Conclusion
following draft report of C1-task group 64 and MC meeting in BA end of October 2008

Draft report of Radon statement

Participants :

From C1 : Dominique Laurier, Margot Tirmarche (Chair)

From C2 : François Paquet, John Harrisson, Eric Blanchardon, James Marsh

From C4 : Jean-François Lecomte

Consultants : John Boice (US), Doug Chambers (Canada), Ladislav Tomasek (Czech Republic), Francesco Bocchichio (Italy), Colin Muirhead (UK)

Objectives of the radon statement group

Following publication 103 recommendations,
should the radon risk for lung cancer be revised ?

- Results of residential exposure studies, published since 1990
- Post Publication 65, new miner results
- Exposure Dose conversions
  - *Epidemiological / Dosimetric*
  - *ICRP / UNSCEAR*

ICRP upper reference levels
600 Bq / m^3 homes
1500 Bq / m^3 workplaces

MC meeting of ICRP in Berlin October 2008

- **Statement on Radon is urgent (6 months), needed for the BSS**
- **Statement shall:**

  Include nominal risk per unit concentration of Rn

  Clearly explain the dose conversion convention

  Take account of recent scientific publications (UNSCEAR report)

  Clarify any apparent or real differences between ICRP and UNSCEAR

Work in progress

- **A draft of the statement is written**
- **Has been examined by C1 and discussed by MC in October 2008**
- **Includes :**

  Synthesis of epidemiological studies, joint analyses from domestic radon and from miners studies

  New calculations / ICRP 65

  Executive summary, followed by a detailed report

Case-control studies in general population

- Comment : no other domestic pollutant has been studied in a more detailed way :
  - Evidence from animal experience, even at « low » doses
  - Evidence from occupational exposure
  - Evidence from 13 epi studies in Europe, 7 from North-America and two from China (plus 2 from Ural region)

Major input of case-control studies :

➔ in field epi studies, able to adjust precisely on individual tobacco consumption, including male and females, smokers and non-smokers

➔ meta-analysis

➔ joint analysis : increase of statistical power

Darby et al. BMJ 2005 and Scand. J Work Environ Health 2006) and Krewski et al. Epidemiology 2005 and J Toxicology Environ Health, 2006)

European case-control studies of residential radon and lung cancer

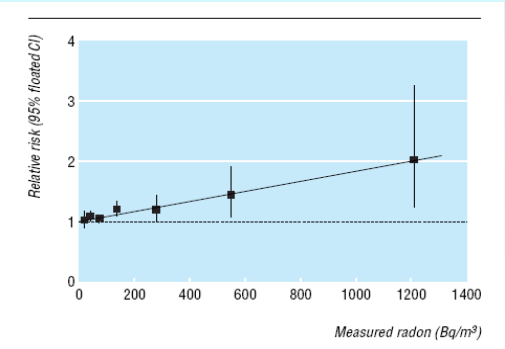
Study	Number of subjects with lung cancer	Number of control subjects
Austria	183	188
Czech Republic	171	713
Finland: nationwide	881	1435
Finland: south	160	328
France	571	1209
Germany: Eastern	945	1516
German: Western	1323	2146
Italy	384	405
Spain	156	235
Sweden: nationwide	960	2045
Sweden: never-smokers	258	487
Sweden: Stockholm	196	375
United Kingdom	960	3126
Total number of subjects	7148	14,208

North American and Chinese case-control studies of residential radon and lung cancer

Study	Number of subjects with lung cancer	Number of control subjects
New Jersey	480 f	442f
Winnipeg	488 m; 250 f	488 m; 250 f
Missouri 1	538 f	1183 f
Missouri 2	512 f	553 f
Iowa	413 f	614 f
Connecticut	527 m; 436 f	442 m; 507 f
Utah; southern Idaho	319 m; 192 f	587 m; 275 f
China		
Shenyang	308	356
Gansu	768	1659

