Lifetime excess absolute risk for lung cancer due to exposure to radon

- The contribution of the PUMA study (Pooled Uranium Miners Analysis)

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Background

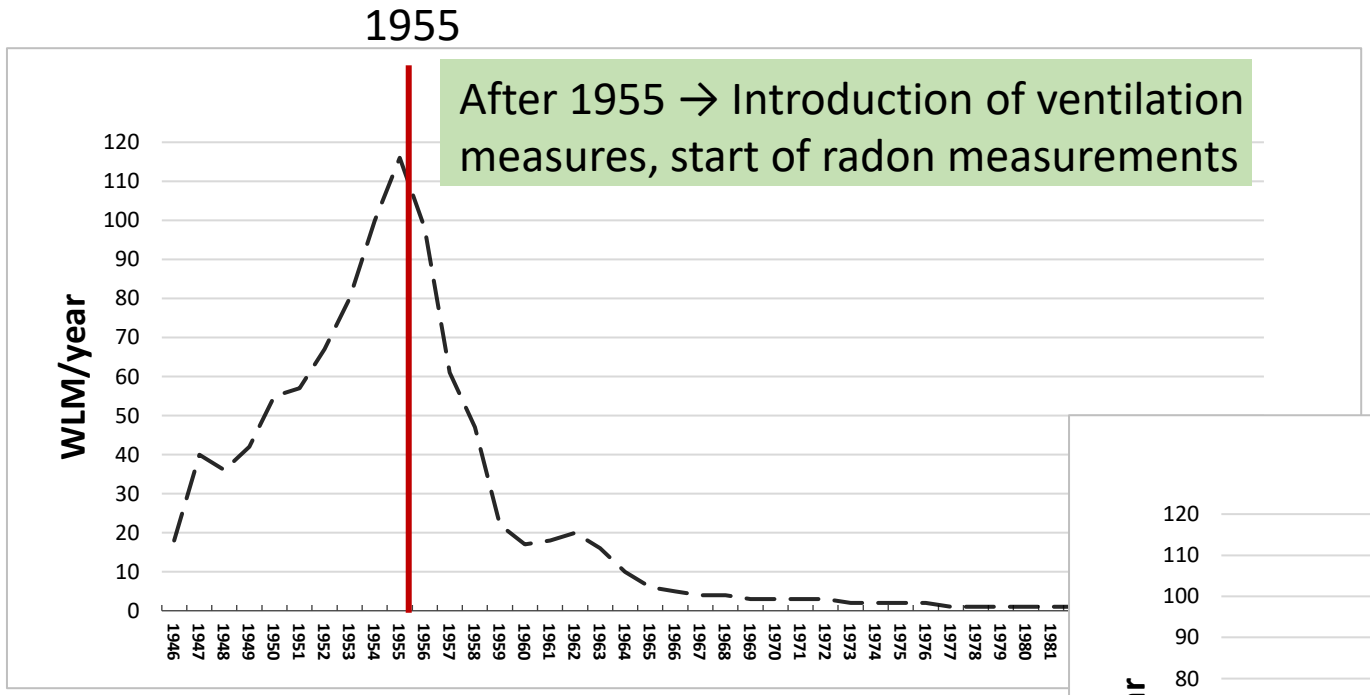
Context

- Radon is a radioactive gas and a leading cause of lung cancer
- Studies of underground miners conducted since the 60’ allowed quantifying the relationship between radon exposure and lung cancer mortality
- These results are a major support for elaborating the system of protection against radon
- Mining conditions and levels of radon exposure in the mines have evolved dramatically over time – studies of uranium miners employed in later periods of mine operations (≥ 1960) provide more accurate exposure information and are more comparable to contemporary settings

