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INSTITUT
DE RADIOPROTECTION
ET DE SÛRETÉ NUCLÉAIRE

Faire avancer la sûreté nucléaire

Risk of Lung Cancer Death Associated to Radon Exposure Corrected for Measurement Error Among Uranium Miners



**R. S. Allodji¹, E. Rage¹, A. C. M. Thiébaud²,
K. Leuraud¹, S. Henry³, J. Bénichou⁴
& D. Laurier¹**

¹ Institut de Radioprotection et de Sûreté Nucléaire (IRSN),

² University of Versailles Saint-Quentin / INSERM U657 /
Institut Pasteur / Raymond Poincaré Garches University
Hospital

³ AREVA group, Medical Council

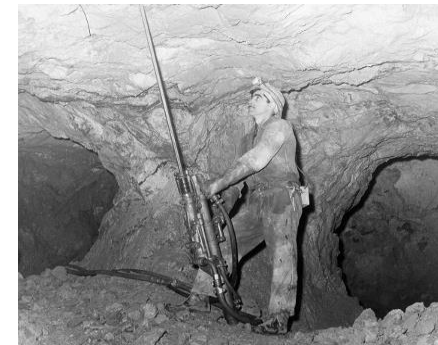
⁴ Rouen University Hospital / University of Rouen

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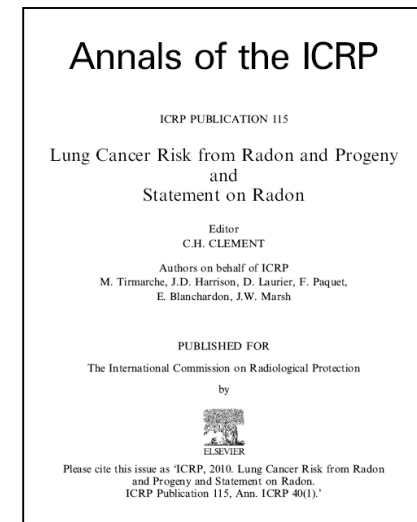
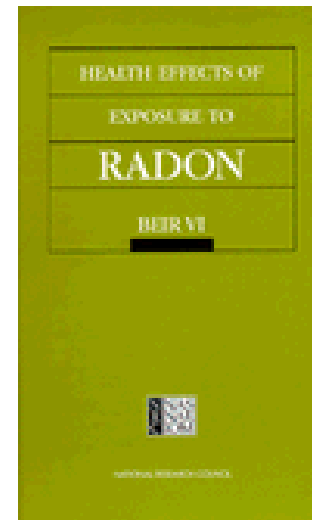
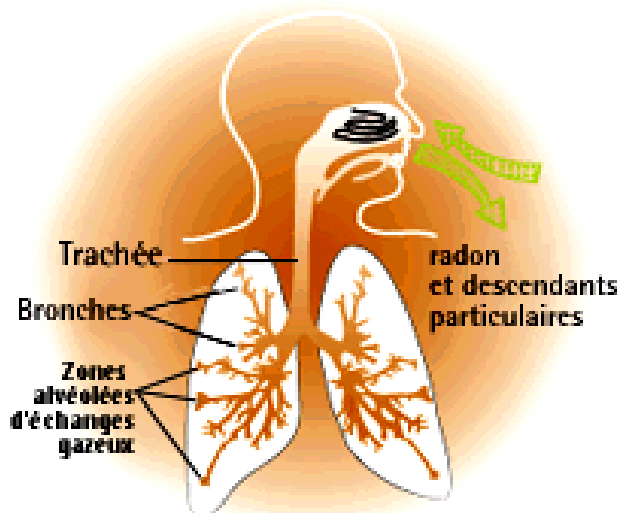
13 - 18 May 2012,
Glasgow, Scotland

Background & Motivation

- **Radon is a radioactive gas of natural origin**
 - concentrates in confined places
 - classified as a known pulmonary carcinogen



Photos PC Guillard



- ⇒
- 20 studies of cohorts of miners in the world,
 - demonstration of an exposure-risk relationship

Background & Motivation

- **Measurement error in covariates has three main effects** (Carroll et al., 2006):
 - It causes bias in parameter estimation for statistical models
 - It leads to a loss of power
 - It hides the features of the data
- A broad variety of methods for measurement error correction has been developed, but they have been rarely applied
- Only one application of correction methods among miners (Stram et al. Health Phys 1999)

