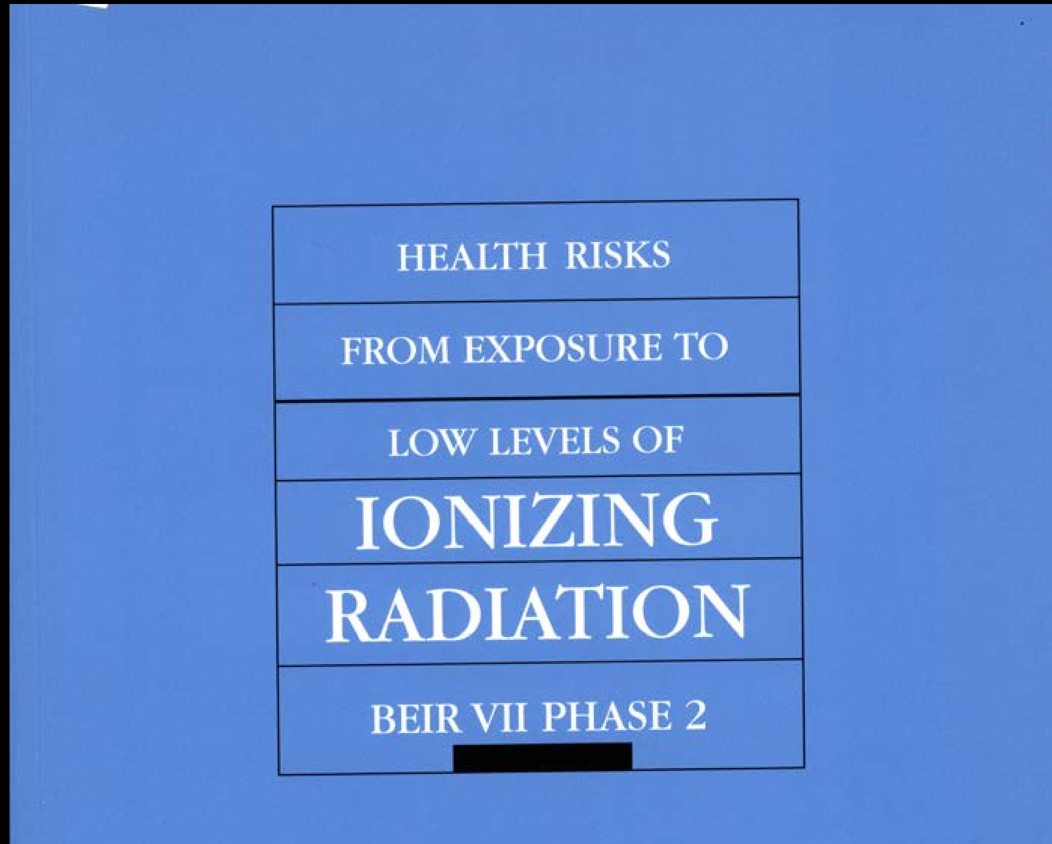

BEIR VII AND ITS IMPLICATIONS ON RISK – FACTS VERSUS MYTHS

Michael K O’Connor, Ph.D.
Dept. of Radiology, Mayo Clinic

Why are we concerned with Radiation Risks?

ORIGINAL INVESTIGATION

Projected Cancer Risks From Computed Tomographic Scans Performed in the United States in 2007

Amy Berrington de González, DPhil; Mahadevappa Mahesh, MS, PhD; Kwang-Pyo Kim, PhD; Mythreyi Bhargavan, PhD; Rebecca Lewis, MPH; Fred Mettler, MD; Charles Land, PhD

Using LNT & BEIR VII report, estimated radiation-related incident cancers

Estimated that 29,000 future cancers could be related to CT scans performed in the U.S. in 2007…..and would translate into about 14,500 cancer deaths.

Arch Intern Med. 2009;169(22):2078-2086 abc NEWS / Health

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CT Scan Radiation May Lead to 29,000 Cancers, Researchers Warn

Popular Diagnostic Scans May Be Overused, Some Worry

REUTERS

EDITION: U.S. | News & Markets | Sectors & Industries | Analysis & Opinio

(Reuters) - Radiation from CT scans done in 2007 will cause 29,000 cancers and kill nearly 15,000 Americans, researchers said on Monday.

By Julie Steenhuysen

CHICAGO | Mon Dec 14, 2009 4:30pm EST

Where does the estimate of 29,000 cancers come from ?

Based on Table 12D from BEIR VII,

+

risk estimates for
56,900,000 patients

TABLE 12D-1 Lifetime Attributable Risk of Cancer Incidence[a]

Cancer Site	Age at Exposure (years) 0	5	10	15	20	30	40				0
Males											
Stomach	76	65	55	46	40	28	27	25	20	14	7
Colon	336	285	241	204	173	125	122	113	94	65	30
Liver	61	50	43	36	30	22	21	19	14	8	3
Lung	314	261	216	180	149	105	104	101	89	65	34
Prostate	93	80	67	57	48	35	35	33	26	14	5
Bladder	209	177	150	127	108	79	79	[illegible]	[illegible]	[illegible]	23
Other	1123	672	503	394	312	198	172	[illegible]	[illegible]	[illegible]	23
Thyroid	115	76	50	33	21	9	3	[illegible]	[illegible]	[illegible]	0.0
All solid	2326	1667	1325	1076	881	602	564	[illegible]	[illegible]	[illegible]	126
Leukemia	237	149	120	105	96	84	84	[illegible]	[illegible]	[illegible]	48
All cancers	2563	1816	1445	1182	977	686	648	591	489	343	174
Females											
Stomach	101	85	72	61	52	36	35	32	27	19	11
Colon	220	187	158	134	114	82	79	73	62	45	23
Liver	28	23	20	16	14	10	10	9	7	5	2
Lung	733	608	504	417	346	242	240	[illegible]	[illegible]	[illegible]	77
Breast	1171	914	712	553	429	253	141	[illegible]	[illegible]	[illegible]	4
Uterus	50	42	36	30	26	18	16	[illegible]	[illegible]	[illegible]	2
Ovary	104	87	73	60	50	34	31	[illegible]	[illegible]	[illegible]	5
Bladder	212	180	152	129	109	79	78	[illegible]	[illegible]	[illegible]	24
Other	1339	719	523	409	323	207	181	148	109	68	30
Thyroid	634	419	275	178	113	41	14	4	1	0.3	0.0
All solid	4592	3265	2525	1988	1575	1002	824	678	529	358	177
Leukemia	185	112	86	76	71	63	62	62	57	51	37
All cancers	4777	3377	2611	2064	1646	1065	886	740	586	409	214

NOTE: Number of cases per 100,000 persons exposed to a single dose of 0.1 Gy.

100,000 women aged 30

Single dose of 100 mGy

Over their lifetime

What is the BEIR VII Report

An estimate of cancer risk from low doses of ionizing radiation!

- Input data:
  - Environmental studies
  - Occupational studies
  - Medical studies
  - Atomic bomb studies
- Model: LNT model (no allowance for dose-rate effects)
- Risk models:
  - ERR (excess relative risk)
  - EAR (excess absolute risk)
  - LAR (lifetime attributable risk)
- Subjective opinion of committee !

