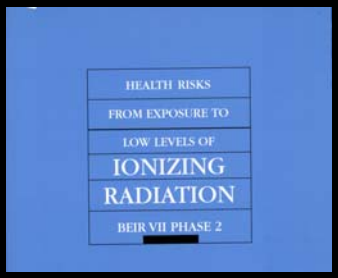


BEIR VII: What It Does and Doesn't Say

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

ORIGINAL INVESTIGATION

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

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

Using 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

abcNEWS / Health

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

Popular Diagnostic Scans May Be Overused, Some Worry

REUTERS

(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

Cancer … msnbc.com

15,000 will die from CT scans done in 1 year

Scans have higher levels of radiation than thought, researchers say

Will You Be one of the 15,000 That Are Killed By CT Scans Next Year?
This is the question being asked as 2009 drew to a close.

Cancercare.com

"Boy I'm lucky I never had one of these done! I was always skeptical of this procedure. It was my intuition that told me don't go there!"….USA Today

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	80
Males								
Stomach	76	65	55	46	40	28	27	7
Colon	336	285	241	204	173	125	122	30
Liver	61	50	43	36	30	22	21	3
Lung	314	261	216	180	149	105	104	34
Prostate	93	80	67	57	48	35	35	5
Bladder	209	177	150	127	108	79	79	23
Other	1123	672	503	394	312	198	172	23
Thyroid	115	76	50	33	21	9	3	0.0
All solid	2326	1667	1325	1076	881	602	564	126
Leukemia	237	149	120	105	96	84	84	48
All cancers	2563	1816	1445	1182	977	686	648	174
Females								
Stomach	101	85	72	61	52	36	35	11
Colon	220	187	158	134	114	82	79	23
Liver	28	23	20	16	14	10	10	2
Lung	733	608	504	417	346	242	240	77
Breast	1171	914	712	553	429	253	141	4
Uterus	50	42	36	30	26	18	16	2
Ovary	104	87	73	60	50	34	31	5
Bladder	212	180	152	129	109	79	74	24
Other	1339	719	523	409	323	207	148	30
Thyroid	634	419	275	178	113	41	14	0.0
All solid	4592	3265	2525	1988	1575	1002	824	177
Leukemia	185	112	86	76	71	62	62	37
All cancers	4777	3377	2611	2064	1646	1065	886	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

Where does Table 12D come from?

Cumulative estimate from 3 risk models
Contains numerous assumptions, opinions

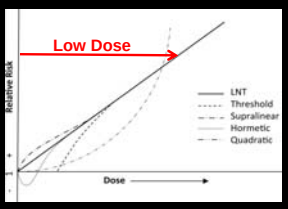
Theory:
Based on Linear No Threshold Hypothesis

Source of Data:
Based almost exclusively on Atomic Bomb Survivors Study

Risk models:
Excess Relative Risk (ERR)
Excess Absolute Risk (EAR)
Lifetime Attributable Risk (LAR)

Parameters:
Dose & Dose Rate Effectiveness Factor (DDREF)
Relative Biological Effectiveness (RBE)
Latency period

Analysis of Radiation Risks in Atomic Bomb Survivor Data is based on the Linear No Threshold Hypothesis



- LNT introduced by Muller in 1902s as a model for the mutagenic effect of x-rays in fruit flies (later proved invalid)
- Muller served as consultant on 1st BEIR committee in 1956 and urged their adoption of this model

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

1 person consumes 1 aspirin daily for 1 year

1 person consumes 365 aspirin in 1 day

365 people consume 1 aspirin in 1 day

Sources of data considered in BEIR VII

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

Sources of data used in BEIR VII
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 (excluded from analysis)
- **Monitored over 60 years & includes both sexes and all ages of exposure – mean dose = 200 mSv**
- **Dose range** 37,000 0-5 mSv
  32,000 5-100 mSv
  17,000 100 mSv – 2000 mSv

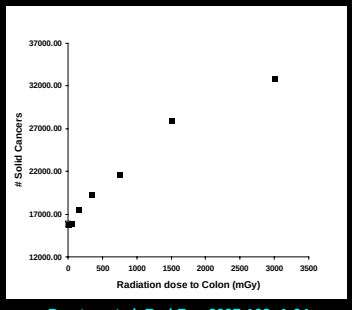
This is the primary source of data for all risk models used in BEIR VII