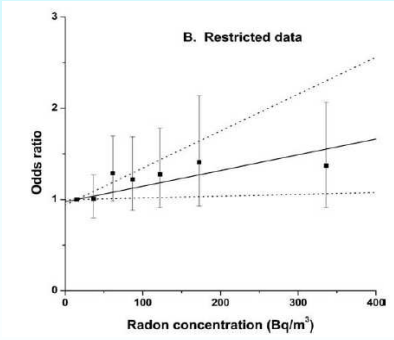
Pooled residential studies

Europe



Darby et al 2005

North America



Krewski et al 2005

Pooled residential studies

Pooling	Studies	Cases	Controls	Relative risk per 100 Bq/m^3 (CI 95 %)
European : *Darby 2006*	13	7148	14208	1.08 (1.03 – 1.16)
North American : *Krewski 2006*	7	3662	4966	1.10 (0.99 - 1.26)
Chinese : *Lubin 2004*	2	1050	1995	1.13 (1.01 - 1.36)

EUROPEAN POOLING Study : non-smokers

Measured radon (Bq/m^3)	% who were lifelong non-smokers
<100	39
100-199	40
200-399	41
400-799	46
800+	48
p for trend	*0.001*

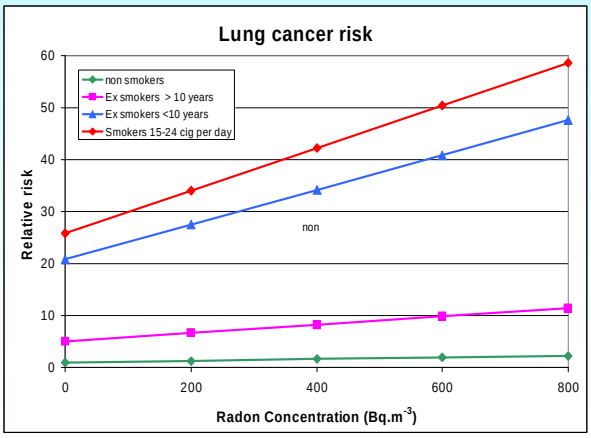
Percentages calculated after stratification for study, age, sex, and region of residence

EUROPEAN POOLING Study :

Effect of stratification for smoking

Stratification	% increase in lung cancer risk per 100 Bq/m^3 measured radon	95% CI	p
A. Study, age, sex, region, smoking in 20 groups	8.4	(3.0, 15.8)	0.0007
B. Study, age, sex, region, smoking in 7 groups	5.2	(1.1, 10.7)	0.009
C. Study, age, sex, region only	2.3	(-0.5, 6.1)	0.64

Joint European analysis: radon risk is a function of the baseline risk of smokers and non smokers



European pooling: Contribution of each study

- **No evidence that effect of radon differed between studies**
- **Influence analysis : analysis repeated by omitting each study in turn**
  (ref Darby et al, table 10,Scan J Work Environ Health 2006, vol32 suppl 1)
  Estimated linear relationship (after stratification by study, age, sex, region of residence and smoking history) changed by less than 10% for 11 of the 13 studies
- **No significant difference**
  when considering lung cancer diagnosis over clinical versus death certificates
  Study with hospital or population based studies
  Wether or not surrogates interviews were used
  Radon measurments detectors were open or closed
  No effect of « windows of exposure »
  If linear or log-linear or linear quadratic RR models were used : quite comparable results were obtained

Combined analysis from North American studies

Krewski , Lubin et al, J TOX ENV H)

- **Odds ratio trend consistent with linearity (p= 0,10)**
- **Excess OR : 0,10 per 100 Bq per m^3 (CI 95 %: -0.01,0.26)**
- **If limited to residence of one or two houses and with alpha track measurments over at least 20 years :**

  EOR = 0.18 per 100 Bq per m^3 (0.02,0.43)

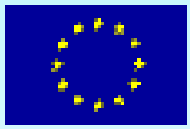
  Estimates are compatible with an EOR of 0.12 per 100 Bq per m^3 (0.02,0.25) predicted by extrapolation from miners studies

