A risk assessment of the potential impacts of radon, terrestrial gamma and cosmic rays on childhood leukemia in France

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Natural radioactivity (NR)

- **Major source** of exposure to ionizing radiation (IR) for **most of the** world **population**
- Exposure from **various sources** and via different **pathways**, notably :
  - Inhalation of radon gas and its decay products
  - External irradiation by cosmic and terrestrial gamma rays (TGR)
  - Food and water ingestion
- **Lung cancer** following radon inhalation is the only clearly established health effect of NR
- Can there be **other health effects** ?

Childhood Leukemia

- One of the cancers **most strongly associated with** exposure to **IR**
- **Shorter latency than most solid cancers**
- **Association** with IR **higher in children**

- Several **ecological studies** suggested an association between NR and CL, including in France (Evrard et al. 2005, 2006)
- **In the UK**, the **proportion of CL attributable** to NR was estimated by a **risk assessment** approach to be circular around **15-20%** (Wakeford et al 2009, Little et al 2009)

… although **considerable uncertainties** surround these figures

Objectives

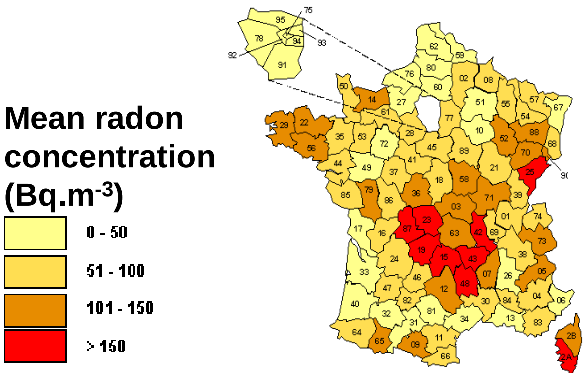
- To **estimate**, via a risk assessment approach, the **proportion of childhood leukemia** cases **potentially related to** 3 components of NR in **France**

  - **radon**
  - terrestrial gamma rays (**TGR**)
  - **cosmic** rays

- … these **components** being those **for which doses** to children can **most reliably be estimated at large scales** for epidemiological studies

Data

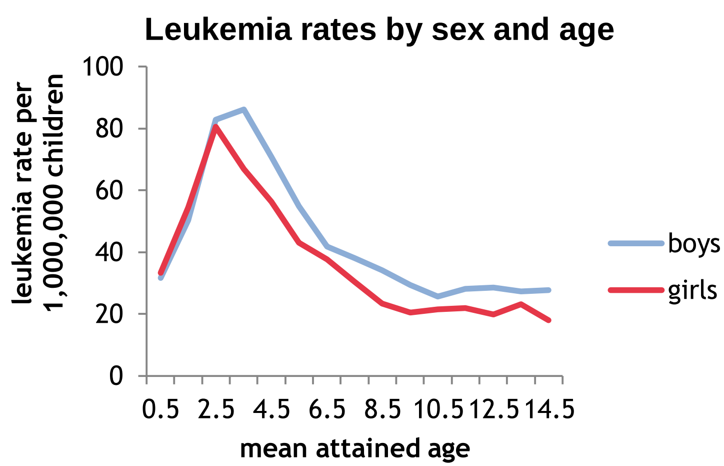
- **Exposure**: average estimates (Billon et al, *RPD* 2005)
  - **radon concentration** in buildings (63 Bq.m^{-3})
  - **dose rates from TGR** (0.49 mSv.y^{-1})
  - **dose rates from cosmic rays** (0.28 mSv.y^{-1})



- **Conversion to RBM** doses
  (Kendall and Smith *JRP* 2002, 2005, Petoussi et al *RPD*, 1991)

- **Leukaemia rates** for French children (**0-14 y**)

provided by the National Registry of Childhood Blood Malignancies (INSERM - RNHE), period **1990-2004**



