THE POOLED URANIUM MINERS ANALYSIS (PUMA)

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Collaborative effort: Pooled Uranium Miners Analysis (PUMA)

Some motivating questions

What are risks of lung cancer associated with lower exposures, and lower exposure rates, to radon progeny?

How long do radon-associated excess lung cancer risks persist? Does susceptibilty vary with age?

Are there radon-associated risks for cancers other than lung?

Are there radon-associated risks of non-malignant diseases?

Study description

Male uranium miners in the Pooled Uranium Miners Analysis (PUMA)

Study	Location	Miners	Follow-up	Period of first hire	Deaths	Person-years
Eldorado	Canada	13 574	1950-1999	1942-1980	4 044	424 549
Ontario	Canada	28 546	1954-2007	1954-1996	8 572	1 002 851
Czech	Czech Republic	9 978	1952-2010	1948-1995	5 564	323 806
CEA-COGEMA	France	5 086	1946-2007	1946-1990	1 924	180 122
Wismut	Germany	53 654	1960-2013	1946-1989	27 143	1 943 231
Colorado Plateau	USA	4 022	1960-2005	1953-1968	2 964	120 437
New Mexico	USA	3 469	1958-2012	1956-1982	1 576	130 537
PUMA	--	118 329	1946-2013	1942-1996	51 787	4 125 533

Rage E, et. Al. PUMA: Pooled Uranium Miners Analysis: Cohort profile. *Occup and Environ Medicine* (2020) 77:194-200

Study description

Study	Radon progeny exposure assessment methods
Eldorado	Port Radium: Area monitoring (1945-1960) Beaverlodge: Area monitoring (1954-1966), personal estimates (1966-1980)
Eldorado- Port Radium	Area monitoring (1945-1960)
Eldorado- Beaverlodge	Area monitoring (1954-1966), personal estimates (1966-1980)
Ontario	Expert rating (1954-57), area monitoring (1958-1967), personal estimates (1968-1999)
Czech	Area monitoring (1948-67), personal estimates (1968-1999)
France	Expert rating (1946-55), area monitoring (1956-82), personal monitoring (1983-99)
Wismut	Expert rating (1946-54), area monitoring (1955-89)
Colorado Plateau	Expert rating (1946-49), area monitoring (1950-89)
New Mexico	Area monitoring (1953-89)

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Study description

Study	Gamma exposure assessment methods
Eldorado-Beaverlodge	Film badges used sporadically in the 1950s; and starting in 1963 a sample of workers wore film badges fulltime. Estimates derived based on average dose rates and time on the job.
Eldorado-Port Radium	Film badges used sporadically in the 1950s; estimates derived based on average dose rates and time on the job.
Ontario	No data (before 1980), Personal dosimeter (1981-)
Czech	Estimated (<1960). Film (1960-69) TLD (1970-99)
France	No data (1946-55), Film (1956-85) TLD (1986-99)
Wismut	Expert rating (1946-54), Area measurements (1955-89)
Colorado Plateau	Not available
New Mexico	Not available

Study	Smoking assessment methods
Eldorado	Nested case-control data derived from interview
Ontario	Medical records, interview, and mail survey
Czech Republic	Nested case-control data derived from medical files and interview
France	Nested case-control data derived from medical files and a questionnaire
Wismut	Nested case-control data derived from medical files and interview
Colorado Plateau	Cigarette use: duration, rate, cessation from surveys in the 1950s, 1960s, and 1985
New Mexico	Cigarette use: duration, rate, cessation (at last exam) from medical files