Synthesis from epi studies of domestic exposure

- **Large number of new epidemiological studies : joint analyses from European, North American and Chinese studies;**
  - ***sufficient statistical power for a demonstration of a risk of lung cancer at low doses,***
  - ***adjustment on smoking habits***
- **Major results**
  - ***Risk of lung cancer is increasing with cumulated exposure to radon decay products***
  - ***Risk of lung cancer observed at levels < 200 Bq/m^3, if exposure cumulated over the 30 years preceding cancer diagnosis***
  - ***Risk increases for smokers and non-smokers***
- **Synthesis : RR increase ≈ 10% per 100 Bq/m^3 (cumulated during 30 years) ,**
  - **if uncertainty linked to past exposure is taken in account, this risk coefficient is higher in most studies (Unscear proposal : 16% increase per 100 Bq/m^3)**
- **Further research required about leukaemia**

The "Uminers + Animal data" European project

Uminers + Animal data
Contract no. FIGH-CT1999-00013
Duration: Feb 2000 – July 2003
Coordinator : M Tirmarche (IRSN)



FP5

Quantification of lung cancer risk after low radon exposure and low exposure rate : synthesis from epidemiological and experimental data

- Epidemiology (cohorts of U miners in Europe)
- Modelling (confrontation of classical and TSCE modelling)
- Animal experiments

8 partners

IRSN (France), BfS (Germany), NRPI (Czech Republic), GSF (Germany), CEA (France), AEAT (UK), NRPB (UK), RIVM (The Netherlands)

Final report : **www.irsn.org**

The Alpha-risk European project

Specific targeted research or innovation project (STREP)
Contract no. 516483 (FI6R)
Duration: July 2005 – June 2009
Coordinator: M Tirmarche (IRSN)

FP6

Quantification of cancer and non-cancer risks associated with multiple chronic radiation exposures

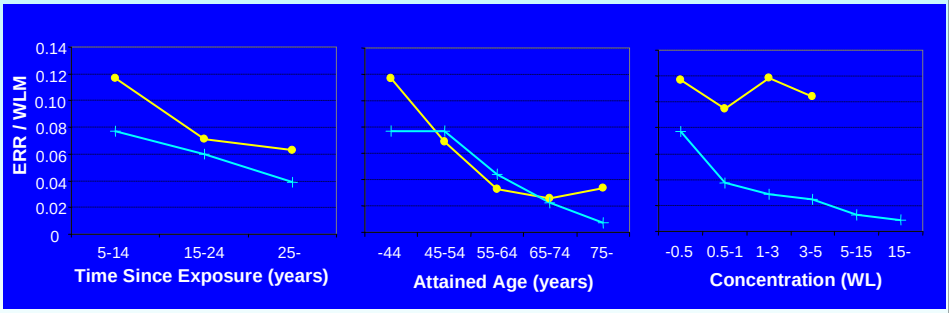
- Epidemiological studies (U miners, nuclear workers) and radon in homes
- Organ dose calculation
- Risk assessment

19 partners

IRSN (France), BfS (Germany), NRPI (Czech Rep), CR-UK (UK), IARC (France), WSC (UK), AWE (UK), HPA (UK), U Salzburg (Austria), GSF (Germany), RIVM (The Netherlands), ISS (Italia), BAuA (Germany), CAATS (France), UK-AEA (UK), SCK-CEN (Belgium), U Ottawa (Canada) , RWE NUKEM (UK), **CREAL** (Spain)

Web site : **www.alpharisk.org**

The Czech-French joint study: risk modifiers

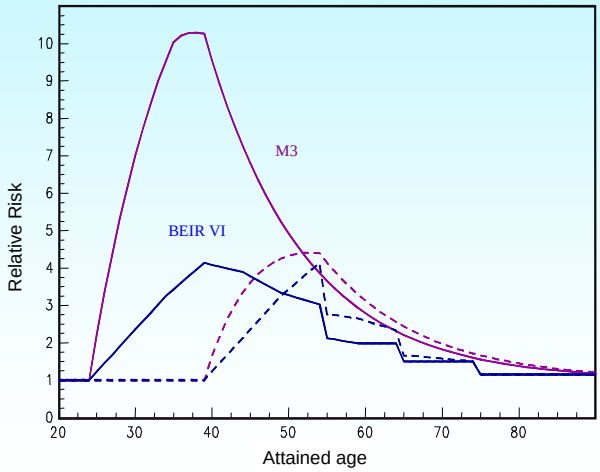


Cz+Fr	10 100 miners – 573 lung cancer deaths – 95% of exposure years at rate < 2 WL
BEIR 6	11 cohorts of miners – 2787 lung cancer deaths – dose rate up to > 15 WL