Risk prediction models

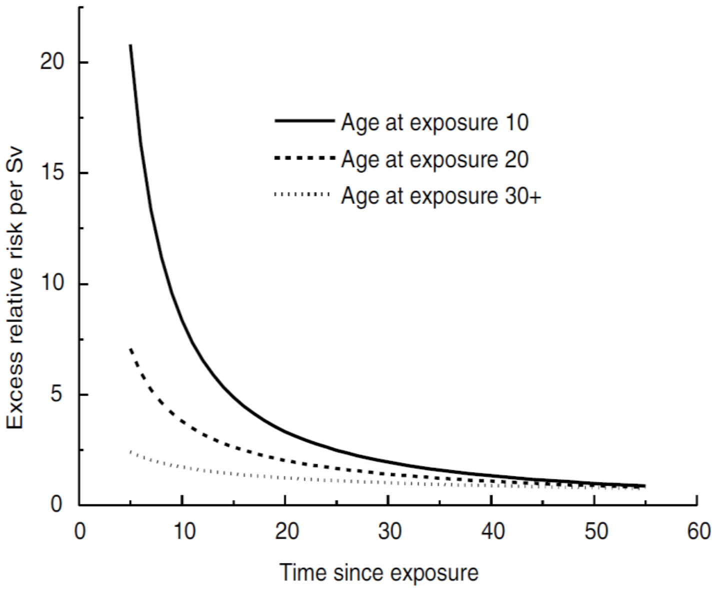
Proposed by international scientific committees :

- United Nations Scientific Committee on the Effects of Atomic Radiation (**UNSCEAR**, 2006)
- U.S. National Research Council, Committee to Assess Health Risks from Exposure to Low Levels of Ionizing Radiation (**BEIR VII**, NRC 2007)

Derived from the cohort of Japanese **A-Bomb survivors** (LSS)

Multiplicative and additive models proposed

Consider **attained age** (and **age at exposure** for some), as **modifiers of the relation** between IR and leukemia



BEIR VII, National Research Council 2006

Results: doses

- RBM dose estimates (in mSv) for average French child

	Radon	TGR	Cosmic rays	Summed doses
In utero (9 months)	0.03	0.33	0.19	0.55
Infant (yearly)	0.29	0.61	0.35	1.24
Child (yearly)	0.34	0.55	0.31	1.21
Cumulated (in utero - 14 years)	5.08	8.64	4.88	18.73
% of cumulated dose	27	47	26	100

- TGR is the major contributor to RBM dose

Results: attributable risk

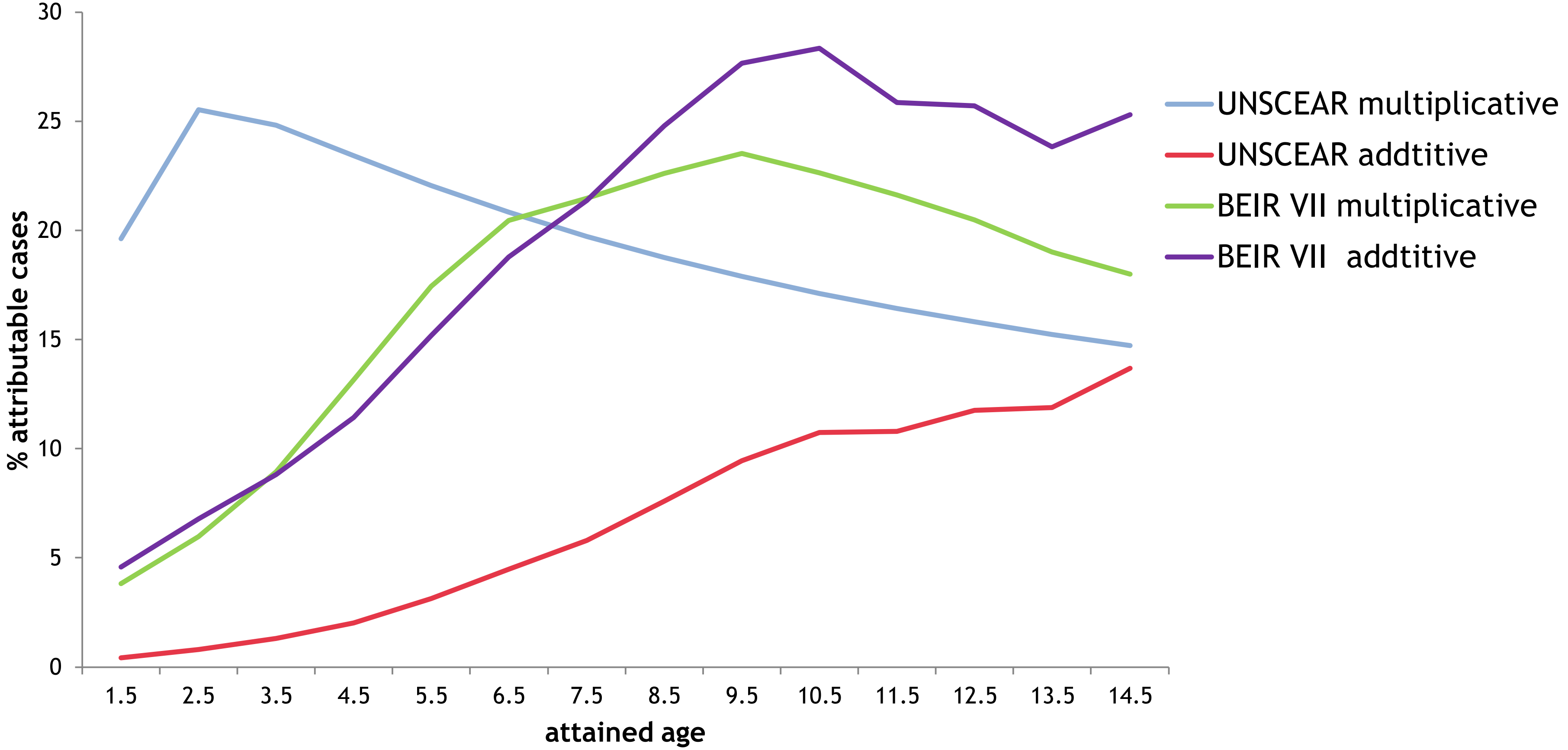
- Point estimates for the attributable % of CL cases for summed doses