Objectives

To investigate the impact of ME on the estimated lung cancer risk associated to radon exposure in the French cohort of uranium miners

- To quantify MEs
- To assess their impact
- To evaluate the effectiveness of ME correction methods
- To estimate a ME corrected exposure-risk relationship



Exposure monitoring in French mines



1946

1956

1983

1999

RADON

**Retrospective
reconstitution
by experts**

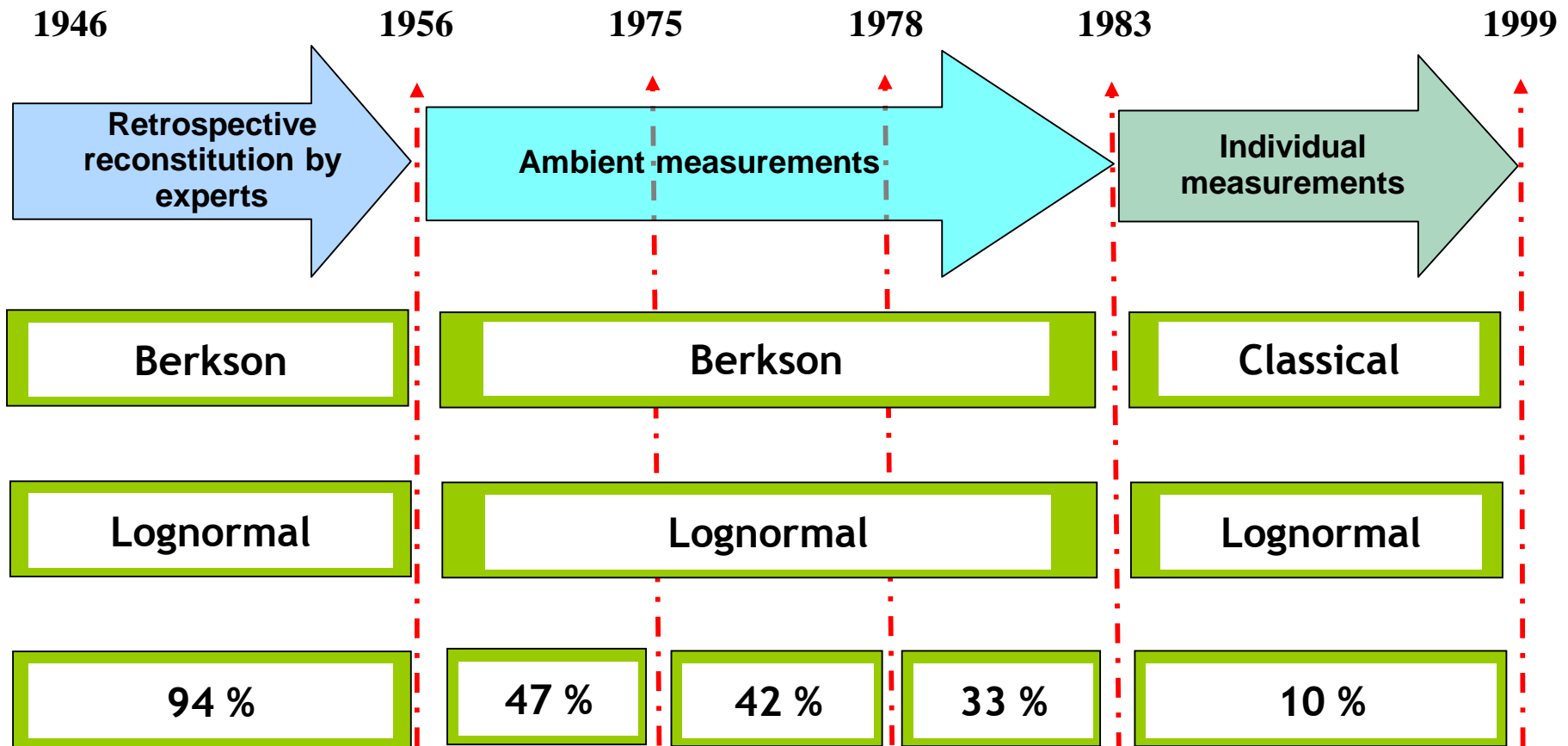
**Individual recording from
ambient measurements**

**Individual
measurements**

**Setting up of
radiation
protection
measures**

Characteristics of measurement error

Root Sum Square Method (Schiager et al, 1981)



