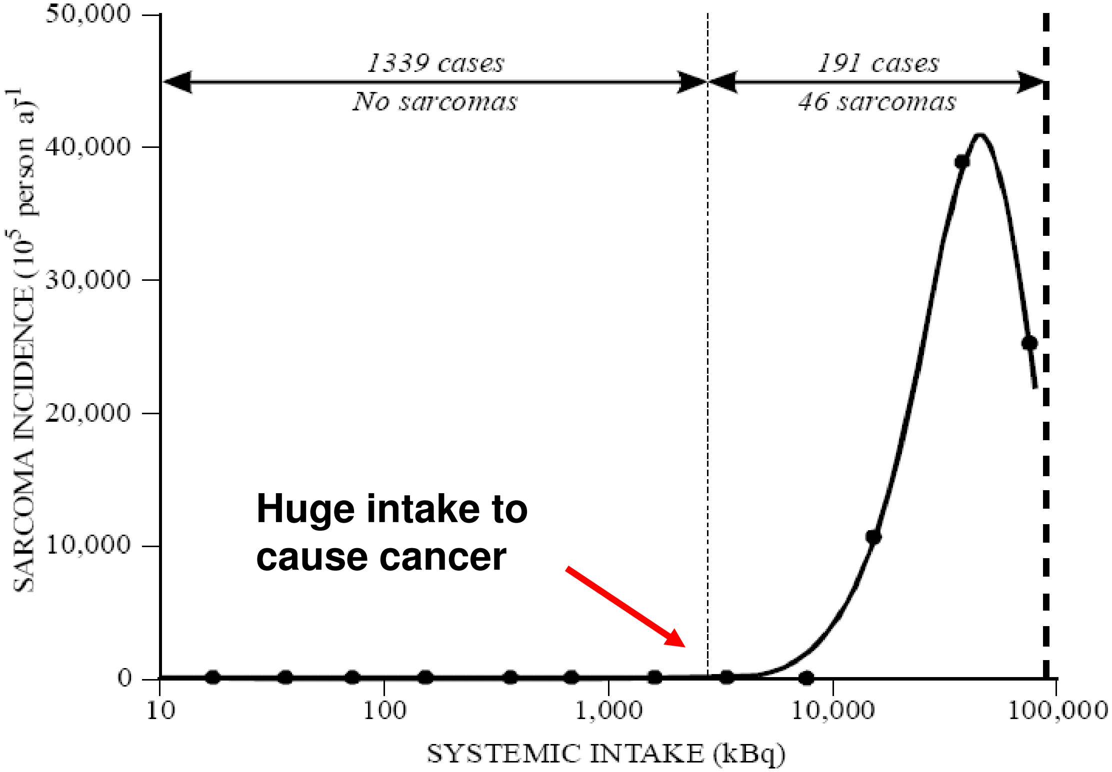




Am. J. Epidemiol. (2002) 155 (3): 290-291.

Bone Cancer in Radium Dial Painters (UNSCEAR 2000)





10 Gy suggested as a “practical threshold” for bone cancer

Bone Cancer, not leukemia

Radium Studies Resulted in Standards that Protected Workers from Internal Radiation

- Evans proposed the radium standard (1941) based on measurements of body burden and radium health effects
- In 1944, the radium standard was used as a basis for setting the plutonium standard
- The Manhattan Project (WW II) in the USA would have suffered without the radium standard (Merrill Eisenbud, 1975)
- Epidemiology and Dosimetry led to Protection

Los Alamos Science Number 23 1995

In the 1930s, Robley D. Evans developed the first quantitative technique for making *in vivo* measurements of radium body burdens. Those measurements were the basis for the radium standard set in 1941.

Protection & Radiation Epidemiology

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From Science to Protection
Radium to Protection
Occupation to Protection
Leukemia – past to present
Breast and Thyroid Cancer
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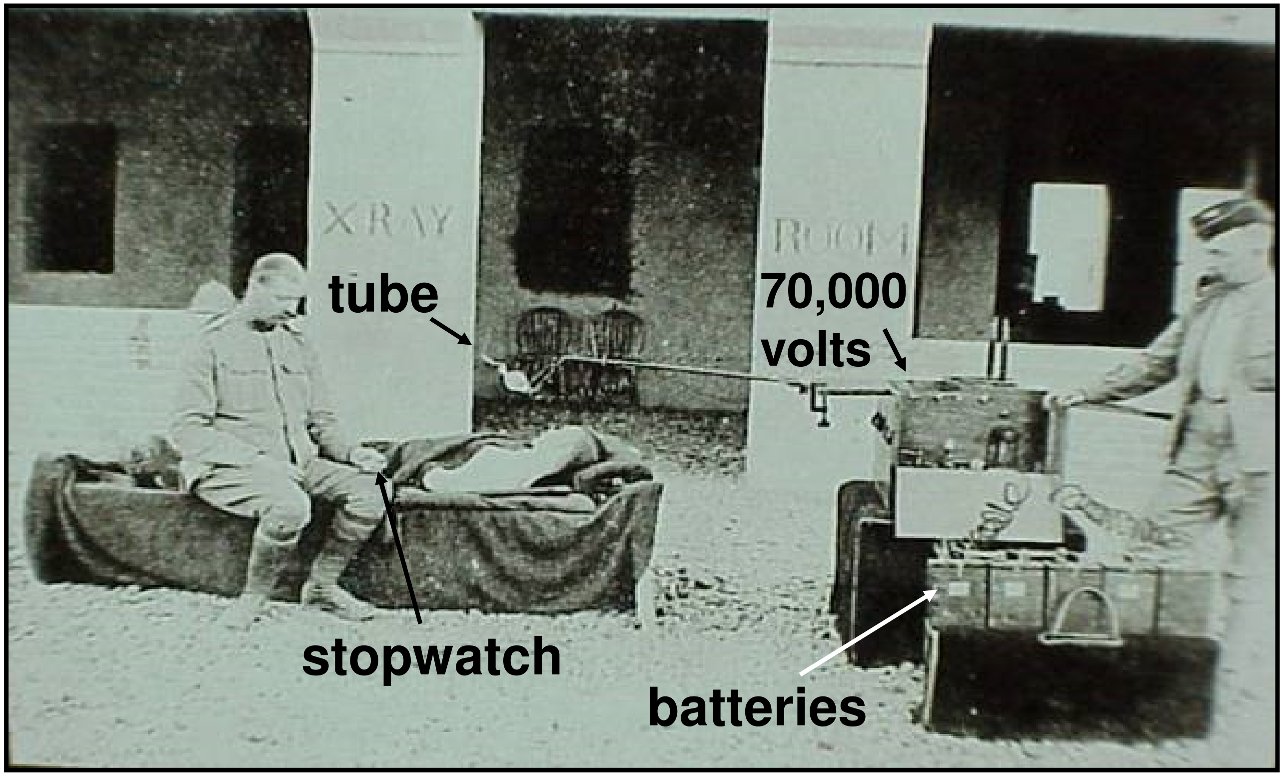
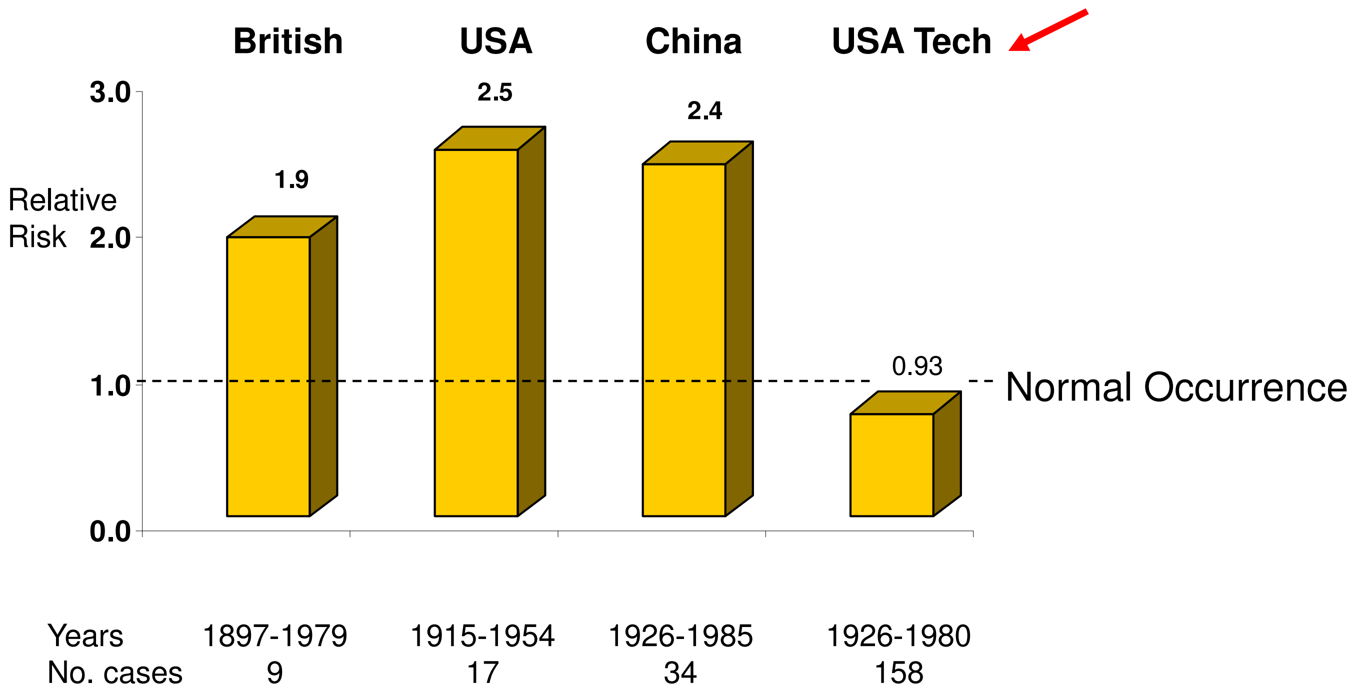
A Million Person Study
What's Next?

Giovanni Silini
Italy
Sievert 1992

Early Radiologists and Technicians
1898 - Sudan



Leukemia Among Early Radiologists / Technologists



Berrington, *Br J Radiol* 74:507, 2001
Seltzer, *Am J Epidemiol* 81:2, 1965
Wang, *Int J Cancer* 45:889, 1990
Mohan, *Int J Cancer*, 2003

Early radiation workers

Radiation Exposure to Radiologists

1930: 1 Gy (100 rad) / y estimated.

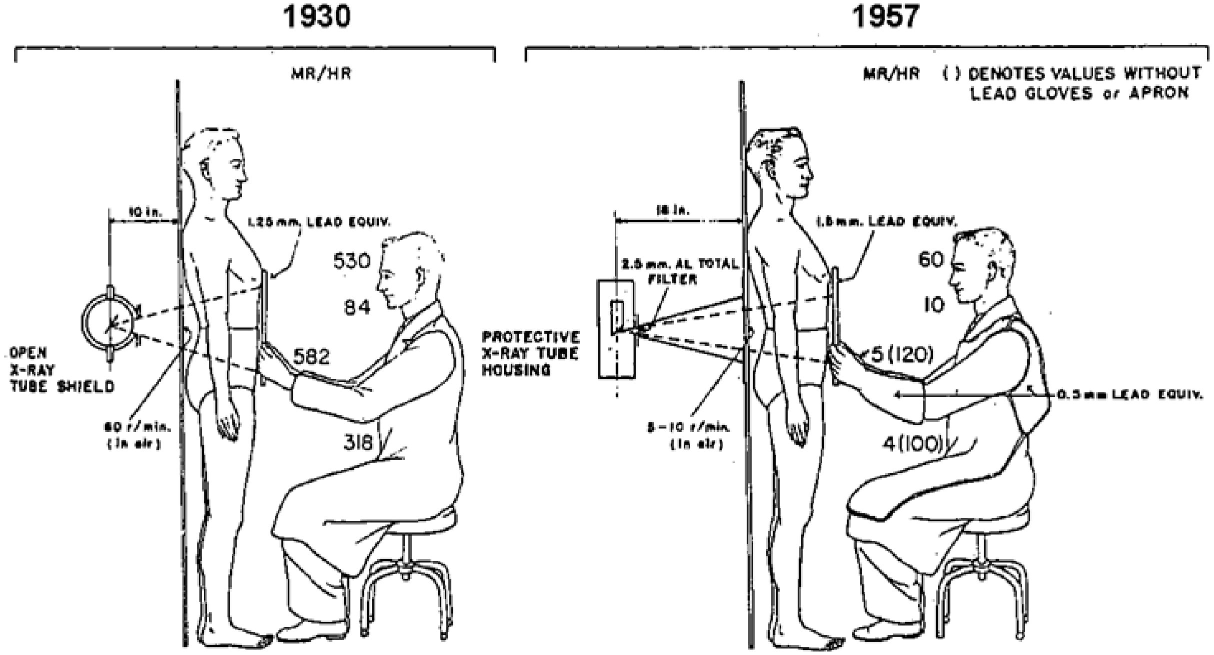


Fig 1. Comparison of stray radiation from vertical fluoroscopes.

Braestrup, *Am J Roentgenol 78:988,* 1957

1940s Studies -- Fractionated Exposures May Cause Leukemia

Leukemia in Radiologists[1]

HERMAN C. MARCH, M.D.
Philadelphia, Penna.

FOR MANY YEARS there has been prevalent an impression of a possible relationship between exposure to radiation and the subsequent development of leukemia. As early as 1911 there appeared the first report on the matter by von Jagic and co-workers (1), in which a brief statement—based in part on hearsay—is made concerning the occurrence of leukemia in four persons who had experienced prolonged exposure to radiation. Of only one of these cases did the authors have any personal knowledge. Since that time there have appeared perhaps a dozen reports on the specific subject of the development of leukemia in persons non-therapeutically exposed to small doses of radiation over prolonged periods. Twenty-three cases have been recorded in the literature, including the four by von Jagic. In a few of the cases details are lacking and the relationship is not well established.

In 1912 Aubertin (2) referred to a case of myeloid leukemia discovered in a French

Lacassagne occurred in persons who were known from definite first-hand information to have experienced prolonged exposures to small amounts of radiation.

Aubertin (7), in 1931, stated that over a period of nineteen years he had the opportunity of seeing five radiologists afflicted with myeloid leukemia, while during the same space of time he had observed only one case in a physician other than a radiologist. Since the radiologists constitute only a small proportion of the medical profession, he concluded, on the basis of his personal experience, that myeloid leukemia is undoubtedly more frequent in radiologists than in other doctors. In the same year Haagensen (8), at the Memorial Hospital, New York, cited a case of leukemia developing in a person exposed to radiation over a prolonged period. The following year a case was added by Nielsen (10) and another by Laubry and Marchal (9). The latter writers quote a case of Znajewska. In 1937 Emile-Weil (11) re-

March HC, *Radiology*, September, 1944

THE INCIDENCE OF LEUKEMIA IN RADIOLOGISTS*

HELMUTH ULRICH, M.D.†
BOSTON

EXPOSURE to x-rays has for some time been regarded as a possible cause of leukemia. This belief is based in part on results obtained by experimental exposure of animals to x-rays[1–4] and in part on several reports of cases of leukemia occurring in workers exposed to radiation.[5–15] Definite proof of such an etiologic relation has not been established, however, and some authors have expressed doubt concerning it. Thus, Evans and Roberts[8] stated in 1928, after a review of the literature to that date, "Although the possibility of causal association cannot positively be denied, the evidence is not conclusive." Haagensen[9] wrote, "Doubt may be raised as to the relationship of the exposure to radiation and the development of leukemia," and Warren and Dunlap,[16] in their comprehensive review published in 1942, stated: "Few examples of leukemia have been described in persons chronically exposed to radiation. Only 24 case reports are found in the literature if one excludes all reports of leukemia following the therapeutic irradiation of lymphatic tumors."

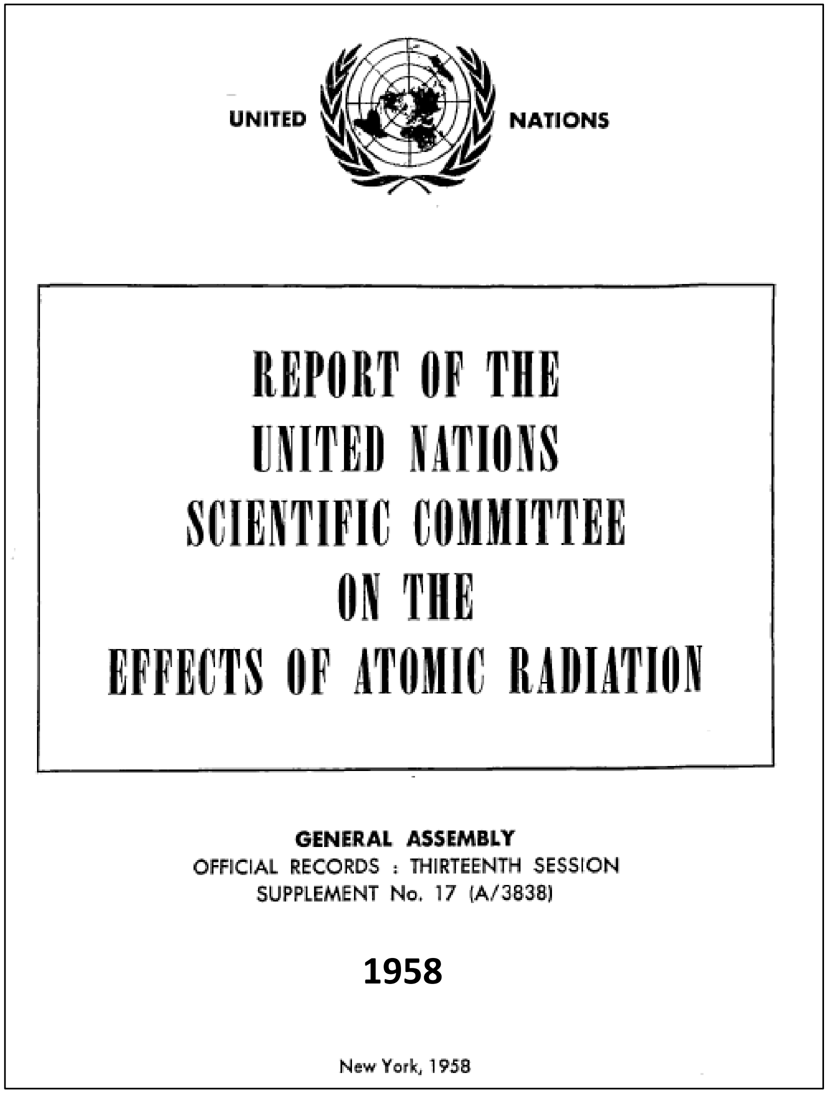
More recently, Henshaw and Hawkins,[17] having found that none of the existing evidence furnishes any direct proof that radiation actually acts as a carcinogenic agent in the induction of leukemia in human beings, determined the incidence of leukemia in physicians from the death notices published weekly in the *Journal of the American Medical Association* and compared it with similar data regarding the general population, derived from the vital statistics of the United States Bureau of the Census. They found that during a ten-year period (1933–1942) 0.53 per cent of physicians died of leukemia, as compared with 0.39 per cent of the general population. After making corrections for differences of age, sex and other factors that influence the outcome, they arrived at the following conclusion: "Leukemia was recognized approximately 1.7 times more frequently among physicians than among white males in the general population." They stated that, although these observations furnished no direct proof that radiation acts to incite leukemia in human beings, they were nevertheless in accord with the findings on experimental animals in which exposure to x-rays had been found to increase the incidence of leukemia.