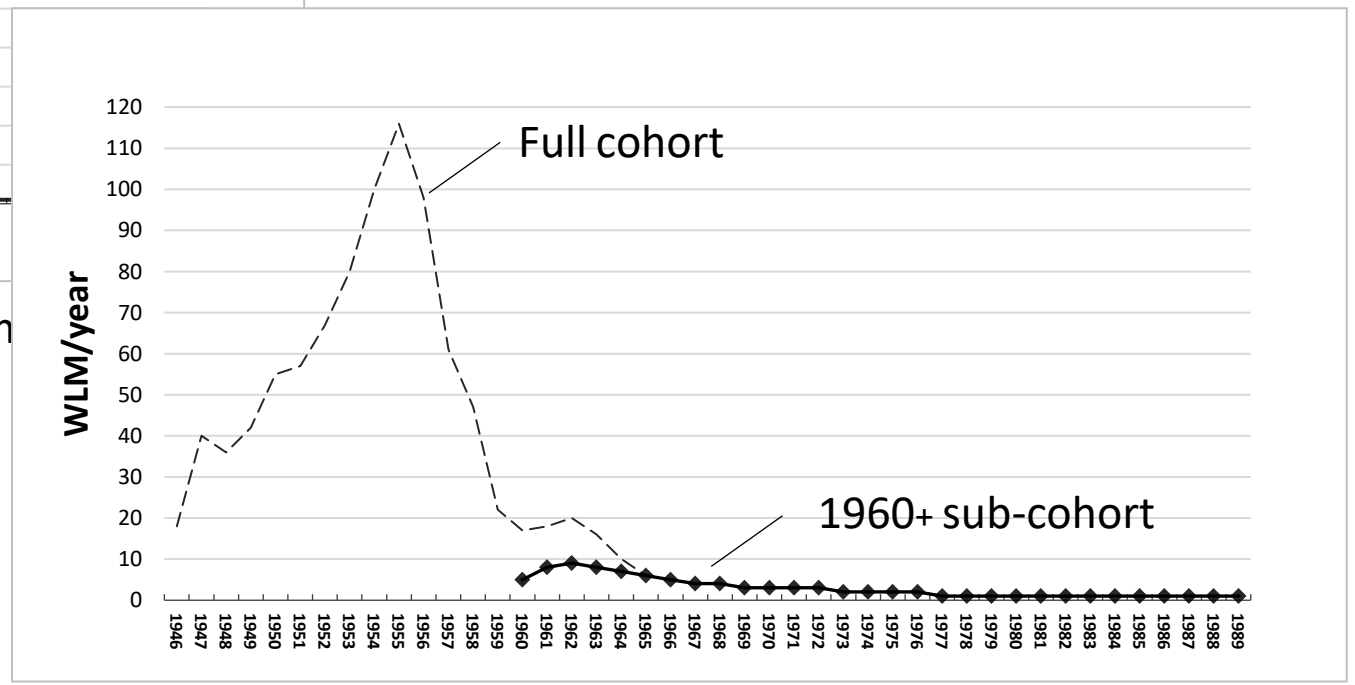
The Pooled Uranium Miner Analysis (PUMA)

- Objective to improve the knowledge of radon related risks (lung cancer, other cancers, non-cancer risks)
- Includes seven cohort studies of uranium miners from Canada, Czech Rep., France, Germany, and the United States
- Cumulated exposure to radon progeny reconstructed individually and expressed in working level months (WLM)
- Association between cumulative radon exposure and lung cancer mortality assessed with the excess relative rate per 100 working level months (ERR/100 WLM)