Sources of data

- Environmental Radiation Studies
- Occupational Radiation Studies
- Medical Radiation Studies
- Atomic bomb survivor Studies

Sources of data used in BEIR VII
Environmental Radiation Studies

Populations living near nuclear facilities

"..no increased risk…with radiation exposure"

Populations exposed to atomic bomb testing

"..some studies (4 out of 10) show some effect"

Chernobyl

High incidence of thyroid cancer

"..no evidence of an increase in any solid cancer type to date"

Natural background (China / India)

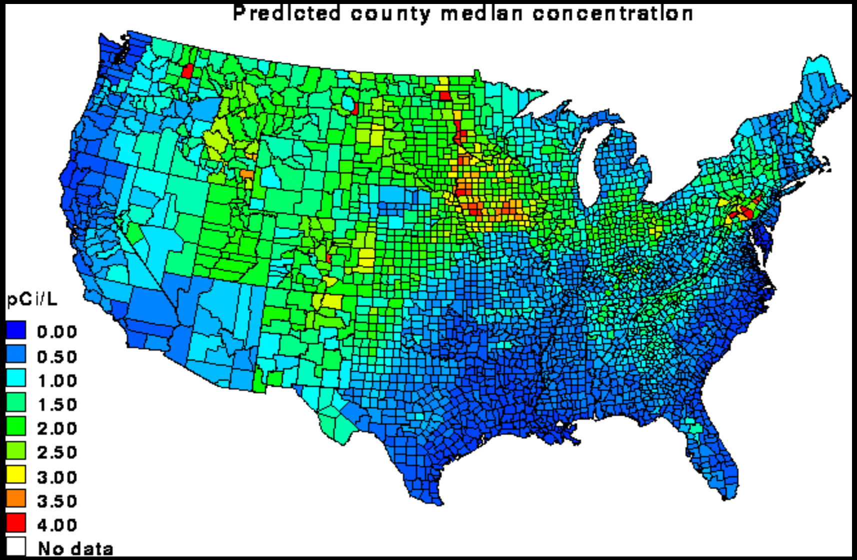
"..did not find higher disease rates in geographical areas with high background levels.."

Cancer Mortality in High Background Radiation Area of Yangjiang, China, 1979-1995

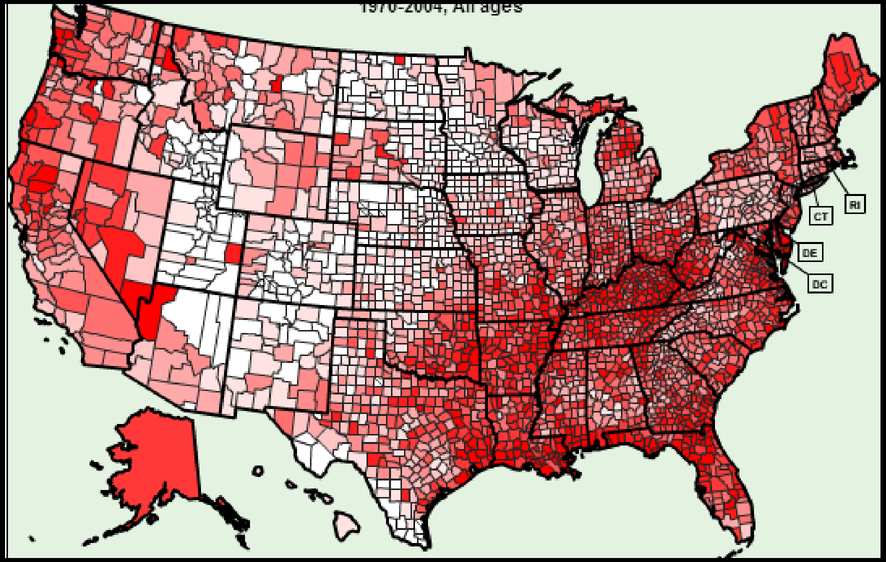
- Estimated cancer risk associated with the low level radiation exposure of 6.4 mSv / year
- 20-year study in 125,079 subjects
- Excess Relative Risk
  ERR/Sv = -0.10 (-0.67 to 0.69)
- Conclusion: the mortality of all cancers in Yangjiang was generally lower than that in control group, but <u>not significant statistically</u>.

(Tao et al, Zhonghua Yi Xue Za Zhi, 1999; 79: 487-492)

Radon Levels



Lung Cancer



Generated from EPA web site (https://www.epa.gov/radon/find-information-about-local-radon-zones-and-state-contact-information#radonmap)

Generated from NCI mortality map (http://ratecalc.cancer.gov/ratecalc/)

Sources of data

- Environmental Radiation Studies
- Occupational Radiation Studies
- Medical Radiation Studies
- Atomic bomb survivor Studies

Occupational Radiation Studies on Workers in the Nuclear Power Industry

"….in most cases, rates for all causes and all cancer mortality in the workers were substantially lower than the reference populations."

Findings explained as "healthy worker effect"

(U.S. Academy of Science, BEIR VII, 2007)

Significant limitation of most occupational studies is absence of an appropriate control group !

Sources of data

- Environmental Radiation Studies
- Occupational Radiation Studies
- **Medical Radiation Studies**
- Atomic bomb survivor Studies

