CHAPTER 11

Combined Spatial-Temporal Analysis of Malformation Rates in Bavaria After the Chernobyl Accident

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Malformation rates in the German state of Bavaria, as a whole, did not increase in 1987, the year following the Chernobyl accident. Also an analysis of the monthly data does not show any association between radiation exposure and malformation rates seven months later. But in a detailed analysis on the level of districts, taking the spatial structure into account, we find an association between malformation rates and the calculated caesium concentration in pregnant women. We used a non-parametric estimation of the dose-response relationship, which gives an increasing malformation risk for regions with higher caesium exposure. The results should be interpreted carefully since the analysis has been conducted as an explorative observational study. The results are not in line with the present understanding of the biological effects, including the existence of a threshold dose, for teratogenic effects of low level ionising radiation.

Background

Ionising radiation is an established risk factor for congenital malformations making them an relevant endpoint in the study of possible health effects from the Chernobyl accident. An increased prevalence of congenital malformations at birth was reported for different European countries after the Chernobyl accident. However, existing databases often do not meet quality criteria required for meaningful epidemiologic analysis. The EUROCAT registry only covers approximately 10% of the European population. Also, under-ascertainment of prevalent cases is a systematic problem in many registers.

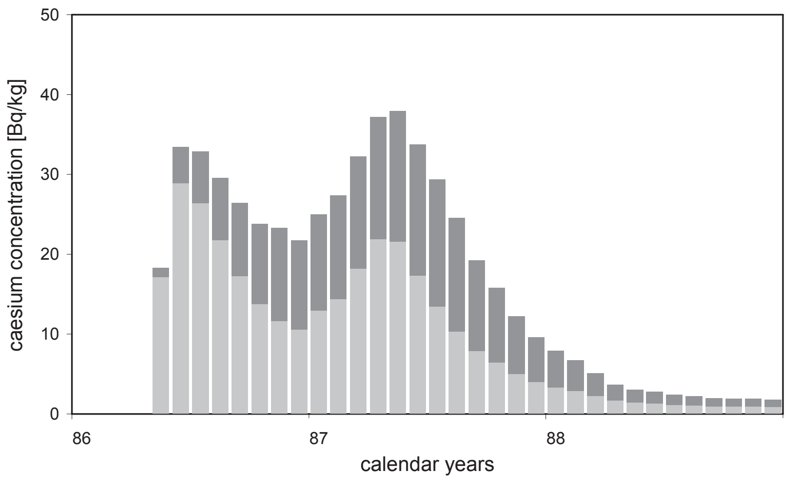
An overview of the literature on malformation rates following Chernobyl is given in a review article by Hoffmann [1]. In northern Turkey, a significant increase of neural tube defects was reported. A rise in congenital malformations after Chernobyl was found in Belarus. In Croatia, an increase of CNS anomalies was detected in aborted foetuses or in newborns that died within 28 days of delivery. The EUROCAT registry, however, revealed no indication of a systematic increase in the prevalence of Down's syndrome, anencephaly, or spina bifida. Most researchers argued that the radiation exposure from the Chernobyl fallout would be too low to cause any measurable increase in malformation rates.

In Germany, data of the prevalence of malformations at birth were collected *a posteriori* in the State of Bavaria, several years before and after Chernobyl (1984 to 1991). Bavaria was the German Federal state with the highest radiation exposure from Chernobyl. A study, conducted by the German Federal Office of Radiation Protection (Bundesamt für Strahlenschutz, BfS), found no significant difference in malformation rates between the higher exposed southern part of Bavaria and the less contaminated northern part following Chernobyl [2].

In a study on perinatal mortality in Germany following the Chernobyl accident, Körblein and Küchenhoff found a small but statistically significant mortality rise in 1987, the year after the Chernobyl accident. Furthermore, an analysis of the monthly data gave an association between caesium burden and perinatal mortality seven months later [3]. There would have been a similar possible effect on congenital malformations as experimental studies on mice have shown that irradiation of the foetus with 200 R during the period of

major organogenesis (day 6 to 13 post conception) resulted in 100% malformed offspring and, to a lesser degree, neonatal deaths [4].
In our study we performed a trend analysis with the same model as in [3]. Then we used ideas of the analysis in [2], in which a comparison of regions was conducted.

