# RADIATION EFFECTS

HPHY 6605

2012

## Basic Types of Radiation Effects

- Heritable effect
  - The effect occurs in the offspring of the irradiated individual (or organism)
  - Are stochastic
- Somatic effect
  - The effect occurs in the irradiated individual (or organism)
  - Can be stochastic or deterministic

## Basic Types of Radiation Effects

- Deterministic effect
  - Degree of effect depends on the amount of absorbed dose
  - A dose threshold exists, below which the effect is not evident
- Stochastic effects
  - Probability of occurrence of the effect depends on absorbed dose
  - Severity of the effect is independent of absorbed dose

## Effects Considered

- Heritable effects
- Deterministic and stochastic effects to Embryo / Fetus
- Deterministic effects in post-natal individuals
- Stochastic effects (cancer) in several categories of post-natal individuals
  - Atomic bomb survivors
  - Occupationally exposed
  - “Down-winders”
  - Those exposed to high natural background
  - Those exposed to elevated radon

## Radiation Effects -- Heritable

- Radiation produces lesions in cell DNA
- Most are repaired but some persist
  - Double strand breaks considered most important
- If male or female germ cells or gametes (egg or sperm) have been affected, the damage could be inherited in the next generation
  - Heritable genetic effects from radiation have been demonstrated clearly in plants and animals
  - Heritable Genetic effects from radiation have not been demonstrated in humans
  - Expert bodies have concluded that humans are likely affected; just not detectable with present studies

## Radiation Effects -- Embryo / Fetus

- Cancer -- data are inconsistent -- rate had been estimated at about 0.02 per Sievert
- One evaluation indicated that quantification was not possible at the time (NCRP 115, 1993)
- A subsequent review by Doll and Wakefield (BJR 70, 130-139, 1997) assert a demonstrable risk of childhood cancer due to fetal irradiation down to one rad (10 mGy)
  - However this study has been criticized extensively in the literature

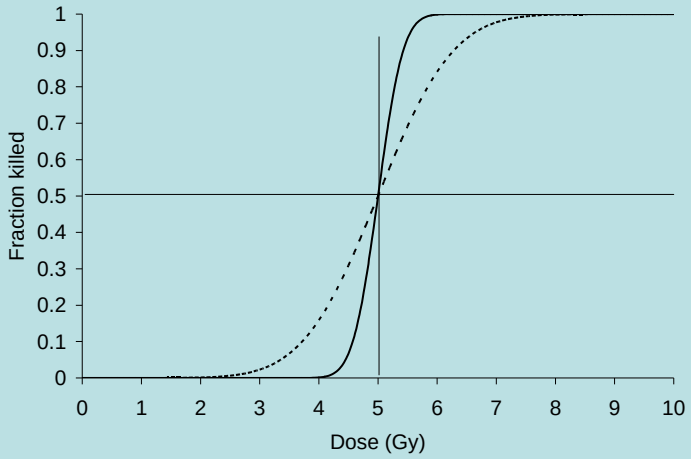
## Radiation Effects -- Heritable

- ICRP 60 assesses risk as 0.013 per Sievert for severe heritable effects for general population
- A doubling dose for effects of 1 Gy has been estimated in several expert committee Reports (BEIR, UNSCEAR)
- Another way of expressing this is 15 defects per million live births following parental exposure to 1 rem (10 mSv) [NCRP 115]
- Chromosome aberrations can be used as crude dosimeter
  - peripheral lymphocytes are used most commonly

## Radiation Effects -- Embryo / Fetus

- Intelligence quotient reduction at 10's of mSv
  - 21 to 29 IQ points per Sievert
- Severe retardation at 100's of mSv
  - rate is about 0.4 per Gy in the 8-15 week group
  - 0.1 per Gy in the 16-25 week group
- Malformations can occur deterministically
  - threshold of 0.05 Gy
- Risk of lethality to fetus
  - about 0.1 Gy

## Radiation Effects -- Deterministic




## Radiation Effects -- Deterministic

- Gastro-intestinal syndrome (nausea, vomiting) >1 Gy whole body
- Arms, legs, hands, and feet can receive large doses (~25 Gy) without leading to death
  - Tissues are often destroyed and amputation is sometimes necessary
  - Seen most commonly in interventional radiography and industrial radiography, especially in the field
- Death to 50% of exposed population in 30 days
  - 3 to 5 Gy ( $LD_{50/30}$ ) whole body

## Radiation Effects -- Deterministic

- Lens opacities (cataracts) > 0.15 Gy per year
  - Recent studies suggest a stochastic component
- Sterility in men (acute dose)
  - 1.5 Gy for temporary sterility
  - 3.5 to 6 Gy for permanent sterility
- Permanent sterility in women - 2.5 to 6 Gy
- Depression of blood forming process - 0.5 Gy
- Skin - erythema, dry and moist desquamation, ulceration - 2 to 25 Gy
- Skin – later effects - pigmentation changes, atrophy, fibrosis

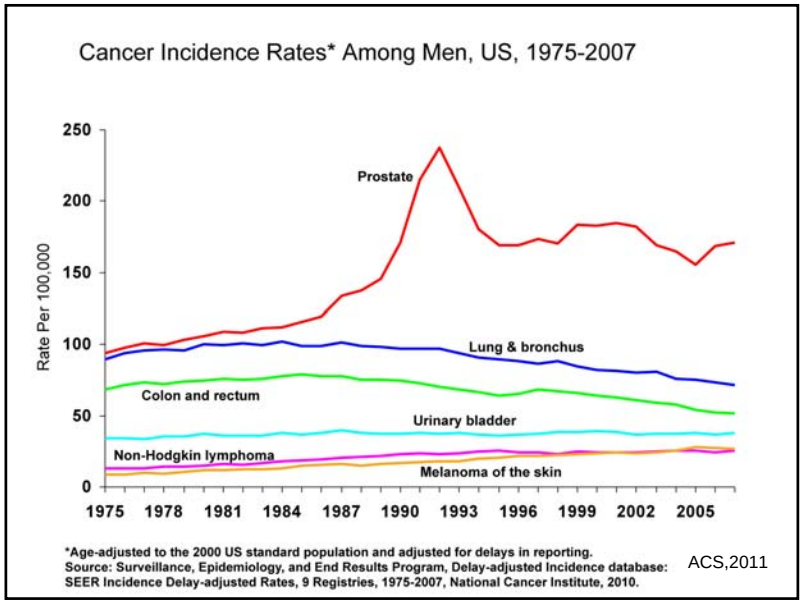
## Example of a Severe Deterministic Effect