Standardized mortality ratios, male uranium miners

Cause (ICD-9 codes)	Observed	SMR	95% CI	
All Causes (all)	51787	1.05	1.04	1.06
All Cancers (140-208)	16633	1.23	1.21	1.25
oral (140-145)	161	0.77	0.66	0.90
pharynx (146-149)	175	0.83	0.71	0.96
esophagus (150)	351	0.92	0.83	1.03
stomach (151)	1058	1.08	1.02	1.15
intestine and colon (152-153)	919	0.89	0.83	0.95
rectum (154)	554	0.96	0.89	1.05
liver and gallbladder (155-156)	549	1.15	1.06	1.25
pancreas (157)	641	0.96	0.89	1.04
larynx (161)	229	1.10	0.97	1.26
trachea, bronchus, lung (162)	7756	1.90	1.86	1.94
pleura (163)	39	1.06	0.75	1.44
prostate (185)	857	0.84	0.79	0.90
kidney (189.0-189.2)	392	0.96	0.87	1.06
bladder and other urinary (188, 189.3-189.9)	421	0.85	0.77	0.94
melanoma and skin (172-173)	133	0.86	0.72	1.02
brain and other nervous system (191-192)	298	0.87	0.77	0.97
Hodgkin's disease (201.0, 201.2, 201.9)	65	0.90	0.70	1.15
non-Hodgkin's lymphoma	321	0.92	0.83	1.03
multiple myeloma (203)	161	0.88	0.75	1.03
leukemia (204-208)	396	0.93	0.84	1.03
Circulatory diseases (390-459)	16921	0.88	0.86	0.89
ischemic heart disease (410-414, 429.2)	9457	0.92	0.91	0.94
Diseases of the respiratory system (460-519)	4508	1.32	1.28	1.36
chronic obstructive pulmonary disease (490-492,496)	1729	0.98	0.93	1.02
silicosis (502)	814	13.56	12.64	14.52
Diseases of the digestive system (520-579, 997.4)	2480	0.93	0.89	0.96
cirrhosis (571)	1415	0.99	0.94	1.05
External causes (E800-E999)	3362	1.41	1.36	1.46

Standardized mortality ratios, male uranium miners

	Period of hire											
	<1955				1955-1964				1965+			
	Obs	SMR	95%CI		Obs	SMR	95%CI		Obs	SMR	95%CI	
Lung cancer	4368	2.48	2.41	2.55	2532	1.50	1.44	1.56	856	1.34	1.26	1.44
	Duration of employment (years)											
	<1				1-<10				10+			
	Obs	SMR	95%CI		Obs	SMR	95%CI		Obs	SMR	95%CI	
Lung cancer	581	1.24	1.15	1.35	3187	1.60	1.54	1.65	3988	2.45	2.38	2.53

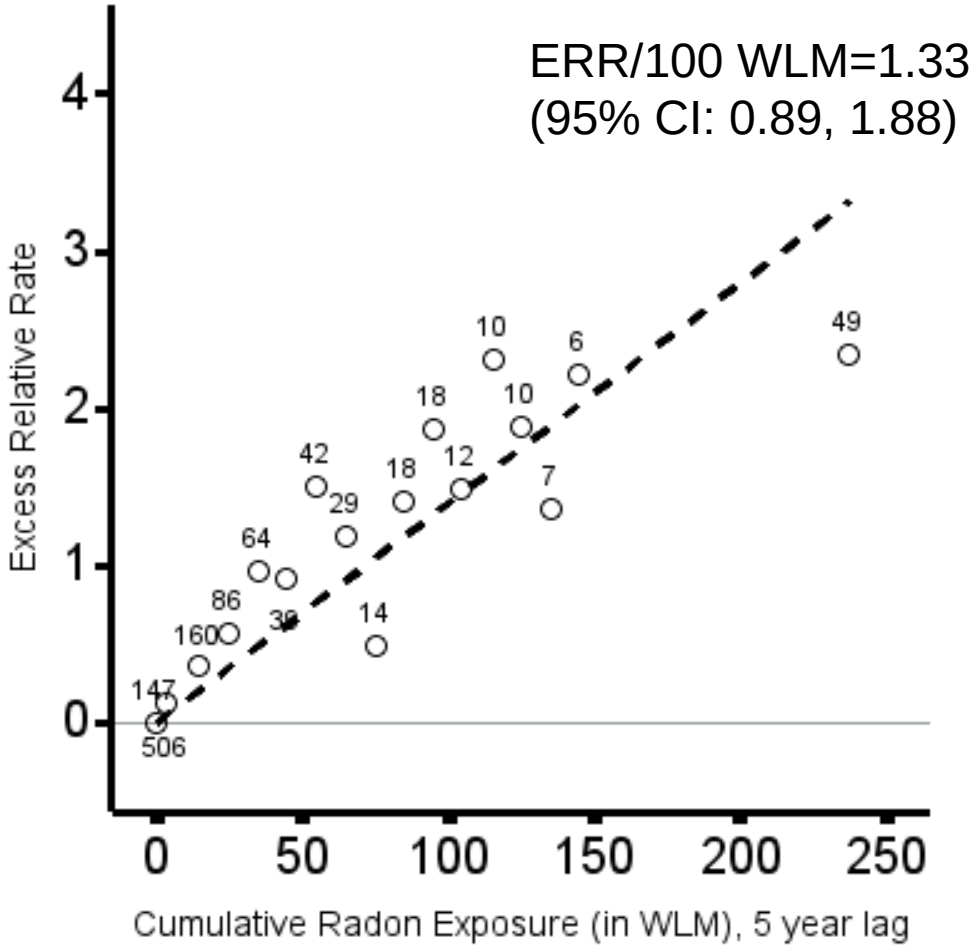
Richardson DB, et. Al. Mortality among Uranium Miners in North America and Europe: The Pooled Uranium Miners Analysis (PUMA). *Int J of Epidemiology* (2020).