Strong decrease of risk with time since exposure
No inverse dose-rate effect

The Czech-French joint study: effect of time and age

Relative lung cancer risk of lung cancer associated to a radon cumulated exposure of 90 WLM (6 WLM per year during 15 years)

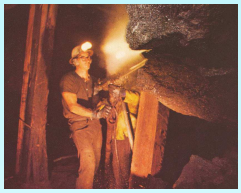


2 scenarii:
Exposure at age 20-34 years (solid lines)
Exposure at age 35-49 years (dashed lines)

2 models:
BEIR VI-age-concentration model (broken lines)
Cz-Fr preferred model (M3) (smoothed lines)

[Tirmarche et al, 2003]

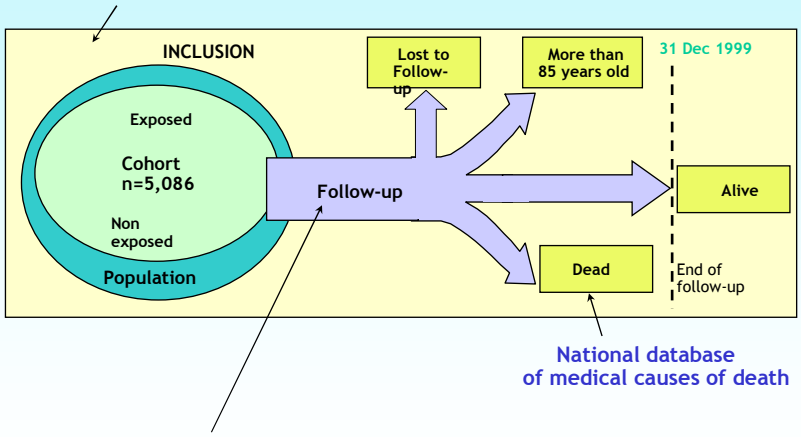
Uranium miners studies



- **Cohorts of uranium miners** (WP1)
  - France, Czech Republic and Germany
  - (> 40,000 miners)
  - Nested case-control studies (tobacco, lung cancer and leukemia risk)
  - Good quality reconstruction of multiple exposures (radon, gamma, ore dus
- **Methodology**
  - Dosimetric models (WP5)
  - Parametric statistical methods and biologically-based modelling approache
  - Consideration of measurement errors and uncertainty
- **Objectives**
  - Time-modifier of the radon-lung cancer risk relationship
  - Risk associated to tobacco, radon and other radiation sources in the mines
  - Risk of cancers other than lung (leukemia, kidney…)
  - Non cancer mortality risk
  - Lifetime lung cancer risk estimates (WP6)
  - Parallel analysis with indoor radon studies (WP6)

Updated data, new endpoint of follow-up

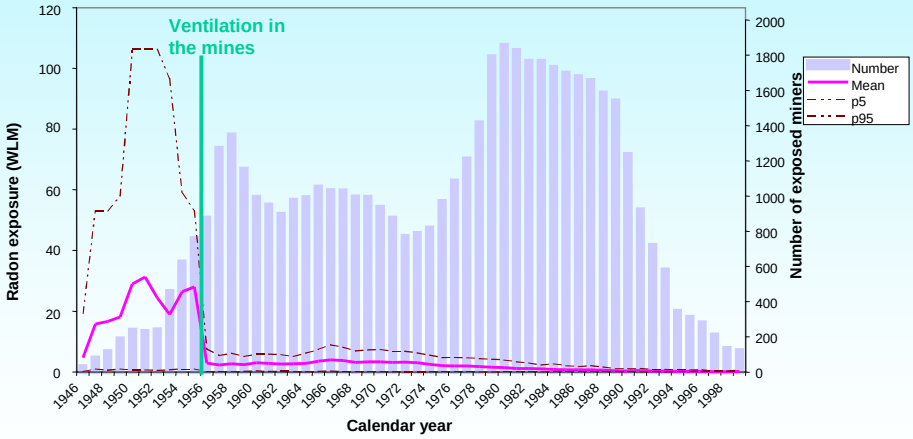
Example French miner cohort :
Criteria of inclusion : Employed at least 1 year between 1946 and 1990