Medical Radiation Studies

Sources of data used in BEIR VII

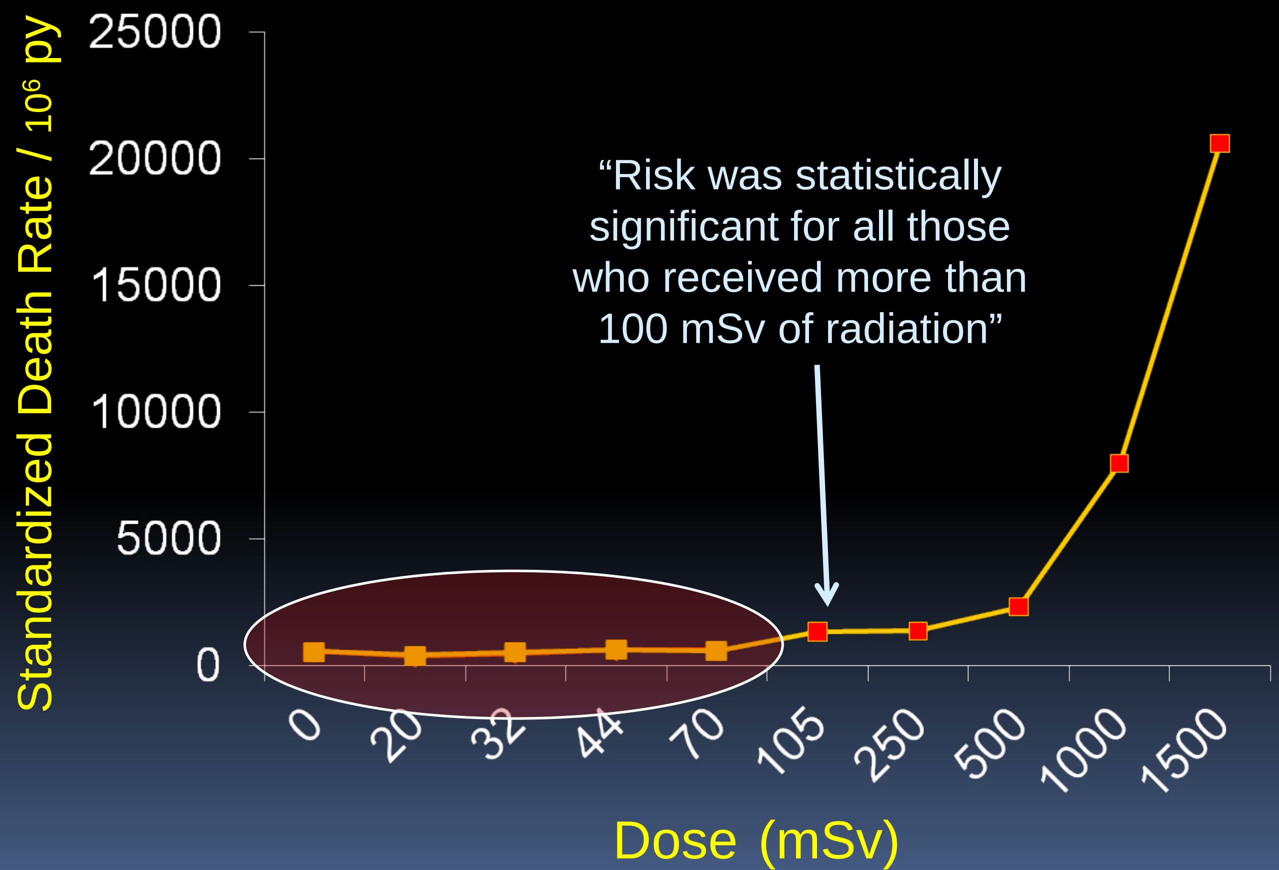
Focus on therapeutic studies

"…most of the information comes from studies of populations with medium to high doses"

Lung Cancer – 9 studies, 40,000 subjects
average dose ~ 1 Gy
Breast cancer – 11 studies, 20,000 subjects
average dose ~ 300 mGy

Mortality from Breast Cancer after Fluoroscopy in Patients being treated for Tubercolosis

31,710 women treated between 1930 - 1952
40-year follow-up
Age range 10-40 years



Miller AB et al, NEJM 1989; 321: 1285-1289.

Mortality from Breast Cancer after Fluoroscopy in Patients being treated for Tubercolosis

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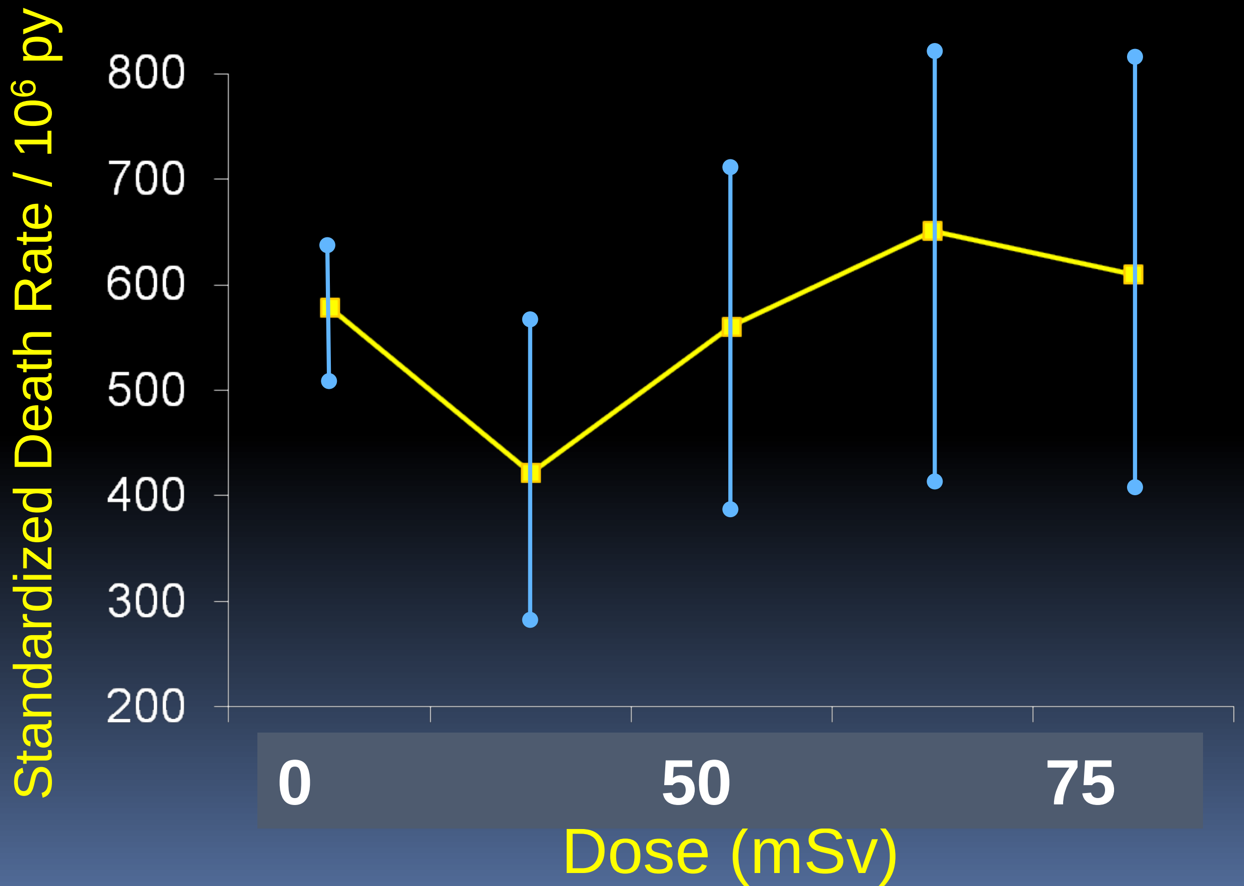
Age range 10-40 years



Sources of data used in BEIR VII

- Environmental Radiation Studies
- Occupational Radiation Studies
- Medical Radiation Studies
- **Atomic bomb survivor Studies**

Atomic bomb survivor Studies

- 120,000 survivors
  93,000 present at time of bombings
  27,000 from locale, but absent at time of the bombing (Not In City group)

- Monitored over 70 years & includes both sexes and all ages of exposure – mean dose = 200 mSv