Wong, L. et al. N Engl J Med 2004;350:e23

The NEW ENGLAND JOURNAL of MEDICINE

## Stochastic Somatic Effects

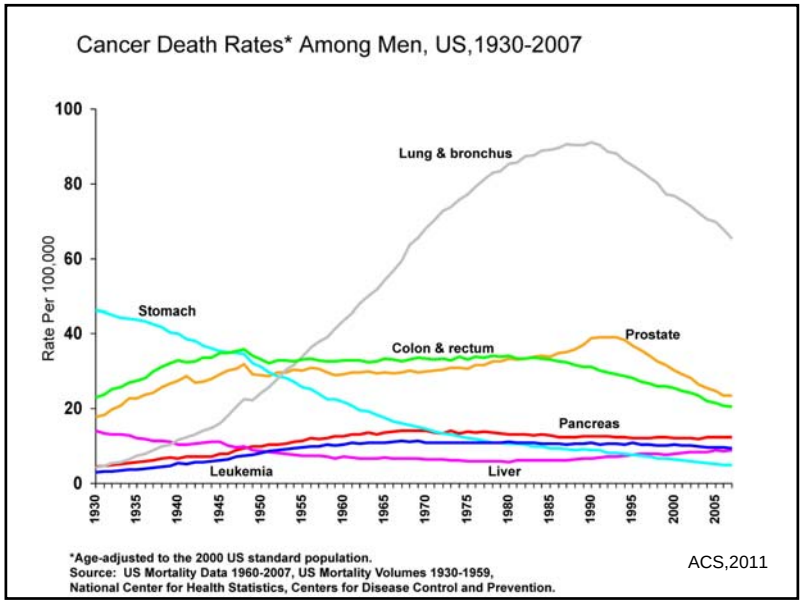
- When a mutation occurs in cells other than germ cells, for example, liver, skin, or blood cells, it might be transmitted to descendant somatic cells if the cell undergoes division
- A somatic mutation cannot be transmitted to or inherited by the next generation of children
- However, the mutations can lead to somatic effects in the irradiated individual
- Cancer is considered to be the most important stochastic effect



ACS,2011

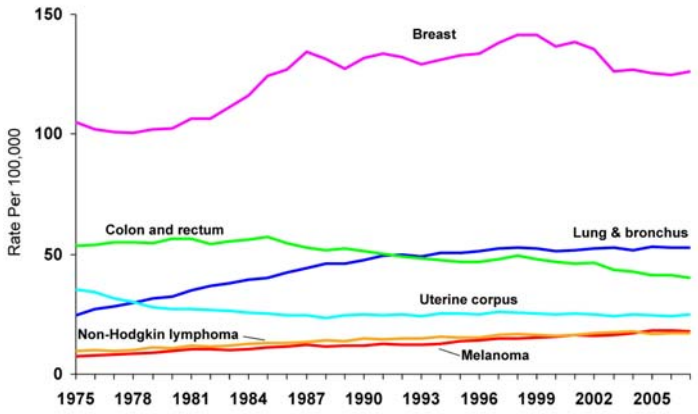
## Radiation Effects -- Cancer

- Cancer etiology is complex and incompletely understood
- Risk depends on kind of cancer, age, sex, kind and amount of radiation, nature of exposure, other carcinogens or promoters, individual predisposition
- Cancers caused by radiation are indistinguishable from other cancers, although research on biomarkers may make distinction possible in future
- Cancer is the cause of about 20% of deaths in the U.S.
- Low level radiation could account for only a small fraction of total cancers



ACS,2011

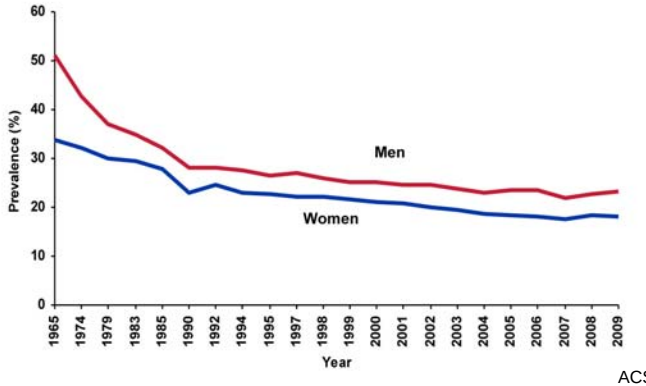
## Cancer Incidence Rates* Among Women, US, 1975-2007




*Age-adjusted to the 2000 US standard population and adjusted for delays in reporting.
Source: Surveillance, Epidemiology, and End Results Program, Delay-adjusted Incidence database: SEER Incidence Delay-adjusted Rates, 9 Registries, 1975-2007, National Cancer Institute, 2010.