Vital status: matching with the national database of individual identification
Exposure: historical reconstruction from 1946 to 1955, and individual records afterward

DISTRIBUTION OF RADON EXPOSURE

**Distribution of yearly radon exposure (WLM)
among the French cohort of uranium miners 1946-1999**



- Unit of radon exposure: Working Level Month (WLM)

RESULTS: Characteristics of the exposure

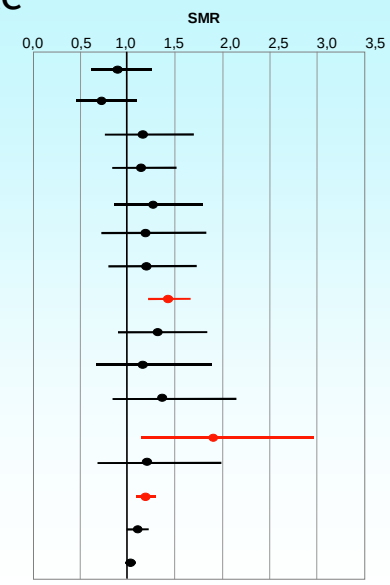
	Follow-up to 1999
Number of exposed miners (%)	4 132 (81)
Mean cumulative radon exposure WLM (Min-Max)	36.6 (<1 - 960)
Mean duration of radon exposure (Min - Max)	13.1 (1 – 35)
Mean age at first exposure (Min – Max)	29.1 (15 - 63)
Mean age at last exposure (Min – Max)	41.1 (16 - 64)

RESULTS: Mortality risk

Causes	Observed	SMR	95% CI
ALL CAUSES	1,404	1.0	1.0 - 1.1
ALL CANCERS	544	1.2	1.1 – 1.3
NON CANCER	867	0.9	0.9 – 1.0
NERVOUS SYSTEM	24	1.1	0.7 – 1.6
CIRCULATORY SYSTEM	319	1.0	0.9 – 1.2
RESPIRATORY SYSTEM	80	1.3	1.0 – 1.6
SILICOSIS	23	7.1	4.5 – 10.7
RESPIRATORY SYSTEM (except SILICOSIS)	57	1.0	0.7 – 1.3
DIGESTIVE SYSTEM	101	1.0	0.8 – 1.2
EXTERNAL CAUSES	196	1.1	0.9 - 1.2

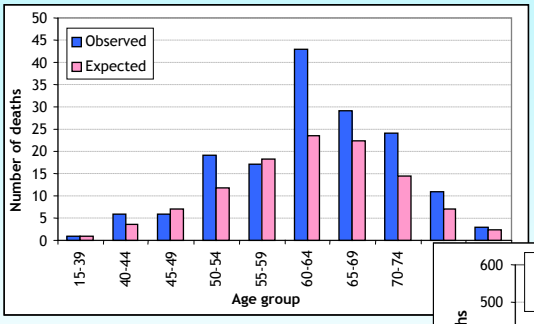
RESULTS: Mortality risk by cancer site

	Observed deaths
Cancer of the oral cavity	33
Oesophagus cancer	22
Stomach cancer	26
Cancer of intestine, colon & rectum	45
Cancer of liver, gallbladder and pancreas	44
Pancreas cancer	20
Larynx cancer	29
Lung cancer	159
Prostate cancer	32
Bladder cancer	17
Brain and central nervous system cancer	21
Kidney cancer	20
Leukaemia	15
All cancer sites	544
All cancers except lung and kidney	365
All cause deaths	1411

