Perinatal mortality in Germany following the Chernobyl accident

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Abstract Perinatal mortality in Germany was investigated with respect to a possible relationship to the nuclear accident in Chernobyl on April 26,1986. Using annual data of perinatal mortality, a trend analysis based on an appropriately chosen statistical model was performed which showed a significant increase in 1987. In addition, we calculated the cesium concentration in women's bodies using data of the cesium concentration in milk. We found two peaks of cesium concentration that were associated with the observed two peaks of monthly perinatal mortality data with a delay of 7 months.

Introduction

The explosion of the nuclear reactor in Chernobyl on April 26, 1986, was the most serious accident in the history of civil use of nuclear power. Large territories in the Ukraine, Belarus, and Russia were highly contaminated by the fallout. A variety of adverse health effects were observed there following the accident [1]. In Belarus, an increased frequency of abnormalities in 5- to 12-week-old embryos from abortions was reported after Chernobyl [2]. In a review article [3], studies from various European countries of the association between the Chernobyl accident and reproductive outcome, with particular reference to congenital anomalies, are summarized. The authors conclude that there is no consistent evidence of a detrimental physical effect of the Chernobyl accident on congenital anomalies.

A significant increase of early neonatal mortality (first 7 days) after the fallout was reported for southern Germany [4]. The authors had compared monthly mortality data for 1986 and 1987 with the extrapolated trend from the years1975 to 1985. The methods were criticized [5], which in turn motivated this work.

Schoetzau et al. [6] compared the rates of abnormalities and perinatal mortality in southern Bavaria with those in northern Bavaria, where the cesium contamination was less. They did not find a significant difference for the 2 years following the Chernobyl accident. However, the populations are relatively small, so the power of the applied statistical test did not allow them to detect small differences.

We report a new evaluation of the German data also using a trend analysis, but with a statistical model different from that in [4] and with data ranging from 1980 to 1993. Thus, a possible increase of the perinatal mortality rate in 1987, the year after the Chernobyl accident, can now be checked by an appropriate statistical test substantially different from a pure trend extrapolation.

Whereas in [4] only early neonatal mortality data were used, our analysis includes the data of stillborn infants, i.e., perinatal mortality data. Data from the former German Democratic Republic (East Germany) are added to broaden the database.

A possible association between radiation from cesium and perinatal mortality rates was checked by evaluating the monthly data. In the first follow-up year, the main radioactive burden from Chernobyl came from ingestion, mainly from cesium in milk and dairy products [7]. As the fetus is considered to be most sensitive to radiation during the period of major organogenesis in the first trimester after conception [8], an increased perinatal mortality rate should, if anything, be observed 6-9 months after exposure. We therefore include in our model the delayed cesium concentration as a further covariate in addition to the trend components.

Materials and methods

The statistical analyses are based on annual as well as on monthly data of perinatal mortality in West Germany (former FRG) and in East Germany (former GDR). The data were provided by the Statistisches Bundesamt in Wiesbaden and Berlin. The perinatal mortality rate is defined as the number of stillbirths plus the number of infant deaths within 7 days of birth, divided by the total number of births (live plus stillbirths).

The classification of 'stillbirth' was changed in 1979 from 'body length greater than 35 cm' to 'birthweight greater than 1000 g' Therefore, 1980 was chosen as the starting point for our data evaluation. Data were available until 1993, so the data ranged over 14 years. Since the same classification was used in the former

GDR and the general trend of perinatal mortality is similar in the study period, the two data sets can be combined for a joint evaluation even for the years before the reunification of East and West Germany in 1990.

We first performed a trend analysis of the annual perinatal mortality rate, where the possible increase in 1987 was modeled by an additional term. For the monthly data, we applied a regression approach with the delayed radioactive exposure as an additional explanatory variable. When deriving the model for the monthly data, we took into account that in the first year following the accident, the main contribution to the radioactive exposure of the German population came from cesium in food [7], mainly milk and dairy products. The cesium concentration in milk reached several hundred Bq/1 immediately after the accident, but it dropped quickly to negligible values due to the rapid grass growth. During the winter feeding period, however, the concentration level increased again, as the cows were fed contaminated grass harvested the preceding summer. After the winter feeding period, in April 1987, the cesium concentration in milk dropped to about 1 Bq/1. Thus, the main dose received from ingestion was limited to the first follow-up year. We used cesium concentration data measured in milk from a farm near Munich and assumed a biological half-life of cesium in the human female body of 86 days and constant daily milk consumption to calculate the course of cesium concentration in the mothers. Two peaks are found, one in mid-1986, the other at the end of April 1987, one year after the accident (Fig. 1). A similar calculation for the cesium concentration after beef consumption shows a first peak in August 1986 and a second in April 1987, but beef plays a minor role compared with milk. Therefore, we focused our investigation on cesium in milk. The concentration in the mothers is only known up to a constant factor as it was calculated using milk data from just one test farm near Munich.