Since the majority of physicians are not subject to exposure to radiation, it seems that a comparison of the incidence of leukemia among radiologists and that among other physicians should give more conclusive results. The present report is based on a statistical study of deaths of physicians reported in the *Journal of the American Medical Association* during the ten-year period 1935–1944.

*From the Department of Internal Medicine, Boston University School of Medicine, and the Department of Internal Medicine, Massachusetts Memorial Hospitals.

†Associate professor of medicine, Boston University School of Medicine.

Ulrich H, *New England Journal of Medicine* Jan 10, 1946


UNITED NATIONS

REPORT OF THE UNITED NATIONS SCIENTIFIC COMMITTEE ON THE EFFECTS OF ATOMIC RADIATION

GENERAL ASSEMBLY
OFFICIAL RECORDS : THIRTEENTH SESSION
SUPPLEMENT No. 17 (A/3838)

1958

New York, 1958

Early Epidemiology

An increased incidence of leukemia has been reported among …

(1) radiologists;
(2) atomic bomb survivors of Hiroshima and Nagasaki;
(3) patients with severe arthritis of the spine who were treated with X-rays for this condition;
(4) children who had been treated with X-rays in to reduce the size of the thymus gland.

Only in the case of a linear dose-effect relation with no threshold value of the dose is it relevant to add the dose contributions from various sources. This can be done in the case of genetic injury and, according to one hypothesis, also in the case of a possible induction of leukemia.

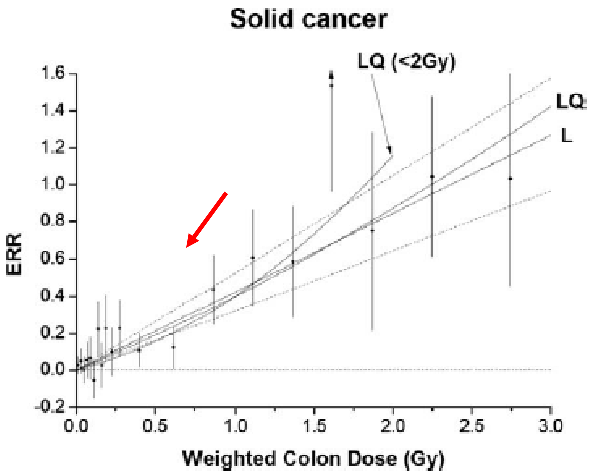
Protection & Radiation Epidemiology

- Radiation Epidemiology
- Heritable Effects and Protection
- From Science to Protection – The Process
- Radium to Protection
- Occupation to Protection
- Leukemia – past to present
- Breast and Thyroid Cancer
- Radon
- A Million Person Study
- What's Next?

Richard Osborne
Canada
11th Sievert 2012

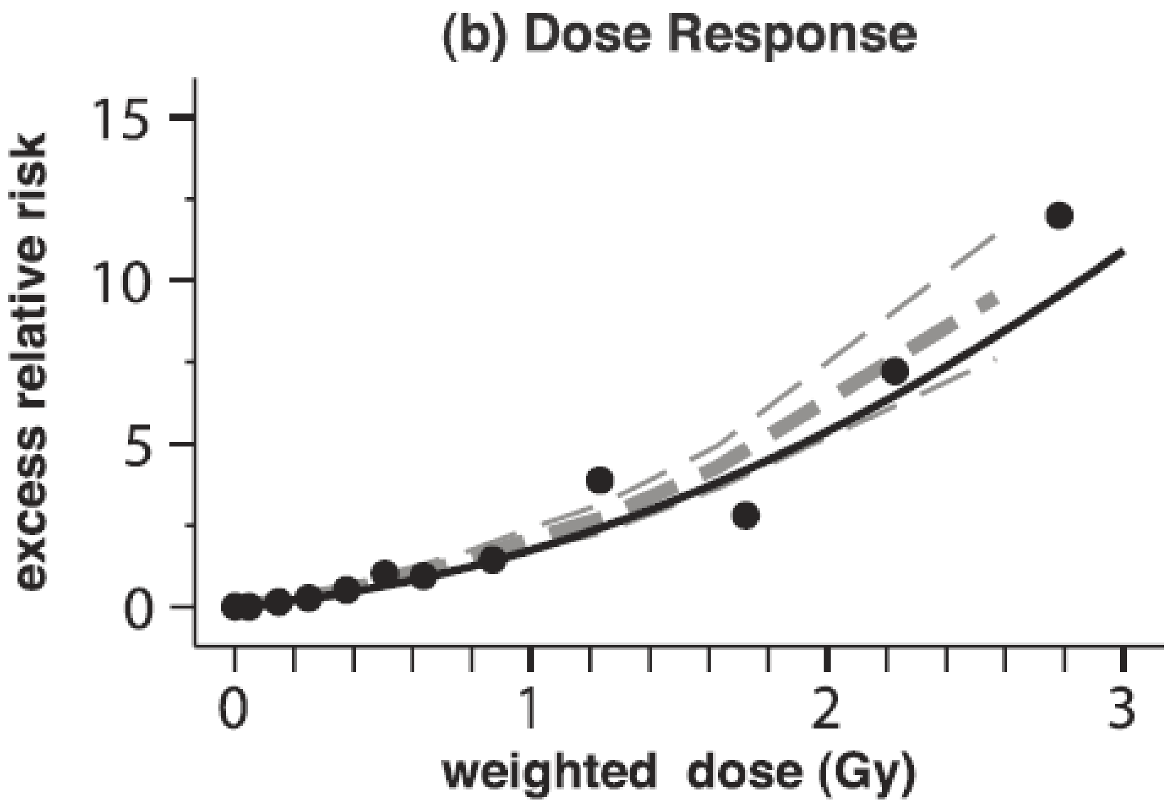
Epidemiologic Studies are the Basis for Cancer Risk Estimates

"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**



Ozasa, *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.

J. Radiol. Prot. **27** (2007) B15–B154

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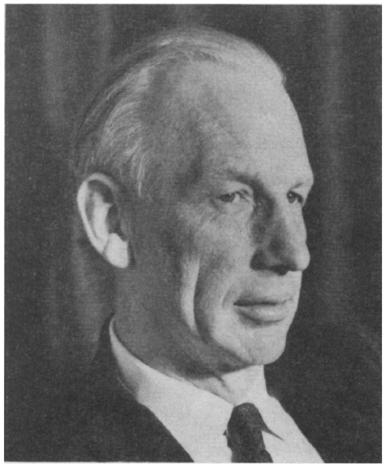
No. 295



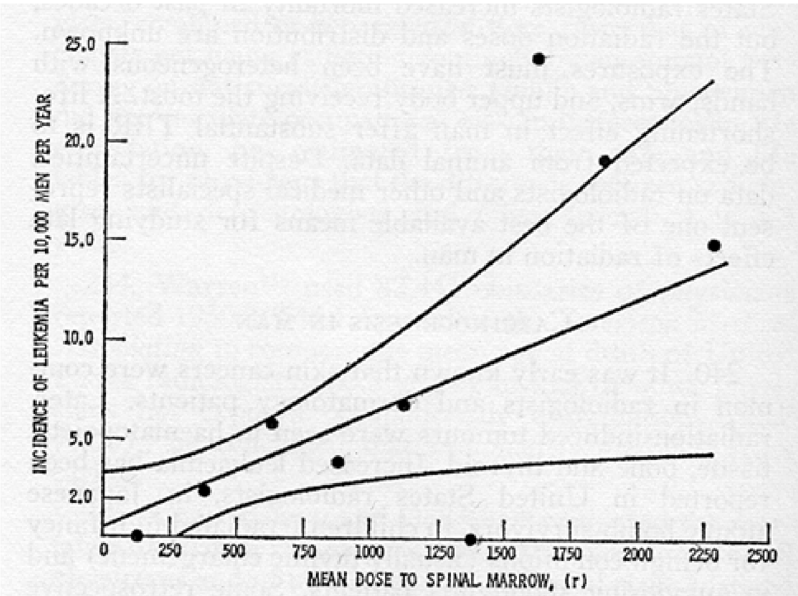
LEUKAEMIA AND APLASTIC ANAEMIA IN PATIENTS IRRADIATED FOR ANKYLOSING SPONDYLITIS

W. M. COURT-BROWN, O.B.E., M.B., B.Sc., F.F.R.
and R. DOLL, O.B.E., M.D., F.R.C.P.

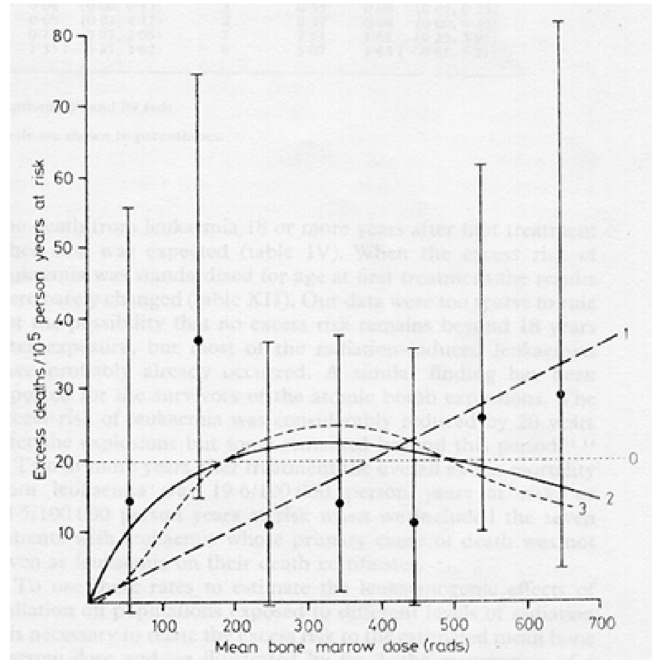
1957

Second study designed to evaluate leukemia dose response

Leukemia - Ankylosing Spondylitis, UK



Court Brown & Doll, UK, 1957
UNSCEAR, 1962

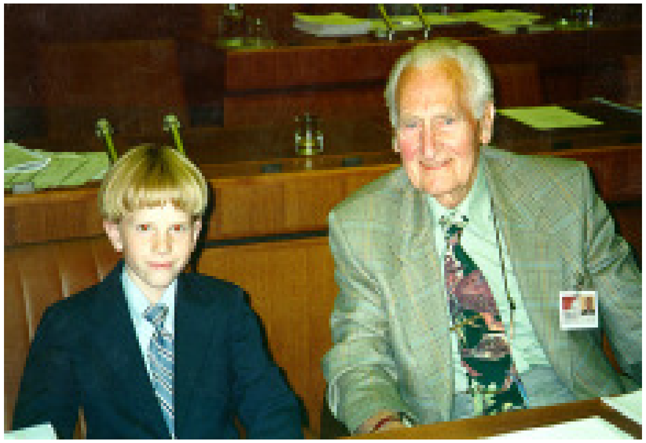


Smith & Doll, *BMJ*, 284:449, 1982
Weiss et al, *Radiat Res* 142:1, 1995

Smith PG. The 1957 MRC report on leukaemia and aplastic anaemia in patients irradiated for ankylosing spondylitis. J Radiol Prot. 2007

Sir Richard Doll on Ankylosing Spondylitis Study

- "My **favouite** paper . . .
- … the second most important piece of work that I have done, after the effects of **smoking**, … it provided the first suggestive evidence of a **linear relationship** for the carcinogenic effect of ionising radiation down to quite small doses.
- In many ways it was the best-designed study I have ever participated in and **possibly my best work**."

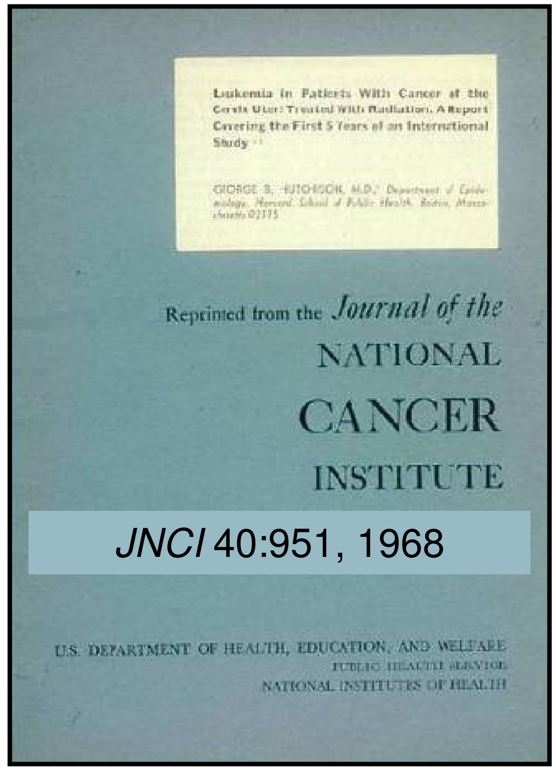


Jason Boice and Sir Richard
UNSCEAR

Darby S 2003 A conversation with Sir Richard Doll *Epidemiology* **14** 375–9

3rd Study of Leukemia Radiotherapy for Cervical Cancer

Third study in 1960s designed to quantify risk of leukemia



Leukemia in Patients With Cancer of the Cervix Uteri Treated With Radiation. A Report Covering the First 5 Years of an International Study

Reprinted from the *Journal of the*
NATIONAL
CANCER
INSTITUTE

JNCI 40:951, 1968

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
NATIONAL INSTITUTES OF HEALTH

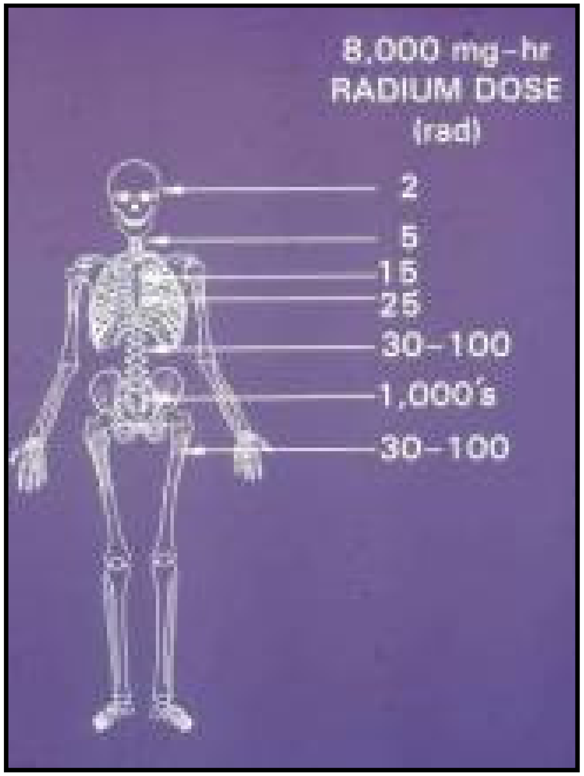
Cervical Cancer and Leukemia Blood Studies and Clinical Follow-Up
30 Radiotherapy Centers in 9 Countries

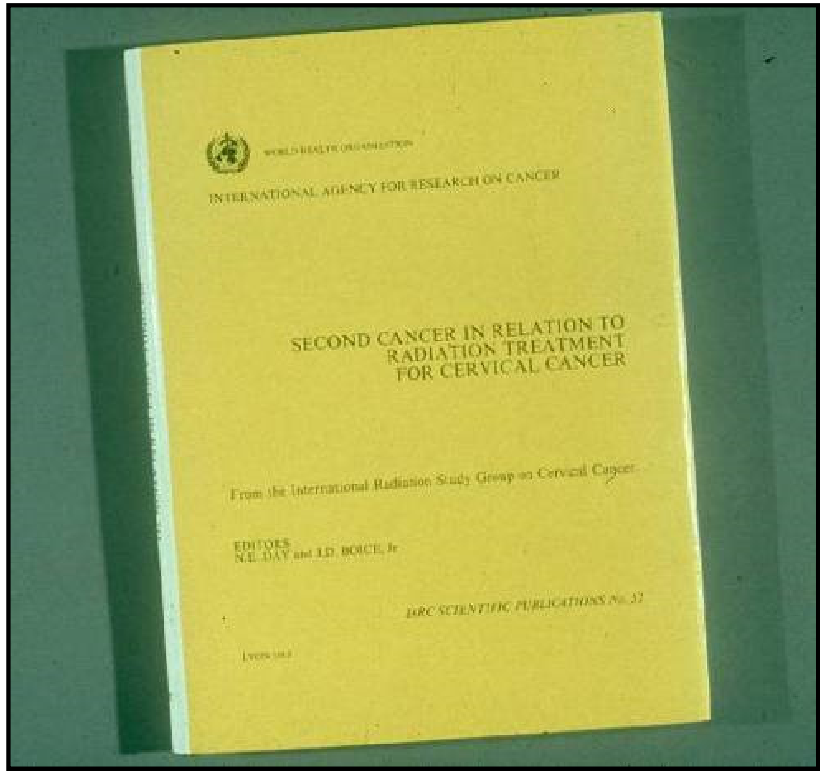
Number	30,000 women
Dose	5 - 15 Gy (marrow)
Leukemia	
Observed	13
Expected	15.5
Risk	**No excess**

Boice & Hutchison, *JNCI* 65:115, 1980

Huge dose but no risk

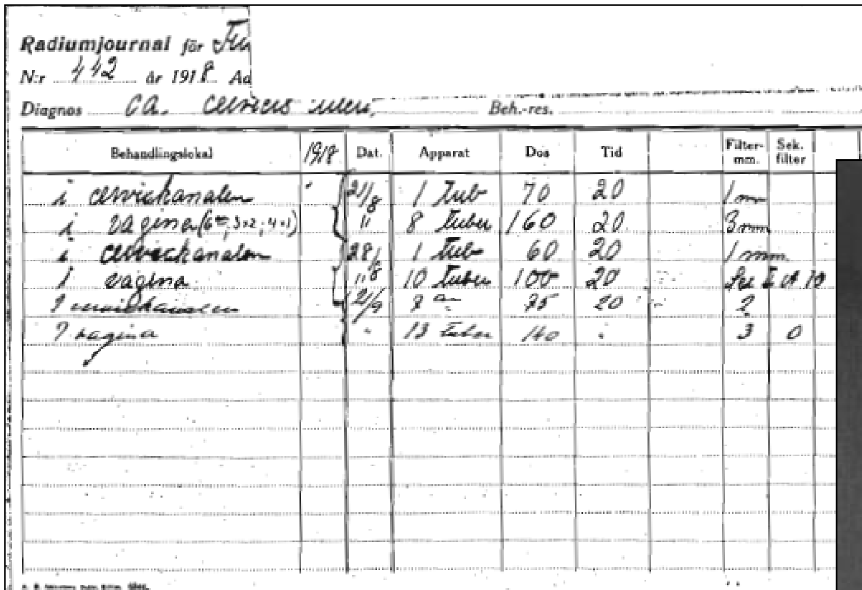
International Cervical Cancer Study Expansion – 16 Radiotherapy Centers and 17 Cancer Registries in 14 Countries





200,000 women

Elis Berven (1885-1966) på Radiumhemmet



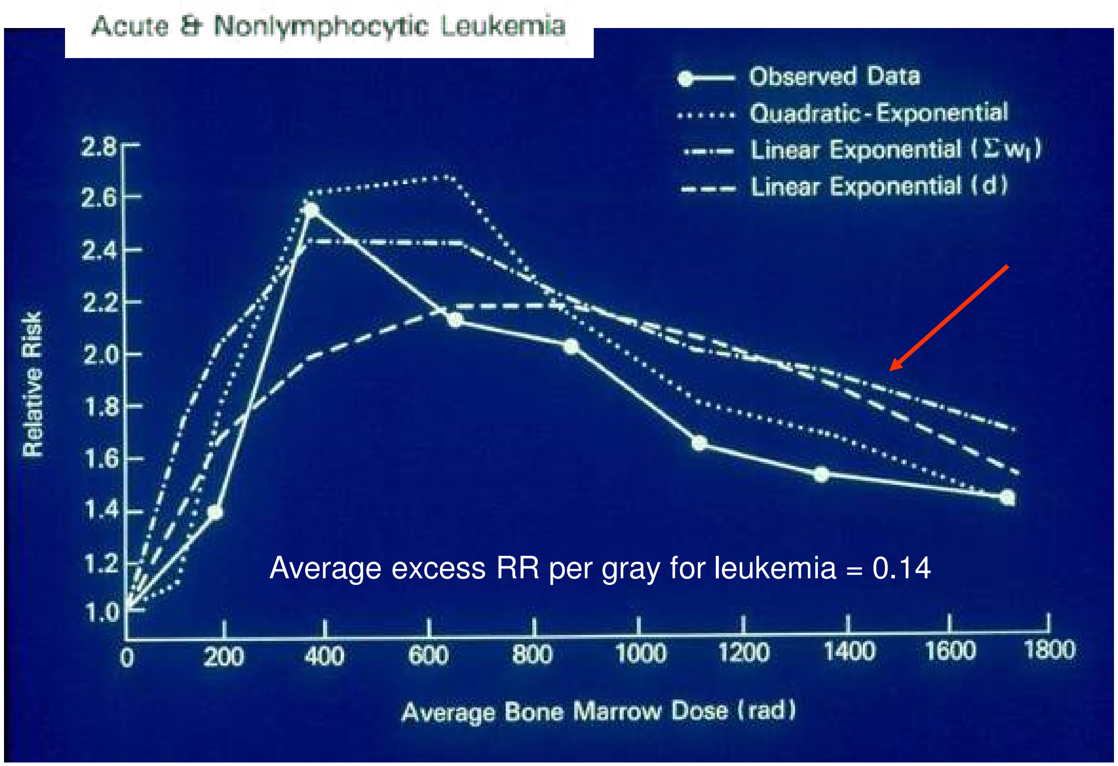
Radiumjournal för [illegible]
N:r 442 år 1918 Ad
Diagnos Ca. cervicis uteri Beh.-res.