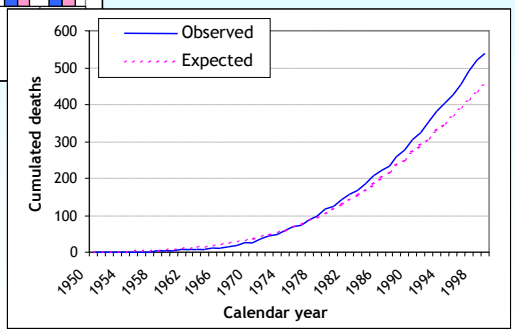


Standardised Mortality ratio (SMR) — 95% Confidence interval

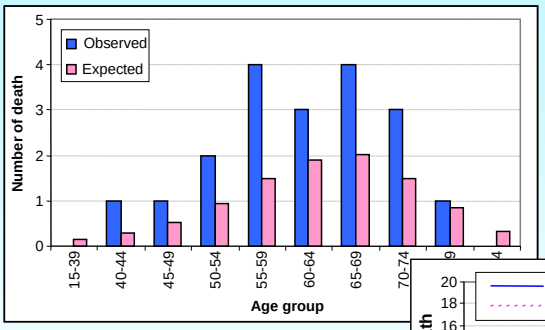
RESULTS: Lung cancer mortality



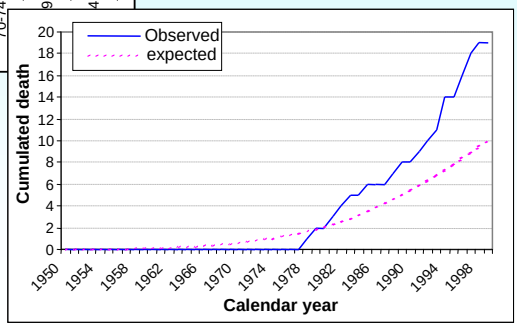
O = 159 ; E = 111.5
SMR = 1.43 [1.21 ; 1.67]



RESULTS: Kidney cancer mortality

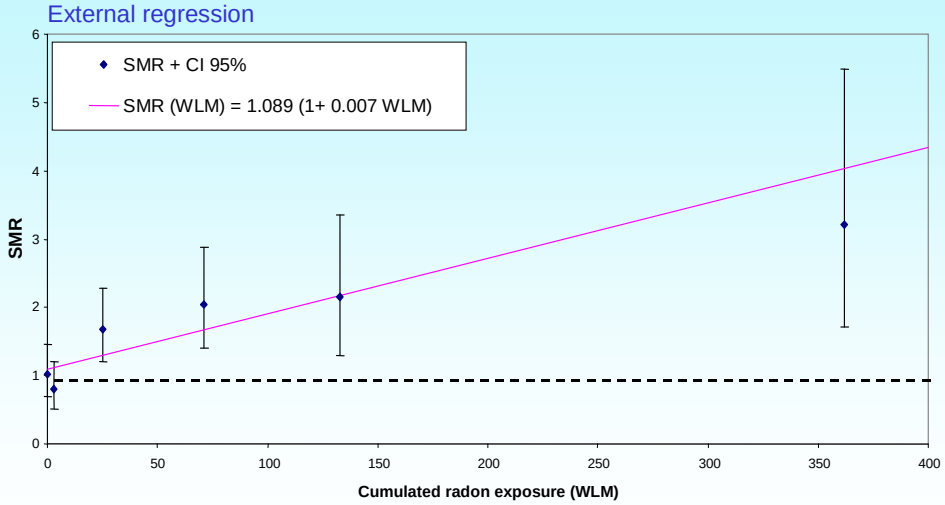


O = 20 ; A = 10,0
SMR = 2,00 [1,22 ; 3,09]



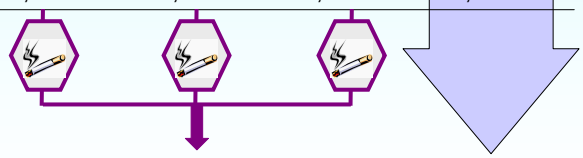
RESULTS: Lung cancer risk and radon exposure

External regression



WP1 Joint analysis on European U miners

	France	Czech Republic	Germany	Total
Population size	5,086	9,979	35,084	50,149
Follow-up period	1946-1999	1952-1999	1955-1998	1946-1999
Person-years	153,047	262,507	908,661	1,324,215
Length of follow-up	30.1	26.3	25.9	26.4
Age at end of study	58.9	56.6	48.6	51.2
Number of death	1,467	3,947	4,519	9,933