Evolution of exposure to radon: German Wismut cohort



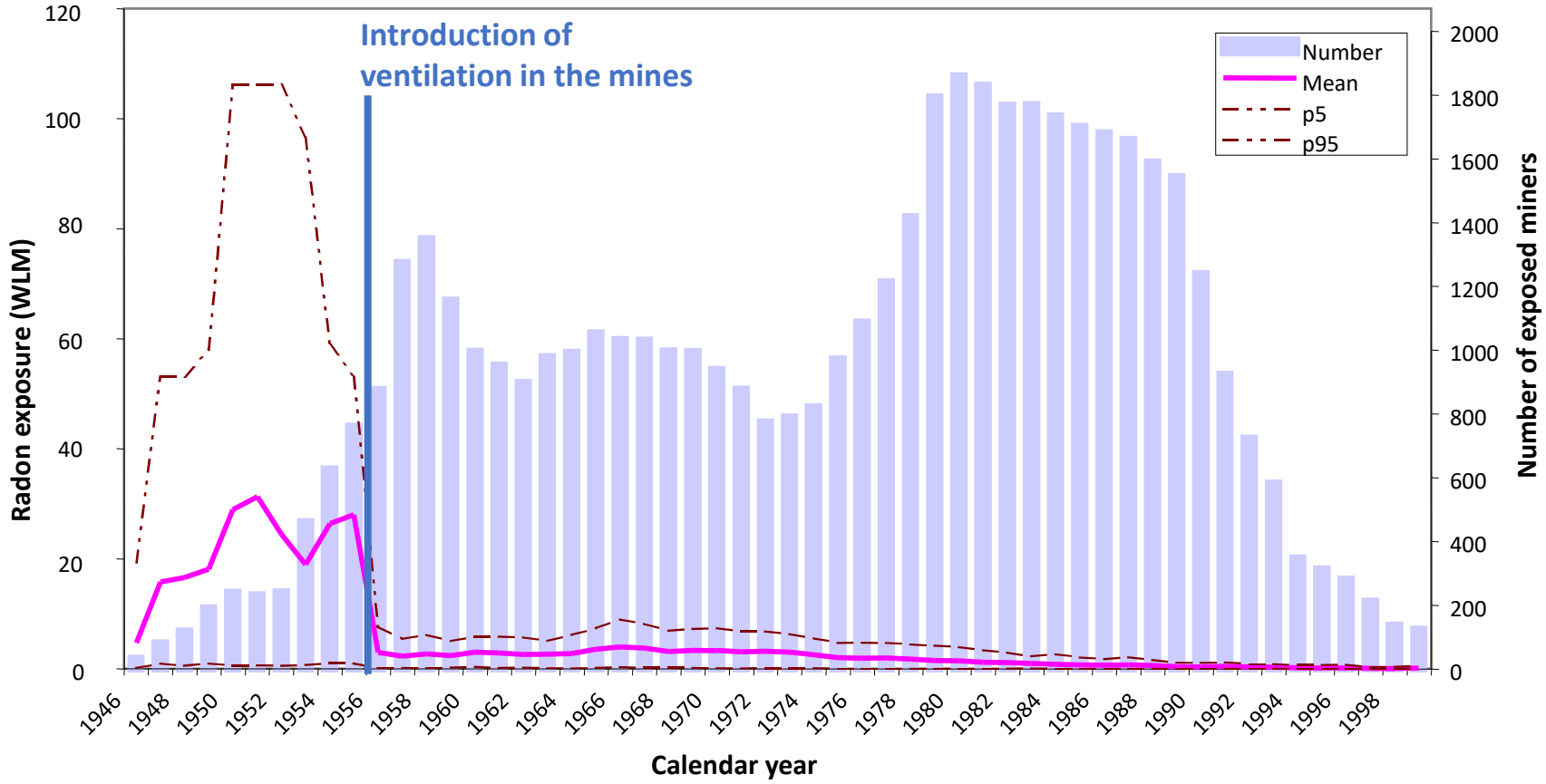
Mean annual exposure to radon progeny in WLM from



Mean annual exposure to radon progeny in WLM from 1946 to 1989

Evolution of exposure to radon: French cohort

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



PUMA – Characteristics of the full cohort (men)

	Period of follow-up	Number of miners	Number of lung cancer deaths	Mean duration of employment [years]	Mean cumulative radon expo [WLM]	Mean annual expo rate [WL]
Eldorado (Canada)	1950-1999	13,574	517	2	122	8.3
Ontario (Canada)	1954-2007	28,546	1,246	5	31	0.9
Czech (Czech Rep.)	1952-2014	9,978	1,176	8	73	0.8
France (France)	1946-2007	5,086	213	17	37	0.8
Wismut (Germany)	1946-2013	54,919	3,759	14	304	1.9
Colorado Plateau (USA)	1960-2005	4,137	612	4	579	11.7
New Mexico (USA)	1957-2012	3,469	231	9	90	9.6
PUMA total	1946-2014	119,709	7,754	10	191	2.9
PUMA without Wismut		64,790	3,995	6	98	3.7

PUMA – Characteristics of the 1960+ sub cohort (men)

	Period of follow-up	Number of miners	Number of lung cancer deaths	Mean duration of employment [years]	Mean cumulative radon expo [WLM]	Mean annual expo rate [WL]
Eldorado (Canada)	1960-1999	6,593	91	2	7	0.2
Ontario (Canada)	1960-2007	15,810	299	6	6	0.4
Czech (Czech Rep.)	1960-2014	5,532	228	6	7	0.2
France (France)	1960-2007	2,159	19	17	12	0.1
Wismut (Germany)	1960-2013	25,067	470	10	18	0.3
Colorado Plateau (USA)	1960-2005	175	16	2	193	7.5
New Mexico (USA)	1960-2012	2,537	94	9	39	4.7
PUMA total	1960-2014	57,873	1,217	8	13	0.5
PUMA without Wismut		32,806	747	6	10	0.7