Behandlingslokal	1918	Dat.	Apparat	Dos	Tid		Filter-mm.	Sek. filter
i cervixkanalen		21/8	1 Tub	70	20		1 mm	
i vagina (6 =; 3×2; 4×1)		〃	8 Tuber	160	20		3 mm	
i cervixkanalen		28/8	1 Tub	60	20		1 mm	
i vagina		〃	10 Tuber	100	20		[illegible]	
i cervixkanalen		2/9	3 [illegible]	75	20		2	
i vagina		〃	13 Tuber	140	〃		3	0

Radiumjournal År 1918

Rolf Sievert's
Hospital

Bone Marrow Dosimetry Downturn at High Doses

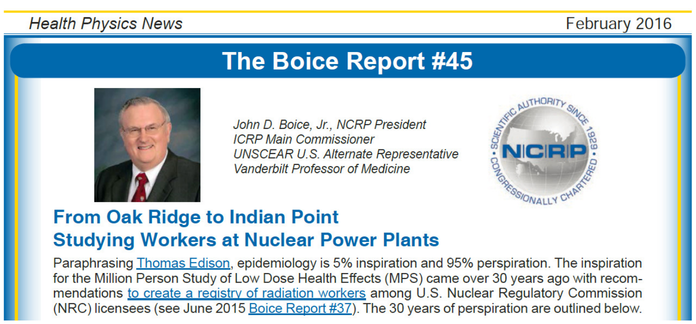


Boice et al, *JNCI* 79, 1987
Blettner and Boice, *Stat Med* 10, 1991

Cancer Treatments

- High dose to small volumes may kill rather than transform most cells – No epidemic of leukemia
- Short latency for leukemia to develop
- Opportunity for low-dose studies – scatter radiation
- New technologies (IMRT, Intensity-Modulated Radiation Therapy) may result in increased dose to all normal tissue

Million Person Study -- Nuclear Power Plant Workers - Dose Distribution



Health Physics News February 2016

The Boice Report #45

John D. Boice, Jr., NCRP President
ICRP Main Commissioner
UNSCEAR U.S. Alternate Representative
Vanderbilt Professor of Medicine

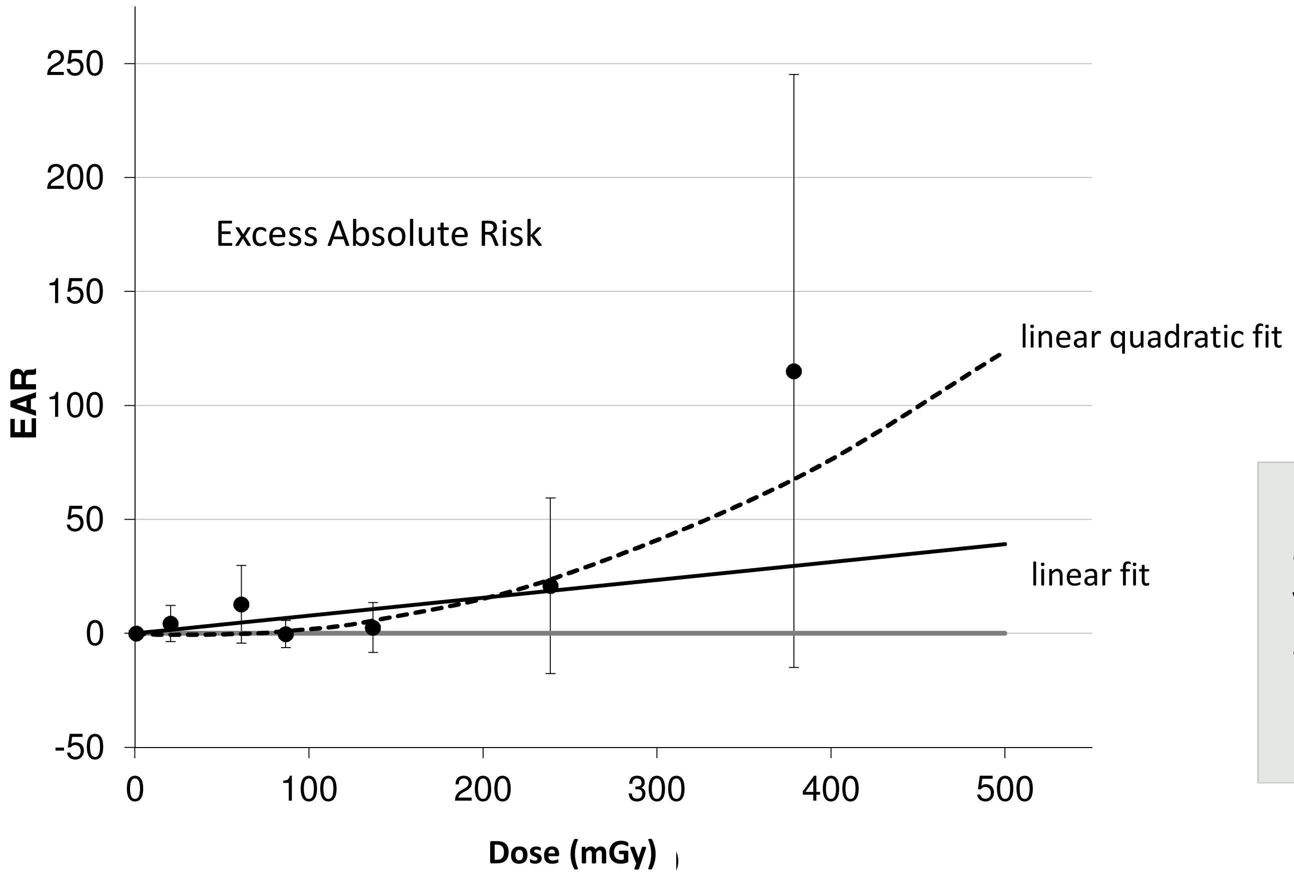
From Oak Ridge to Indian Point
Studying Workers at Nuclear Power Plants

Paraphrasing Thomas Edison, epidemiology is 5% inspiration and 95% perspiration. The inspiration for the Million Person Study of Low Dose Health Effects (MPS) came over 30 years ago with recommendations to create a registry of radiation workers among U.S. Nuclear Regulatory Commission (NRC) licensees (see June 2015 Boice Report #37). The 30 years of perspiration are outlined below.

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) EAR Dose Response Nuclear Power Plant Workers (preliminary)



ERR of 0.25 (90% CI 0.0, 0.5) at 100 mGY, 333 cases vs 0.41 (90% CI 0.3, 0.6) atomic bomb survivors, 98 male cases, mortality (UNSCEAR 2008)

Million Person Study

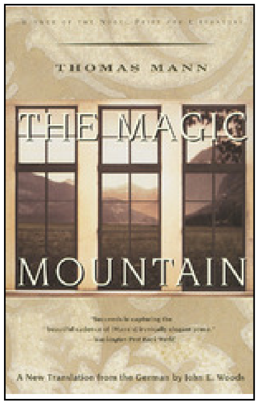
- Guidance on DRREF, specifically DREF
- Precise estimates for all cancer sites
- Precise estimates of risks among women and men
- Both external and internal exposures assessed

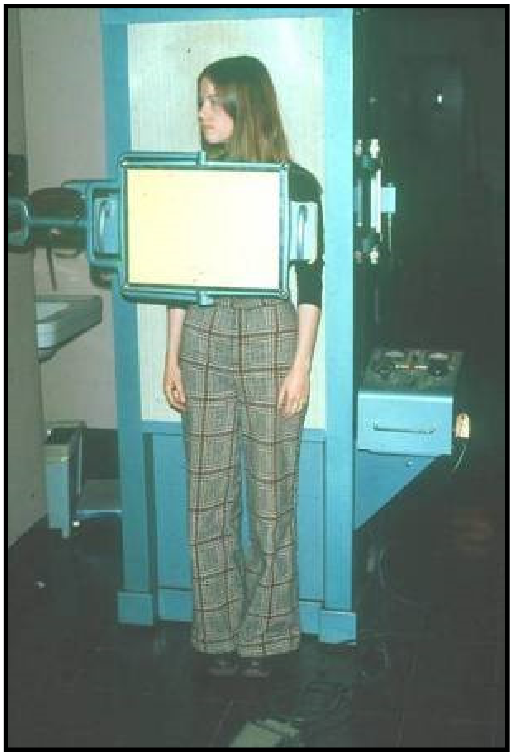
Protection & Radiation Epidemiology

- Radiation Epidemiology
- Heritable Effects and Protection
- From Science to Protection – The Process
- Radium to Protection
- Occupation to Protection
- Leukemia – past to present
- Breast and Thyroid Cancer – Straight lines
- Radon
- A Million Person Study
- What's Next?

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

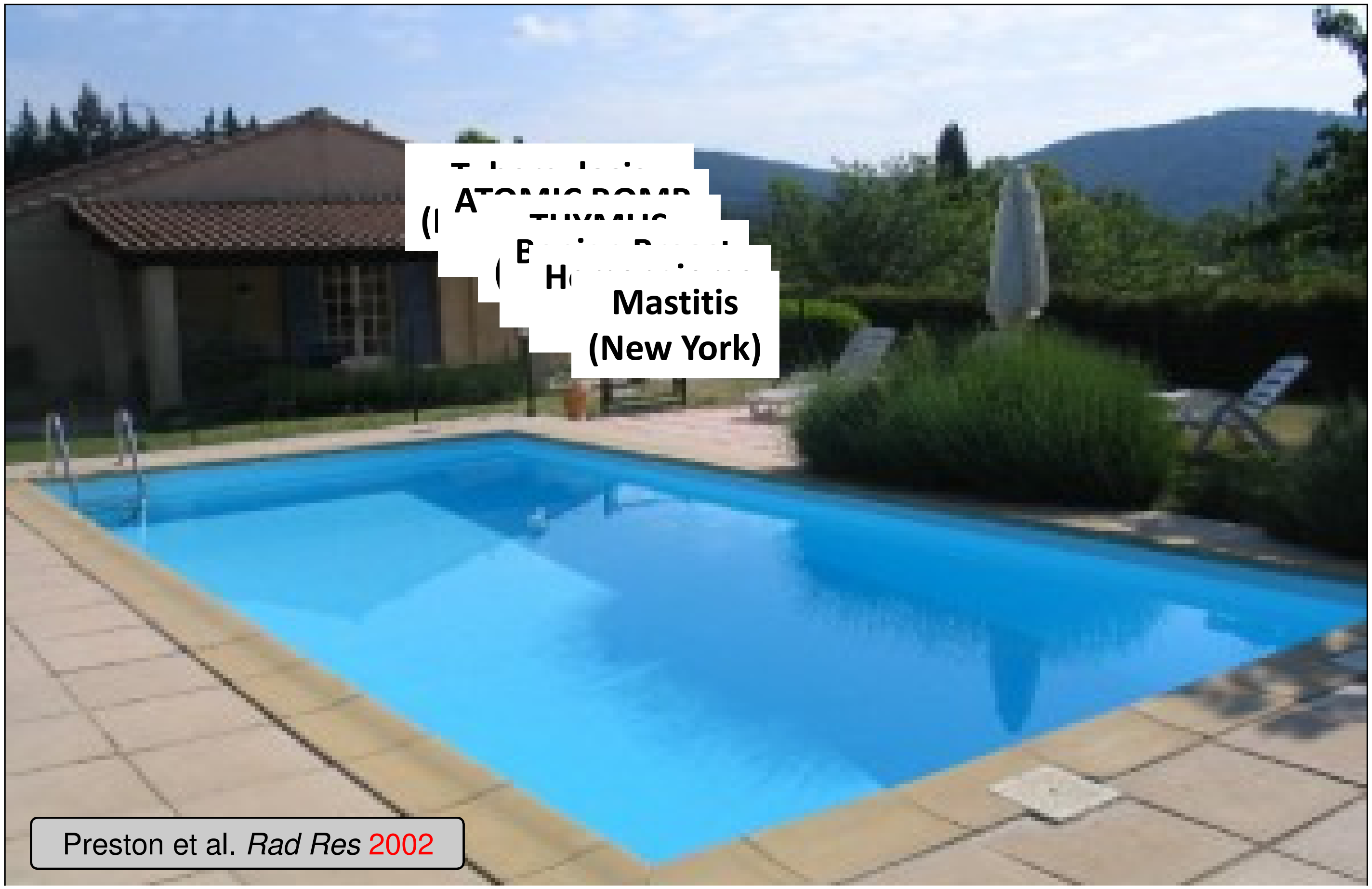
	Exposed	Nonexposed
No. of women	2,573	2,367
No. chest fluoroscopies, ave	88	--
Dose (ave) [*Dale Trout*]	790 mGy	--
Breast cancers		
Observed (O)	147	87
Expected (E)	114	101
O/E	1.29	0.86

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

29% Excess

ERR/Gy ~ 0.4

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

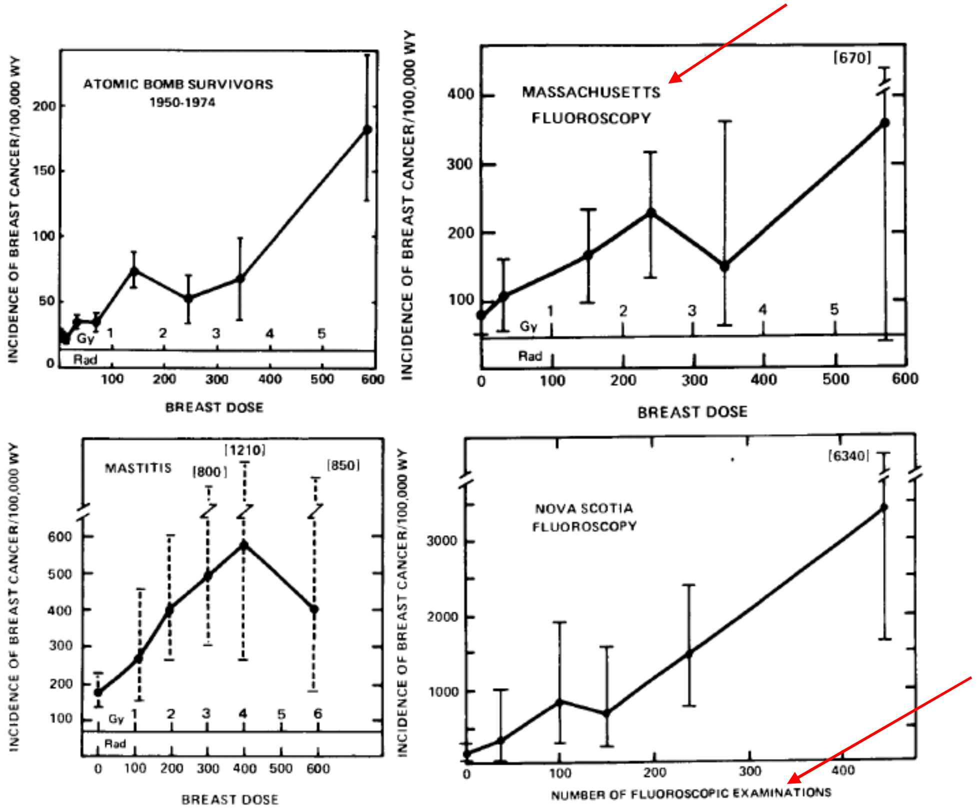


Preston et al. *Rad Res* 2002

Dose Response – Pooled Analysis of Breast Cancer Studies

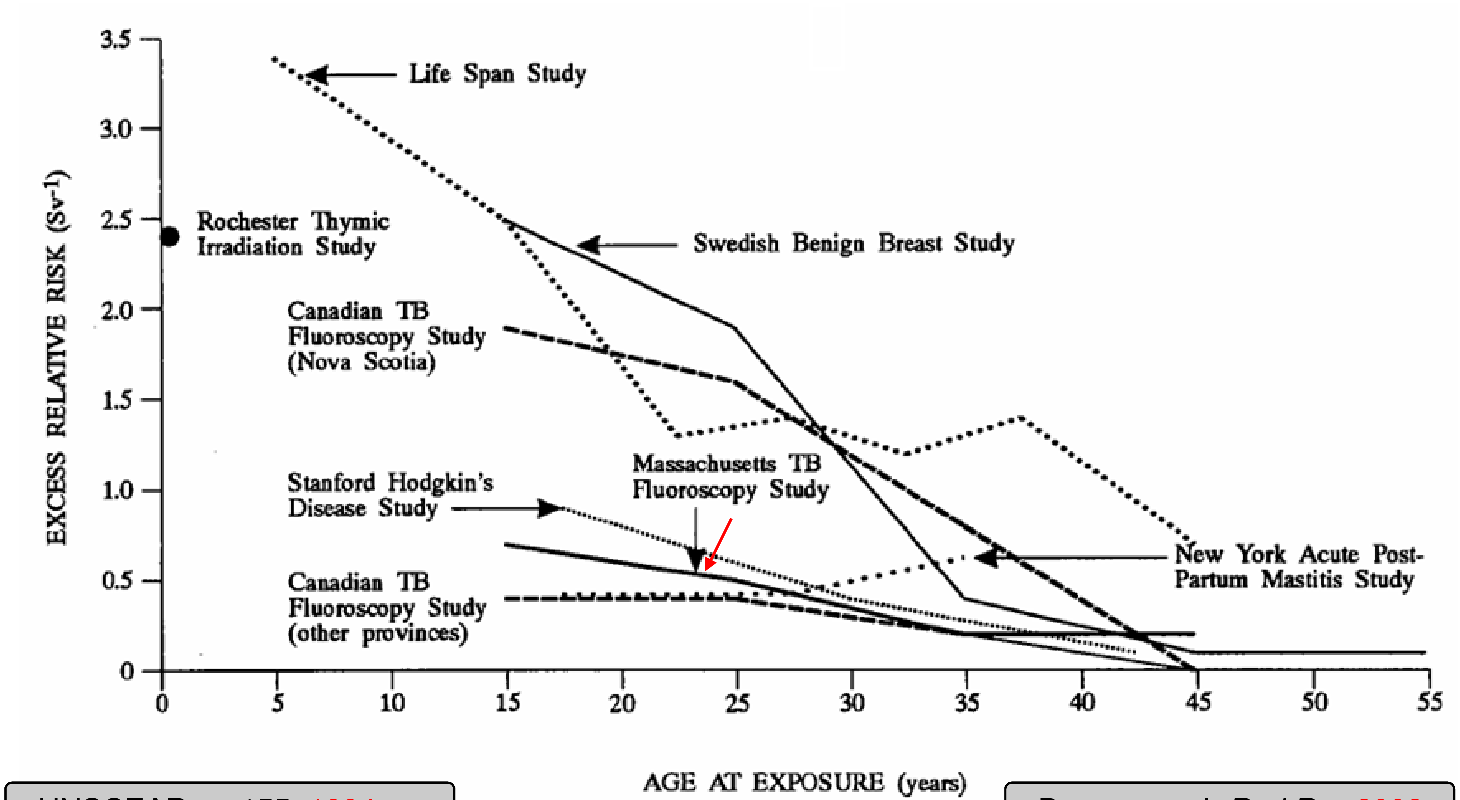
Breast Cancer

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 Cancer
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