Lung cancer deaths and person-years by covariates. PUMA, male miners hired in 1960 or later

	Lung cancers	Person-years
Study cohort		
Eldorado, Canada	91	164,487
Ontario, Canada	299	466,968
Czech Republic	228	195,348
France	19	62,447
Wismut, Germany	470	894,313
New Mexico, USA	94	95,291
Colorado Plateau, USA	16	8,238
Attained age (years)		
<40	19	889,610
40 - 49	142	488,494
50 - 59	359	331,405
60 - 69	489	142,918
70 - 79	190	30,806
≥80	18	3,859
Duration of employment (years)		
< 5	529	979,454
5- <10	174	367,064
≥10	514	540,574
Total	1217	1,887,092

ERR of lung cancer mortality in male miners hired in 1960 or later (per 100 WLM)

Linear exposure-response model for the association between cumulative exposure to radon progeny and lung cancer mortality.



Observations on radon-lung cancer associations in PUMA

The ERR of lung cancer (per 100 WLM):

Diminishes with older attained age

Diminishes with increasing time-since-exposure

Diminishes with radon concentration

High concentrations (>1 WL) have smaller associations with lung cancer than lower concentrations.

Current and planned research topics within PUMA

Research topic	**Specific aim**
Analysis of associations between radon exposure and mortality due to cancer other than lung	- Radon exposure and risk of solid cancers other than lung - Radon exposure and risk of hematologic cancers
Analysis of associations between radon exposure and mortality due to non-cancer disease	- Radon exposure and risk of circulatory diseases - Radon exposure and risk of non-malignant respiratory diseases
Analysis of associations between radon exposure and mortality due to lung cancer	- Lung cancer risk at low exposure/exposure rates of radon - Temporal effect modifiers for radon-associated risk of lung cancer. - Lung cancer and combined effects of radon and smoking
Risks associated with other ionizing radiation exposure	- Health effects of gamma exposures in uranium miners
Lifetime risk exposure	- Assessment of lifetime risks for lung cancer associated with radon exposure

Challenges and Opportunities

Comparability of information between cohorts
- restricted to uranium miners
- restricted to contemporary workers

Methods for exposure assessment changed over time and place
- in general, improvement over time
- analyses restricted to later operation periods

Limited information on many potential confounders/modifiers
- sampled information on smoking for cohorts
- indirect assessments

Pooling
- Permits analyses of outcomes for which no single cohort is sufficient.
- Allows for improved characterization of effect modifiers.

International collaboration
- Fosters sharing of perspectives
- Cross-validation
- Evaluation of homogeneity

Contemporary relevance

Underground work settings

phosphate, fluorspar, talc and slate mines
subway tunnels
utility service ducts
underground parking

Above ground work settings

fertilizer plants
natural gas and oil piping facilities
oil refineries
water treatment plants
schools
hospitals
prisons

Domestic radon exposures

A ubiquitous air pollutant