NATIONAL CANCER INSTITUTE

Division of Cancer Epidemiology and Genetics

Rockville, Maryland

Radiation Epidemiology Course

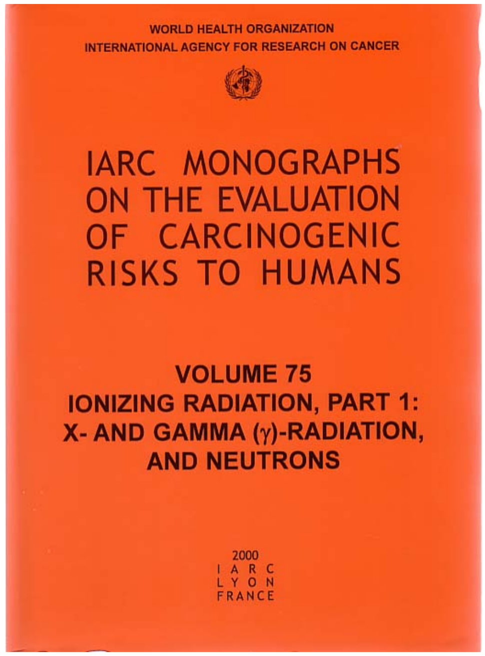
13 May 2004

"Natural Background"

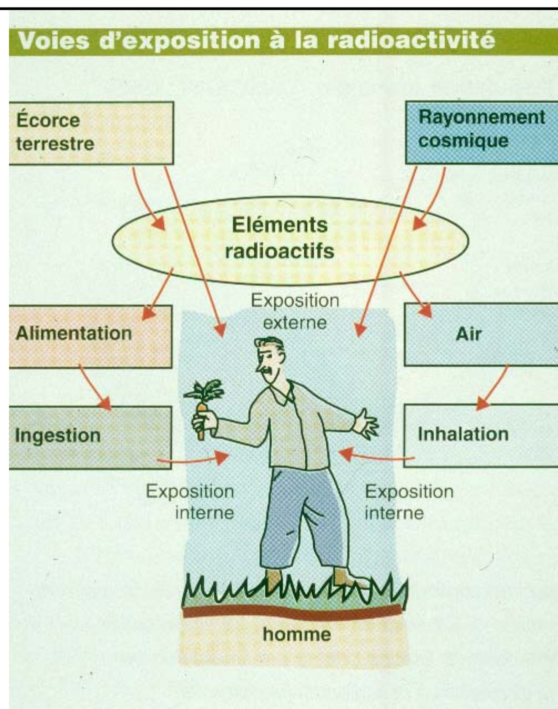
John D. Boice, Jr (IEI, Vanderbilt)

Outline

- Introduction
- Descriptive Epidemiologic (Ecologic) Studies
- Analytic Studies
  - China
  - Childhood Cancer
  - Air Crew
- Other Studies



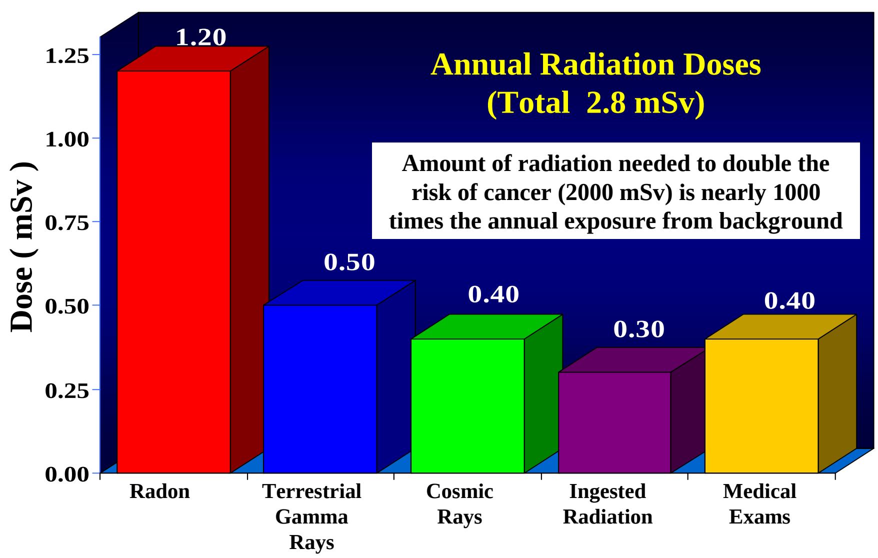
Sources of Radioactivity



Attributable Percents

Risk Factor	Percentage (%)
Tobacco	30
Adult diet / obesity	30
Sedentary lifestyle	5
Occupational factors	5
Family history of cancer	5
Viruses and other biologic agents	5
Perinatal factors / growth	5
Reproductive factors	3
Alcohol	3
Socioeconomic status	3
Environmental pollution	2
Ionizing / ultraviolet radiation	2
Prescription drugs / medical procedures	1
Salt / other food additives / contaminants	1

Harvard Report on Cancer Prevention. *Cancer Causes Control* 7 (suppl 1), 1996



Estimated radiation doses received each year from natural and medical sources of radiation *(UNSCEAR 2000)*

DESCRIPTIVE STUDIES

Descriptive (geographical correlation or ecologic) studies attempt to correlate disease outcomes with data collected on groups of persons in defined geographical areas.