Sources of data used in BEIR VII
Atomic bomb survivor Studies

Data from Table 4, Preston et al, 2007

 # solid cancers adjusted to per 100,000 people

"Based on fitting with lower threshold, best estimate of threshold was 40 mGy with upper bound of 85 mGy (90% CI) However model not significantly better than LNT"



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

Sources of data used in BEIR VII
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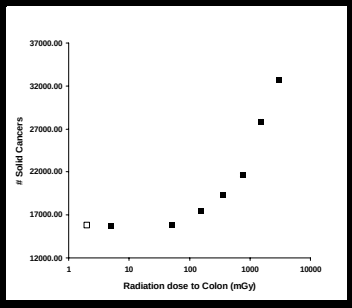

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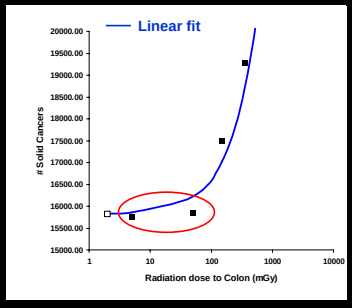


Preston et al, Rad Res 2007;168: 1-64.
(Radiation Effects Research Foundation)

Sources of data used in BEIR VII
Atomic bomb survivor Studies

"in the presence of available data, it is neither sound statistical interpretation nor prudent risk evaluation to take the view that the risk should be considered zero in some low-dose range…"

BEIR VII Committee

Sources of data used in BEIR VII
Medical Radiation Studies

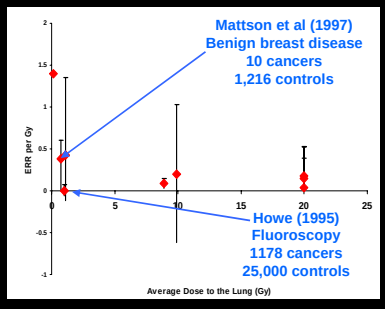
Focus on therapeutic studies

"…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

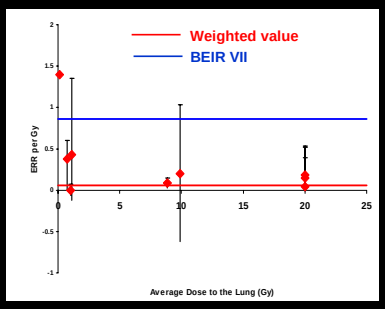
Medical Radiation Studies
Cancer Incidence from radiation exposure to the lungs
9 studies, >40,000 subjects

ERR
Excess risk relative to background risk



Calculation of ERR - Medical Radiation Studies
Cancer Incidence from radiation exposure to the lungs
9 studies, >40,000 subjects

ERR
Excess risk relative to background risk

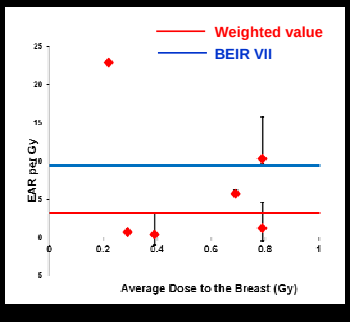


MAYO CLINIC

Calculation of EAR - Medical Radiation Studies

Cancer Incidence from radiation exposure to the breast 6 studies, >30,000 subjects

EAR Excess absolute above background risk



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Calculation of EAR - Medical Radiation Studies

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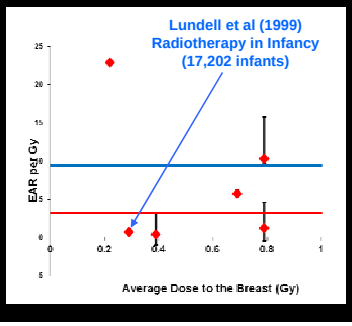
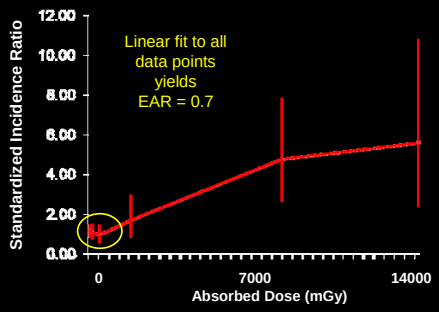