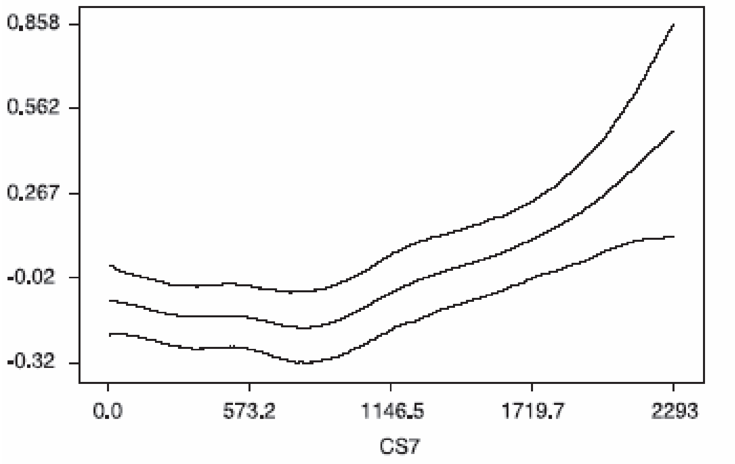
Figure 1: Development of caesium concentration in pregnant women following the Chernobyl accident. The light columns are the contributions from milk, the dark columns the additional contributions from beef, pork and cereals.



Data
Out of a total of 29,961 newborn with malformations only 7,171 cases were considered appropriate for evaluation; the others were excluded for different reasons by the German Federal Office of Radiation Protection (*Bundesamt für Strahlenschutz, BfS*). Each case was recorded with diagnosis, sex, date of birth and residence of the mother. This data set was provided by *BfS* for evaluation.

Data for the caesium-137 soil contamination on a district level (96 districts) were also obtained from *BfS*. Daily measurements of the caesium concentration in cows milk in Munich from May 1986 until the end of 1988 were provided by the state supported Society for Environment and Health (*Gesellschaft für Umwelt und Gesundheit*, *GSF*).
Monthly values of the caesium concentration of pregnant women, were calculated on the basis of 4 main food components (milk, beef, pork, cereals) and average consumption rates. They are displayed in Figure 1. There is a first peak in the caesium burden in June/July 1986, and a second in April/May 1987. During the winter 1986/87 cows were fed contaminated grass harvested in summer 1986. Therefore the caesium concentration in pregnant women shows a second increase in the winter season 1986/87.

Figure 2: Estimated effect of the caesium term (CS7) on malformation rates, Bayes' model. The numbers on the y-axis are the logarithms of the odds ratios. The upper and lower curves indicate the 95% confidence limits.



Methods

In a first step, the model used by Körblein and Küchenhoff in [2] is applied to fit the monthly malformation rates in Bavaria:

$$P(Y=1)=\alpha+\exp(\beta_0+\beta_1 t)+\beta_2(cs(t-7))$$

In a second step, a combined spatial-temporal analysis is conducted. The monthly malformation rates in all 96 Bavarian districts and in 96 months (1984-1991) are analysed as a function of place and time.

As a proxy for the internal caesium exposure in district k at time t, a caesium term cs(k,t) is formed which is the product of the time dependent concentration cs(t) in pregnant women and the caesium soil contamination cs(k) in district k with k = 1, .. , 96. We use a nonparametric logistic regression model of the following form:

$$P(Y(k,t)=1)=G(\alpha_k+f(cs(k,t-7)+g(t))$$

Here $G(z)=1/(1+\exp(-z))$ is the logistic function.