Epidemiological studies of cancer associated with natural background radiation

Country/region (reference)	Characteristics of study
Scotland (Court Brown *et al.*, 1960b)	Mortality from leukaemia in 10 major areas of Sco compared with natural background radiation in fou
Irelan (Allwright *et al.*, 1983)	Ecological study of cancer mortality rates and natu background radiation measured outdoors (*n* = 2756 indoors (*n* = 145); highest and lowest doses differe factor of approximately 5 (McAulay & Colgan, 19 ~370 000 individuals included
United Kingdom (Muirhead *et al.*, 1991; Richardson *et al.*, 1995)	Incidence of childhood leukaemia in 459 county di compared with exposure to indoor radon and γ-radi outdoor γ-radiation
United Kingdom (Gilman & Knox, 1998)	Mortality from childhood solid cancers and leukae 1953 64 (9363 deaths) compared with residence, s radon and terrestrial γ-radiation
France (Tirmarche *et al.*, 1988)*	Cancer mortality in seven 'départements' with high background γ-radiation compared with national rat
Italy (Forastiere *et al.*, 1985)	Lung cancer mortality in 31 villages in volcanic an volcanic areas in central Italy correlated to outdoor γ-radiation and cigarette sales
Italy (Forastiere *et al.*, 1998)	Five controls matched to each of 44 men who had acute myeloid leukaemia compared with indoor rad γ-radiation

Court Brown et al 1960 related mortality from leukemia in Scotland to residence at death and estimated bone marrow dose. Substantial variations in rates in 10 areas likely due to incomplete ascertainment, economic status or bkgd radiation.

IARC *Vol 75*, 2000

Epidemiological studies of cancer associated with natural background radiation (cont)

Country/Region (reference)	Characteristics of study	Main results
Sweden (Stjernfeldt *et al.*, 1987)*	One control chosen for each of 15 cases of childhood cancer, and exposure to indoor ã-radiation and radon measured	No difference in cumulative exposure to γ-radiation or radon daughters; low statistical power
Sweden (Edling *et al.*, 1982)	Cancer incidence in 24 Swedish counties correlated to γ-radiation measured in 1500 homes	Correlation for lung and pancreatic cancer but borderline correlation for leukaemia. Degree of urbanization and smoking most likely influenced the results.
Sweden (Flodin *et al.*, 1990)*	172 controls randomly selected for 86 cases of acu leukaemia; background radiation approximated fro construction materials in homes and work places	
Yangjiang, China (Tao & Wei, 1986; Wei *et al.*, 1990; Chen & Wei, 1991; Wei & Wang, 1994)	Ecological study of cancer mortality rates in thoriu monazite areas and a control area	
Japan Noguchi *et al.*, 1986)	Correlation between background radiation and can mortality during 1950–78	
India (Nambi & Soman, 1987)	Cancer incidence in 5 Indian cities correlated to ba γ-radiation of 0.3–1 mSv	
USA (Mason & Miller, 1974)	Correlation of cancer mortality and altitude in 53 counties at an altitude > 3000 ft [> 900 m]	No significant difference in comparison with US national rates

Epidemiological studies of cancer associated with natural background radiation (cont)

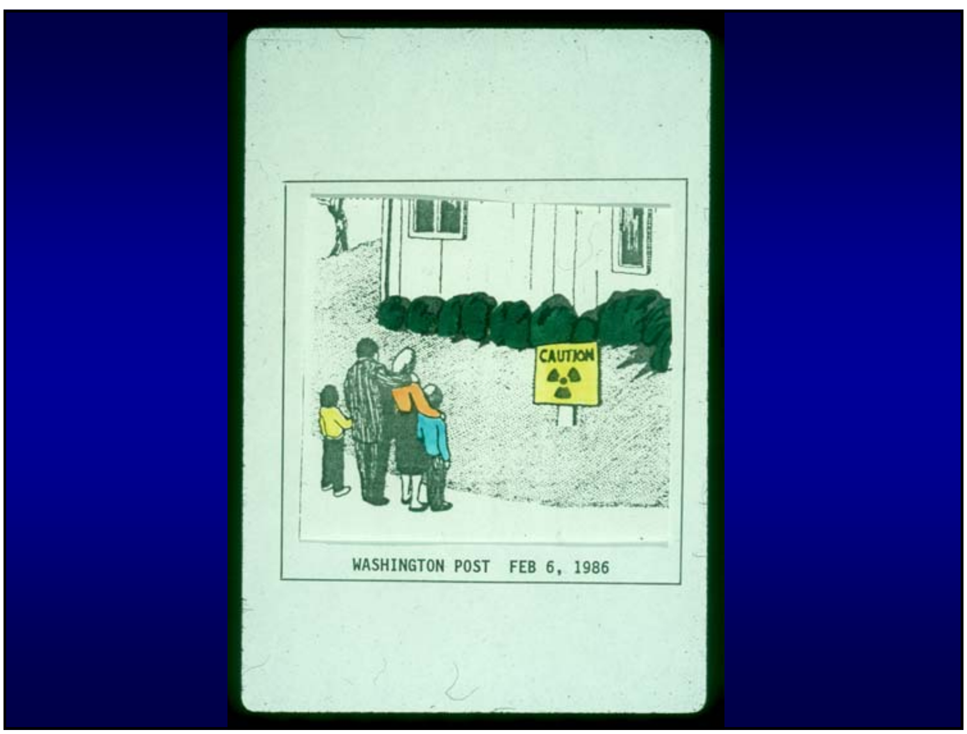
Country/Region (reference)	Characteristics of study	Main results
USA (Amsel *et al.*, 1982)	Relationship between altitude, urbanization, industrialization and cancer in 82 US counties	Generally, deficits in cancer mortality rates at high altitude
Connecticut, USA (Walter *et al.*, 1986)	Cancer incidence related to background radiation, populat density and socioeconomic status in data for 1935–74	
USA (Weinberg *et al.*, 1987)	Correlation between cancer mortality, altitude and background irradiation in US cities at an altitude > 900 ft [> 250 m]	