MAYO CLINIC

Breast Cancer Risk after Radiotherapy in Infancy

Pooled analysis of 17,202 Infants – Mean follow-up of 45 Years



Lundell et al, Radiation Research 1999; 151: 626-632

MAYO CLINIC

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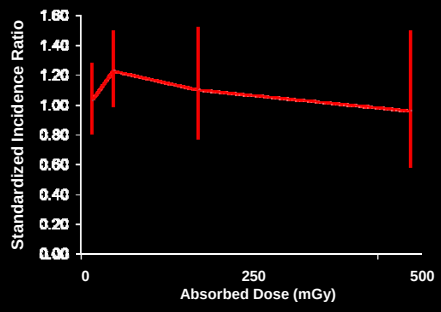


Lundell et al, Radiation Research 1999; 151: 626-632

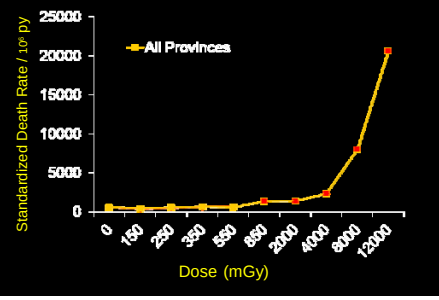
MAYO CLINIC

Mortality from Breast Cancer after Irradiation during Fluoroscopic Examinations in Patients being treated for Tubercolosis

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

31,710 women treated between 1930 - 1952

"Risk was statistically significant for all those who received more than 700 mGy of radiation"



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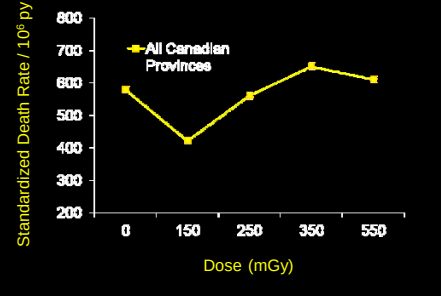


Sources of data used in BEIR VII
Occupational Radiation Studies

U.S. – 9 studies
U.K. – 6 studies
Canada – 1 study
France – 1 study

Six large combined cohort studies
Combined study population > 500,000 subjects with 30- 40 years of follow-up

Cumulative dose levels: 30-60 mSv

Sources of data used in BEIR VII
Occupational Radiation Studies

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

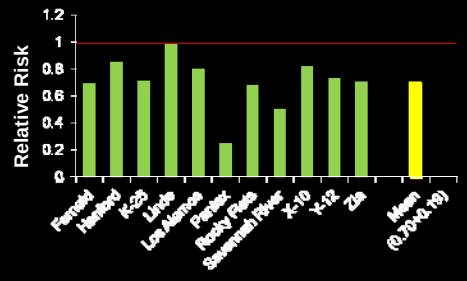
Effect explained as "healthy worker effect"

"Because of uncertainty in occupational risk estimates….., the committee has concluded that the occupational studies are not suitable for the projection of population-based risks."

Breast Cancer Mortality

Study of 67,979 women who worked with radiation in Nuclear Weapons facilities before 1980 (relative to unmonitored women in same facilities)

Expected mortality = 18,106 deaths / Observed mortality = 13,671 deaths



Wilkinson et al. Nat Inst Occup Safety Health, June 2000

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 not significant statistically.

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

Most radioactive place in the world - Ramsar, Iran (due to Radium-226)
Background radiation = 100-260mSv / year
No epidemiological evidence of adverse affects
Residents demonstrate a marked increase in DNA repair.

Co-60 Contamination in Taiwan Buildings

1982-1983: Taiwan buildings constructed using steel heavily contaminated with Co-60. Extent of problem discovered in late 1990s.

180 buildings, schools and small businesses (> 1600 apartments)

~10,000 residents affected, many for ~20 years

Cohort	# People	Cumulative dose 1983-2003 (mSv)
High	1,100	4000
Medium	900	420
Low	8,000	120

(Chen et al. Dose Response 2007; 5:63-75.)

