Radiation Epidemiology Course
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Lung Cancer Risk and Radon Exposure

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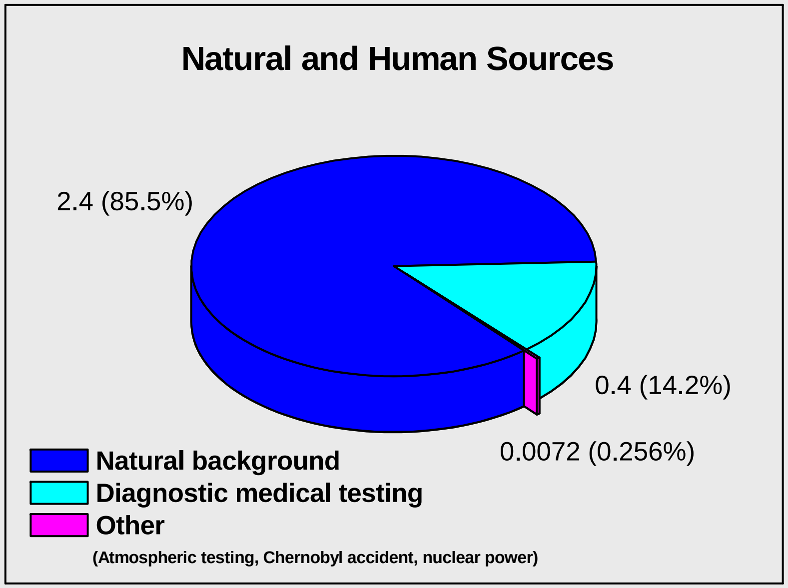
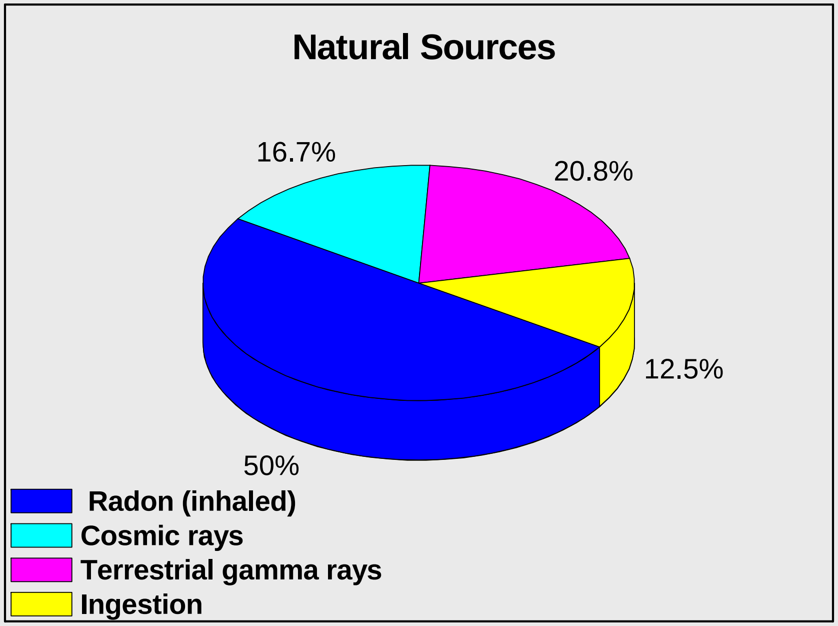
Lung Cancer Risk and Radon Exposure

- Background
- Studies of underground miners
- Studies of radon in houses
- Public health burden
- Future

Annual Per Capita Effective Dose (mSv)



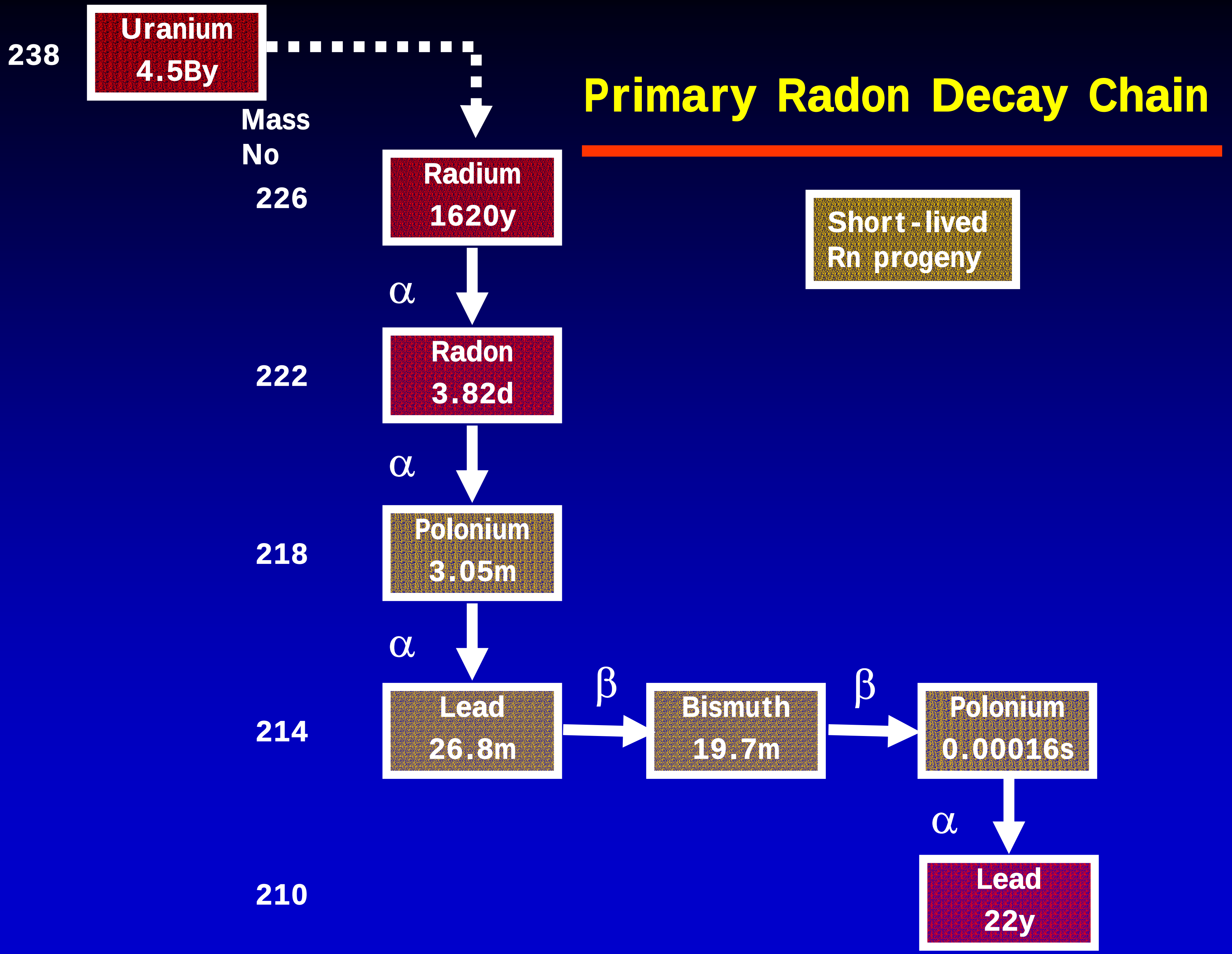


UNSCEAR, 2000

What is radon (^{222}Rn)?

- Noble gas
- Decay product of ^{238}U and ^{236}Ra
- Alpha emitter
- Half-life 3.8 d
- High LET radiation

Primary Radon Decay Chain



Units of Concentration/Exposure

- **Mines: radon and progeny**
  - **1 WL: any combination of short-lived decay products resulting in 1.3x10^{5} MeV of " energy**
  - **WLM (Working Level Months):**

    3 **WL_i x dur_i with duration in units of 170 hrs**

- **Residential studies:**
  - **1 becquerel/m^{3} = 1 decay/sec/m^{3} (SI units)**
  - **1 Curie/l = 3.7 x 10^{10} decays/sec/l (old units)**
  - **37 bq/m^{3} = 1pCi/l**
  - **at equilibrium: 37 Bq/m^{3} = 1 pCi/l = 0.01 WL**

Measuring Radon in Homes

	Concentration		Exposure (25y)
	Bq/m^3	pCi/l	WLM
EPA Action Level 5% of houses	148	4	20
			3 WL_i x dur_i
U.S. homes (mean)	46	1.2	
	37	1	5
1 decay/sec/m^3	1		

Computing Exposure in Houses

1 yr @ 37 Bq/m³ (at equilibrium):

0.01 WL x (365x24/170) = 0.52 WLM/yr

and @ 40% equilibrium:

