Lung cancer mortality among Eldorado uranium workers: A comparison of the TSCE and ERR model[1]

M. Eidemüller, P. Jacob, R. Lane, S.E. Frost and L. Zablotska

The Study Cohort
The study addresses lung cancer mortality risk after exposure to Radon Decay Products (RDP) in the Eldorado cohort. The Eldorado cohort included workers from the Beaverlodge and Port Radium uranium mines and workers from the Port Hope radium and uranium refinery and processing facility [2].
- 16,236 male workers
- 618 lung cancer deaths
- Follow-up time: 1950-1999
- Mean RDP exposure: 52 WLM

Risk Models
Two-stage clonal expansion (TSCE) model:
- Baseline confounders include birthyear, people who worked less than 6 months, and a correction for the clonal expansion rate at older ages.
- Only radiation effect on clonal expansion rate, strong increase at low exposure rate, leveling at higher exposure rates.
- This dose response might be explained by a radiation-induced bystander effect.

Model uncertainties are large below exposure rates of about 10 WLM.

Clonal expansion rate and possible relation to a bystander effect
Non-targeted radiobiological effects such as radiation-induced genomic instability or bystander effect may be incorporated into mechanistic models such as the two-stage model with clonal expansion (TSCE model). The consequences of these effects on cancer risk can then be estimated [3,4].

Results
The lung cancer mortality risk depends strongly on the radiation modifiers attained age, time since exposure and exposure rate. In the figures the dependence of the excess relative risk per exposure dose (ERR_{rd}) on age is shown for typical exposure scenarios in the cohort: age at exposure of 30 years, duration of exposure of 2 and 5 years with a total of 50 and 500 WLM.
- ERR_{rd} decreases with attained age.
- ERR_{rd} increases for lower exposure rates in all models.
- 68% CI for TSCE model are shown, based on statistical uncertainty of parameter values.
- Uncertainty intervals of parametric ERR model are of similar size.
- Uncertainty intervals of BEIR VI model cannot be estimated due to very large correlations between the parameters.
- In addition to statistical uncertainty, there is a large model uncertainty involved due to complex dependence on several modifiers; model uncertainty can be larger than statistical one.
- Risk estimates are significant until about 10 WLM.
- Model uncertainties are large below exposure rates of about 10 WLM/year.

Clonal expansion rate and possible relation to a bystander effect
Non-targeted radiobiological effects such as radiation-induced genomic instability or bystander effect may exhibit non-linear exposure dependencies for low and moderate exposures. These exposure responses can be incorporated into mechanistic models such as the two-stage model with clonal expansion (TSCE model). The consequences of these effects on cancer risk can then be estimated [3,4].

For lung cancer in the Eldorado cohort, the clonal expansion rate, \( \gamma = \alpha - \beta - \mu \), depends on the annual exposure rate in a non-linear way:
- Strong increase for small exposure rates until about 20 WLM/year.
- Linear increase above.

Uncertainty intervals of BEIR VI model cannot be estimated due to very large correlations between the parameters.

References