Radiation Epidemiology Course
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Cancer Risk and Radon Exposure

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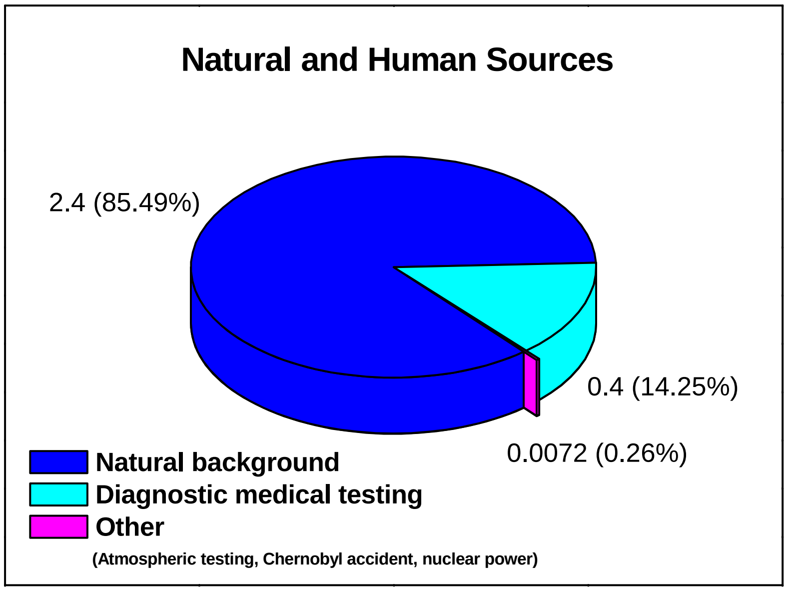
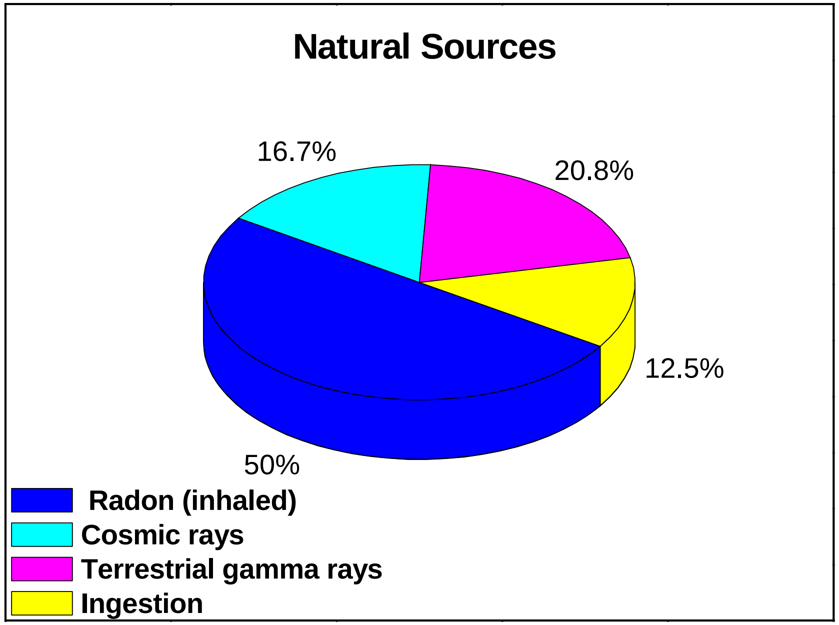
Radon Exposure and Risk of Lung and Other Cancers

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

Annual Per Capita Effective Dose (mSv)



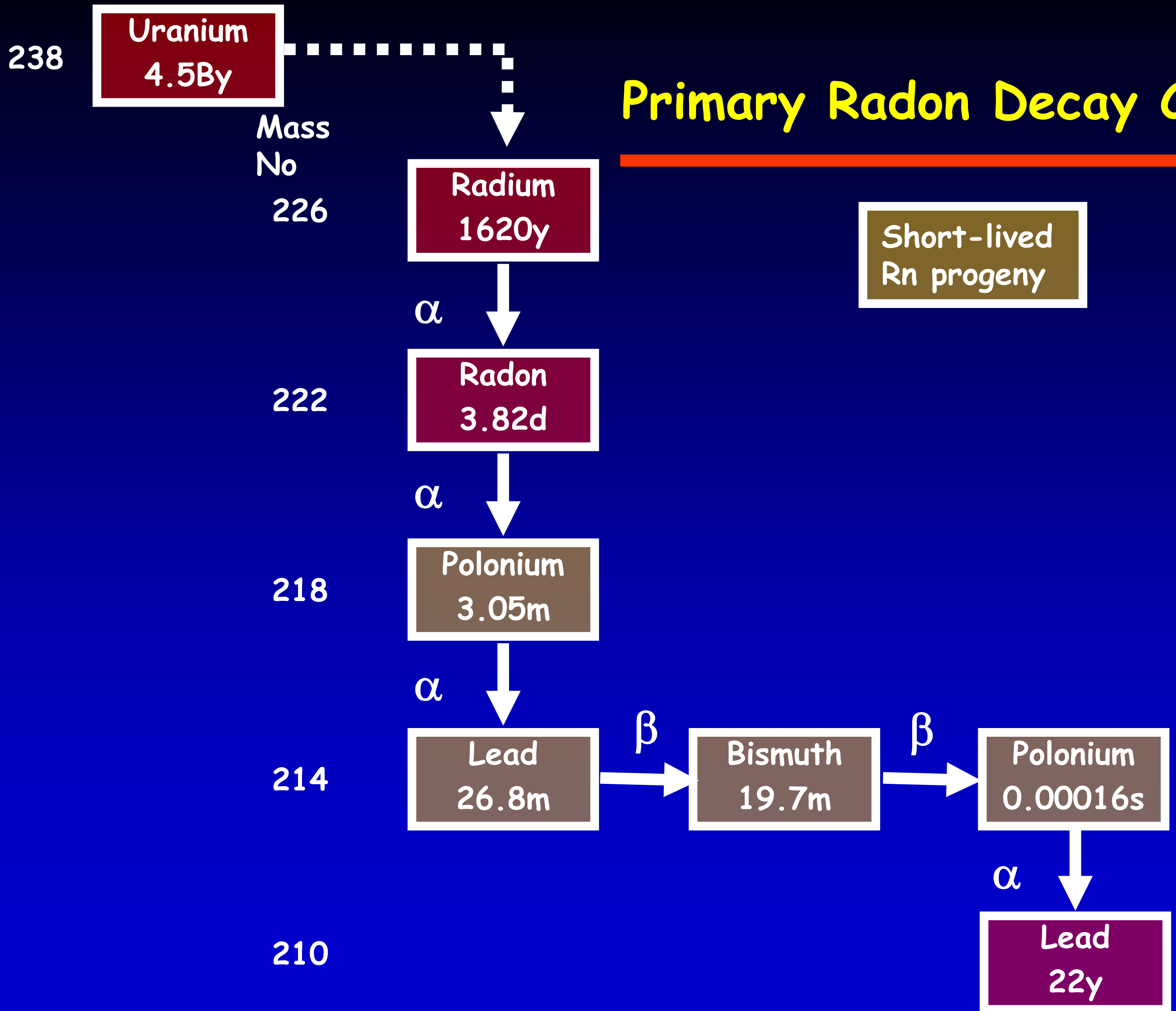


UNSCEAR, 2000

What is radon (^{222}Rn)?

- Noble gas
- Decay product of ^{238}U and ^{226}Ra
- Alpha emitter
- Rn half-life is 3.8 d
- High LET radiation

Primary Radon Decay Chain



Radon and Cancers Other Than Lung

Stomach: NRC, Radon in Water, 1999

Leukemia:

Miners:	Pooled miner data	Darby JNCI 1995	N
	E. Germany	Mohner AJIM 2006	N
	Czech	Rericha EPH 2006	Y
Adults:	Iowa (eco)	Smith Stat Med 2007	N
Children:	ALL (c/c study)	Lubin JNCI 1998	N
	France (eco)	Evrard Eur J Ca Prev 2005	Y
	UK (eco)	Henshaw BJC 1990	Y

Units of Concentration/Exposure

- Mines: Rn and Rn progeny
  - 1 WL: 1.3×10^5 MeV of α energy from short-lived decay products
  - WLM (Working Level Months): $\sum WL_i \times dur_i$ with duration in units of 170 hrs
  - 1 WL = 2.08×10^{-5} J/m^3; 1 WLM = 3.5×10^{-3} Jh/m^3

