Analysis of kidney cancer mortality among uranium miners

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Kidney cancer mortality among uranium miners

- **Context**
- **Data & method**
- **Results**
- **Discussion & Prospects**
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- **Ionizing radiations and cancer among uranium miners**

  - Sources of ionizing radiation in uranium mines:
    - Radon (radioactive gas)
    - Gamma radiation
    - Long-lived radio-nuclides (dust)


  ➤ **Other cancers induced by exposure?**

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- **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
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- 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 radon exposure in Czech uranium miners cohort (Kulich 2011, *Environ. Res.*)

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- **Wismut company**
  - 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)
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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
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- **Covariates**

- **Covariates of interest**
  - Radon (Working Level Month WLM), gamma radiation (mSv), long-lived radio-nucleides (kBq/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
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**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 dependent covariates
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**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
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Kidney cancer

- Among the 10 most common cancers in Western Communities

- Most frequent among males

- Kidney cancer mortality: 14th cancer mortality among men in the world in 2008 (IARC/GLOBOCAN)

- Risk factors: cigarette smoking, hypertension, obesity, …, occupational exposures