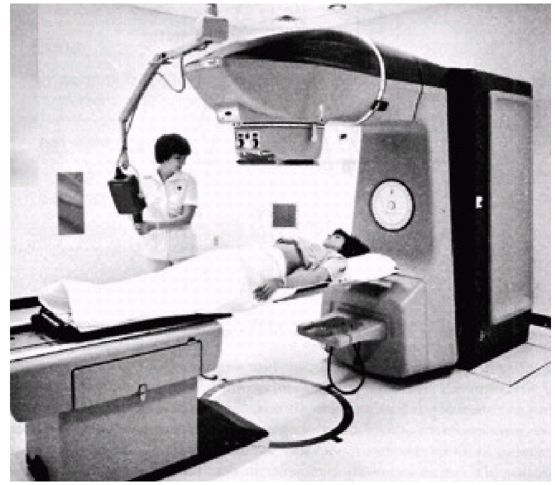
- Tissues respond differently to the effects of fractionated doses ~DDREF >9 for lung, DDREF ~ 1 for breast
- Age at exposure modifies effect – relevance for mammography
- Be cautious when generalizing – one size doesn't fit all – all models are wrong, some are useful
- US and Canadian studies re-activated – Stay tuned!

NCRP REPORT No. 170

SECOND PRIMARY CANCERS AND CARDIOVASCULAR DISEASE AFTER RADIATION THERAPY

2012

http://NCRPonline.org



COMMENTARY

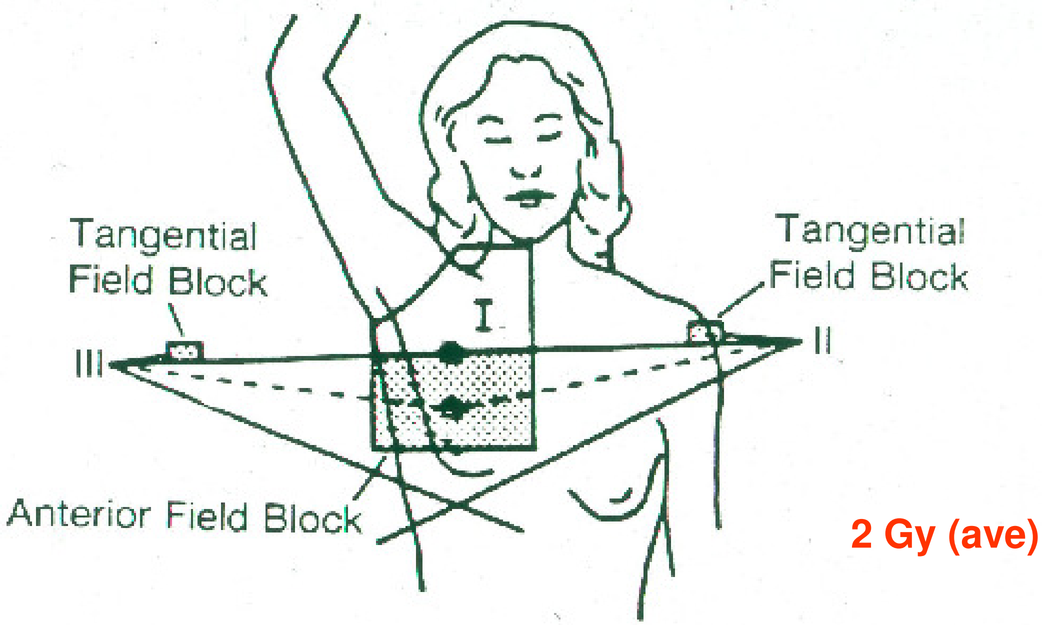
Second Malignant Neoplasms and Cardiovascular Disease Following Radiotherapy

Lois B. Travis, Andrea K. Ng, James M. Allan, Ching-Hon Pui, Ann R. Kennedy, X. George Xu, James A. Purdy, Kimberly Applegate, Joachim Yahalom, Louis S. Constine, Ethel S. Gilbert, John D. Boice Jr

Travis et al. JNCI 104:1, 2012

Scatter doses can also be studied

Radiotherapy for Breast Cancer



RADIOTHERAPY
DOSE TO CONTRALATERAL
BREAST

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
$\geq$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
$\geq$45	1.01	0.8-1.4

*655 Cases, 1,189 Controls

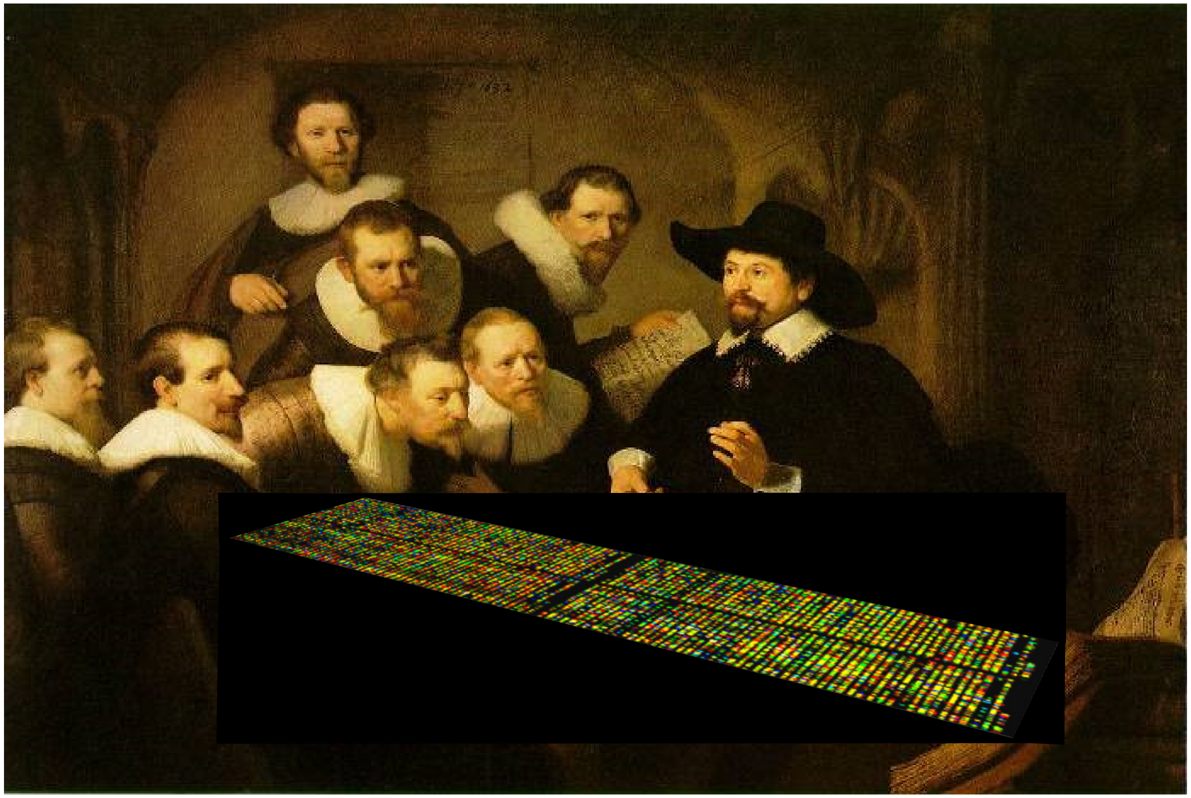
Boice et al, *NEJM* 326:781, 1992

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

Rembrandt: "Anatomy Lesson" of Dr. Tulp (1632)

Courtesy of Dr Lois Travis, Roswell Park Medical Center

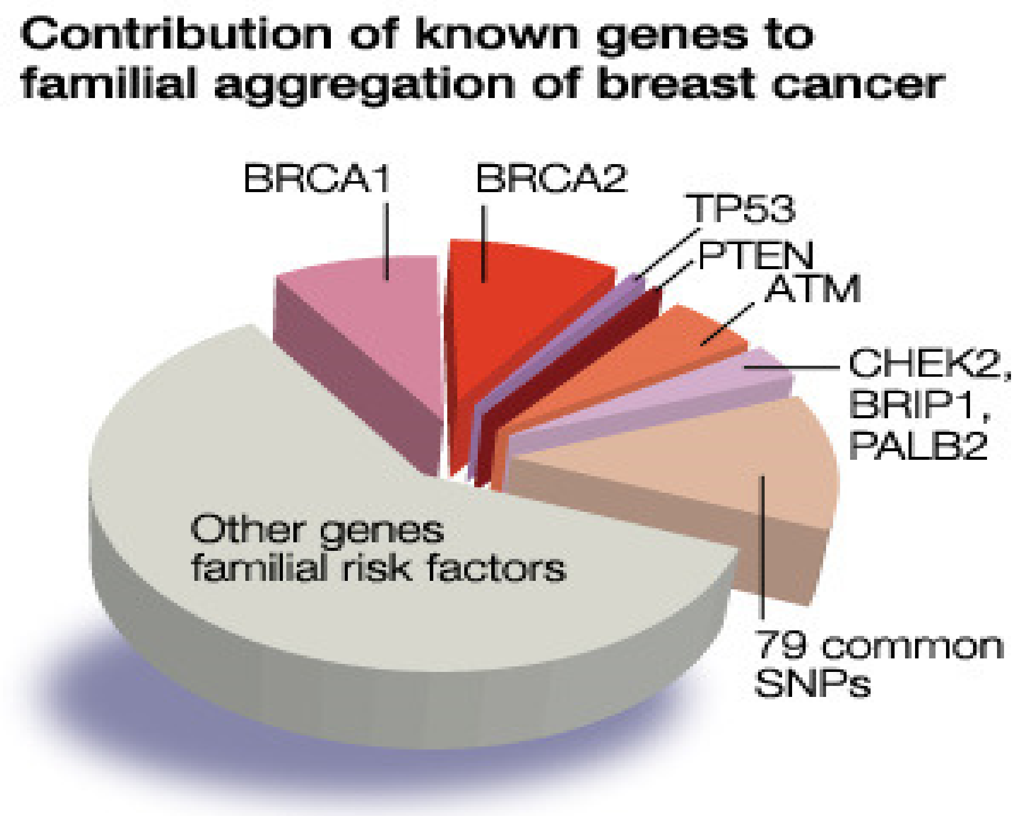
If Rembrandt were alive Today
The *Genomics* "Anatomy Lesson"



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

Courtesy of Dr Lois Travis, Roswell Park Medical Center

Genetic Epidemiology of Breast Cancer



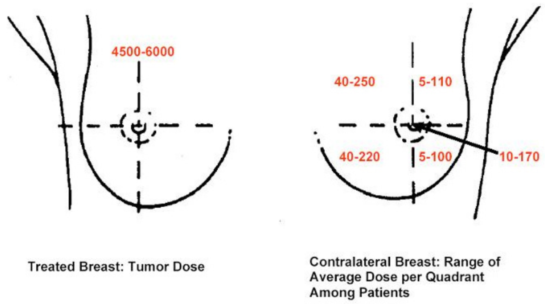
Couch, F Mayo Clinic

Thanks Jonine Bernstein

Unanswered Question Genetic Susceptibility? Second Breast Cancer

WECARE, 2nd breast (n = 800) to study Interaction Between Radiation and Genes

Exposure	RR	95% CI
BRCA1 mutation	4.5	2.8-7.1
BRCA2 mutation	3.4	2.0-5.8
1 Gy (<40 y)	1.6	1.1-2.5
1 Gy (≥45 y)	1.0	0.9-1.3



Dose estimated to the location of the 2nd breast cancer

Stovall, *IJROBP*, 2008
Bernstein, *Breast Ca Res*, 2004

Whether Risk of Breast Cancer Among Carriers Following Low-Dose Radiation Exposure is Higher than Noncarriers Remains Unknown

THE LANCET Oncology

Screening mammography and risk of breast cancer in *BRCA1* and *BRCA2* mutation carriers: a case-control study

Steven A Narod, Jan Lubinski, Parviz Ghadirian, Henry T Lynch, Pal Moller, William D Foulkes, Barry Rosen, Charmaine Kim-Sing, Claudine Isaacs, Susan Domcheck, Ping Sun, for the Hereditary Breast Cancer Clinical Study Group*

Cancer Epidemiology, Biomarkers & Prevention

Effect of Mammography on Breast Cancer Risk in Women with Mutations in *BRCA1* or *BRCA2*

Deborah Goldfrank,[1] Shannon Chuai,[2] Jonine L. Bernstein,[2] Teresa Ramon y Cajal,[3] Johanna B. Lee,[1] M. Carmen Alonso,[3] Orland Diez,[3] Monserrat Baiget,[3] Noah D. Kauff,[1] Kenneth Offit,[1] and Mark Robson[1]

RESEARCH HIGHLIGHTS

BREAST CANCER

Radiation risk in *BRCA* carriers

Lisa Hutchinson

Original article Pijpe, A. *et al*. Exposure to diagnostic radiation and risk of breast cancer among carriers of BRCA1/2 mutations: retrospective cohort study

BMJ

BMJ 2012;345:e5660 doi: 10.1136/bmj.e5660 (Published 6 September 2012) Page 1 of 15

Exposure to diagnostic radiation and risk of breast cancer among carriers of BRCA1/2 mutations: retrospective cohort study (GENE-RAD-RISK)

OPEN ACCESS

Anouk Pijpe *postdoctoral research fellow*[1], Nadine Andrieu *senior researcher*[2 3 4], Douglas F Easton *professor*[5], Ausrele Kesminiene *study coordinator*[6], Elisabeth Cardis *professor*[7], Catherine Noguès

VOLUME 24 · NUMBER 21 · JULY 20 2006

JOURNAL OF CLINICAL ONCOLOGY — ORIGINAL REPORT

Effect of Chest X-Rays on the Risk of Breast Cancer Among *BRCA1/2* Mutation Carriers in the International *BRCA1/2* Carrier Cohort Study: A Report from the EMBRACE, GENEPSO, GEO-HEBON, and IBCCS Collaborators' Group

Nadine Andrieu, Douglas F. Easton, Jenny Chang-Claude, Matti A. Rookus, Richard Brohet, Elisabeth Cardis, Antonis C. Antoniou, Teresa Wagner, Jacques Simard, Gareth Evans, Susan Peock, Jean-Pierre Fricker, Catherine Nogues, Laura Van't Veer, Flora E. Van Leeuwen, and David E. Goldgar

Thanks Jonine Bernstein

No Evidence that Risk of CBC Among *BRCA1/2* Carriers is Modified by Radiation Exposure

Carrier Status	Dose (Gy)	Case	Control	RR*	95% CI
No BRCA	No	256	223	1.0	
	0 < 1.0	133	508	1.0	0.8 - 1.3
	≥1.0	118	406	1.2	0.9 - 1.6
BRCA1/2	No	40	9	1.0	
	0 < 1.0	35	27	1.9	0.7 - 4.6
	≥1.0	21	26	1.1	0.4 - 2.6

Adjusted for exact age, are adjusted for age at menarche, number of full term pregnancies, age at menopause, family history, treatment (chemo, hormone), histology, and stage.

Bernstein et al. Eur J Cancer, 2013

Thanks Jonine Bernstein

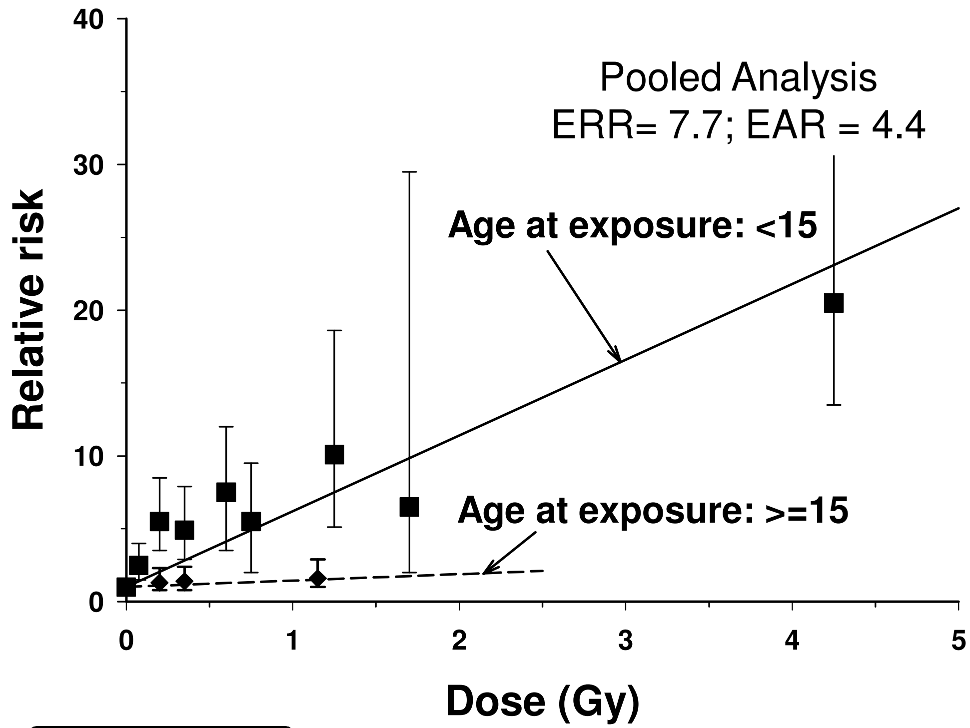
Breast Cancer Treatment

- Long latency (time) for second cancers to occur
- Age at exposure can have a profound effect – little risk for exposures over 40 y
- Genetic susceptibility at low doses is uncertain
- However, GWAS analyses (WECARE 2) found evidence of a radiation-sensitive sub-population of women with breast cancer (eg <40 y, 5+ latency) and combined 57 SNPs.
- Effecting only a small number of women in WECARE and needs to be replicated. Stay tuned.