As mentioned above, a standard technique for analyzing such data consists in conducting a trend analysis. Thus, the first step of our analysis concerns the model fit to the annual data. The data suggest a nonlinear regression model with an exponential trend and a constant term as follows:

(1) $E(Y(t)) = \alpha + \exp(\beta_0 + \beta_1 t)$

where E(Y(t)) is the expected perinatal mortality rate in year t with t ranging from 1 to 14, t = 1 representing 1980. Denoting the number of births in year t by N(t), the random variable Y(t)·N(t) is binomially distributed with

$Var(Y(t)) = E(Y(t)) \cdot (1 - E(Y(t))) / N(t)$

Model (1) above is justified as follows. On the one hand, it reflects the trend apparent in the data, which displays a decrease in the perinatal mortality rate from 1980 to 1993 by about a factor of 2. This trend, given by $\beta_1 t$, is essentially due to better medical care. The exponential term, however, yields an expected perinatal mortality rate of zero for time t tending to infinity. This effect is compensated, on the other hand, by introducing the additional parameter α which allows for a natural limit of perinatal mortality for reasons other than medical care. It is also worth mentioning that for practical purposes, the exponential term of the model is identical to a logistic one which is typically applied in such fields of investigation.

We further allow for random deviations from the exact trend by introducing an unknown random effect u(t) to model (1), so the expected mortality rate conditioned on u(t) is expressed as follows

(1a) $E(Y(t) \mid u(t)) = \alpha + exp(\beta_0 + \beta_1 t) + u(t)$

Following [9], we assume E(u(t)) = 0 and $Var(U(t)) = \rho^2 E(Y(t)) (1-E(Y(t)))$ for the random effect, where ρ^2 is an unknown constant. These assumptions mean that u(t) does not yield a systematic deviation from the trend and that its variance is essentially proportional to E(Y(t)).This implies that the unconditional expected mortality is still the same as in model (1). Noting that the sample sizes in each year are nearly the same in our data, the variance of *Y(t)* can be calculated as

(2) $Var(Y(t)) = OD \cdot E(Y(t)) \cdot (1 - E(Y(t))) / N(t)$

where OD is the so-called overdispersion factor which depends on ρ^2 and has to be estimated from the data (for a detailed derivation see [9], p. 192ff). Overdispersion results in an observed variance of the response variable Y(t) greater than it should be under the assumed binomial model. Since overdispersion is a common problem in practical situations, 'it seems wise to be cautious and to assume that overdispersion is present to some extent unless and until it is shown to be absent' (see [10], p. 125). Ignoring the effect of overdispersion can lead to seriously misleading results, because in that case. among others, the calculated standard errors of the point estimators of the model parameters will be too small.

In the next step, the model has to be slightly modified to take into account a possible change in the perinatal mortality rate in 1987. This is done by introducing an additional term in model (1):

(3) $E(Y(t)) = \alpha + \exp(\beta_0 + \beta_1 t) + \beta_2 I_{1987}(t)$

with $I_{1987}(t) = 1$ for t = 8. i.e., in 1987, and zero otherwise. Our hypothesis of an increased perinatal mortality rate in 1987 can thus be checked by a statistical test (one-sided t-test) of β_2, i.e., the null hypothesis of $\beta_2 \leq 0$ has to be tested versus the alternative $\beta_2 > 0$.