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

Measuring Radon in Homes

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

Computing Exposure in Houses

1 yr @ 37 Bq/m^3 (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

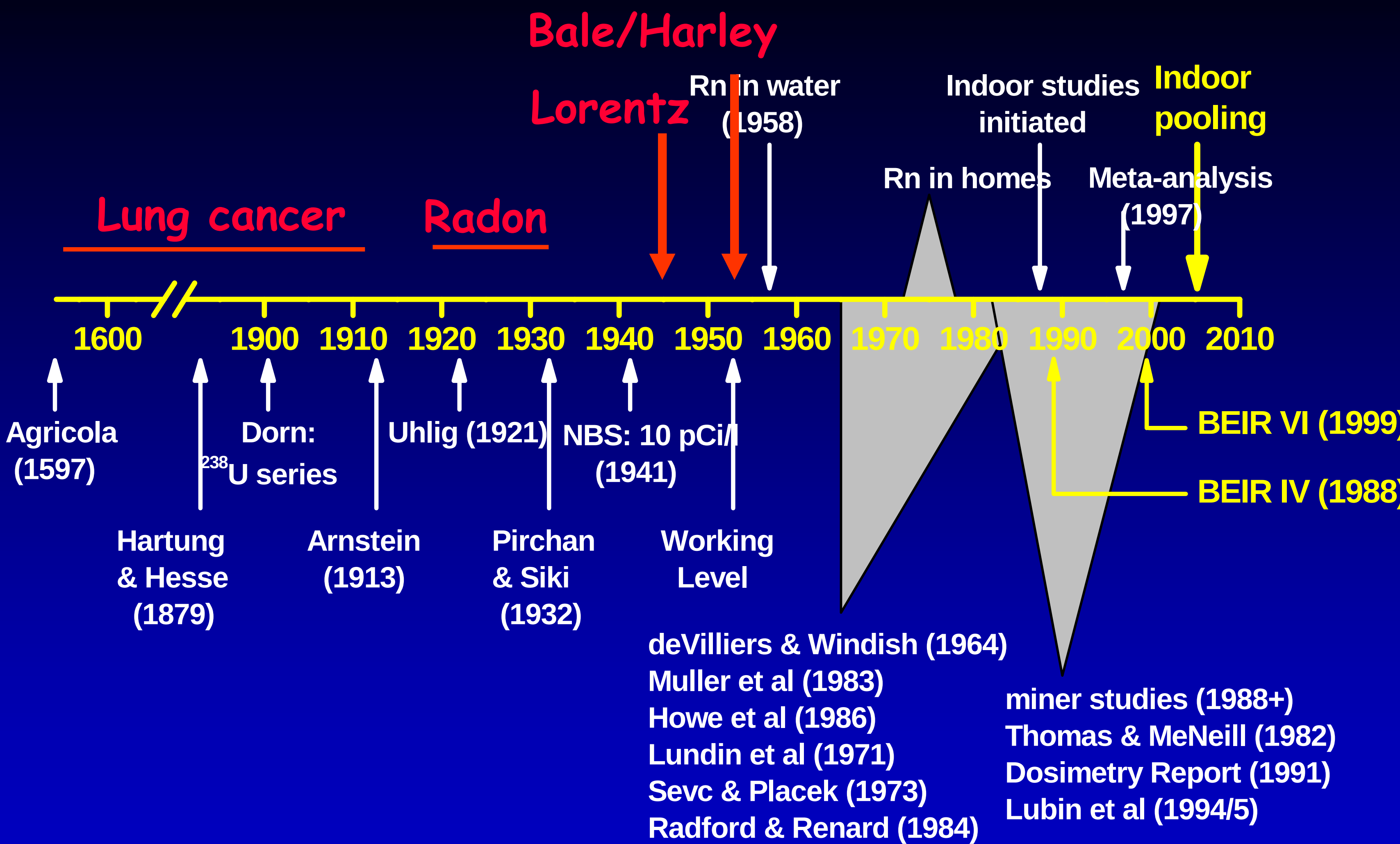
and with 75% occupancy:

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

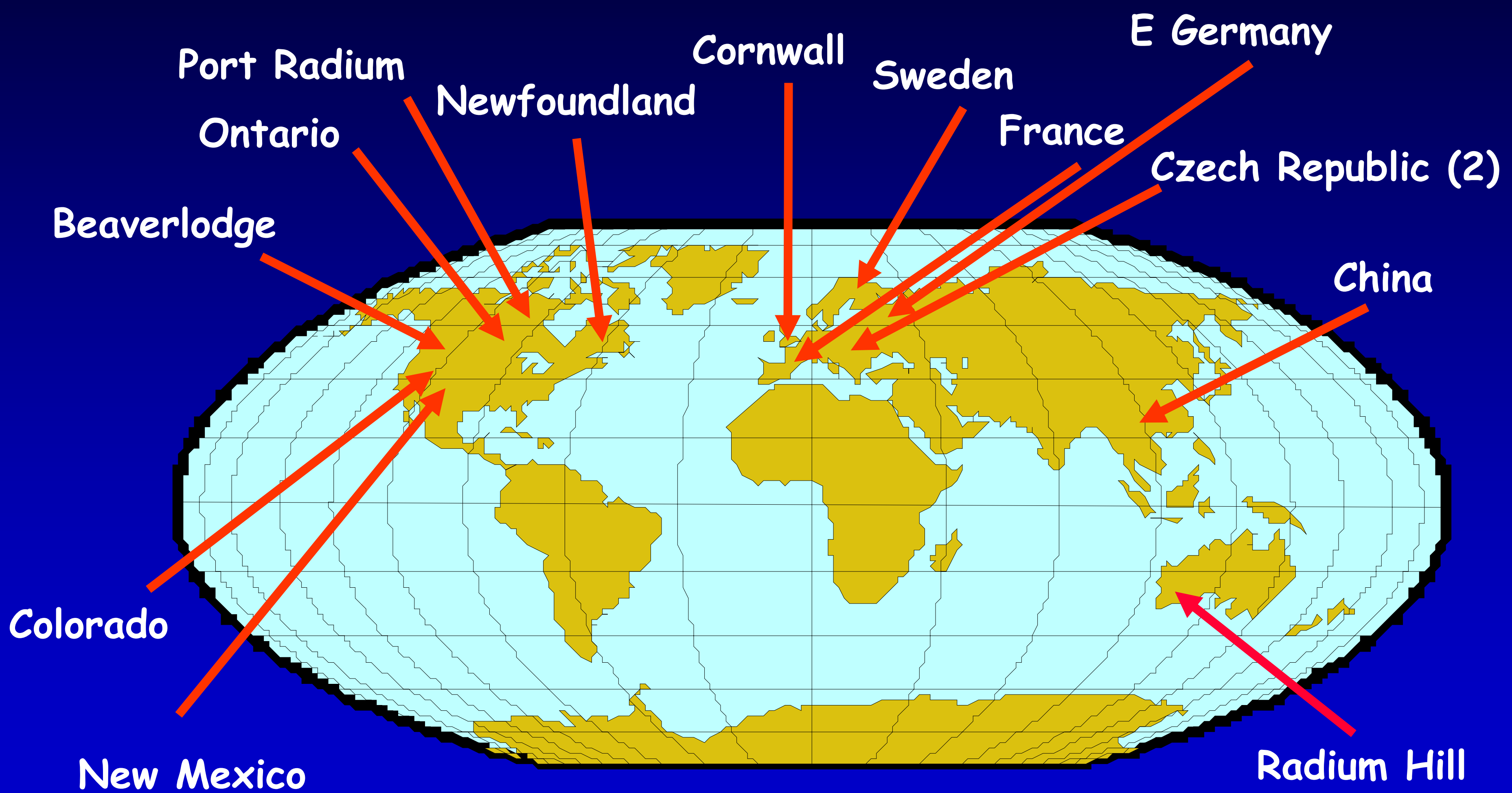
Residing 25 yr @ 37 Bq/m^3 ≈ 3 - 5 WLM



Chronology of Important Radon Events

Studies of Underground Miners

Studies of Radon-Exposed Miners



Pooled Analysis of Miners

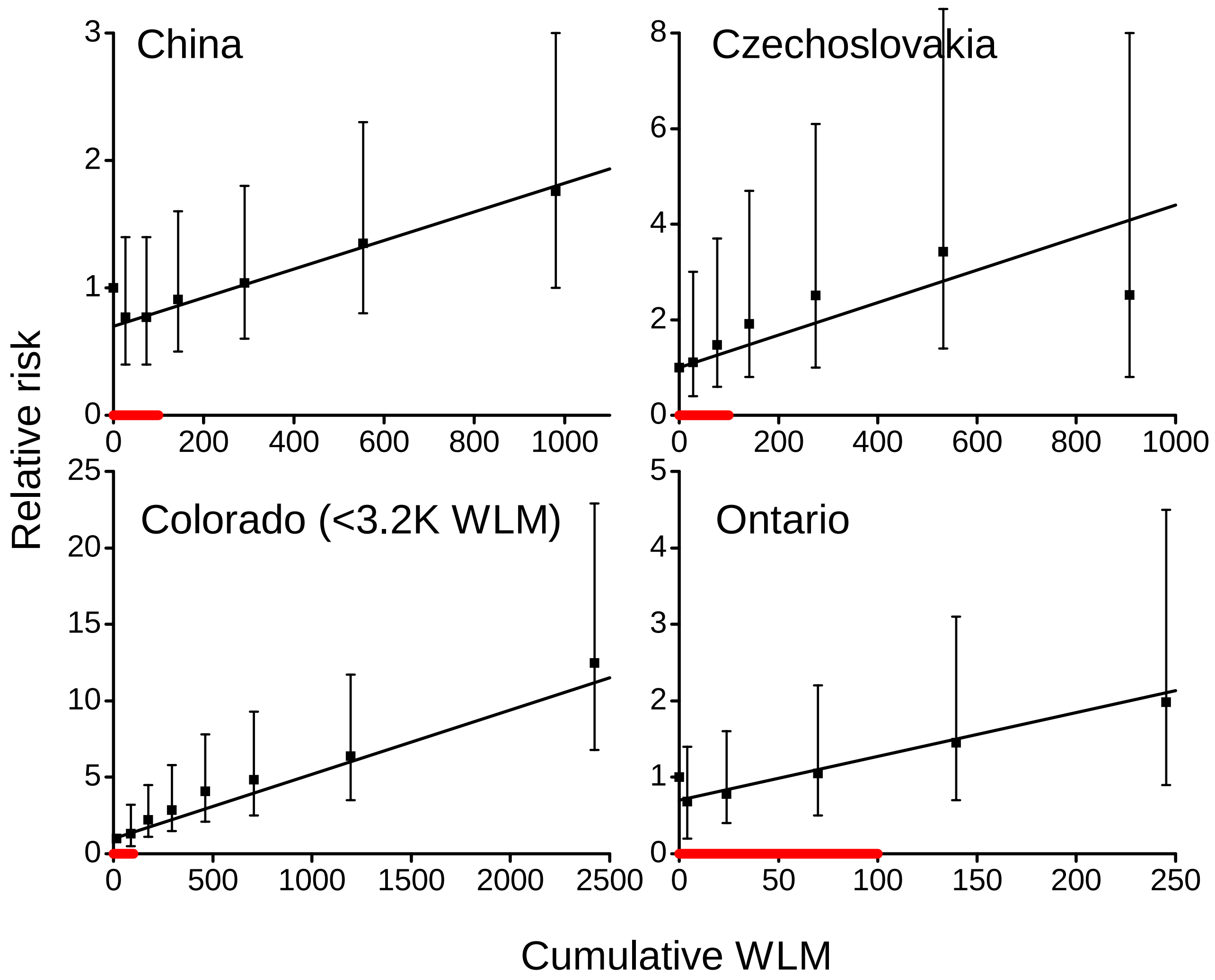
Study	Lung ca	P-yrs
China *	980	175,342
Czech Republic	705	106,924
Colorado *	336	87,821
Ontario	291	380,719
Newfoundland *	118	48,742
Sweden *	79	33,293
New Mexico *	69	55,964
Beaverlodge	65	118,385
Port Radium	57	52,677
Radium Hill *	54	51,624
France	45	43,962
Total	2,787	1,155,453