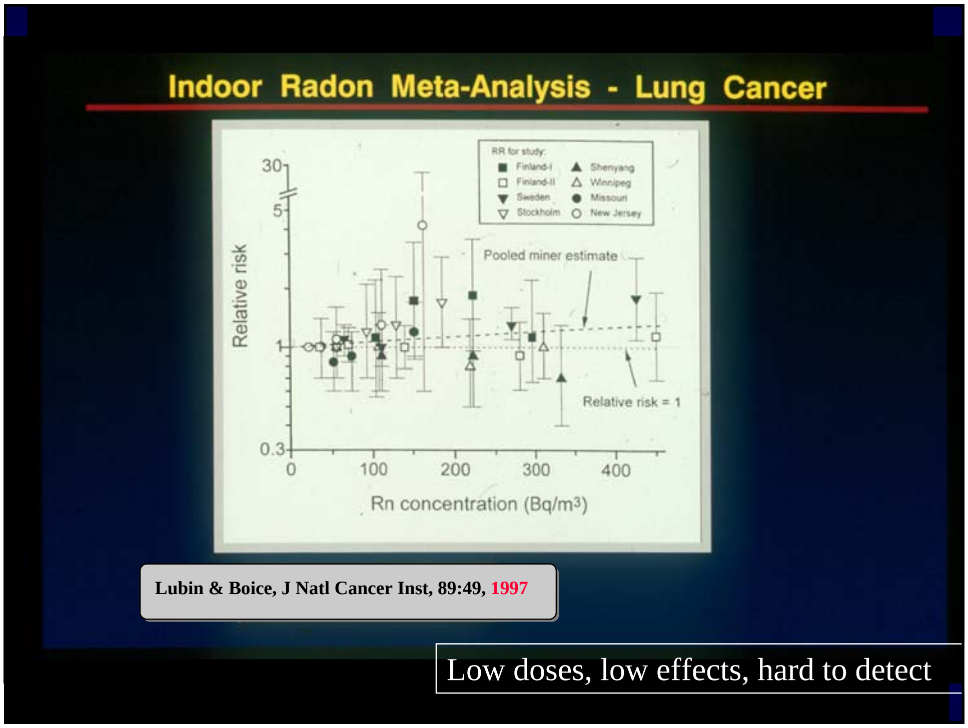
* Not described in text

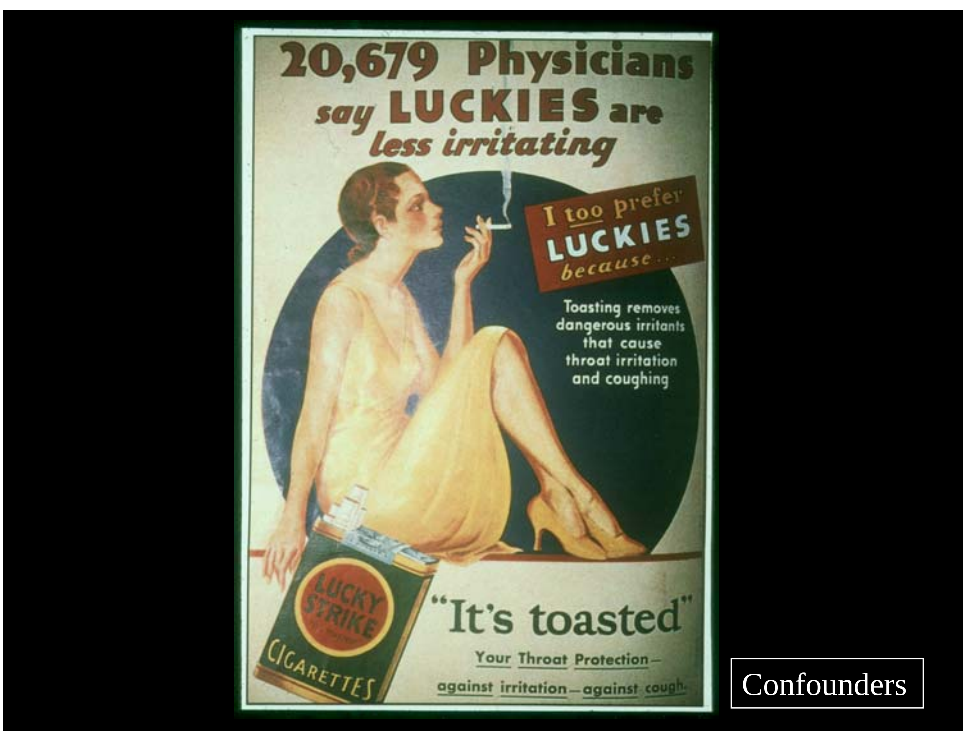
Connecticut Tumor Registry, 1935-74 and gamma rays, 169 towns. No association. Notable were use of incidence rather than mortality, fairly high levels and reasonable variation.