0.01 WL x (365x24/170) x 0.40 = 0.21 WLM/yr

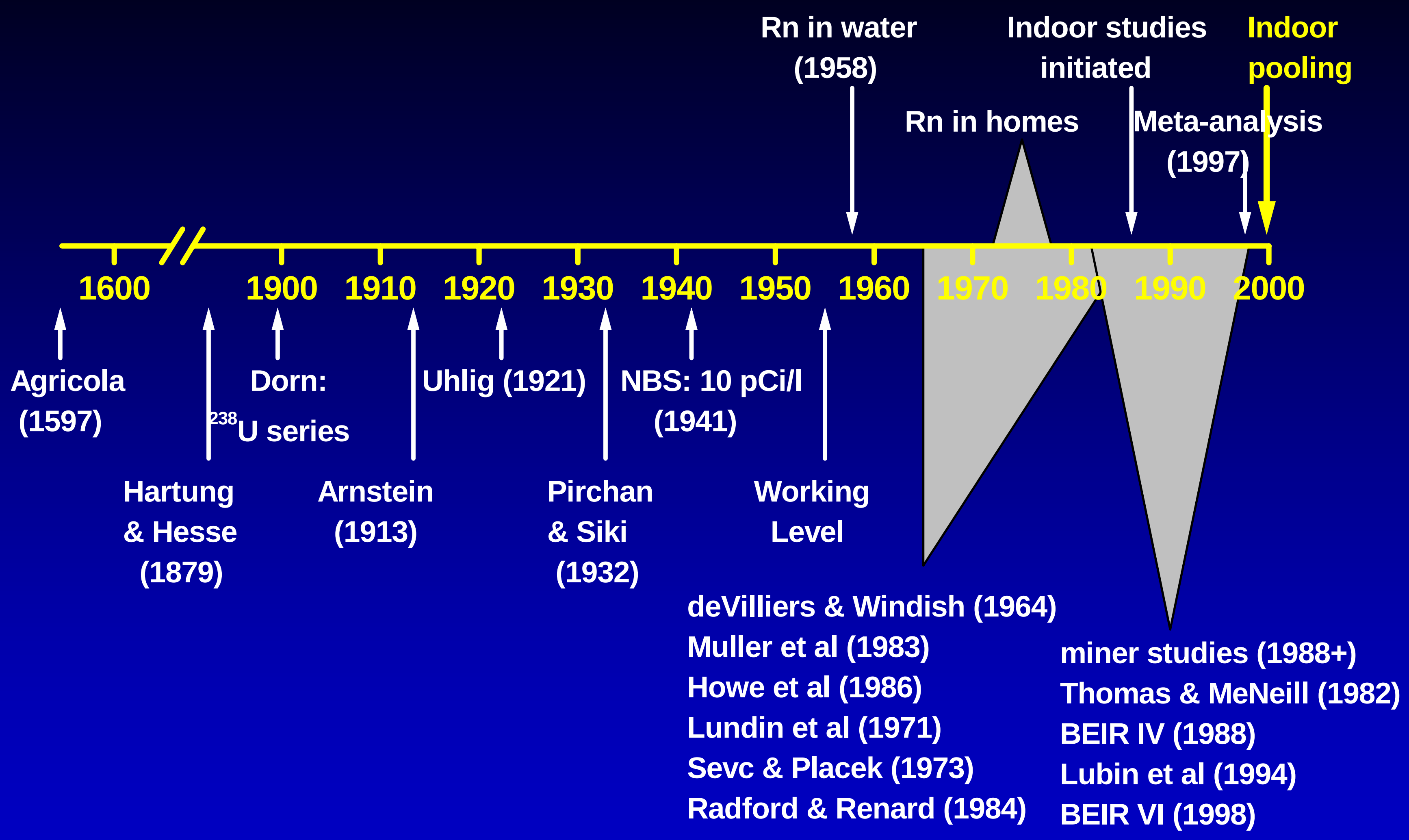
and with 75% occupancy:

0.01 WL x (365x24/170) x 0.40 x 0.75 = 0.15 WLM/yr

for a 25y exposure period:

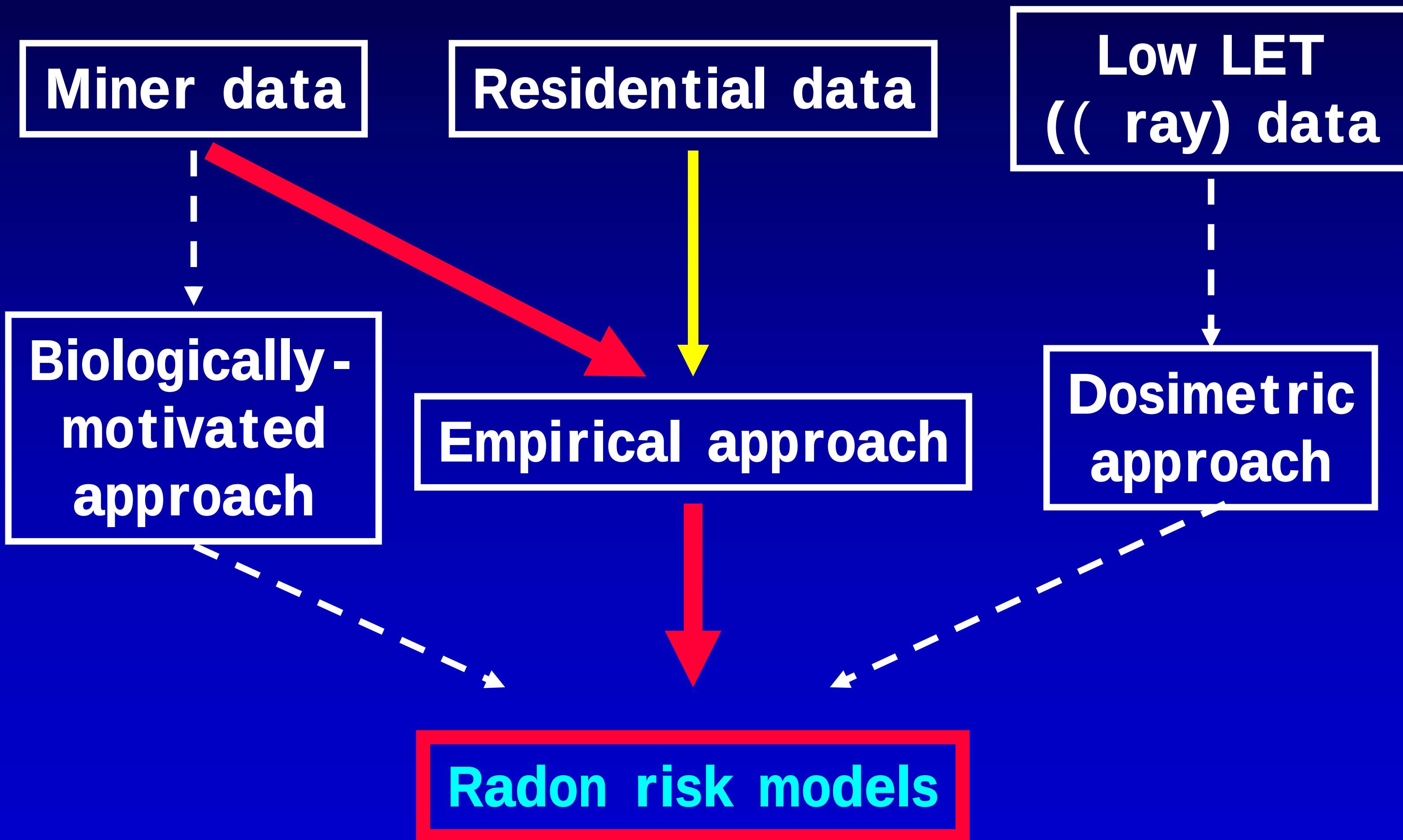
0.01 WL x (365x24/170) x 0.40 x 0.75 x 25= 3.9 WLM