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

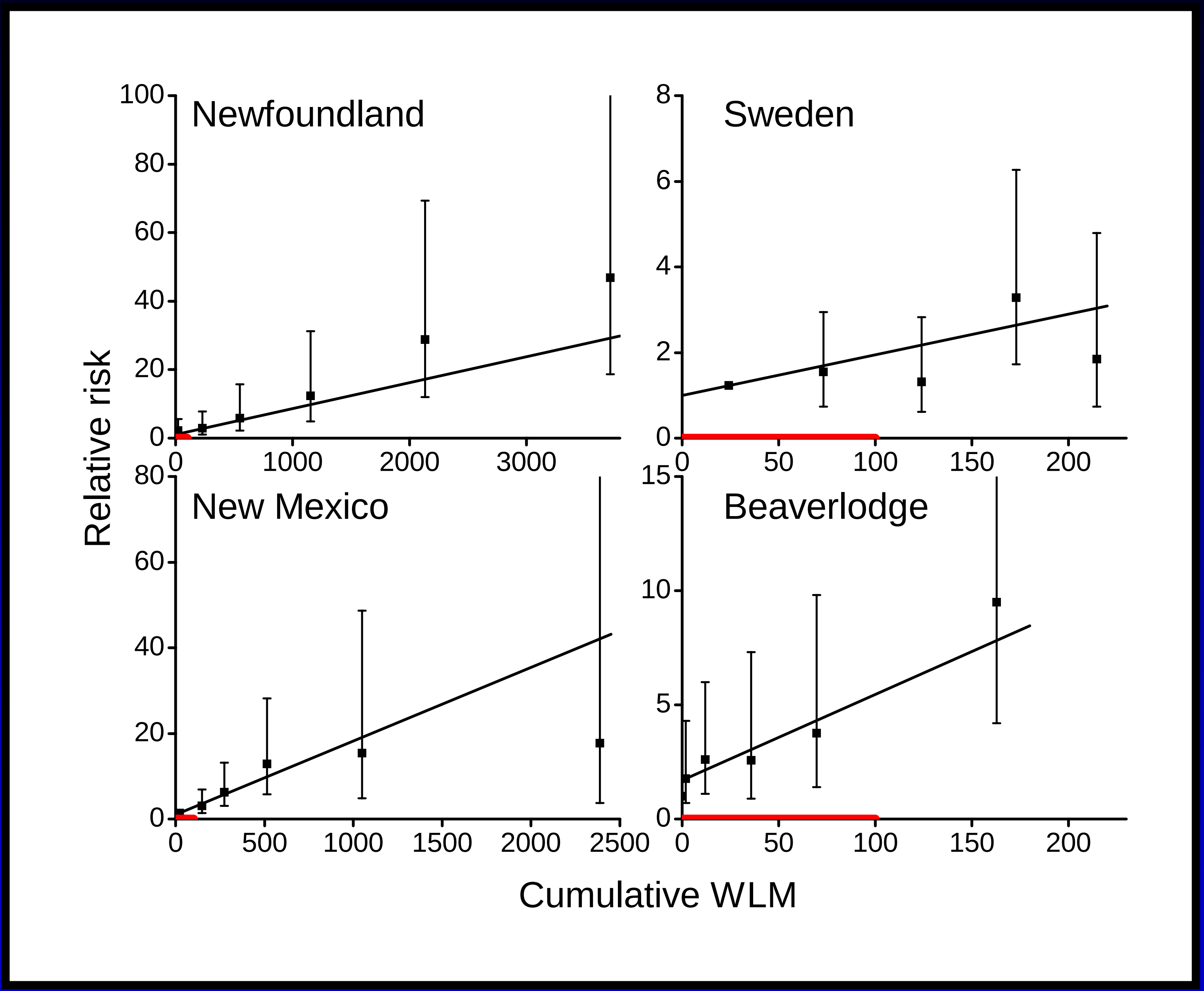
* Cohorts with smoking info

Lubin et al 1995
BEIR VI, 1999

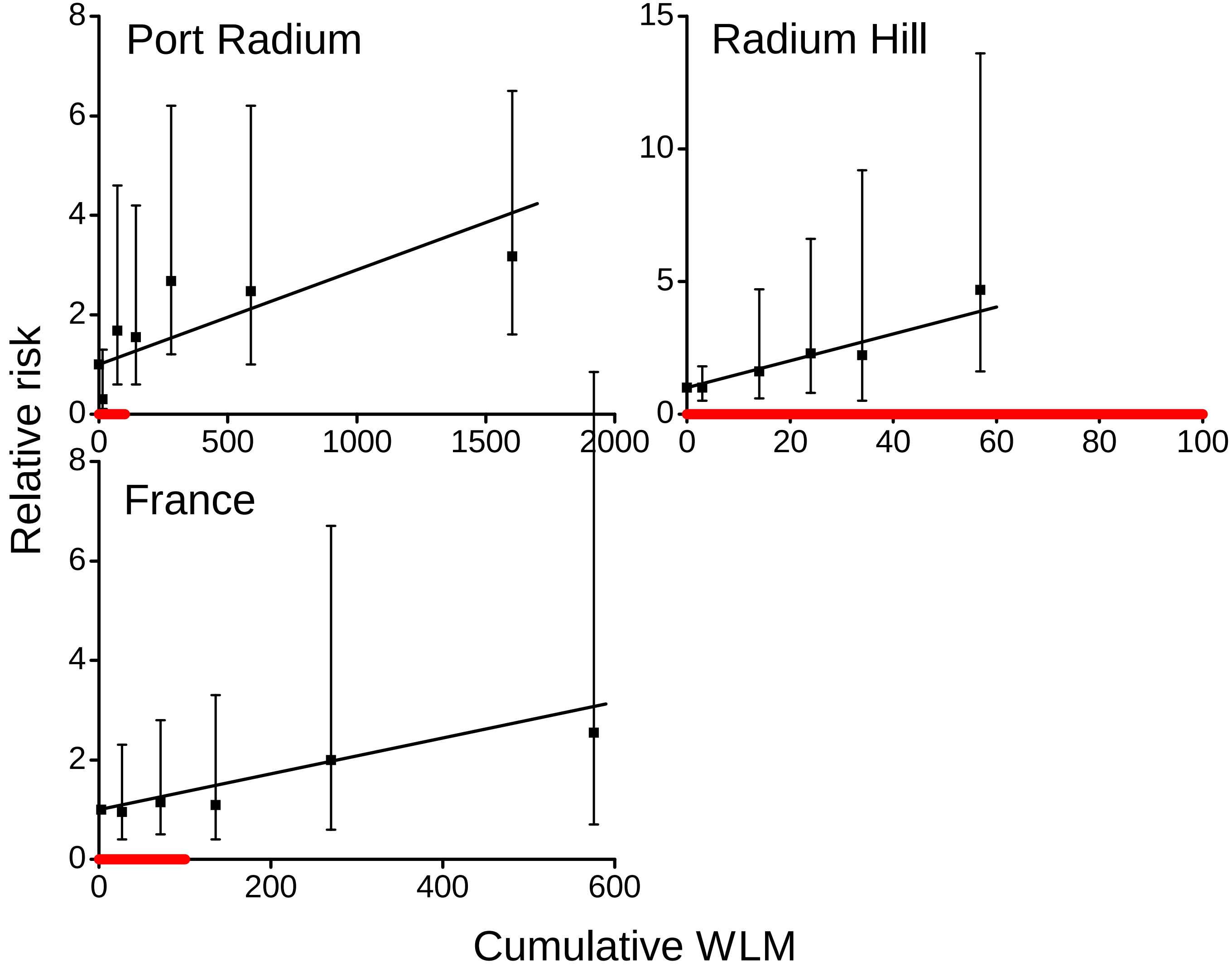
Dose-Response in Miner Studies (I)



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:

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

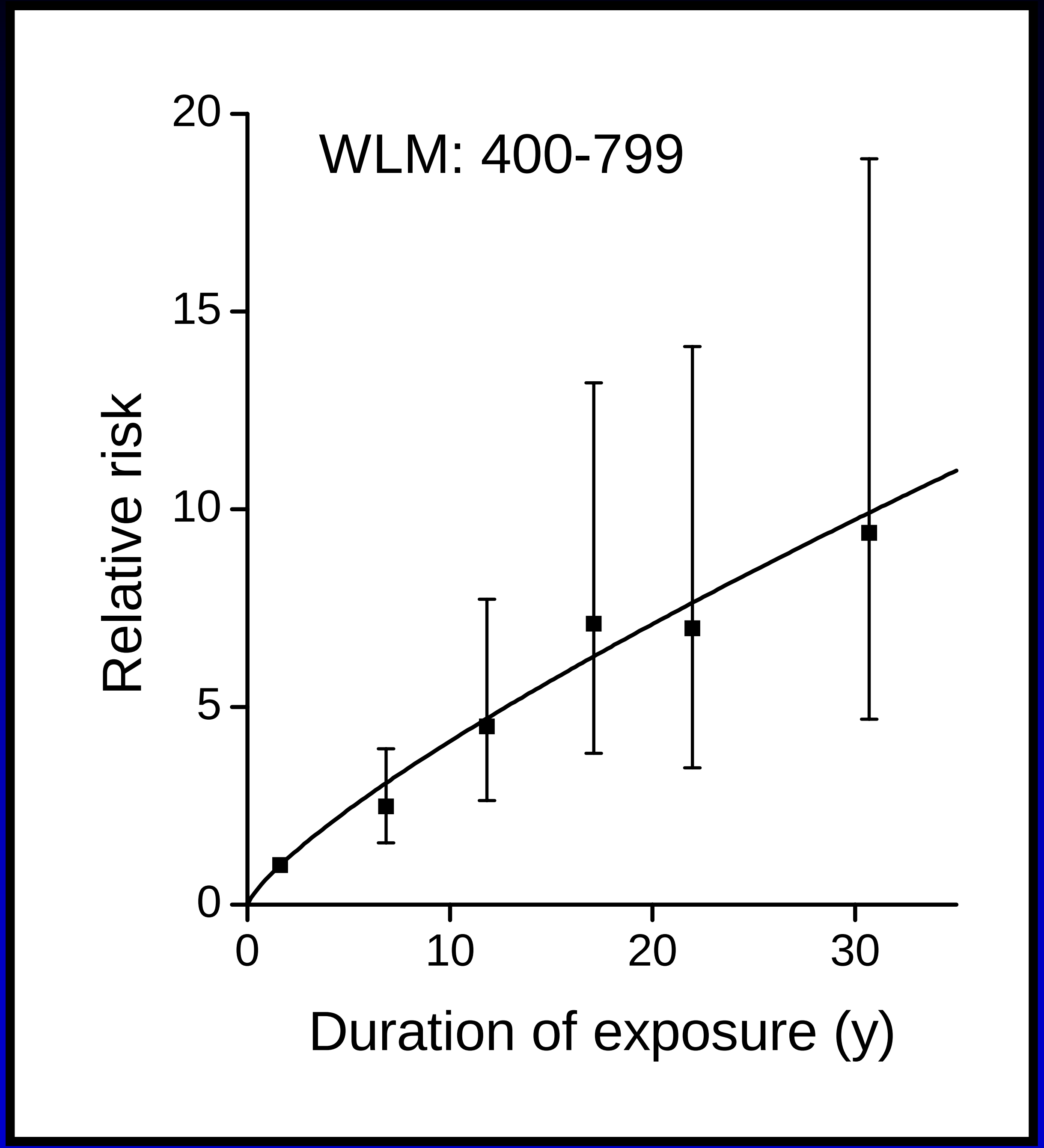
WLM^{*} = WLM weighted by time since exposure

