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INSTITUT
DE RADIOPROTECTION
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Faire avancer la sûreté nucléaire

Analysis of kidney cancer mortality among uranium miners

D Drubay¹, M Kreuzer², F Dufey², M Sogl², D Laurier¹, E Rage¹

1 : Institut de Radioprotection et de Sûreté Nucléaire, 92262, Fontenay-aux-Roses, France

2 : Federal Office for Radiation Protection and Health, Ingolstaedter Landstr. 1, 85764 Neuherberg, Germany.

- **Context**
- Data & method
- Results
- Discussion & Prospects

➤ Ionizing radiations and cancer among uranium miners

■ Sources of ionizing radiation in uranium mines:

- Radon (radioactive gas)
- gamma radiation
- Long-lived radio-nuclides (dust)

■ Significant relationship between radon and lung cancer among uranium miners (Walsh 2010, *Radiat. Res.*; Vacquier 2008, *Radiat. Environ. Biophys.*)

➤ Other cancers induced by exposure?

■ Significant excess of KCM among French uranium miners without relationship with cumulated radon exposure (Vacquier 2008, *Occup. Environ. Med.*)

➤ Occupational exposures

- Strong presumption of link between Trichloroethylene (TCE) and KCM (Kelsh 2010, *Epidemiology*)
- Significant relationship with diesel exposure (Boffeta 2001, *Cancer Causes Control*)
- Significant relationship with cutting fluids exposure during uranium processing (Ritz 1999, *Occup. Environ. Med.*)

➤ Low dose radiation exposure could be involved?

- Nephrotoxicity of uranium (Vicente 2010, *Toxicol. Sci.*)
 - Morphological renal modifications
 - Altered renal function

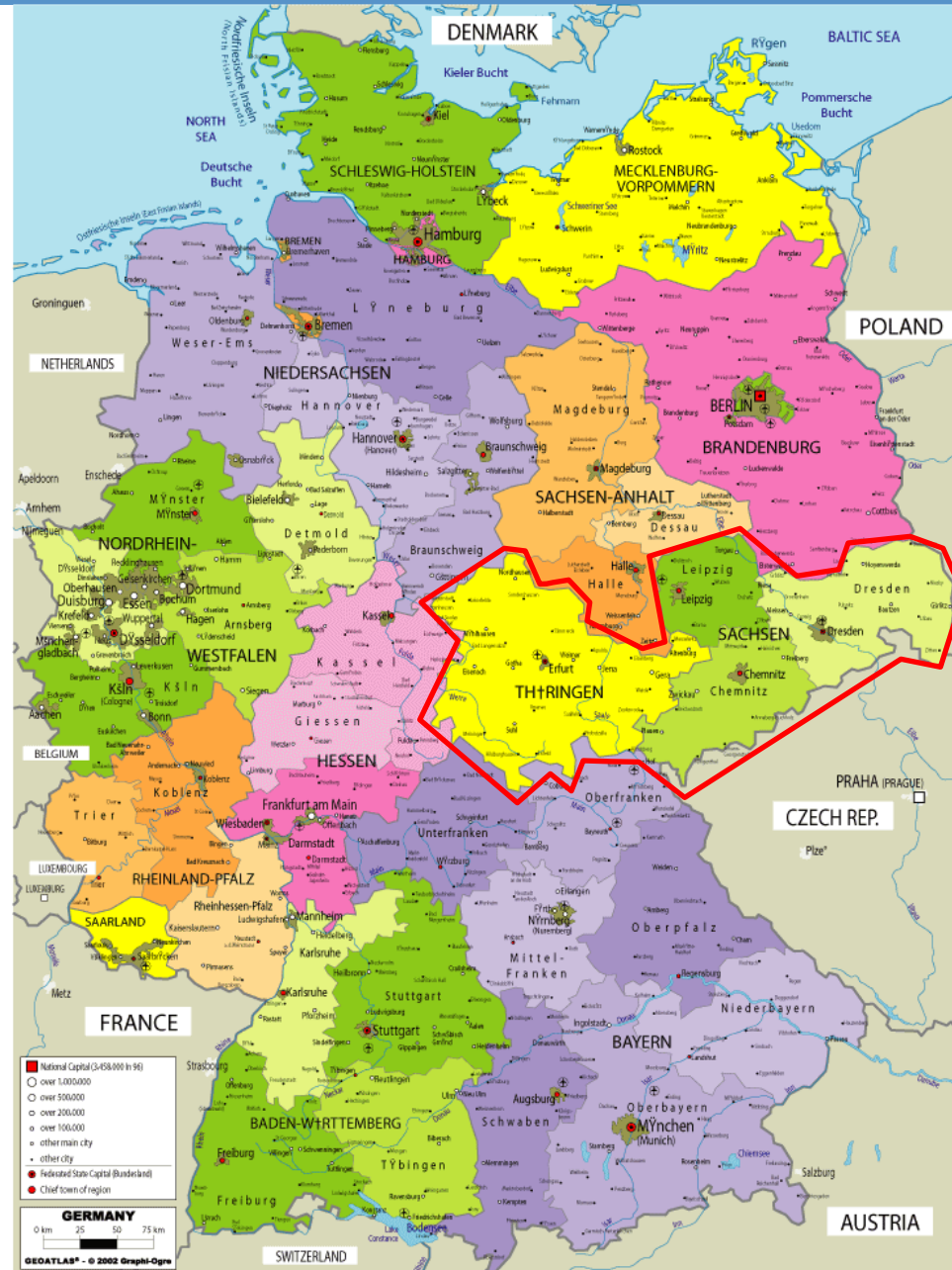
➤ Ionizing radiations and kidney cancer : Previous epidemiological results