Using now the monthly data on perinatal mortality as the response variable, we consider the following model:

(4) $E(Y(t)) = \alpha + \exp(\beta_0 + \beta_1 t) + \beta_2 \cos(2\pi(2t - \beta_3)) + \beta_4 (x(t - \beta_6))^{\beta_5}$

where t represents the time measured in years. As the data suggest a seasonal effect with a period of half a year, a periodic term with parameters β_2 and β_3 is introduced in model (3). To model the influence of radiation on perinatal mortality, the term $\beta_4 (x(t - \beta_6))^{\beta_5}$ is added. The variable $x(t - \beta_6)$ denotes the cesium concentration in the human body at time $t - \beta_6$. Parameter β_6 represents the time-lag to be estimated from the data.

We are now concerned with adequate methods for the statistical inference. Model (3) with (2) and model (4) with (2), respectively, are quasi-likelihood models (see e.g. [11, 12]). The distribution of Y(t) can be well approximated by a normal distribution, because the population sizes $N(t)$ are very large. Estimates of the parameters are obtained by the method of iteratively weighted least squares. In model (4), it is also necessary to minimize the profile likelihood depending on the parameter β_6 by a grid search. The factor OD can be estimated by the standardized sum of weighted least squares.

Statistical tests for the influence of certain parameters in each model can be performed by the F-test using

$$\frac{(SSE_2 - SSE_1)/p}{SSE_1/(T-q)}$$

where SSE_1 and SSE_2 denote the weighted sum of squares under the full model and under the null hypothesis, respectively. Here p is the number of parameters to be tested, T is the number of observed mortality rates ($T = 14$ for the annual data and $T = 168$ for the monthly data), q the number of parameters in the full model, and $T - q$ the degrees of freedom. The expression in the denominator is the estimator of OD. Based on this test statistic, confidence intervals can be constructed for single parameters using the relationship between tests and confidence intervals. For this purpose, the so-called profile sum of squares (SSE_2 as a function of the parameter of interest) has to be calculated. An alternative for testing a single parameter consists in calculating the Wald confidence intervals (t-test). Note that these two test procedures differ since our model is nonlinear. The F-test has the advantage of being less sensitive to non-linearity ([12], p. 191ff.), while the t-test can be conducted one-sided. Finally, OD is tested, with SSE_1 being approximately $\chi^2 (T - q)$-distributed under the null hypothesis OD = 1.

Results

Annual Data

In Fig. 2, the observed annual perinatal mortality rates and the estimated regression curve (with $\beta_2 = 0$) are plotted. It can be seen that the estimated curve is very close to the observed values. The data point with the greatest deviation from the curve is the observed mortality rate in 1987, which reflects the significance of the parameter β_2 shown by the corresponding t-test mentioned below.

Conducting the regression analysis based on model (2) yields an estimated value of α of 0.0030 which turns out to be significantly different from zero at the 1 % level (F-test). The parameters β_0 and β_1 are estimated as -4.7 and -0.10, respectively. The OD resulting from the data is 1.6. Though this value is not significantly different from 1, we use it for the analyses, i.e., the covariance matrix of the estimated parameters is inflated by 1.6 before investigating the null hypothesis of no increase in 1987. Taking this overdispersion into account, the results obtained from the calculated statistical tests are more conservative, i.e., the P values are larger than they would if we ignored the overdispersion. Now, the null hypothesis of no increase in 1987 can be checked by testing the hypothesis of $\beta_2 \leq 0$ versus the alternative of $\beta_2 > 0$. Estimating β_2 results in 0.36 per thousand (t value = 2.8), which is significantly greater than zero ($P < 0.01$, t-test). This increase translates to 317 additional perinatal deaths in 1987 with a 95% confidence region ranging from 65 to 569.

Monthly Data

The parameter estimates for the trend parameters α (0.0030), β_0 (-4.7). and β_1 (-0.10) are equal to those obtained from estimating model (2) with the annual data. The two parameters of the seasonal component β_2 and β_3 are estimated as 0.00030 and 0.86, with β_2 being significantly different from zero (F-test, $P < 0.001$). The importance of the seasonal component can also be seen from the weighted sum of squares, which is 226.3 with the seasonal component and 298.4 without it. Figure 3 displays the monthly perinatal mortality data from 1980 to 1993 and the result of the fit to the monthly data.

The main result of fitting model (3), however, is the highly significant effect of the delayed cesium concentration on perinatal mortality. Including the cesium term in the model leads to a reduction of the weighted sum of squares from 222.6 to 200.0. The corresponding F-test is highly significant ($P < 0.001$). The regression yields $\beta_5 = 3.5$ (95% confidence interval: 1.5 - 7.5). Thus, the excess perinatal mortality is a strongly nonlinear function of the cesium concentration at very small dose rates.