ACS,2011

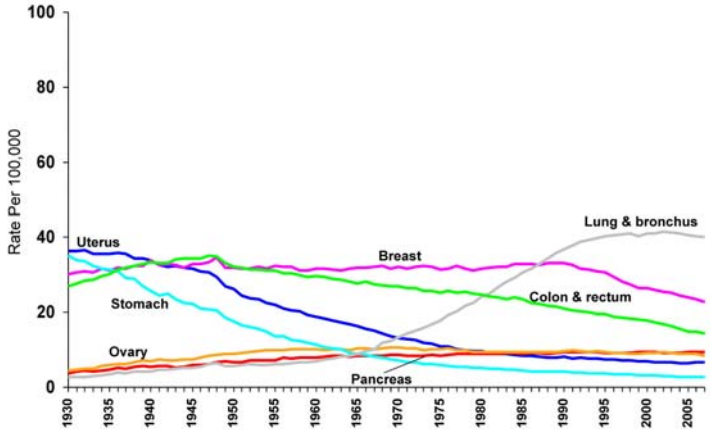
## Trends in Cigarette Smoking Prevalence* (%), by Sex, Adults 18 and Older, US, 1965-2009




ACS,2011

*Redesign of survey in 1997 may affect trends. Estimates are age adjusted to the 2000 US standard population using five age groups: 18-24, 25-34 years, 35-44 years, 45-64 years, and 65 years and over.
Source: National Health Interview Survey, 1965-2009, National Center for Health Statistics, Centers for Disease Control and Prevention, 2010.

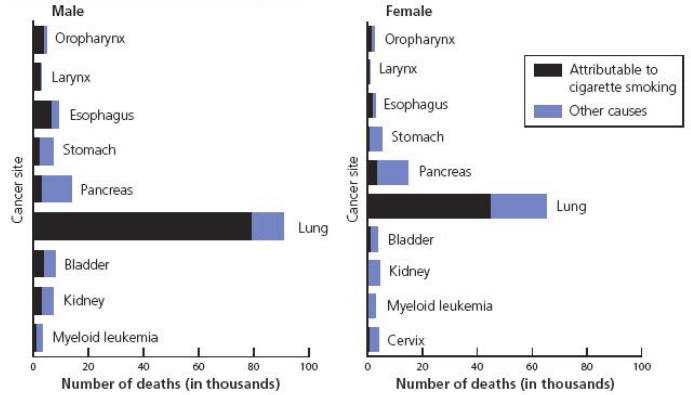
## Cancer Death Rates* Among Women, US,1930-2007




*Age-adjusted to the 2000 US standard population.
Source: US Mortality Data 1960-2007, US Mortality Volumes 1930-1959, National Center for Health Statistics, Centers for Disease Control and Prevention.

ACS,2011

## Annual Number of Cancer Deaths Attributable to Smoking, Males and Females, by Site, US, 1997-2001

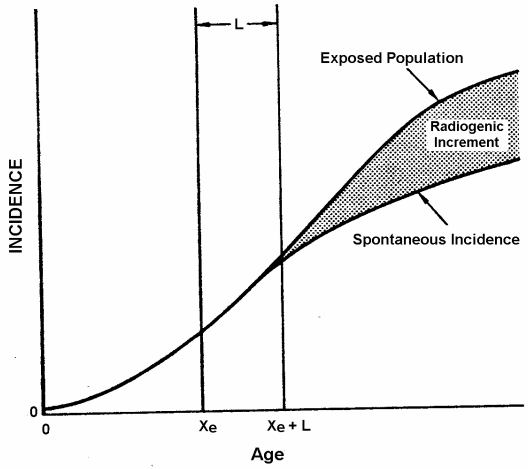



**Source:** Centers for Disease Control and Prevention, Annual smoking-attributable mortality, years of potential life lost, and productivity losses – United States, 1997-2001. *MMWR Morb Mortal Wkly Rep.* 2005;54(25):625-628.

ACS,2008

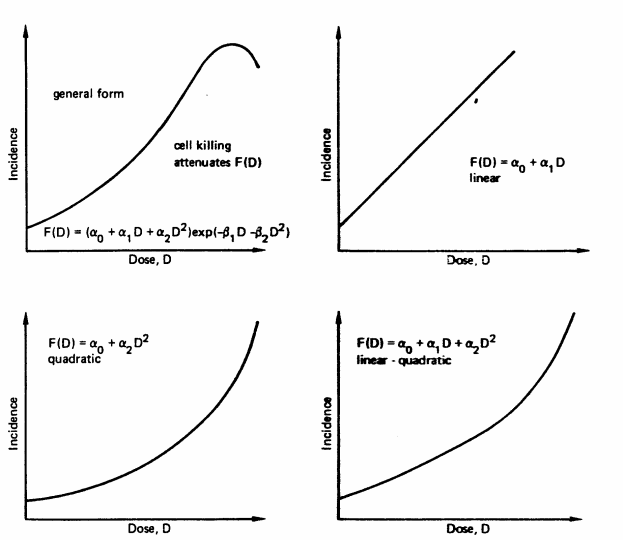
# Radiation Effects -- Cancer

- Cancer in exposed populations is predicted from cellular and animal studies and observed in numerous human epidemiological studies
- Until recently observations were limited to elevated doses, > 0.2 Gy
- More recently, claims have been made in the literature of observations at doses as low as 0.05 Gy in humans and as low as 0.01 Gy for childhood cancer resulting from fetal exposures, but these are controversial




*Xe is age at exposure, L is the minimum latent period

From BEIR III

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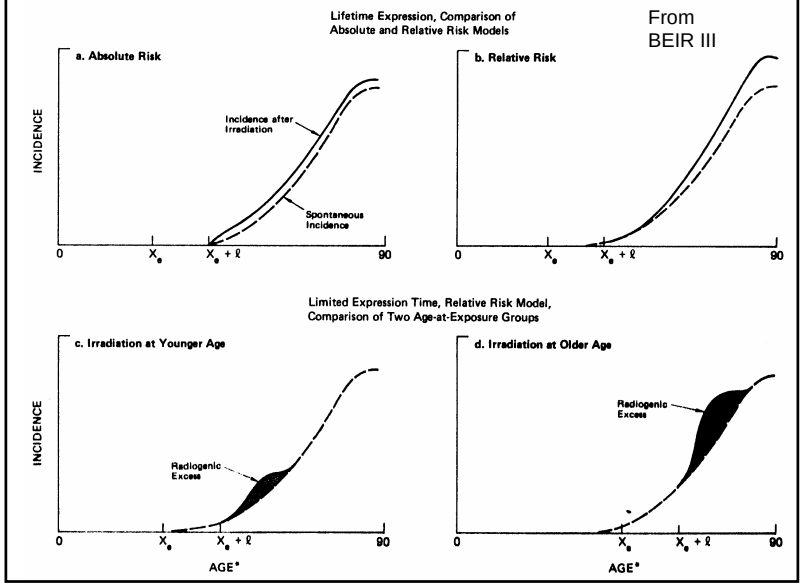