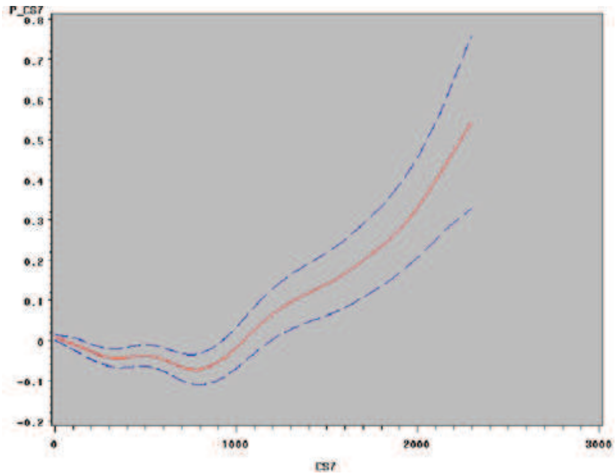
The probability of a malformation of child i in region k and in month t is denoted by $P(Y(k,t)=1)$.

The expression f(cs(k,t-7)) is a smooth function which associates the malformation rates with the delayed caesium concentration cs(k,t-7) (time-lag 7 months). This association is estimated by nonparametric methods. Furthermore, the spatial structure is taken into account by assuming a random regional effect which has a correlation dependent on the distance between the regions. The function g(t) is a flexible smooth overall trend component.

For the calculation we use a Bayesian approach by Fahrmeir and Lang [5]. The function f is estimated by a penalised spline approach. The calculations were performed by the program Bayes X [6].

For a sensitivity analysis we fitted other less complicated models, including a parametric logistic model with polynomial trend and polynomial caesium term, and a nonparametric logistic model with a regional effect without assuming a spatial structure. These analyses were performed by the program package SAS. We also conducted the analyses with time-lags of 6 and 8 months between exposure and delivery.

Figure 3: Estimated effect of the caesium term on malformation rates, non-parametric model. The numbers on the y-axis are the logarithms of the odds ratios. The broken lines indicate the 95% confidence limits.



Results
The first model does not give any significant association between caesium exposure and the malformation rates in Bavaria as a whole.
In the second model, the dose response relationship given in Figure 2 is found.
Although formal test procedures have not been performed, the pointwise confidence limits give a clear indication for an association between caesium exposure and malformation risk. The result was confirmed in parametric approaches and in a nonparametric approach without the spatial effect (see Figure 3).

Discussion
To summarise, no association between malformation rates and caesium exposure was found in the first part of the analysis. In a second explorative analysis, using a regression model on an area level, an association between the delayed caesium exposure in pregnant women and malformation rates was found (time-lag 7 months). There is an apparent decrease of risk at low values of the caesium exposure which, however, should not be over-interpreted since the data are also compatible with a practical threshold at low doses. But the decrease at low doses might explain the fact that no caesium effect is found in the data of Bavaria as a whole.
In 1996, the German radiation protection commission (*SSK*) estimated the effective radiation dose from Chernobyl in the highest exposed German areas near the Alps (*Voralpengebiet*) as 0.65 mSv for the first follow-up year. The ICRP 90 recommendations [7] state that the malformation risk is greatest during the period of major organogenesis (3-7 weeks post conception), with an estimated dose threshold of around 100 mSv foetal dose of low-LET radiation, and that the induction of malformations at low doses may therefore be discounted (quoted in the recent WHO report on the Health Effects of the Chernobyl

Accident from July 26, 2005). Since the radiation exposure in Bavaria was 2 orders of magnitude below this threshold dose, no effect on malformations should have been expected.

Our results challenge the concept of a threshold dose of about 100 mSv for the induction of malformations and suggest that the form of the dose response curve at very low doses is non-monotonous. According to Burlakova [8], radiation effects are best characterised by a bimodal dose response curve with a low dose maximum, followed by a plateau region or even a decrease, and a subsequent increase at higher doses. The proposed mechanism involves an increase of DNA repair efficiency by low level radiation exceeding a certain trigger dose.

In conclusion, we believe that the biological effects of very low dose ionising radiation, as yet, are not well understood and deserve further attention.

References

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