In Fig. 4, the profile sum of squares as a function of the time-lag (parameter β_6) is plotted. The minimum of the sum of squares is obtained for a time-lag of 7 months. The broken line gives an estimate of the 95% confidence interval from 6 to 8 months based on the F-test.

In Fig. 5, the residuals resulting from the regression, i.e., the deviations between observed and expected monthly perinatal mortality rates, are presented for the models with and without the delayed cesium term in units of standard deviations. Without the cesium term, the moving average exhibits two peaks, one in the beginning and one at the end of 1987, which are no longer present when the model is adjusted for cesium. The greatest monthly deviation from the model without cesium is found in November 1987, where perinatal mortality is increased by 1.5 per thousand, which means a relative increase of 20%.

OD is now estimated as 1.25, indicating that the model fits remarkably well.

Discussion

Summarizing the above results, we find a significant increase of German perinatal mortality in 1987, the year following the Chernobyl accident. The model which was used for the data analysis fit the data very well (cf. Fig. 1). We furthermore analyzed the monthly data and noticed a highly significant association between cesium concentration and excess perinatal mortality rates. Although we know that, in general, such an observational study cannot prove a causal relationship, we feel that the results deserve further attention.

Thus, for instance, their biological plausibility has to be discussed. The dose rates received by the embryo from internal cesium radiation were of the order of the background radiation. The doses were 2 to 3 orders of magnitude smaller than in animal experiments [13,14]. The consequence of adopting the radiation explanation would be that there is either no threshold dose for radiation damage to the human embryo or the threshold is smaller than the additional exposure in Germany after Chernobyl.

After the atmospheric bomb testing in the 1960's, an increased first-day neonatal mortality was observed in USA and in England and Wales [15]. Then millions of individuals over many years were exposed to ionizing radiation, mainly from strontium in the food that accumulates in the human bones. With the fallout from Chernobyl, a similar amount of fission products contaminated Germany within just a few days. However, in Germany, in contrast to the atmospheric tests, strontium played a minor role in the Chernobyl fallout compared with cesium. While the biological half-life of strontium in humans is many years, for cesium it is only some months. This is why the development of the cesium concentration in the human body after Chernobyl shows two marked peaks which could both be correlated with the observed two peaks of perinatal mortality in the beginning and at the end of 1987.

Further confirmation of our findings could come from evaluating monthly perinatal data from countries nearer to Chernobyl such as Poland, Belarus, and Ukraine which, to our knowledge, has not yet been done.

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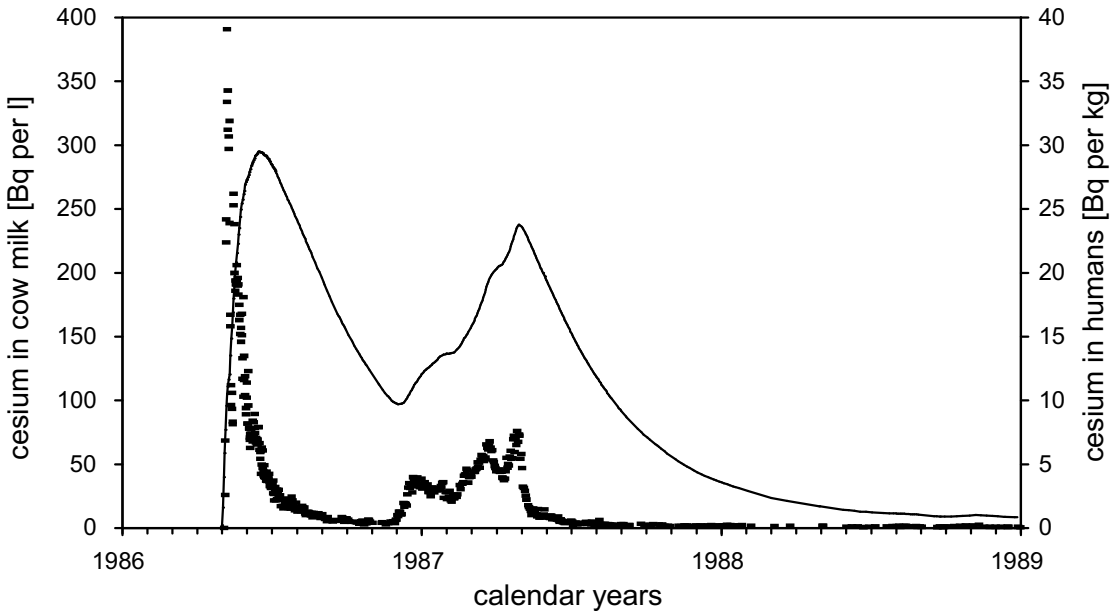