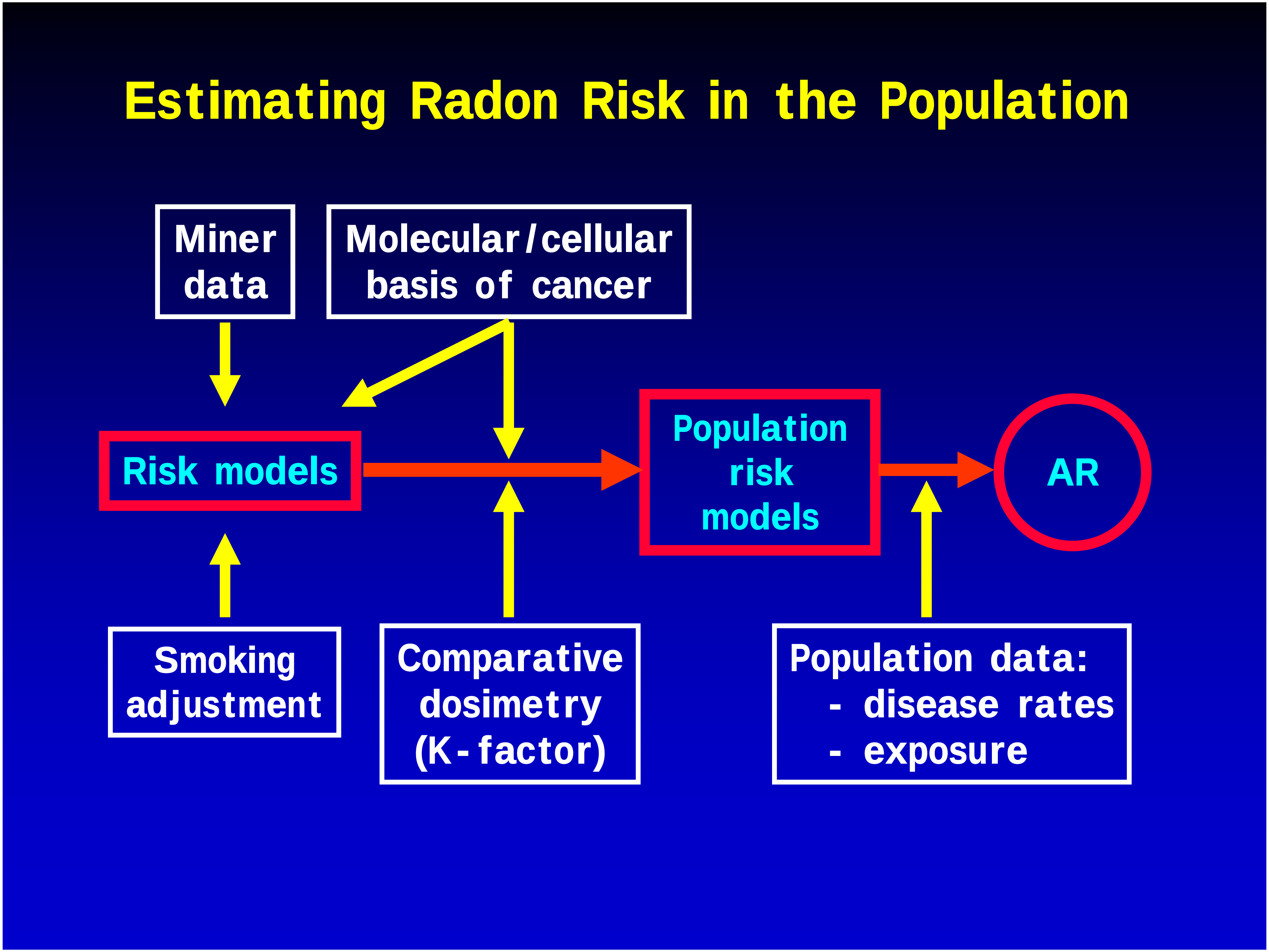
Residing 25 yr @ 37 Bq/m3 ≈ 3 - 5 WLM



Chronology of Important Radon Events

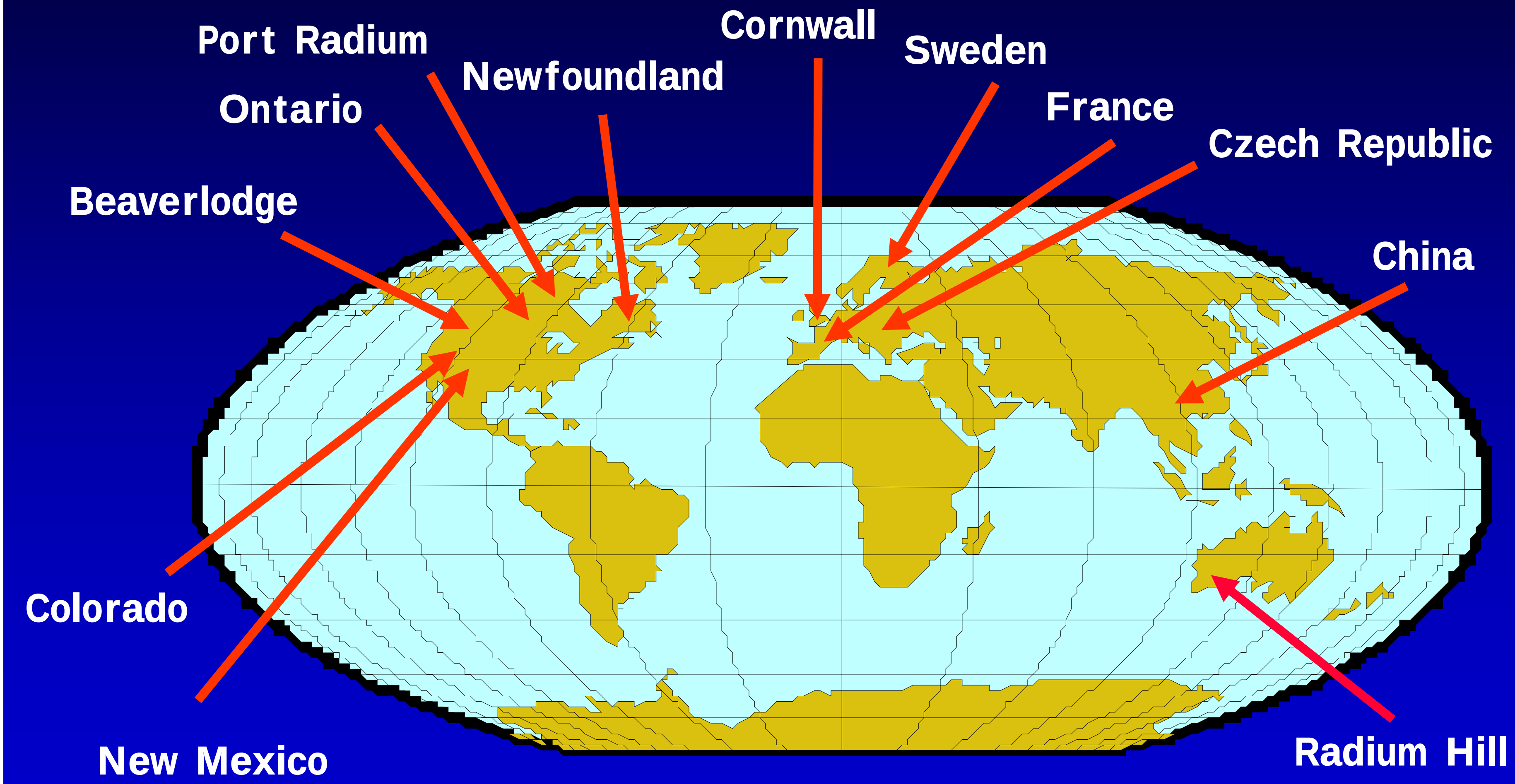
Methodologies for Generating Risk Estimates for Exposure to Radon




Estimating Radon Risk in the Population
Miner data
Molecular/cellular basis of cancer
Risk models
Population risk models
AR
Smoking adjustment
Comparative dosimetry (K-factor)
Population data:
- disease rates
- exposure

Studies of Underground Miners

Studies of Radon-Exposed Miners



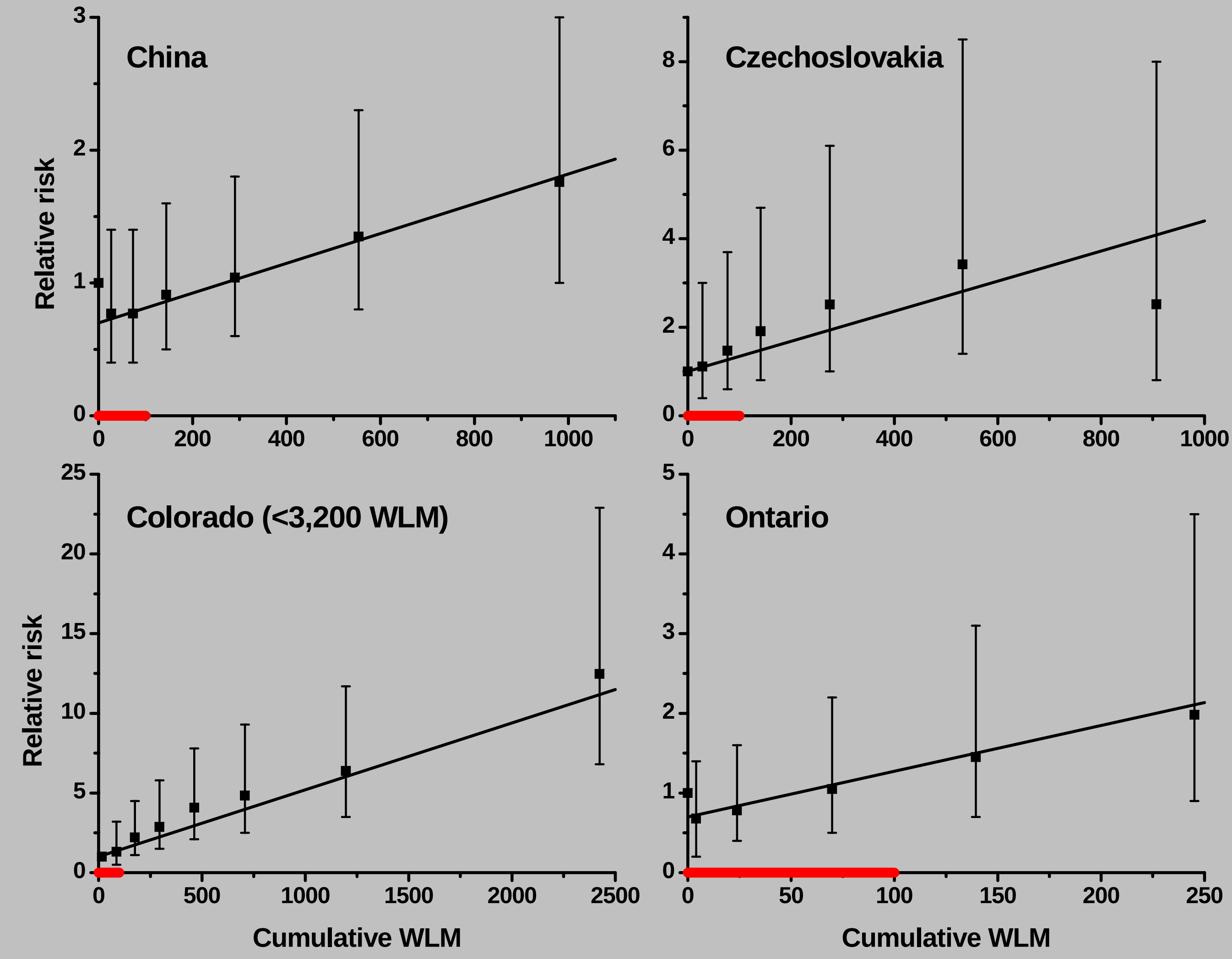
Pooled Analysis of Miners

Study	Lung ca	P-yrs
China *	980	175,342
Czech Republic	705	106,924
Colorado *	336	87,821
Ontario	291	380,719
Newfoundland *	118	48,742
Sweden *	79	33,293
New Mexico *	69	55,964
Beaverlodge	65	118,385
Port Radium	57	52,677
Radium Hill *	54	51,624
France	45	43,962
Total	2,787	1,155,453