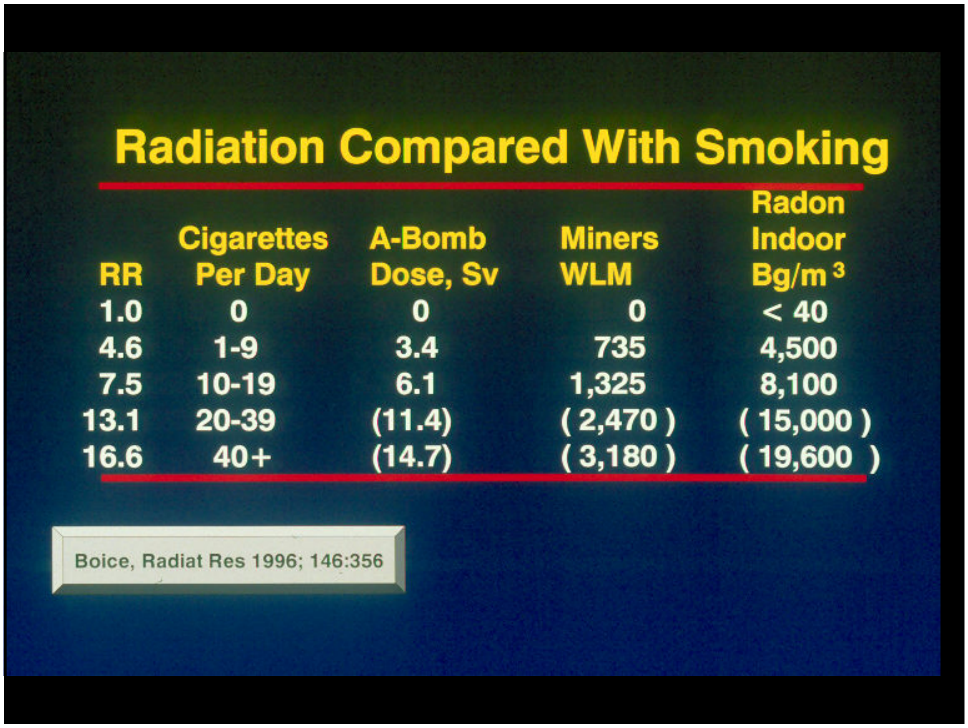
ECOLOGIC STUDIES

Ecological (or geographic correlation) studies are the weakest type of epidemiologic survey. Doses are not known for individuals, exposure is estimated for groups of people averaged over populations, migration and selection of residence can distort inferences, and there is inadequate control of confounding variables.




Indoor Radon Meta-Analysis - Lung Cancer
RR for study:
Finland-I
Finland-II
Sweden
Stockholm
Shenyang
Winnipeg
Missouri
New Jersey
Relative risk
30
5
1
0.3
Pooled miner estimate
Relative risk = 1
0
100
200
300
400
Rn concentration (Bq/m3)
Lubin & Boice, J Natl Cancer Inst, 89:49, 1997
Low doses, low effects, hard to detect


20,679 Physicians
say LUCKIES are
less irritating
I too prefer
LUCKIES
because...
Toasting removes
dangerous irritants
that cause
throat irritation
and coughing
LUCKY STRIKE
CIGARETTES
"It's toasted"
Your Throat Protection—
against irritation—against cough.
Confounders