Calculation of Lifetime Excess Absolute Risk (LEAR)

Calculation

- **Exposure scenario**
  - Males exposed to 2 WLM per year from age 18 to 64 years (94 WLM cumulated over 47 years)
  - Cumulated risk up to the age of 94 years
- **Risk model**
  - ERR per 100 WLM derived from the PUMA full cohort (Kelly-Reif et al. 2023) and the PUMA 1960+ sub-cohort (Richardson et al. 2022)
  - Modifying effect of time since exposure, age, and exposure rate (concentration)
- **Baseline mortality**
  - Survival function and lung cancer rate
  - Euro-American-Asian mixed population (ICRP 2007)

Interpretation

- **Cumulated absolute risk estimate:** number of lung cancer deaths attributable to radon exposure over lifetime in a population of 10,000 individuals
- **Comparable**: best way to compare the impact of different risk models depending on modifying factors, comparable to previously published LEAR estimates obtained using the same scenario
- **Support to radiological protection**: confrontation with the radiation detriment associated with external radiation exposure

PUMA – BEIR VI model* and LEAR

	BEIR VI	PUMA full cohort	PUMA 1960+ sub-cohort
ERR / 100 WLM (95% CI)	7.68	4.68 (2.88, 6.96)	6.98 (1.97, 16.15)
Time since exposure (years)			
5-14	1.0	1.0	1.0
15-24	0.78	0.77 (0.56, 1.05)	0.64 (0.17, 2.43)
25-34	0.51	0.54 (0.38, 0.76)	0.89 (0.34, 3.01)
35+	-	0.39 (0.26, 0.58)	-
Attained age (years)			
<55	1.0	1.0	1.0
55-64	0.57	0.55 (0.38, 0.82)	0.64 (0.25, 1.68)
65-74	0.29	0.38 (0.25, 0.57)	0.22 (0.06, 0.67)
75+	0.09	0.40 (0.24, 0.66)	0.17 (n.d., 0.85)
Exposure rate (WL)			
<0.5	1.0	1.0	1.0
0.5-1.0	0.49	0.60 (0.31, 1.08)	1.00 (0.38, 2.36)
1.0-3.0	0.37	0.42 (0.31, 0.64)	0.29 (0.11, 0.68)
3.0-5.0	0.32		
5.0-15	0.17	0.17 (0.12, 0.25)	
15+	0.11		
LEAR per WLM ($\times 10^4$)	5.97	5.38	7.50

*BEIR VI time since exposure – age - concentration ERR model type (NRC 1999)

Comparison with previously published LEAR: full cohorts

Study	Publication	Lung cancer deaths	PYRs at risk (10^6)	Mean WLM	LEAR per WLM ($x10^{-4}$)
7 miner study (Jacobi)	ICRP 1993	1,047	0.6	120	3.20
BEIR VI, 11 miners cohort	NRC 1999	2,787	1.2	164	5.97
Eldorado	Lane et al. 2010	618	0.5	117	8.20
Wismut (F-Up 2013)	Kreuzer et al. 2018	3,942	2.3	280	2.50
Czech cohort	UNSCEAR 2020	1,141	0.3	73	4.22
Wismut (F-Up 2018)	Kreuzer et al. 2023	4,329	2.5	280	3.13
PUMA	Kelly-Reif et al. 2023	7,754	4.3	191	5.38
PUMA without Wismut	Kelly-Reif et al. 2023	3,995	2.2	98	8.78

Comparison with previously published LEARS: low-exposed cohorts

Study	Publication	Lung cancer deaths	PYRs at risk (10^6)	Mean WLM	LEAR per WLM ($x10^{-4}$)
Czech + French cohort	Tomasek et al. 2008	547	0.2	47	4.58
Cz+Fr+Eldorado (<100 WLM)	Lane et al. 2019	408	0.4	36	4.56
Wismut 1960+ (F-Up 2013)	Kreuzer et al. 2023	495	1.0	17	9.22
Wismut 1960+ (F-Up 2018)	Kreuzer et al. 2023	663	1.1	17	6.10
PUMA 1960+	Richardson al. 2022	1,217	1.9	13	7.50