Co-60 Contamination in Taiwan Buildings

Results	No. Deaths over 20 yr.	Notes
Natural (expected) cancer deaths	232	Includes 4–5 leukemia
Predicted cancer deaths (BEIR VII)	302	232 natural plus 70 caused by radiation
Observed cancer deaths	7	3% of general public cancer death rate

"The observation that the cancer mortality rate of the exposed population is only about 3 percent of the cancer mortality rate of the general public is particularly striking and is consistent with the radiation hormesis model."

Risk Models

- **Excess Relative Risk (ERR)**
  - **Excess risk expressed relative to background risk**
- **Excess Absolute Risk (EAR)**
  - **Excess risk expressed as difference between total risk and background risk**
- **Lifetime Attributable Risk (LAR)**
  - **Uses one of the above to calculate lifetime risk of cancer**

Risk Models

Excess Relative Risk (ERR)

vs.

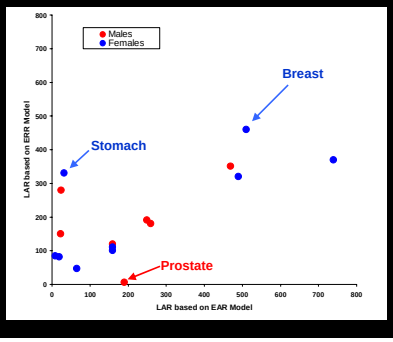
Excess Absolute Risk (EAR)

Which model is correct ?

Final Risk model = x.ERR + (1-x).EAR
where x is determined by committee !

Same Data – 2 different Risk Models

Comparison of LAR using ERR and EAR



Modifying Parameters

- **Dose & Dose Rate Effectiveness Factor (DDREF)**
  - **Range of values 1.1 – 2.5**
- **Relative Biological Effectiveness (RBE)**
  - **Range of values 1 - 4**
- **Latency period**
  - **Range 2 – 10 years**
- **Ethnicity, Environment (diet, lifestyle)**
  - **Convert cancer risk in Japanese subject in 1940's to American subject in 2011 !**

Risk Models

- Lifetime Attributable Risk (LAR)
  - Uses different final risk models for different organs
  - Assumptions about modifying parameters
  - Risk models then applied to cancer rates for U.S. population
  - **Cancer incidence in Table 12D is based on this parameter !**

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

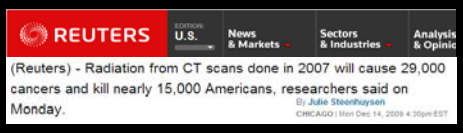
Cancer Site	Males: LAR Based on Relative Risk Transport[a]	Males: LAR Based on Absolute Risk Transport[a]	Males: Combined and Adjusted by DDREF[b] (Subjective 95% CI[c])	Females: LAR Based on Relative Risk Transport[a]	Females: LAR Based on Absolute Risk Transport[a]	Females: Combined and Adjusted by DDREF[b] (Subjective 95% CI[c])
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[e]	2060[e]	1310
All solid cancer models[d]	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)

Risk Models

- **Lifetime Attributable Risk (LAR)**
  - **"Because of the various sources of uncertainty it is important to regard specific estimates of LAR with a healthy skepticism, placing more faith in a range of possible values" (BEIR VII, page 278)**


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

Based on Table 12D BEIR VII, and risk estimates for 56,900,000 patients

For comparison: 9,700,000 people will die of cancer

IF they all lived in Minnesota, (bkg rad = 3 mSv)
we would expect 576,000 deaths from background radiation

IF they all lived in Colorado, (bkg rad = 4.5 mSv)
we would expect 863,000 deaths from background radiation

Differences in residence = 287,000 cancers, or ~20 CT scans/patient

BEIR VII:

What it does say:

- All estimates are based on multiple models and assumptions
- Regard specific estimates with a healthy skepticism
- Confidence intervals are "subjective" and partly based on opinion

Don't quote cancer estimates from BEIR VII as if they were a proven scientific fact !!!

If you believe I'm wrong and BEIRVII is correct, here are a few suggestions to keep you safe !!

- Don't stand close to anyone - stay single, no close friends !
  - we all are radioactive, even your dog
  - if you want a pet, pick a goldfish!
- Don't fly on airplanes (cosmic rays)
- Don't live or visit mountain areas (radon / cosmic rays).
- Don't breath too much air (radon is in the air).
- Don't eat fruits and vegetables (they contain radioisotopes)