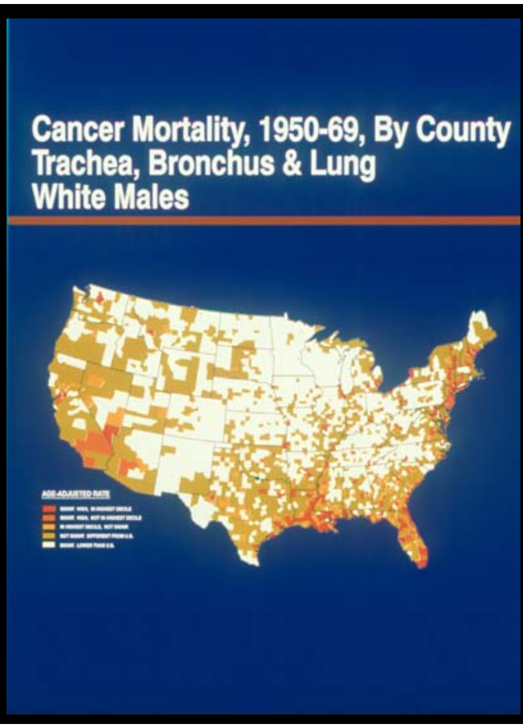
Radiation Compared With Smoking

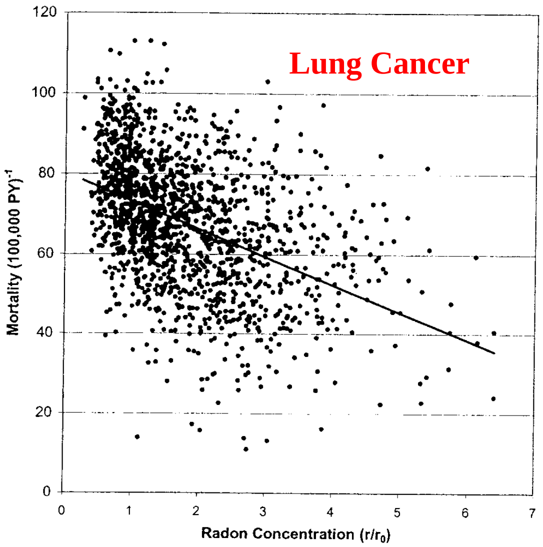
RR	Cigarettes Per Day	A-Bomb Dose, Sv	Miners WLM	Radon Indoor Bg/m^3
1.0	0	0	0	< 40
4.6	1-9	3.4	735	4,500
7.5	10-19	6.1	1,325	8,100
13.1	20-39	(11.4)	(2,470)	(15,000)
16.6	40+	(14.7)	(3,180)	(19,600)

Boice, Radiat Res 1996; 146:356

ECOLOGIC -- RADON

Another ecologic study that has received considerable attention is one showing a decrease in lung cancer mortality over mean radon levels within U.S. counties (Cohen, 1993). There has been considerable discussion in the literature on the potential pitfalls associated with such data where smoking and migration cannot be determined and for which individual exposures to indoor radon are unknown (NAS, BEIR VI, 1999).

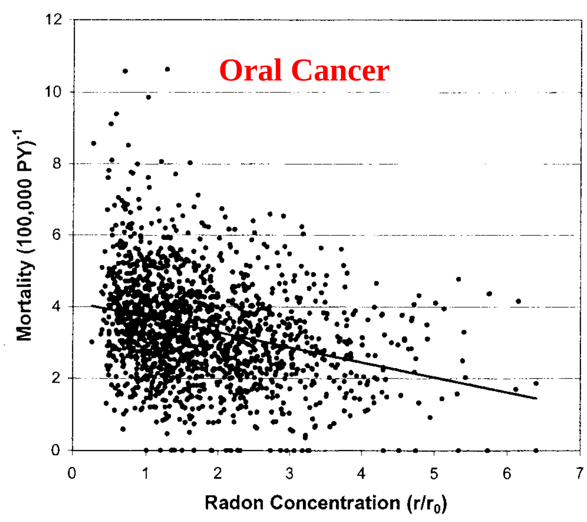




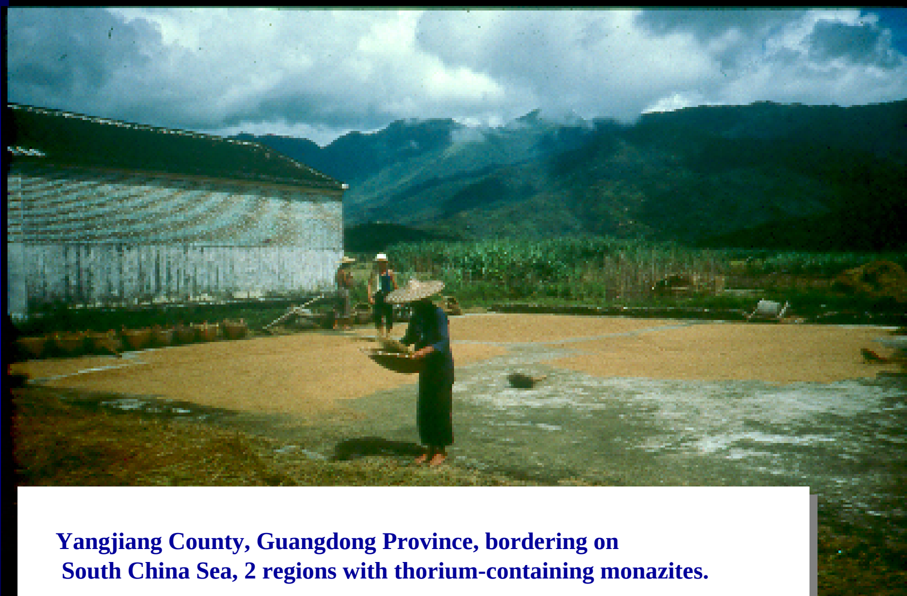
County lung cancer mortality (1970-1994) for white males vs. measured average radon concentration (Puskin, *Health Phys* 2003).

ECOLOGIC -- RADON 3

Recently, Puskin concluded that the negative association between radon levels and lung-cancer mortality can be largely explained by a negative correlation between smoking and radon levels. He found an inverse association for other smoking-related cancers that are not linked to radon exposure (Health Phys 2003).



County oral cancer mortality (1970-1994) for white males vs. measured average radon concentration (Puskin, *Health Phys* 2003).