From BEIR III

# Radiation Effects -- Cancer

- Some important data sets are for:
  - Atomic bomb survivors
  - Ankylosing spondylitis patients
  - Canadian fluoroscopy patients
  - Massachusetts fluoroscopy patients
  - New York post partum mastitis
  - Israel tinea capitis (ringworm)
  - Rochester thymus
  - Underground miners (treated separately)

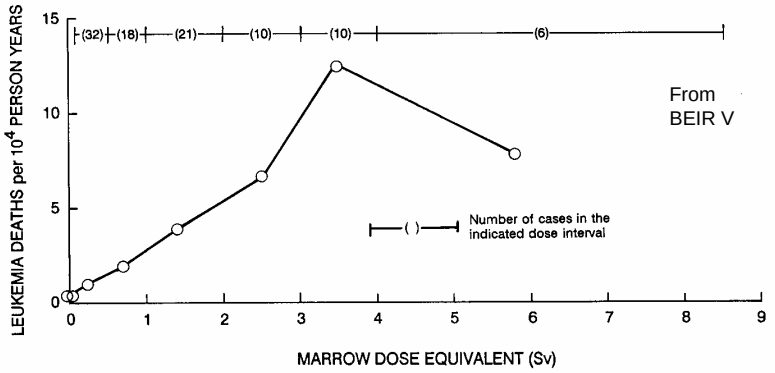
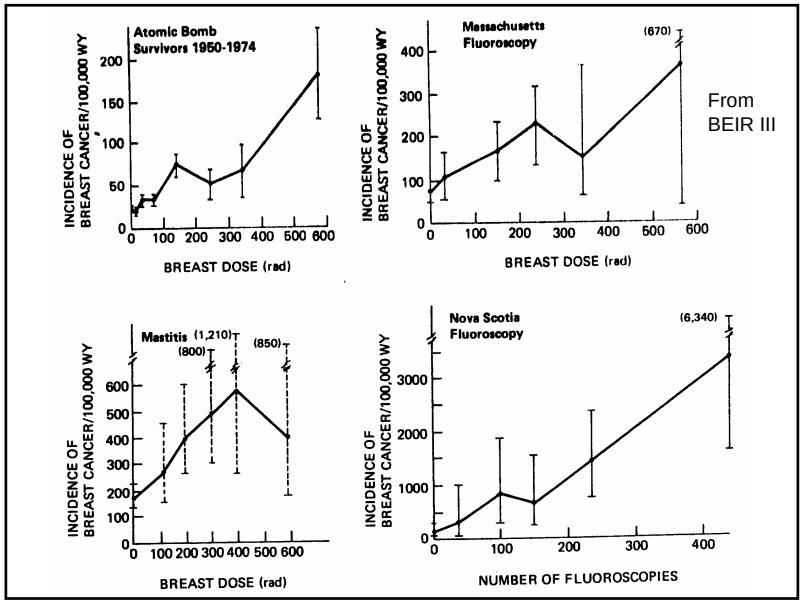
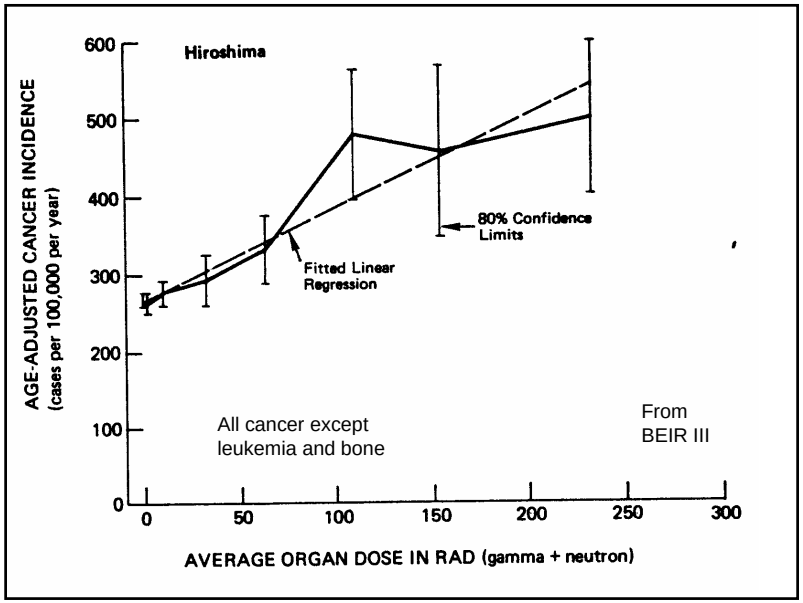