Model	UNSCEAR multiplicative	UNSCEAR additive	BEIR VII multiplicative	BEIR VII additive
CL percentage attributable to NR	19.8	4.6	13.8	14.9

  - -> large contrasts depending on the model considered

Results: variation with attained age

- Models behave differently according to attained age : point estimates of the % of cases attributable to summed exposures (radon, TGR, cosmic)



- Consistent with findings in the UK (Wakeford et al, *Leukemia* 2009)

Uncertainties and extrapolation hypotheses

- Uncertainties in **red bone marrow** dose estimates (especially for radon)
- Difference in **radiation quality** between LSS exposure and NR in France
- **Dose level extrapolation** (some influential observations at high doses in the LSS)
- **Dose rate extrapolation** (acute LSS exposure vs chronic NR exposure)
- **Risk at young ages:** sparse data on risk at youngest ages and shortest time since exposure periods
- **Transposition**: from a mid-20th century Japanese population to contemporary French children

Uncertainties

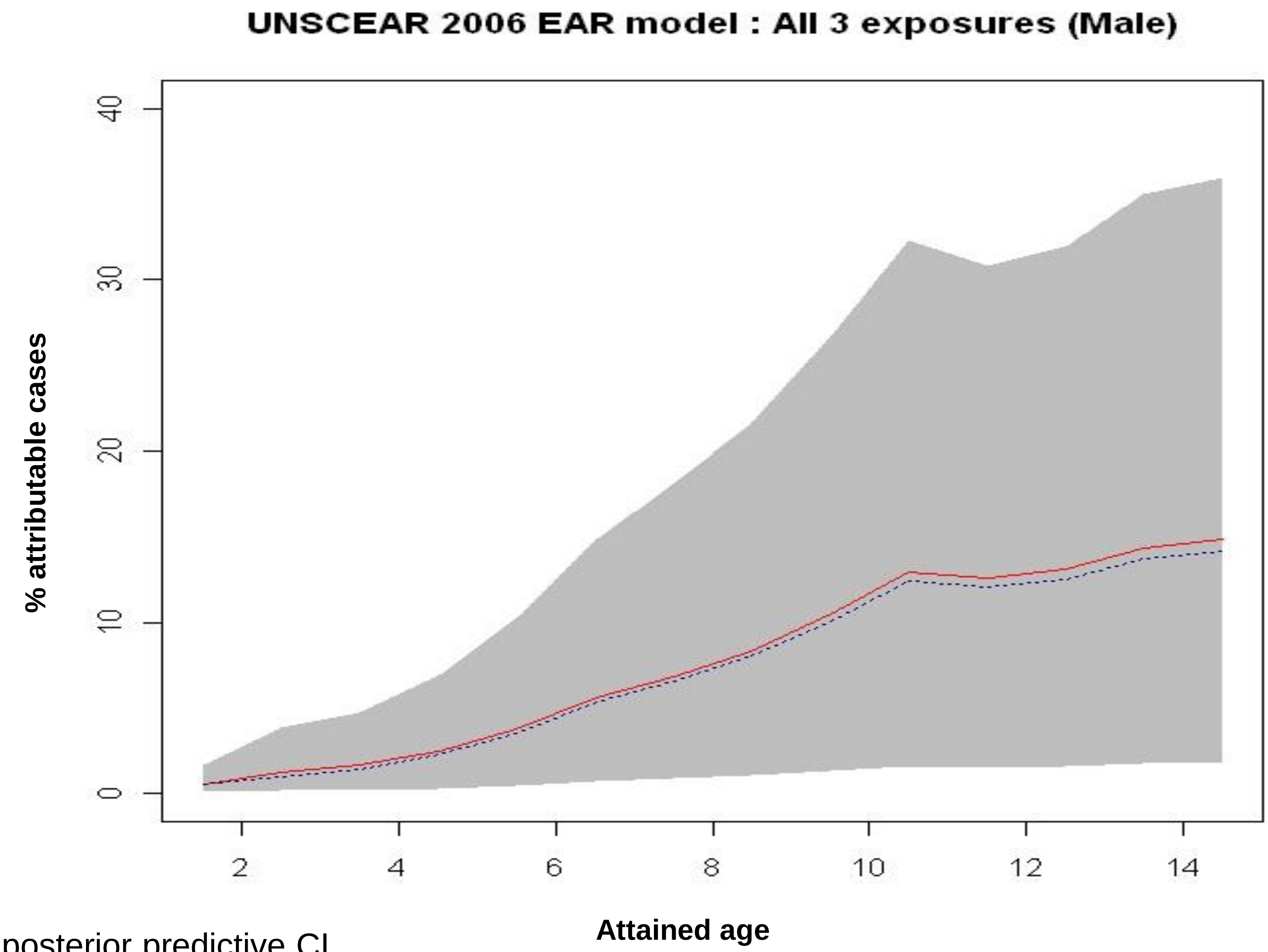
- **So far, "point estimates"** only! Uncertainties not quantified…