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

Natural Background
China Mortality

	High Background		Control
Number (1979-86)	80,640		32,651
Doses			
Effective (mSv y^{-1})	6.4		2.4
Radon (WLM y^{-1})	0.38		0.16
Deaths (1979-95)			
Lung	62		32
Leukemia	33		11
All cancer	710		293
RR (95% CI)			
Lung	0.81	(0.53-1.24)	
Leukemia	1.12	(0.56-2.22)	
All	0.99	(0.87-1.14)	

Boice. *J Radiol Prot* 22:102-4 2002

Low power to reject predicted risk

Natural Radiation (UNSCEAR 2000)
China

Study	Strengths	Limitations
Yangjiang [T12, A11, Z2, S35, T25, T26]	• Large cohorts in high background and control areas • Stable population • Extensive dosimetry for region • Assessment of potential confounders	• Mortality follow-up • Small numbers for some cancer types • Low doses

Natural Background China, Thyroid

	High Background		Control
Number examined	1,001		1,005
Thyroid dose (cGy)	14.0		5.0
Nodular disease	9.5%		9.3%
Single nodules	7.4%		6.6%
RR (95% CI)	1.13	(0.8-1.6)	

Wang et al. *J Natl Cancer Inst*, 82:478, 1990

Table 6. Average laboratory values from serum and urine tests of women residing in high background radiation and control areas in China

Test	Background radiation		*P* value
	High	Control	
Serum T4 (μg/dL)	7.65 ± 0.10	7.70 ± 0.14	.770
Serum T3 (ng/mL)	1.05 ± 0.02	1.04 ± 0.03	.750
Serum TSH (μU/mL)	*	*	—
Serum AMA (% binding)	8.63 ± 0.50	8.36 ± 0.40	.670
Urinary iodine-creatinine ratio (μg/g)	132.20 ± 5.96	93.85 ± 5.25	<.001
Urinary iodine (μg/dL)	6.62 ± 0.24	8.10 ± 0.72	<.001
	No. of subjects tested		
Thyroid assays	289	261	
Urinary iodine	152	127	

Wang et al. *J Natl Cancer Inst*, 82:478, 1990

No difference in thyroid function

Table 7. Summary of cytogenetic findings among women residing in high background radiation and control areas in China

Characteristic	Background radiation		*P* value
	High	Control	
No. of subjects	100	100	
No. of metaphases scored	10,000	10,000	
Proportion of metaphases* (± SE) with			
Stable aberrations†	0.29 (0.06)	0.18 (0.04)	.14
Translocations	0.14 (0.03)	0.12 (0.04)	.69
Inversions	0.07 (0.03)	0.05 (0.02)	.55
Deletions	0.09 (0.04)	0.02 (0.01)	.10
Unstable aberrations‡	0.16 (0.04)	0.06 (0.02)	.04
Total, stable + unstable aberrations	0.44 (0.07)	0.23 (0.05)	.02

Wang et al. *J Natl Cancer Inst*, 82:478, 1990

Chromosomal differences

Outline

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  - **Childhood Cancer** ←
  - **Air Crew**
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UK Childhood Cancer Study - Gamma

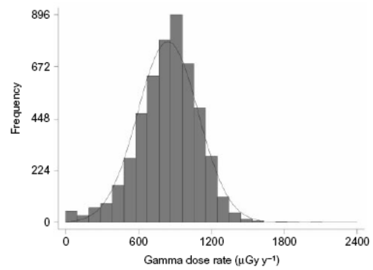


Figure 2 Frequency of absorbed dose rate in control houses.

"There is no indication of increased risk with increasing dose rates either in matched or unmatched analyses, with or without adjustment for deprivation."

Dose Rate(uGy/yr)	Cases	Controls	OR	95% CI
<650.3	418	742	1	–
650.3 – <798.5	436	724	1.10	0.90 – 1.35
798.5 – <916.2	459	702	1.17	0.95 – 1.44
916.2 – < 1045.3	423	737	1.04	0.84 – 1.29
>=1045.3	429	732	0.97	0.78 – 1.21

Br J Ca 86, 1727, 2002

NCI Childhood Leukemia - Radon

	Radon concentration, Bqm^{-3}			
	<37	37–73	74–147	≥148
	Matched analysis			
No. of case subjects	116	90	48	27
No. of control subjects	120	74	59	28
Mean	20.1	53.7	97.4	300.7
RR (95 CI)‡	1.00 (reference)	1.22 (0.8–1.9)	0.82 (0.5–1.4)	1.02 (0.5–2.0)

"Conclusions: **In contrast to prior ecologic studies, the results from this analytic study provide no evidence for an association between indoor radon exposure and childhood ALL."**

Lubin et al. *J Natl Cancer Inst*, 90:294, 1998

UK Childhood Cancer Study - Radon

Figure 1 Regional study centres of the UKCCS

	Unadjusted for deprivation	
Radon level (Bq m^{-3})	OR[a]	95% CI
Pre-defined groupings		
0–24	1.00	–
25–49	**0.82**	**0.71 – 0.95**
50–99	0.89	0.71 – 1.10
100–199	**0.56**	**0.37 – 0.87**
200+	0.91	0.47 – 1.75
Trend Test	χ^2=9.39	P=0.002

"The study suggests that control houses had more features, such as double glazing and central heating, leading to higher radon levels than case houses. Further, case houses have features more likely to lead to lower radon levels, e.g. living-rooms above ground level. Consequently the case – control differences could have arisen because of differences between houses associated with deprivation that are not adequately allowed for by the deprivation score."