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

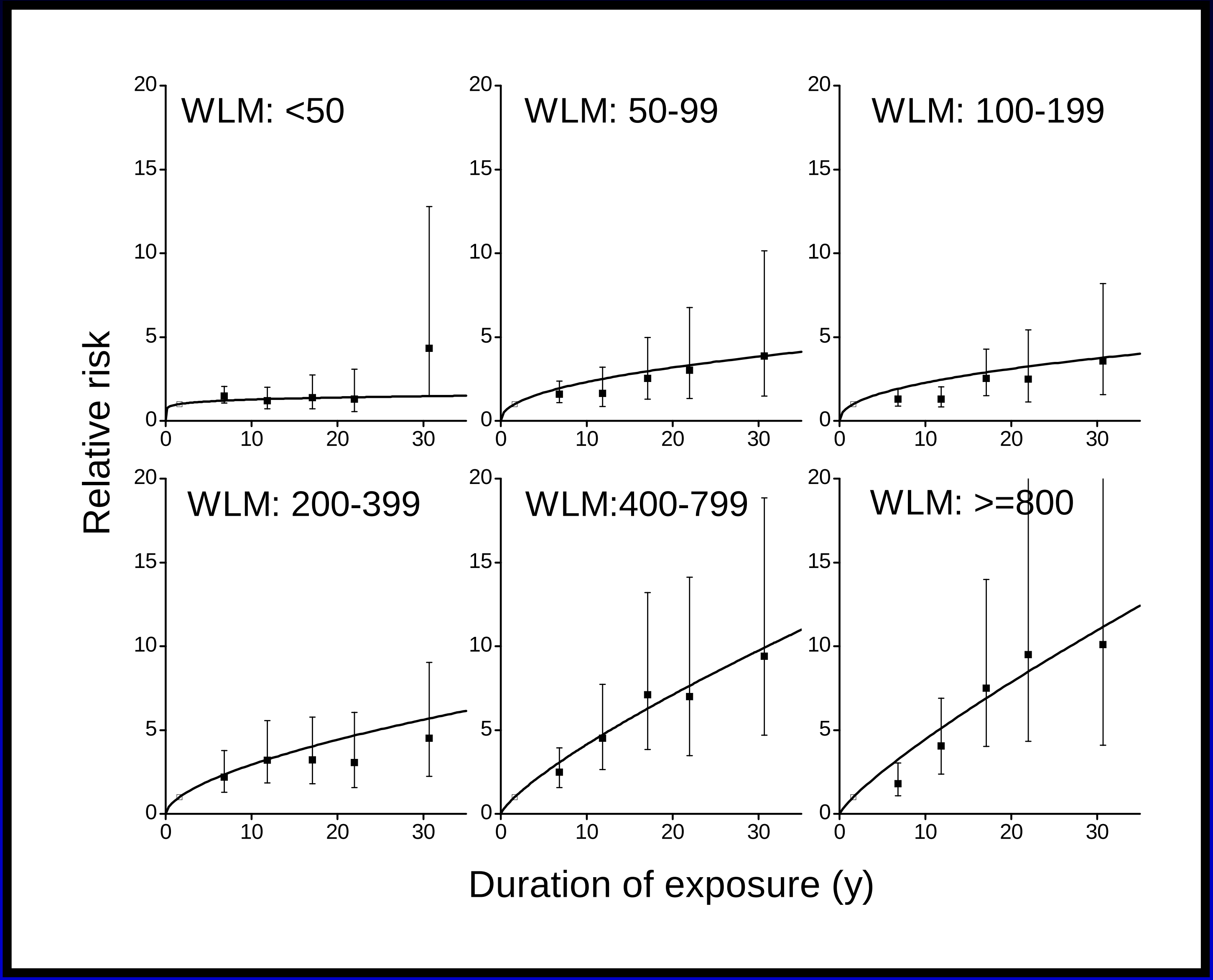
Time Since Exposure Effects

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

RR Patterns and the Inverse Dose-Rate Effect

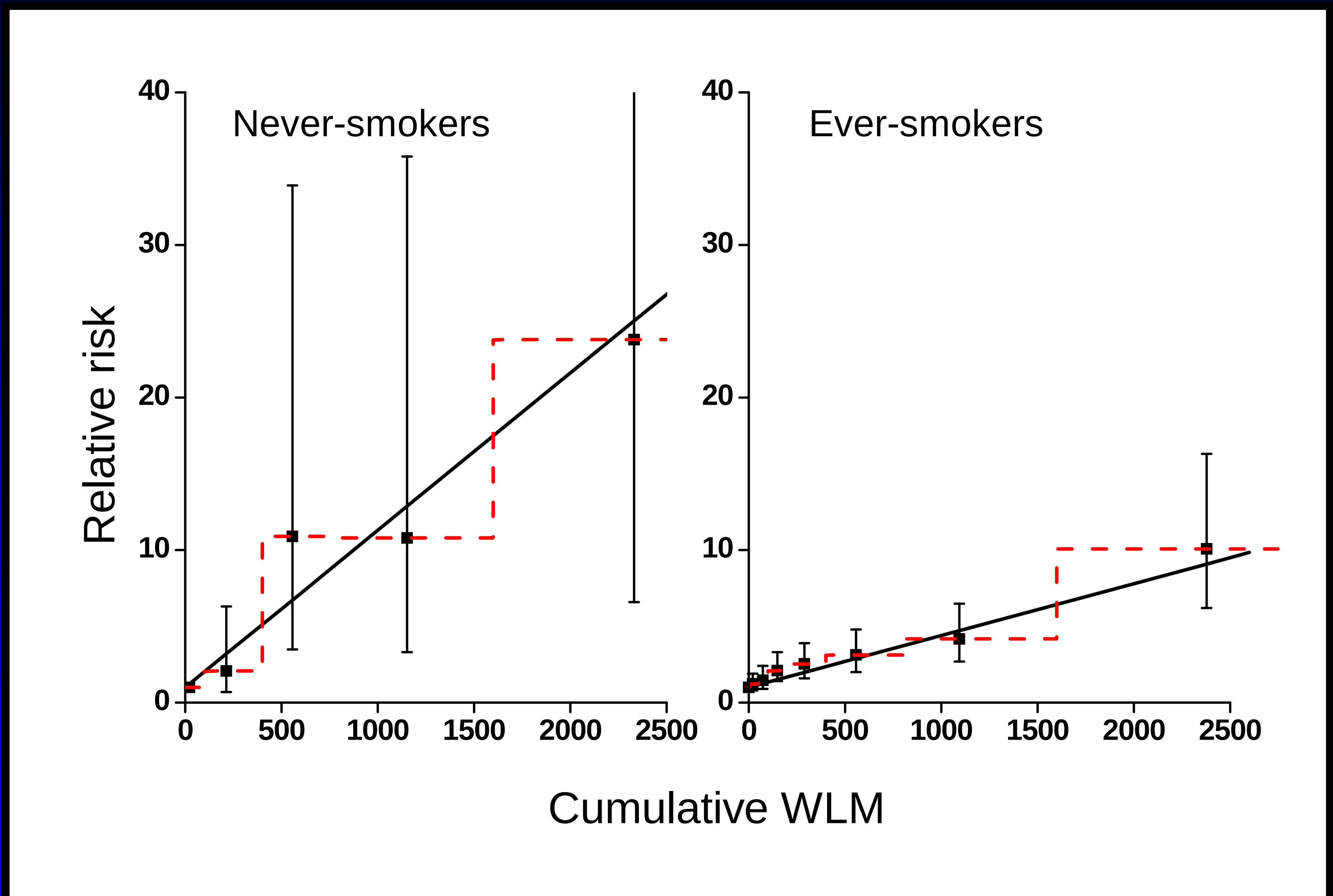


The Inverse Dose-Rate Effect for Radon



Lubin et al 1995

RRs for Ever/Never Smoking Miners



Additional Lung Cancer Studies Since BEIR VI

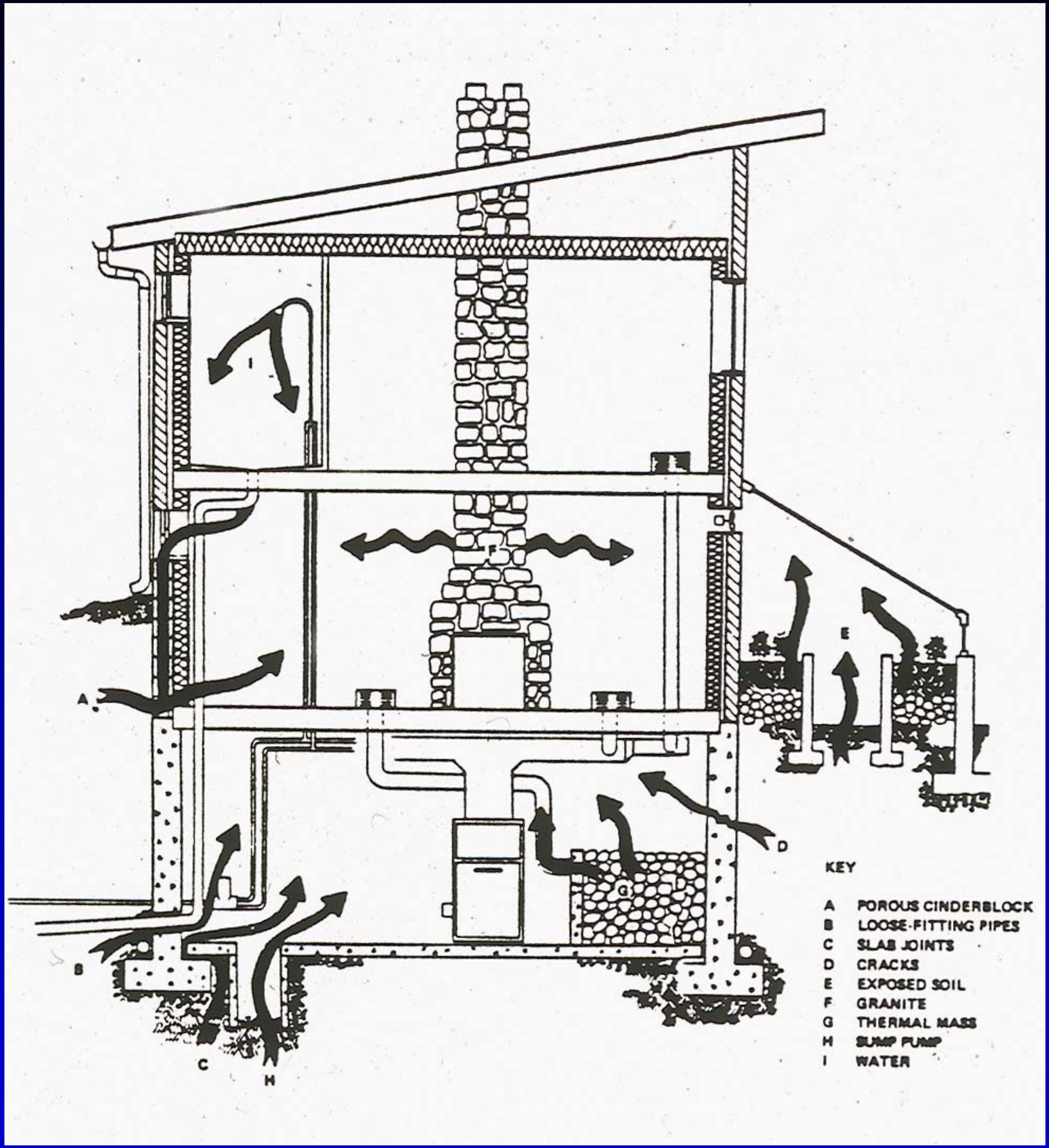
- Czech miners
  - West Bohemia: lung cancer; Tomasek, Rad Res 1999
- French miners
  - Laurier, Eur J Epi 2004; Rogel, J Rad Prot 2002
- Newfoundland fluorspar miners
  - Villeneuve, Health Phys 2007
- Beaverlodge & Port Radium (Canada)
- Brazilian coal miners
  - Veiga, Radiat Env Biophys 2006
- GDR miners (WISMUT)
  - Grosche, BJC 2006; Kreuzer, Health Phys 2002