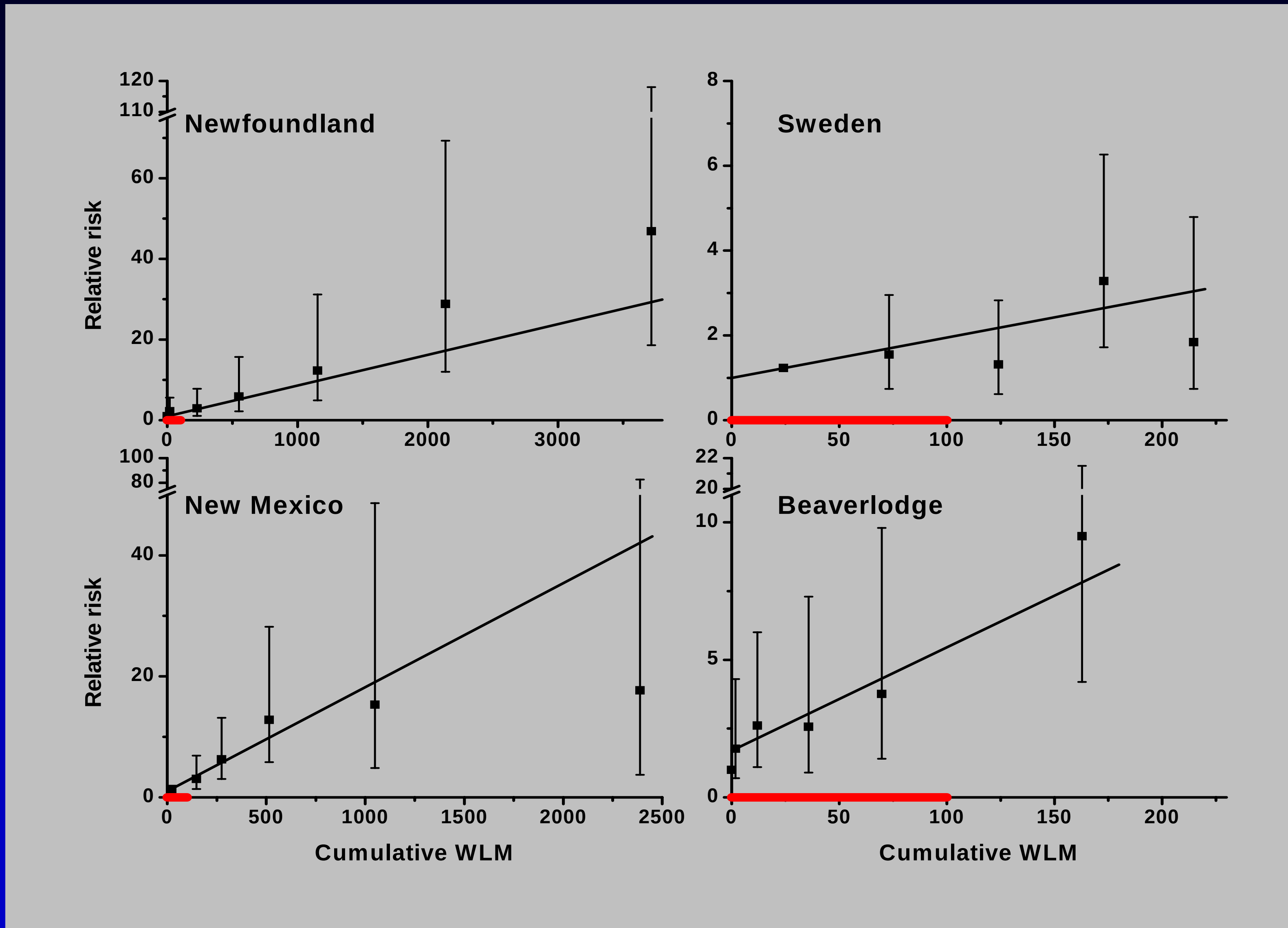
Mean: WLM = 164, WL=2.9, Dur=5.7 y

* Cohorts with smoking info

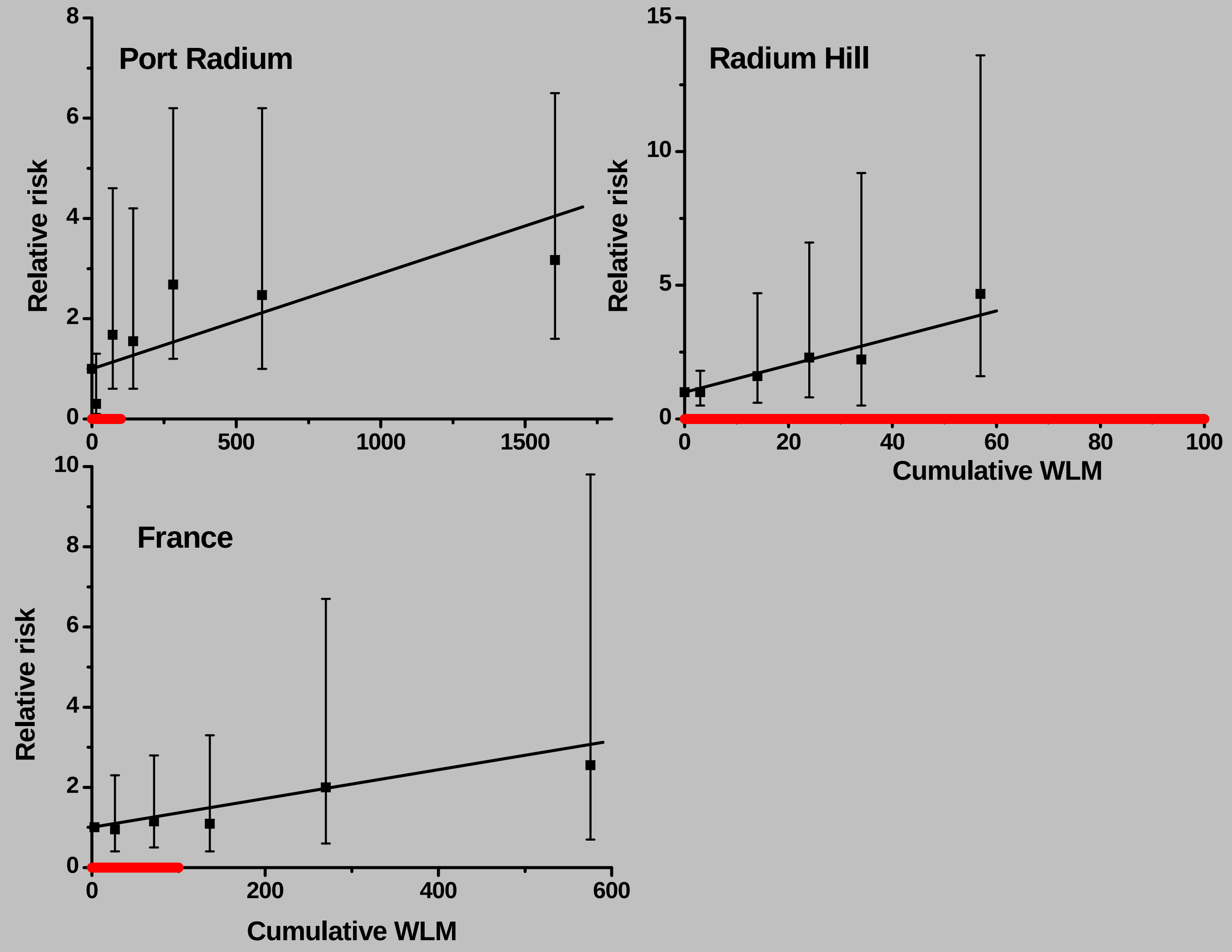
Dose-Response in Miner Studies (I)



Dose-Response in Miner Studies (II)



Dose-Response in Miner Studies (III)



Risk models for Lung Cancer (NAS 1999)

Exposure-age-duration model:

$$RR = 1 + \beta(age,dur) \times WLM^{*}$$

Exposure-age-concentration model:

$$RR = 1 + \beta(age,WL) \times WLM^{*}$$

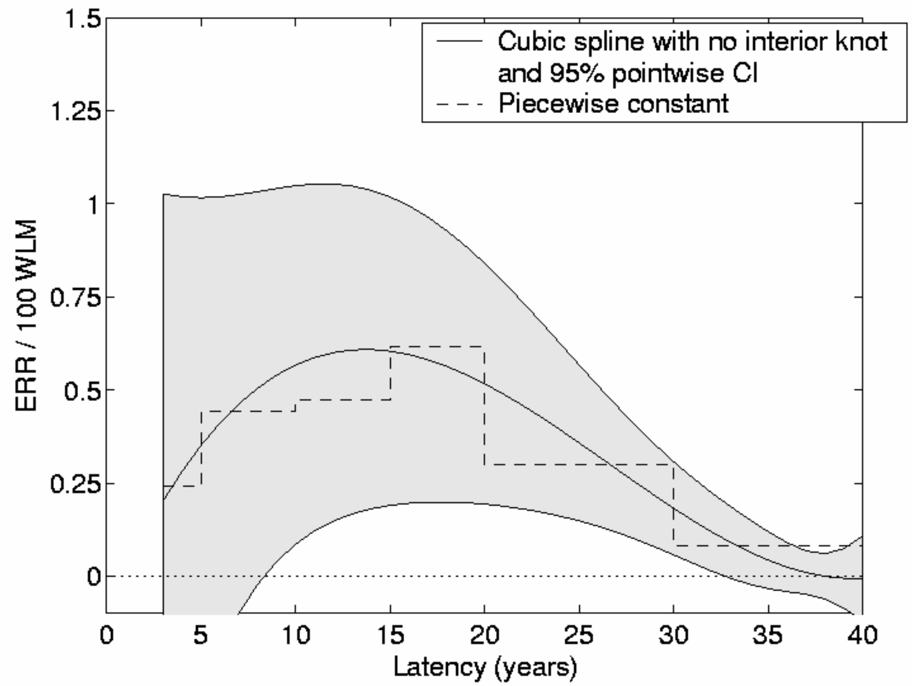
WLM^{*} = WLM weighted by time since exposure