[Allodji et al., J Radiol Prot 2012]

Simulation study

Aim: to investigate the impact and correction of measurement error

➤ generation of a simulated cohort (1,000 replications) with characteristics similar to the French Uranium Miners Cohort

Date of birth, date of employment, exposed or unexposed status, date of first exposure, yearly radon exposure from 1946 to 1999, and deaths from lung cancer or other causes

➤ lung cancer deaths generated with different true Excess Relative Risk (ERR) values: 0.7 and 2 per 100 Working Level Months (WLM)

➤ Addition of ME of different nature, size, type

Simulation study: data characteristics

■ Characteristic of the French Uranium Miners Cohort Study and simulated data

	Real data	Mean of 1000 replications*
Population	5,086	5,086
Person-years	153,076.6	153,568.8
Age at entry into the cohort: mean (S.E.)	28.8 (7.6)	28.8 (8.0)
Age at end of follow-up: mean (S.E.)	58.9 (13.2)	59.0 (13.2)
Percentage of radon-exposed miners	81.3%	81.0%
Age at first exposure: mean (S.E.)	29.1 (7.8)	28.4 (8.6)
Duration of exposure: mean (S.E.)	13.1 (9.3)	12.5 (9.0)
Cumulative radon exposure (WLM*): mean (S.E.)	36.6 (71.1)	33.4 (44.3)

*working level months

➤ Very minor differences between real and simulated data

Simulation study: impact of ME

■ Impact of measurement error on the Excess Relative Risk

		Mean ERR	Relative Bias (%)	2.5th- 97.5th percentiles	Coverage Probability (CP)	Empirical Power (%)
True ERR value: 0.7	Without ME	0.719	2.69	0.206 – 1.495	0.951	64.1
	With ME	0.268*	-61.65	0.048 – 0.591	0.163°	49.9
True ERR value: 2.0	Without ME	2.023	1.15	1.170 – 3.252	0.952	100
	With ME	0.756*	-62.19	0.406 – 1.246	0.014°	100

ERR = Excess Relative Risk per 100 WLM; ME = Measurement error; *Significant difference with true ERR value (0.7 or 2.0 per 100 WLM); °Significant difference with 95%

[Allodji et al., Rad Environ Biophys 2012]

➤ Measurement error:

➤ Strong attenuation vs true association (about 60%)

➤ CP value significantly lower than the nominal value 0.95

➤ Sensitivity analyses: Nature, size, structure and distribution of measurement error strongly influence the impact of measurement error

ME Correction methods

- **3 correction methods selected for our simulation study**
- **Substitution Method** (also called Regression Calibration) denoted RC-SM (Hu et al, Biometrics 1998)
- **Estimate Calibration Method** (Regression Calibration variant) denoted RC-ECM (Rossner et al, Stat Med 1989)
- **Simulation Extrapolation Method** denoted SIMEX (Cook and Stefanski, JASA 1994)

Simulation study: performance of ME correction methods

- Performance of correction in case of perfect knowledge of measurement error characteristics

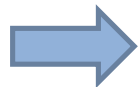
True ERR : 2.0	Without correction of error	After correction of measurement error		
		RC-SM	RC-ECM	SIMEX
Mean ERR	0.756*	1.355*	1,481*	1.538*
Relative Bias (%)	-62.19	-32.25	-25,94	-23.13
2.5th- 97.5th percentiles	0.406 - 1.246	0.714 - 2.277	0.598 -3,542	0.759 - 2.581
Coverage Probability	0.014°	0.534°	0.471°	0.694°
Empirical Power (%)	100	99.8	100	100

*Significant difference with true ERR value (2 per 100 WLM) bias before correction was -62%; ° Significant difference with 95%CI

- Similar performances of the 3 ME correction methods
- ERR increased by about a factor 2 compared to the naïve estimate
- Estimated ERR remains lower than the true one

Conclusions

- ME decrease strongly with the improvement of radiation protection and exposure monitoring in the mines
- ME lead to a reduction of the estimated ERR/WLM compared to the true relationship
- The performance of the three correction methods highly depended on the accurate determination of measurement error characteristics
- The 3 methods allow to correct for the ME bias, but not completely
- The corrected ERR/WLM estimates are higher than the naïve one (between 30 and 120% increase on the real cohort data)



Potential important impact of radiation protection of miners if confirmed by other studies

Thank you
for your attention