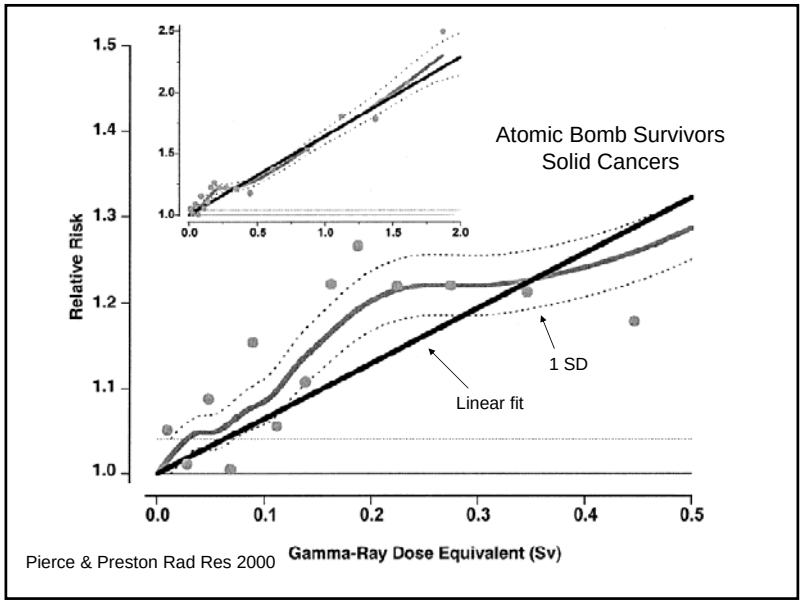

FIGURE 5-1 Cumulative leukemia mortality in Hiroshima and Nagasaki as a function of the estimated dose equivalent to the bone marrow under DS86. By 1985, there were 51 cases in the 0 Sv category and 31 cases in the 0.01-0.1 Sv stratum.

# Radiation Effects -- Cancer

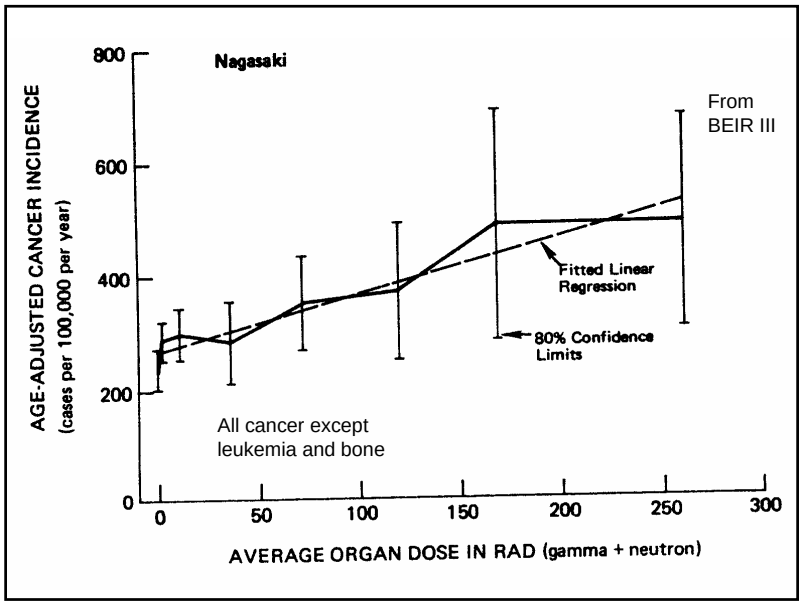
- Atomic bomb survivor data are basis of most quantitative estimates of risk
- Problems include differences in dose and dose rate between atomic bomb victims and most of those exposed occupationally or environmentally
- Further complication results from differences in baseline cancer rates and possible differences in radiation response between Japanese and other populations

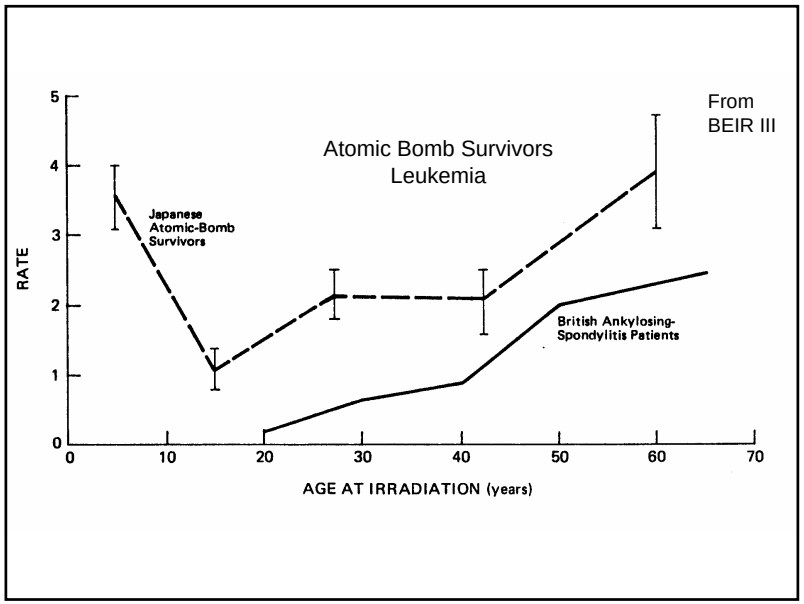


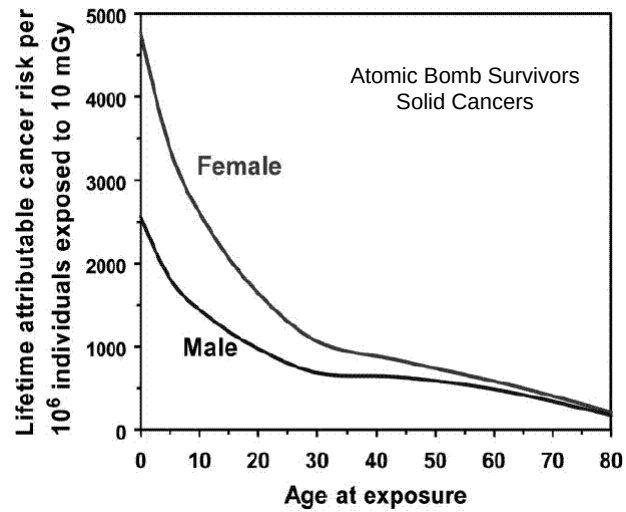



Pierce & Preston Rad Res 2000





Hall & Brenner Brit J of Radiol 2008

## Radiation Effects -- Cancer

- Interpretation of data by National Academy of Science (BEIR V)
  - Natural background (~ 1 mSv/y) may be responsible for about 3% of total cancer
  - Cancer is significant at doses>10mSv for children exposed in uterus
  - Continuous occupational exposure at 10 mSv per year may increase the natural cancer rate by 16%
  - A single exposure to 100 mSv may cause about 4% increase in the natural cancer rate
  - The lifetime absolute mortality risk to exposure of 1 Sv is approximately 0.08
  - Oxford survey of childhood cancer found risk elevated 40% up to age 5 after 10-20 mSv exposures