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



Pooling of Residential Radon Studies

- Workshops (1989, 1991, 1995)
  - annual/semi-annual meetings since 1995
- North America/Europe/China
- World pooling

Pooling of Residential Radon Studies

	No.	Cases	Controls
N America	7	4,108	5,301
China	2	1,076	2,015
Europe	13	7,148	14,208
Total		12,332	21,524

Results of Indoor Rn studies: EOR at 100 Bq/m^3

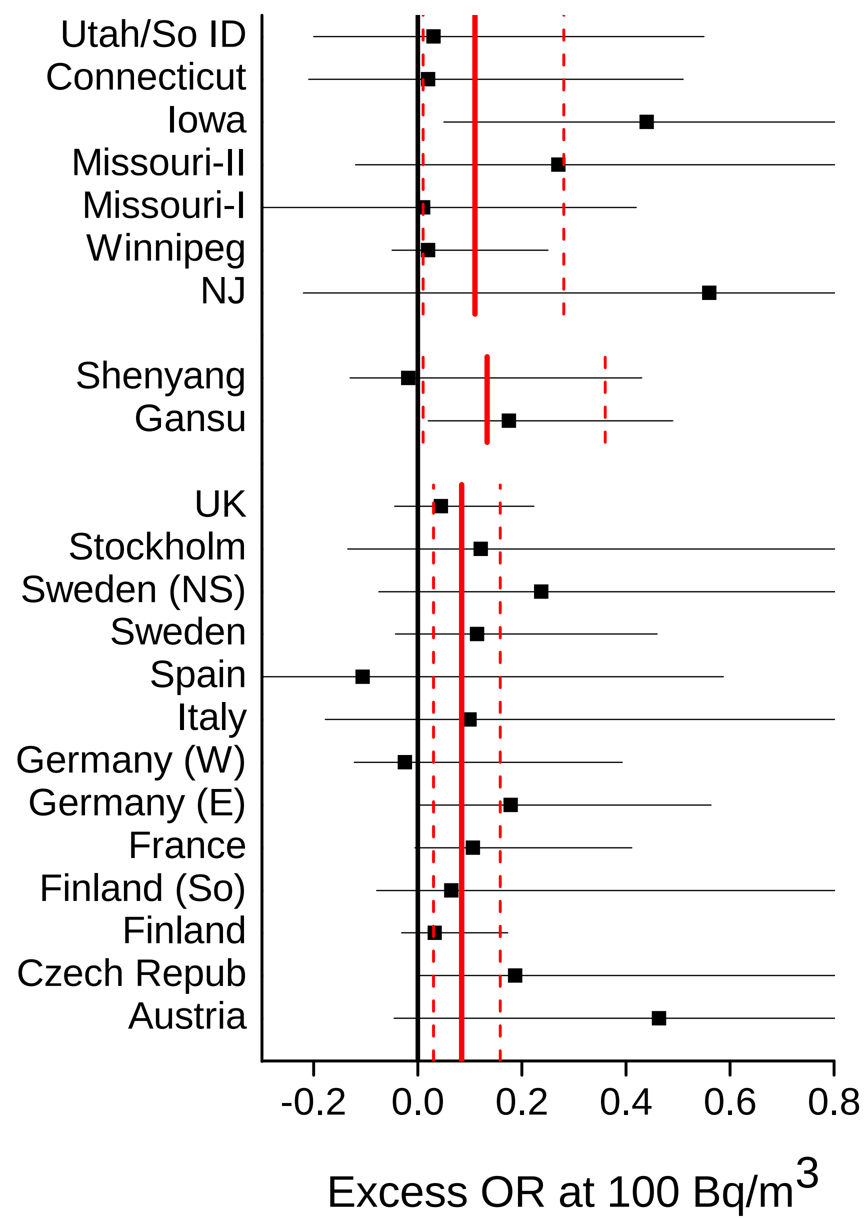
$OR = 1 + \beta \times Bq/m^3$

China: Lubin 2004

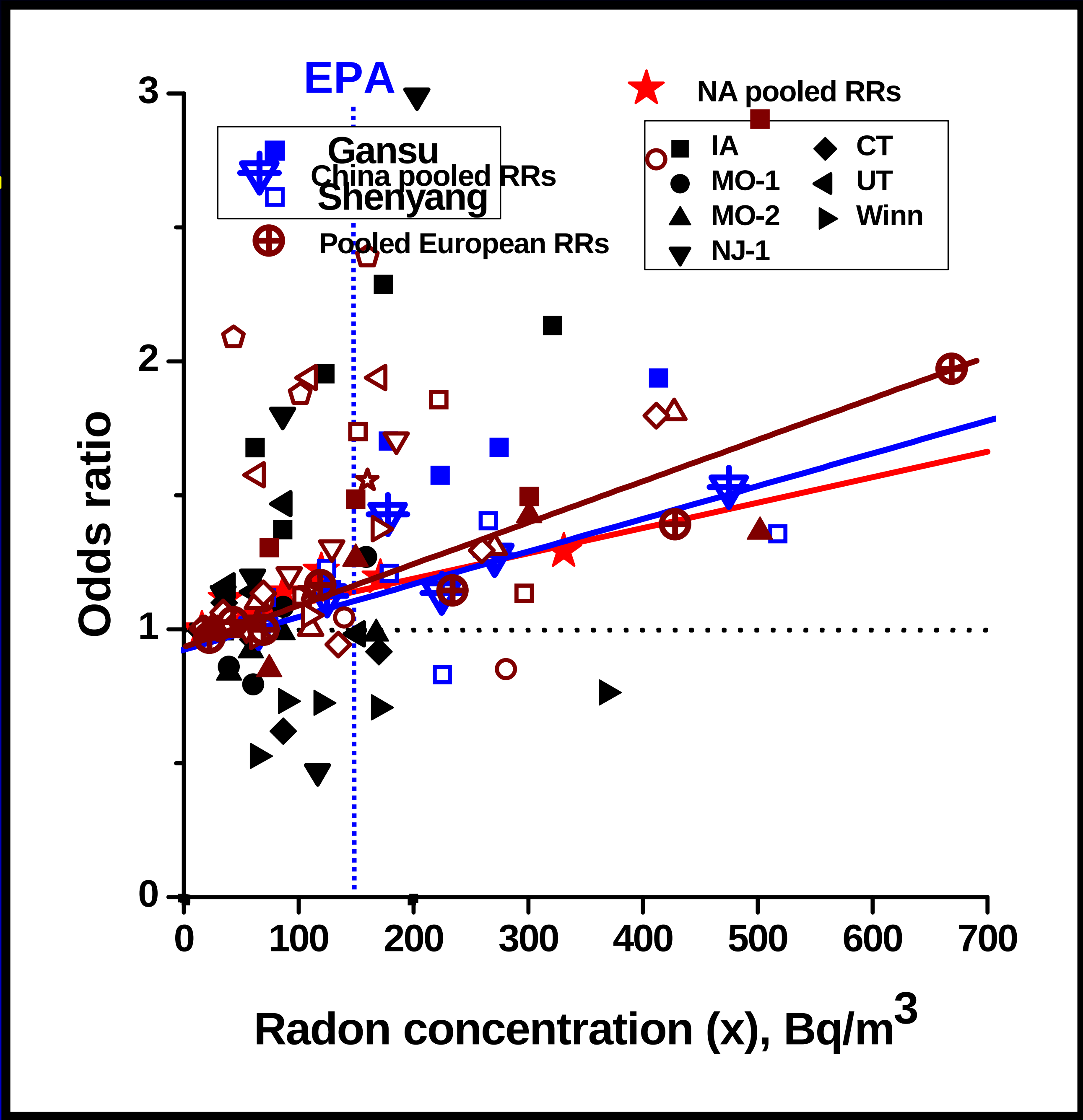
Eur: Darby 2004

NA: Krewski 2005

World: 2007/8



Comparability of Results of Indoor Radon Studies of Lung Cancer



Attributable Risk of Lung Cancer

AR of Lung Cancer in the US from Indoor Radon

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

Assumptions for Extrapolating Risk from Miners to the General Population