Smokers: $0.9 \times \beta$; never-smokers: $2.0 \times \beta$

Time Since Exposure Effects

$$WLM^{*} = 1.0xW_{5-14} + 0.8xW_{15-24} + 0.3xW_{25+}$$

Latency (TSE) Pattern in CO Miners using B-splines



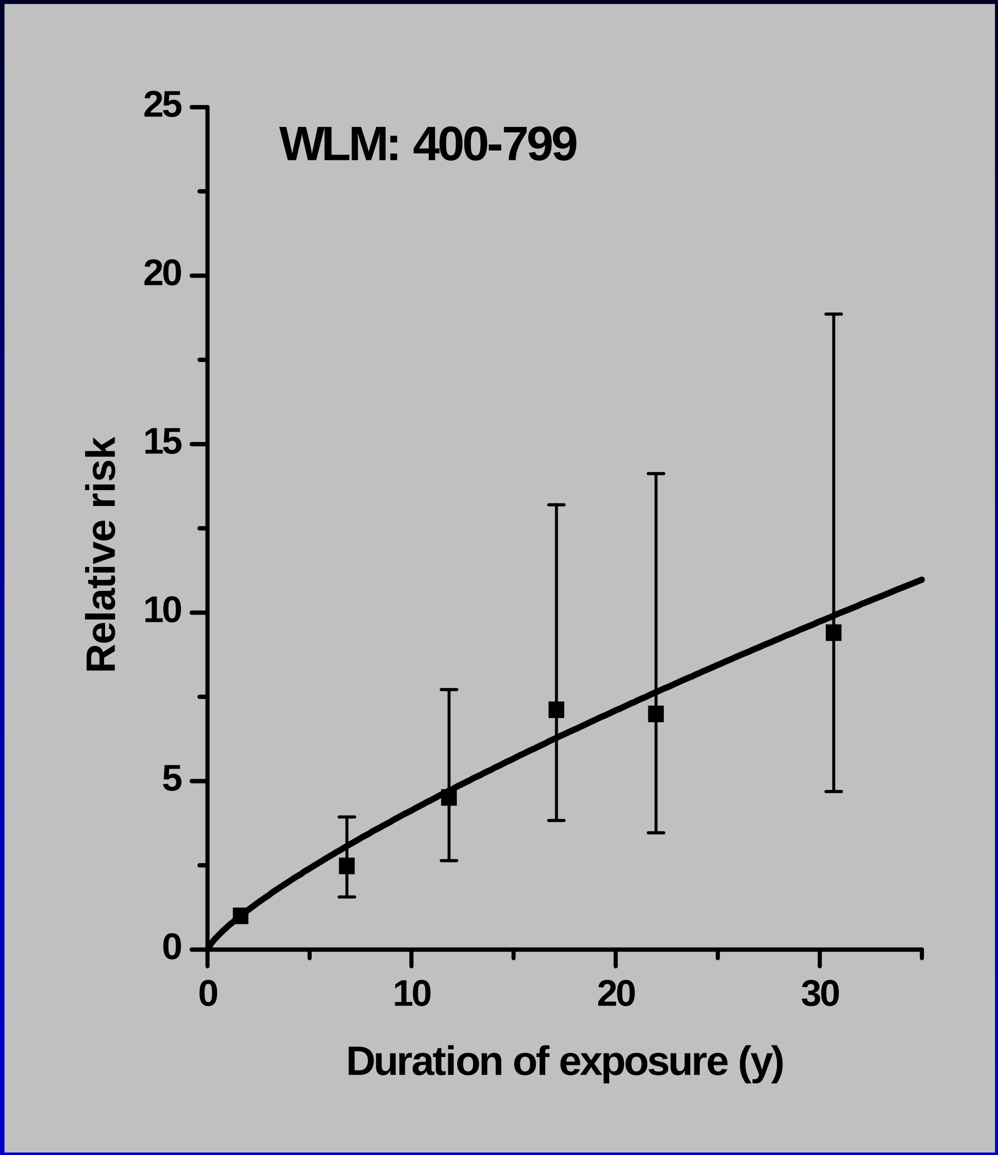
Hauptmann 2001

Dose-Rate Effects: Alpha-Particle Hits Per Year

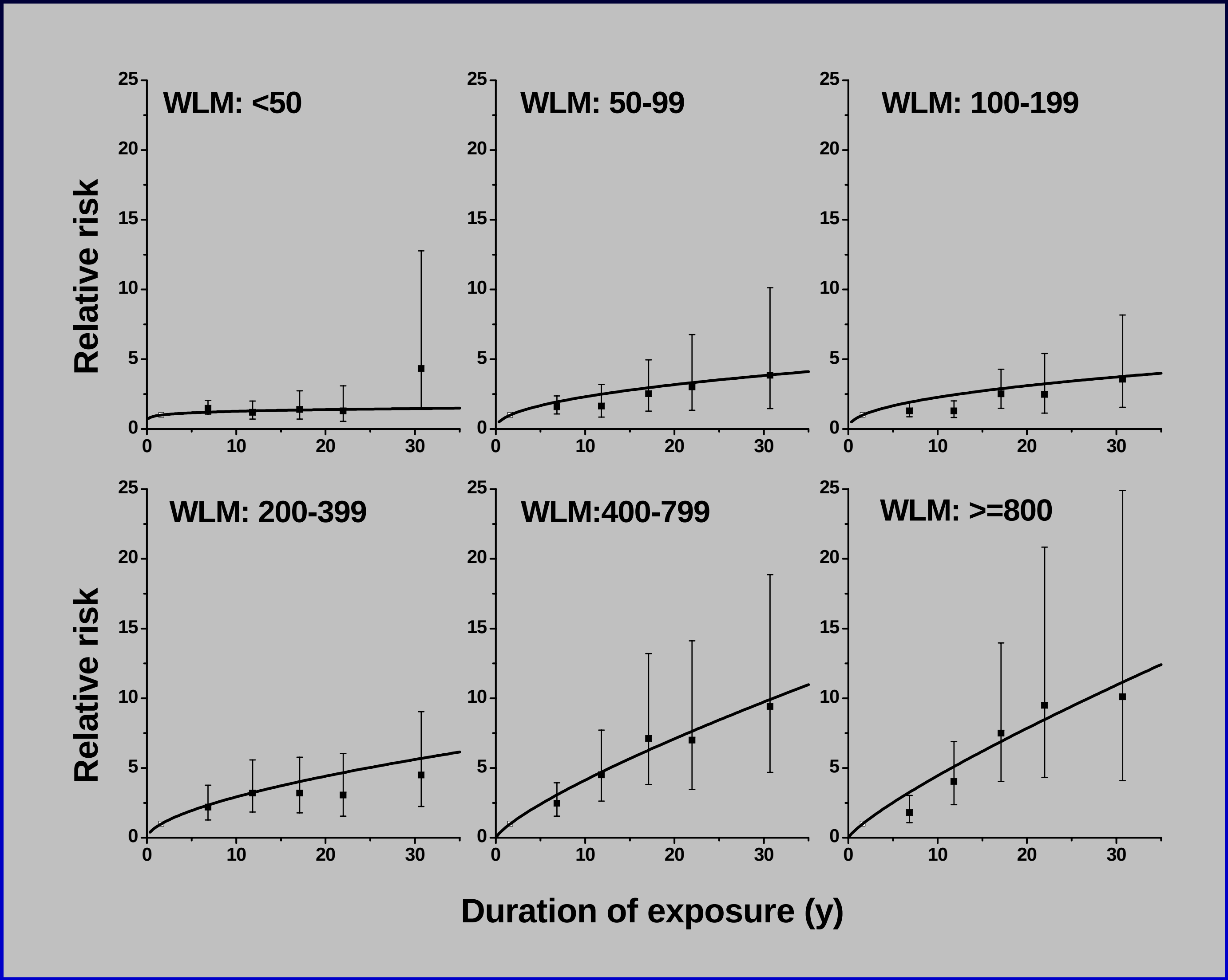
Mean alpha particle hits per year at a cell location in bronchial region			
Target	800 WLM in 5 yrs	8 WLM in 1.1 yrs	50 Bq/m^3 in 70 yrs
Basal cell nuclei	1.3	0.058	0.0022
Basal cell cytoplasm	3.8	0.17	0.0062
Secretory cell nuclei	5.3	0.23	0.0086
Secretory cell cytoplasm	77	3.32	0.12

NAS, BEIR VI (1999)