- Dose range

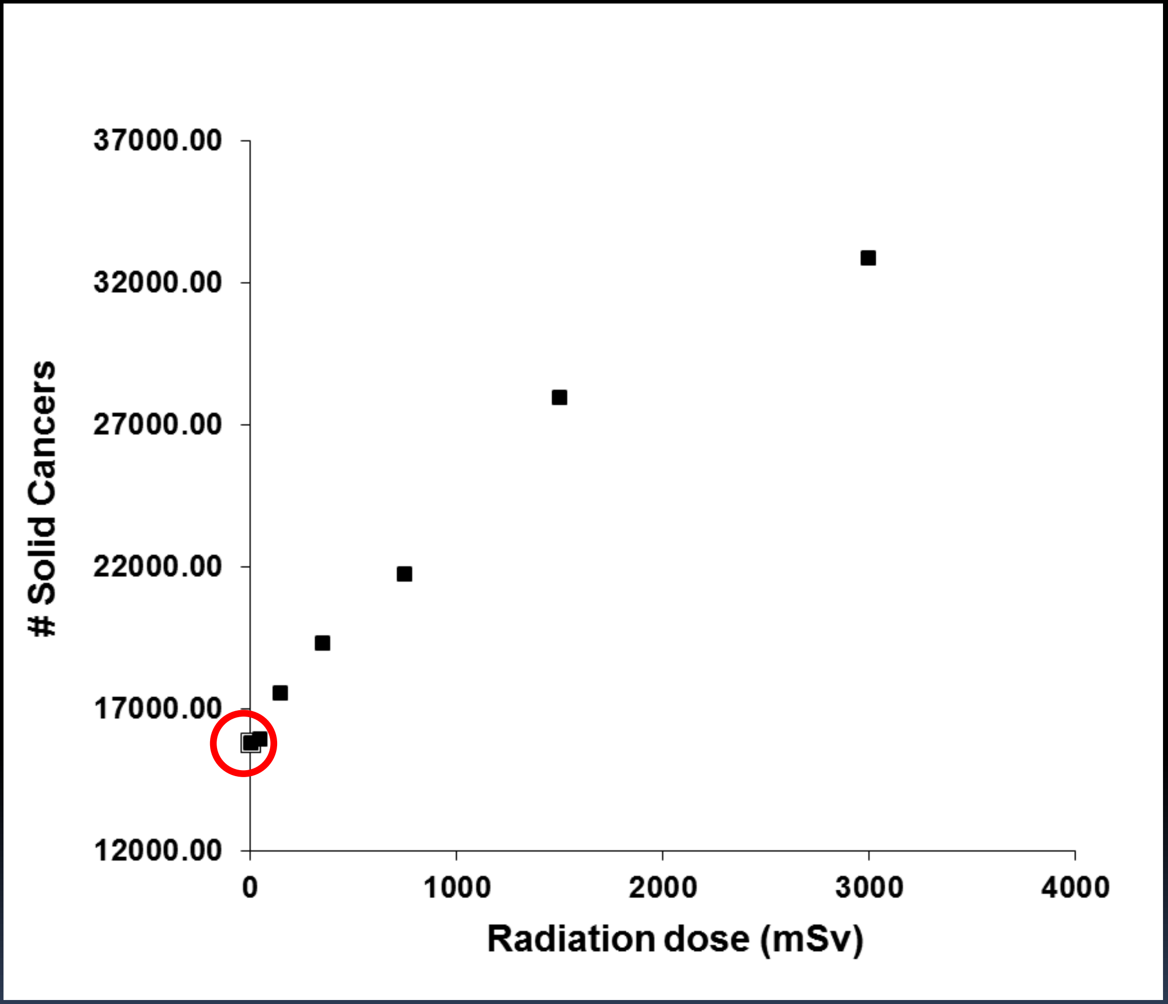
Dose range	37,000	0-5 mSv
	32,000	5-100 mSv
	17,000	100 mSv – 2000 mSv

This is the primary source of data for LNT risk models

Atomic bomb survivor Studies

Data from Table 4, Preston et al, 2007

 # solid cancers adjusted to per 100,000 people

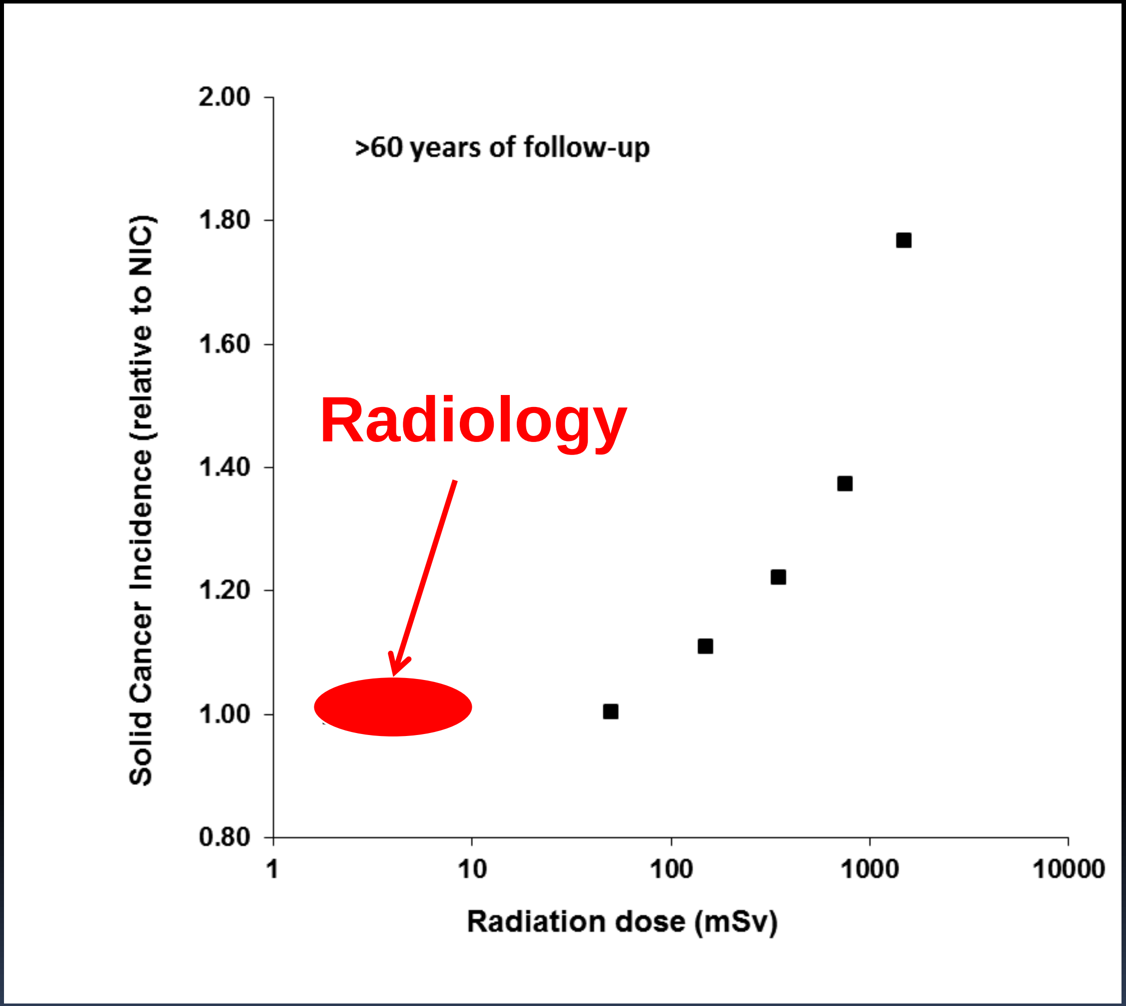


Preston et al, Rad Res 2007;168: 1-64.
(Radiation Effects Research Foundation)