Fig. 1 Cesium concentration in milk (*dots*) and in the female human body (*solid line*)

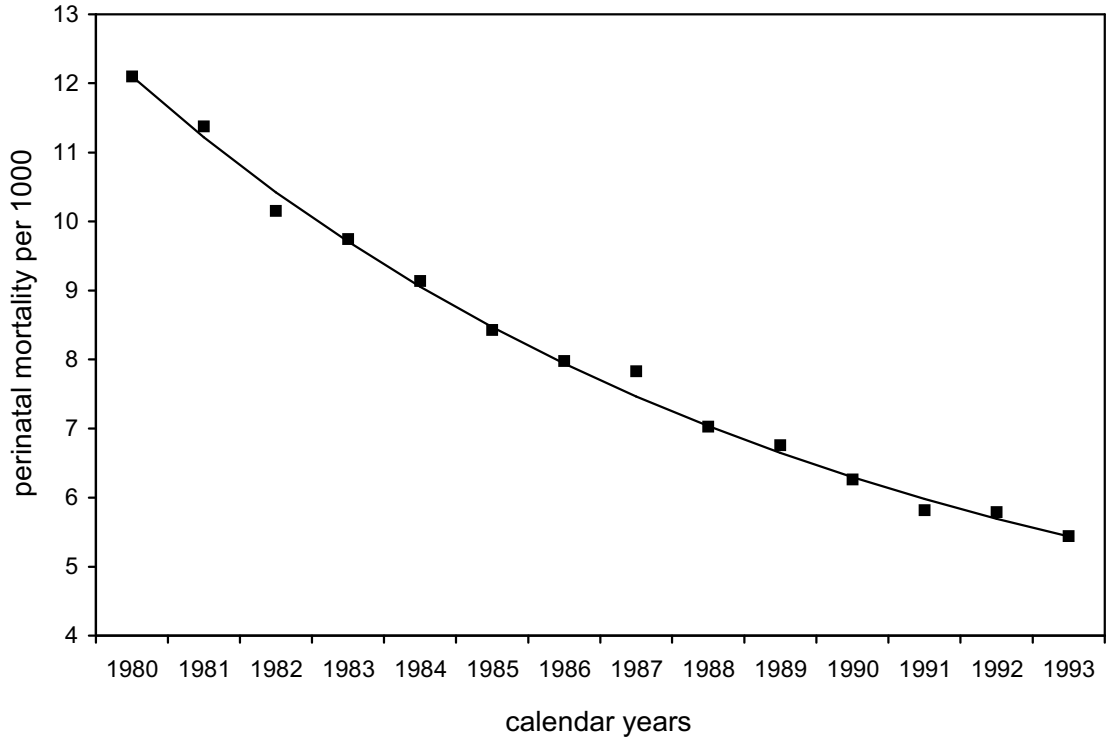

Fig. 2 Observed annual perinatal mortality rate in Germany and estimated trend curve