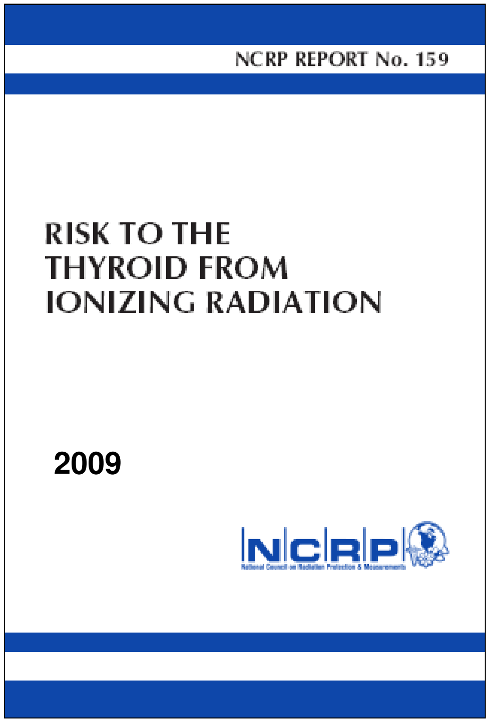
Protection & Radiation Epidemiology

- Radiation Epidemiology
- Heritable Effects and Protection
- From Science to Protection – The Process
- Radium to Protection
- Occupation to Protection
- Leukemia – past to present
- Breast and Thyroid Cancer – Straight lines
- Radon
- A Million Person Study
- What's Next?

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



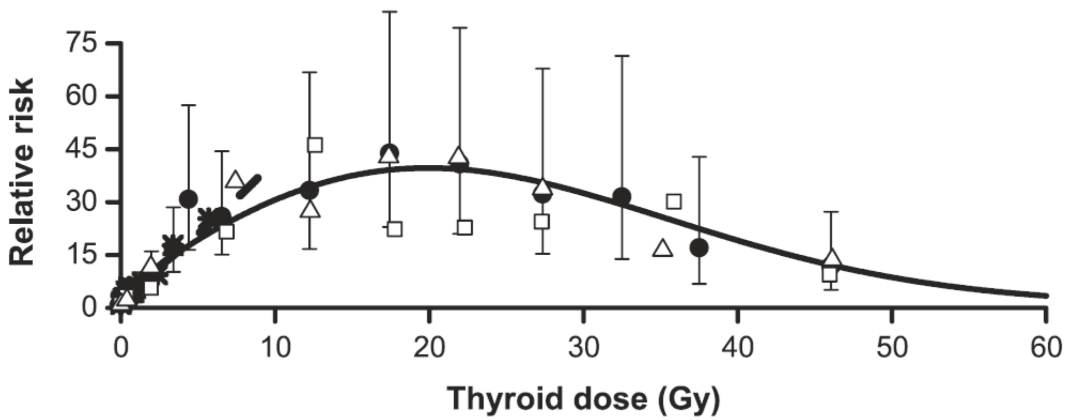
Ron et al, 1995



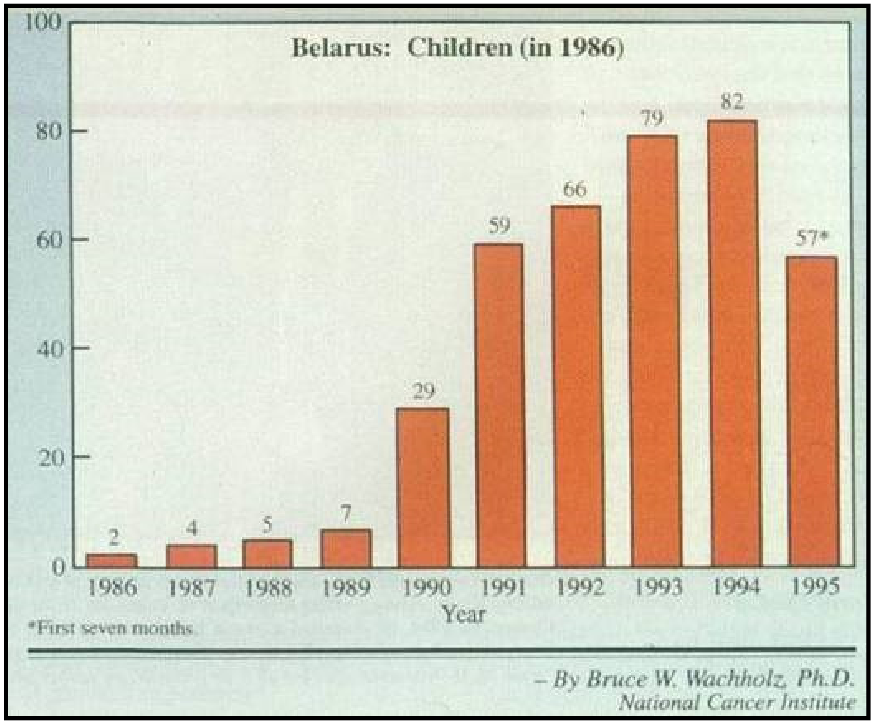
New Study - Thyroid Cancer (May 2016)

Thyroid Cancer after Childhood Exposure to External Radiation: An Updated Pooled Analysis of 12 Studies.

Lene H. S. Veiga,[a,c] Erik Holmberg,[d] Harald Anderson,[e,f] Linda Pottern,[g] Siegal Sadetzki,[h] M. Jacob Adams,[i] Ritsu Sakata,[j] Arthur B. Schneider,[k] Peter Inskip,[a] Parveen Bhatti,[l] Robert Johansson,[m] Gila Neta,[b] Roy Shore,[j] Florent de Vathaire,[n] Lena Damber,[m] Ruth Kleinerman,[a], Michael M. Hawkins,[o] Margaret Tucker,[a] Marie Lundell[p] and Jay H. Lubin[a,1]

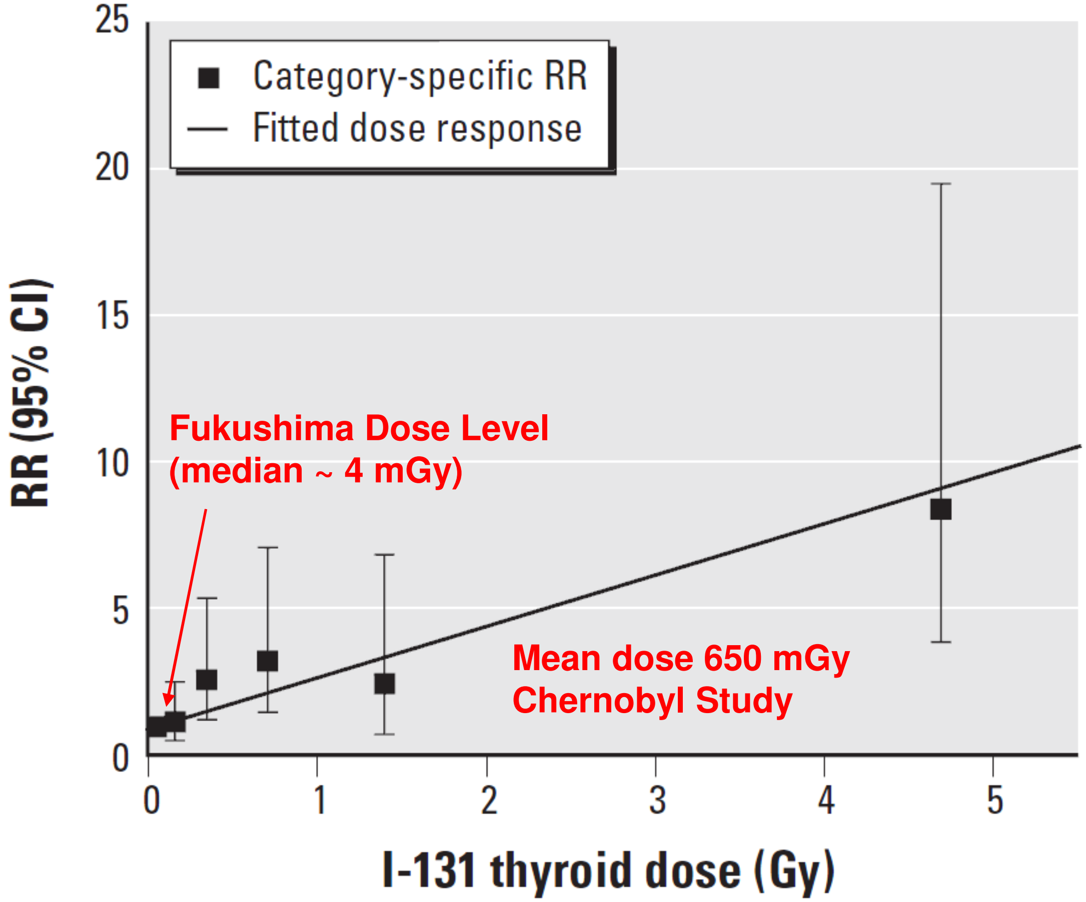


Radioactive Iodines in the Environment Resulted in Epidemic of Thyroid Cancer in Children Who Drank Contaminated Milk



Belarus: 10,000 Bq/L milk vs 300 Bq/L limit

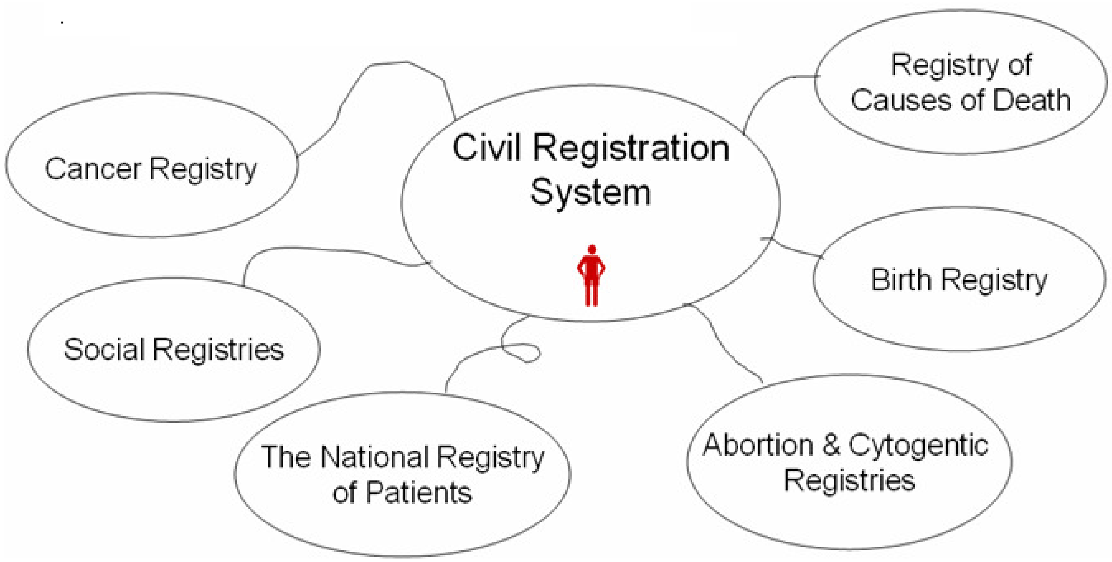
Ukrainian – American Chernobyl Thyroid Study



A. Brenner et al EHP 2011

Scandinavia – Epidemiologic Gold Mines

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



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

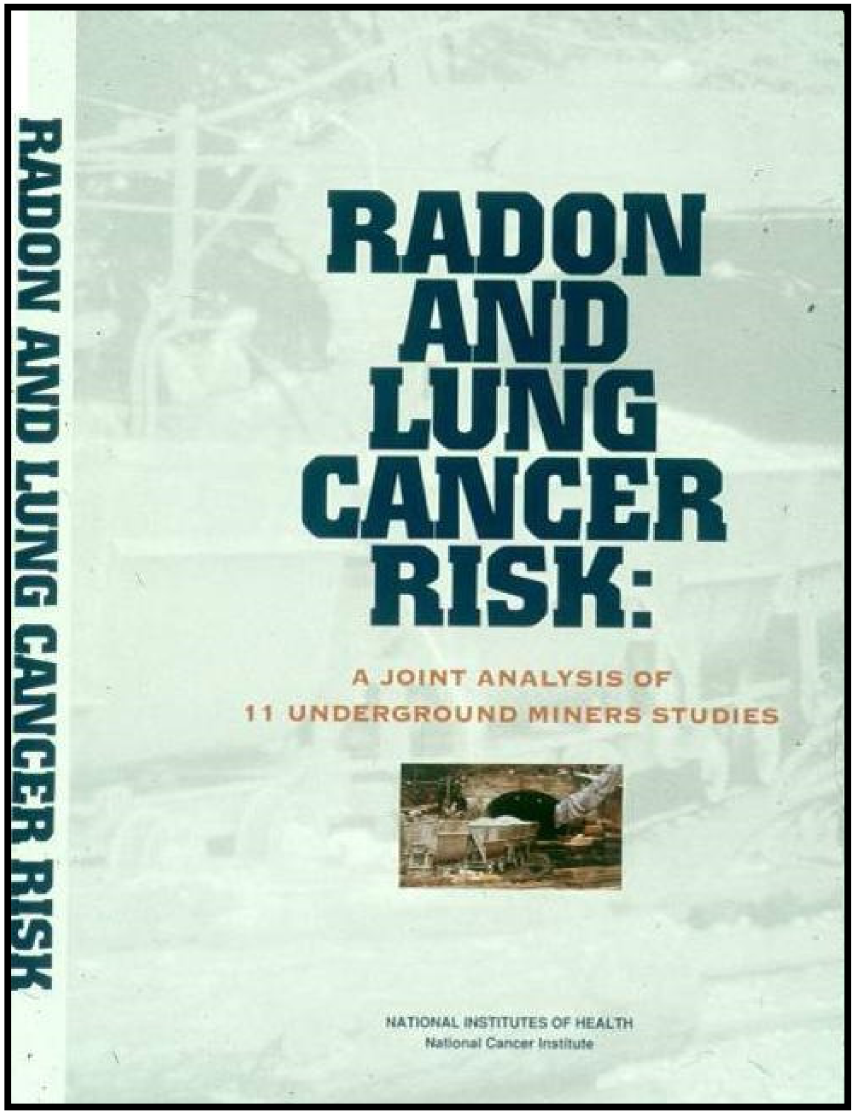
Hall et al, *Radiat Res,* 145:86, 1996

Thyroid Cancer Studies

- Very high risk among children < 15 y
- Very low risk among adults > 20 y
- Stockpiling KI around nuclear power plants or administering KI after a major nuclear incident should concentrate mainly (only?) on the children

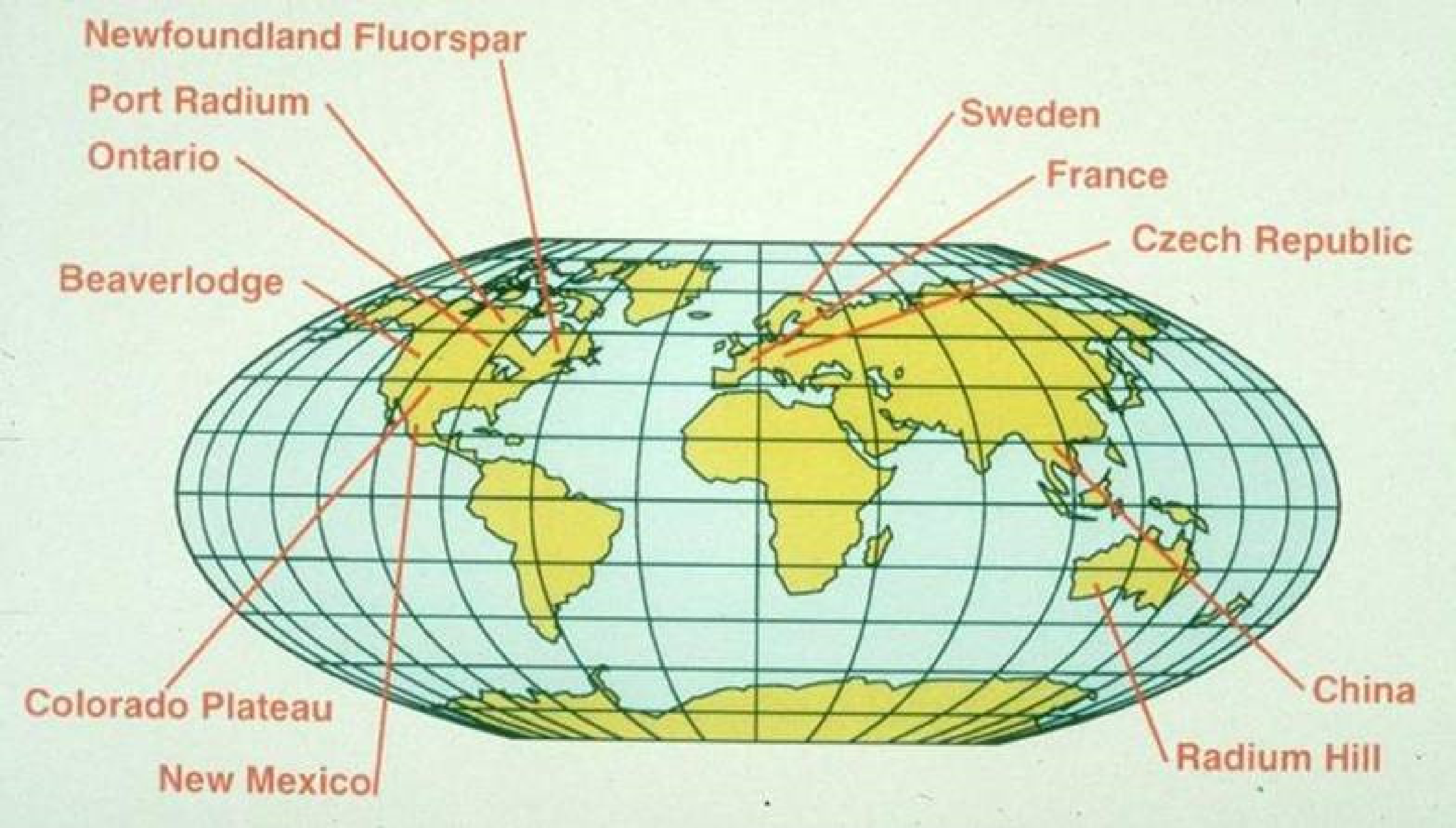
Protection & Radiation Epidemiology

Radiation Epidemiology
Heritable Effects and Protection
From Science to Protection – The Process
Radium to Protection
Occupation to Protection
Leukemia – past to present
Breast and Thyroid Cancer – Straight lines
Radon from Mines to Homes
A Million Person Study
What's Next?