Atomic bomb survivor Studies

Data from Table 4, Preston et al, 2007

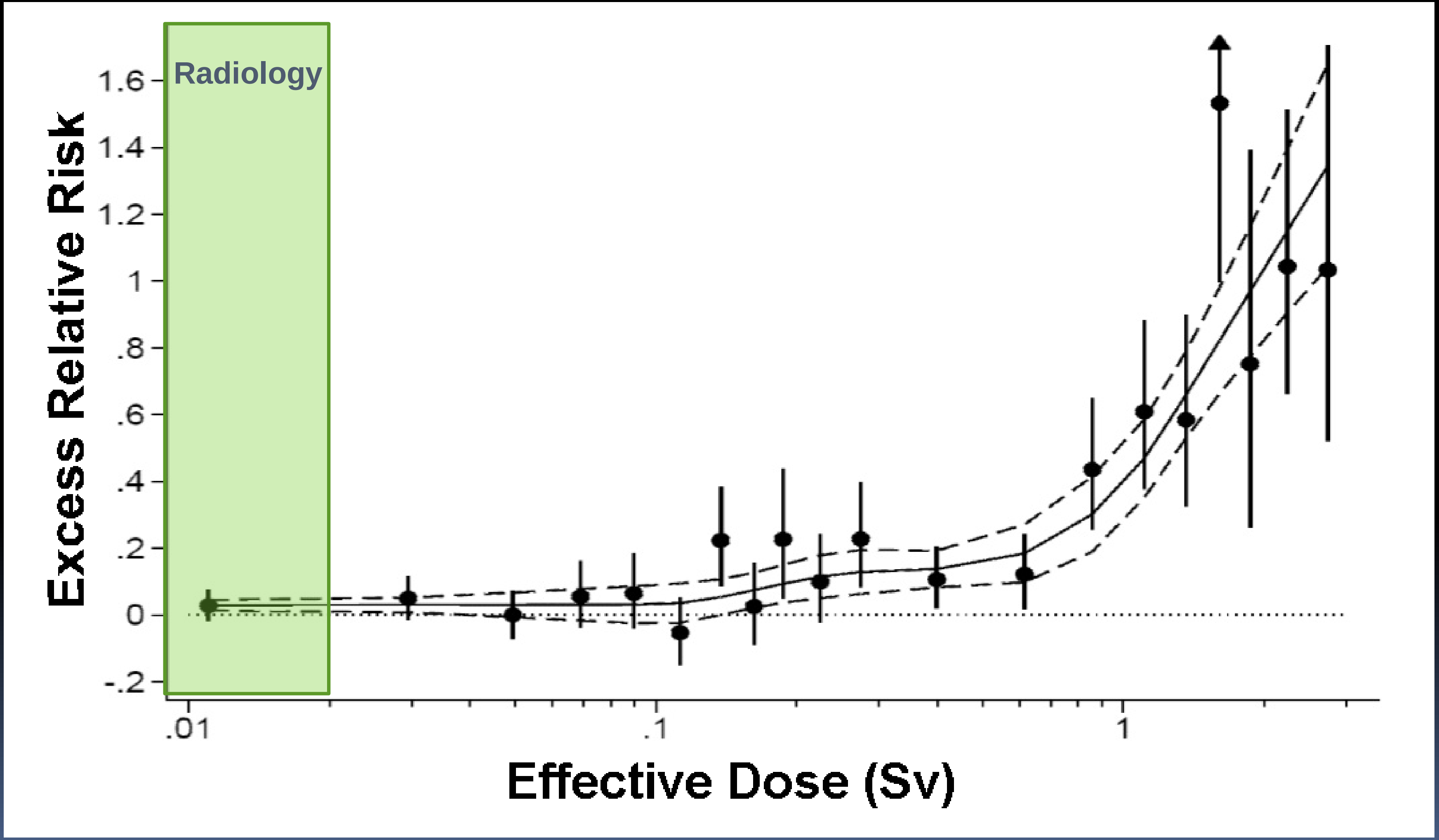
 # solid cancers adjusted to per 100,000 people



Preston et al, Rad Res 2007;168: 1-64. (Radiation Effects Research Foundation)

Atomic bomb survivor Studies

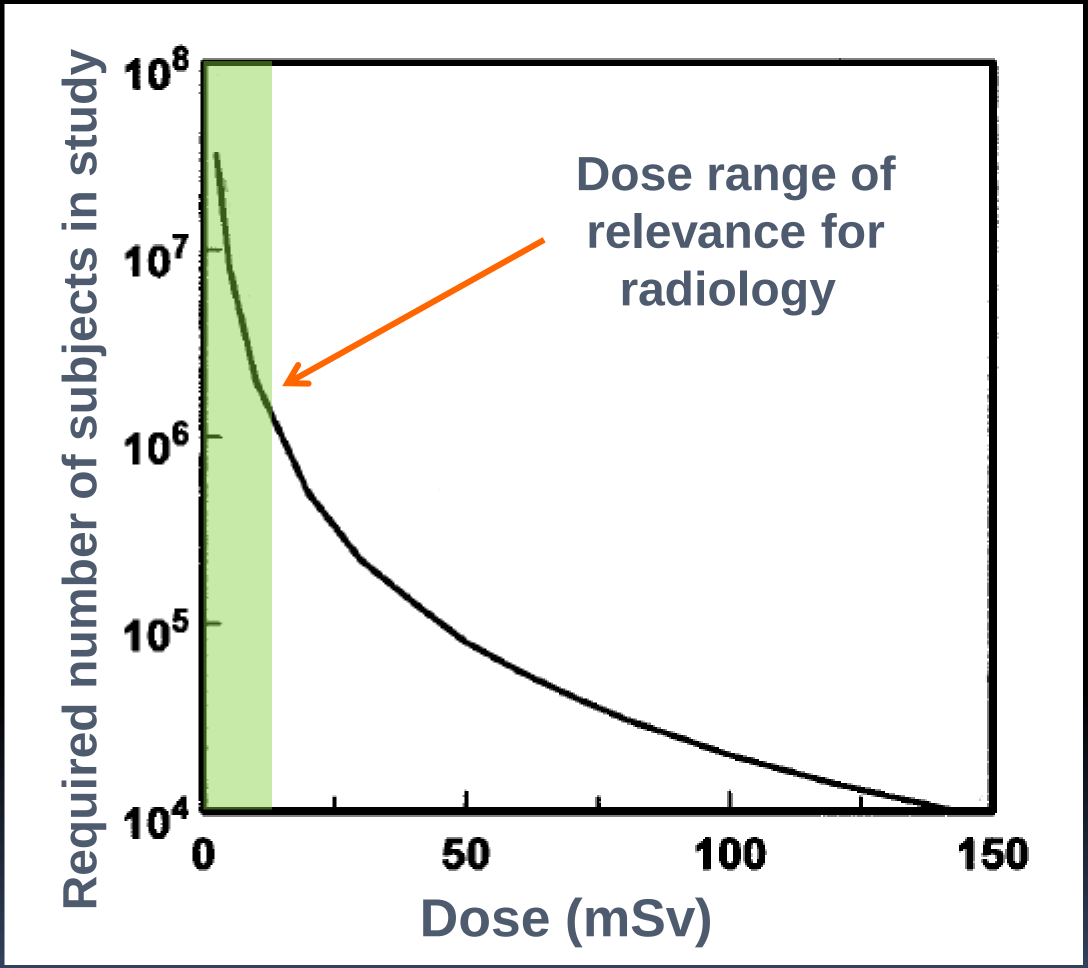
Ozasa et al, 2013, Doss et al 2012



Low Dose Risk Estimates require "Impracticably Large" sample requirements

- Does the radiation from mammography (about 1 mSv) cause breast cancer?
  - Cohort study: about 100 million (20-year follow-up)!
  - Case-control: about 1 million cases (4:1 ratio)