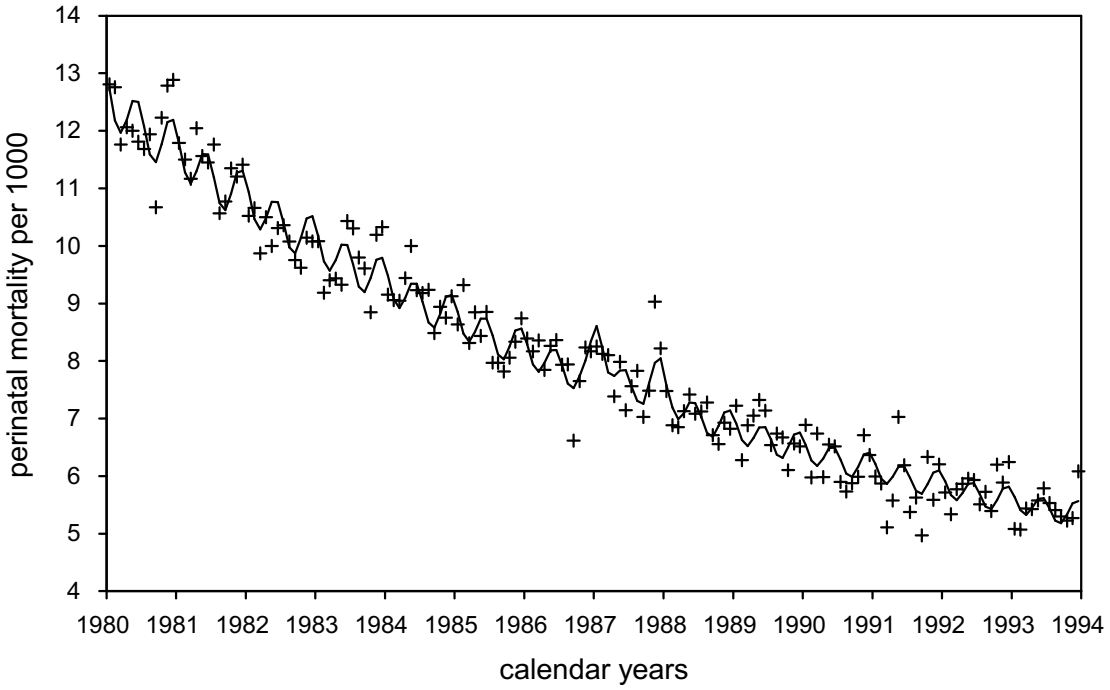

Fig. 3 Observed monthly perinatal mortality rate in Germany and estimated model curve

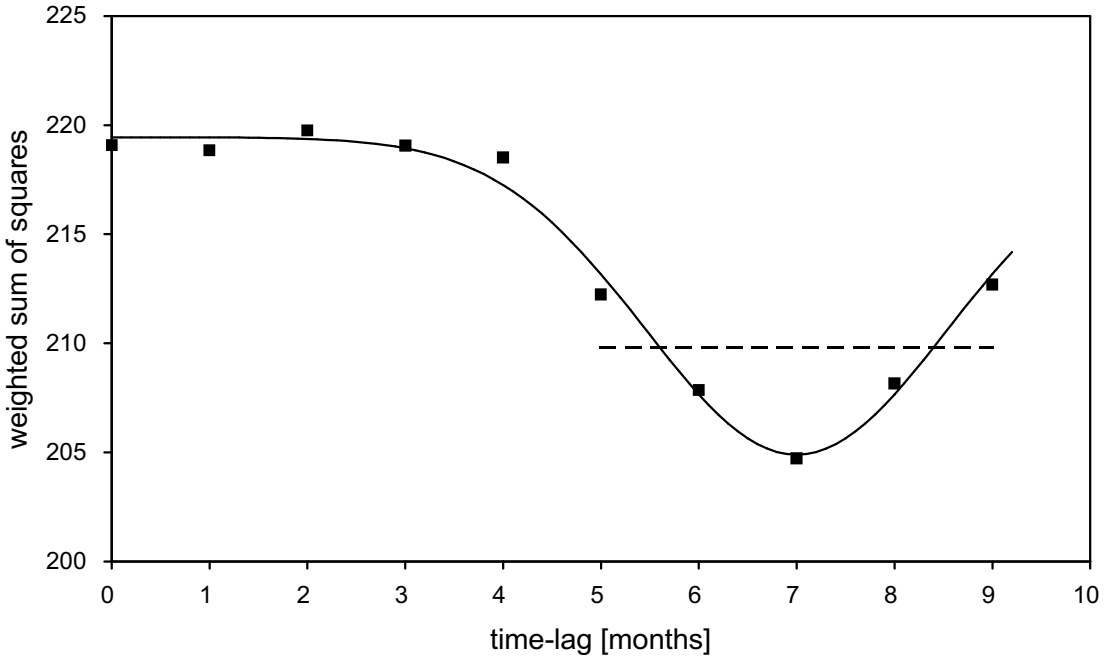

Fig. 4 Weighted sum of squares resulting from regressions to monthly German perinatal mortality data with different time-lags between cesium concentration in the femals body and perinatal mortality data. The best fit is obtained for a time-lag of seven months. The broken line yields the 95% confidence interval which ranges from 5.5 to 8.5 months.