## Radiation Effects -- Cancer

- Analyses of data have become more sophisticated
- Life table techniques have been used to incorporate age-dependent risk
- Relative risk models have been selected for projections
- A linear quadratic model has been selected for leukemia
- Linear models were chosen for all other cancers

## Radiation Effects -- Cancer

- Interpretation of data by International Commission on Radiological Protection (ICRP Report 60)
  - Lifetime mortality risk to exposed workers can be estimated as 0.04 per Sv (effective dose)
  - Lifetime mortality risk to exposed members of the general population can be estimated as 0.05 per Sv (effective dose)
- Difference between BEIR V and ICRP 60 is that effects of dose rate and age at exposure are considered

## BEIR VII

- The National Academy of Science / National Research Council has prepared a another report on radiation risk, BEIR VI
- Report has drawn some criticism
- A simplified comparison table follows
  - BEIR V and UNSCEAR results have been adjusted to reflect the assumptions made in BEIR VII on dose and dose rate effectiveness factor (DDREF) and on “risk transport” from a Japanese to a Caucasian population
- Differences mainly reflect longer follow-up

## Radon

- Another important source of data relating radiation to cancer are occupational exposures to radon decay products
- Nearly any poorly ventilated cavity within the earth will have elevated radon levels
- Studied occupational groups are primarily
  - Uranium miners
  - Other underground miners
- Some examples follow

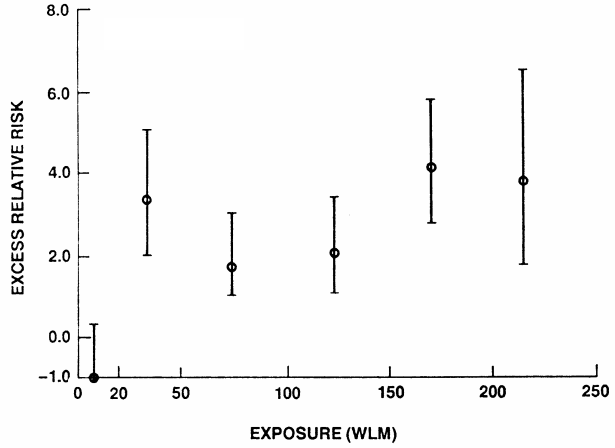
## BEIR VII

Excess deaths for a population of 100,000 of all ages exposed to 0.1 Gy

| Cancer Mortality | BEIR V 1990 | UNSCEAR 2000 | BEIR VII 2005 |
|---|---|---|---|
| Males | | | |
| Leukemia | 110 | 50 | 59 |
| Solid Cancers | 440 | 380 | 410 |
| Females | | | |
| Leukemia | 80 | 60 | 52 |
| Solid Cancers | 490 | 660 | 610 |