RR Patterns and the Inverse Dose-Rate Effect

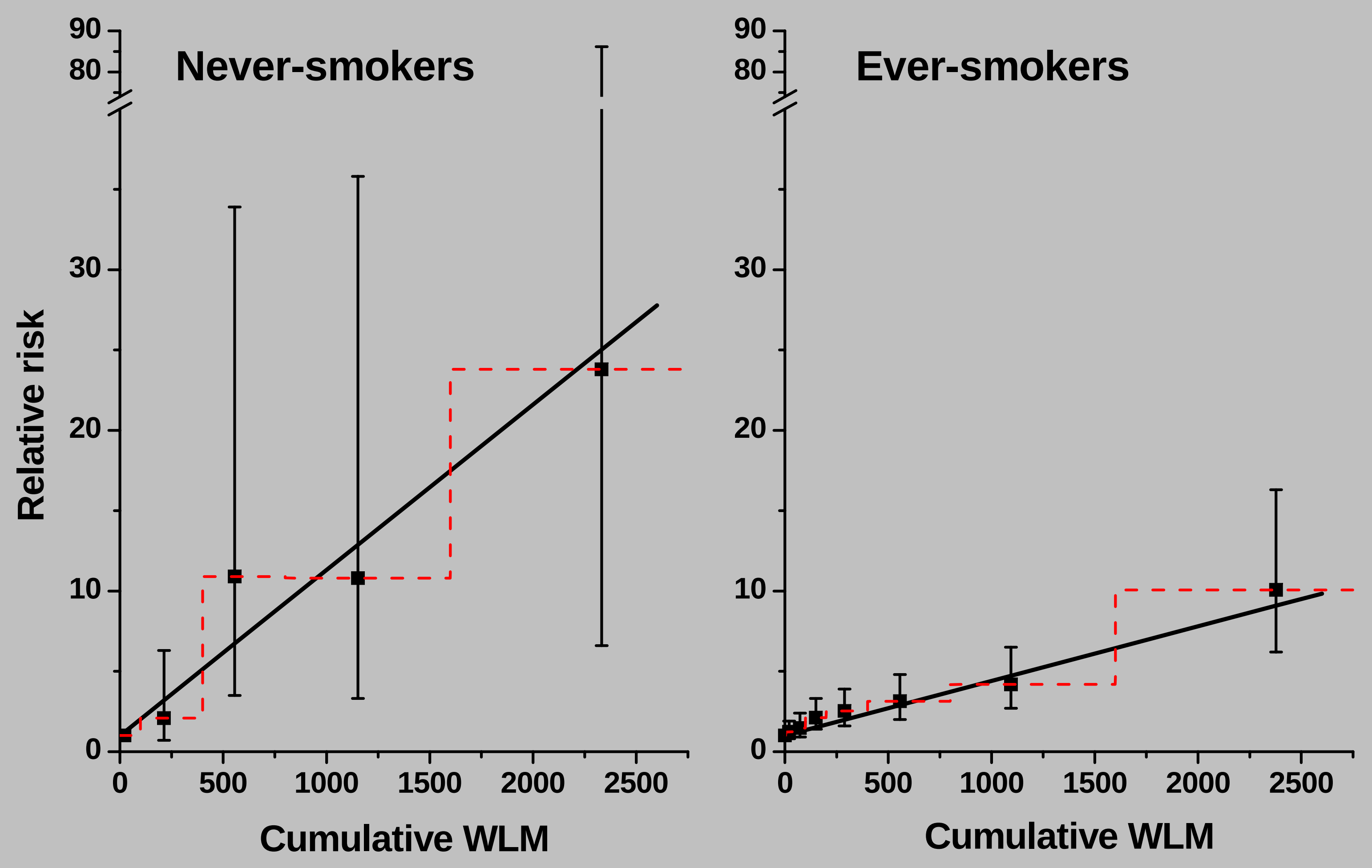


The Inverse Dose-Rate Effect for Radon



Lubin et al 1995

RRs for Ever/Never Smoking Miners

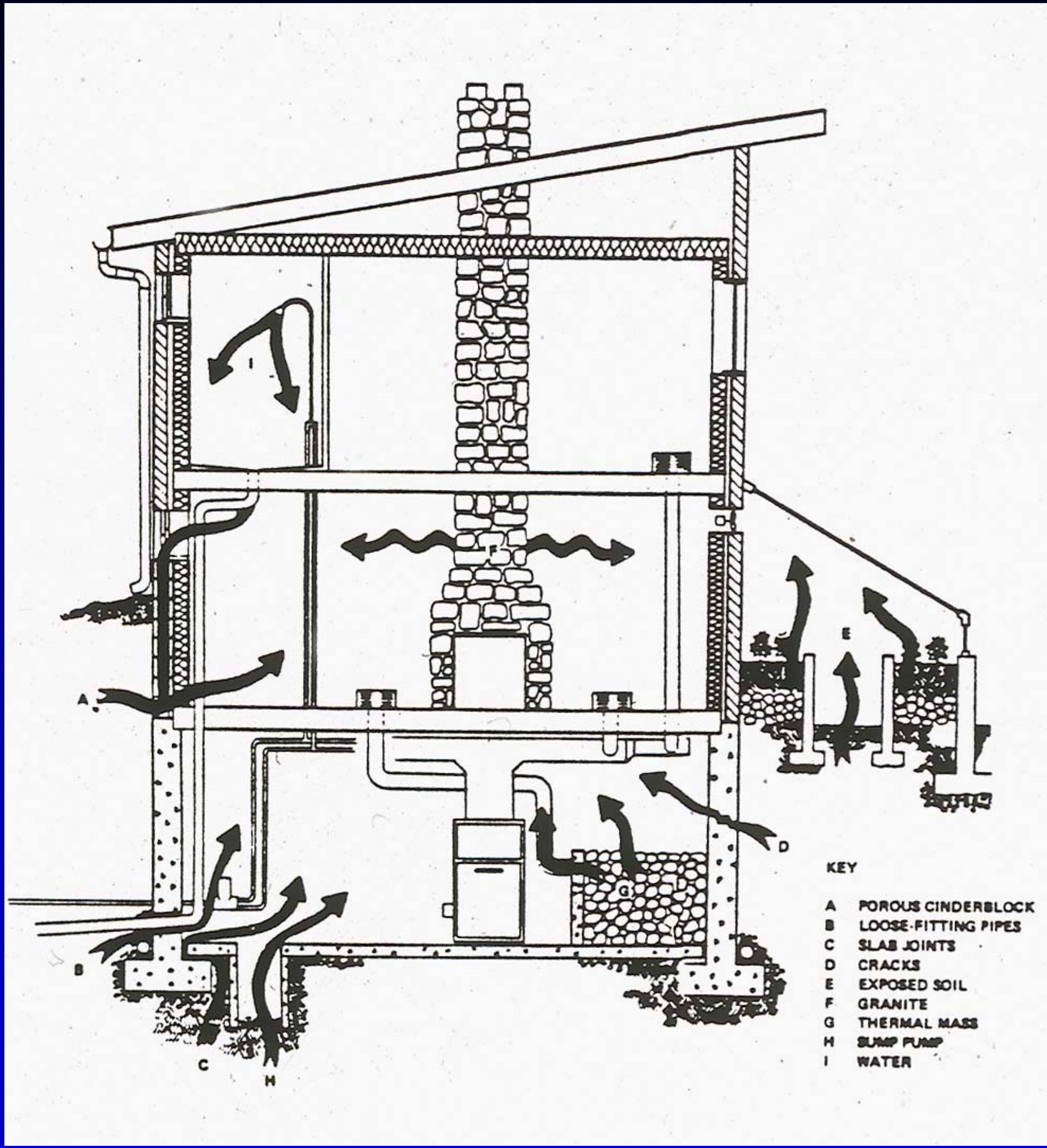


Residential Studies of Radon

Case-Control Studies of Lung Cancer and Residential Radon

- Compare residential risks with miner extrapolations
- Direct estimate of exposure-response relationship
- Evaluate other factors, e.g., females, children

Routes of Entry of Radon into Houses



Residential Radon Studies

	Cases	Controls
N Amer	4,108	5,301
China	1,076	2,015
Europe	8,652	15,856
Total	13,836	23,172

Study	Cases	Controls	Bq/m^3	Status
		North America		
New Jersey - 1	433	402	29	T
Winnipeg	738	738	141	T
Missouri - 1	538	1,183	63	T
Missouri - 2	512	553	55	T
Iowa	413	614	129	T
Connecticut	963	949	33	T
Utah-So Idaho	511	862	57	T
		China		
Shenyang	308	356	85	T
Gansu	768	1,659	225	T
		Europe		
Stockholm	210	379	133	T
Sweden	1,360	2,054	96	T
So Finland	161	328	213	T
Finland	863	1,166	102	T
SW England	982	3,126	55	T
E. Germany	1,053	1,667	75	T
W. Germany	1,449	2,297	50	T
Sweden (NS)	258	487	75	T
France	552	1,103		2003
Czech Rep	206	824		2003
Ardennes-Eiffel	1150	552		2003
Rome	408	424		2003

Results of Indoor Rn studies: OR at 100 Bq/m³

$OR = 1 + \beta \times Bq/m^3$

Study	OR	95% CI
Finland-I	1.19	1.1-1.6
Finland-II	1.17	1.1-1.6
New Jersey	1.50	1.2-2.9
Shenyang	0.89	0.8-0.9
Winnipeg	0.97	0.9-1.1
Stockholm	1.50	1.3-2.5
Sweden	1.13	1.1-1.3
MO-I	1.08	0.9-1.4
MO-II	1.74	1.7-3.1
UK	1.12	1.0-1.4
W Germany	1.92	2.0-3.5
Iowa	1.27	1.3-1.6
Gansu	1.29	1.1-1.7

Lubin 1999

Pooling of Residential Radon Studies

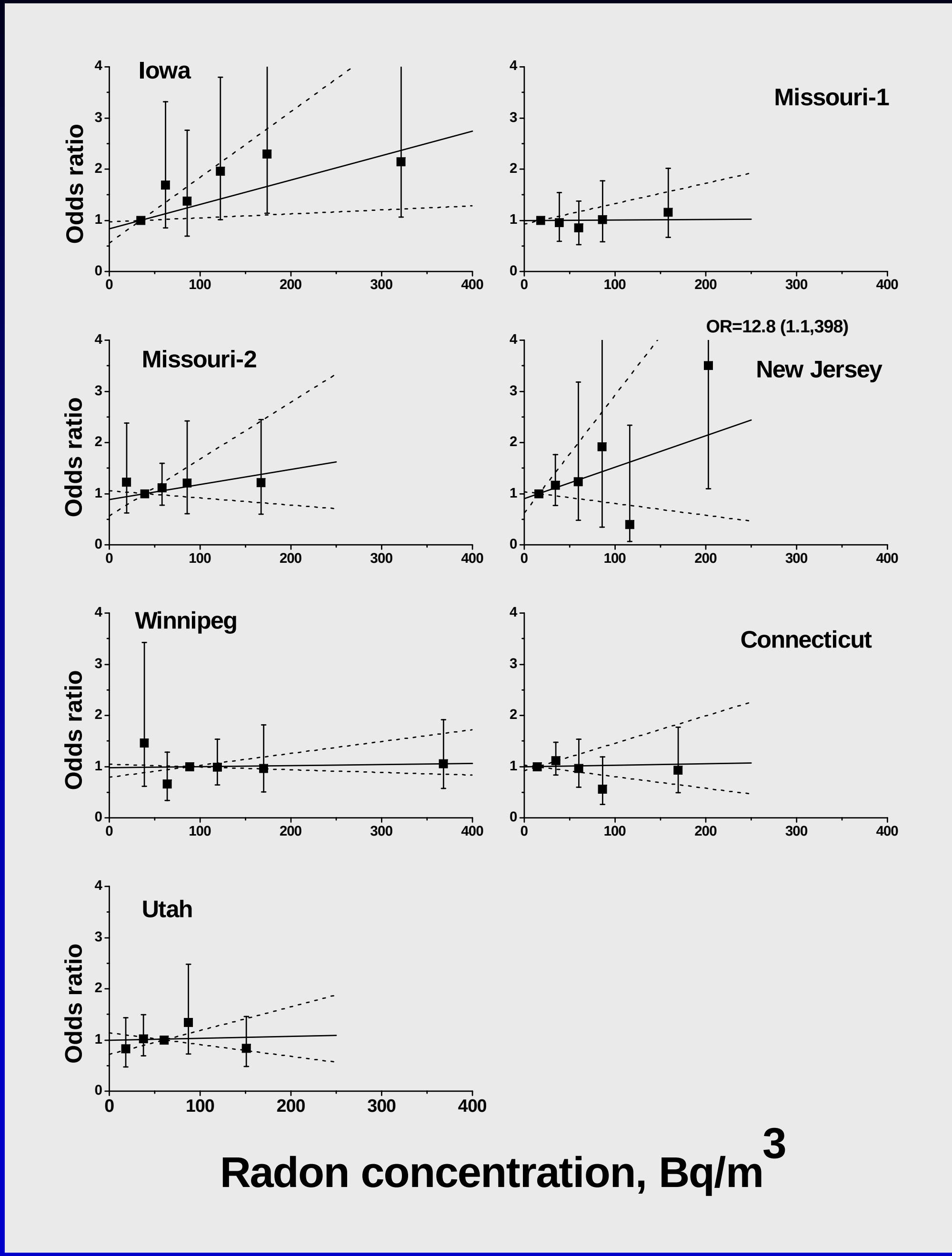
- Workshops (1989, 1991, 1995)
  - periodic meetings and exchanges since 1995
- North America/Europe/China
- World pooling

Pooling of N.A. Residential Radon Studies

- North American pooling project
  - studies with 200+ cases
  - long-term radon detectors
  - 4,101 cases and 5,281 controls

– New Jersey	Schoenberg 1990, 1992
– Winnipeg	Létourneau 1994
– Missouri-1	Alavanja 1994
– Missouri-2	Alavanja 1999
– Iowa	Field 2000
– Connecticut	Sandler 2003
– Utah	Sandler 2003