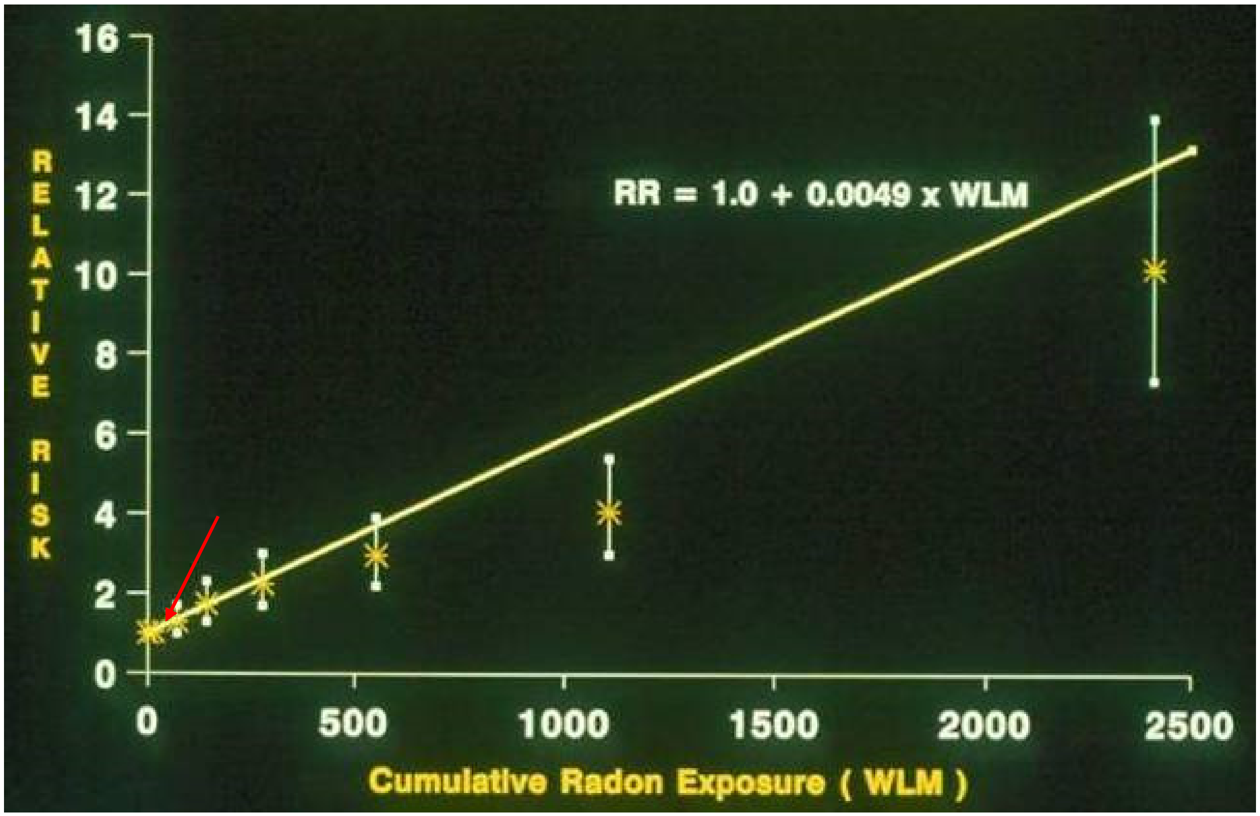


Jay Lubin
USA
National Cancer Institute

Pooled Analysis of Underground Miner Studies



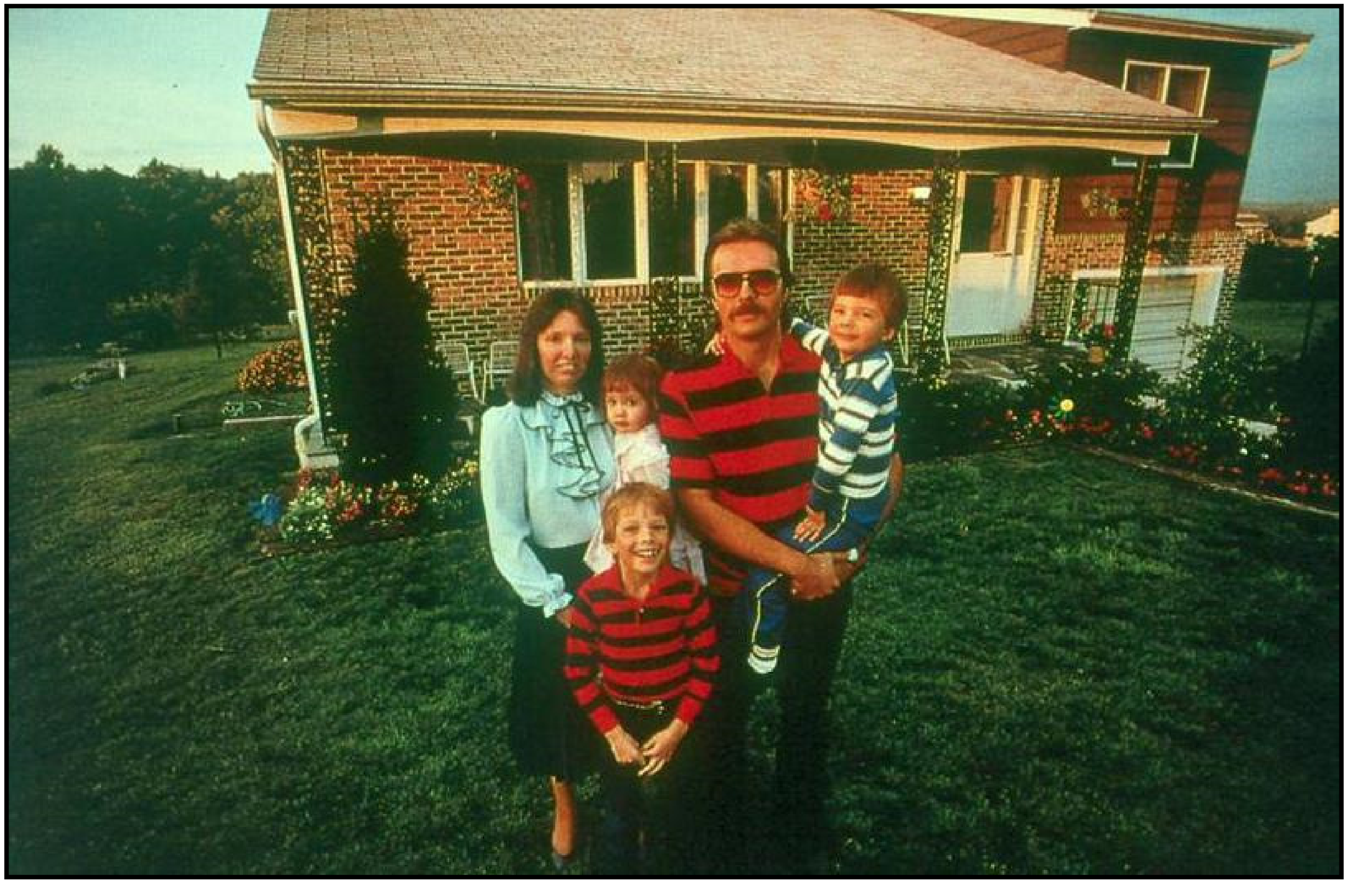
11 Underground Miner Studies
68,000 Miners – 2,700 Lung Cancers



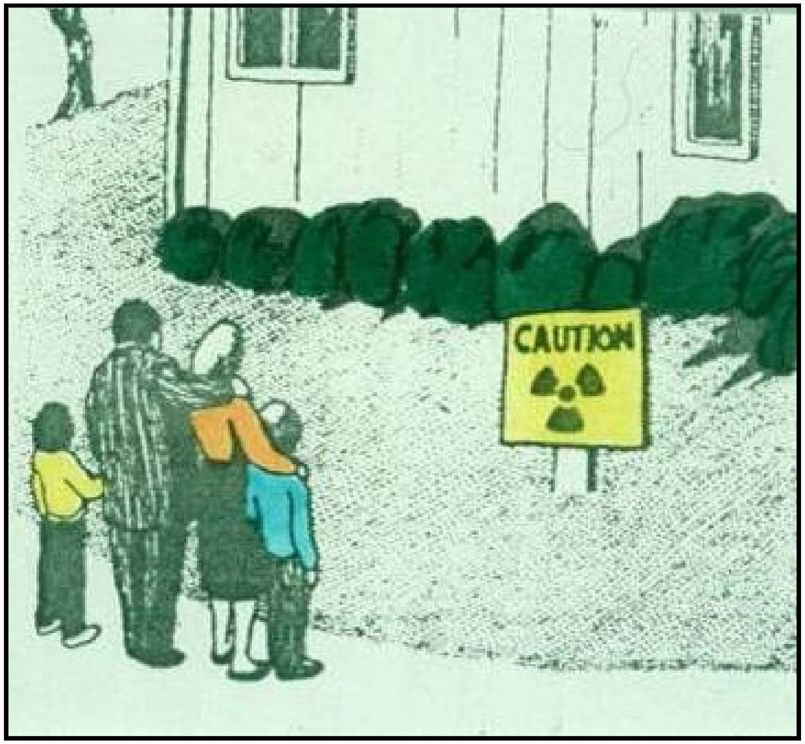
Lubin et al, 1993

37 Bq/m^3 = 1 pCi/l ~ 0.2 WLM / yr.

1986 Home in Pennsylvania ~ 100,000 Bq/m^3



New Meaning to "The Nuclear Family"



Washington Post, February 6, 1986

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

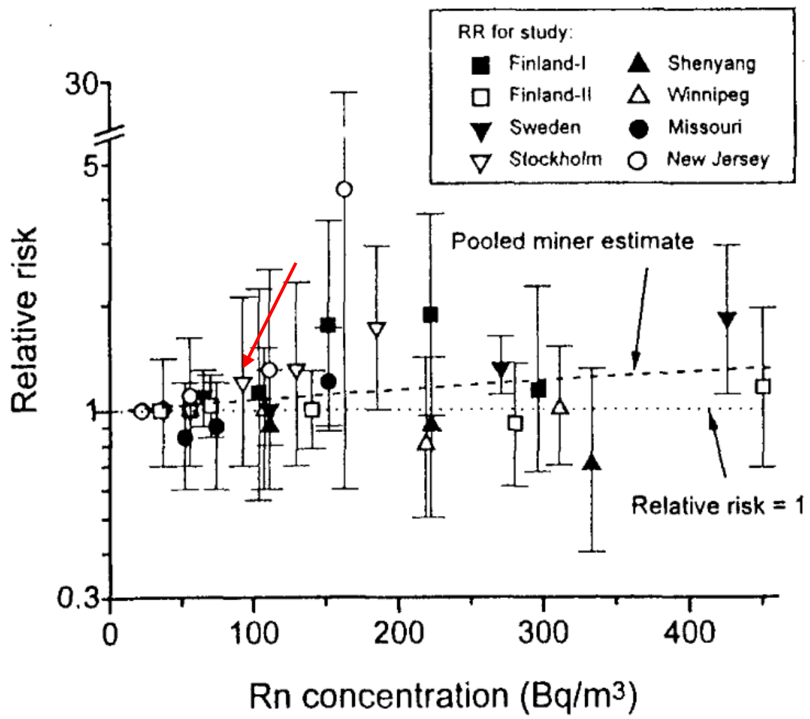
China
- √ Shenyang
- √ Gansu

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

Shenyang

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

Indoor Radon Meta-Analysis
4,263 Lung Cancers

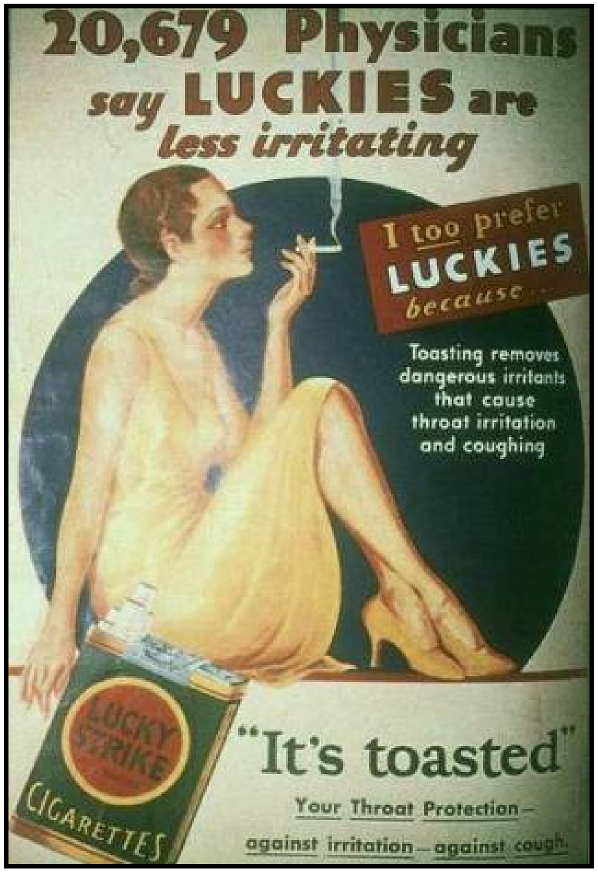


Difficult to detect low-dose risks, yet significant trend when studies combined!

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

4 pCi/l = 150 Bq/m^3

Radon Interacts with Smoking to Enhance Risk



Smoking <10 cig/day equivalent to being high dose A-bomb survivor

RR	Cigarettes per Day	A-Bomb Dose, Sv	Miners WLM	Radon Indoor Bq/m^3
1.0	0	0	0	<40
4.6	1 - 9	3.4	735	4,500*

NRC, BEIR, 1999

Boice, *Radiat Res*, 146:356, 1996

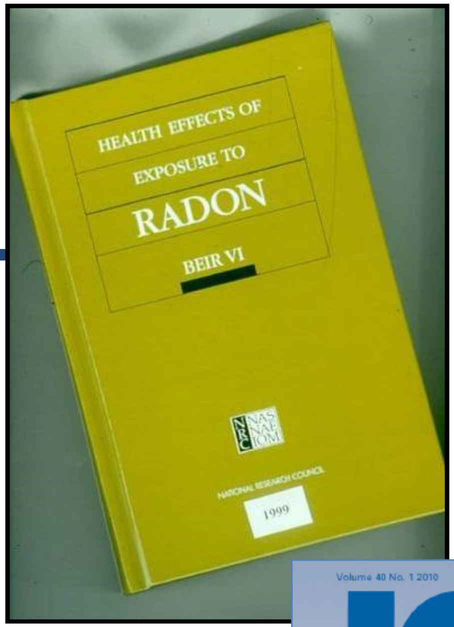
Discovery of a Very High Radon Area

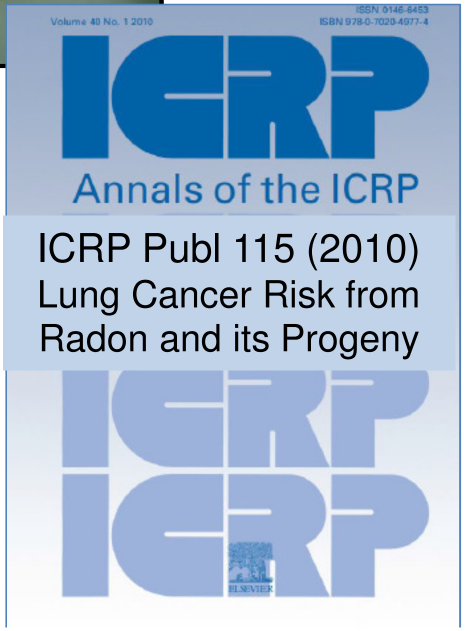
- Mitigator informs DEP of home > 40,000 Bq/m^3 in early October 2015
- Radon Division does a targeted 'hot spot' survey mailing to over 500 homes
- Begin to see homes with 4,000s to 40,000s of Bq/m^3
- Mid-November one home over 100,000 Bq/m^3 and in early December one with over 140,000 Bq/m^3 !!!

Slide from Dave Allard, Pennsylvania

Radon and Epidemiology

- The epidemiology is consistent
- Linearity fits all the data
- Indoor risk low but case-control studies consistent with miner study predictions
- Interaction with smoking nearly multiplicative
- Best way to lower radon risk -- stop smoking
- Science from the National Acadamies BEIR VI 1999, UNSCEAR Annex E, 2006
- Guidance from ICRP Publ 115 2010, the US Environmental Protection Agency





Protection & Radiation Epidemiology

- Radiation Epidemiology
- Heritable Effects and Protection
- From Science to Protection – The Process
- Radium to Protection
- Occupation to Protection
- Leukemia – past to present
- Breast and Thyroid Cancer – Straight lines
- Radon from Mines to Homes
- A Million Person Study – Really?
- What's Next?

IRPA

NCRP
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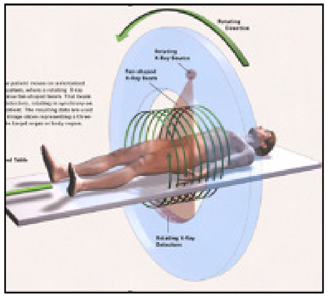
Studying One Million Persons Exposed to Radiation
Why?

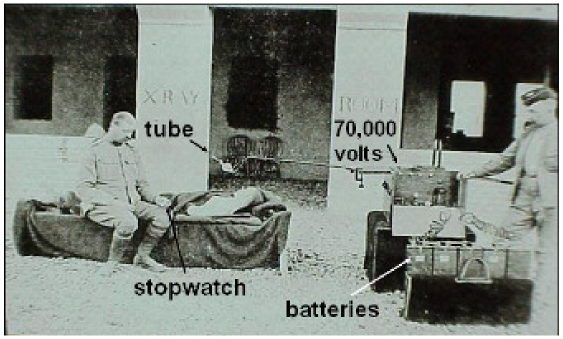
Much is know about radiation effects when exposure is received all at once (briefly), but the gap in understanding is when radiation is received over years (prolonged).