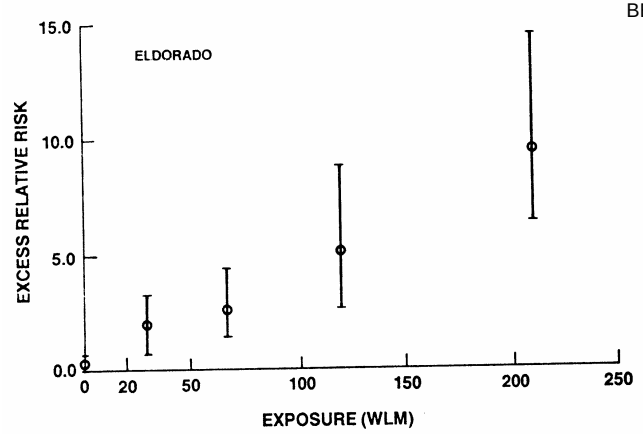
Malberget, Sweden

From BEIR IV

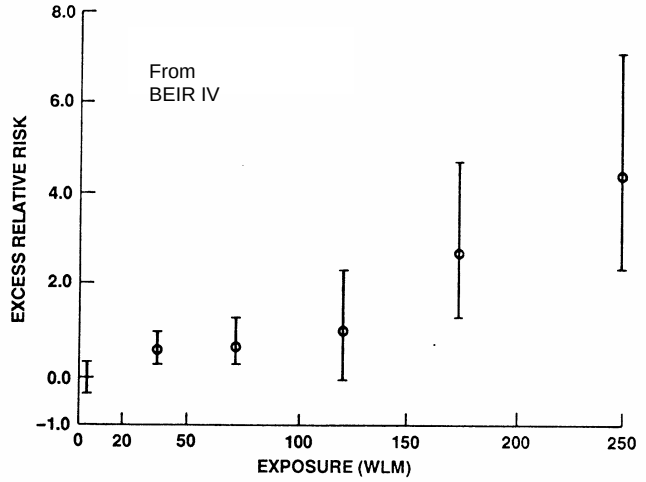


Eldorado Mine, Beaverlodge, Saskatchewan

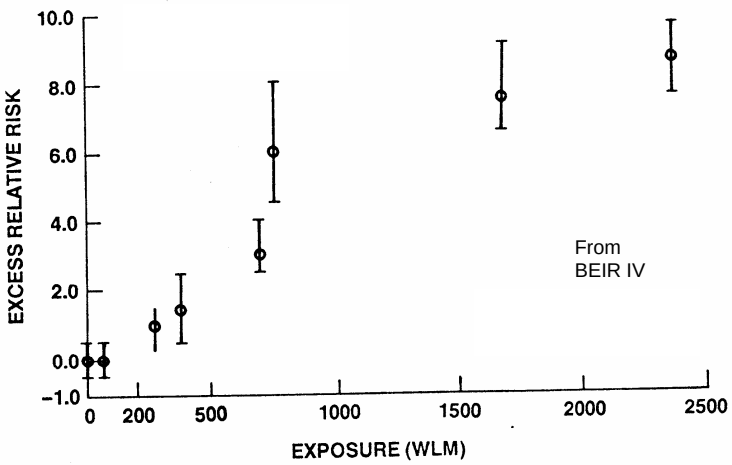
From BEIR IV




Multiple mines, Ontario, Canada



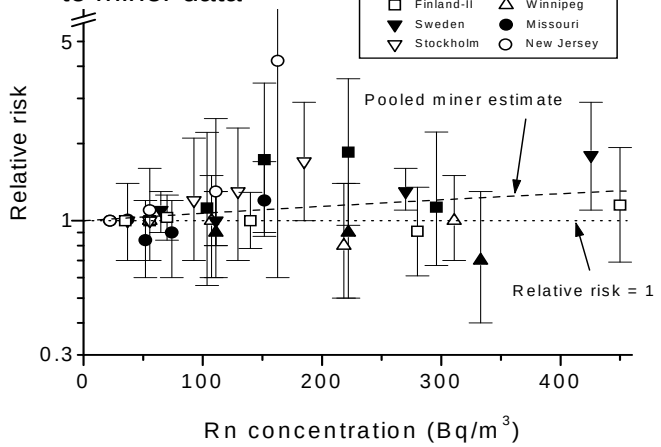

Multiple mines, Colorado Plateau



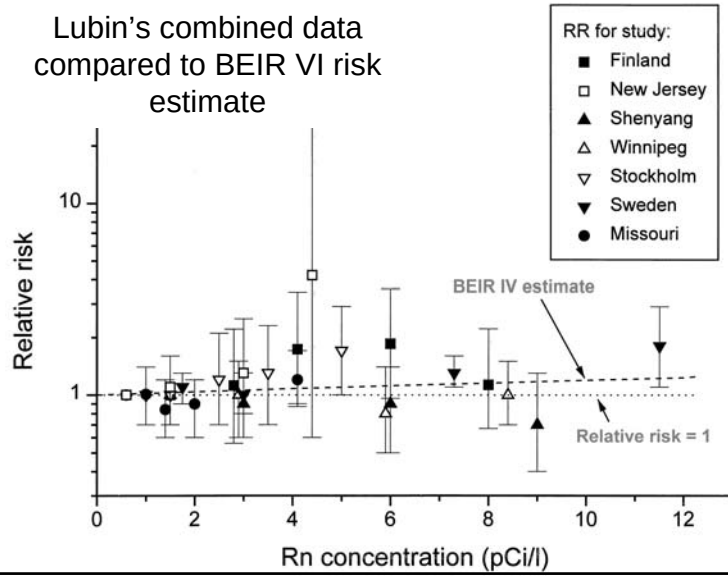

## Residential Radon

- Radon studies have been equivocal and hotly debated
- Lubin has demonstrated a positive correlation between radon exposure and lung cancer by combining the data from 8 case-control studies
- Neuberger and Gesell found no increase among non-smokers
- Recent European studies indicate a demonstrable risk

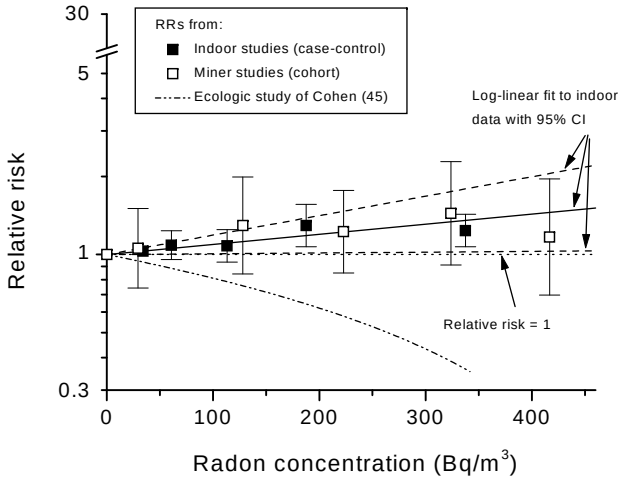
## Lubin's combined residential data compared to miner data




## Lubin's combined data compared to BEIR VI risk estimate



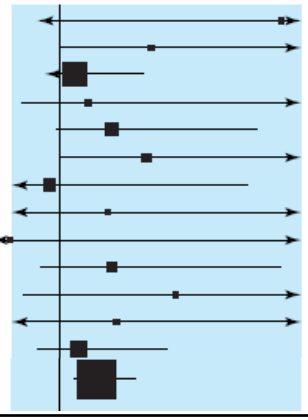

## Lubin's meta-analysis




## European Radon Studies

Darby et al, 2005

| Study (P=0.94 for heterogeneity) | No of lung cancers/ controls | Percentage increase in risk per 100 Bq/m³ |
|---|---|---|
| Austria | 183/188 | 46 |
| Czech Republic | 171/713 | 19 |
| Finland (nationwide) | 881/1435 | 3 |
| Finland (south) | 160/328 | 6 |
| France | 571/1209 | 11 |
| Germany (eastern) | 945/1516 | 18 |
| Germany (western) | 1323/2146 | -2 |
| Italy | 384/405 | 10 |
| Spain | 156/235 | -11 |
| Sweden (nationwide) | 960/2045 | 11 |
| Sweden (never smokers) | 258/487 | 24 |
| Sweden (Stockholm) | 196/375 | 12 |
| United Kingdom | 960/3126 | 4 |
| **Overall, using measured radon** | 7148/14 208 | 8 |