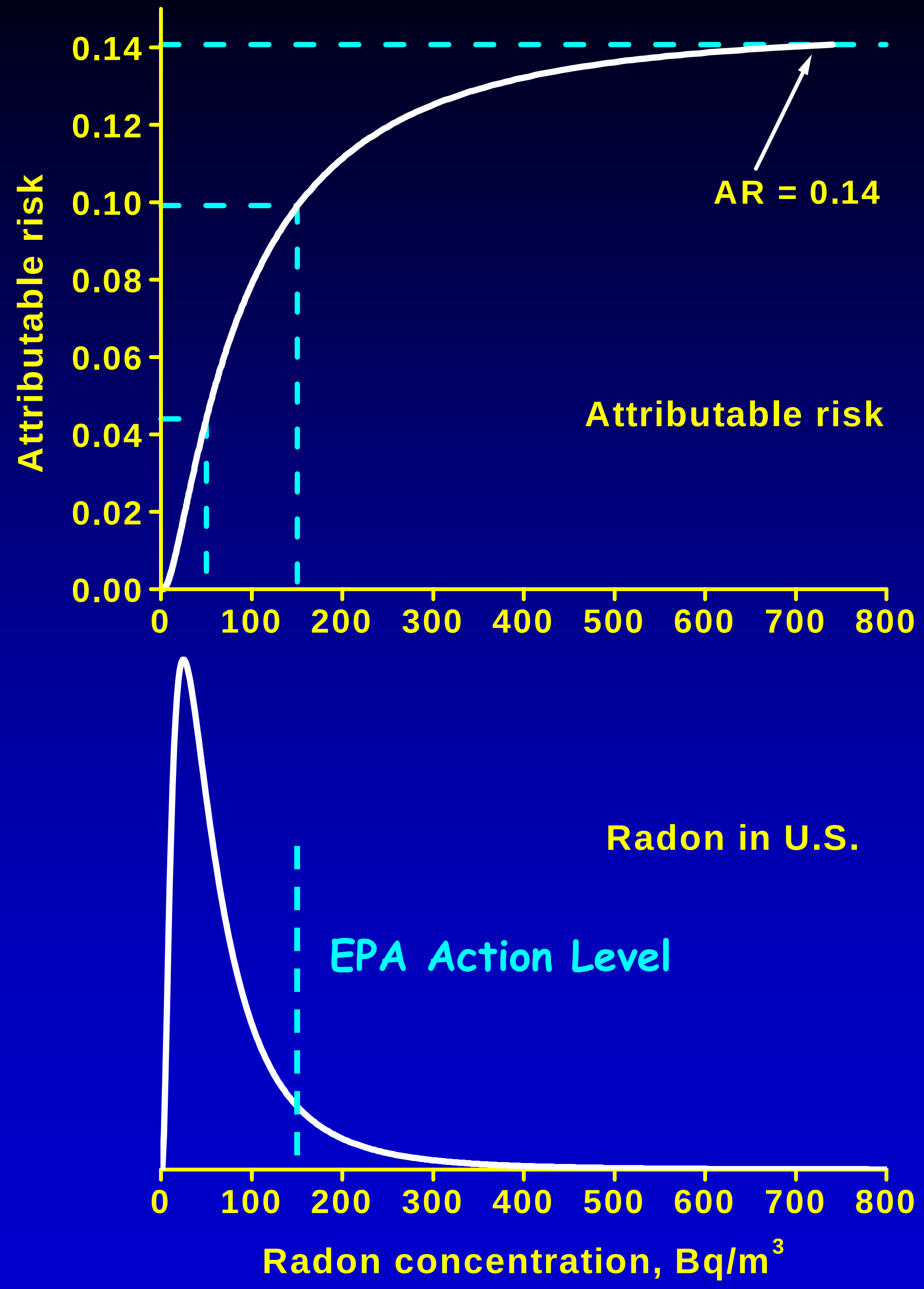
Factor	Assumption
Shape dose-response	Linear ERR
Exposure rate	Comparable risks for rates <0.5 WL or durations longer than 35 yr
Sex	ERR/exposure same in F and M
Age at exposure	ERR/exposure same for all ages
Cigarette smoking	Sub-multiplicative interaction: never-smokers - $2.0 \times \beta$ ever-smokers - $0.9 \times \beta$
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



Attributable Risk for Radon

USA:	10-14%	(3,000-30,000)	BEIR VI 1999
Missouri:	1-4%		Alavanja Envir Intl 1996
Canada:	7.8%	(1,400)	Brand Risk Anal 2005
France:	2-12%	(543-3,108)	Catelinois EHP 2006
Germany-W:	7%	(500-8,200)	Steindorf IJE 1995
Germany:	2-13%	(650-5,000)	Wichmann Epidemiol 2006
Europe:	9%		Darby BMJ 2004

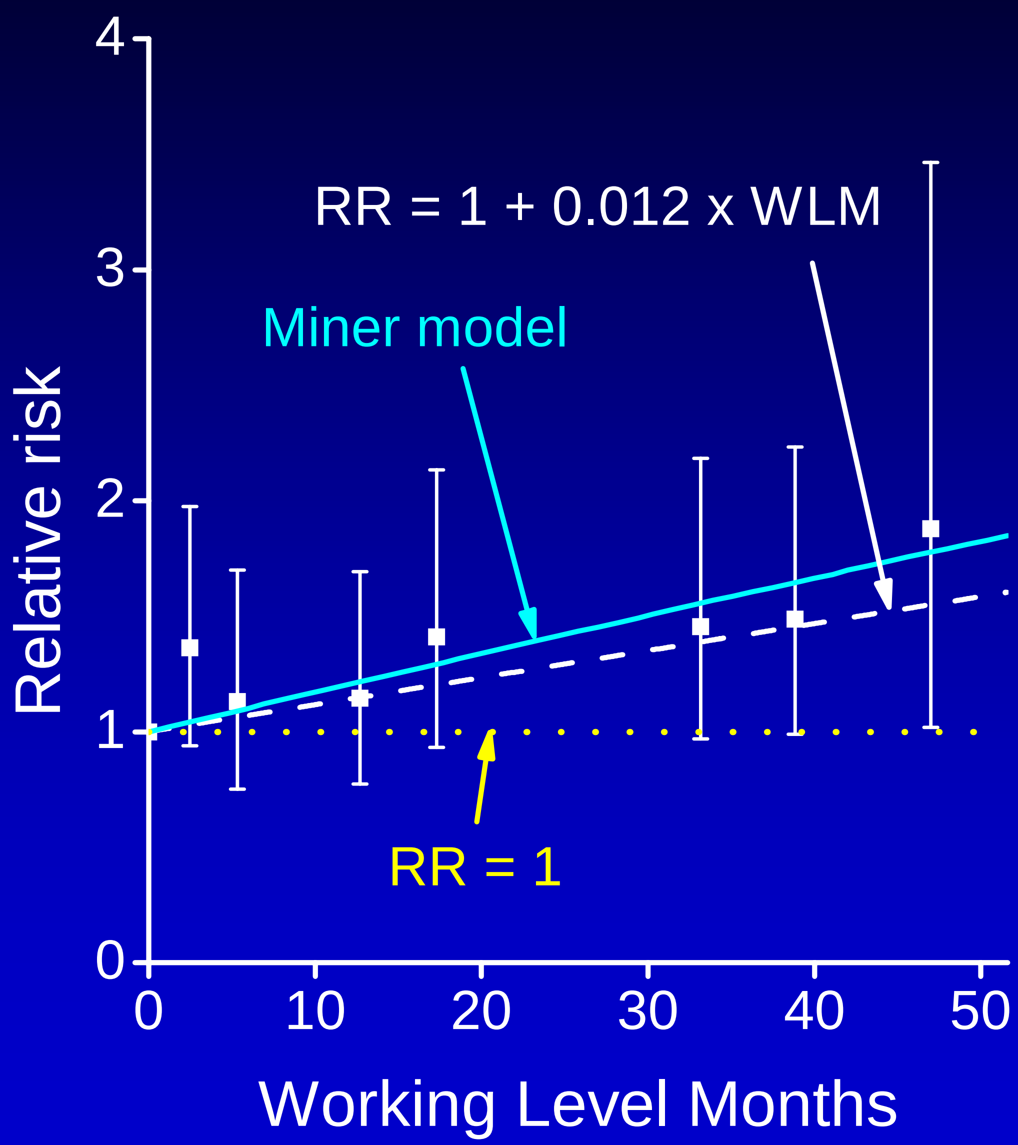
Validity of Attributable Risk Estimates

(1) Are miner-based models internally consistent for low-exposed miners?