Br J Ca 86, 1721, 2002

" Apparently, flying no higher than 1,000 feet saves
Air travelers from the perceived ravages of cosmic radiation."

ESTIMATED EXPOSURE TO AIRCREW

	mSv per year Ave.	Max.
Friedberg (1989); FAA (1990)	0.2 - 9.1	---
UK (Hughes, 1989)	2	---
Concorde (Davies, 1993)	3 - 6	6 - 10
Air France (Montagne, 1993)	2 - 3	---
Lufthansa (Regulla, 1993)	3 - 5	---
Australia (Wilson, 1994)	1 - 1.8	3.8
Finnair (Pukkala, 1995)	2 - 3	---
Air Canada Pilots (Band, 1996)	6	---
Canadian Aircrew (Tume, 1998)	0.7 - 4.2	---

Air crew on high altitude flights may receive roughly 1 - 10 mSv annually

4

ICRP 60, 1991: 33-34

… the Commission recommends that there should be a requirement to include exposures to natural sources as part of occupational exposure only in the following cases:

…

(c) Operation of jet aircraft

…

Case (c) will relate principally to the aircraft crew, but attention should also be paid to groups such as couriers who fly more often than other passengers.

5

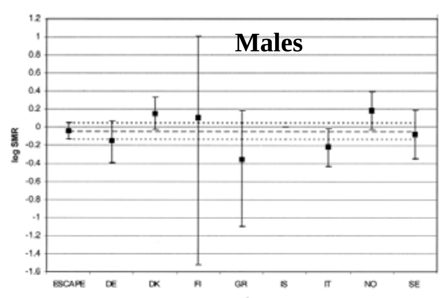
Airline Crew

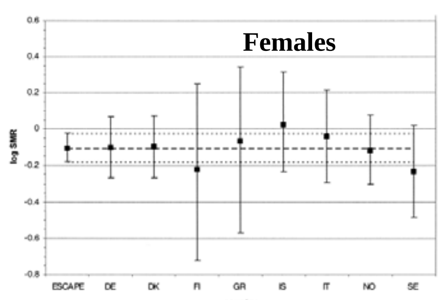
Seven Countries – pilots (Radiat Env Bioph, 2004)
Eight Countries - air crew (AJE 158:35, 2003)
Finland (BMJ 311:649, 1995)
Iceland (CCC 12:95, 2001)
Norway (Int J Epi 30:825, 2001)
California (CCC 13:317, 2002)
Canada (AJE 143:137, 1996)
Italy (Int J Occup Environ Health 8:87, 2002)
Germany (AJE 156:556, 2002)
Sweden (Aviat Space Environ Med 73:2, 2002)
Denmark (Lancet 354:2029, 1999)
Overview (Boice, Health Phys 79:576, 2000)

Airline Attendants - Europe
Cancer Mortality
(AJE 158:35, 2003)

Males	SMR	95% CI
All cancer	0.90	(0.7 -1.1)
Leukemia	0.78	(0.0 -4.7)
Melanoma	1.93	(0.7 -4.4)
AIDS	19.6	(15 - 23)
Aircraft accidents	24.7	(13.8-41)

Females	SMR	95% CI
All cancer	0.78	(0.7-1.0)
Breast	1.11	(0.8 -15)
Aircraft accidents	59.0	(39 - 87)





Breast Cancer Among Female Aircrew

Country	Number	Outcome	Obs	Exp	Obs/Exp	95% CI
Norway	3,105	Incidence	38	34.0	1.1	0.8-1.5
Germany	16,014	Mortality	24	18.5	1.3	0.7-2.2

"Postponement of childbearing is common in this occupational group"

Blettner et al, *Am J Epidemiol* 156:556, 2002

Haldorsen et al, *Int J Epidemiol*, 30:825, 2001

Leukemia – Cockpit Crew

Dose (mSv)	Number	SMR	95% CI
0–	5	1.08	0.34 - 2.5
5.0–	7	1.71	0.69 - 3.7
15.0–	4	1.09	0.29 - 2.9
25.0+	3	1.05	0.22 - 3.2

Langmer et al, *Radiat Envir Biophy* 42:247, 2004

CONCLUSIONS

- Groups exposed to increased natural background
- No clear patterns except
  - Low overall mortality
  - High risk of aircraft accidents
- Comparison group important (bias)
  - SES
  - Lifestyle

- Potential confounders
  - Cabin pollutants
  - Engine fuel / emissions
  - Other
- Low statistical power (exposure & assessment)
  - Limited range of cumulative doses
  - QF (weighting factor) incorporated for neutrons/protons