Sample size required to detect a significant increase in cancer mortality, assuming lifetime follow-up

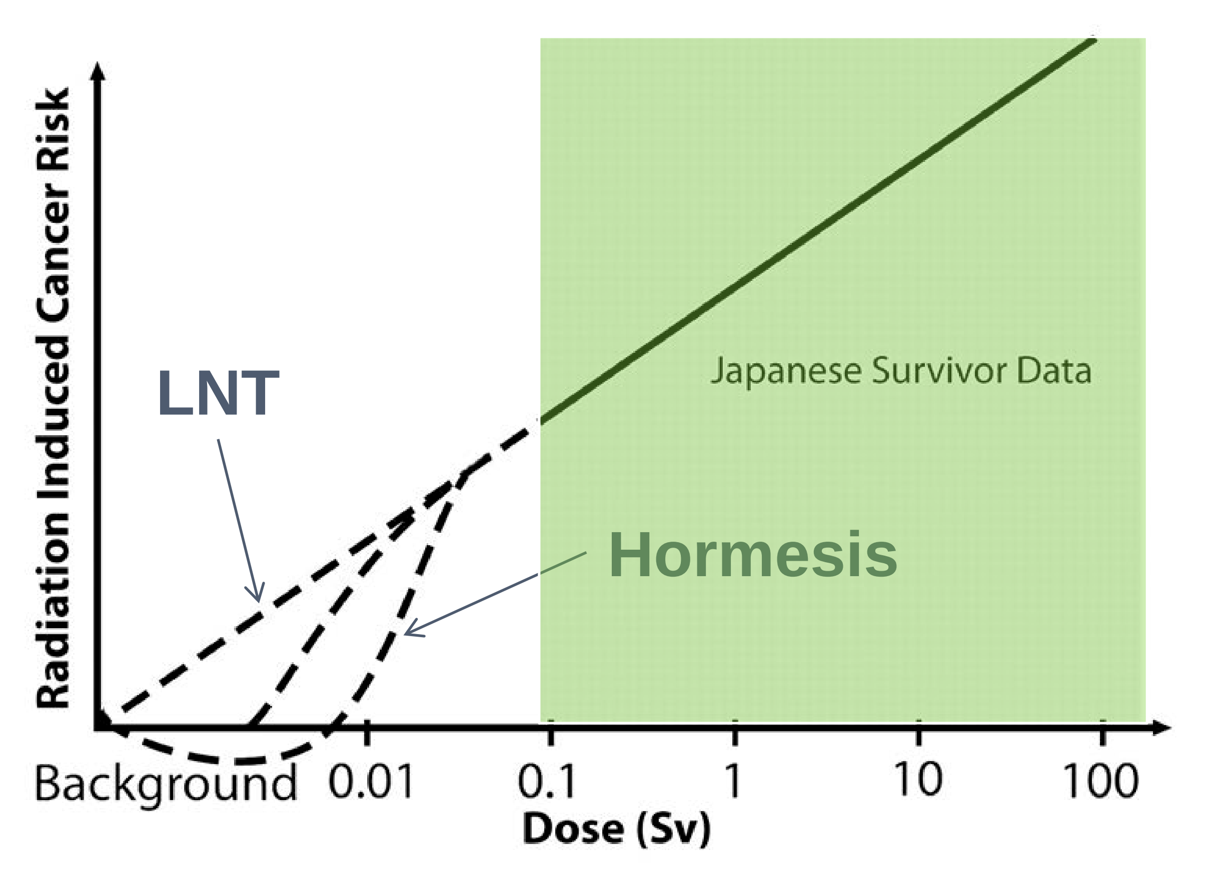


National Research Council (1995) *Radiation Dose Reconstruction for Epidemiologic Uses* (Natl. Acad. Press, Washington, DC).

MAYO CLINIC

Effect of Low Doses - 3 Theories

Linear No Threshold (LNT) Model
Threshold Model
Hormesis Model



MAYO CLINIC

Linear No-Threshold Hypothesis

LNT & Radiation

- 1930’s: developed by Herman Mueller to explain mutagenesis in fruit flies
- 1950: Mueller persuaded BEIR committee in 1950 to use his LNT hypothesis to explain carcinogenesis

LNT assumes that

- any amount of radiation exposure, no matter how small, can increase the chance of cancer.
- probability of cancer from radiation exposure increases with cumulative lifetime dose.