(2) Are miner-based models consistent with indoor Rn studies?

(3) Is there radiobiological/ epidemiological evidence for low-dose effects at indoor Rn levels?

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

Validity of AR Estimates for Rn-Associated Lung Cancer

(1) Are miner-based models internally consistent for low-exposed miners?

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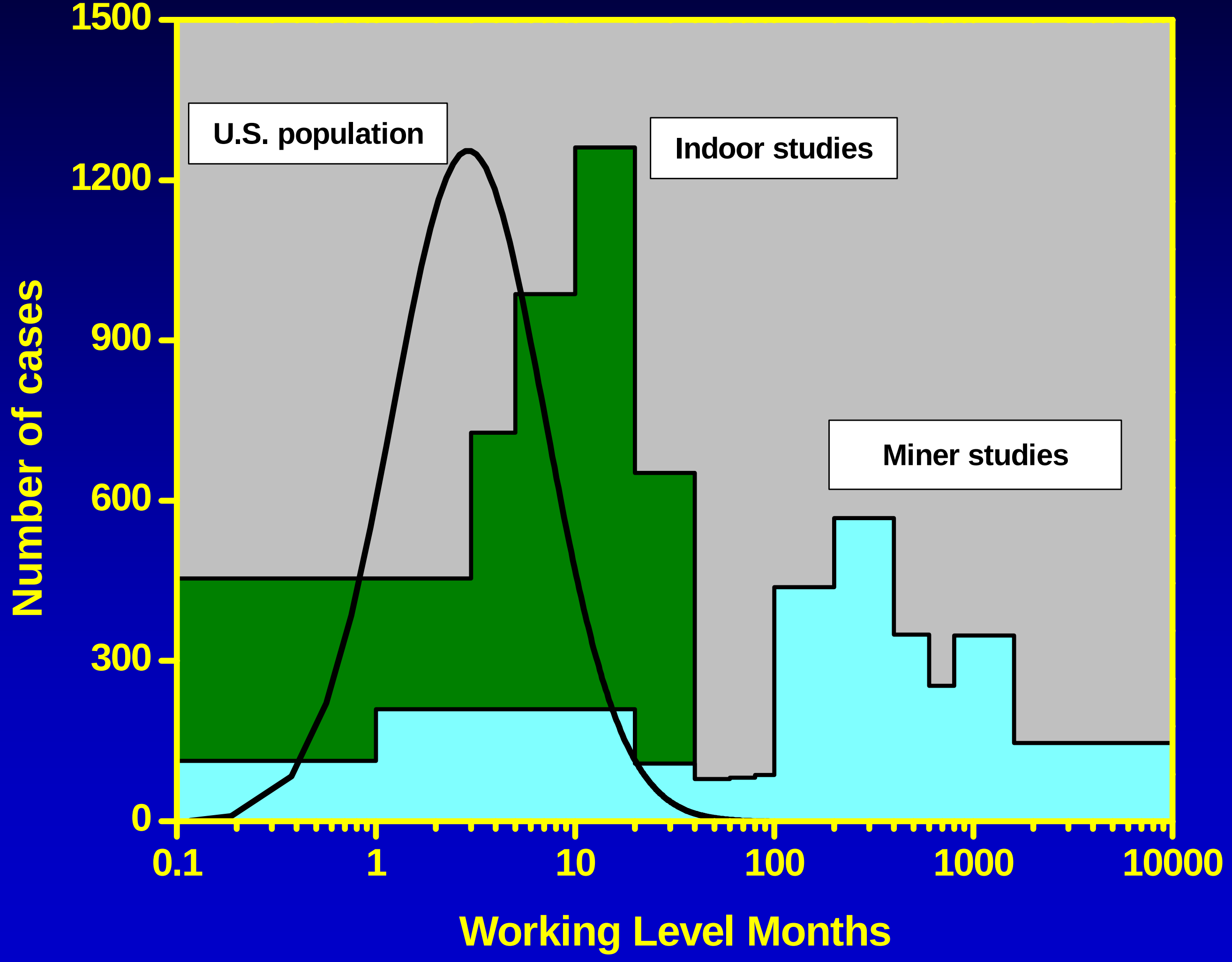
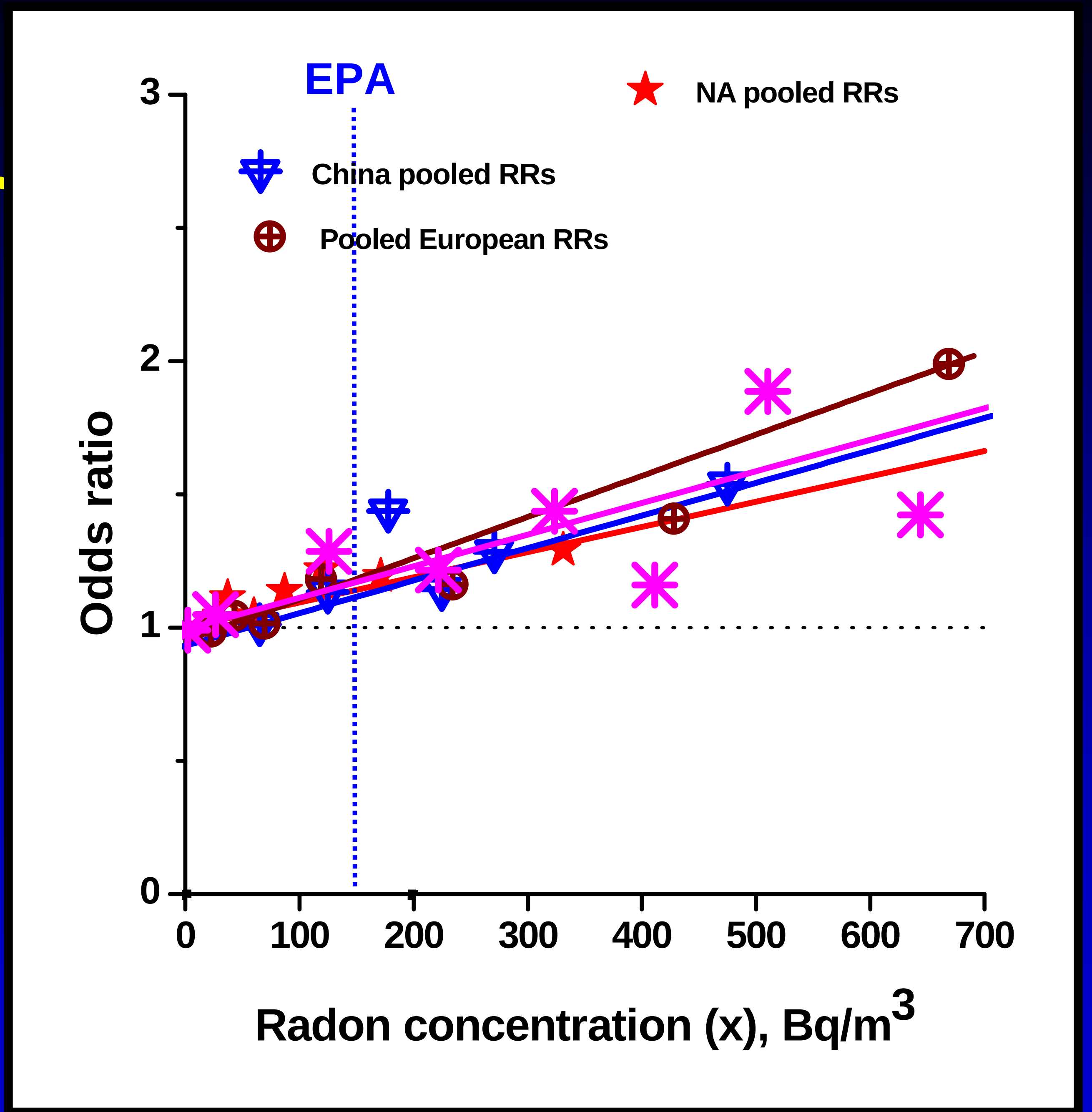
Distribution of radon exposure for cases



Comparability of Results of Indoor Radon Studies of Lung Cancer



Validity of AR Estimates for Rn-Associated Lung Cancer

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(3) Is there radiobiological/epidemiological evidence for low-dose effects at indoor Rn 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 consistent with linear dose-response at low doses.

Brenner 1998

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 "low-doses", estimates always have some uncertainty