Medicine



Accidents or Terrorism

Occupation

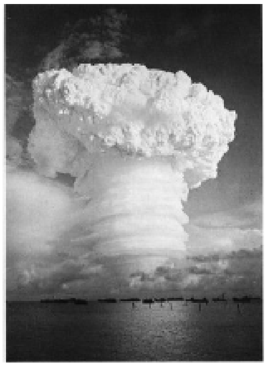


Environment, Fracking

Population:
One Million Persons Exposed to Radiation

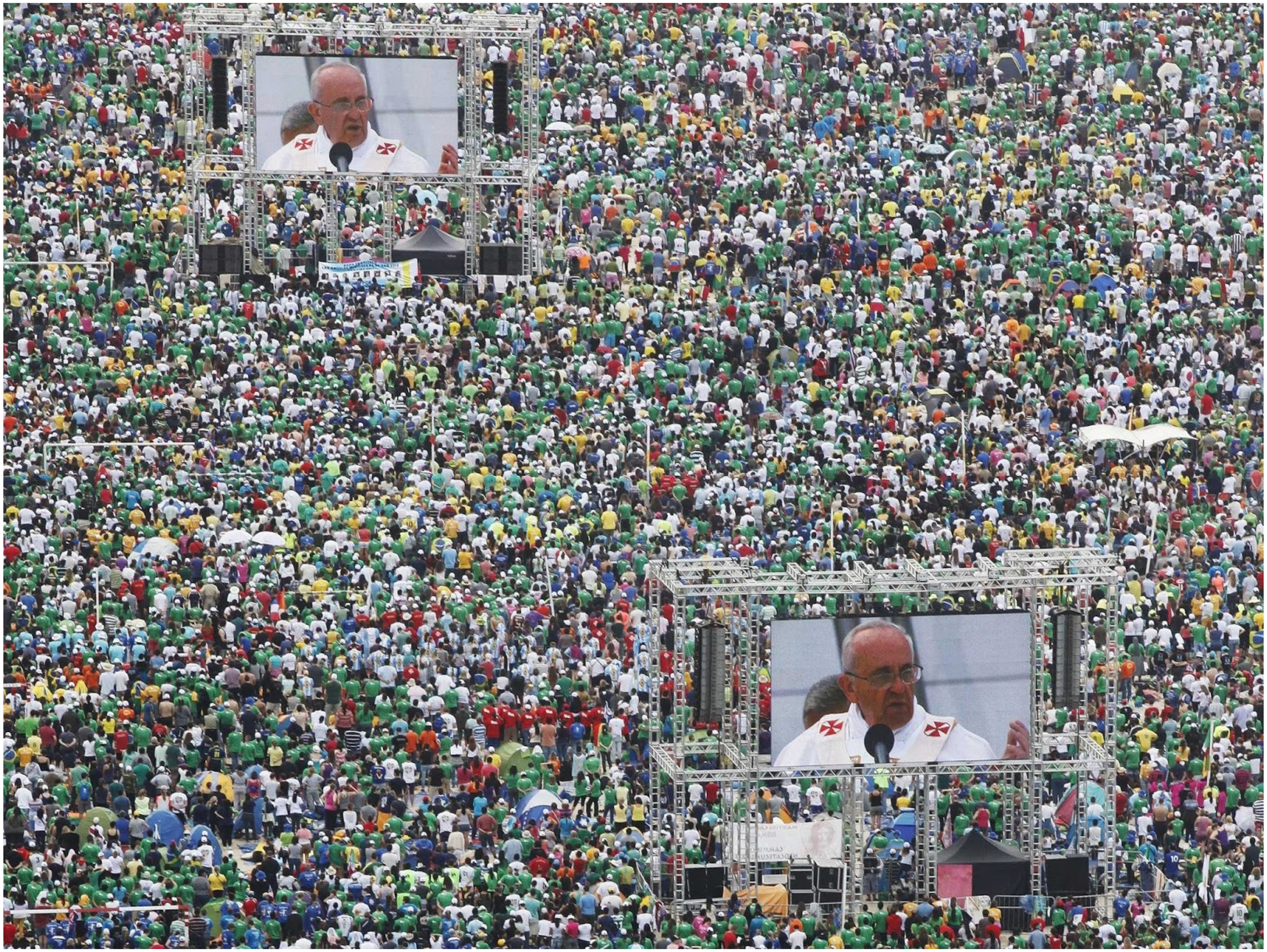
Robert Oppenheimer, General Leslie Groves, Enrico Fermi, Hans Bethe, Theodore Hall

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



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

Health Physics News October 2012

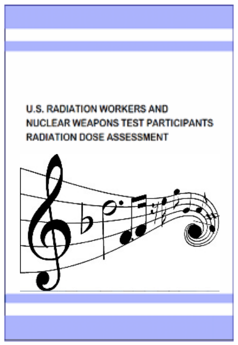


The Pope visits Philadelphia 2015

1 Million People

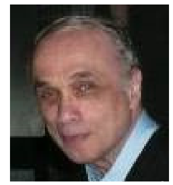
Dosimetry is Key to Good Epidemiology

SC 6-9: U.S. Radiation Workers and Nuclear Weapons Test Participants Radiation Dose Assessment




A Bouville
Chairman

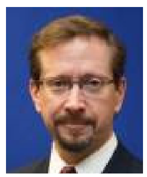

R Toohey
Co-Chairman


H Beck

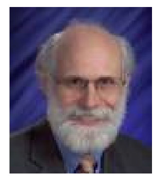

T Brock


L Dauer


K Eckerman


D Hagemeyer


R Leggett

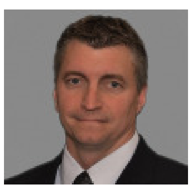

B Napier


K Pryor


M Rosenstein


S Balter

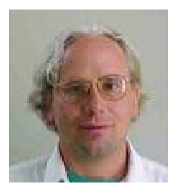
5 Committee Members here at IRPA

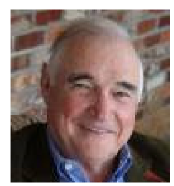

J Thompson


D Schauer


S Sherbini


D Miller


D Stram


J Till

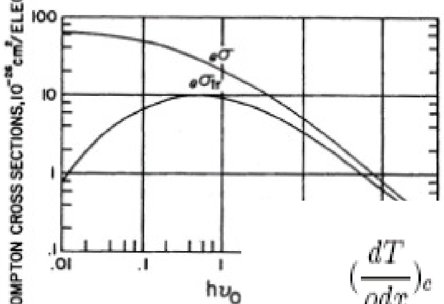

C Yoder

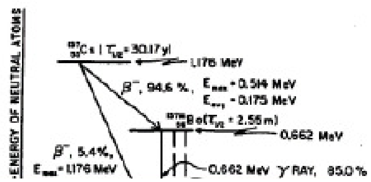

C Zeitlin

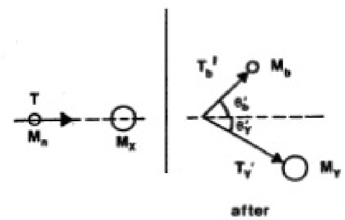
Bouville et al. Dosimetry for the Million Worker Study Health Physics Feb 2015

Dosimetry & Radiation Protection Issues

$${}_e\sigma_{tr} = 2\pi r_0^2\left[\frac{2(1+\alpha)^2}{\alpha^2(1+2\alpha)} - \frac{1+3\alpha}{(1+2\alpha)^2} - \frac{(1+\alpha)(2\alpha^2-2\alpha-1)}{\alpha^2(1+2\alpha)^2} - \frac{4\alpha^2}{3(1+2\alpha)^3} - \left(\frac{1+\alpha}{\alpha^3} - \frac{1}{2\alpha} - \frac{1}{2\alpha^3}\right)ln(1+2\alpha)\right]$$





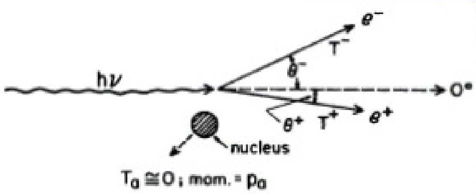


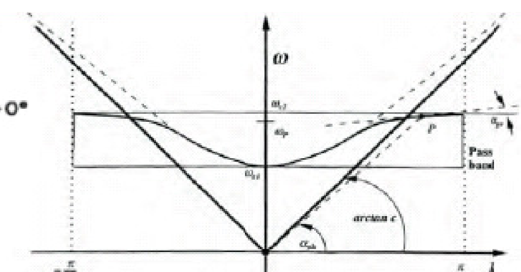
$$\left(\frac{dT}{\rho dx}\right)_c = 0.3071\frac{Zz^2}{A\beta^2}\left[13.8373 + \ln\left(\frac{\beta^2}{1-\beta^2}\right) - \beta^2 - \ln I\right]$$

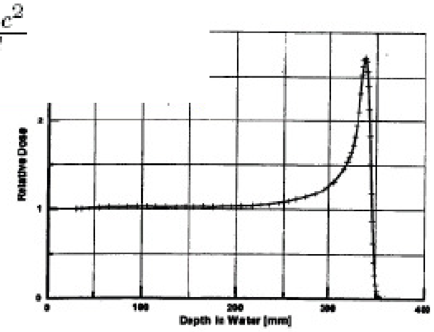
$$-\frac{2\sqrt{M_a M_b T T_b'}cos\theta_b'}{M_Y}$$

$$\frac{d\sigma}{d\Omega} = \frac{r_0^2}{2}\left[\frac{1+}{[1+\alpha(1}\right.$$

$$f = \frac{qB}{2\pi M} = \frac{qB}{2\pi M_0}\sqrt{1-\beta^2} = f_0\frac{M_0c^2}{E}$$







$$d({}_a\kappa) = \frac{\sigma_0 Z^2 P}{h\nu - 2m_0c^2}dT^+$$

$$\vec{\nabla}\bullet\mathbf{E} = \frac{\rho}{\varepsilon_0}, \qquad \vec{\nabla}\times\mathbf{E} = \frac{\partial\mathbf{B}}{\partial t},$$

$$\vec{\nabla}\bullet\mathbf{B} = 0, \qquad c^2\,\vec{\nabla}\times\mathbf{B} = \frac{\mathbf{j}}{\varepsilon_0} + \frac{\partial\mathbf{E}}{\partial t},$$

$$\left(\frac{dT}{\rho dx}\right)_c = 0.3071\frac{Zz^2}{A\beta^2}\left[13.8373 + \ln\left(\frac{\beta^2}{1-\beta^2}\right) - \beta^2 - \ln I\right]$$

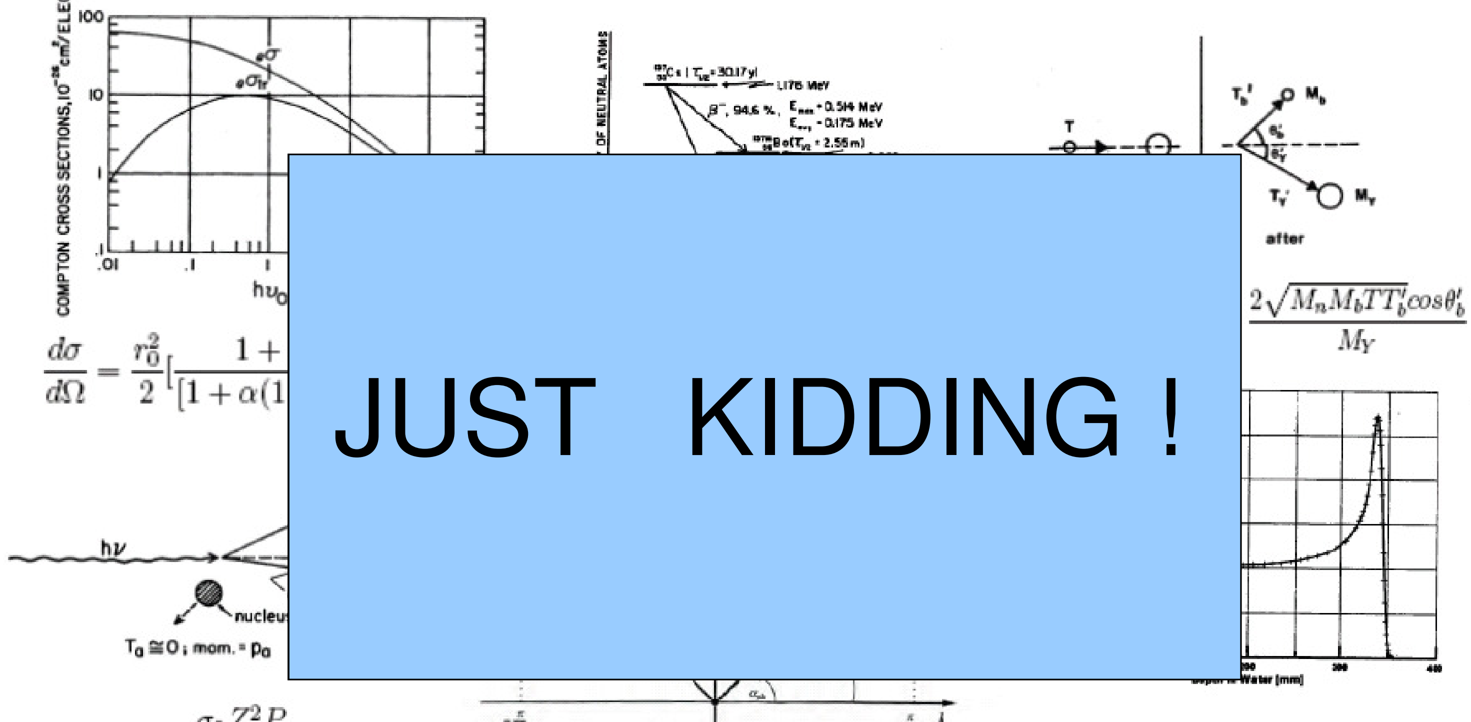
$$f = \frac{qB}{2\pi M} = \frac{qB}{2\pi M_0}\sqrt{1-\beta^2} = f_0\frac{M_0c^2}{E}$$

Wayne State University School of Medicine

Thanks to Mike Joiner

Dosimetry & Radiation Protection Issues

$$_e\sigma_{tr} = 2\pi r_0^2\left[\frac{2(1+\alpha)^2}{\alpha^2(1+2\alpha)} - \frac{1+3\alpha}{(1+2\alpha)^2} - \frac{(1+\alpha)(2\alpha^2-2\alpha-1)}{\alpha^2(1+2\alpha)^2} - \frac{4\alpha^2}{3(1+2\alpha)^3} - \left(\frac{1+\alpha}{\alpha^3} - \frac{1}{2\alpha} - \frac{1}{2\alpha^3}\right) ln(1+2\alpha)\right]$$



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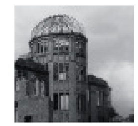
$$\left(\frac{dT}{\rho dx}\right)_c = 0.3071\frac{Zz^2}{A\beta^2}[13.8373 + \ln(\frac{\beta^2}{1-\beta^2}) - \beta^2 - \ln I]$$

$$f = \frac{qB}{2\pi M} = \frac{qB}{2\pi M_0}\sqrt{1-\beta^2} = f_0\frac{M_0c^2}{E}$$

WAYNE STATE UNIVERSITY
SCHOOL OF MEDICINE

Comparison with Atomic Bomb Survivor Study

External Dose (mSv)	Million Person 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



* Sampled for study

**4x more high dose subjects

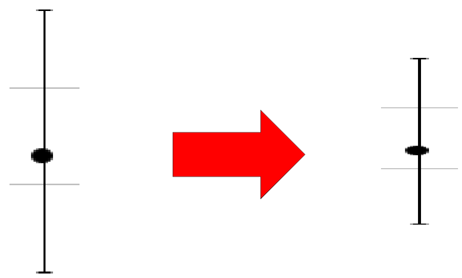
Epidemiology, Protection and Mars

Million Person Study – NASA bases its regulations on epidemiology - relevance to space protection.

- Going to Mars – Precise Risk Estimates Matter
- Going to Mars – Sex Matters
- Going to Mars – Dementia?
- Cardiovascular disease

Value of Precision from Epidemiology is more time in Space

- A US astronaut is not permitted to receive a cumulative dose in space that would exceed a predicted lifetime excess risk of cancer death of 3%, but specifically the 95% upper confidence level about the 3% estimate
- A narrowing of the confidence limits would allow more time in space simply because one component of the uncertainty would be reduced.



Epidemiology, Protection and Mars

Million Person Study – relevance to space protection. NASA bases its regulations on epidemiology

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- Going to Mars – Sex Matters
- Going to Mars – Dementia?
- Cardiovascular disease

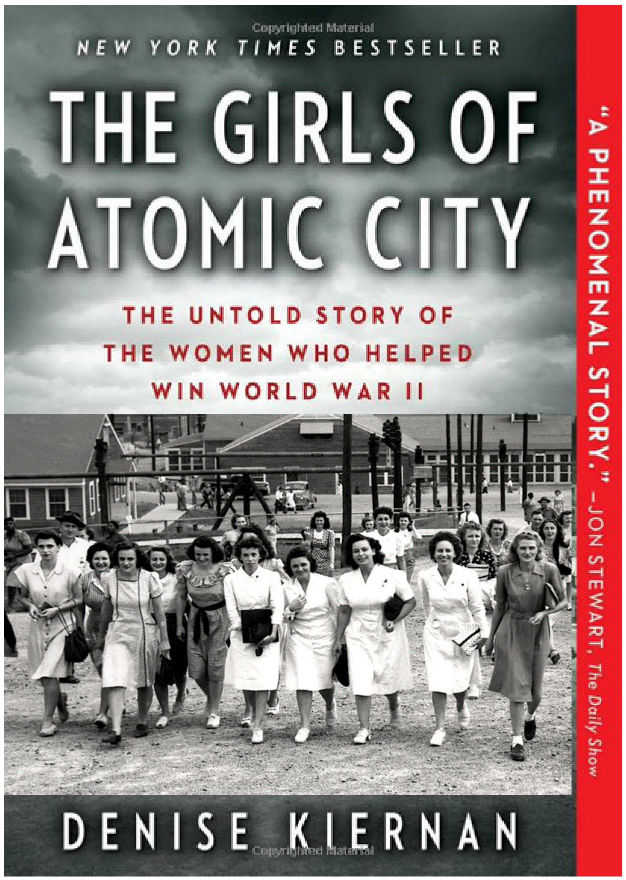
Differences Between Sexes in Risks of Cancer

Cancer Type – Atomic Bomb Survivors	Female to Male Ratio of ERRs
All solid cancers	**2.1**
Esophagus	4.3
Stomach	3.7
Colon	1.4
Liver	1.6
Gallbladder	0.4
Lung	2.7
Bladder	1.7
Sex Specific ERR Gy^{-1}	*ERR Gy^{-1}*
Female breast	1.5
Female ovary	0.8
Male prostate	~0.0
Male testes	~0.0

from Ozasa *et al.* 2012

Kristina Rex interviews Jessica Meir last month

Women in the Million Person Study



DOE workers	83,000
NPP workers	5,000
Industrial radiographers	13,000
Medical workers	140,000
Total	241,000

Number of adult Japanese female atomic bomb survivors in 1945 ~30,000

Epidemiology, Protection and Mars

Million Person Study – relevance to space protection. NASA bases its regulations on epidemiology

- Going to Mars – Precise Risk Estimates Matter
- Going to Mars – Sex Matters
- Going to Mars – Dementia – should it be added to detriment?
- Cardiovascular disease

NCRP COMMENTARY No. 25

POTENTIAL FOR CENTRAL NERVOUS SYSTEM EFFECTS FROM RADIATION EXPOSURE DURING SPACE ACTIVITIES
PHASE I: OVERVIEW

February 2016

SCIENTIFIC AUTHORITY SINCE 1929 · NCRP · CONGRESSIONALLY CHARTERED

OPEN ACCESS Freely available online PLOS | ONE

Galactic Cosmic Radiation Leads to Cognitive Impairment and Increased Aβ Plaque Accumulation in a Mouse Model of Alzheimer's Disease

Jonathan D. Cherry[1], Bin Liu[2], Jeffrey L. Frost[2], Cynthia A. Lemere[2], Jacqueline P. Williams[3], John A. Olschowka[4], M. Kerry O'Banion[4]*

COGNITIVE NEUROSCIENCE

What happens to your brain on the way to Mars

Vipan K. Parihar,[1] Barrett Allen,[1] Katherine K. Tran,[1] Trisha G. Macaraeg,[1] Esther M. Chu,[1] Stephanie F. Kwok,[1] Nicole N. Chmielewski,[1] Brianna M. Craver,[1] Janet E. Baulch,[1] Munjal M. Acharya,[1] Francis A. Cucinotta,[2] Charles L. Limoli[1]*