LNT Hypothesis

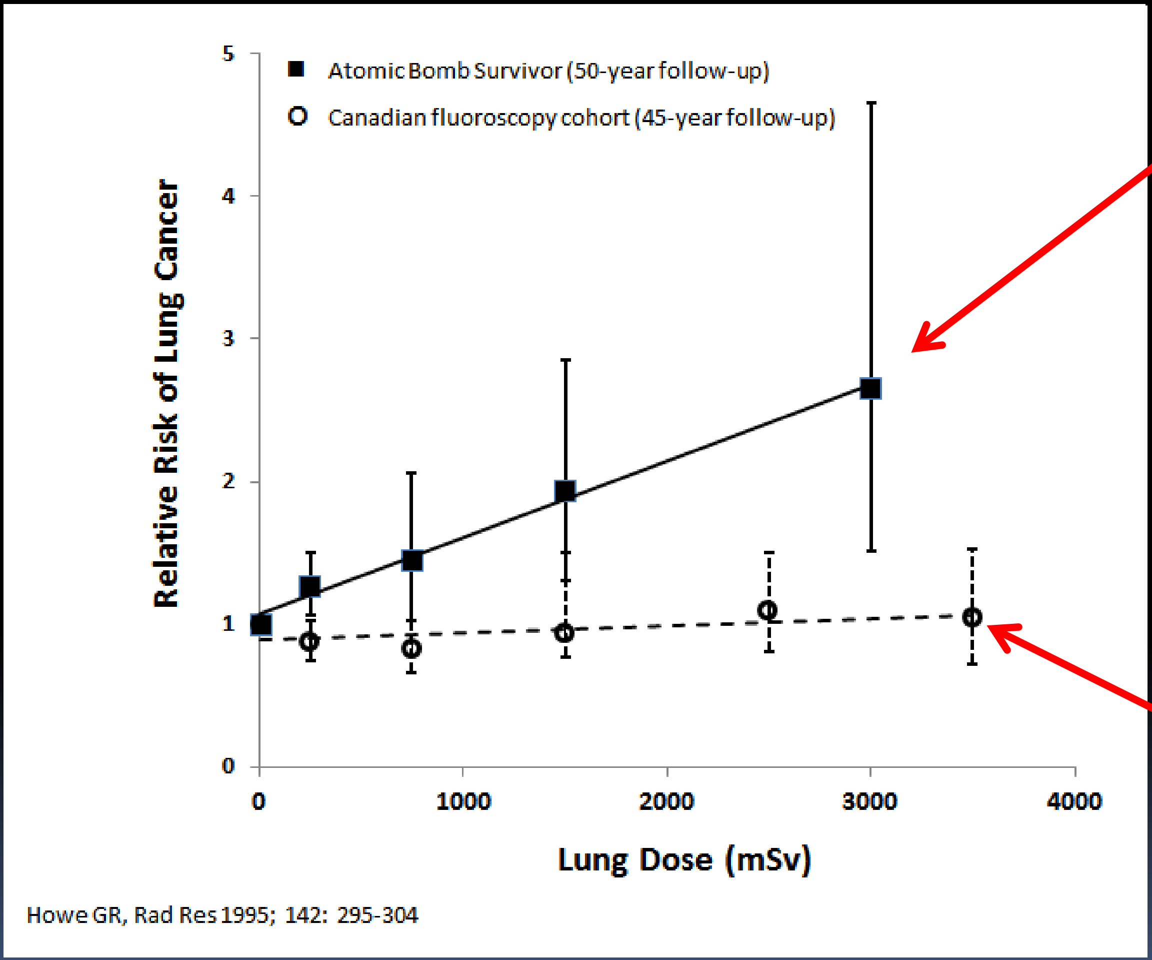
For example: Using the LNT model the following are equivalent in terms of their effect

1 person jumps off a 100-foot cliff

100 people jump off a 1-foot cliff

1 person jumps off a 1-foot cliff 100 times

Lung Cancer Mortality vs. Dose Rate



Dose delivered instantaneously

According to LNT they should be the same !

Dose delivered Over 3 years
(avg. dose / session = 11 mSv)

Risk Models used in LNT

Excess Relative Risk (ERR) model

The ERR is the rate of disease in an exposed population divided by the rate of disease in an unexposed population, minus 1.0.

(This is a useful model if the population under investigation is similar to the population on which the model was based.)

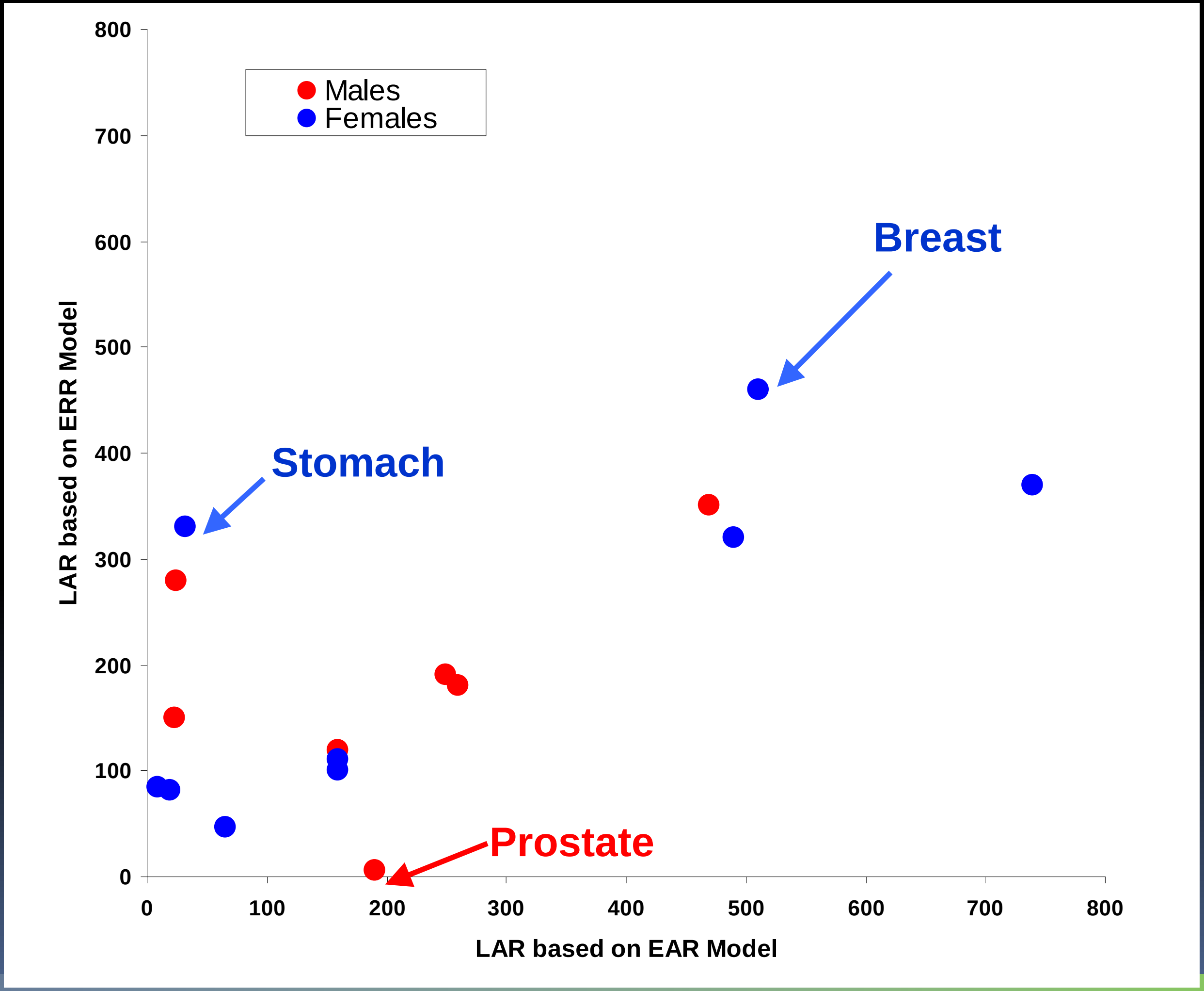
Excess Absolute Risk (EAR) model

The EAR is the rate of disease in an exposed population minus the rate of disease in an unexposed population.

(This model is more suited if there are significant differences (ethnicity, diet, etc) between the population under investigation and that on which the model was based.)

Same Data – 2 different Risk Models

Comparison of Lifetime Risk of Cancer using ERR and EAR



Risk Models used in LNT

Excess Relative Risk (ERR)

vs.

Excess Absolute Risk (EAR)

Which model is correct ?

For each organ, final risk model
= x.ERR + (1-x).EAR
where x is determined by committee !