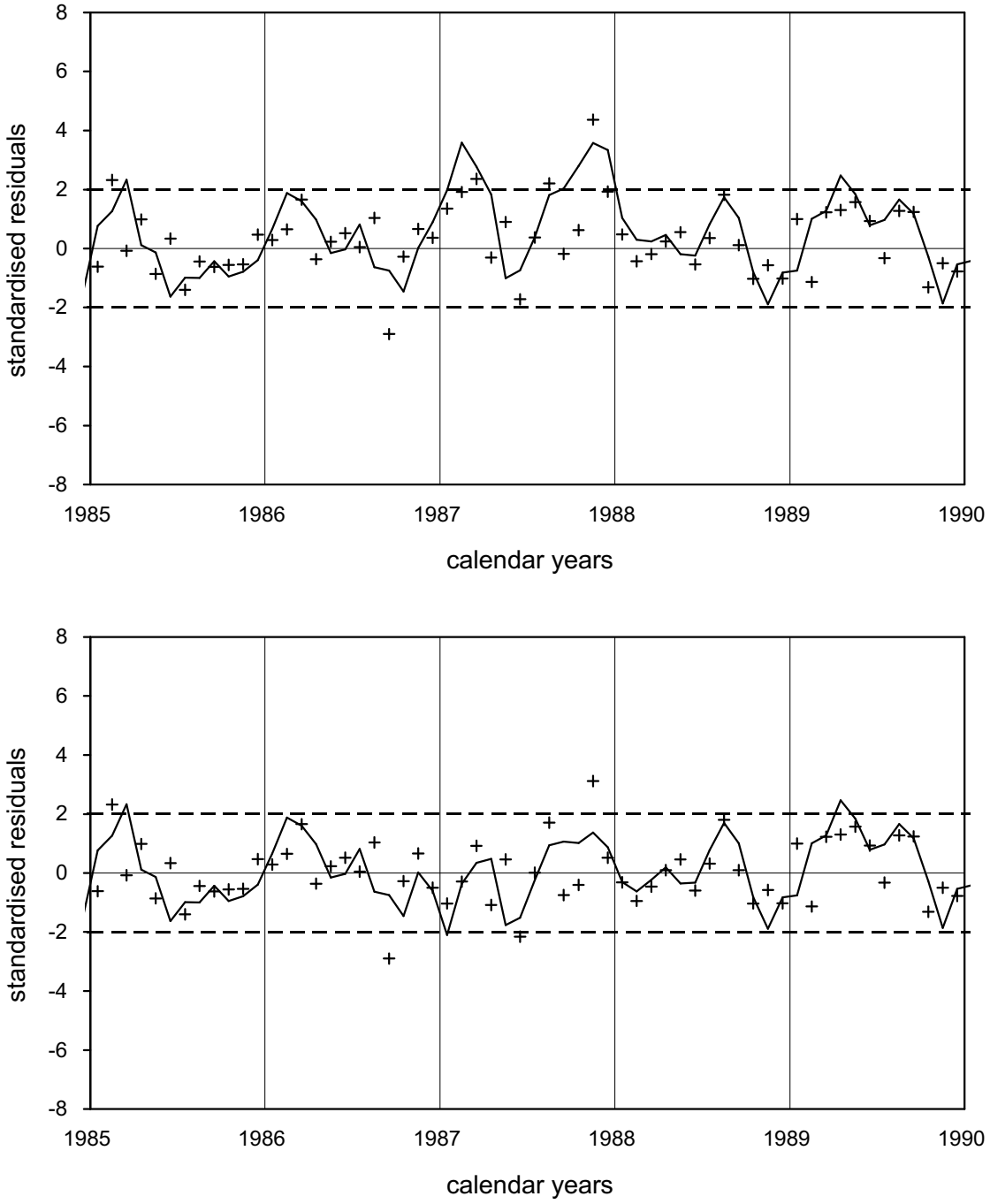

Fig. 5 Residuals from regressions to monthly perinatal mortality data (*dots*) without (*upper diagram*) and with (*lower diagram*) the cesium term. The solid line is the moving average of the residuals, the broken line indicates the range of two standard deviations (2σ-range).