Discussion

PUMA

- **Largest and most informative database** to date to estimate the risk of death from lung cancer due to cumulative radon exposure in studies of uranium miners
- **Coherence of risk models**: Positive association between cumulative radon exposure and lung cancer mortality risk, modified by age, time since exposure and exposure rate
- **LEAR estimates ranging between 5.4 (full cohort) and 7.5 (1960+ sub-cohort) x10^{-4} per WLM**

Difference in LEAR estimates between the PUMA full cohort and the 1960+ sub-cohort

- **Full cohort:**
  - Wider range of exposure levels
  - Larger statistical power
  - Longer duration of follow-up and older age at end of follow-up
- **1960+ sub-cohort:**
  - Exclusion of early miners with extreme levels of exposure
  - Better quality assessment of radon exposure and working conditions closer to contemporary environments
  - Less heterogeneity in risk models between studies

Conclusions

The LEAR per WLM estimates derived from risk models reported for previously published uranium miner studies range from 2.5 to 9.2 x10^{-4}
The PUMA results lie in the upper half of this range

PUMA strengthens knowledge on the radon-related lung cancer LEAR, a useful way to translate models for policy purposes

Cohorts of miners with low exposure rates or focused on more recent periods are in principle preferable, and their follow-up needs to be extended

To know more

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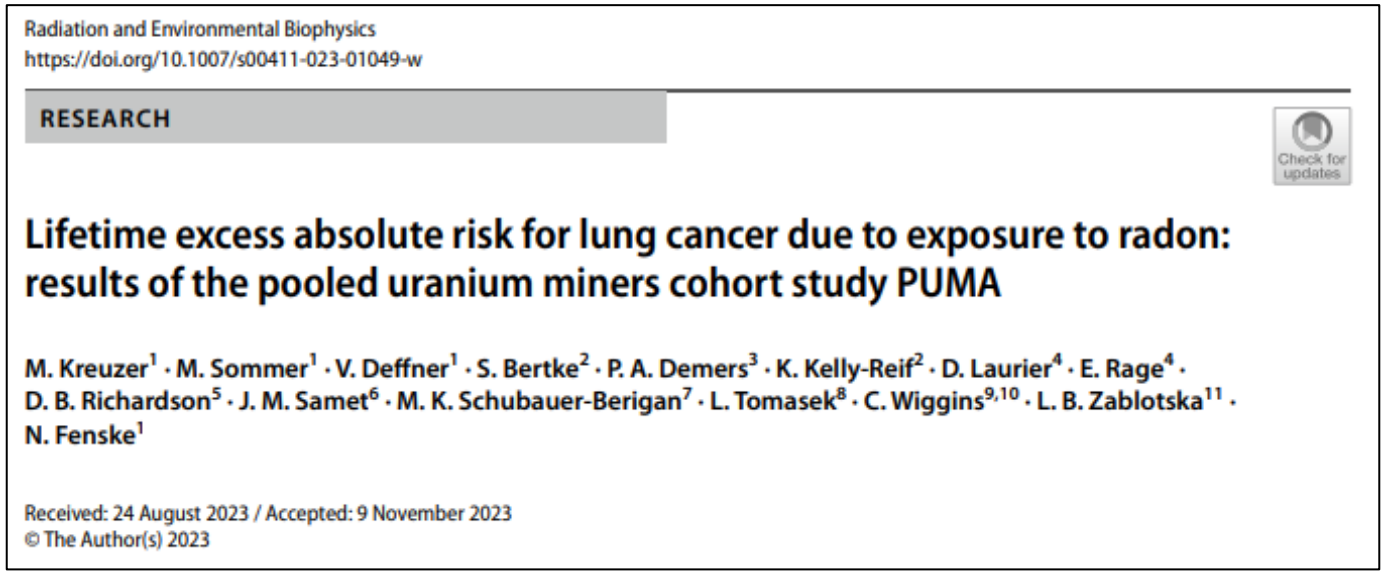

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RESEARCH

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Lifetime excess absolute risk for lung cancer due to exposure to radon: results of the pooled uranium miners cohort study PUMA

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