Analysis on 1236 cas and 2678 controls with information on tobacco consumption

Joint analysis

Synthesis from epi studies of occupational exposure

- **Updated U miners studies, joint analysis of Czech and French miners, German study, several Canadian studies :**

  Major results :

  Linear exposure response relationship, modified by time since exposure and age at exposure:

  - ***Risk decreases when time since exposure increases***
  - ***No inverse dose-rate effect at low cumulated exposures***
  - ***Tobacco does not modify dose-response relationship (limited data)***

Open issues

1 New results from miners studies

2 Comparison with risk coefficients from indoor studies

3 Underlying hypotheses to the dose conversion convention,
and potential impact on the coefficients

Miner data

ICRP Publication 65 (1993)

ERR / 100 WLM = 1.34 (0.8 – 2.1)

➔ 31,486 miners, 7 cohorts (USA, Canada, Czech Republic, France, Sweden)

BEIR VI (1999)

ERR / 100 WLM = 0.59

➔ 60,705 miners, 11 cohorts (+ China, Australia)

UNSCEAR (2008)

ERR / 100 WLM = 0.59 (0.35 - 1.0)

➔ 14 cohorts (+ Germany)

Miner data
low cumulated exposures, over long periods

Reference	Analysis	ERR / 100 WLM
BEIR VI (1999)	< 100 WLM	0.81 (0.30 - 1.42)
	< 50 WLM	1.18 (0.20 - 2.53)
	< 0.5 WL	3.41
Tomasek (2008)	French-Czech (47 WLM)	2.7 (1.7 - 4.3)

remark: 1 WLM over 30 years = 30 WLM
1 WLM per year equivalent to 230 Bq per m^3 per year
(assuming F=0.4 and 7000 h per year)

Miner data ➔ Lifetime Excess absolute Risk

Reference	Model	Background	Risk x 10^{-4} WLM^{-1}
ICRP (1993)	Pub 65	Pub 60, M+F	**2.83**
EPA (1999)	BEIR VI	USA	5.1
Tomasek (2008)	Pub 65	Pub 103, M+F	2.7
	BEIR VI	Pub 103, M+F	**5.3**
	Czech-French	Pub 103, M+F	**4.4**

proposal of task group : ➔ USE revised 5 x 10^{-4} per WLM lung cancer risk

Lifetime risk

Primary risk coefficient : study population, modifying factors, exposure range

Lifetime risk : lifetime duration, survival function, other causes of death

Risk projection model : multiplicative / additive

Background rates : gender, country, period

ICRP65 approach

- **Scenario used :**
  - ***Exposure to 2WLM from age 18-age 64***
  - ***Follow-up from age 18_to age 90 : lifetime risk calculation***
  - ***Mixed female and male population: Euro-american population***
  - ➔***background rate of cumutative lung cancer mortality***
  - ➔***ERR model (+modifying factors) gives the Lifelong risk calculation for exposed population***
  - ➔***LEAR of lung cancer mortality per WLM***
  - ➔***Is considered as the total detriment and compared with total detriment linked to external exposure (ICRP103)***
  - ➔***Value of mSv effective dose per WLM for domestic and workers exposure***

Main points

- Lung cancer risk is demonstrated on residential radon case-control studies : risk is increasing with increasing cumulated exposure (exposure window studied : period of 30 years preceding the lung cancer diagnosis)
- Risk exists both for smokers and nonsmokers
- Risk is observed at levels close to < 200 Bq / m^3
- Risk management on the basis of exposure to radon gas is possible (annual averaged concentration weighted by number of hours)

• if Conversion in mSv effective dose☹(ICRP65 approach)

Based on miner data, the revised LEAR (life time excess absolute risk) of lung cancer estimate is 5×10^{-4} per WLM

•Comparison of LEAR with total detriment gives effective dose of 9 mSv per WLM for the public and 12 mSv per WLM for the workers:

•➔taskgoup proposes a unique value of 10 mSv per WLM

•Exposure to dose conversion is not different from dosimetric models approach
➔different ways with similar results