Risk Models

Cancer incidence from ionizing radiation

- Based almost exclusively on atomic bomb survivor studies
- Uses a combination of ERR and EAR
- Uses different combinations for different organs
- Includes additional assumptions about modifying factors such as latency
- Risk models (developed from Japanese population, wartime conditions) then applied to cancer rates for U.S. population

TABLE 12-5A Lifetime Attributable Risk of Solid Cancer Incidence

Cancer Site	Males: LAR Based on Relative Risk Transport[a]	Males: LAR Based on Absolute Risk Transport[b]	Males: Combined and Adjusted by DDREF[c] (Subjective 95% CI[d])	Females: LAR Based on Relative Risk Transport[a]	Females: LAR Based on Absolute Risk Transport[b]	Females: Combined and Adjusted by DDREF[c] (Subjective 95% CI[d])
Incidence						
Stomach	25	280	34 (3, 350)	32	330	43 (5, 390)
Colon	260	180	160 (66, 360)	160	110	96 (34, 270)
Liver	23	150	27 (4, 180)	9	85	12 (1, 130)
Lung	250	190	140 (50, 380)	740	370	300 (120, 780)
Breast				510 Not used	460	310 (160, 610)
Prostate	190	6	44 (<0, 1860)			
Uterus				19	81	20 (<0, 131)
Ovary				66	47	40 (9, 170)
Bladder	160	120	98 (29, 330)	160	100	94 (30, 290)
Other	470	350	290 (120, 680)	490	320	290 (120, 680)
Thyroid	32	No model	21 (5, 90)	160	No model	100 (25, 440)
Sum of site-specific estimates	1400	1310[e]	800	2310[f]	2060[e]	1310
All solid cancer model[g]	1550	1250	970 (490, 1920)	2230	1880	1410 (740, 2690)

NOTE: Number of cases per 100,000 persons of mixed ages exposed to 0.1 Gy.

…range of plausible values for LAR is labeled a "subjective confidence interval" to emphasize its dependence on opinions in addition to direct numerical observation (BEIR VII, page 278)

BEIR VII Risk Estimates

Risk estimates are “subjective” and partly based on the opinion of members of the BEIR VII committee

Risk estimates at low doses are extrapolated from high doses and are not supported by current low-dose studies

The following organizations have clearly stated that the use of the LNT Hypothesis to compute the effects of small doses on large populations is inappropriate

- International Commission on Radiological Protection
- American Association of Physicists in Medicine
- Health Physics Society
- Academie Nationale de Medecine, France
- National Council on Radiation Protection & Measurement
- United Nations Scientific Committee on Effects of Atomic Radiation

2012 UNSCEAR Report

- "The Scientific committee <u>does NOT recommend</u> multiplying very low doses by large numbers of individuals to estimate numbers of radiation-induced health effects within a population exposed to incremental doses at levels equivalent to or lower than natural background levels"

Report of the United Nations Scientific Committee on the Effects of Atomic Radiation

Fifty-ninth session

(21-25 May 2012)

United Nations • New York, 2012

Background Radiation: 2 – 10 mSv / year worldwide

ANS / HPS Program: Oct 1st-3rd 2018 Pasco, WA

- 3-day program on applicability of radiation response models to low dose protection standards
- 200-300 participants divided into 3 primary camps
  - LNT (~10%)
  - Threshold (~70%)
  - Hormesis (~20%)
- Regulatory bodies
  - ICRP
  - UNSCEAR
  - NCRP / IAEA / NRC / EPA

RESEARCH ARTICLE

Was the Risk from Nursing-Home Evacuation after the Fukushima Accident Higher than the Radiation Risk?

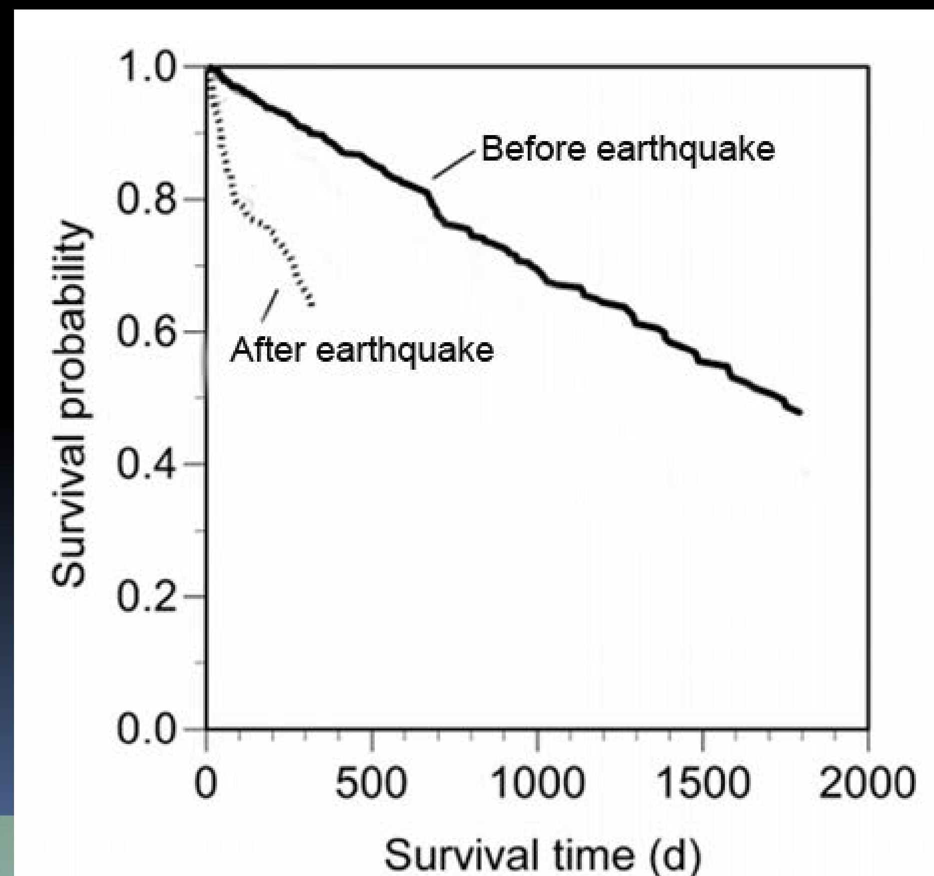
Michio Murakami[1¤]*, Kyoko Ono[2], Masaharu Tsubokura[3], Shuhei Nomura[4], Tomoyoshi Oikawa[5], Tosihiro Oka[6], Masahiro Kami[3], Taikan Oki[1]

PLOS ONE | DOI:10.1371/journal.pone.0137906 September 11, 2015

Radiophobia Fukushima

The number of deaths indirectly related to the earthquake in Fukushima Prefecture was >1700 .

Deaths were due to the physical / mental stresses related to the evacuation.



ICRP Recommendations

Encourage & support low-dose and low-dose-rate research

Improve messaging about risks at very low doses

Promote reasonableness in <u>optimization of protection</u>, avoiding over-conservatism, in:

- Standards
- Regulations
- Practice (including regulatory practice)

UNSCEAR Recommendations:

For legislators to exclude from the law low-dose exposure situations that are unamenable to be controlled

For regulators to exempt from regulations low-dose exposure situations that do not warrant control.