20

IEI

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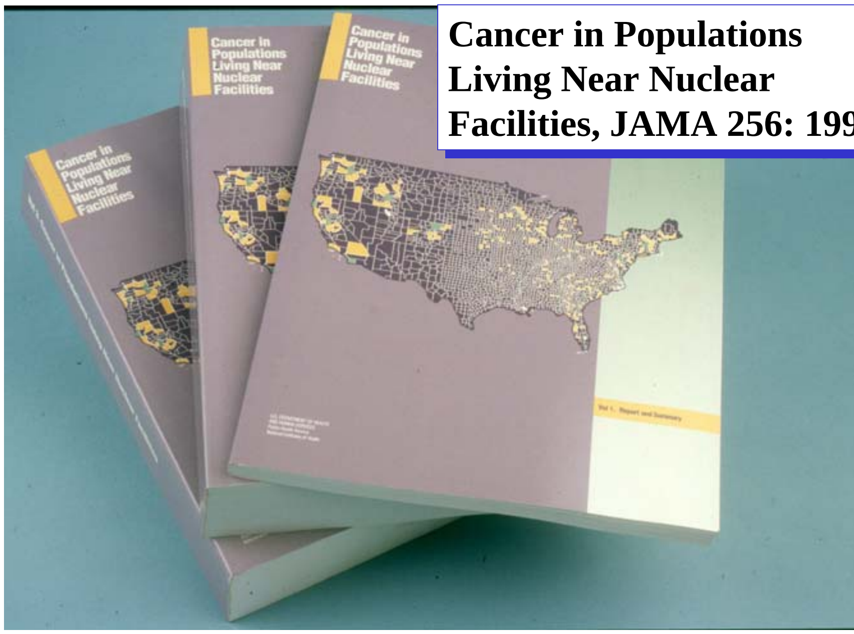
SELLAFIELD, U.K. - Descriptive

Preconception Radiation
Leukemia / Non-Hodgkin's Lymphoma < 25 yr

Study		RR at 100 mSv	(95% CI)
Sellafield (U.K.)	Gardner (BMJ 300:423, 1990) Dickinson (Int J Ca 99:436, 2002)	6.4 1.6	(1.6- 26.3) (1.0-2.2)
British Rad Workers	Draper (BMJ 315:1181, 1997)	0.92	(0.28-2.98)
Ontario Rad Workers	McLaughlin (BMJ 307:959, 1993)	0.75	(0.07-3.31)
USA Rad Workers Hanford, Idaho Oak Ridge	Sever (NIOSH 1997) Wakeford (J Radiol Prot 20:331, 2000)	0.75	(<0.75-3.5)
Japanese Atomic Bomb Survivors	Yoshimoto (Am J Hum Genet 46:1041, 1990)	0.76	(0.31-1.03)

Little, J Radiol Prot 16: 25, 1996

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

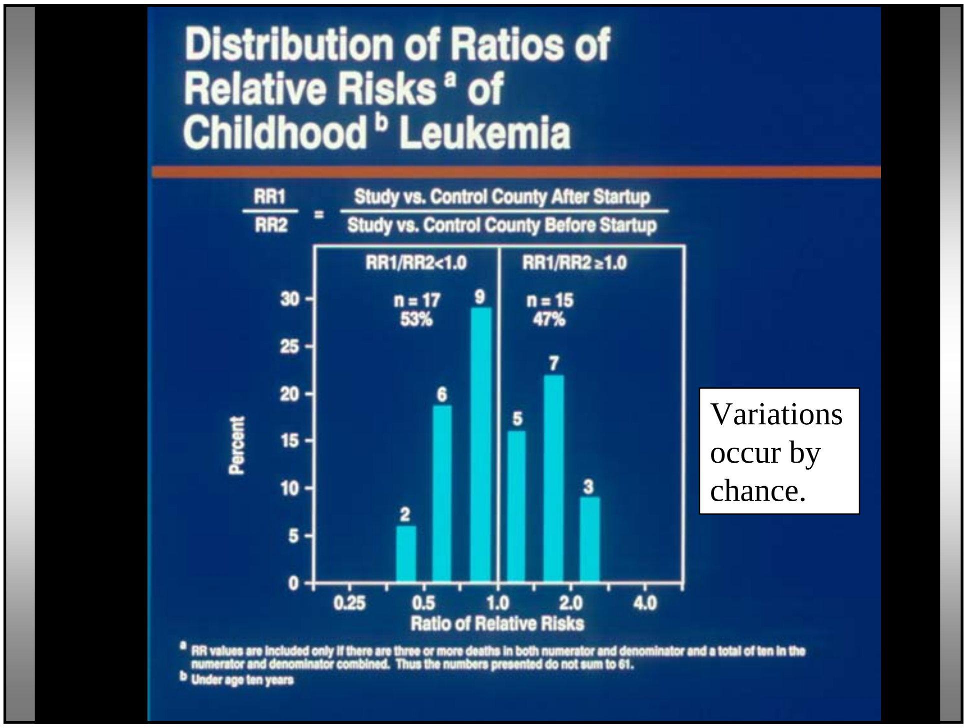


Overall Relative Risks

Disease	Before Startup	After Startup
Leukemia		
- Childhood	1.08	1.03
- All Ages	1.02	0.98

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

Time Pattern



Environmental Exposures (not UNSCEAR 2000) Nuclear Facilities

Study	Strengths	Limitations
Nuclear Facilities correlation Study	• Large numbers in most studies • Protracted exposures over many years	• Uncertainties in assessing exposures (unknown) • Migration (in and out) • Confounding possible since no risk factor information on individuals • Doses small for most subjects

Final Comment

- Most of the estimated population risk of radiation-induced cancers comes from natural background sources.
- The overwhelmingly negative results of studies of natural background radiation suggest that the carcinogenic risk of low natural levels of radiation is unlikely to be substantial (IARC 2000)