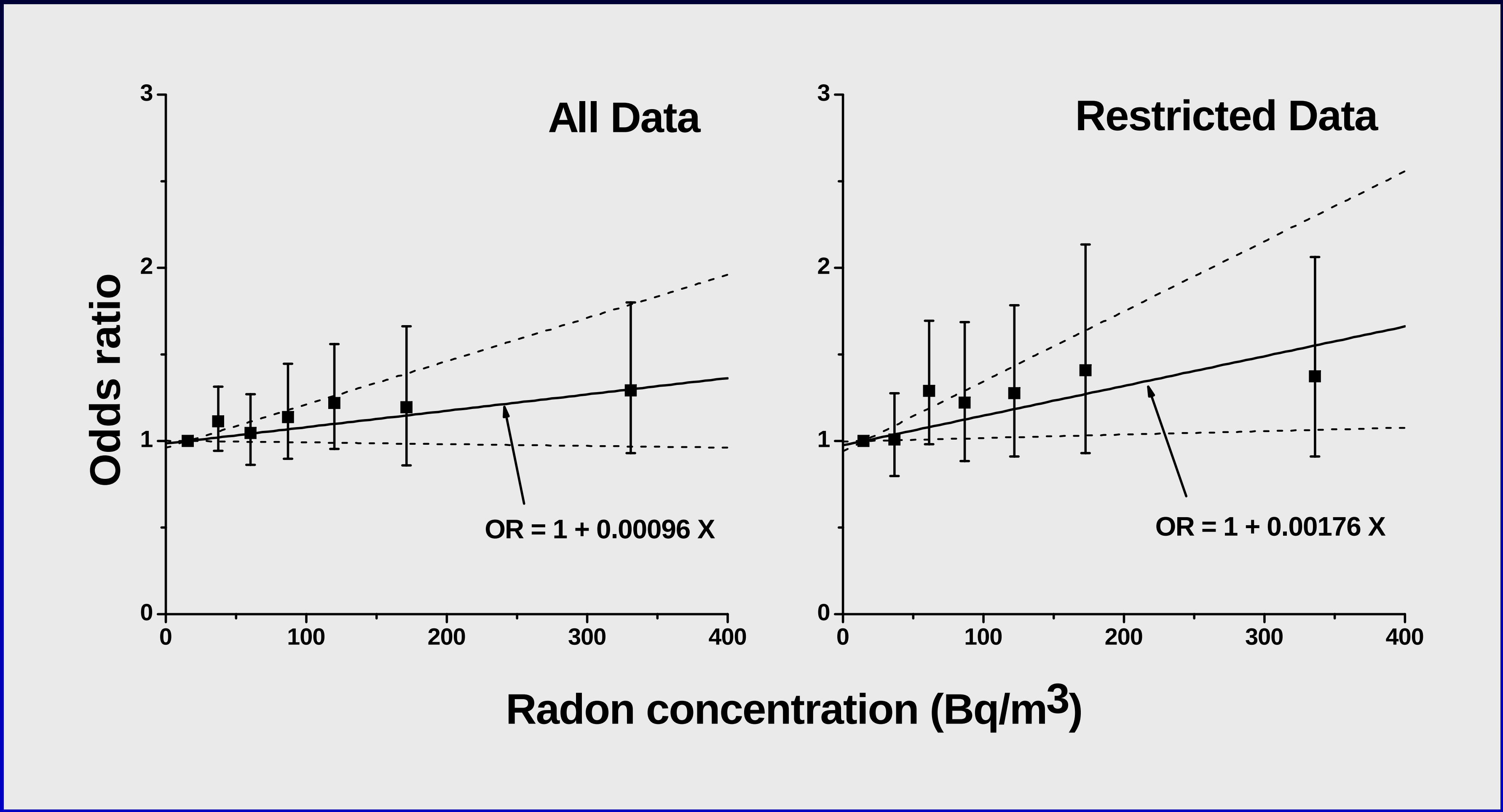
ORs by Rn Level for North American Radon Studies



$P_{homogeneity} = 0.56$

Krewski et al
(Epidemiol, JTEH In press)

ORs by Radon Level for North American Studies

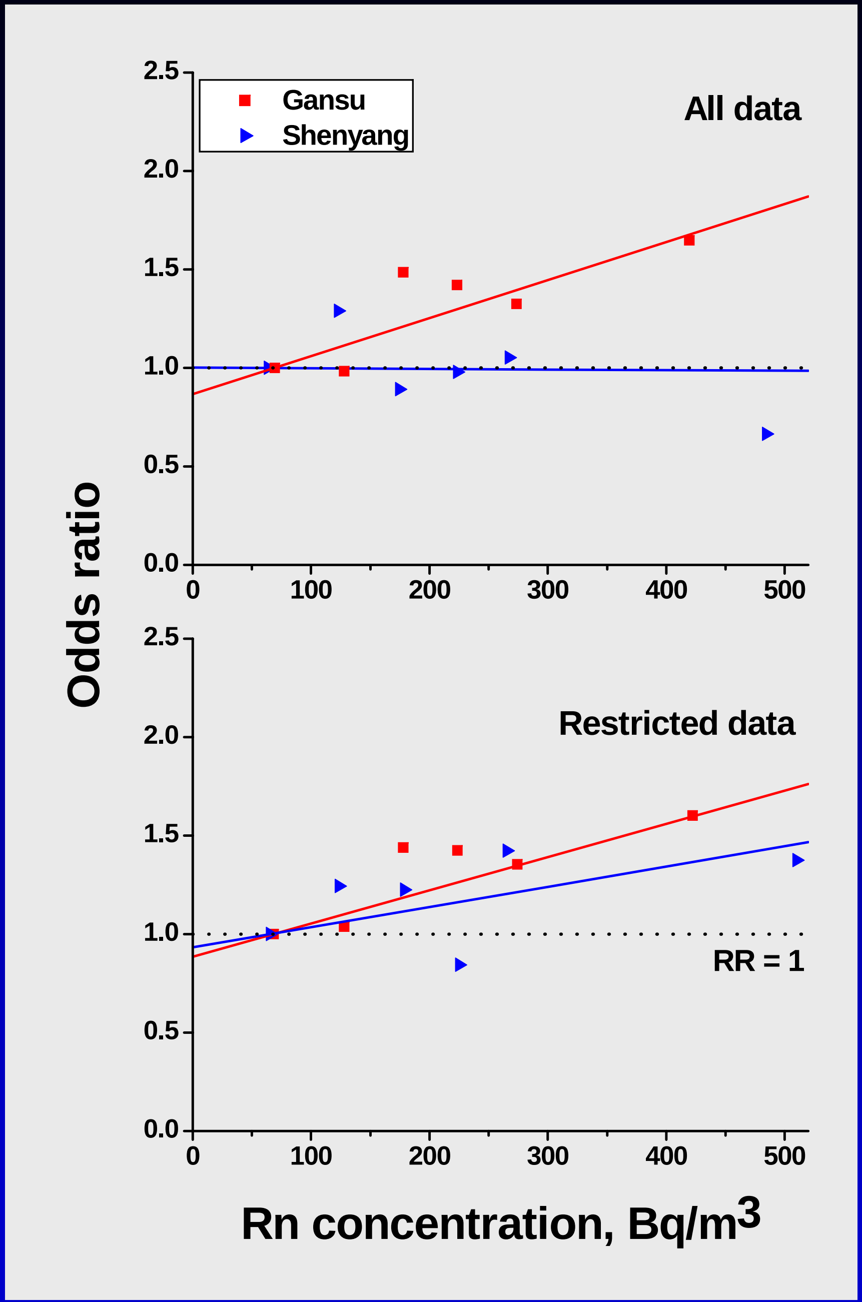


Restriction:1-2 houses; 20+ yrs α-track

Pooling of China Radon Studies

Shenyang: 308/356 Blot 1990
Gansu: 768/1,659 Wang 2002

Lubin, IJC 2004



Restriction: 100% coverage in 5-30y ETW

Attributable Risk of Lung Cancer

AR of Lung Cancer in the US from Indoor Radon

- **Assumptions for residential extrapolation**
- **Radon concentration in US houses (EPA):**
  Log-Normal
  GM = 24.8 Bq/m^3, GSD = 3.1
- **1985-89 US mortality rates**

Assumptions for Extrapolating Risk from Miners to the General Population

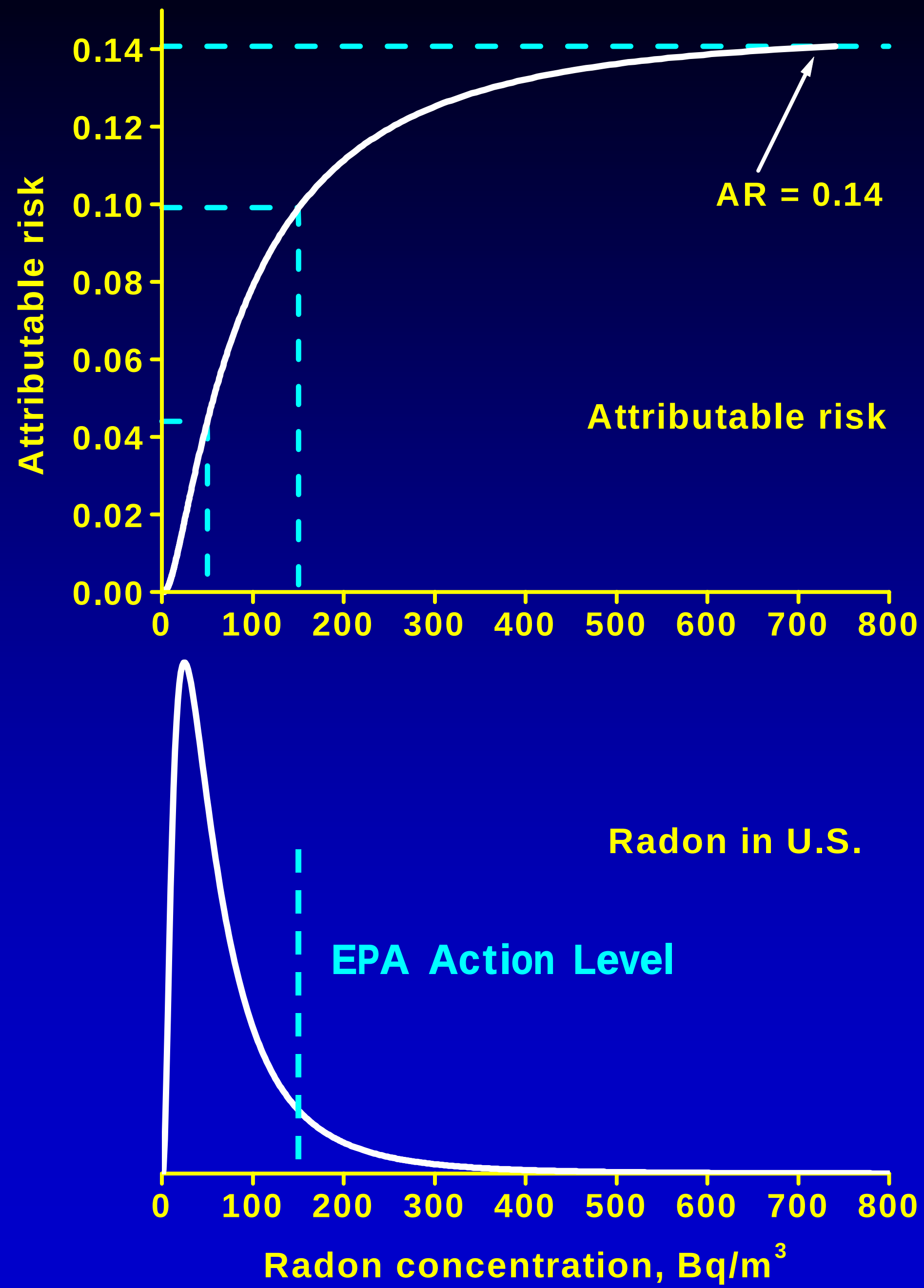
Factor	Assumption
Shape dose-response	Linear ERR
Exposure rate	Comparable risks for rates <0.5 WL or durations longer than 35 yr
Sex	ERR/exposure same in F and M
Age at exposure	ERR/exposure same for all ages
Cigarette smoking	Sub-multiplicative interaction: never-smokers - 2.0×β ever-smokers - 0.9×β
Particle size/distn, activity, bronchial morphology	No modification, K=1
Other differences	ERR/exposure the same