Study: Deep-Space Radiation Could Damage Astronauts' Brains

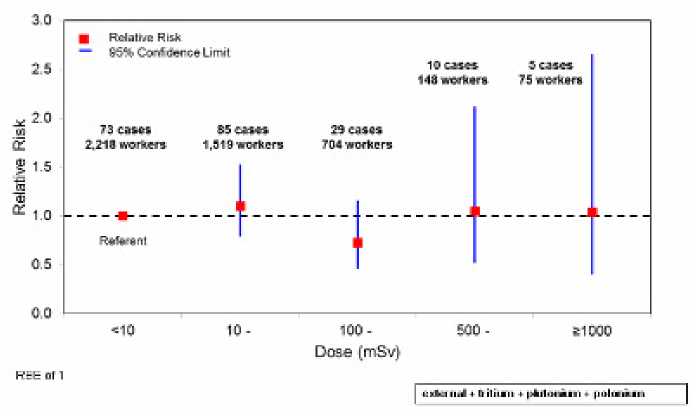
Cosmic rays could leave travelers to Mars confused, forgetful and slow to react

Mound, Dayton, Ohio
Polonium-210 (7,291 Workers)

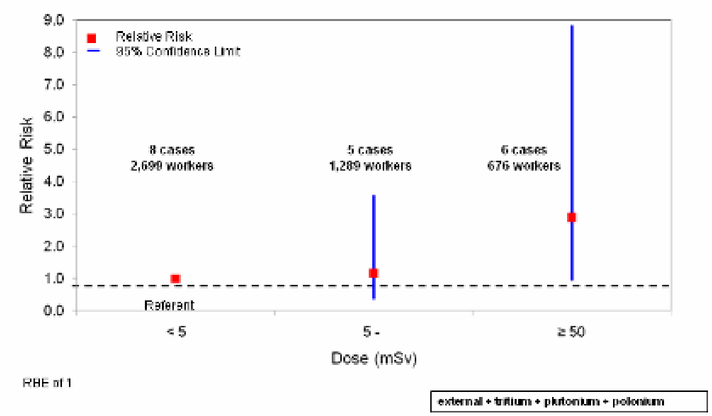
Mortality Among Mound Workers Exposed to Polonium-210 and Other Sources of Radiation, 1944–1979

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]

Lung Cancer - Mound



Esophageal Cancer - Mound

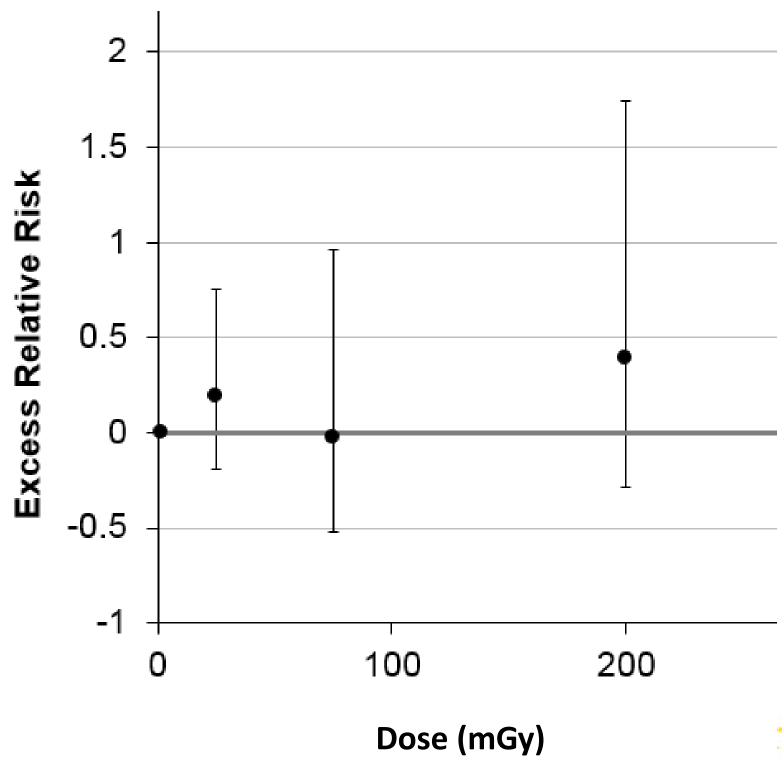


Brain Dose for Dementia, Alzheimer's, Parkinson's and Motor Neuron Disease (*e.g.*, ALS) among Mound Polonium Workers

Dose is to the brain and includes a high-LET alpha particle component from Po-210.

Outcome: Combined (Dementia, Alzheimer's, Parkinson's, Motor Neuron Disease)

Dose (mGy)	N Workers	N Deaths	RR	95% CI
<5	2,662	69	1.0	Ref
5 – <50	1,262	47	1.19	0.81 – 1.75
50 – <100	328	9	0.97	0.48 – 1.96
100+	324	10	1.39	0.71 – 2.74
p for trend (two sided) 0.06 RR at 100 mGy (95 % CI) 1.23 (0.99 – 1.54)				



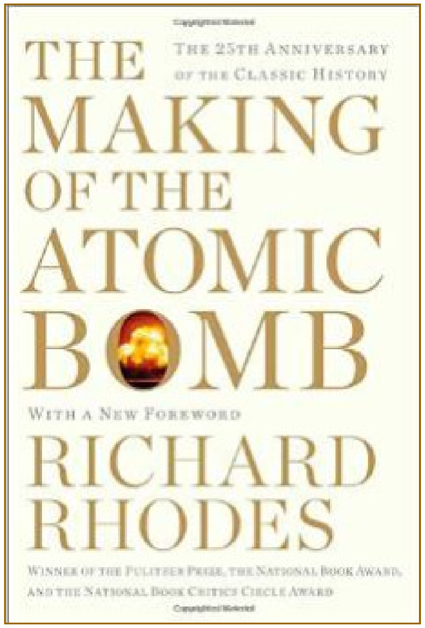
Alpha Particle Dose to the Brain also associated with Plutonium, Americium, and Radium

Epidemiology, Protection and Mars

Million Person Study – relevance to space protection. NASA bases its regulations on epidemiology

- Going to Mars – Precise Risk Estimates Matter
- Going to Mars – Sex Matters
- Going to Mars – Dementia?
- Cardiovascular disease

Trinity - Alamogordo, NM, 16 July 1945 - Atomic Veterans



- Note the film badges

Toward Estimating Risks in the low mGy Range:
David Brenner - NCRP April 2016

- **Epidemiologic evaluation of cancer risks in the 10 mGy region would be valuable**
- **Even if risks can't be detected, generating upper–limits of risk extremely valuable.**

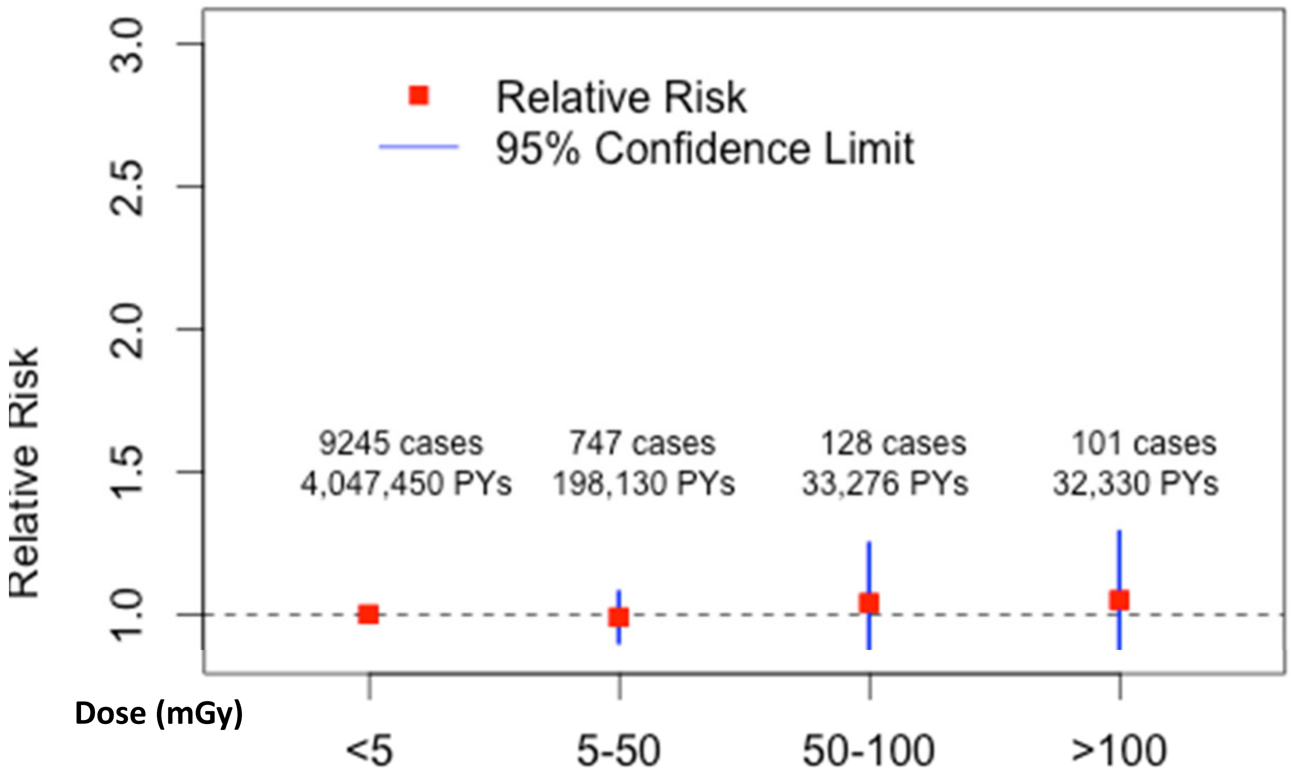
Ischemic Heart Disease Among Atomic Veterans[1] Preliminary

	Dose (mGy)					
	0	0 –	5 –	10 –	20 +	Total
IHD cases	9,072	2,672	2,390	1,561	1,101	16,786
Full cohort	59,676	18,472	16,781	11,148	7,923	114,270
Relative risk	**1.0** [2]	**0.97**	**0.97**	**0.99**	**0.94**	
95% confidence interval		0.93 – 1.01	0.93 – 1.02	0.93 – 1.04	0.88 – 1.01	

[1] Adjusted for test site, rank (enlisted/officer), year of birth, and year of first participation at a weapons test and sampling fraction. Use a 10 y dose lag.

[2] Referent category.

Combined Heart Analyses (Mound + Rocketdyne)



Zhang J, Stram DO, Cohen SS, Pawel D, Sesso H, Boice J. Radiation Research Society Annual Meeting September 2014

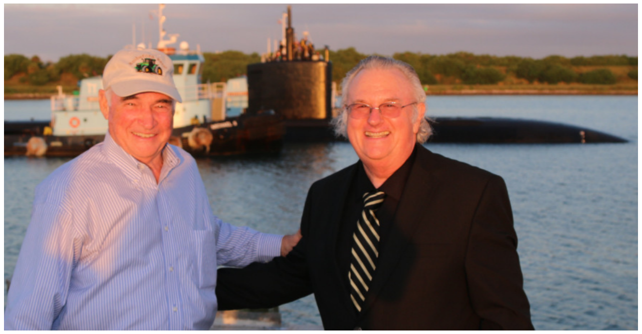
51K cases of heart disease in these few studies compared with 14K among atomic-bomb survivors (Shimizu BMJ 2009)

Study	Heart Disease
Mound	4,979
Rocketdyne	9,135
Mallinckrodt	648
Atomic Vets	22,512
Industrial Rad.	5,937
Nuclear Power	8,111
Total	**51,322**

Epidemiologists Will Go to Any DEPTH in the Public Interest - 85,033 Nuclear Submariners

USS
Montpelier

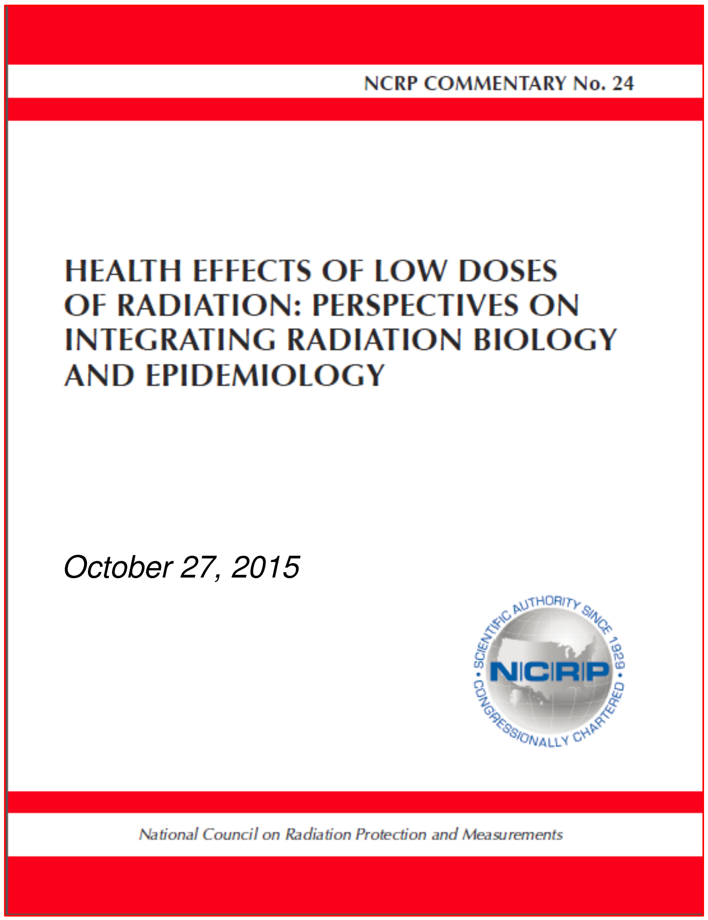
At 600 feet



Protection & Radiation Epidemiology

- Radiation Epidemiology
- Heritable Effects and Protection
- From Science to Protection – The Process
- Radium to Protection
- Occupation to Protection
- Leukemia – past to present
- Breast and Thyroid Cancer – Straight lines
- Radon from Mines to Homes
- A Million Person Study
- What's Next?

SC 1-21: On Integrating Radiation Biology with Epidemiology


NCRP COMMENTARY No. 24

HEALTH EFFECTS OF LOW DOSES OF RADIATION: PERSPECTIVES ON INTEGRATING RADIATION BIOLOGY AND EPIDEMIOLOGY

October 27, 2015

National Council on Radiation Protection and Measurements

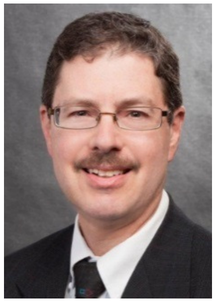
Sally Amundson, *Chairman*
Columbia University Medical Center
New York, New York

Jonine Bernstein, *Vice-Chairman*
Memorial Sloan-Kettering Cancer Center
New York, New York

NCRP – Current Need for Guidance

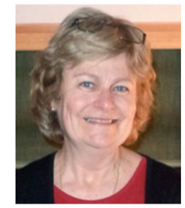
NCRP Council Committee 1 (CC-1): to update the bases of the System of Protection against Radiation for the United States, and the fundamental recommendations to limit exposures and their subsequent consequences.

Ken Kase
Former IRPA
President

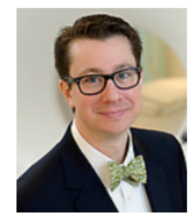


Don Cool
ICRP Chair
C4

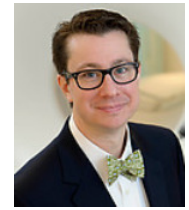
SC 1-23: Guidance on Radiation Dose Limits for the Lens of the Eye



Chairs Ellie Blakely and Larry Dauer

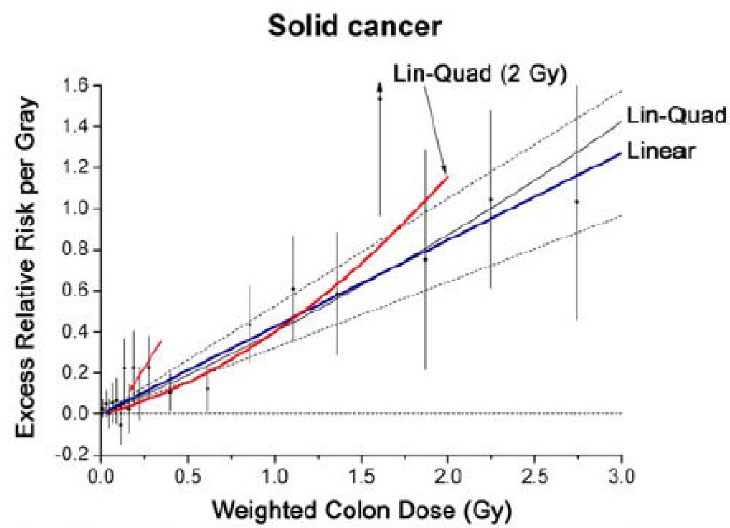


SC 1-25: Recent Epidemiologic Studies and Implications for the Linear-Nonthreshold Model



<u>Purpose</u>: SC 1-25 will prepare a commentary reviewing recent epidemiologic studies and evaluate whether the new observations are strong enough to support or modify the linear nonthreshold (LNT) model as used in radiation protection today.

Roy Shore, *Co-Chair*
Larry Dauer, *Co-Chair*
John Boice
Scott Davis
Randall Hyer
Fred Mettler, Jr.
Julian Preston
John Till
Daniel Stram
Richard Wakeford
Linda Walsh
Richard Vetter, *Staff Consultant*



Graph used with permission of K. Ozasa and *Radiation Research*

SUMMARY

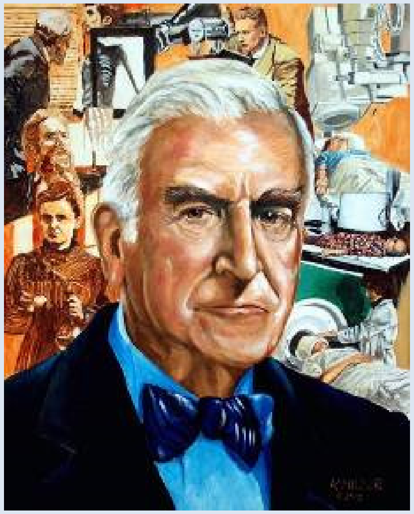
- Epidemiology forms the basis for protection
- Committees synthesize the epidemiology and other science
- ICRP and NCRP make recommendation considering UNSCEAR and NAS BEIR Reports
- Authorities decide on standards and regulations
- There's much to be done as society expand its uses of ionizing radiation! Stay tuned !

Thanks!
Also To IRPA and Health Physics Society

1929: U.S. Advisory Committee on X-Ray and Radium Protection

1946: U.S. National Committee on Radiation Protection

1964: National Council on Radiation Protection and Measurements chartered by Congress (Public Law 88-376)



Laurie Taylor, USA
Sievert 1980

IRPA

HEALTH PHYSICS SOCIETY
FOUNDED 1956

SCIENTIFIC AUTHORITY SINCE 1929
NCRP
CONGRESSIONALLY CHARTERED

VANDERBILT
UNIVERSITY