# Expressions of Radon Risk

- 1992 EPA risk assessment of lifetime cancer mortality per pCi/L (per 37 Bq/m$^3$)
  - 2.5 x $10^{-3}$ for smokers
  - 2.5 x $10^{-4}$ for non smokers
  - 14,000 excess lung cancer deaths/year in US assuming an average radon concentration of 1.25 pCi/L (46 Bq/m$^3$)
  - Range estimated to be 7,000 – 30,000
- 1999 NAS/NRC BEIR VI estimate
  - 15,000 or 21,800 excess lung cancer deaths/year depending on choice of model

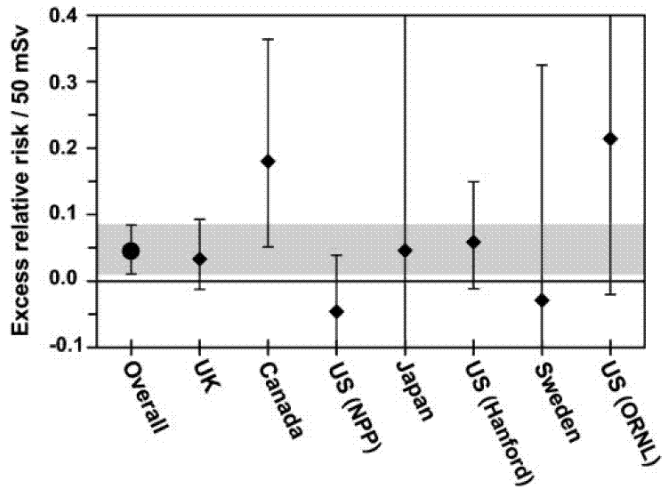
Cardis et al (1995) 3-country nuclear worker study

| Type | Deaths | ERR Sv$^{-1}$ | 90% CI | RR (10 rad) |
|---|---|---|---|---|
| **All Cancers** | **3976** | **-0.02** | **-0.34, 0.35** | **1.00** |
| Except leukemia | 3830 | -0.07 | -0.39, 0.30 | 0.99 |
| All leukemia | 146 | 1.55 | -0.21, 4.7 | 1.16 |
| Except CLL | 119 | 2.18 | 0.13, 5.7 | 1.22 |
| ALL | 11 | -0.89 | <0, 7.3 | 0.91 |
| CLL | 27 | -0.95 | <0, 9.4 | 0.91 |
| AML | 32 | 3.38 | <0, 14.9 | 1.34 |
| CML | 28 | 11 | 2.9, 30.9 | 2.10 |

# Risk from Environmental and Diagnostic Levels of Radiation

- Equivocal or no association between radiation exposure and cancer has been found in several studies of groups exposed to environmental and diagnostic levels of radiation
  - Myeloid leukemia (diagnostically exposed)
  - Nevada Test Site “downwinders”
  - Participants in nuclear weapons tests, US British, and Canadian
  - Leukemia due to global fallout
  - Populations near nuclear installations
  - Exposed workers (except uranium miners)
  - Residential radon exposures

Cardis et al (2005, 2007)15-country nuclear worker study



## High Natural Background Areas


## High Natural Background Areas

- Studies showing insignificant or lower rates of cancer in areas of high natural background have been "explained" in terms of the correlation of high background areas with altitude and the benefits of lower atmospheric pressure
- Studies of populations exposed to environmental levels of radiation serve to provide confidence that risks developed from higher exposures do not underestimate risks at lower exposures

## High Natural Background Areas

No definitive cancer increases in high background areas around the world but chromosome aberrations have been observed

- Guarapari, Brazil - chromosome aberrations
- Iran - chromosome aberrations
- Kerala, India - chromosome aberrations; possibly Down syndrome, but Down syndrome has not been associated with radiation in other contexts; cancer not significant
- Yanjiang County, China – cancer increases and decreases depending on dose, but not significant

## Statements of the National Academy of Sciences

- "Hence expectations based on linear extrapolation from the known effects in man of larger doses delivered at higher dose rates in the range of rising dose-incidence relationship may well overestimate the risks of low-LET radiation at low dose rates and may, therefore be regarded as upper limits of risk for low-level, low-LET irradiation.
- (the possibility of zero is not excluded by the data)." (NAS, 1972)

## Statements of the National Academy of Sciences

- "The Committee does not know whether dose rates of gamma or x rays of about 100 mrads/yr are detrimental to man.
- Any somatic effects at these dose rates would be masked by environmental or other factors that produce the same type of health effects as does ionizing radiation." (NAS, 1980)

## Statements of the National Academy of Sciences

- "Moreover, epidemiologic data cannot rigorously exclude the existence of a threshold in the millisievert (100's of mrem) range.
- Thus the possibility that there may be no risks from exposures comparable to external natural background radiation cannot be ruled out.
- At such low doses and dose rates it must be acknowledged that the lower limit of the range of uncertainty in the risk estimates extends to zero." (NAS, 1990)

## Statements of the National Academy of Sciences

"No increase in the frequency of cancer has been documented in populations residing in areas of high natural background radiation" (NAS, 1990)

## Statements of the National Academy of Sciences

- BEIR VII suggests that linearity is the best model and does not make disclaimers concerning the possibility of a threshold similar to those found in the 1972, 1980 and 1990 reports of the BEIR committees.
- BEIR VII does state that “Because of limitations in the data used to develop risk models, risk estimates are uncertain, and estimates that are a factor of two or three larger or smaller cannot be excluded.”
- BEIR VII defined low dose as 0-100 mSv; 0.1mGy/min over months or a lifetime.