Attributable Risk of Lung Cancer from Indoor Radon

	AR	Deaths/yr
Total	14%	20,500 (3,000-30,000)
Ever-smokers	12%	18,000
Never-smokers	23%	2,500

Cumulative AR for Radon

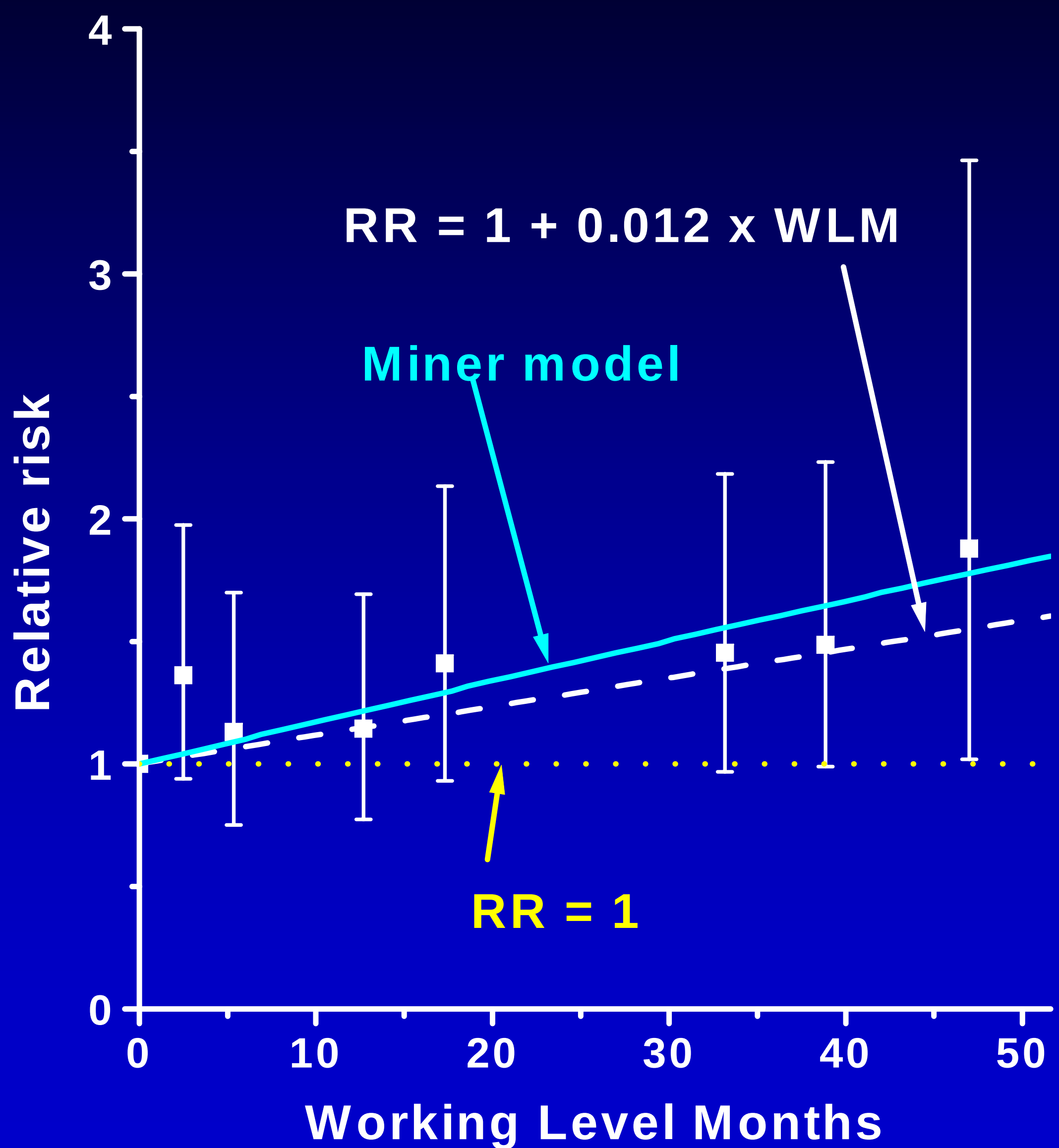
~ 1/3 from houses above EPA action level



Are estimates of AR for radon-associated lung cancer believable?

Does the miner-based model predict risk in low-exposed miners?

RRs for Miner Exposures (<50 WLM)

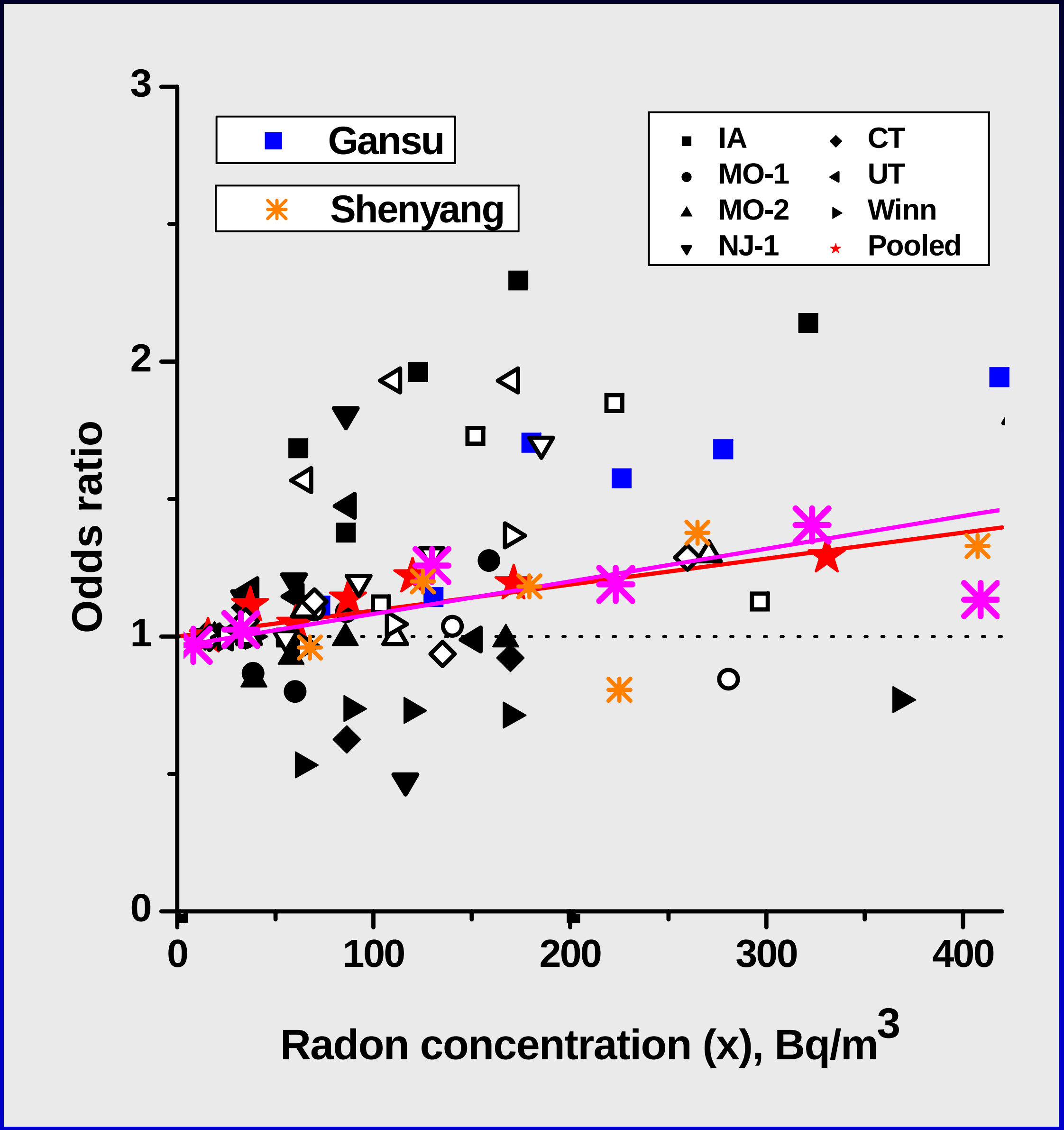


Models Fit to Restricted (<50 WLM) Miner Data

Model	Deviance	P for fit
Exp-age-dur (fixed)	1,753.8	
Exp-age-cond (fixed)	1,754.3	
Exp-age-dur (free)	1,751.3	0.87 $
Exp-age-conc (free)	1,749.0	0.57 $
$RR = 1 + \beta \times WLM$	1,754.2	0.52

Are miner-based models consistent with current indoor radon studies?

Comparability of Results of Indoor Radon Studies of Lung Cancer



Is there radiobiological and epidemiological evidence for low-dose linearity at indoor radon levels?

Cellular studies show that a single alpha particle can cause substantial damage to a cell, which can lead directly or indirectly to adverse chromosomal effects.

Low doses result in at most single particle traversals of cells. Further decreasing dose proportionally reduces the number of cells traversed, but not the degree of insult to a cell.

Cellular studies, radiobiology and epidemiology indicate linearity of dose-response at low doses.

Unanswered Questions for Extrapolating Risk to Indoor Radon

- Do miner-based risk models include all important risk factors?
- Are effect modifiers (smoking, etc.) in miner risk models valid for indoor exposures?
- Do miner-based risk models apply for lifelong exposures at low exposure rates?
- Is the K-factor (≈1) correct?
- Are risk models valid for males and for females?
- Do children have any special sensitivity to radon?

Summary

- **Miner studies, residential studies, animal studies and radiobiology implicate indoor radon as a cause of lung cancer**
- **In US, radon may cause 20,500 lung cancer deaths/yr, with a range of 3,000 to 32,000 (2nd leading cause of lung cancer)**
- **AR greater in never-smokers, but radon-attributable lung cancer deaths greater in ever-smokers**
- **About 1/3 of AR preventable (148 Bq/m^3)**
- **Due to limited low-dose data, estimates uncertain**

Future Studies of Radon

Areas of Research

epidemiology: pooling residential studies

molecular markers: identify markers of exposure, signature of “radon” lung cancer

cofactor effects: mechanistic formulation of cofactor effects to guide modeling of epidemiologic data

genomic instability, apoptosis, bystander effects: effects on dose-response

cellular repair mechanisms: improved modeling of risk reduction with time since exposure

susceptible sub-populations