- No significant relationship with radionucleides concentration of well water ingested by Finn drilled wells users (Kurttio 2006, *Am. J. Kidney Dis.*)
- No significant relationship with radiation exposure among atomic bomb survivors of Life Span Study (Ozasa 2012, *Radiat. Res.*)
- No significant relationship with radon exposure in Czech uranium miners cohort (Kulich 2011, *Environ. Res.*)

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➤ Wismut compagny

- East Germany (Saxony and Thuringia)
- Wismut creation in 1946 (after the WW2) by Soviet Union
- Nearly 350 mines before 1954
- 3rd largest producer of uranium
- Mining abandoned after the German unification (1990)



➤ Wismut cohort

■ Inclusion criteria :

- Men only
- First employment between 1st January 1946 and 31st December 1989
- Minimum employment time of 180 days
- Year of birth after 1899

■ Specifications :

- 58986 uranium miners
- 152 cases of kidney cancer deaths
- Follow-up : 1946 → 2003 (mean=34.35 years)
- 3 time periods :
 - A : before 1955 : Lack of occupational safety measures
 - B : 1955 to 1971 : improvement of working conditions (forced ventilation, wet drilling...)
 - C : 1971 to 1989 : international standards

➤ Covariates

➤ Covariates of interest

- Radon (Working Level Month WLM), gamma radiation (mSv), long-lived radio-nucleides (kBqh/m³) exposures
- Kidney doses (alpha and non-alpha) (Gy) estimated using AlphaMiners software

➤ Adjustment/Stratification

- Mine location, job type, physical activity, age at first exposure, exposure time

➤ Lag

- Delayed effect of exposure

➤ Analysis

- Standardized mortality ratio (SMR) corrected for missing causes of death (Rittgen & Becker 2000, *Biometrics*) :

$$SMR^* = \frac{SMR}{p} \quad \text{with} \quad SMR = \frac{O}{E}$$

and $p = \frac{\text{Number of known causes of death}}{\text{Number of death}}$

- Count data analysis : Poisson, Binomial negative and Quasi-Poisson model
- Survival analysis : Cox model with time dependant covariates

➤ Analysis

■ Nephrotoxicity of uranium

- Decreased renal function
- Morphological renal modifications

■ Radon known as carcinogenic product for the lung

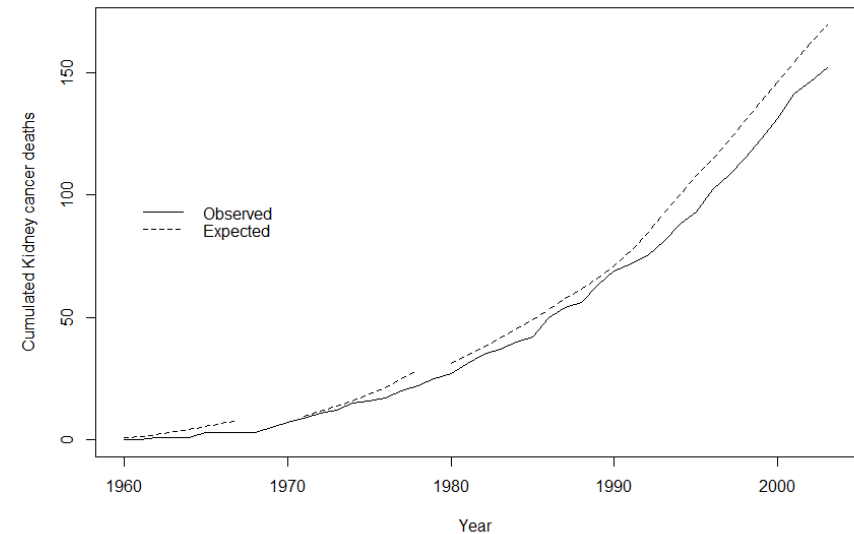
➤ Competing risks

- Competing risks model : Fine & Gray model for left-truncated and right-censored data
 - Cox model with Inverse Probability of Censoring Weighting (IPCW) method (Geskus 2011, *Biometrics*)

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➤ Results

- No significant excess of KCM :
SMR= 0.97 [0.82;1.13], $p=0.71$
- Count data analysis : very sensitive results to the choice of categorization
- No significant association with each type of cumulated exposure (lag 0 to 20 years)
- No significant effect of cumulated time of exposure (lag 0 to 20 years)
- No significant effect of cumulated time of diesel exposure



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➤ Limits

- Lack of statistical power? No real effect of radiation exposure?
- Lack of information concerning other risk factors (cigarette smoking, hypertension, obesity,...)

➤ Prospects

- Further analyses with competing risks models
- Comparison with French uranium miners cohort after extension of follow-up

Thank you for your attention

➤ Kidney cancer

- Among the 10 most common cancers in Western Communities
- Most frequent among males
- Kidney cancer mortality : 14 mortality among men in the world in 2008 (IARC/GLOBOCAN)
- Risk factors : cigarette smoking, hypertension, obesity, ..., occupational exposures

