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W. Friedland, P. Jacob (Editors)



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Using Splines to Analyse the Effect of Time since Exposure on the Risk of Lung Cancer in the French Uranium Miners

Agnes Rogel, Anne Fouillet, Dominique Laurier, Margot Tirmarche

Institute of Radioprotection and Nuclear Safety, BP17 92262 Fontenay-aux-Roses, France

Cancer appears as a late effect of exposure to ionising radiation. Analysis of temporal variations of exposure-risk relationship is of great importance for radiation-risk assessment. When chronic exposure is received at low level during a long period of time, such analysis requires precise individual exposure history, for example on an annual basis, as in occupational cohort studies.

Two methods were applied to analyse exposure-time-risk relationship. Piecewise constant model has been used, where cumulative exposure was divided into various 'exposure windows' defined by time intervals. This method gave a good overview of the relation, but depended on the choice of cut-points and size of intervals, and changes in risk occur in 'jumps'. The second method is a generalisation of this approach, weighting each year of exposure by a time-dependant function describing the temporal effect of exposure on the cancer risk. B-spline was used to model this weighted function, since it is a smoothing method with high flexibility.

Both methods were applied to evaluate the effect of time since exposure on lung cancer risk among French uranium miners exposed to radon. The cohort comprised 5098 miners with a mean cumulative radon exposure of 37 WLM¹, and followed up from 1945 to 1994, during a mean duration of 26 years. A total of 125 lung cancer deaths were observed. The excess relative risk model was used, and parameters were estimated by maximising the likelihood, using either Poisson or Cox regression. Several possibilities were examined: on one hand, different sizes and numbers of intervals, on other hand, different orders of the B-splines and numbers and position of knots.

A significant effect of time since exposure was suggested using both methods. Results from the piecewise constant model with three windows of exposure showed that exposure-risk relationship was higher when exposure was received 5 to 14 years earlier. This effect was no longer significant when 6 windows were used. Results from the B-splines model showed that excess relative risk reached a maximum around 10 years after exposure, and then gradually decreased toward zero with increasing time since exposure. According to the order of splines, the number and position of knots and the use of Poisson or Cox regression, we obtained slightly different shape of the time-weighted function of the exposure-risk.

These methods are superior to the approach using either time since first exposure or time since end of exposure. They can be used for the analysis of other modifying factors, such as age at exposure and period of exposure.

¹ WLM : Working Level Month