-> Under the Bayesian paradigm:

- To characterize the full posterior distributions of leukemia risk model coefficients by fitting these anew to the LSS data*
- To propagate these distributions throughout the risk assessment process

*by applying the methodology described in Little et al, Rad Res 169, 660–676 (2008)

Uncertainties: preliminary results



95% posterior predictive CI

posterior predictive median

point predictive value obtained from frequentist analysis

Conclusion and perspectives

- Point estimates suggest that an important proportion of CL cases might be attributable to radon, TGR and cosmic rays

- Preliminary results reveal important uncertainties related to leukemia risk predictions models

⇒ **Need for further analysis of uncertainties**

⇒ **Need to better investigate the relation between NR and CL**

- An INSERM-IRSN epidemiological study of NR and CL is ongoing in France as part of the Geocap program *

*Presentation by C Demoury, TS10c: Radon Thursday, May 17, 10:15

Thank you for your attention

UNSCEAR 2006 leukemia models

Generalized ERR model

$$h_0(s,a)\cdot\left[1+(\alpha\cdot D+\beta\cdot D^2)\cdot\exp[\kappa_1\cdot\ln[a]]\right]^{a}$$

Generalized EAR model

$$h_0(s,a)+(\alpha\cdot D+\beta\cdot D^2)\cdot\exp[\kappa_1\cdot 1_{s=female}+\kappa_2\cdot\ln[a-e]]^{a}$$

[a] D = radiation dose (Sv); a = attained age, e = age at exposure, s = sex,

Wakeford et al, *Leukemia* 2009

IRSN

BEIR VII leukemia models (NRC, 2006)

Generalized ERR model

$$h_0(s,a)\cdot\left[1+\beta_s\cdot(D+\theta\cdot D^2)\cdot\exp\begin{bmatrix}\gamma_-\cdot\min(e-30,0)/10+\delta\cdot\ln[(a-e)/25]+\\ \phi\cdot\ln[(a-e)/25]\cdot\min(e-30,0)/10\end{bmatrix}\right]^a$$

Generalized EAR model

$$h_0(s,a)+\beta_s\cdot(D+\theta\cdot D^2)\cdot\exp\begin{bmatrix}\gamma_-\cdot\min(e-30,0)/10+\\ \phi\cdot\ln[(a-e)/25]\cdot\min(e-30,0)/10\end{bmatrix}^a$$

[a] D = radiation dose (Sv); a = attained age, e = age at exposure, s = sex,

Wakeford et al, *Leukemia* 2009